Synthesis, Characterization, and Hydrolytic Degradation of PLA/PEO/PLA Triblock Copolymers with Long Poly(L-lactic acid) Blocks

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ABSTRACT: A series of triblock PLA/PEO/PLA copolymers were synthesized by polymerization of L-lactide in the presence of PEG2000, a bifunctional OH-terminated poly(ethylene glycol) ($\bar{M}_n$ = 1800) using Zn metal or CaH_2 as catalyst. The resulting copolymers were analyzed by various techniques including ^1H and ^{13}C nuclear magnetic resonance, size-exclusion chromatography, X-ray diffractometry, optical microscopy, and differential scanning calorimetry. NMR spectra showed that Zn and CaH_2 catalyzed lactide polymerization under the selected experimental conditions to yield long PLA blocks at both ends of the PEG macroinitiator. The copolymer composition was comparable to that of the feed even after purification by dissolution/precipitation. Hydrolysis of the triblock copolymers conclusively showed that the early stages of ester bond cleavage proceeded at random along the PLA blocks. As degradation advanced, a highly swollen hydrogel layer expanded from the surface of a still compact, partially degraded specimen. According to NMR analysis, this layer was composed of PLA/PEO/PLA copolymers bearing short PLA blocks which resulted from the degradation of parent long blocks. It remained attached to the surface via physical interactions within hydrophobic microdomains composed of clustered PLA segments.

Introduction

In a previous paper, we reported the synthesis and characterization of triblock copolymers constituted of a central poly(oxyethylene) (PEO) block ended at both sides by short poly(L-lactic acid) (PLA) sequences.[1] These PLA/PEO/PLA triblock copolymers were obtained by polymerization of L-lactide at high temperatures (140−145 °C) in the presence of poly(ethylene glycol) (PEG) and CaH_2. Both PEG and PLA are of great interest for temporary therapeutic applications, especially as matrices for sustained release drug delivery systems.[2,3] PEG presents outstanding properties, e.g. solubility in water and in organic solvents, lack of toxicity, and absence of antigenicity and immunogenicity, which are essential for drug formulations.[4] PLA polymers have been used in clinics for many years as sutures and osteosynthesis devices and have been widely investigated for other biomedical applications because of their biocompatibility and bioresorbability.[3] However, both polymers present shortcomings. PLA is a rather hydrophobic and brittle polymer, whereas PEG is hydrophilic and not biodegradable. However, intravenously administered PEG is readily excreted through the kidney and, thus, the biostability is not a problem provided its molecular weight (MW) is rather low.[5]

The copolymerization of PEG with lactides is now regarded as a good means to obtain new polymeric materials with original physical, chemical, and biological properties adaptable to specific uses.[6−12] A number of catalysts have been used to attach PLA blocks to OH-terminated PEG, e.g. stannous octoate, SnO, SnO_2, Sb_2O_3, PbO, GeO_2, $SnCl_2$, and NaH.[6−12] Among these catalysts, stannous octoate is the most frequently mentioned in literature because it leads to high yields and high molecular weights.[8,12] However, stannous octoate, as many other catalysts, is difficult to remove from the resulting polymeric compounds, and residues might present some cytotoxicity.[13] On the other hand, catalyst-free polymerization of lactides in the presence of PEG yielded only low molecular weight PLA blocks attached to the PEO central block.[10]

In this paper, we wish to report recent results concerning the polymerization of L-lactide in the presence of PEG, using zinc metal or CaH_2 as catalyst. Zinc has been successfully utilized by our group for nearly 20 years as a life-friendly standard initiator for the synthesis of PLA polymers.[14] Zn^{2+} ions are nontoxic at trace doses, and the residual Zn particles can be easily eliminated by filtration after polymerization. CaH_2 was selected because residual calcium ions were obviously nontoxic. Low molecular weight PEG was selected because it can be excreted easily through the renal route. Biological, material, and physico-chemical properties of triblock copolymers depend very much on macromolecule structures and, thus, on polymerization conditions and mechanisms, especially when one deals with bioresorbable blocks. Therefore, it is of critical importance that such copolymers be well characterized. The PLA/PEO/PLA triblock copolymers with similar PEO central blocks investigated in this work were prepared under original conditions and were characterized comparatively by optical microscopy, ^1H and ^{13}C nuclear magnetic resonance (NMR), size-exclusion chromatography (SEC), differential scanning calorimetry (DSC), and X-ray diffractometry. Last, but not least, hydrolytic degradation of one of the copolymers was undertaken in water and preliminary results are reported herein.

