Summary: The degradation behavior of the diblock copolymers PPDX-*b*-PCL was studied under in vitro conditions, in samples with high PPDX content. Molded films were immersed in phosphate buffer solution at pH = 7.4 and 37 °C for 9 months. The samples were periodically extracted, dried and evaluated by weighing, SEC, ^{1}H NMR, DSC, and POM. The results point out that an increase in PCL content reduced the weight loss in the diblock copolymers. ^{1}H NMR and DSC analysis showed that degradation occurred almost exclusively in the PPDX block during the first 9 months of hydrolysis. POM results for the diblock copolymer with high PPDX content (77%) indicated the presence of some typical homo-PPDX spherulites in the 0.8 months degraded sample when no weight loss was detected. This result demonstrated that random chain scission during the early stages of degradation can produce homo-PPDX chains that cannot be dissolved in the hydrolysis medium because their molecular weight is still too high. It was found that a small increase in PCL content in the diblock copolymers produced a synergistic increase in the PPDX block degradation stability. This is a direct result of the inter-digitized lamellar morphology present in the copolymers where PCL and PPDX lamellae are alternated within mixed spherulites. In view of its much higher resistance to hydrolysis, the PCL lamellae offer a barrier-type protection to the PPDX within the copolymer. A schematic morpholog-ical model is proposed to explain the observed changes during the different degradation stages encountered by the diblock copolymers.
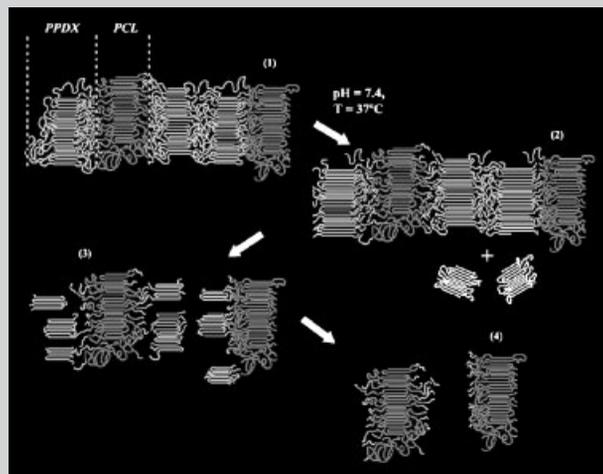
Proposed scheme for the hydrolytic degradation process of PPDX-*b*-PCL diblock copolymers.

Hydrolytic Degradation of Double Crystalline PPDX-*b*-PCL Diblock Copolymers

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Introduction

The study of biodegradable systems has a growing interest in the pharmaceutics and medical field.[1] In this frame, aliphatic polyesters like poly(lactic acid) (PLA),[2−6] poly-(glycolic acid) (PGA),[7−9] poly(*p*-dioxanone) (PPDX)[10−15] and poly(ε-caprolactone) (PCL),[16,17] their blends and copolymers have been widely investigated and employed, e.g. as sutures, surgical pins or drug delivery systems, in order to improve healthcare. Therefore, the changes experienced by the material during the bio-assimilation process are of crucial importance and structural changes must be monitored and understood in detail.

PPDX is a poly(ester-*alt*-ether) commercially employed for the manufacture of medical sutures and pins (PDSII® from Ethicon). Recently a review dealing with the synthesis and properties of PPDX and its copolymers was published.[10] Sabino et al.[11−14] have studied the morpholog-ical changes experienced by PPDX fibers and melt pressed samples during the in vitro degradation. Their most recent work[14] presents a detailed study concerning with the effect of the hydrolysis time on the spherulitic and lamellar

morphology as the degradation proceeds. The samples were degraded either in distilled water or in a phosphate buffer solution at 37 °C. The hydrolytic degradation of PPDX occurs in an approximate two-stage process where the amorphous regions of the sample are attacked faster than the crystalline regions. A schematic morphological model that details the changes experienced by the material as degradation time increases was also presented.

Pezzin and co-workers[15] evaluated the hydrolytic degradation of PPDX films prepared by solvent casting and a phase separation method. They concluded that film preparation methods have consequences in the degradation rate of the PPDX and might determine the final biomedical application.

In order to tune the lifetime of biodegradable medical devices that could be bio-assimilated by the human body and the changes in properties during hydrolytic degradation, blends and copolymers of biopolymers have been developed and are commercially used.[18] Since PCL is a polymer whose degradation rate by hydrolysis is very slow, a combination with a fast hydrolysable polymer like PPDX can allow the design of a range of new materials with different life times. In the literature it can be found works related with the synthesis of low molecular weight random copolymers of ε-CL, PDX and other esters for medical applications. These materials show minimal tissue reaction in animals and acceptable drug release properties.[19] Lendlein et al.[20] synthesized multiblock copolymers of PPDX-co-PCL from macrodiols. The hydrolytic degradation study showed that the mass loss was a function of the PPDX composition. They prepared fibers and found shape memory effects and good tissue compatibility.

No other precedents could be found in the literature where both PCL and PPDX were combined to prepare biodegradable materials. However, a great deal of literature is available where blends or copolymers of other biodegradable polyesters have been used and their hydrolytic degradation studied. Li[21] published a review about the hydrolytic degradation of aliphatic polyesters derived from PLA and PGA. The most important findings are that degradation induces morphological and compositional changes, and that the mechanism of degradation is generally heterogeneous. Other authors have reported the hydrolysis of poly(ester-urethane)s made with PLA and diisocyanates, concluding that the weight loss is influenced by the stereostructure of the lactic group.[22] Saito et al.[23] synthesized diblock copolymers of poly(D,L-lactic acid) with poly(ethylene glycol) that could be used as bone morphogenic proteins carriers, concluding that the composition of the copolymer influenced the degradation rate and the swelling ratio.

