Synthesis of ε-caprolactone-*b*-L-lactide block copolymers by mean sequential polymerization, using diphenylzinc as initiator

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Abstract Block copolymers of ε-caprolactone (CL) and L-lactide (L-LA) were synthesized by sequential polymerization using diphenylzinc as initiator. The composition of the copolymers was adjusted changing the comonomers in ratio. Copolymers were characterized by ^{1}H-NMR, ^{13}C-NMR, DSC, and GPC. Results indicate that poly(ε-caprolactone)-*b*-poly(L-lactide) (PCL-*b*-PLA) block copolymers had a narrow molecular weight distribution and well-controlled sequences without random placement.

Keywords Block copolymer · Diphenylzinc · L-Lactide · ε-Caprolactone

Introduction

Pollution caused by waste derived from synthetic polymers is one of the most serious ecological problems, which is mainly attributable to these materials are inert toward microorganisms, reason why they do not spontaneously degrade in the environment. Ecological awareness has led to the development of environmentally friendly biodegradable polymers which can be substituted for conventional polymeric materials. Of the variety of biodegradable polymers known, aliphatic polyesters nowadays constitute the most attractive class of synthetic polymers, both in the terms of their degradability in contact with living tissues or under outdoor conditions [1–4]. Among these polymers, the poly(ε-caprolactone) (PCL) and poly(L-lactide) (PLA) are among the most important biodegradable and biocompatible polymers, which are widely used in pharmaceutical and medical applications [3–8]. PCL degrades very slow and can be permeable to many kinds of drugs

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[4, 9–14], while PLA degrades too fast and hardly permeable to most drugs [8–15]. The combination of the permeability of PCL with the faster biodegradation of the PLA widens the range of application of these polyesters, a reason why the synthesis of the copolymers of CL and L-LA has received increasing attention [9–29]. The changes in both the composition and the microstructure of the copolymers obtained allow obtaining materials with different mechanical and physical properties, which facilitate the adjustment of the times of degradation and drug release [10].

These copolymers have been synthesized by ring-opening copolymerization of CL and L-LA using as initiators metal halides and their complexes [10, 16], by metal alkoxides [9–11] as well as by organometallic compounds with the addition of water or alcohols [12–29]. These various initiators bring about lactones polymerization via a "coordination-insertion" mechanism, commonly referred to as "pseudo-anionic" polymerization. In the case of the block copolyesters, two synthesis strategies have been used wherein the order of addition depends on the initiator system used. In the first of which a hydroxyl-terminated polymer is previously prepared using an organometallic compound as initiator and subsequently this prepolymer is copolymerized with another lactone in the presence of the same initiator [12–14, 16, 18, 19, 25, 28–32], and the other is based on the living nature of the initiator system consists to perform a sequential addition of a desired monomer on the living growing chain end of a first monomer [11, 15, 33].

Recently, in our laboratory we have been using diphenylzinc as initiator in the polymerization of lactones and it has been proposed as a living polymerization mechanism [20, 34, 35]. Based on the "living" nature of this polymerization, this paper, describes the synthesis of block copolymers of CL and L-LA by means of sequential polymerization with CL polymerizing first.

Experimental

Materials

L-Lactide (L-LA) (Aldrich Chemical Co.) was used as received. ε-caprolactone (CL) (Aldrich Chemical Co.) was dried over calcium hydride for 24 h at room temperature, then distilled at reduced pressure (4 mmHg) and the 80–82 °C fraction was collected. Diphenylzinc (Aldrich Chemical Co.) was purified by bulb-to-bulb fractional distillation at 10^{-5} mmHg, and stored in calibrated ampoules, provided with a break seal. The diphenylzinc was dissolved in dry benzene, and the solution concentration was measured by complexometric titration of Zn with ethylene diaminetetraacetic acid (EDTA).

Tetrahydrofuran (THF) was dried over sodium for 24 h at room temperature and then a small amount of benzophenone was added. The mixture was refluxed until the appearance of blue color and then it was distilled into a flask containing sodium. Benzophenone was used as indicator for the purity of the THF. Benzene was purified by conventional methods, and finally distilled from sodium wire and stored over calcium hydride, in the absence of air. Chloroform (Burdick & Jackson) was used as received.

Copolymerization

Copolymerization were conducted in Pyrex reactor provided with two necks equipped with magnetic stir bars, which were previously flamed and purged with argon. These were loaded using the technique of high vacuum line. In a typical experiment, CL (1.5 mL, 1.50 g, 13.54 mmol) and diphenylzinc solution in benzene (463.90 μL, 0.068 mmol) were transferred by syringe through a rubber septum, under a positive pressure of argon, and subsequently THF (5 mL) was cryodistilled into the reactor. The reaction mixture was degassed and then vessel was sealed off from the vacuum line and left at 90 °C for 72 h. After, the reactor was connected back into the vacuum line, and a sample of the living polymer was picked out from reactor and precipitated into methanol for characterization by size exclusion chromatography (SEC); then L-LA (1.30 g, 9.03 mmol) dissolved in THF (5 mL) was transferred into the reactor by syringe through a rubber septum, under a positive pressure of argon. The reaction mixture was degassed and then vessel was sealed off from the vacuum line and left at 110 °C for 72 h. The polymerizations were terminated by addition of chloroform containing a small amount of acetic acid. This was required to precipitate the initiator. Subsequently, initiator residues were removed by centrifugation, and the copolymers were isolated by precipitation with methanol and finally dried in vacuum at 25 °C, to constant weight. By a similar method, a series of block copolymers with different compositions were prepared keeping constant the amount of CL but varying the amount of L-LA in feed.