Experimental Section

Materials. L-Lactide was purchased from Purac and recrystallized from acetone before use. PEG2000 was supplied by Fluka and used without further purification. The actual number average molecular weight ($\bar{M}_n$) of this PEG was found

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Table 1. $PLA_x/PEO_y/PLA_x$ Triblock Copolymers Obtained from Polymerization of L-Lactide in the Presence of PEG2000 Using Zn or CaH_2 as Co-Initiator

copolymer PLA/PEO/PLA	LA/EO in feed	LA/EO[a] in product	$\overline{DP}_{PEO}$[b]	$\overline{DP}_{PLA}$[b]	$\bar{M}_n$[c]
$PLA_{14}/PEO_{41}/PLA_{14}$(Zn)	0.6	0.6	41	14	3 800
$PLA_{44}/PEO_{41}/PLA_{44}$(Zn)	2.0	2.1	41	44	8 090
$PLA_{109}/PEO_{41}/PLA_{109}$(Zn)	5.0	5.3	41	109	15 650
$PLA_{205}/PEO_{41}/PLA_{205}$(Zn)	9.9	10.0	41	205	31 320
$PLA_{340}/PEO_{41}/PLA_{340}$(Zn)	19.8	19.0	41	340	57 890
$PLA_{21}/PEO_{41}/PLA_{21}(CaH_2)$	1.0	1.0	41	21	4 800
$PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$	2.0	2.1	41	43	7 950
$PLA_{117}/PEO_{41}/PLA_{117}(CaH_2)$	5.0	5.7	41	117	18 600
$PLA_{194}/PEO_{41}/PLA_{194}(CaH_2)$	9.5	9.1	41	194	29 760
$PLA_{382}/PEO_{41}/PLA_{382}(CaH_2)$	19.9	18.7	41	382	56 850

[a] Determined by using the integration ratio of resonances due to PEO blocks at 3.65 ppm (-O-CH_2-CH_2) and to PLA blocks at 1.46 ppm (CH_3) in the ^{1}H NMR spectra. [b] $\overline{DP}_{PEO} = 1800/44 = 41$, $\overline{DP}_{PLA} = \overline{DP}_{PEO} \times (LA/EO)/2$. [c] $\bar{M}_n = 44 \times \overline{DP}_{PEO} + 2 \times 72 \times \overline{DP}_{PLA}$.

to be 1800 when determined by SEC using PEG standards. GR zinc powder and CaH_2 powder of 40 mesh size were purchased from Merck and from Janssen, respectively.

Polymerization. The procedure was comparable to that of the homopolymerization of lactides.[14] Predetermined amounts of L-lactide and PEG2000 were introduced into a flask. The selected catalyst, zinc powder (0.05 wt %) or CaH_2 (in 1/1 mole ratio with respect to hydroxyl end groups of PEG2000), was then added. After degassing, the flask was sealed under vacuum and placed in an oil bath at 140 °C equipped for continuous stirring. The flask was opened after 7 days when Zn was the co-initiator and 4 days in the case of CaH_2. Typically, the polymer was recovered by dissolution in $CHCl_3$ and precipitation in ethanol after filtration on sintered glass. Diethyl ether was used as nonsolvent in the case of copolymers with high PEG2000 contents. In all cases, the polymeric products were filtered out and dried over P_2O_5 under reduced pressure.

Hydrolytic Degradation. Parallelepiped plates (10 × 10 × 2 mm) were prepared by compression molding and machining as in the case of previous investigations.[15] The specimens were soaked in distilled water at 37 °C. Periodically, the specimens were recovered, weighed, and vacuum dried before analysis. Relative hydrophilicity values of the various copolymers were evaluated from the content in absorbed water which was determined by weighing.

