Influence of the Synthesis Conditions on the Structural and Thermal Properties of Poly(L-lactide)-b-Poly(ethylene glycol)-b-Poly(L-lactide)

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ABSTRACT: The poly(L-lactide)-b-poly(ethylene glycol)-b-poly(L-lactide) block copolymers (PLLA-b-PEG-b-PLLA) were synthesized in a toluene solution by the ring-opening polymerization of 3,6-dimethyl-1,4-dioxan-2,5-dione (LLA) with PEG as a macroinitiator or by transterification from the homopolymers [polylactide and PEG]. Two polymerization conditions were adopted: method A, which used an equimolar catalyst/initiator molar ratio (1–5 wt %), and method B, which used a catalyst content commonly reported in the literature (<0.05 wt %). Method A was more efficient in producing copolymers with a higher yield and monomer conversion, whereas method B resulted in a mixture of the copolymer and homopolymers. The copolymers achieved high molar masses and even presenting similar global compositions, the molar mass distribution and thermal properties depends on the polymerization method. For instance, the suppression of the PEG block crystallization was more noticeable for copolymer A. An experimental design was used to qualify the influence of the catalyst and homopolymer amounts on the transreactions. The catalyst concentration was shown to be the most important factor. Therefore, the effectiveness of method A to produce copolymers was partly due to the transreactions. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40419.

INTRODUCTION

Amphiphilic copolymers are of great academic and technological interest because their properties can be designed by the nature and proportion of their constituents and by their molecular architecture. Such characteristics brings a wide range of application possibilities, such as surfactants,[1,2] biobased materials,[3] stimuli-responsive polymers,[4,5] drug delivery,[6,7] and many other classes of materials, for all kinds of final applications from the noblest to the most ordinary. The ring-opening polymerization (ROP) reaction is a profitable route for the synthesis of copolymers from cyclic monomers. The mechanism of ROP is characterized as chain-growth polymerization.[8,9] There are three ROP variants: cationic, anionic, and coordination–insertion routes. The coordination–insertion route uses metallic alkoxide catalysts. One mechanism described in the literature is the coordination of the cyclic monomer to the catalyst–initiator pair. This mechanism assumes that the catalytic group must undergo uncoordination from the growing chain and then became available to start new polymer chain growth.[10] However, Yoon et al.[11] showed that the catalyst group remained coordinated to the growing polymer chains even after several washings with different solvents.

Recent literature has described the synthesis of many lactide copolymers with a wide range of compositions and architec-tures. The most used catalyst, tin(II)−2-ethylhexanoate [Sn(Oct)$_2$], does not present a precoordinated alkoxide group, which must be provided in a pre-activation step. Therefore, the initiator group can be set as desired. The initiator is a Brönsted acid and, in general, water or alcohols are used.[10–14]

The main contribution of this study is the proposal and execution of two studies that aim to understand the influence of the catalyst on the copolymerization efficiency and on the properties of the poly(L-lactice)-b-poly(ethylene glycol)-b-poly(L-lactide) triblock copolymers. The motivation of this study lied in the experimental observation of the byproducts, such as homopolymers, in our previous studies of copolymerization, using catalyst in very small amounts, as will be discussed and as in the studies carried out by Yoon et al.,[11] Buwalda and coworkers,[15,16] and Kricherldorf and Meier-Hack,[17] whose results support the hypothesis that the metal remains bonded to the growing polymer chains.

Buwalda and coworkers[15,16] synthesized eight-armed PEG–polylactide (PLA) star block copolymers, studying the influence of the block linkage nature on the gelation behavior. It is important to note that these researchers used considerably high amounts of catalyst to achieve the desired architecture. The effectiveness of high amounts of catalyst was correlated early by

Kricherldorf and Meier-Hack,[17] who synthesized PLLA-*b*-PEG-*b*-PLLA block copolymers, adopting equimolar amounts of PEG macroinitiator and Sn(Oct)$_2$ catalyst, and achieving full PEG consumption and no side reactions.

In addition to the ROP, transreactions plays an important role in determining the architecture of the macromolecules, as pointed out by Morbidelli et al.[18] and Ryan et al.[19] Morbidelli et al.[18] reported the occurrence of ester-interchange reactions and showed that the catalyst/initiator molar ratio influences the mechanism of ROP and the product characteristics. Both the monomers/catalyst and initiator/catalyst molar ratios were directly responsible for the ester-interchange reactions; this led to a very well described kinetic modeling based on mechanistic proposals from Penczek et al.[10]

For biomedical applications, the molar mass of the PEG block should not be high, so the development of a multiblock copolymer is necessary.[20] Ryan et al.[19] synthesized high-molar-mass multiblock copolymers with controlled compositions on the basis of the transesterification of low-molar-mass PEG/succinic acid polyester and PLLA with titanium(IV) isopropoxide as a catalyst. They also demonstrated the dependence of the PEG crystallinity on the copolymer composition and architecture.

Our studies were a result of our observation of the low effectiveness of the copolymerization at low catalyst/initiator molar ratios. Moreover, Morbidelli et al.[18] and Ryan et al.[19] showed that transreaction events become more important with increasing the catalyst amount. Our purpose was to investigate the effectiveness of the copolymerization of 3,6-dimethyl-1,4-dioxan-2,5-dione (LLA) with a PEG macroinitiator as a function of the catalyst/initiator and monomer/initiator molar ratio and the effectiveness of the transesterification between PEG and PLA to produce block copolymers.

EXPERIMENTAL

PEG with a molar mass of 8 kg/mol [Fluka; it showed a molar mass of 43 kg/mol and a polydispersity index (PDI) of 1.05 in comparison to polystyrene (PS) standards in dimethylformamide (DMF)] was subjected to lyophilization to remove residual water. Commercial polylactide PLA (Nature Works, Cargill-Dow grade 2002D) free from additives [X-ray fluorescence analysis revealed the presence of only 0.0023 wt % iron; no additive could be extracted by Soxhlet extraction with polar (ethyl alcohol) and nonpolar (*n*-heptane) solvents], with a molar mass of 217 kg/mol and a polidispersity index (PDI) of 1.38, was also subjected to lyophilization before use. LLA (Sigma) was recrystallized twice in ethyl acetate and dried *in vacuo* for 24 h. Before use, LLA was lyophilized to remove residual water. Toluene was dried by stirring with CaCl$_2$; this was followed by filtration and distillation in the presence of metallic sodium to obtain a water-free solvent for the synthesis. Sn(Oct)$_2$ (Sigma) was used as received in a dry toluene solution.