PCL has been combined in the form of blends and copolymers with several other polyesters as well as polyethers. In order to increase the hydrophilic character of PCL, this polyester was copolymerized with poly(ethylene oxide) (PEO). The in vitro degradation of PCL-b-PEO micelles showed good biocompatibility and physical stability in the presence of cells during 24 h of incubation.[24] In the case of the PCL-co-PEO multiblock copolymer the inclusion of polyether sequences increased the water absorption and weight loss of the material, but the degradability of the PCL block was not improved.[25] Random copolymerization with cyclo-(α-amino acid-α-hydroxy acids) (depsipeptide) proved to increase the degradation rate with respect to the PCL homopolymer, due to a decrease in the degree of crystallinity.[26]

Recently, diblock copolymers of PPDX and PCL have been obtained by controlled ring opening polymerization techniques.[27] The poly(p-dioxanone-block-ε-caprolactone) diblock copolymers (PPDX-b-PCL) have been extensively studied from the viewpoint of the nucleation and crystallization since both components can crystallize and influence each other.[28,29] Several evidences point out that these diblock copolymers are in the weak segregation regime, and their structure and morphology have been also studied.[29] In the present work, we studied for the first time the hydrolytic degradation behavior of two PPDX-b-PCL diblock copolymers with PPDX contents of 77 and 65 wt.-%, and we compared their behavior with a PPDX homopolymer of similar molecular weight. The polymers have been characterized as a function of degradation time by DSC, ^{1}H NMR, size exclusion chromatography (SEC) and polarized optical microscopy (POM). A schematic morphological picture of the degradation process has been drawn from the analysis of the results.

Experimental Part

Materials

The synthesis of PPDX and PPDX-b-PCL diblock copolymers has been previously described.[27] Table 1 denotes the principal characteristics of the materials employed. In the diblock copolymers, subscripts denote the composition in weight fractions and superscripts the molar mass (in $kg \cdot mol^{-1}$).

Table 1. Molecular characteristics of the PPDX homopolymer and the PPDX-b-PCL diblock copolymers.

Composition[a]	M_{PCL}	$\bar{M}_w/\bar{M}_n$	$\bar{M}_{PPDX}$	F_{PCL}
	$g \cdot mol^{-1}$		$g \cdot mol^{-1}$	wt.-%
$D_{65}C_{35}^{42}$	15 320	1.07	26 200	35
$D_{77}C_{23}^{43}$	10 280	1.07	32 280	23
$PPDX^{15}$	–	–	15 190[b]	0

[a] D and C denote PPDX and PCL blocks, respectively; the superscripts indicate their molar mass (in thousands) and the subscripts refer to their weight fractions.
[b] Average molecular weight determined by capillary viscometry ($\bar{M}_v$) in phenol/1,1,2,2-tetrachloroethane (2:3 v/v) at 25 °C.[12]

Hydrolytic Degradation

Compression molded films of $10 \times 15 \times 0.1$ mm^3 were melt pressed at 120 °C for 7 min in the diblock copolymers case and for 3 min for the PPDX homopolymer and then quenched to room temperature. The films were immersed in 15 mL of a 0.2 M phosphate buffer saline solution (pH = 7.4) at 37.2 ± 0.2 °C for 9 months. The buffers solutions were replaced every 10 d in order to maintain the pH of the medium constant during the hydrolytic degradation process. The samples were extracted monthly and dried at 25 °C until the weight was constant (approximately 48 h).

DSC

A Perkin Elmer DSC-7 apparatus was calibrated with indium and hexatricontane standards, under an ultrahigh purity nitrogen atmosphere. The samples (5 mg) were encapsulated in aluminum pans. Samples were first heated from 25 °C to 130 °C at 10 °C · min^{-1}, and the first heating scans were recorded, where the accumulated thermal history of processing (compression molding) and immersion in the hydrolysis medium at 37 °C were evaluated. After erasing the thermal history at 130 °C for 3 min, the cooling scans were recorded down to −25 °C, and finally a second heating scan was recorded up to 130 °C (10 °C · min^{-1}).

POM

The hydrolytically degraded samples were melt pressed between two glass cover slips at 130 °C for 3 min, then they were rapidly cooled to the desired crystallization temperatures in a Linkam TP-91 hot stage, observed in a Zeiss MC-80 optical microscope and the images were recorded with a digital camera.

Characterization

The compositions of the diblock copolymers were calculated from ^{1}H NMR spectra recorded using a Bruker AMX-300 in 1,1,2,2-tetrachloroethane-*d$_2$* (C$_2$D$_2$Cl$_4$)/TMS, knowing the molar mass of PCL segment and the relative intensities of the methylene protons of the PPDX repetitive units at 4.38 ppm and methylene protons of PCL repetitive units at 2.32 ppm. SEC of poly(*p*-dioxanone-*block*-ε-caprolactone) block copolymers (PPDX-*b*-PCL) were performed in CHCl$_3$ at 40 °C by using a Polymer Laboratories liquid chromatograph equipped with a PL-DG802 degasser, an isocratic HPLC pump LC 1120 (flow rate = 0.6 mL · min^{-1}), a manual injector (loop volume: 200 μL, solution conc.: 1 mg · mL^{-1}), a PL-DRI refractive index detector and three columns: a PL gel 10 μm guard column and two PL gel Mixed-B 10 μm columns. The molecular weight of the PPDX homopolymer (see Table 1) was determined by capillary viscosimetry using a mixture of phenol/1,1,2,2 tetrachloroethane (2:3 v/v) at 25 °C as it was previously reported.[12]

Results and Discussion

The hydrolytic degradation process of aliphatic polyesters starts with the scission of the ester linkage and thereby cleavage of the chains involved. Weight loss and variations of the polymer properties are significant when the degradation products can be dissolved in the degradation medium.

Weight loss data (expressed as weight retention) as a function of hydrolysis time are plotted for PPDX homopolymer and the diblock copolymers in Figure 1. As can be observed, the data points were fitted to sigmoidal shape curves that can be divided in three zones which reflect the behavior throughout the process: an induction period, an abrupt weight loss region and a final stabilization plateau. In the case of PPDX[15], the shape of the curve is a crude estimate based on the behavior reported in the literature[14] for a PPDX of higher molecular weight because data was not collected between the third and the fifth month. The hydrolysis mechanism in which the hydrolysis media takes places over the amorphous and crystalline phases follow the same pattern in spite of the differences in molecular weight between the PPDX previously reported and the homopolymer used in this work.