Characterization

Molecular weight distributions of copolymers were determined by size exclusion chromatography (SEC) with a Waters chromatograph, model 150 CV, operated at 40 °C and equipped with four columns connected in series and packed with Ultrastyragel 10^3, 10^4, 10^5 and 10^6 Å. Tetrahydrofuran (THF) was used as solvent and the instrument was calibrated to a first approximation with polystyrene of known molecular weight.

Infrared measurements were carried out with a Perkin-Elmer 2000 Fourier transform infrared (FTIR) spectroscope. Thin films of the samples were cast from the $CHCl_3$ solution onto NaCl pellets. The films were dried at room temperature until $CHCl_3$ was removed completely. The ^1H-NMR spectra of copolymers were recorded at 400 MHz with a Bruker AVANCE spectrometer and a 5-mm sample tube. $CDCl_3$ containing tetramethylsilane (TMS) as internal reference was used as solvent and the spectra were obtained at 25 °C with 32 scans, 1.99-s acquisition time, and 10 μs pulse width.

The ^{13}C-NMR spectra of the copolymers were run in $CDCl_3$ and were recorded at 100 MHz with 1,300 scans, 1.48-s acquisition time, a 12.20 μs pulse width, and delay of 3 s between pulses.

The reaction conversion was determined by weighing the purified copolymers and by NMR spectroscopy.

Thermogravimetric curves were obtained in a Perkin-Elmer TGA 7, from a heating scan of a sample of about 10 mg from 20 to 600 °C, at 10 °C/min under a nitrogen atmosphere.

Differential scanning calorimetry (DSC) measurements were carried out with a Perkin-Elmer DSC-7. The sample size was 10–15 mg and the heating rate was 10 °C/min.

Results

Previous investigations have shown that diphenylzinc is effective initiator for the polymerization of lactones [20, 34, 35]. It was proposed that the reaction occurs via a living polymerization mechanism in which the initiator is involved in the active chain end. Taking advantage of this, in this work, the preparation of block copolymers of CL and L-LA was investigated. The structure of the monomer first polymerized in the sequential polyaddition is of critical importance [11–16, 18, 19, 25, 27–33]. Thus, two preliminary experiments were carried out in which it was attempted to prepare these copolymers using two feed sequences. One in which the L-LA was polymerized in the presence of Ph$_2$Zn to form PLA active chains which we attempt to make them react with CL. However, analysis of the obtained polymers through spectroscopic techniques showed that only PLA homopolymer was formed. This result showed that active species deriving from L-LA failed to initiate the polymerization of CL, due to the less nucleophilicity and self-coordination for the active lactide sites [9, 20].

Considering this, the opposite feed sequence was used. CL was first polymerized and then L-LA solution was added into the living system, and in this case the block copolymers were obtained. The method of synthesis is show in Scheme 1.

Characterization of the copolyester

SEC chromatograms obtained in the two stages of the synthetic procedure are presented in Fig. 1. It is shown that in block copolymer, the peak is shifted toward a high molecular weight region compared with that of its original PCL prepolymer with little change in molecular weight distribution, thus reflecting an increase of molecular mass certainly arising from further incorporation of L-LA into the copolymer. A peak in the low molecular weight region is observed and it can be attributed to some unreacted PCL prepolymer.

To gain insight into the chemical structure of the copolymerization product, it was subjected to spectroscopic analysis. The FTIR technique is one of the several powerful tools to obtain information on copolymerization, such as the creation of new chemical bonds, the existence of specific interaction and so forth [30]. Figure 2 displays the carbonyl-stretching region of the FTIR spectra for PCL, PLA and the product obtained. The carbonyl-stretching vibration of PCL consists of peak centered at 1,725 cm^{-1}, whereas PLA has a carbonyl-stretching absorption centered at 1,758 cm^{-1}. The characteristic peaks of carbonyl-stretching vibration of both
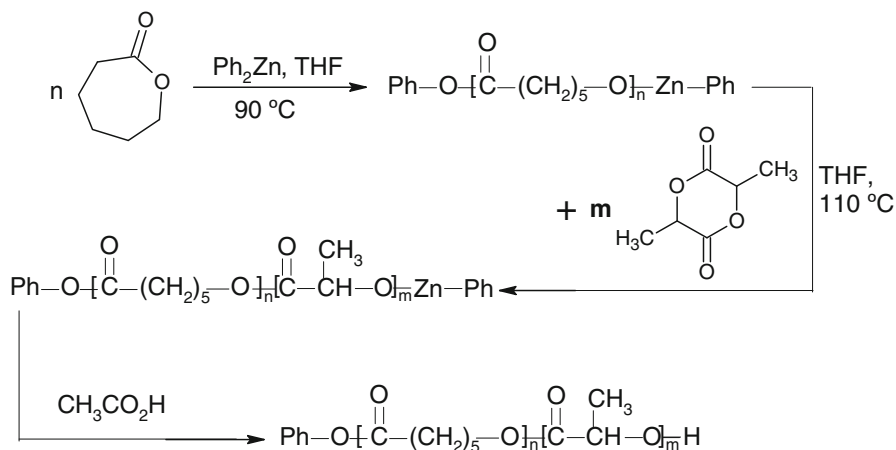
Scheme 1 Synthetic pathway to PCL–PLA blocks copolymers
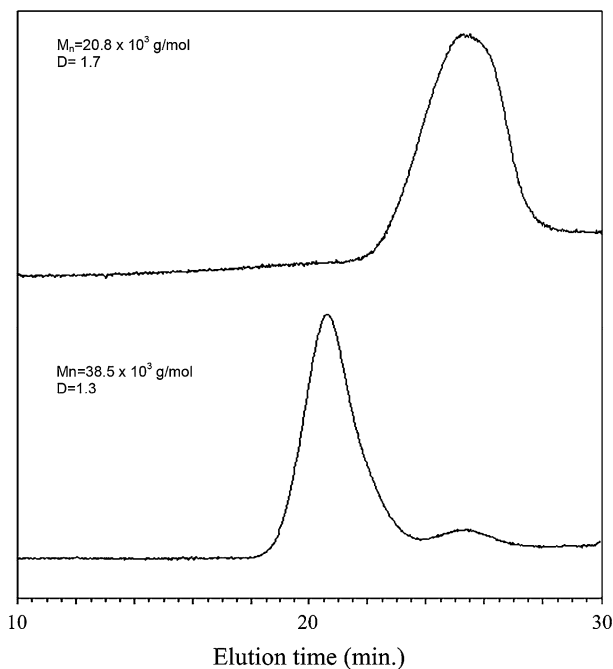