Synthesis of the Copolymers
The copolymers were synthesized in anhydrous toluene solutions. The catalyst Sn(Oct)$_2$ and PEG macroinitiator were added in controlled amounts to a flask kept under toluene reflux (ca. 110°C) with moderate stirring and an N$_2$ atmosphere for 1 h.

After this preactivation of the catalyst, the LLA was added, and the reaction medium was allowed to reflux with stirring under N$_2$ for 44 h. The products were then purified by precipitation of the toluene solution in commercial diethyl ether and dried *in vacuo* at 50°C for 24 h.

Influence of the Catalyst/Initiator Ratio on the Yield of Polymerization
To investigate the influence of the catalyst/initiator molar ratio (n_{cat}/n_{PEG}, where n_{cat} is the number of moles of catalyst and n_{PEG} is the number of moles of PEG) on the yield of polymerization and characteristics of the products, different n_{cat}/n_{PEG} molar ratios were used to polymerize LLA. Two groups of experiments were conducted, according to methods A and B.

In method A, an equimolar ratio of the catalyst and PEG hydroxyl group initiators was used. The molar mass of the PLLA block was defined on the basis of the molar mass of PEG, specifically on the numbers of moles of EG (n_{EG}). Thus, copolymers with different molar masses were obtained starting from five different molar ratios of LLA to EG ($n_{LLA}/n_{EG} = 0.3$, 0.5, 1.0, 1.5, and 2.0, where n_{LLA} is the number of moles of LLA). These materials were named LP-A0.3, LP-A0.5, LP-A1.0, LP-A1.5, and LP-A2.0, respectively.

In method B, the amount of catalyst used was related to the monomer LLA. The average LLA/Sn(Oct)$_2$ molar ratio was $n_{LLA}/n_{cat} = 5000$. Five different molar ratios of LLA to EG were used ($n_{LLA}/n_{EG} = 0.3$, 0.5, 1.0, 1.5, and 2.0). These materials are named LP-B0.3, LP-B0.5, LP-B1.0, LP-B1.5, and LP-B2.0, respectively.

Table I summarizes the data relating to the compositions of the reaction constituents.

The products were characterized by ^{1}H-NMR, gel permeation chromatography (GPC), differential scanning calorimetry (DSC), and thermogravimetric analysis (TGA).

Blend Preparation
We obtained the PEG/PLLA blends by solubilizing the homopolymers at a mass ratio of 1:2 ($n_{LLA}/n_{EG} = 0.62$) in tetrahydrofuran and then precipitated the product in commercial diethyl ether and drying *in vacuo* at 50°C for 24 h. PLLA synthesized by method A (number-average molar mass (M_n) of 130 kg/mol, and a PDI of 1.30) was used to prepare the blends.

Transreaction Study
The PEG homopolymer used was the same used for the catalyst study synthesis, whereas a nonstereoregular commercial homopolymer, PLA, was used instead of PLLA.

The desired quantities of the PEG homopolymer, Sn(Oct)$_2$ catalyst, and anhydrous toluene were loaded into a flask, and the solution was kept under toluene reflux (ca. 110°C) with moderate stirring and an N$_2$ atmosphere for 1 h. PLA homopolymer was then added to the reaction medium, and the reaction was conducted under the same reaction conditions as used for the copolymer syntheses.

A fractional factorial experimental design (2^{3-1}) was adopted to maximize the results with a few reactions. Three factors with

Table I. Reaction Medium Compositions, Copolymer Compositions, Yields, and M_n, M_w, and PDI (M_w/M_n) Values

		Reaction medium					Copolymer			
		n_{LLA}/n_{EG}	n_{LLA}/n_{cat}	n_{cat}/n_{PEG}	n_{LLA}/n_{EG}	PEG (wt %)	Yield (%)	M_n (kg/mol)	M_w (kg/mol)	M_w/M_n
PEG		—	—	—	—	—	—	43	45	1.05
PLLA[a]		150	10,000	—	—	—	88	130	171	1.31
PEG/PLLA[b]		—	—	—	0.62	33.3	—	—	—	—
Method A	LP-A0.3	0.30	24	2.2	0.11	73.5	63	52	60	1.15
	LP-A0.5	0.50	42	2.1	0.33	48.3	68	72	86	1.19
	LP-A1.0	0.99	78	2.3	0.90	25.4	92	102	129	1.26
	LP-A1.5	1.49	135	2.0	1.33	18.7	88	98	144	1.47
	LP-A2.0	1.99	181	2.0	1.90	13.9	90	103	142	1.38
Method B	LP-B0.3	0.30	5200	0.01	0.01	96.2	46	49	53	1.08
	LP-B0.5	0.49	4600	0.02	0.09	78.1	44	50	55	1.10
	LP-B1.0	0.98	4600	0.04	0.44	41.2	50	65	75	1.15
	LP-B1.5	1.47	5200	0.05	0.95	24.3	70	84	97	1.15
	LP-B2.0	1.98	5000	0.07	1.68	15.4	87	110	127	1.15

[a] Homopolymer of LLA synthesized as a reference with ethylene glycol as the initiator.
[b] PEG/PLLA blend made from the PEG and PLLA homopolymers.

two levels were adopted, as shown in the table footnote. Table II presents the experimental levels of this experimental design.

The solvent of the reaction medium was removed by distillation, and the residual materials were dried *in vacuo* and not subjected to any kind of purification to prevent the loss of residual reactants, products, and byproducts.

These materials were characterized by GPC, DSC, and TGA.

Characterization

The ^{1}H-NMR spectra of the polymer solutions (20 mg in 0.6 mL of CDCl$_3$) were obtained on a Bruker AC/P 250-MHz spectrometer (operating at 25°C, 250 MHz, 5.87 Tesla, pulse delay of 1 s, acquisition time of 3.16 s, 128 scans with 32,000 points and an free induction decay resolution of 0.15 Hz).