Measurements. NMR spectra were recorded at room temperature with a Bruker spectrometer operating at 250.13 MHz (^{1}H) and 50.32 MHz (^{13}C) by using 6% (^{1}H) and 14% (^{13}C) solutions in $CDCl_3$. Chemical shifts (δ) were given in ppm using tetramethylsilane (TMS) as an internal reference. SEC of the triblock copolymers was performed on a Waters apparatus equipped with a differential refractometer as detector and a Waters 5 μm PLgel Mixed-C column. Tetrahydrofuran (THF) was used as the mobile phase with a flow rate of 1.0 mL/min. Thermograms were obtained by using a DuPont DSC series 99 equipped with a DSC 910 accessory, the heating rate being 10 °C/min. X-ray diffractometric analyses were carried out using a diffractometer equipped with a Cu Kα ($\lambda = 0.154$ nm) source, an INEL monochromator, and a goniometric plate. For optical microscopy measurements, a Leitz SMPOL optical polarizing microscope equipped with a heating device was used. The sample was placed on a glass lamella, heated to the melting temperature (T_m), and then cooled at 10 °C/min to 25 °C.

Results and Discussion

Various PLA/PEO/PLA triblock copolymers were obtained from the copolymerization of L-lactide in the presence of PEG2000 ($\overline{DP}_{PEO} = 41$) and small amounts of Zn metal or CaH_2 (Table 1). The LA/EO mole ratio in the feed ranged from 0.6/1 to 19.9/1. For the sake of clarity, the various copolymers were denoted $PLA_x/PEO_y/PLA_x$(catalyst), x and y being the number average degree of polymerization of PLA and PEO blocks ($x = \overline{DP}_{PLA}$ and $y = \overline{DP}_{PEO}$). $\overline{DP}_n$, LA/EO ratio, and $\bar{M}_n$ values of the copolymers were evaluated from ^{1}H NMR spectra.

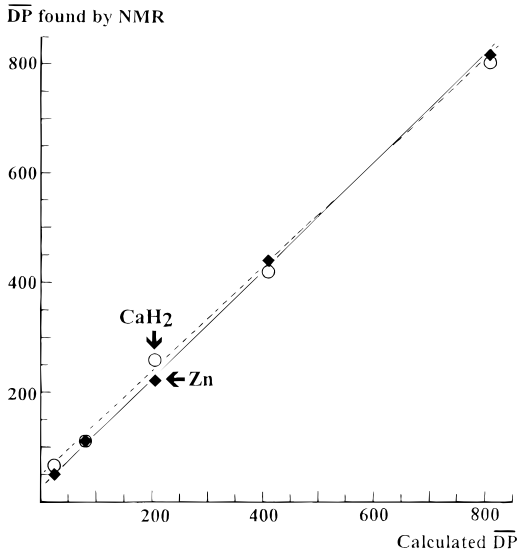

Figure 1. Average degree of polymerization of PLA blocks in the copolymers obtained from calculations and from ^{1}H NMR.

NMR Analyses. All the polymeric compounds presented well-defined NMR spectra with similar characteristics which corresponded well to what had been reported in the literature for triblock copolymers synthesized with other initiator systems.[7,8,11]

^{1}H NMR. ^{1}H NMR spectra of PLA/PEO/PLA triblock copolymers were used to determine LA/EO ratios from the integration ratio of resonances due to PEO blocks at 3.65 ppm (−O−CH_2−CH_2 singlet) and to PLA blocks at 1.46 ppm (CH_3 doublet) and 5.19 ppm (−CH quartet), according to a procedure already described in the literature.[7,8] After purification, all the resulting triblock copolymers exhibited LA/EO molar ratios very close to those of corresponding feeds (Table 1). This finding suggested that all monomer molecules were engaged in polymer chains, since all lactyl units were present within the purified materials. $\bar{M}_n$ of the polymeric precipitates also depended on feed compositions. The higher the LA/EO ratio in the feed, the higher the $\bar{M}_n$. The values of $\overline{DP}_{PLA}$ derived from ^{1}H NMR were in good agreement with calculated data, assuming total conversion of L-lactide (Figure 1). These findings well agree with data obtained for triblock copolymers prepared in the presence of stannous octoate.[12]

^{13}C NMR. Figure 2 shows the ^{13}C NMR spectrum in $CDCl_3$ of the copolymer $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$ and the assignments of resonances to carbon atoms of the