Fig. 1 SEC curves of PCL prepolymer and PCL-*b*-PLA copolymers

PCL and PLA are shown in the spectrum of the product obtained. This suggests that block copolymer was obtained [12–14].

To verify this, the analysis of the copolymer microstructure was performed by means of NMR spectroscopy. It is well known that the ^{13}C-NMR spectroscopy is a

Fig. 2 FTIR spectra (carbonyl region) of *a* PLA, *b* PCL and *c* product obtained
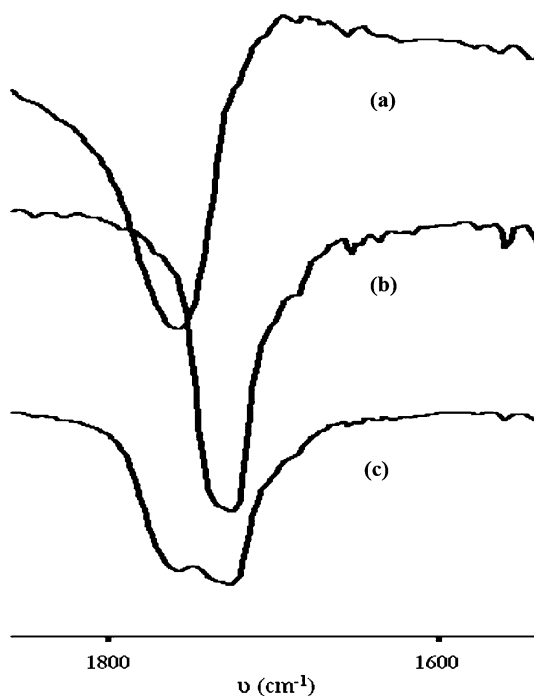
technique very sensitive to the chemical environment of nuclei and is therefore a powerful tool for analyzing the sequential structure of the comonomer units in the copolymers [9, 36]. In the case of copolyesters, it has been established that the most appropriate signal to analyze the effect of the sequences is the carbonyl group (C=O), due to its greater sensitivity to such effect in relation to the signals corresponding to the carbon methyl (CH_3), methylene (CH_2) and methyne (CH) [9, 10, 12, 15, 17, 18, 20–27, 30, 31, 36–41]. Considering the above, Fig. 3, shows the spectra of ^{13}C-NMR (carbonyl region), and it can be seen that the products of reaction (c spectrum) obtained show the chemical shift of the carbonyl groups in the same region of the homopolymers, that is to say, the presence of two signals corresponding to each carbonyl group of lactyl units (–O–CH–(CH_3)–**C**=O, $\delta = 170$ ppm) and caproyl units (–O–(CH_2)$_5$–**C**=O, $\delta = 174$ ppm), respectively. This indicates, without doubt, that the polymeric products obtained do not have random copolymer structures but rather that is a block copolymer (PCL-*b*-PLA) [12, 15, 25, 37].

Effect of the CL/L-LA feed ratios on the copolymerization

Various PCL-*b*-PLA copolymers with different composition were synthesized via sequential copolymerization in tetrahydrofuran (THF), by adjusting the mole ratio of reaction mixture. To remove possible unreacted PCL homopolymer and other possible collateral products from transesterification reaction [10, 18, 20, 31], all
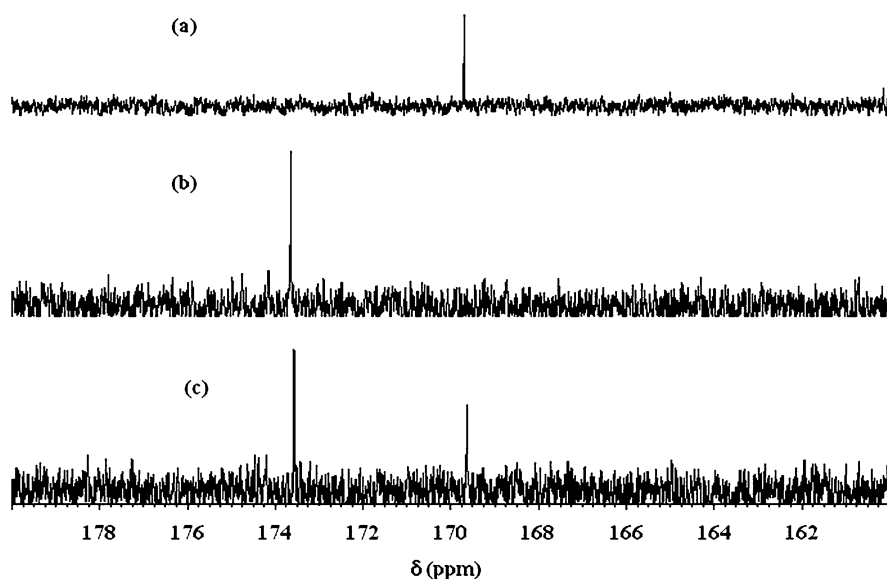
Fig. 3 Carbonyl signal in the ^{13}C NMR spectra of: *a* PLA, *b* PCL and *c* PCl-*b*-PLA (62/38)