The induction period is the zone where the decrease in weight retention is not significant. This is related to the early stages of degradation where random scissions first occur and the molecular weight of the degraded chains is too high for solubilization in the hydrolysis medium. POM evidences that support the presence of insoluble long chains products on the early degradation stages will be presented below. The abrupt weight loss stage can be attributed, as stated above, to the solubilization of low molecular weight products in the hydrolysis medium. Finally, when the concentration of hydrolysable chains
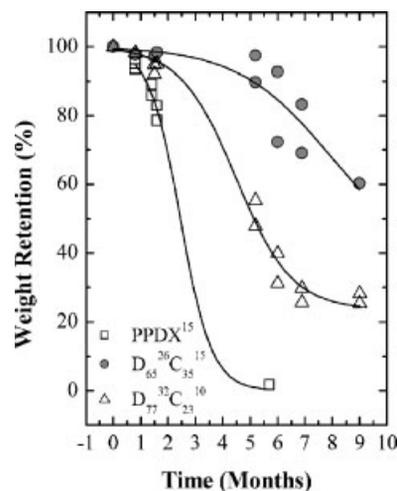
Figure 1. Weight loss as a function of hydrolysis time, under in vitro condition (pH = 7.4, *T* = 37 °C), for PPDX[15] and the indicated PPDX-*b*-PCL diblock copolymers.

decreases to a minimum the weight retention curve reaches a constant value.

For the PPDX^{15} homopolymer, the material was found to be completely degraded by exposure to the hydrolysis medium after 6 months. In the case of $D_{77}C_{23}^{43}$ the induction time related to the onset of a considerable weight loss is close to 2.2 months and the curve is finally stabilized at 23% weight retention after 9 months which fits with the PCL weight fraction in the diblock copolymer. When the content of PCL in the diblock copolymer increases, as in the case of the $D_{65}C_{35}^{42}$, the induction time increases to 4.9 months and the weight retention did not reach a constant value during the 8.5 months experiment duration. Previous results of PPDX-*b*-PCL diblock copolymers with high PCL content (≈85%) where the buffer solution was not kept at constant pH (i.e., the buffer was not replaced during the course of the hydrolysis experiment) showed that a weight loss of 15% had occurred over 10 weeks.[30] This means that, in spite of the increment of the acidic character of the hydrolysis medium as degradation time elapsed, the increase in PCL content in the PPDX-*b*-PCL copolymer decreases the weight loss rate. For PCL homopolymers, several authors have found no significant weight loss under similar degradation conditions, during comparable time intervals.[25] The lack of significant PCL degradation during 9 months implies that the weight loss detected in the diblock copolymers is mainly due to the degradation of the PPDX block. This was corroborated by ^{1}H NMR and DSC results presented below.

Figure 2 shows the first heating DSC scans of the degraded samples after they had been carefully removed from the hydrolysis medium at the indicated time intervals and dried to constant weight. The melting peak (see also Table 2 and 3) corresponding to the PCL block in all samples exposed to the hydrolysis medium is considerably higher than that of the neat sample and slightly increases with degradation time. This is a consequence of the temperature employed during hydrolysis (37 °C) which causes annealing of PCL crystals.

Table 2 and 3 also list relevant transition temperatures and enthalpies for the diblock copolymer samples determined during a controlled cooling (at 10 °C · min^{-1}) after the first heating scan, and also equivalent values measured during a subsequent second heating scan. During the second heating scan, the thermal history of the sample was given during the previous cooling at 10 °C · min^{-1}, therefore the annealing effect on the PCL crystals has been removed (i.e., no increase in PCL melting point is reported in the second heating DSC scans as degradation time increased).

For $D_{77}C_{23}^{43}$ the melting point (T_m) values corresponding to the PCL block determined in the second heating scan (see Table 2) do not change with degradation time, indicating that the PCL block has not suffered any degradation by hydrolysis in the 9 months exposure to the phosphate buffer solution at 37 °C. Only in the 5.2 months sample the T_m suffers a slight decrease. In the case of $D_{65}C_{35}^{42}$ (Table 3) there is a minor reduction in T_m of the PCL block after 5 months of hydrolysis or more. However, the degree of crystallinity is practically invariant with degradation time for the PCL block in the copolymers. Therefore if there was some chain scission, it is probable that the molecular weight of the degraded chains was too high for dissolution in the hydrolytic degradation medium. This is consistent with the weight loss behavior (see Figure 5 and its discussion and comparison with Figure 1 below).

Previous degradation studies in homo-PPDX have indicated that during the first few months of exposure to the degradation media, the peak melting temperature may

(a)
ENDO
Heat Flow (mW)
5 mW
0
0.8
1.2
5.7
6.1
7.6
8.5
40
60
80
100
120
Temperature (°C)
(b)
ENDO
Heat Flow (mW)
5 mW
0
0.8
1.5
5.2
6.0
6.9
9.0
40
60
80
100
120
Temperature (°C)
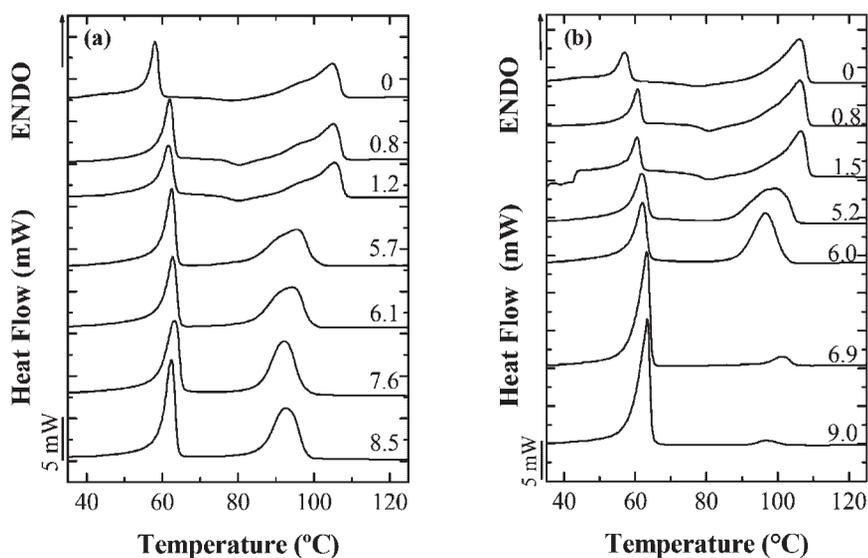
Figure 2. DSC scans showing the first heating (10 °C · min^{-1}) of (a) $D_{65}^{26}C_{35}^{15}$ and (b) $D_{77}^{32}C_{23}^{10}$ diblock copolymers at the indicated hydrolysis time (in months).

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Table 2. DSC derived thermal data for $D_{77}^{32}C_{23}^{10}$.