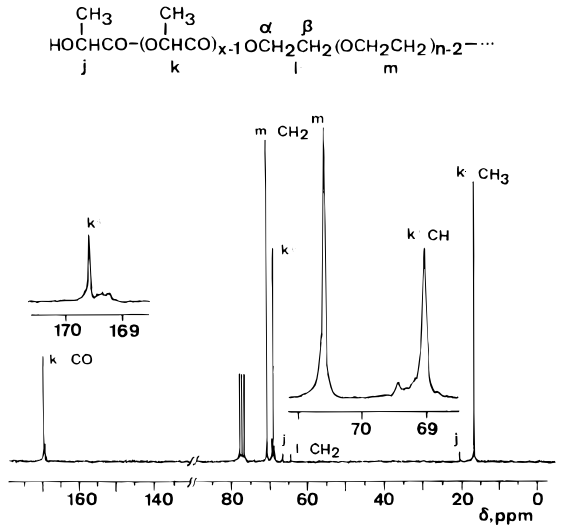

Figure 2. ^{13}C NMR spectrum ($CDCl_3$) of the copolymer $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$.

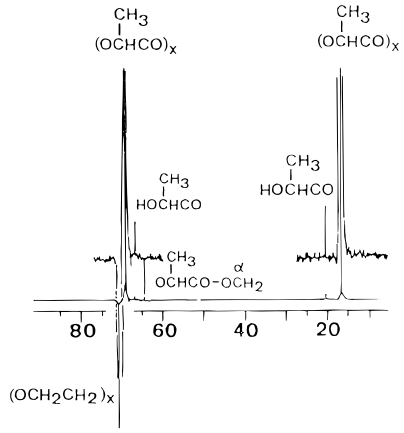

Figure 3. ^{13}C NMR spectra ($CDCl_3$) of the copolymer $PLA_{109}/PEO_{41}/PLA_{109}(Zn)$ taken by the INEPT technique.

different repeating units, namely, $-CH_2-CH_2$ of EO units (**m**) in PEO blocks at 70.3 ppm, $-CH_2-CH_2$ of EO units ($\mathbf{l}_\alpha$) bound to PLA blocks via an ester bond at 64.15 ppm, $-CH_3$, $-CH$, and $-CO$ of LA units (**k**) in PLA blocks at 16.35, 69.04, and 169.56 ppm, respectively, and $-CH_3$ and $-CH$ of OH-ended lactyl units (**j**) at 20.20 and 66.40 ppm, respectively. These assignments, which well agreed with literature data,[8] were confirmed by the insensitive nuclei enhanced polarization transfer (INEPT) technique, as shown in Figure 3. In both spectra, $\mathbf{l}_\alpha$ and **j** resonances had similar areas, suggesting EO–LA junctions and OH-ended lactyl chain ends were in comparable amounts. This good correlation and the absence of other detectable peaks ruled out the presence of COOH-ended lactyl units within the considered triblock compounds. Therefore, if COOH-ended lactyl units relax at a similar rate as OH-ended ones, one can conclude that no or less than 0.5% COOH-ended PLA chains or blocks were formed under the selected polymerization conditions, OH-ended lactyl units (**j**) being still detectable within $PLA_{205}/PEO_{41}/PLA_{205}(Zn)$. On the other hand, it was not possible to detect any signal assignable to $-O-CH_2-CH_2-OH$ or $-O-CH_2-CH_2-$ OH carbon atoms belonging to OH-ended PEG groups. This finding showed that PEG hydroxyl end groups were totally esterified and that neither residual PEG nor PLA/PEG diblock copolymer was present in the final products, at least with respect to NMR sensitivity. Therefore, it was concluded that the polymeric compounds recovered from the polymerization of L-lactide in the presence of PEG and Zn metal or CaH_2 could be considered as exclusively composed of OH-terminated PLA/PEO/PLA triblock chains.

The presence of OH-ended lactyl units in the triblock copolymers (as reflected by the **j** resonances) indicated that, similar to L-lactide polymerization initiated with $CH_3O^-Na^+$ or with $-(OCH_2CH_2)_nO-CH_2CH_2O^-Na^+$,[16,17] the reaction proceeded via acyl–oxygen bond cleavage. It is of interest to point out that, in the absence of Zn metal or of CaH_2, no significant copolymerization occurred under the selected conditions.