DSC was performed on a MDSC 2910 from TA Instruments operating at a 20°C/min rate and with the following program adopted: (1) heating from 25 to 200°C, (2) isotherm for 2 min, (3) cooling from 200 to −100°C, (4) isotherm for 2 min, and (5) heating from −100 to 200°C.

The thermal degradation of the copolymers was evaluated by TGA on a Seiko TG/DTA 6200 instrument under an argon atmosphere (with a 50 mL/min flow rate) at a 10°C/min heating rate from 30 to 600°C.

Table II. Reaction Medium Compositions and M_n, M_w, and PDI (M_w/M_n) Values Determined with GPC for the Materials Obtained in the Transreaction Study

	Reaction medium						Final material			
	Design experiment			Composition			Composition	Molar mass		
	Catalyst (wt %)	PLA (g)	PEG (g)	PLA (wt %)	n_{LA}/n_{EG}	n_{cat}/n_{PEG}	PLA (wt %)[b]	M_n (kg/mol)	M_w (kg/mol)	PDI
PEG	—	—	—	—	—		—	43	45	1.05
PLA	—	—	—	—	—		—	217	299	1.38
TR 1[a]	0.05 (−)	0.5 (−)	1 (+)	33	0.16	0.01	35	54	63	1.18
TR 2	5 (+)	0.5 (−)	0.5 (−)	50	0.33	1.97	52	59	66	1.12
TR 3[a]	0.05 (−)	1 (+)	0.5 (−)	66	0.65	0.03	68	172; 46	229; 48	1.34; 1.05
TR 4	5 (+)	1 (+)	1 (+)	50	0.29	1.97	49	55	60	1.09

In the catalyst column, (−) indicates 0.05 wt % catalyst and (+) indicates 5 wt % catalyst (in relation to the whole polymer mass). In the PLA and PEG column, (−) indicates 0.5 g, and (+) indicates 1.0 g.
[a] This material showed a bimodal mass distribution.
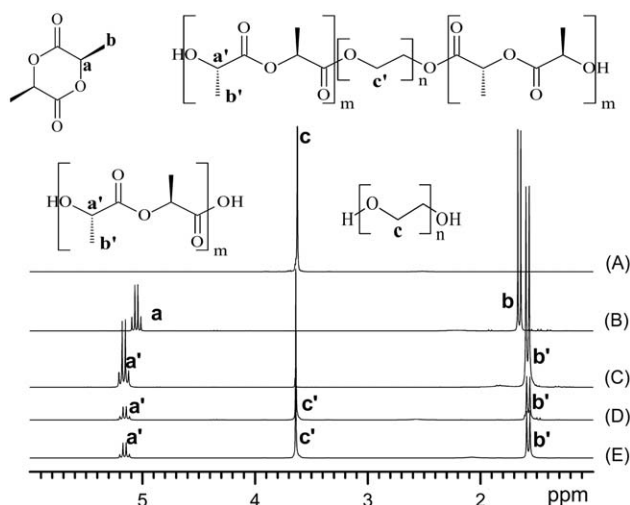[b] Determined from the TGA data.

Figure 1. ¹H-NMR spectra obtained with CDCl₃ for (A) PEG, (B) LLA monomer, (C) PLLA homopolymer, (D) PLLA-b-PEG-b-PLLA copolymer, and (E) PEG/PLLA blend. The monomer conversion could be verified through a comparison of hydrogens **a** and **b** of the monomer and **a′** and **b′** of the polymer.

The number-average molar mass (M_n) weight-average molar mass (M_w), and polidispersity index of the polymers (M_w/M_n) were determined with GPC performed on a Viscotek GPCmax VE 2001 instrument with a Viscotek VE 3580 refractive index detector and a Viscotek UV 2500 detector, Viscotek TGuard 10 × 4.6 mm² guard column, and 3 X Viscotek T6000M 300 × 7.8 mm² (10-μm particles) columns. The column system was kept at 60°C. A 10 mmol/L LiBr solution in DMF was used as an eluent at a flow rate of 1.0 mL/min. The polymer solutions of 8.0 mg/mL were prepared with this eluent solvent (injection volume = 100 μL). The molar masses were relative to PS standards (Viscotek - molar masses from 1050 to 3,800,000 g/mol).

RESULTS AND DISCUSSION

Catalytic Study

Two series of materials were synthesized with methods A and B as described in the Experimental section. These materials were named LP-Xy, where X indicates the method (A or B) and y is the LLA to EG molar ratio used in the synthesis (see Table I).

Figure 1 shows the ¹H-NMR spectra for the precursors, copolymers, and a PLLA/PEG blend. The hydrogens labeled **a** and **b** in the LLA monomer molecule underwent chemical environmental changes after the reaction to give new chemical shifts, which are indicated as **a′** and **b′** in the polymer chain (Figure 1), an evidence of the LLA polymerization. However, these were not enough to determine the block copolymer formation. The global composition of the products was determined by ¹H-NMR.

The main difference between methods A and B was the amount of catalyst used in comparison with the amount of PEG initiator. In method A, an equimolar ratio of catalyst and PEG reactive hydroxyl groups was desired to ensure the coordination of all of the hydroxyls to the catalyst molecules, a necessary step in ROP. For method B, commonly reported in the literature for ROP, the catalyst amount was set relative to the monomer content. This meant that the catalyst/hydroxyl group of the PEG molar ratio was approximately constant and on the order of 10^{-2}. Table I presents the reaction medium compositions, copolymer compositions (determined from the ¹H-NMR spectra), LLA monomer conversion, reaction yield, and molar mass (relative to PS standards, as determined from GPC chromatograms).