Time	First heating ($10\,°C \cdot min^{-1}$)								Cooling ($10\,°C \cdot min^{-1}$)	
months	PCL Block				PPDX Block				T_c	ΔH_c
	T_m	ΔH_m	$\Delta H_m^{*a)}$	χ_c^*	T_m	ΔH_m	ΔH_m^*	χ_c^*	°C	$J \cdot g^{-1}$
	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%		
0	57.0	18.8	81.7	58.6	106.2	56.5	73.4	52.0	29.0	−53.8
0.8	60.7	19.2	87.3	62.6	106.3	57.4	73.6	52.1	29.8	−52.5
1.5	60.5	19.7	85.7	61.4	106.5	58.1	75.5	53.4	29.0	−55.1
5.2	61.8	34.2	76.0	54.5	99.7	60.0	109.1	77.3	26.0 33.8	−52.8
6.0	62.0	49.3	−	−	96.5	64.0	−	−	33.3	−48.1
6.9	63.2	88.9	108.4	77.7	101.2	10.6	58.9	41.7	35.1 70.0	−64.5 −5.0
9.0	63.3	89.4	89.4	64.1	96.8	4.9	−	−	36.3 58.3	−68.8 −0.9

Time	Second heating ($10\,°C \cdot min^{-1}$)							
months	PCL Block				PPDX Block			
	T_m	ΔH_m	$\Delta H_m^{*a)}$	χ_c^*	T_m	ΔH_m	ΔH_m^*	χ_c^*
	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%
0	57.5	17.0	73.9	53.0	106.4	56.6	73.5	52.1
0.8	57.2	16.8	76.4	54.7	106.2	59.3	76.0	53.9
1.5	57.2	16.7	72.6	52.0	106.4	60.9	79.1	56.0
5.2	54.0	29.1	64.7	46.4	96.4	47.5	86.4	61.2
6.0	53.4 56.2	31.7	44.0	31.6	93.2	46.6	−	−
6.9	57.4	70.4	85.9	61.5	99.7	6.2	34.4	24.4
9.0	57.9	75.7	75.7	54.3	93.4	3.2	−	−

a) * Indicates normalized values with respect to the composition calculated by ¹H NMR analysis.

decrease slightly but the heat of fusion corresponding to the melting of the PPDX block tends to increase. Several authors have interpreted similar results in PPDX and in other hydrolysable polymers associating them with the loss of entanglements in the amorphous phase, and the successive incorporation of these chains into the crystalline regions, increasing their number. This phenomenon has been termed "cleavage-induced crystallization".[14,31] Obviously, the crystallinity will eventually decrease once the crystal regions in the sample are heavily attacked by hydrolysis during the later stages of degradation.

Cleavage-induced crystallization probably occurred in the PPDX block of both diblock copolymer samples employed here, as the composition normalized values of the crystallinity degrees tended to increase as a function of degradation time (see Table 2 and 3). The values were normalized with respect to recalculated values of composition after ¹H NMR measurements were performed to degraded samples, see Figure 5 below. For $D_{65}C_{35}^{42}$ the effect saturated at the highest degradation time employed, while in the case of $D_{77}C_{23}^{43}$ the crystallinity eventually decreased since the PPDX block in this case was almost completely degraded after a 9-month immersion in the hydrolytic medium.

When the hydrolysis time increased, the degradation of the amorphous and interlamellar regions induced the frag-

mentation of the lamellar phase and facilitates their degradation. The attack on the lamellar regions occurred throughout the crystal surfaces and therefore mainly through the fold planes, thereby progressively reducing the lamellar thickness (and therefore the melting points of the material) until eventually only low molecular weight material remained that could be dissolved in the hydrolysis medium.

Figure 3a compares the variations in heats of fusion (determined from the first DSC heating scans) with degradation time for homo-PPDX and the PPDX block within the two studied copolymers. The homo-PPDX and the PPDX block first experienced an initial slight increase in crystallinity degree, which could be related to the cleavage-induced crystallization process explained above. Then, at longer degradation times, homo-PPDX degraded completely and after 5.5 months almost no material was left. For the PPDX block within the copolymers, the degradation depended on the amount of covalently linked PCL. After 9 months of hydrolysis for the $D_{77}C_{23}^{43}$ copolymer, the PPDX block heat of fusion eventually decreased to just 4.9 $J \cdot g^{-1}$. However, for $D_{65}C_{35}^{42}$ the PPDX block endotherm was displaced to lower temperatures, but the experimental heat of fusion did not decrease as in the other copolymer. The increment in PCL content in the copolymer increased the

Table 3. DSC derived thermal data for $D_{65}^{26}C_{35}^{15}$.

Time	First heating ($10\,°C \cdot min^{-1}$)								Cooling ($10\,°C \cdot min^{-1}$)	
months	PCL Block				PPDX Block				T_c	ΔH_c
	T_m	ΔH_m	$\Delta H_m *$[a]	$\chi_c *$	T_m	ΔH_m	$\Delta H_m *$	$\chi_c *$	°C	$J \cdot g^{-1}$
	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%		
0	58.2	28.5	75.0	53.8	104.8	45.9	74.0	52.4	32.0	−57.1
0.8	62.0	31.8	85.9	61.6	105.2	48.1	76.3	54.1	32.6	−59.7
1.2	61.7	31.8	81.5	58.5	105.5	46.0	75.4	53.4	31.8	−59.1
5.7	62.5	41.7	94.8	67.9	95.5	56.2	100.4	71.1	34.1	−67.2
6.1	62.7	41.7	90.7	65.0	94.3	56.2	104.1	73.7	34.8	−67.6
7.6	63.3	49.5	95.2	68.2	92.2	58.6	122.1	86.5	23.0 32.6	−68.2
8.5	62.5	53.4	95.4	68.4	92.7	56.5	128.4	91.0	24.0 33.0 43.1	−66.4