The ^{13}C NMR spectrum of $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$ exhibited extra signals with low intensities around 169.35 and 69.40 ppm besides those characteristic of isotactic PLA sequences at 169.56 and 69.04 ppm, respectively (Figure 2).[17] These extra resonances were not present in the spectra of Zn-catalyzed copolymers. Therefore, in the case of CaH_2-catalyzed PLA blocks, LD heterotactic enchainments were formed which are normally forbidden in the case of configuration-respecting ring opening polymerization of optically pure L- or D-lactides which are cyclic dimers bearing two asymmetric carbon atoms of the same configuration.[17] This finding showed that copolymerization in the presence of Zn yielded triblock copolymers containing isotactic PLA blocks, whereas some racemization occurred in the case of CaH_2. It is of interest to note that no racemization was detected in the case of CaH_2-catalyzed triblock copolymers with short PLA chains.[1] This difference can be assigned to differences in polymerization conditions, in particular a shorter reaction time (14 h for short PLA chains *vs* 96 h in the present work).

Morphological Characterizations. X-ray Diffraction. X-ray diffraction spectra of PEG2000 and of some of the copolymers are shown in Figure 4. PEG2000 exhibited the two main diffraction peaks of crystalline PEG at 9.7 and 11.8°,[18] which were also observed in PLA/PEO/PLA triblock copolymers with very short PLA blocks.[1] These peaks were not detected in the spectra of the present copolymers which were crystallized without any special thermal treatment. The absence of PEO peaks suggested that crystallizability of PEO blocks was very much decreased when they were covalently bound to rather long PLA blocks at both ends. In contrast, two peaks were observed at 8.5 and 9.4°, which are characteristic of the crystalline phase of poly(L-lactic acid). As determined by weighing, crystallinity was 32% for both $PLA_{205}/PEO_{41}/PLA_{205}(Zn)$ and $PLA_{109}/PEO_{41}/PLA_{109}(Zn)$ whereas it was lower (14%) for $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$. The lower crystallinity observed for the latter could be due to the smaller length of PLA blocks in agreement with the literature of triblock copolymers obtained without catalyst.[10] It is likely that the partial racemization shown in the case of CaH_2-type polymers also contributed to lower the crystallinity. Last, but not least, the crystallinity increase of copolymers leveled off as the length of PLA blocks exceeded 109 lactyl units, the limit being apparently in the range of the 32% crystallinity usually reported for poly(L-lactic acid).

Visual Examination. Samples of a high molecular weight poly(L-lactic acid) and of the copolymer $PLA_{205}/PEO_{41}/PLA_{205}(Zn)$ were allowed to crystallize under 10 °C/min cooling after melting on glass lamellae. Both compounds showed spherulitic crystallites, as observed by using optical microscopy. However, the spherulites of poly(L-lactic acid) were more numerous and much

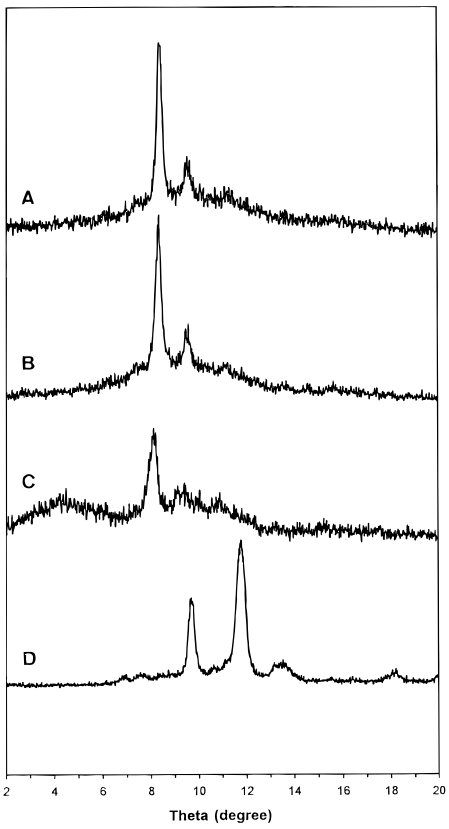

Figure 4. X-ray diffraction patterns of (A) $PLA_{205}/PEO_{41}/PLA_{205}$(Zn); (B) $PLA_{109}/PEO_{41}/PLA_{109}$(Zn); (C) $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$; (D) PEG2000.

