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Synthesis of poly(ε-caprolactone)-poly(L-lactide) block copolymers by melt or solution sequential copolymerization using nontoxic dibutylmagnesium as initiator

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Summary

Poly(ε-caprolactone)-poly(L-lactide) (PCL-PLLA) block copolymers were synthesized via melt or solution sequential copolymerization of ε-caprolactone (ε-CL) and L-lactide (L-LA) using nontoxic dibutylmagnesium as initiator. The formation of block structure was confirmed by ^{1}H-, ^{13}C NMR, GPC, and FT-IR, it can be concluded that the block copolymers PCL-PLLA have been successfully synthesized by both melt and solution sequential copolymerization methods. Two melting endothermic peaks (T_m) during heating and two crystallization exothermal peaks (T_c) during cooling were observed in DSC curves. XRD patterns of the copolymers were approximately the superposition of both the PCL and PLLA homopolymers. The results indicated the coexistence of both PCL and PLLA crystalline microdomains, and the microphase separation took place in the block copolymers.

Introduction

Biodegradable aliphatic polyesters have received great attention for their potential applications in medical materials, such as sutures, scaffolds, bone fixation, and drug release carriers [1, 2]. Among them, poly(ε-caprolactone) (PCL) is permeable to many drugs, but its degradation is very slow. In contrast, poly(L-lactide) (PLLA) is hardly permeable to most drugs, and its half-time is much shorter. Thus, copolymerization of ε-caprolactone (ε-CL) and L-lactide (L-LA) is an effective strategy of combing the great permeability of PCL and the rapid biodegradation of PLLA component [3-9]. Owing to their microphase separation and morphology, the block copolymers showed several advantages over the corresponding the random copolymers, especially when used as drug carriers.

On the other hand, continuous efforts have been devoted to the development of new catalysts and initiators for the polymerization of lactones[6,8,10-16]. Stannous octoate has been frequently used as one of the effective catalyst. However, like many other

catalysts, the cytotoxicity and difficulties in removal of the catalyst from the resulting polymer have limited its use in many cases. For medical and pharmaceutical applications, the synthetic polymers without containing any toxic heavy metal ions are reasonably desirable.

Magnesium ions are required by the metabolism of living organism, including human body, therefore, the magnesium compounds is a potential catalyst for its nontoxicity. Some previous studies showed that dibutylmagnesium (Bu_2Mg) is an effective initiator for the polymerizations of lactones [17-20]. In the present paper, we attempt to synthesize PCL-PLLA block copolymers using Bu_2Mg as initiator by the sequential copolymerization of ε-CL and L-LA in solution or melt, and employ ^{1}H-NMR, ^{13}C-NMR, GPC and FT-IR analysis techniques to confirm the block structure. Their thermal behaviors and crystallization are also evaluated by DSC and XRD.

Experimental

Materials

Monomers L-LA and ε-CL and solvent 1,4-dioxane were purified by recrystallization or distillation prior to use. Bu_2Mg (1 M in heptane,) was used without further treatment. All other reagents were used as received.

Polymerization

Melt sequential copolymerization reactions were carried out in a previously flamed and N_2-purged flask. The first monomer ε-CL and Bu_2Mg were injected into the flask by syringes. The flask was immersed into a thermostated oil bath at 130°C for 24 h. A part of the reaction mixture was withdrawn for NMR and GPC analysis. Then the second monomer L-LA was weighted into the flask, and the polymerization continued 24 h. The product was dissolved in chloroform and precipitated in an acidic diethyl ether and then dried under vacuum.

Solution sequential copolymerizations of ε-CL and L-LA were carried out at 70°C with 1,4-dioxane as solvent following the above procedure.