Figure 2(a) shows the molar fraction of LLA in the copolymers (x_{LLA}-copolymer) against the molar fraction of LLA used in the synthesis (x_{LLA}-reaction medium), and Figure 2(b) shows the relative conversions of the monomer LLA as a function of n_{LLA}/n_{EG} in the reaction medium. The analysis of the materials obtained from different methods revealed that the copolymers obtained by method A showed a final composition closer to the reaction medium in comparison with the method B copolymers. Moreover, method A resulted in a higher monomer conversion. However, these results did not allow us to conclude whether the products were copolymers or blends because the homopolymerization of LLA was possible when water or other potential initiators were present. The GPC chromatograms, shown in Figure
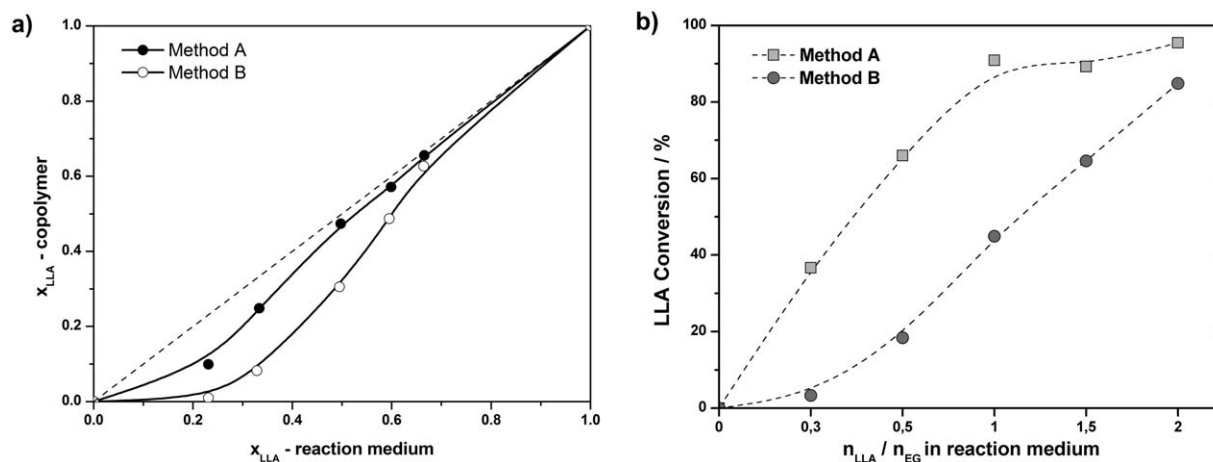

Figure 2. (a) LLA molar fraction in the copolymers versus the LLA molar fraction in the reaction medium and (b) LLA conversion as a function of n_{LLA}/n_{EG} in the reaction medium.
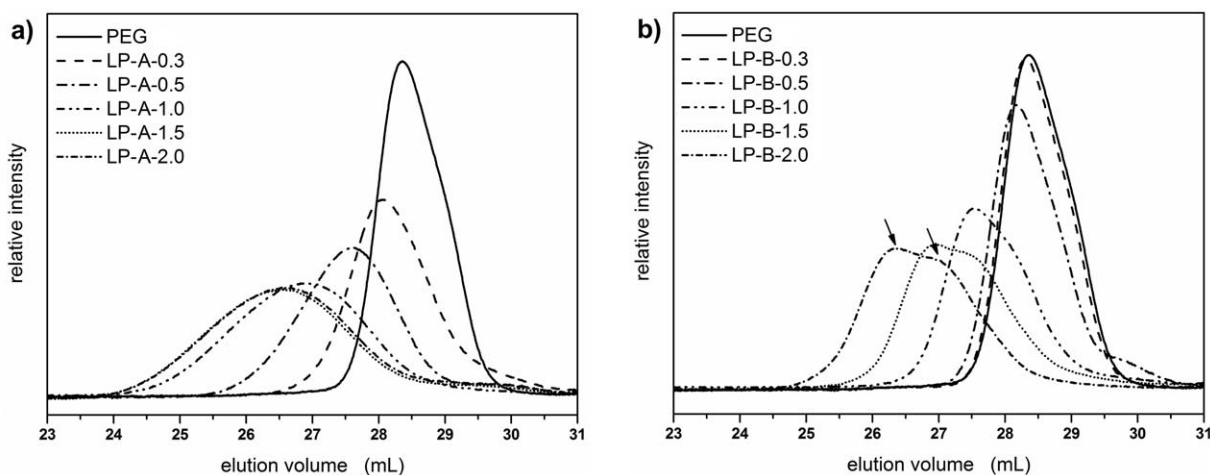
Figure 3. Gel permeation chromatograms (DMF, 60°C, and 1 mL/min flow rate) for products synthesized with methods (a) A and (b) B.

3, allowed us to elucidate this question. The copolymers presented molar masses between 50,000 and 110,000 g/mol. However, the copolymers obtained by method A exhibited a single molar mass distribution, and materials synthesized by method B exhibited a bimodal molar mass distributions; this suggested that these materials were mixtures, possibly of the copolymers, PLLA and PEG.

Other evidence that the products of methods A and B were different was provided by DSC analysis. Both PEG and PLLA are semicrystalline polymers. In block copolymers, the crystallinity of each constituent depends on the composition, architecture of the polymeric chains, and molar masses of the whole copolymer and the blocks. Figure 4 shows the DSC curves normalized with respect to the sample mass and corresponding to the cooling and second heating scans for PEG, PLLA, and a PEG/PLLA blend. PEG presented a crystallization temperature (T_c) at 31°C, a melting temperature (T_m) at 65°C, and a glass-transition temperature (T_g) near −50°C. However, the last one was hardly detected by DSC because of the high crystallinity of PEG. PLLA presented T_g and T_m values of 65 and 173°C, respectively. However, PLLA did not crystallize during the cooling step at 20°C/min, and cold crystallization occurred around 120°C during the second heating scan. The PEG/PLLA blend (mass ratio = 1:2) presented two crystallization peaks and two melting peaks in the cooling and second heating scan, respectively, at temperatures corresponding to the crystallization and melting of both polymers. The main difference between the thermal behavior of the neat PLLA and this polymer in the blend was the crystallization during cooling in the second case. The presence of PEG in the blend seemed to facilitate PLLA crystallization under cooling from the melt.