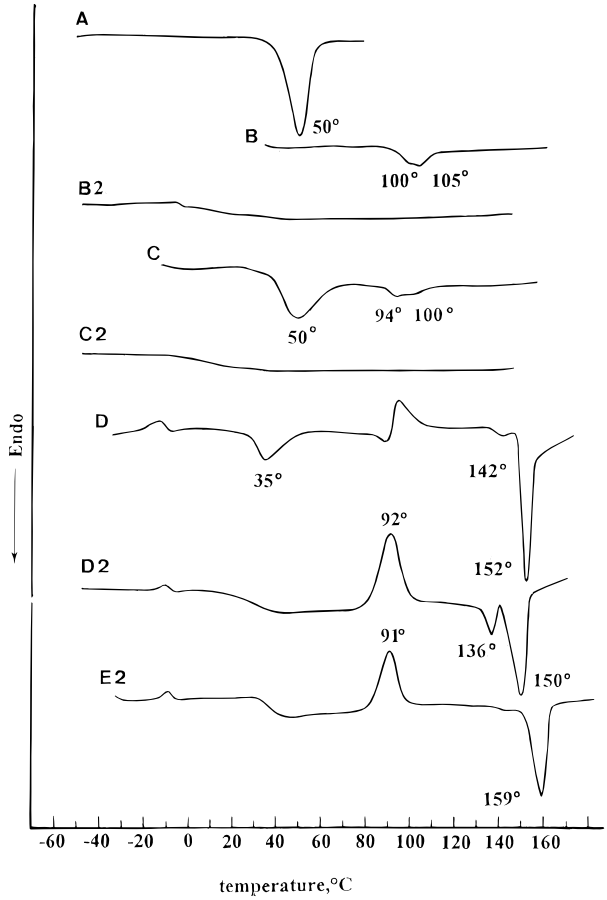

Figure 5. DSC thermograms: (A) PEG2000; (B) $PLA_{44}/PEO_{41}/PLA_{44}$(Zn); (C) $PLA_{117}/PEO_{41}/PLA_{117}(CaH_2)$; (D) $PLA_{109}/PEO_{41}/PLA_{109}$(Zn); (E) $PLA_{205}/PEO_{41}/PLA_{205}$(Zn). (2: second run, 10 °C/min cooling from the melt.)

smaller than those of the copolymer. A "Maltese cross" appeared neatly for the larger spherulites of the copolymer. This finding well agreed with the lower crystallizability suggested by X-ray data.

Thermal Analysis. DSC thermograms of PEG2000 and of different copolymers, namely $PLA_{44}/PEO_{41}/PLA_{44}$(Zn), $PLA_{117}/PEO_{41}/PLA_{117}(CaH_2)$, $PLA_{109}/PEO_{41}/PLA_{109}$(Zn), and $PLA_{205}/PEO_{41}/PLA_{205}$(Zn), are presented in Figure 5. PEG2000 exhibited an endothermal melting transition at 50 °C, as usual.[18] The copolymer $PLA_{44}/PEO_{41}/PLA_{44}$(Zn) exhibited only a small melting peak at 100−105 °C which disappeared at the second run, showing that the crystallizability of PLA blocks as long as PEO ones is rather low. In the case of $PLA_{117}/PEO_{41}/PLA_{117}(CaH_2)$, a broad endothermal peak was detected at 50 °C followed by a small melting peak at 94 °C, in agreement with the low stereoregularity of CaH_2-type PLA blocks due to racemization. The peak at 50 °C could be assigned to the glass transition and relaxation phenomena of largely amorphous PLA domains,[19] PEO segments being in the amorphous state in these copolymers with long PLA blocks, as shown by X-ray diffractometry (Figure 4). In contrast, the sharp endothermal peak found at 152 °C for $PLA_{109}/PEO_{41}/PLA_{109}$(Zn) well agreed with melting characteristics of poly(L-lactic acid) of intermediate average molecular weight and low polydispersity. At the second run, this copolymer showed clearly a glass transition at 35 °C, a crystallization peak at 92 °C, and a double melting peak at 136 and 150 °C. Insofar as $PLA_{205}/PEO_{41}/PLA_{205}$(Zn) was concerned, the melting peak appeared at 159 °C during the second run, i.e. 9 deg above the T_m observed for $PLA_{109}/PEO_{41}/PLA_{109}$(Zn), in agreement with the presence of longer stereoregular PLA blocks. Therefore, DSC thermograms of PLA/PEO/PLA triblock copolymers with a rather short PEO segment reflected an increasing crystallizability of the PLA blocks with increasing length and stereoregularity, in agreement with X-ray diffraction data and visual examination.