Measurements

^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker DRX 400 NMR spectrometer with $CDCl_3$ as solvent. FT-IR spectra were recorded on a Nicolet 5DX spectrometer using film samples cast on a KBr plate from $CHCl_3$ solution. GPC was conducted with PL-220 using THF as eluent at 40°C, and the polymer molecular weights were calibrated with polystyrene standards. DSC was carried out on a Mettler Toledo DSC 822^e instrument from −60 to 200°C at 10°C/min under N_2. XRD was performed on a Dmax-Ultima+ X-ray diffractometer with Ni-filtered Cu/K-α radiation at the scanning rate of 0.02° θ/s from 5.0° to 50.0°.

Results and discussion

Some PCL-PLLA block copolymers were synthesized by melt or solution sequential copolymerization of ε-CL and L-LA with a nontoxic Bu_2Mg initiator. ^{1}H NMR spectra of the PCL prepolymer and the PCL-PLLA copolymer were shown in Figure 1. The signals

of $-CH_2OH$, methylene protons of the hydroxyl end groups of the PCL prepolymers at 3.58 ppm disappeared, and new signals of $-CH(CH_3)OH$, methyne proton (δ=4.18 ppm) of the hydroxyl end of the copolymer were observed. These indicated that the PCL reactive chains have succeeded the polymerization of the second monomer L-LA.

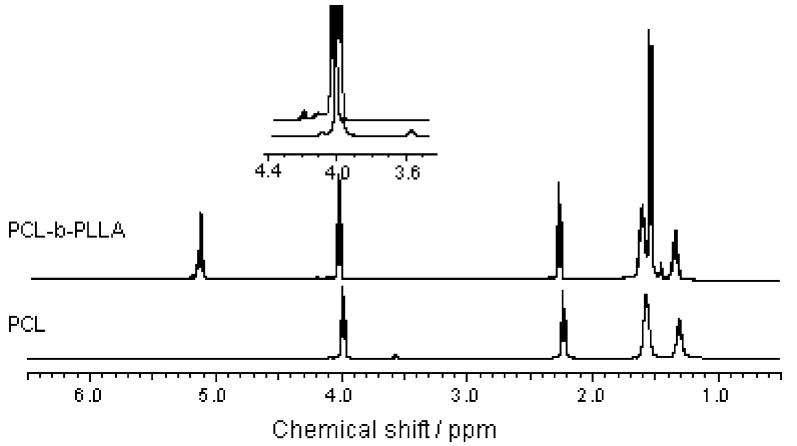


Figure 1 ^{1}H NMR spectra of PCL prepolymer and the resulting PCL-PLLA copolymer (Sample M2)

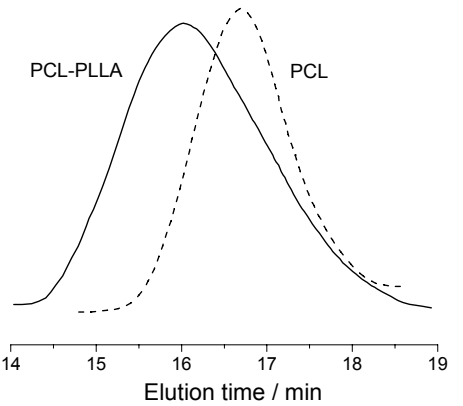


Figure 2 GPC curves of the PCL prepolymer and the PCL-PLLA copolymer (Sample M1).

Then, we employed GPC technique to trace the copolymerization process. If the PCL prepolymer did not initiate the polymerization of L-LA, there should be double or triplet peaks on the GPC curve of the product [5]. The GPC curves (Figure 2) of the prepolymer and the copolymer were all single and symmetric and the latter peak left-shifted to the small elution volume, which indicated that PCL prepolymer was not detectable in the copolymerization product.