Figure 5 shows the DSC curves for the copolymers. The glass transition of the PEG block in most of the copolymers was observed around −40°C in the cooling curves [Figure 5(a)]. On the other hand, the glass transition of PLLA occurred in the same temperature range of the crystallization and melting of PEG and could be identified only when the crystallization of

the PEG blocks was completely suppressed. For example, the glass transition of PLLA was observed in the second heating curves in the temperature range from 25 to 35°C for the LP-A2.0, LP-B1.5, and LP-B2.0 copolymers; these temperatures were lower than that observed for the PLLA homopolymer
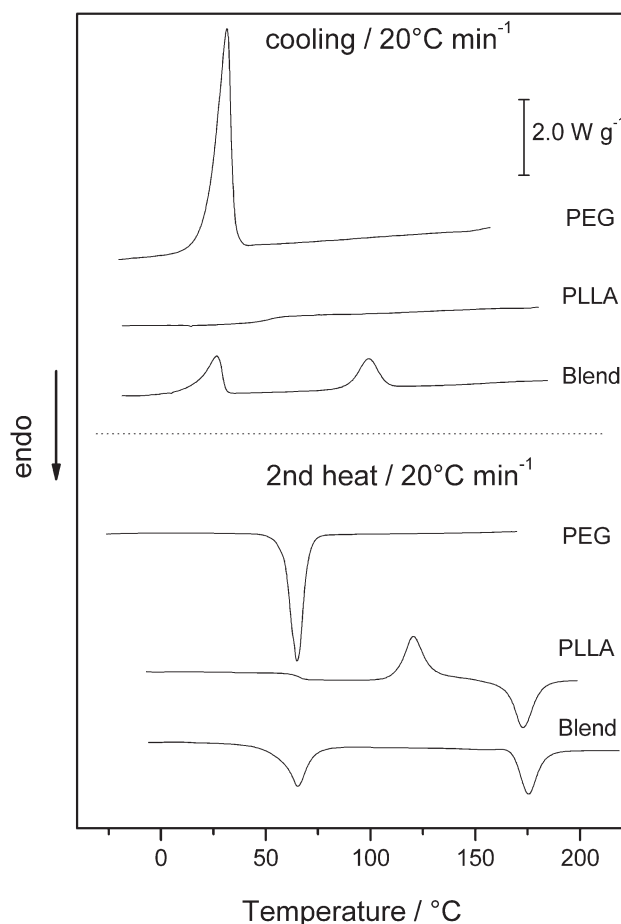

Figure 4. DSC curves for PEG, PLLA, and the PEG/PLLA blend.
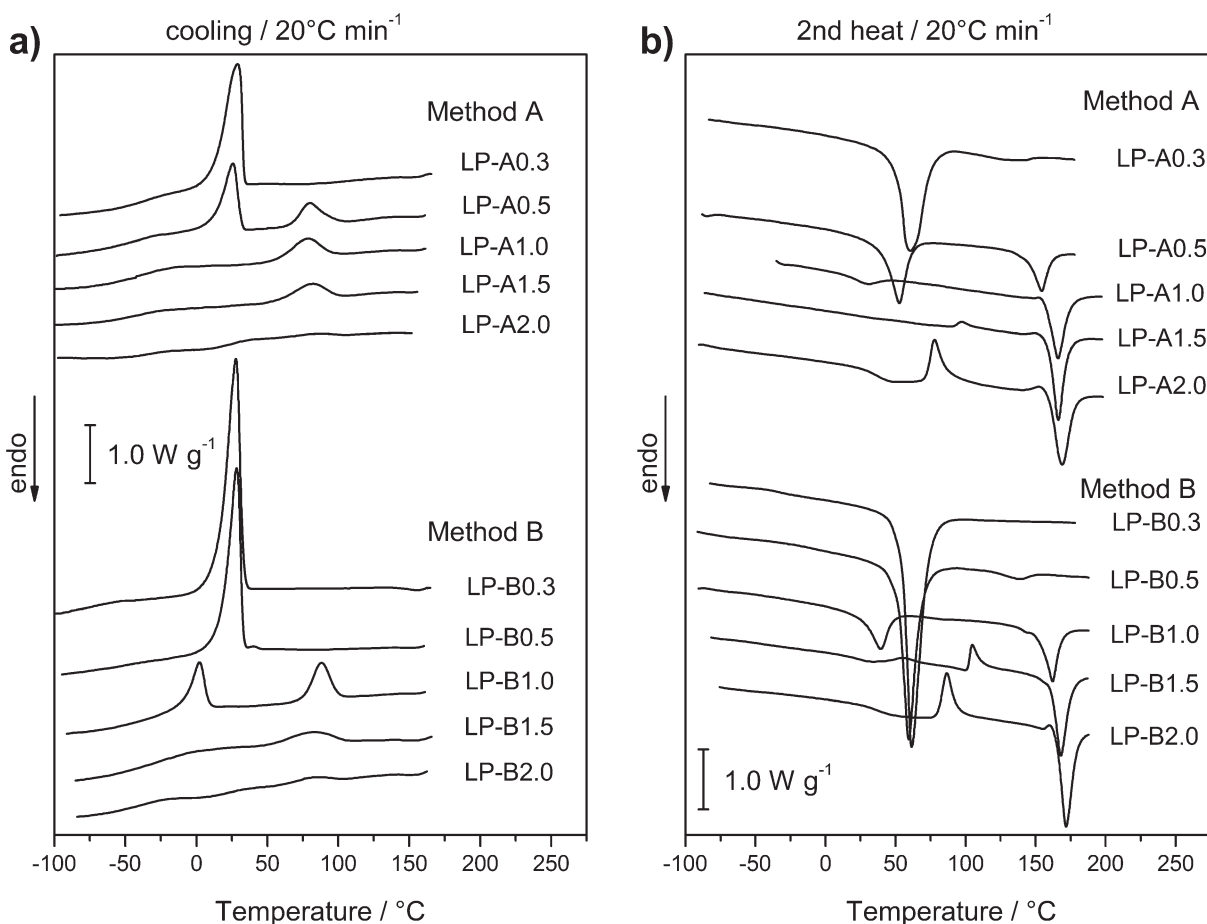
Figure 5. DSC curves for the copolymers synthesized with methods A and B: (a) cooling and (b) second heating.