reaction products were subjected to fractionated precipitation [15]. In this regard, the samples were dissolved in CHCl$_3$ and methanol was added slowly to the solution. When the solution becomes cloudy, it is centrifuged and the two phases were separated. Thereafter, the copolymers were characterized. The SEC curves of the purified polymers exhibited a monomodal molecular weight distribution, which evidences that block copolymerization reaction was effective. This was verified by spectroscopic analysis of the polymers and it could be observed that FTIR and ^{13}C-NMR spectra were similar to those shown in the Figs. 2 and 3. The molecular characteristic of the obtained copolymers is shown in Table 1. In the copolymer JP1, the molar composition of CL was lower than that of the feed of the comonomer, which indicates the probability of partial formation of PCL-rich copolymer and PCL homopolymer, which may be removed in the purification step. In the copolymers JP2–JP5, the mole composition of copolymers was consistent with that of the reaction mixture; however, the yields of copolymers were lower than that of the feeds of comonomers. This could be related with the fact that during the purification process by fractional precipitation, the product extracted was essentially PCL homopolymer unreacted, which makes copolymer yields lower than expected based on the amount of monomer in the feed. This latter fact could lead to a slight enrichment of lactyl units in some of the obtained copolymers.

Besides these relatively low yields could be indicating that L-LA is not fully polymerized by the PCL macroinitiator formed during the reaction of CL with Ph$_2$Zn and thus end-capped by a secondary zinc alkoxide (Scheme 1). In the PLA growing chain, this secondary zinc alkoxide is in the position β with respect to a carbonyl function being able to produce an intramolecular coordination of the Zn-active species onto carbonyl function with formation of a five-membered ring:

Table 1 Molecular characteristics of the obtained copolymers at various feed monomer ratios

Exp. no.	$f_{\varepsilon\text{–CL}}/f_{\text{L-LA}}$ (mol%)[a]	$F_{\varepsilon\text{–CL}}/F_{\text{L-LA}}$ (mol%)[b]	Yield (%)[c]	$M_n \times 10^{-3}$ (g/mol)[d]	D[d]
JP1	80/20	66.5/33.5	81.0	25.3	1.9
JP2	60/40	62.0/38.0	84.5	38.5	1.3
JP3	50/50	56.5/43.5	77.0	33.5	1.6
JP4	40/60	35.0/65.0	74.0	28.3	1.7
JP5	20/80	13.5/86.5	62.7	22.2	1.3

CL/I = 200; (CL) = 2.71 mol/l; (Ph$_2$Zn) = 0.013 mol/l; Mn (PCL macroinitiator) = 20.8 × 10^3 g/mol

[a] Contents of L-lactide and ε-caprolactone in feed (mole% ratio)

[b] Contents of L-lactide and ε-caprolactone in copolymer, determined by ^{1}H NMR spectra (mole%)

[c] Based on initial comonomers

[d] From SEC, measured in THF at 40 °C
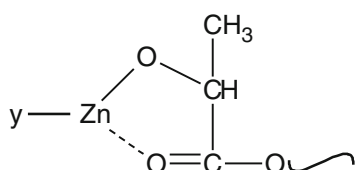
Thus, the coordination-insertion polymerization of L-LA is then unusually slow, which reflect a loss of reactivity of the zinc alkoxide species by internal coordination [9, 20, 28].

The Mn of copolymers shows a tendency to increase with the contents of ε-CL in the feed composition ($f_{\varepsilon\text{-CL}}$). This could be associated with the fact that the molecular weight of the PLA homopolymer is lower than that of PCL homopolymer, in accordance with the lower reactivity of LA in this type of polymerization [20].

Thermal properties of the obtained copolymers

Thermogravimetric analysis (TGA)

TGA was used to study the decomposition pattern and thermal stability of the polymers obtained. Figure 4 shows the thermal degradation profile of JP2 ($F_{\text{CL}}/F_{\text{L-LA}} = 62/38$), that is typical of all copolymers, along with PCL and PLA homopolymers and a reference mixture of PCL and PLA homopolymers. In Table 2 the temperatures at each inflection point (T_i) and the total weight loss percentages (ΔW) calculated at the end of the each volatilization step are reported. It can be noted that both homopolymers have a degradation process in a single step being the PLA less stable than the PCL. PCL-b-PLA copolymers exhibited two-step degradation. Their temperature values and, above all, the comparison between the percentage of volatilized material after each step and the composition of the copolymer suggest that the first step can be ascribed to the degradation of PLA portion and the second one to the PCL portion. For instances, the PCL content in the copolymers JPC2, JPC4, JPC5 and the blend of both homopolymers are 72.1, 46.0,
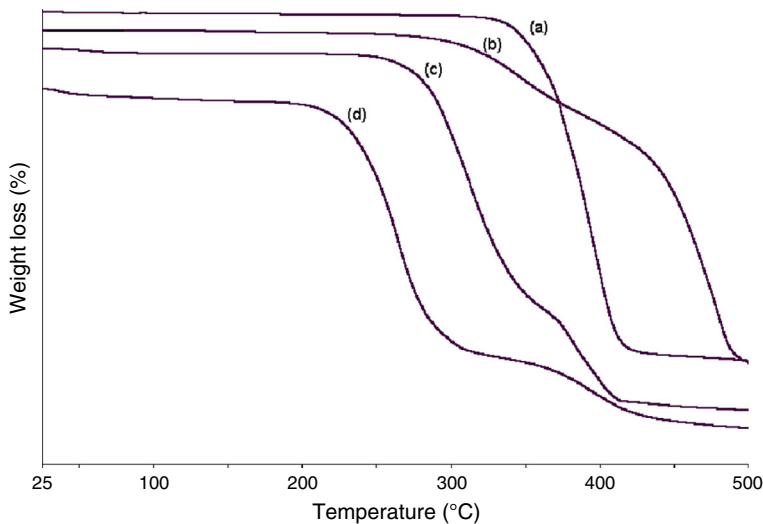
Fig. 4 TGA traces of *a* PCL, *b* block copolymers 62/38; *c* blend 17/83; *d* PLA