In a previous paper, we have shown that PEO bearing short PLA isotactic sequences (2−8 units) at both ends showed PEO-type crystallization and that an increase in the length of PLA sequences led to a decrease of the T_m of PEO crystallites.[1] The trend was preserved in the cases of similar chains containing longer PLA blocks. When the total length of the two PLA blocks was close to that of the PEO block, as in the cases of $PLA_{14}/PEO_{41}/PLA_{14}$(Zn) and $PLA_{21}/PEO_{41}/PLA_{21}(CaH_2)$, neither the PEO blocks nor the PLA ones could crystallize spontaneously, whereas with PLA blocks longer than the PEO ones ($PLA_{44}/PEO_{41}/PLA_{44}$(Zn), $PLA_{109}/PEO_{41}/PLA_{109}$(Zn), etc.), it was the PLA blocks which crystallized, T_m increasing asymptotically with the PLA chain length. Therefore, from literature data[10] and the X-ray diffraction and DSC data reported herein, one can conclude that PEO and PLA can both crystallize in separate domains when PEO and PLA blocks are both long enough. On the other hand, both short and long PEO blocks can crystallize in the presence of very short PLA blocks,[1,10] whereas in the presence of long PLA blocks, short PEO chains cannot crystallize.

Swelling Properties. In order to evaluate the hydrophilicity of the copolymers prepared in the presence of Zn metal or CaH_2, large size specimens were soaked in distilled water at 37 °C, using high molecular weight poly(L-lactide) of the Zn type ($\bar{M}_n$ = 86 000 as referred to polystyrene standards) as a reference. Water

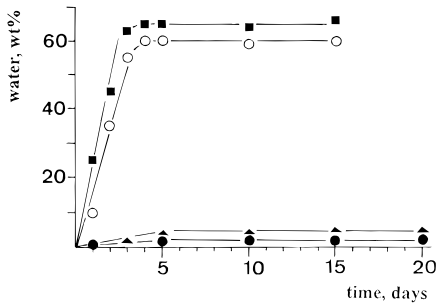

Figure 6. Water absorption for (●) poly(L-lactic acid), (▲) $PLA_{109}/PEO_{41}/PLA_{109}$(Zn), (○) $PLA_{44}/PEO_{41}/PLA_{44}$(Zn), (■) $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$.

absorption data are presented in Figure 6. Two typical behaviors can be distinguished: highly crystalline poly(L-lactide) and $PLA_{109}/PEO_{41}/PLA_{109}$(Zn) absorbed small amounts of water, whereas slightly crystalline copolymers $PLA_{44}/PEO_{41}/PLA_{44}$(Zn) and $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$ which had relatively higher PEO contents appeared very hydrophilic. At equilibrium, a water content of about 60% was attained after 4 days for the second group. It is of interest to note that water absorption equilibrium was reached in only a few minutes in the case of PLA/PEO/PLA copolymers with PLA block lengths comparable with that of $PLA_{117}/PEO_{41}/PLA_{117}(CaH_2)$ but with longer PEO blocks ($\overline{DP}_{PEO} \approx 180$).[11] Therefore, the relative length of the PEO block seems to be an important factor insofar as the rate of water absorption is concerned.