(65°C). A shift in the glass transition of the PEG richer phase was also observed ($T_g \approx -30$°C); this suggested a partial miscibility of the PEG and PLLA blocks. The miscibility of PEG and PLLA has been discussed in the literature without any definitive conclusions.[21–23]

Figure 6 shows the dependency of the T_m and melting enthalpy (ΔH_m) for the PEG and PLLA components on n_{LLA}/n_{EG} of reaction products. In these figures, the data of the PEG/PLLA blend are also plotted.

The PEG/PLLA blend, whose DSC curves are shown in Figure 4, presented the expected behavior for a heterogeneous blend; that is, the phase transitions of both components were observed in the same temperature range as that of the corresponding neat polymers. The unchanged T_m's for PEG and PLLA in the blend [see Figure 6(a)] indicated that the PEG and PLLA homopolymers had no variation in the crystallization behavior and presented crystallites with the same characteristics as their homopolymers. Figure 6(b) shows a small decrease in the PEG ΔH_m for this blend. This result was possible because of the spatial hindrance imposed by the PLLA crystalline phase, the major component, and probably the matrix of the blend.

A depression in the T_m values of the blocks of the PLLA-*b*-PEG-*b*-PLLA copolymers in comparison with those of the respective

homopolymers was expected; this was due to the linkage between the blocks. In fact, a progressive depression in the PEG T_m and ΔH_m with increasing n_{LLA}/n_{EG} and even the total suppression of the PEG crystallinity was observed for n_{LLA}/n_{EG} values greater than 0.5 [as shown in Figure 5(a,b)]. The crystallization behavior of the PEG central block of the copolymers was strongly influenced by the PLLA blocks, which crystallized at higher temperatures during cooling [Figure 5(a)] from the melt and suppressed PEG crystallization because of spatial hindrance. This effect depended on the PLLA block length, as the T_m of the PEG blocks decreased with increasing molar mass of the PLLA block.[22,24] On the other hand, for the PEG/PLLA blend, which had an n_{LLA}/n_{EG} value of 0.62, no depression in T_m for the PEG phase was observed, whereas the loss of crystallinity was assigned to spatial hindrance.

For the products from method A, the PEG block melt temperature depressions were more significant than those observed for the polymers synthesized by method B. This result indicated that the nature of the final material, even when it presented the same n_{LLA}/n_{EG} ratio, may have been different. These results suggested that the products obtained by method B may have been complex mixtures of the PLLA, PEG, and PLLA-*b*-PEG-*b*-PLLA copolymer, as indicated also by the multimodal molar mass distribution.
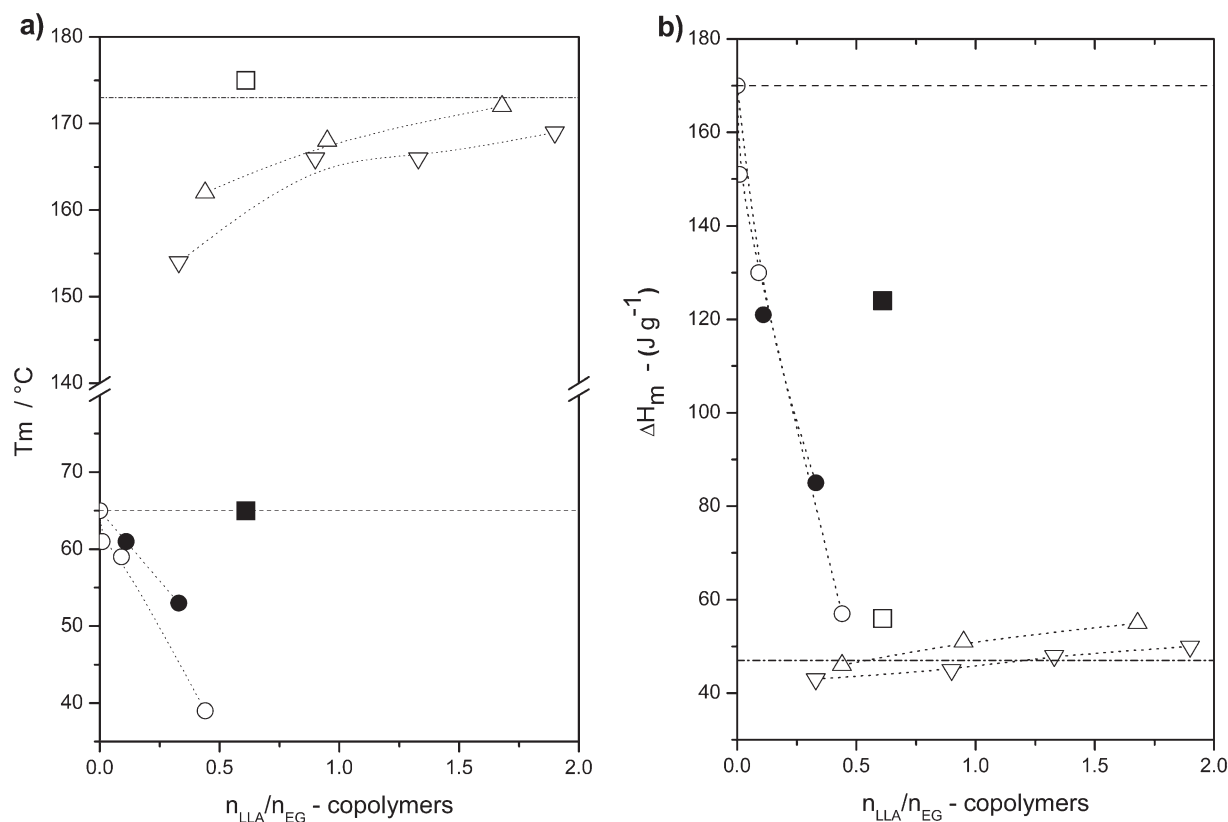
Figure 6. (a) T_m and (b) ΔH_m for (●) PEG and (▽) PLLA in copolymers synthesized with method A; for (○) PEG and (△) PLLA in copolymers synthesized with method B and for (■) PEG and (□) PLLA in the PEG/PLLA blend.

At this point, it was acceptable to indicate method A as more efficient in obtaining the PLLA-*b*-PEG-*b*-PLLA block copolymers. Thus, the next question to be answered was as follows: how did the concentration of catalyst in method A contribute to this efficiency? The trivial hypothesis, that more catalyst results in higher yields, was very fragile and failed when the results presented previously were considered. There were substantial differences in the products obtained by methods A and B themselves. Thus, it was necessary to investigate whether some others reactions were occurring.