Time	Second heating ($10\,°C \cdot min^{-1}$)							
months	PCL Block				PPDX Block			
	T_m	ΔH_m	$\Delta H_m *$	$\chi_c *$	T_m		ΔH_m	$\Delta H_m *$	$\chi_c *$
	°C	$J \cdot g^{-1}$	$J \cdot g^{-1}$	%	°C		$J \cdot g^{-1}$	$J \cdot g^{-1}$	%
0	58.2	25.9	68.2	48.9	95.5	105.0	46.1	74.4	52.7
0.8	58.2	26.7	72.2	51.7	95.5	105.2	48.5	77.0	54.5
1.2	58.2	25.8	66.2	47.4		105.5	48.1	78.9	55.9
5.7	55.5	33.2	75.5	54.1	81.7	94.9	48.0	85.7	60.7
6.1	55.9	34.5	75.0	53.8	80.0	93.7	48.0	88.9	63.0
7.6	54.7	39.2	75.4	54.0	77.4	89.2	42.5	88.5	62.7
8.5	55.0	41.3	73.8	52.9	78.5	91.0	39.2	89.1	63.1

[a] * Indicates normalized values with respect to the composition calculated by ^1H NMR analysis.

hydrolytic resistance of the diblock copolymer, in such a way that in the time limit explored, no significant decreases in the PPDX heat of fusion was observed. It is well known that the amorphous regions are first degraded since they are less dense and the diffusion of water molecules less hindered. Longer degradation times are needed for significant degradation on the crystalline regions in the case of the PPDX block within $D_{65}C_{35}^{42}$.

The DSC results are consistent with the weight loss data presented in Figure 1. It is clear that the PCL component is
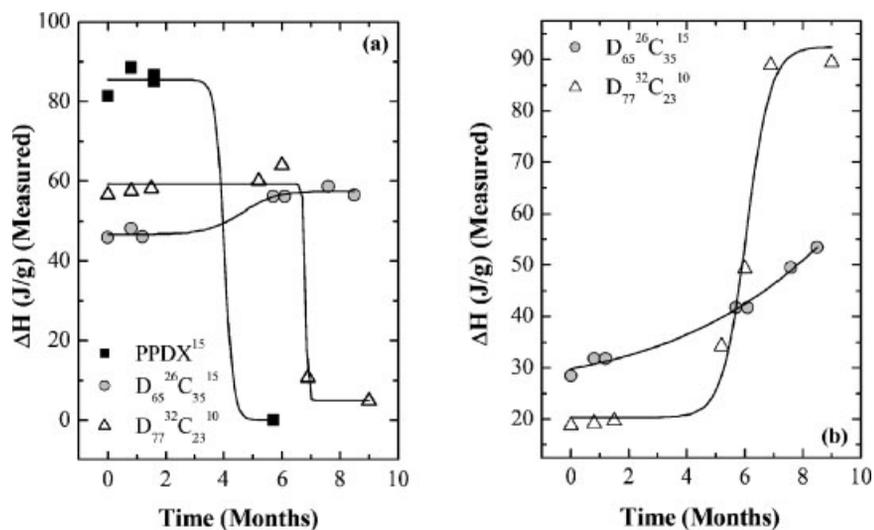
Figure 3. Experimental heat of fusion (DSC first heating scans) of (a) PPDX[15], PPDX block and (b) PCL block within PPDX-b-PCL diblock copolymers.

offering a protection to the PPDX block that is a strong non-linear function of composition. For instance, after 6 months degradation time, homo-PPDX was completely dissolved in the hydrolysis medium. The PPDX component within $D_{77}C_{23}^{43}$ experienced a weight loss of approximately 60% after 6 months exposure to the hydrolysis medium, while the PPDX block within $D_{65}C_{35}^{42}$ only suffered a 20% weight loss. This stabilization can be considered synergistic, since even when the PCL component had not degraded at all in 6 months exposure to the hydrolysis medium, the diblock copolymers (and specially the one with 35% initial PCL content) were much more stable than expected on the basis of the degradation rate of homo-PPDX. Such stabilization effect is a direct result of the morphology of PPDX-*b*-PCL diblock copolymers as discussed in greater detail below.

The stability of the PCL block seems unaffected by being covalently linked to a polymer that can be easily degraded by hydrolysis. In the case of PLLA-*b*-PEO-*b*-PLLA tri-block copolymers, the hydrophilic character of the PEO block increases the degradation rate of the PLLA block as compared to that of homo-PLLA.[31] In this way, we expected that being the PPDX covalently linked to PCL, the degradation rate of the PCL block could be perhaps increased. However, the PCL block melting point did not show a considerable decrease during the entire period of exposure to the hydrolytic degradation medium employed in this work, in agreements with the literature.[25] Figure 3b shows how the experimentally determined heat of fusion for the PCL block increased with degradation time. Such increase is due to the change in composition experienced by the copolymers as PPDX was being degraded, since the values are calculated on the basis of the total mass of each sample. If we normalize the experimentally determined values with the composition at each degradation time, the PCL heat of fusion was found to be constant during the entire degradation period (results not shown).

It is worth noting in Table 2 and 3 that the initial degree of crystallinity in homo-PPDX and in the PPDX block of the two diblock copolymers employed in this work was approximately the same before the hydrolysis process. This indicates that the difference in degradation rate between homo-PPDX and the PPDX block within the copolymers is only a function of the PCL content of each diblock copolymer (and therefore also on the diblock copolymer morphology) and cannot be attributed to differences in the amount of amorphous material within each PPDX component under consideration. For this reason, the diblock copolymer composition is the key parameter, which determines the degradation rate. The degradation depends of the quantity of PCL phase, which serves as barrier for the more hydrolytically unstable PPDX phase.

Using the relation between the methylene protons of the PPDX and the PCL repeating units obtained by ^{1}H NMR analysis,[27] we can estimate the composition change of
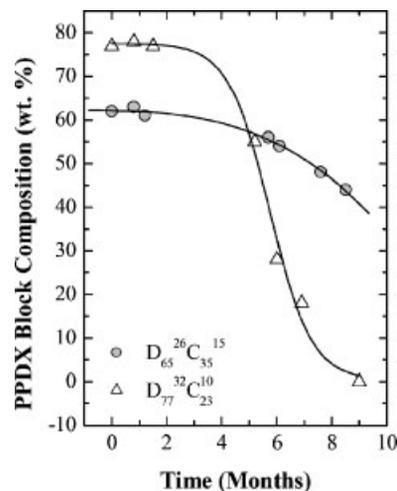
Figure 4. Changes in PPDX block composition during hydrolytic degradation, obtained by ^{1}H NMR measurements.

each block during the hydrolysis. Figure 4 summarizes the ^{1}H NMR results obtained as a function of degradation time, where the real PPDX content of each sample has been plotted. The composition was approximately constant during the induction time. After 5 months, the PPDX content decreased in both copolymers. In the case of $D_{77}C_{23}^{43}$, the initial PPDX content was 77% and it gradually decreased until it becomes 0% after 9 months of degradation time. It is noteworthy that the weight retention at that time in Figure 1 for this copolymer was very close to 23%. This result confirms that the hydrolytic degradation mainly affects the PPDX block in the time scale explored here. On the other hand, for $D_{65}C_{35}^{42}$ the composition changed from an initial PPDX content of 65% to roughly 45% after 8.5 months of hydrolytic degradation. Therefore, a much longer degradation time would be required to completely degrade the PPDX block within this diblock copolymer because of the protection provided by the PCL component.