Table 2 TGA data obtained for PCL, PLA and copolymers

Exp. no.	$F_{CL}/F_{L\text{-}LA}$	Composition CL/L-LA	First step		Second step	
	(mol%)	(% p/p)	T_i^a (°C)	ΔW^b (%)	T_i^a (°C)	Δw^b (%)
PCL	100/0	100/0	328.6	95.6	–	–
JP1	66.5/33.5	75,9/24.1	274.7	21.3	372.7	77.8
JP2	62.0/38.0	72.1/27.9	279.2	22.5	387.5	71.3
JP3	56.5/43.5	64.10/35.90	268.8	43.8	372.9	56.3
JP4	35.0/65.0	46.0/54.0	266.7	56.90	375.0	40.0
JP5	13.5/86.5	19.8/80.2	254.2	78.70	370.3	20.1
PLA	0/100	0/100	230.4	98.13	–	–
Blend	17.0/83.0	24.5/75.5	235.4	70.0	362.5	27.5

[a] Temperature at the inflection point

[b] Total weight loss percentage at the end of step

19.8 and 24.5 %, respectively. These values are very close to the weight loss relative to the second volatilization step for the same copolymers: 71.3, 40.0, 20.1 and 27.5 %, respectively. Furthermore, mass losses occur in the temperature range similar to the respective homopolymers.

Differential scanning calorimetry (DSC) analysis of the block copolymers

To check the dependence of the thermal behavior of the copolymers on their composition, DSC measurements were carried out. All samples were subjected to a first heating from −40 to 200 °C to remove its thermal history and then were cooled

Table 3 DSC data for PCL-*b*-PLA, PCL, PLA and blend of both homopolymers

Exp. no.	$F_{CL}/F_{L\text{-}LA}$ (mol%)	T_c (°C)[a]		T_m (°C)[b]		ΔH_m (J/g)[c]	
		I	II	I	II	I	II
PCL	100/0	25.80	–	58.53	–	56.55	–
JP1	66.5/33.5	14.63	–	45.70	146.20	26.45	8.302
JP2	62.0/38.0	11.80	–	43.53	145.53	34.20	8.023
JP3	56.5/43.5	23.30	91.80	51.70	158.37	16.65	8.816
JP4	35.0/65.0	9.633	–	46.37	154.20	18.10	16.65
JP5	13.5/86.5	18.63	95.80	49.37	168.53	5.99	44.12
PLA	0/100	–	105.13	–	175.53	–	63.87
Blend	17.0/83.0	21.96	104.30	55.70	174.20	21.96	33.63

I PCl block, *II* PLA block

[a] Values of crystallization temperatures

[b] Values of melting temperatures

[c] Values of melting enthalpies

to −40 °C and finally subjected to a second heating to 200 °C at a rate of heating and/or cooling of 10 °C/min. Thermograms (crystallization and second heating) of copolymers with increasing content of L-LA units together with a reference mixture of PCL and PLA homopolymers are shown in Fig. 5. Table 3 shows the results of transitions and enthalpies of fusion obtained from DSC.