The most promising hypothesis was that transreactions between the polymer chains took place during the polymerization and any undesired PLLA homopolymer chains growing in the reaction medium could be consumed. The results of Ryan et al.[19] indicate that this hypothesis would explain why method A was more effective in copolymer synthesis and also caused an increase in PDI, as verified in these materials. To verify this hypothesis, a transreaction study was carried out.

Transreaction Study
The ROP mechanism takes place at the ester group of a cyclic monomer. The mechanism described in the literature for ROP catalyzed by Sn(Oct)$_2$ starts by the coordination of the monomer to the Sn–OR bond, followed by the insertion of the monomer. In method A, there was one catalyst molecule for each hydroxyl group of the PEG macroinitiator. This high amount of reactive groups increased the probability that trans-

reaction between the reactive polymer chains (chains coordinated to catalyst groups) and polyester chains took place.

Figure 7 shows the thermogravimetric curves for the transreaction study materials under an argon atmosphere. PLA and PEG thermal degradation occurred in one step in the temperature ranges of 225–275 and 350–425°C, respectively. The thermogravimetric curves for the copolymers presented two steps of mass loss, one of them at a temperature close to the thermal degradation step of PEG. The other step, due to the PLA block degradation, shifted strongly to lower temperatures, an approximately 90–105°C reduction in relation to the temperature corresponding to the maximum mass loss rate. This indicated that some kind of modification took place in the PLA chain. Thermal degradation of PLA and similar polyesters depends on several factors, such as the structure, molar mass, morphology, and residual catalyst concentration. Different mechanisms of thermal degradation have been postulated, among which are competition between random chain scission via a cis- elimination (to generate an acrylic ester unit) and cyclic rupture via intramolecular transesterification (releasing lactic acid).[25] In this study, the presence of the catalyst in the products must be the major reason for the thermal stability loss, as it is capable of catalyzing the transesterification of the chains. Despite the temperature displacement, the mass loss in each step corresponded to the amount of blocks in the copolymers. Table II shows the amounts of PLA used in the reaction medium and those found in the final materials by thermogravimetry. The values were very close.
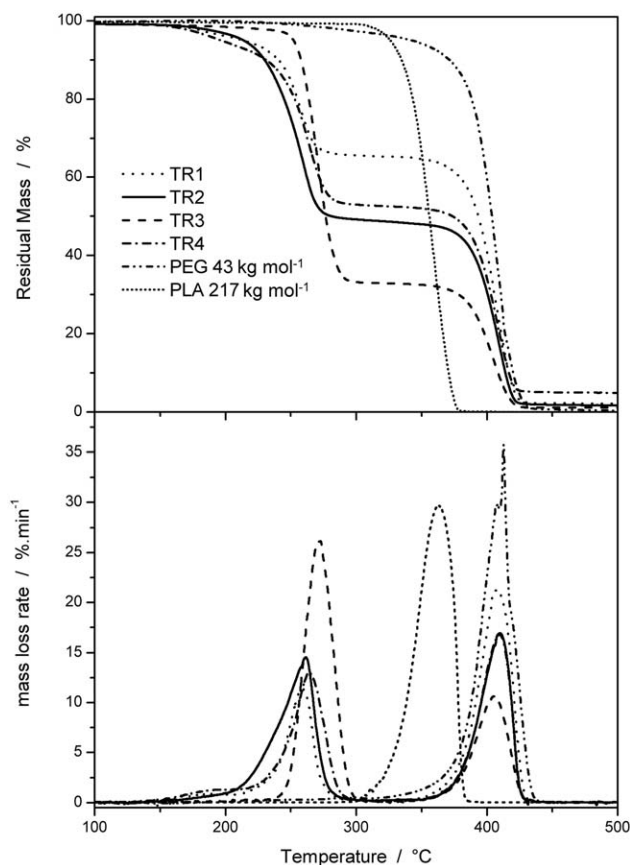
Figure 7. Thermogravimetric curves in an argon atmosphere for the homopolymers and the products of the transreaction study.

The main technique used to investigate the transreactions in this case was GPC. Not coincidentally, the molar masses of the precursors were chosen to be distinct (see the first curve homopolymers in Figure 8) to allow us to monitor any event of chain scission or growth. Figure 8 shows that the chromatograms of the products obtained in the transreaction experiments presented some level of difference with respect to the homopolymers and to each other. Table II shows the molar mass data for these materials.

In analyzing the chromatograms in Figure 8 and the molar mass data in Table II, we verified that all of reaction conditions resulted in some degree of modification of the homopolymers. Products TR2 and TR4 showed a peak located between the peaks for PLA and PEG; therefore, the products had intermediate molar masses in comparison with the homopolymers. This result was very significant because it not only clearly indicated the consumption of the PLA chains, but it also indicated the consumption of PEG chains and, therefore, their insertion into the copolymer. The TR1 chromatogram showed a peak that was slightly shifted in relation to the PEG peak, and a shoulder shifted in relation to the PLA peak. This indicated that the PLA chains were consumed, but a fraction of the PEG chains was not. This was due to the low n_{LLA}/n_{EG} (0.16) and n_{cat}/n_{EG} (0.01). On the other hand, the chromatogram of the product of experiment TR3 showed two peaks that were only slightly shifted from the peaks of the homopolymers; this indicated a

low degree of modification of the homopolymers in comparison with the products of experiments TR2 and TR4.