The results presented in Figure 4 are fully consistent with the DSC results presented in Figure 2. In fact, a similar calculation of composition changes was performed on the basis of the enthalpy of fusion changes in the case of $D_{77}C_{23}^{43}$ and parallel results to those shown in Figure 4 were obtained.

The ^{1}H NMR measurements (as well as DSC and SEC) were performed to samples that had been directly removed from the hydrolysis medium after the indicated time (they were dried to constant weight and then dissolved in $C_2D_2Cl_4$). Therefore, these samples may contain a mixture of diblock copolymer chains and lower molecular weight PPDX chains whose molecular weight was high enough to prevent their dissolution in the hydrolysis medium before their removal. SEC demonstrated that this was indeed the case, see below. Then, the PPDX content in Figure 4 cannot be directly equated to diblock copolymer composition

without incurring an error whose magnitude will depend on the amount of homo-PPDX chains present in each sample.

The molecular weight distributions of diblock copolymer samples were obtained after 5 months hydrolysis. It should be noted that the neat samples cannot be dissolved in $CHCl_3$ because of the poor solubility of relatively high molecular weight PPDX. Therefore, it was only after 5 months of degradation that the samples had a low enough molecular weight to be soluble in $CHCl_3$. Transparent solutions were obtained, allowing SEC analysis.

Figure 5 shows SEC traces for 3 different degradation times and for both diblock copolymers. The resulting traces show the presence of several chain populations, which could be related with the random hydrolytic cleavages of PPDX-b-PCL block copolymers chains leading to the formation of low molecular weight chains. We can identify one chain population at low retention volumes (higher molecular weights) that did not change in position. In the $D_{77}^{43}C_{23}$ case, Figure 5(a), the SEC trace shows a marked decrease in the signals present at high retention volume for the sample recovered after the 9-month degradation time. This sample, according to ^{1}H NMR and weight loss data (see Figure 1 and 4) should contain almost no PPDX. Furthermore, from the results previously obtained by DSC and ^{1}H NMR we know that the hydrolysis occurred mainly in the PPDX block. Therefore, it can be concluded that the chain lengths associated with higher retention volumes in the SEC traces are related to the formation of low molecular weight PPDX chains by hydrolysis, whereas the signal at lower elution volume (that is almost constant with degradation time) corresponds to diblock copolymer chains and/or with homo-PCL chains, depending on the hydrolysis time. However, it must be emphasized that, although the samples hydrolyzed after 5 months were soluble to "the

naked eye", one cannot exclude that they were not fully soluble (microscopically) in $CHCl_3$. Indeed, it is worth recalling that $CHCl_3$ is not a good solvent for high molecular weight PPDX in contrast to PCL.

The spherulitic superstructure of PPDX and PPDX-b-PCL diblock copolymers has been studied in detail in previous work along with spherulitic growth kinetics.[28,32,33] In general, isothermal crystallization of PPDX or PPDX-b-PCL diblock copolymers yields well-developed banded spherulites at crystallization temperatures below 55 °C. In the diblock copolymer case, at such low temperatures usually mixed spherulites (formed by both PCL and PPDX lamellae) are formed. If the crystallization is performed at temperatures between 55 and 75 °C, a very different morphology can be obtained for homo-PPDX and for the diblock copolymer. At these temperatures, PPDX still forms well-developed banded spherulites; however, in the case of the diblock copolymer the PCL block will be molten at such temperatures. The corresponding superstructural morphology observed is that of irregular granular spherulites that exhibit a very faint Maltese cross, and no discernible banding. At very high crystallization temperatures, the spherulitic structure of neat PPDX can also change to a more granular superstructural aggregate with distorted banding and faint Maltese cross (this change is more easily seen in very high molecular weight PPDX at crystallization temperatures of 80 °C or higher, see ref.[13]).

In the present case, the neat samples of PPDX[15], $D_{77}^{43}C_{23}$ and $D_{65}^{42}C_{35}$ exhibited the expected spherulitic morphologies depending on their crystallization temperatures as described above. When isothermal crystallization was performed in the temperature range between 60 and 70 °C, well-developed banded spherulites were only observed for PPDX[15], while in the case of both diblock copolymer samples, only granular superstructural aggregates were
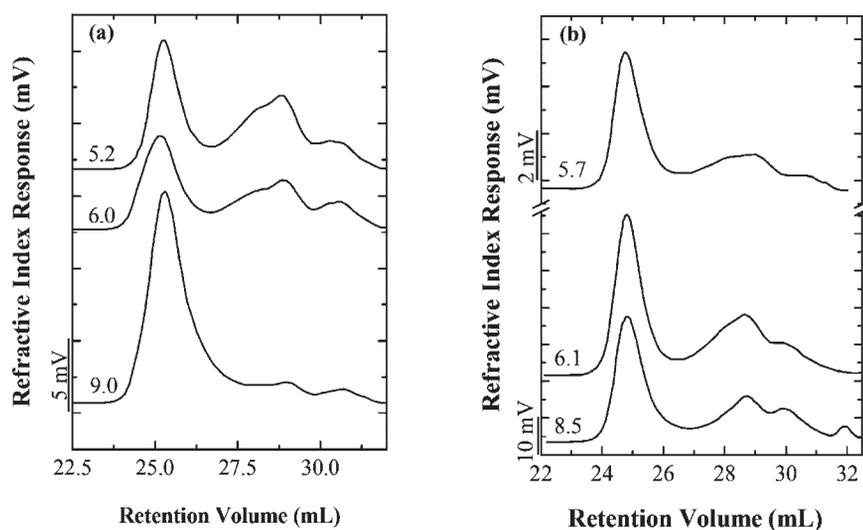
Figure 5. SEC traces of (a) $D_{77}^{32}C_{23}$ and (b) $D_{65}^{26}C_{35}^{15}$ diblock copolymers. The inset indicates degradation time (in months).