Hydrolytic Degradation. The copolymer $PLA_{43}/PEO_{41}/PLA_{43}(CaH_2)$ was retained for hydrolysis studies. This copolymer was slightly crystalline according to X-ray diffraction analysis. Once placed in the aqueous medium, the plates absorbed large amounts of water with swelling due to the hydrophilic nature of the PEO blocks. After 25 days, a highly swollen hydrogel layer was observed at the surface. After 45 days, the layer had grown several millimeters thick but remained attached to the still compact core. It could not be separated either by shaking the flasks or by sonication. The ^1H NMR spectrum of the swollen material showed that, after physical separation from the bulk, it was predominently composed of PEO chains. In contrast, the bulk showed only a LA/EO ratio decrease of 15% during the first 25 days. This finding was in good agreement with the increase of PEO content observed for the residual material of hydrolytically degraded multiblock PLA/PEO copolymers.[20] At the later stages of degradation, the LA/EO ratio in the bulk did not change as degradation proceeded. This well agrees with the fact that PLA oligomers had to remain entrapped until they are small enough to become soluble in the aqueous medium. Later on, ultimate degradation byproducts, i.e. lactic acid and lactyllactic acid, became detectable by ^1H and ^{13}C NMR. It is of interest to note that it is a decrease in PEO content which was observed in the case of the hydrolytic degradation of PCL/PEO/PCL copolymers.[21]

Presently, the following mechanism is proposed to account for the slow formation of a rather thick layer of hydrogel largely composed of physically cross-linked PEO chains at the surface of a still slightly swollen and partially degraded PLA/PEO/PLA matrix (Figure 7). When introduced in the aqueous aging medium, the copolymer absorbed water and swelled. Hydrolytic cleavage of PLA blocks started immediately, probably at random as in the case of PLA polymers.[15] The LA/EO ratio decreased in the triblock chains, but this decrease was rather limited because of the entrapment of the free PLA segments within the polymeric matrix. However, as the length of the PLA blocks decreased, the hydrophilic PEO segments were pulled off the surface into the aqueous medium, short PLA blocks being still attached. This process attracted progressively the PLA residual short blocks in the aqueous phase where they formed hydrophobic tiny clusters acting as physical cross-links, thus explaining the formation of a rather thick, highly swollen hydrophilic network of loose PEO segments attached to the still compact and partially degraded bulk. This interpretation was strongly supported by the fact that PEO sequences as long as $\overline{DP}_{PEO} = 49$ became insoluble in water when short PLA segments ($\overline{DP}_{PLA} = 8$ and 12) were attached.[1] Such behaviors well agree with the fundamentals of micellization and gelation of symmetrical triblock copolymers,[22] when they are combined with the fundamentals of the hydrolytic degradation of PLA devices.[23]

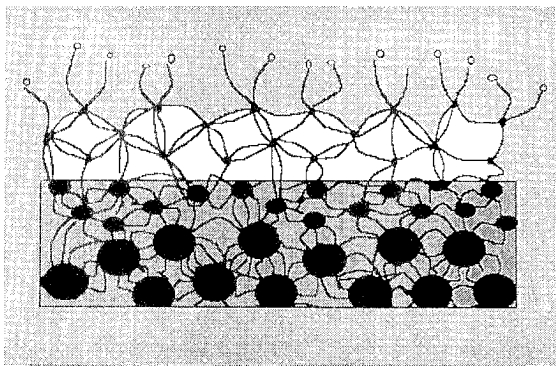

Figure 7. Schematic representation of PLA/PEO/PLA triblock copolymers during hydrolysis: (●) microdomains composed of high molecular weight PLA; (●) microdomains composed of partially degraded PLA; (•) microdomains composed of largely degraded PLA; (∼∼∼∼) PEO blocks.

Conclusions

In this work, we have shown that Zn powder and CaH_2 are efficient catalysts for the preparation of PLA/PEO/PLA triblock copolymers with rather long PLA blocks. The copolymer composition corresponded very well to that of the feed, even after purification by dissolution/precipitation, thus showing an excellent conversion of L-lactide. The presence of unreacted PEO and of PLA homopolymer was ruled out on the basis of NMR spectra. CaH_2 led to some racemization whereas Zn metal appeared as configuration-respecting as in the case of homopolymerization of L-lactide. It was also shown that hydrolysis of the ester bonds occurred at random along the PLA blocks, which led to a decrease in length and generated a swollen hydrogel layer at the surface of the specimen. The properties of these copolymers and their hydrolytic degradation should depend very much on a number of factors such as initial $\overline{DP}$ of PLA and PEO blocks, crystallinity of PLA blocks, LA/EO ratio, processing history, etc. Further studies are under way to evaluate quantitatively the effects of these factors on the hydrolytic degradation of PLA/PEO/PLA triblock copolymers.

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