Experimental design data allows one to quantify the effect of each factor considered in the experimental design. A full factorial experiment design consists of executing all possible combinations between discrete possible levels across the factors of interest and allows one to study the effect of each factor (as well their interactions) on the response variable. In a fractional factorial design, some of the combinations of the full factorial experiment are omitted without a loss of information. In this study, a 2^{3-1} fractional factorial design was used.[26] By considering M_n as the response variable, we were able to calculate the effect of changing each factor between its levels, that is, changing the PLA, PEG, and catalyst proportions, as depicted in Table II. The effects represented the change applied to M_n when each factor was changed from level ($-$) to level ($+$), and for the catalyst, PLA, and PEG, these effects values were found to be -81, 32, and -36, respectively. The catalyst proved to be the most important factor influencing the molar mass of the copolymers, as expected from the results, because method A (which used higher contents of catalyst) was shown to be more efficient in
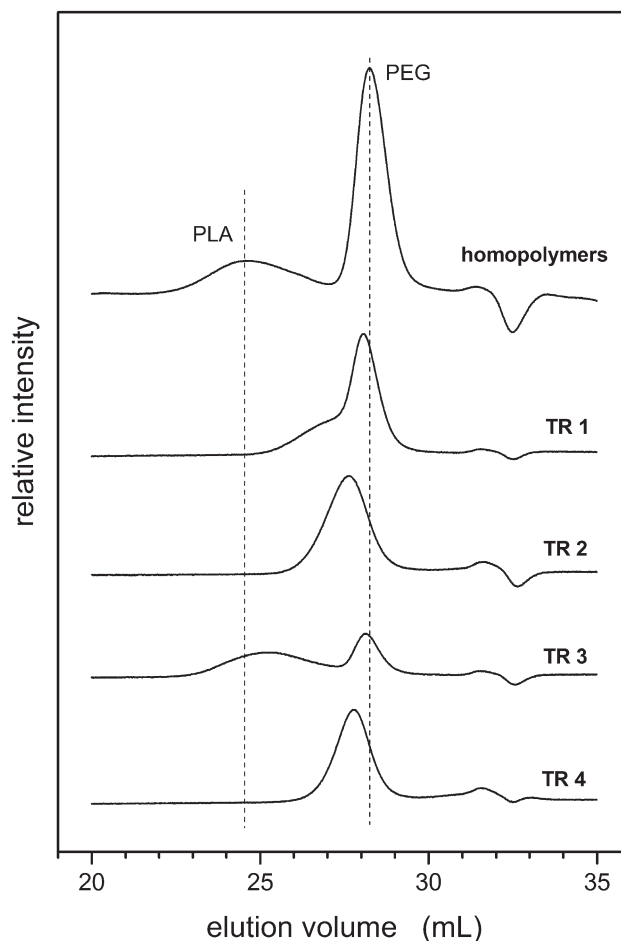

Figure 8. Gel permeation chromatograms (DMF, 60°C, and 1 mL/min flow rate) for the transreaction products. The dashed lines mark the maxima of the peaks in the chromatograms for the PLA and PEG homopolymers.
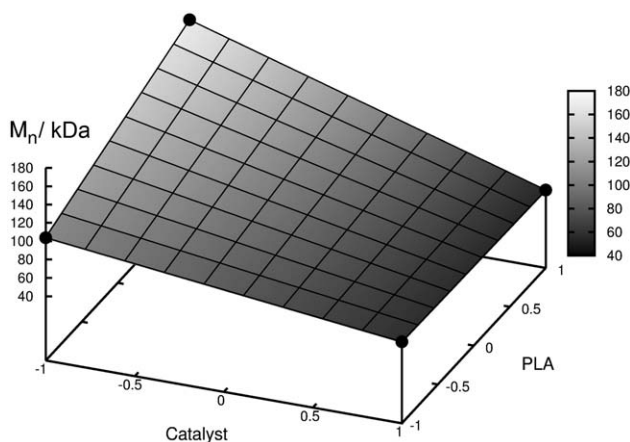
Figure 9. Molar masses of the products as functions of the Sn(Oct)$_2$ (catalyst) and PLA levels (the PEG level was set to zero).

producing the copolymers. The almost antagonistic effects found for PLA (+32) and PEG (−36) content were expected. In fact, these results indicated that both factors may have been replaced by a single factor: the PLA and PEG concentration ratio (e.g., the mass or molar ratio between PEG and PLA).

A useful way to visualize these results is to plot the variation in the molar mass as a function of the reaction medium composition. Figure 9 shows this graphical representation. The M_n molar mass was plotted as a function of the Sn(Oct)$_2$ (catalyst) content and PLA levels, where the PEG level was set to zero. The increasing catalyst concentration was more effective in promoting the transreaction, which was accompanied here by a reduction in the molar mass of the PLA homopolymer.

Considering the transreaction study results, we found it possible to set the characteristics of method A to make it more advantageous than method B. Although both methods were capable of producing copolymers, the method A conditions were such that any PLLA homopolymer synthesized as a byproduct would be consumed by the transreaction events; this led to a high efficiency in obtaining the PLLA-*b*-PEG-*b*-PLLA copolymer. These results were in agreement with those reported by Morbidelli et al.[18] for LLA homopolymerization, which showed a catalyst/initiator molar ratio near that used by us in method A. According to these authors, this condition favored the occurrence of transreactions between the chains, whereas the method B condition favored the occurrence of chain activity transference.[21]

In light of these findings, it was possible to understand this strange result. Although the method B materials presented a bimodal molar mass distribution, their PDI values (i.e., the M_w/M_n value) were lower than those found for the method A materials (Table I). This meant that the method B materials were a combination of copolymers and homopolymers obtained with a very low PDI. In method A, transreactions must have extended the molar mass distribution and thus increased the PDI because of the random transreaction of the polymer chains.

CONCLUSIONS

In summary, PLLA-*b*-PEG-*b*-PLLA copolymer synthesis was achieved in toluene solution. Method A, in which an equimo-

lar amount of catalyst and initiator was used, was the most efficient with respect to yield, monomer conversion, and copolymer production. The differences between methods A and B did not involve mechanism alteration, but the higher catalyst amount used in method A led to transreaction events that resulted in the consumption of any PLLA homopolymer byproduct that may have been generated. Because of these so-called side reactions, the method A and B products had different thermal properties. In fact, the structural difference between them (the copolymers in method A and a complex blend of copolymers and homopolymers in method B) led to a significant modification in the crystallization and thermal degradation.

The occurrence of these transreactions was already reported for PLLA homopolymer synthesis;[18,21] therefore, the accomplishment of this study is an expansion of the understanding of ROP applied to the synthesis of block copolymers. Another important new achievement is the production of a block copolymer from two homopolymers, which opens a wide range of possibilities in the synthesis of new block copolymers starting with preformed polymers.

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