obtained. When samples that had been exposed to hydrolytic degradation for 0.8 months were examined a curious phenomenon was observed for the $D_{77}C_{23}^{43}$ sample. The sample exhibited two types of spherulites, the majority looked just like those seen in the neat diblock copolymer, and they were granular superstructural aggregates with faint Maltese crosses (see Figure 6a). However, a few well-developed spherulites with very clear Maltese cross and banding extinction patterns were also present (see Figure 6b). It is worth noting that after 0.8 months of degradation, the sample had not shown any appreciable weight loss, since probably any chain scission produced in the PPDX segments of the copolymer was confined to the amorphous regions and yielded PPDX chains that had lower molecular weights than the PPDX block but were still too high for dissolution in the hydrolysis medium. Therefore, we propose that spherulites such as those shown in Figure 6b were formed by degraded homo-PPDX chains that can segregate during crystallization from the melt. A confirmation that this is indeed the origin of such structures was obtained by determining spherulitic growth rates. In the case of the $D_{65}C_{35}^{42}$ sample (with 0.8 month of exposure to the hydrolysis medium) the presence of homo-PPDX spherulites was not observed, maybe because of its lower PPDX content.

We have demonstrated in previous works[28,29,32] that the spherulitic growth rate of PPDX-*b*-PCL diblock copolymers at temperatures where PCL cannot crystallize ($T_c > 50\,^\circ\text{C}$) is much lower than that of a corresponding homo-PPDX of equivalent molecular weight. It was demonstrated that the presence of the covalently linked PCL greatly increases the energy barrier for secondary nucleation or spherulite growth in such a way that a retardation on the growth rate of almost an order of magnitude can be achieved depending on the crystallization temperature. This is shown in Figure 7 when the spherulitic growth rate of PPDX[15] is compared to that of neat $D_{77}C_{23}^{43}$ diblock copolymer.

Figure 7 also includes spherulitic growth data for PPDX[15] after 0.8 month exposure to hydrolytic degradation and data corresponding to the growth of the spherulites believed to be the result of the crystallization of lower molecular weight homo-PPDX molecules derived from the random scission of the PPDX block within $D_{77}C_{23}^{43}$, in other words, spherulites similar to those shown in Figure 6b.

The solid lines in Figure 7 are fits to the Lauritzen and Hoffman secondary nucleation theory, using the parameters, equations and procedure previously reported.[32] For homo-PPDX[15] a typical bell shape curve has been observed. After 0.8 month of hydrolytic degradation, the spherulitic growth rate increased in the low crystallization temperature range. This is a consequence of the lower molecular weight, since the low T_c range or left hand side of the typical bell shape G versus T_c curve was regulated by diffusion. Lower $\overline{M}_n$ molecules will have faster diffusion at lower temperatures and also lower T_g temperatures. These facts can explain the general shift of the curve to slightly lower temperatures.

The most striking result presented in Figure 7 is the difference in spherulitic growth rate (G) exhibited by spherulites like those shown in Figure 6b (i.e., present in $D_{77}^{32}C_{23}^{43}$ after 0.8 months degradation) and neat $D_{77}^{32}C_{23}^{43}$ spherulites. In the former case G is very similar to the value obtained for neat PPDX spherulites, while in the latter case G is nearly an order of magnitude lower.

The obvious difference with the spherulitic growth rate of PPDX when it is covalently bonded with PCL (neat $D_{77}C_{23}^{43}$ results in Figure 7) demonstrates that these spherulites (Figure 6b) are mainly composed of PPDX chains as we suspected from their morphological differences (compare Figure 6a and 6b). Therefore, it is clear that in the first stages of the degradation process in PPDX-*b*-PCL diblock copolymers, hydrolytic chain scissions occurred preferentially on the PPDX block and produced PPDX homopolymer that remained blended in the system since its molecular weight was probably high enough to prevent its
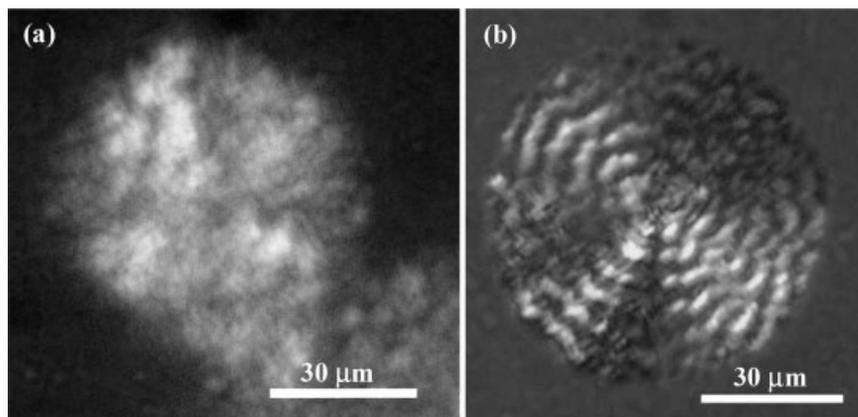
Figure 6. POM images for $D_{77}^{32}C_{23}^{43}$ diblock copolymer: (a) neat at $T_c = 60\,^\circ\text{C}$ and (b) after 0.8 months hydrolytic degradation at $T_c = 70\,^\circ\text{C}$.
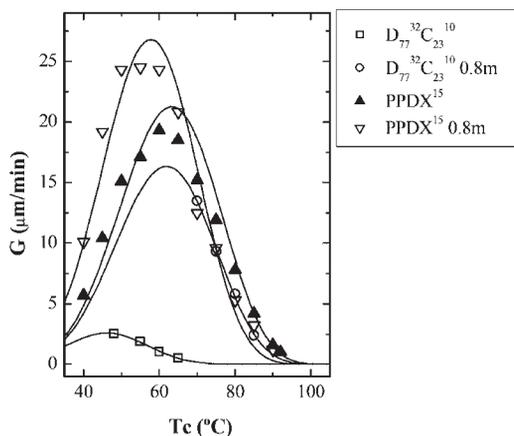
Figure 7. Growth rate as a function of crystallization temperature (T_c) for neat and degraded PPDX[15] and $D_{77}^{32}C_{23}$ diblock copolymer. The solid lines represent fits to the Lauritzen and Hoffman crystallization theory.

dissolution in the reaction medium. Spherulites similar to those presented in Figure 6a have a growth rate kinetics that is similar to that of neat $D_{77}C_{23}^{43}$ (results not shown).