Trace a in Fig. 4 illustrates the thermal behavior of a PCL–PLA physical blend, and it can be seen that the thermograms exhibits two exoterms and two endoterms, at temperatures of crystallization and of melting similar to those obtained for both homopolymers, a clear sign of immiscibility [42]. The observed lack of mutual influence between PCL and PLA suggests that the polymeric component phase separates into domains of sufficient size to preserve the individual properties of both homopolymers [43]. A similar macrophase separation cannot take place in the copolymer sample, since the two homopolymeric components are covalently bonded. The peak crystallization temperatures (Fig. 5A) and the melting temperatures (Fig. 5B) are affected by composition as can be observed in Table 3. In general, it can be noted that the melting point (and the peak crystallization temperature) of the PCL phase in the block copolymers is depressed as the content of PLA increases. This decrease can be explained considering that PLA block crystallize first when the samples are cooled from the melt, which could create worse conditions for crystallization of the PCL [12, 42, 43]. Finally, Table 3 also shows that both T_c and T_m for the PLA phase in the block copolymers decrease as the content of PCL increase. This could indicate that the crystallization PLA block is kinetically hindered [32, 45], which means that when the copolymer is cooled from the melt, the chain mobility in the PLA block is restricted since this is bound to PCL block that is in the molten state (amorphous state). This could lead to a delay in crystallization PLA block. The decreases in the value of Tm of PLA block reach a value of 30 °C for sample JPC2; which could be associated at the partial miscibility, so PCL may be acting as diluent depressing both T_m and T_c of the PLA rich phase [43, 44].
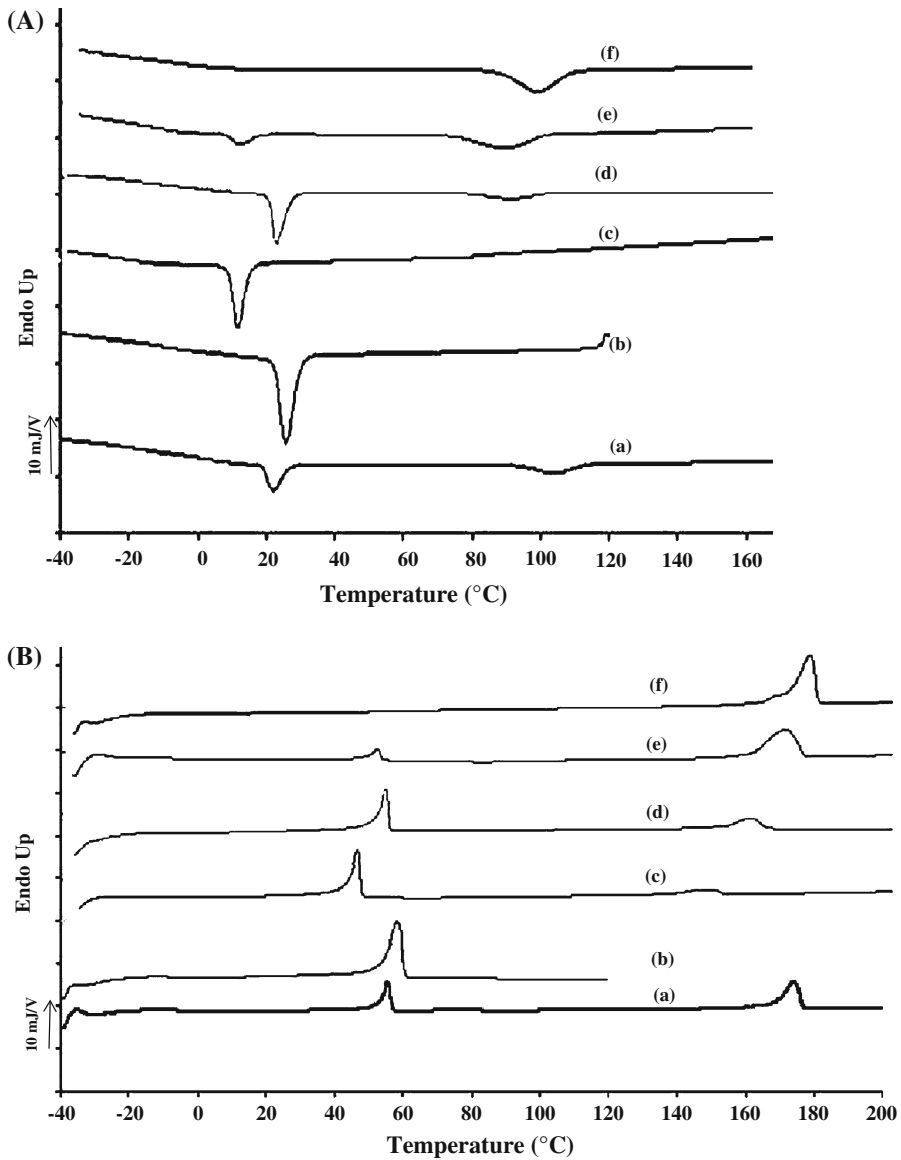
(A)

(B)

Fig. 5 Typical DSC curves of polyester: **A** DSC cooling scans; **B** DSC heating scans: *a* blend 17/83; *b* PCL; *c* block copolymer 62/38; *d* block copolymer 56.5/43.5; *e* block copolymer 13.5/86.5, *f* PLA

Conclusions

PCL-*b*-PLA copolymers have accordingly been synthesized successfully by the sequential polymerization of the CL/L-LA comonomer pair initiated by Ph$_2$Zn, thus they were obtained copolymers with different amounts of caproyl and lactyl units in the polymeric chain by adjusting the feed ratio of comonomer. The mutual reactivity

of the two comonomers determines the order of their addition: CL must be first polymerized followed by L-LA. Random sequences were not observed by spectral analysis of the copolymers, indicating that these have a sequential distribution of the comonomeric units in the manner of diblocks. TGA data indicate that the copolymers show thermal stability between both homopolymers, and also that thermal degradation involves the occurrence of two distinct processes related to the degradation of PLA and of the PCL blocks, respectively. Thermal transition of the both PCL and PLA is affected by composition.