The crystallization of PPDX-*b*-PCL diblock copolymers proceeds from a weakly segregated melt.[28,32] Recently, Atomic Force Microscopy (AFM) evidences showed that these copolymers crystallize forming lamellar structures regardless of composition, a typical behavior of weakly segregated diblock copolymers.[32] When only PPDX crystallizes at higher temperatures, PPDX lamellae are formed

in a molten PCL matrix. When both components crystallize at lower crystallization temperatures, mixed spherulites with inter-dispersed or inter-digitized lamellae are formed. A schematic diagram is presented in Figure 8 where an idealized picture describes how the amorphous and crystalline regions of each block could be alternated in the diblock copolymer sample before degradation (Figure 8, Scheme 1). This morphology has a tremendous impact on the degradation process since the PCL regions cannot be easily hydrolyzed and act as hydrolysis barriers while the PPDX regions are susceptible to hydrolysis. This is the main reason behind the synergistic stabilization effect caused by the PCL content in the PPDX block in the PPDX-*b*-PCL diblock copolymers.

In the first stage of the degradation, the ester linkages located in the amorphous phase of the PPDX blocks (see Figure 8, Scheme 2) are preferentially hydrolyzed. This PPDX block is covalently linked to PCL whose amorphous and crystalline zones may act as physical obstacles (due to their lower susceptibility to hydrolysis) that protect PPDX block regions, delaying water penetration and subsequent hydrolysis, and therefore decrease the degradation rate of the PPDX block as compared to homo-PPDX. The degradation of the amorphous zones within the PPDX block may produce the formation of new crystals, i.e. via cleavage-induced crystallization. Moreover, random chain scissions of the PPDX blocks can also generate chains of homo-PPDX that cannot be dissolved by the hydrolysis medium due to their molecular weights, and may form lamellae on their own (and spherulites like those of Figure 6b).
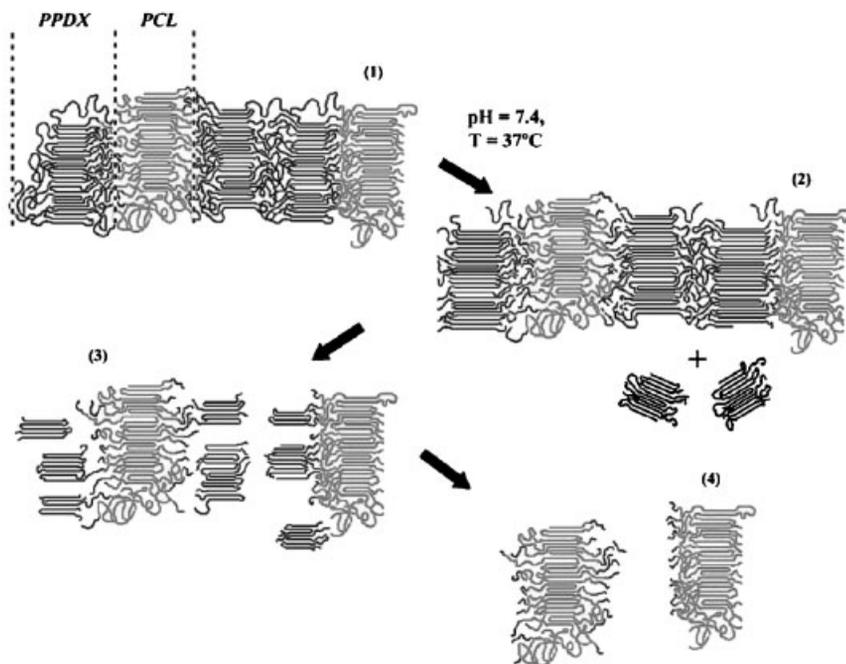
Figure 8. Proposed scheme for the hydrolytic degradation process of PPDX-*b*-PCL diblock copolymers.

The advance of the PPDX block hydrolysis (Figure 8, Scheme 3) leads to the fragmentation of interlamellar and lamellar regions until many PPDX chains get solubilized by the media. Finally (Figure 8, Scheme 4), most of the PPDX block has been depleted, for example after 9 months of degradation in sample $D_{77}C_{23}^{43}$, and we would expect that the hydrolysis may increasingly occur in the PCL block at longer times. However, significant hydrolysis of the PCL block could not be observed during the progress of our experiment, or at least not extensively since no dissolution of PCL chains was detected and only slight changes in T_m were encountered for $D_{77}C_{23}^{43}$ (and none for the other diblock copolymer) while the degree of crystallinity remained constant. This is in perfect agreement with the very slow hydrolytic degradation of PCL compared to its enzymatic degradation. Indeed, highly crystalline PCL was reported to totally degrade in 4 d, the crystallinity decreasing during degradation, in contrast to hydrolytic degradation which takes several years.[31,34]

Conclusion

The hydrolytic degradation process was studied in PPDX-*b*-PCL diblock copolymers. The PCL block did not experience any significant degradation by hydrolysis (at 37 °C) during the 9 months experiment. ^{1}H NMR and DSC analysis showed that the PPDX block within $D_{77}C_{23}^{43}$ copolymer was completely degraded over the 9 months of hydrolysis. When the PCL composition increased, that is the case of $D_{65}C_{35}^{42}$ the weight lost was 40% after 8.5 months and the composition of the PPDX in the copolymer just decreased 20%. These results indicate that the difference in degradation rate between the diblock copolymers is a non-linear function of the PCL content. POM results for $D_{77}C_{23}^{43}$ indicate the presence of some typical homo-PPDX spherulites in the 0.8 month degraded sample when no weight loss was detected. We conclude that random chain scission during the early stages of degradation can produce homo-PPDX chains that cannot be dissolved in the hydrolysis medium because their molecular weight is still too high. It was found that the PCL content in the diblock copolymers produced a synergistic increase in the PPDX block degradation stability. This is a direct result of the inter-digitized lamellar morphology present in the copolymers where PCL and PPDX lamellae are alternated within mixed spherulites. Due to its much higher resistance to hydrolysis, the PCL lamellae offer a barrier-type protection to the PPDX within the copolymer.

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