References

1. Van de Velde K, Kiekens P (2002) Material properties. Biopolymers: overview of several properties and consequences on their applications. Polym Test 21:433–442. doi:10.1016/S0142-9418(01)00107-6
2. Siracusa V, Rocculi P, Romani S, Dalla Rosa M (2008) Biodegradable polymers for food packaging: a review. Trends Food Sci Tech 19:634–643. doi:10.1016/j.tifs.2008.07.003
3. Nair L, Laurencin C (2007) Biodegradables polymers as biomaterials. Prog Polym Sci 32:762–798. doi:10.1016/j.progpolymsci.2007.05.017
4. Woodruff MA, Hutmacher DW (2010) The return of a forgotten polymer- Polycaprolactone in the 21st century. Prog Polym Sci 35:1217–1256. doi:10.1016/j.progpolymsci.2010.04.002
5. Albertson A, Varma I (2003) Recent developments in ring opening polymerization of lactones for biomedical applications. Biomacromolecules 4:1466–1486. doi:10.1021/bm034247a
6. Vert M, Chabot F, Leray J, Christel P (1981) Stereoregular bioresorbable polyesters for orthopedic surgery. Makromol Chem Suppl 5:30–41. doi:10.1002/macp.1981.020051981103
7. Vert M (1989) Bioresorbable polymers for temporary therapeutic applications. Makromol Chem 166(167):155–168. doi:10.1002/apmc.1989.051660111
8. Dechy-cabaret O, Martin-Vaca B, Bourissou D (2002) Controlled ring-opening polymerization of lactide and glycolyde. Chem Rev 104:6147–6176. doi:10.1021/cr040002s
9. Vanhoorne P, Dubois P, Jerome R, Teyssie P (1992) Macromolecular engineering of polylactones and polylactides. 7. Structural analysis of copolyesters of ε-caprolactone and L- or D, L-lactide initiated by Al(O^{i}Pr)$_3$. Macromolecules 25:37–44. doi:10.1021/ma00027a008
10. Shen Y, Zhu KJ, Shen Z, Yao K (1996) Synthesis and characterization of highly random copolymer of ε-caprolactone and D, L-lactide using rare earth catalyst. J Polym Sci Part A Polym Chem 34:1799–1805. doi:10.1002/(SICI)1099-0518(19960715)34:9<1799:AID-POLA18>3.0.CO;2-1
11. Deng X, Zhu Z, Xiong Ch, Zhang L (1997) Synthesis and characterization of biodegradable block copolymers of ε-caprolactone and D, L-Lactide Initiated by potassium poly (ethylene glycol) ate. J Polym Sci Part A Polym Chem 35:703–708. doi:10.1002/(SICI)1099-0518(199703)35:4<709:AID-POLA14>3.0.CO;2-R
12. Qian H, Bei J, Wang S (2000) Synthesis, characterization and degradation of ABA block copolymer of L-lactide and ε-caprolactone. Polym Deg Stab 68:423–429. doi:10.1016/S0141-3910(00)000318
13. Huang M, Li S, Vert M (2004) Synthesis and degradation of PLA-PCL-PLA triblock copolymer prepared by successive polymerization of ε-caprolactone and DL-lactide. Polymer 45:8675–8681. doi:10.1016/j.polymer.2004.10.054
14. Liu F, Zhao Z, Yang J, Wei J, Li S (2009) Enzyme-catalyzed degradation of poly(L-lactide)/poly(ε-caprolactone) diblock, triblock and four-armed copolymers. Polym Deg Stab 94:227–233. doi:10.1016/j.polymdegradstab.2008.10.023
15. Stridsberg K, Albertson A (2000) Copolymerization of glycolide and e-caprolactone of L-lactide and 1,5-dioxepan-2-one forming a triblock copolymer. J Polym Sci Part A Polym Chem 38:1774–1784. doi:10.1002/(SICI)1099-0518(20000515)38:10<1774:AID-pola620>3.0.co
16. Zhong Zh, Yu D, Meng F, Gan Zh, Jing X (1999) Controlled synthesis of L-lactide-b-ε-caprolactone block copolymers using a rare earth complex as catalyst. Polym J 31:633–636

17. Bero M, Kasperczyk J, Adamus G (1993) Coordination polymerization of lactides, 3 copolymerization of L, L-lactide and ε-caprolactone in the presence of initiators containing Zn and Al. Makromol Chem 194:907–912. doi:10.1002/macp.1993.021940314

18. In't Veld P, Velner E, Van de Witte P, Hamhuis J, Dijkstra P, Feijen J (1997) Melt block copolymerization of ε-caprolactone and L-lactide. J Polym Sci Part A Polym Chem 35:219–226. doi:10.1002/(SICI)1099-0518(19970130)35:2<219:AID-POLA3>3.0.CO;2-N

19. Kon Kim J, Park D, Lee M, Ihn K (2001) Synthesis and crystallization behavior of poly(L-lactide)-block-poly(ε-caprolactone) copolymer. Polymer 42:7429–7441. doi:10.1016/S0032-3861(01)00217-8

20. Contreras J, Dávila D (2006) Ring-opening copolymerization of L-lactide with ε-caprolactone initiated by diphenylzinc. Polym Int 55:1049–1056. doi:10.1002/pi.2050

21. Kasperczyk J, Bero M (1991) Coordination polymerization of lactides, 2. Microstructure determination of poly(L, L-lactide)-co-(ε-caprolactone) with 13C nuclear magnetic resonance spectroscopy. Makromol Chem 192:1777–1787. doi:10.1002/macp.1991.021920812

22. Bero M, Kasperczyk J (1996) Coordination polymerization of lactides, 5. Influence of lactide structure on the transesterification processes in the copolymerization with ε-caprolactone. Macromol Chem Phys 197:3251–3258. doi:10.1002/macp.1996.021971015

23. Kasperczyk J, Bero M (1993) Coordination polymerization of lactides, 4. The role of transesterification in the copolymerization of L, L-lactide and ε-caprolactone. Makromol Chem 194:913–925. doi:10.1002/macp.1993.021940315

24. Grijpma DW, Pennings AJ (1991) Polymerization temperature effects on the properties of L-lactide and ε-caprolactone copolymers. Polym Bull 25:335–341. doi:10.1007/BF00316903

25. Pensec S, Leroy M, Akkouche H, Spassky N (2000) Stereocomplex formation in enantiomeric diblock of poly (ε-caprolactone) and polylactide. Polym Bull 45:373–380. doi:10.1007/s002890070010

26. Fukuzaki H, Yoshida M, Asamo M, Kumakura M, Mashimo T, Yuasa H, Imai K, Yamanaka H (1990) Synthesis of low-molecular-weight copoly(L-lactic acid/ε-caprolactone) by direct copolycondensation in the absence of catalysts, and enzymatic degradation of the polymers. Polymer 31:2006–2014. doi:10.1016/0032-3861(90)90031-S

27. Dobrzynski P (2002) Synthesis of biodegradable copolymers with low-toxicity zirconium compounds. III. Synthesis and chain-microstructure analysis of terpolymer obtained from L-lactide, glycolide, and ε-caprolactone initiated by zirconium (IV) acetylacetonate. J Polym Sci Part A Polym Chem 40:3129–3143. doi:10.102/pola.10401

28. Kurcok P, Dubois P, Sikorska W, Jedliński Z, Jérôme R (1997) Macromolecular engineering of lactones and lactides. 24. Controlled synthesis of (R, S)-β-butyrolactone-b-ε-caprolactone block copolymers by anionic and coordination polymerization. Macromolecules 30:5591–5596. doi:10.1021/ma970212p

29. Hiki S, Miyamoto M, Kimura Y (2000) Synthesis and characterization of hydroxyl-terminated [RS]-poly(3-hydroxybutyrate) and its utilization to block copolymerization with L-lactide to obtain a biodegradable thermoplastic elastomer. Polymer 41:7369–7379. doi:10.1016/S0032-3861(00)00086-0

30. Chen Ch, Fei B, Peng S, Wu H, Zhuang Y, Chen X, Dong L, Feng Z (2002) Synthesis and characterization of poly(β-hydroxybutyrate) and poly(ε-caprolactone) copolyester by transesterification. J Polym Sci Part B Polym Phys 40:1893–1903. doi:10.1002/polb.10242

31. Kricheldorf HR, Rost S (2005) A-B-A-triblock and multiblock copolyesters prepared from ε-caprolactone, glycolide and L-lactide by means of bismuth subsalicylate. Polymer 46:3248–3256. doi:10.1016/j.polymer.2005.02.004

32. Barakat I, Dubois P, Grandfils Ch, Jérôme R (2001) Poly(ε-caprolactone-b-glycolide) and poly(D, L-lactide-b-glycolide) diblock copolyesters: controlled synthesis, characterization, and colloidal dispersions. J Polym Sci Part A Polym Chem 39:294–306. doi:10.1002/1099-0518(20010115)39:2<294:AID-POLA50>3.0.CO;2-A

33. Zhao ZH, Yang L, Hu Y, Wei J, Li S (2007) Enzymatic degradation ob block copolymers obtained by sequential ring opening polymerization of L-lactide and ε-caprolactone. Polym Deg Stab 92:1769–1777. doi:10.1016/j.polymdegradstab.2007.07.012

34. Vivas M, Contreras J (2003) Ring-opening polymerization of ε-caprolactone initiated by diphenylzinc. Eur Polym J 39:43–47. doi:10.1016/S0014-3057(02)00190-8

35. Vivas M, Mejías N, Contreras J (2003) Ring-opening polymerization of lactones initiated by diphenylzinc-coinitiator systems. Polym Int 52:1005–1009. doi:10.1002/pi.1183

36. Kricheldorf H, Mang T, Jonté J (1984) Polylactones. 1. Copolymerization of glycolide and ε-caprolactone. Macromolecules 17:2173–2181. doi:10.1021/ma00140a051

37. Liu L, Wei YZ, Qi M (2007) Synthesis and characterization of biodegradable aliphatic polyesters using dibutylmagnesium as initiator. Chin Chem Lett 18:744–746. doi:10.1016/j.cclet.2007.04.011

38. Kricheldorf HR, Bornhorst K, Hachmann-Thiessen H (2005) Bismuth (III) *n*-hexanoate and tin(II) 2-ethylhexanoate initiated copolymerization of ε-caprolactone and L-lactide. Macromolecules 38:5017–5024. doi:10.1021/ma047873o

39. Hamitou A, Jérôme R, Teyssié P (1977) Soluble bimetallic μ-oxoalcoxides. IX. ε-caprolactone and β-propiolactone block copolymerization. J Polym Sci Polym Chem Ed 15:1035–1041. doi:10.1002/pol.1977.170150502

40. Kasperczik J (1996) Microestructural analysis of poly [(L,L-lactide)-co-(glycolide)] by ^{1}H and ^{13}C n.m.r. spectroscopy. Polymer 37: 201–203. doi:10.1016/0032-3861(96)81088-3

41. Kasperczik J (1999) Copolymerization of glycolide and ε-caprolactone, 1. Analysis of the copolymer microstructure by means of ^{1}H and ^{13}C n.m.r. spectroscopy. Makromol Chem Phys 200:903–910. doi:10.1002/(SICI)1521-3935(19990401)200:4<903:AID-MACP903>3.0.CO;2-6

42. Hamley IW, Parras P, Castelleto V, Castillo RV, Müller AJ, Pollet E, Dubois P, Martin CM (2006) Melt structure and its transformation by sequential crystallization of the two blocks within poly(L-lactide)-*block*-poly(ε-caprolactone) double crystalline diblock copolymers. Macromol Chem Phys 207:941–953. doi:10.1002/macp.200600085

43. Cerrai P, Tricoli M, Andruzzi F, Paci M, Paci M (1989) Polyether-polyester block copolymers by non-catalyzed polymerization of ε-caprolactone with poly(ethylene glycol). Polymer 30: 338–343. doi:10.1016/0032-3861(89)90126-2

44. Hamley IW, Castelleto V, Castillo RV, Müller AJ, Pollet E, Martin CM, Pollet E, Dubois P (2005) Crystallization in poly(L-lactide)-*b*-poly(ε-caprolactone) double crystalline diblock copolymers: a study using X-ray scatteing, differential scanning calorimetry and polarized optical microscopy. Macromolecules 38:463–472. doi:10.1002/ma0481499

45. Liu KL, Goh SH, Li J (2008) Controlled synthesis and characterization of amphiphilic poly[(R, S)-3-hydroxybutyrate]-poly(ethylene glycol)-poly[(R, S)-3-hydroxybutyrate] triblock copolymers. Polymer 49:732–741. doi:10.1016/j.polymer.2007.12.017