^{13}CNMR is a powerful tool for determining the chain microstructure and the randomizing effects of transesterification reactions, because the carbonyl carbon signals were sensitive to sequence effects [21, 22]. Figure 3 showed that no peaks appeared between 173.9 ppm (carbonyl group of PCL block) and 169.9 ppm (carbonyl

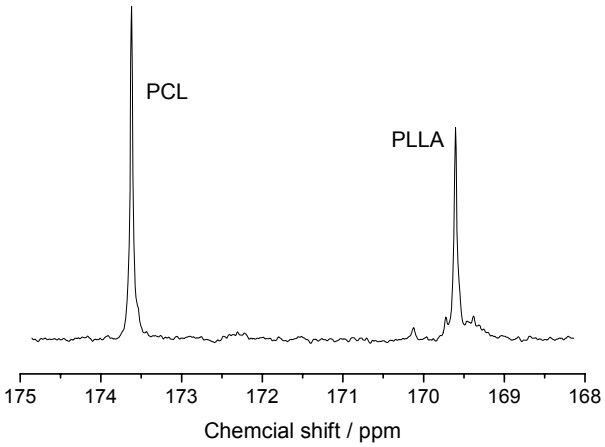


Figure 3 CO signal in ^{13}C NMR spectrum of the PCL-PLLA block copolymer (Sample M2)

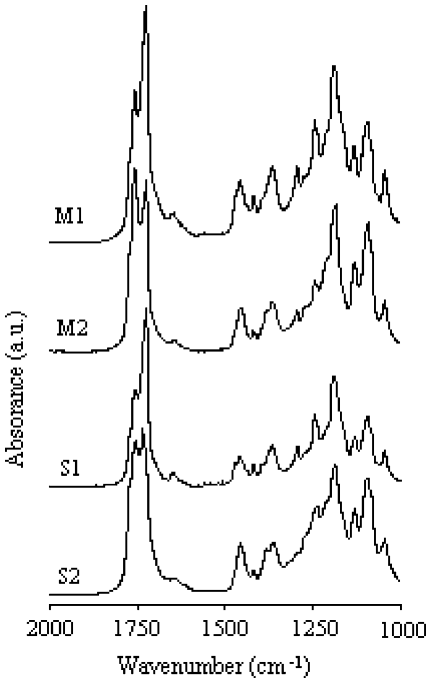


Figure 4 Expanded FT-IR spectra of the PCL-PLLA block copolymers (Samples in Table 1)

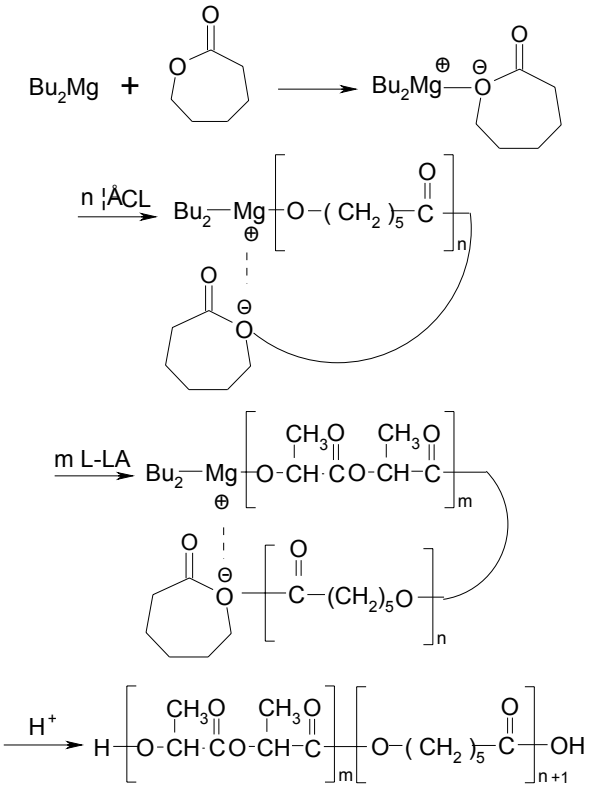
group in PLA block), which undoubtedly indicated that there is no occurrence of transesterification in the copolymerization.

In addition, FT-IR spectra of the copolymers provide a new evidence of the formation of block copolymers. Two absorption peaks of the ester carbonyl groups, one at 1750 cm^{-1} due to PLLA block, and the other at 1730 cm^{-1} due to PCL block, were observed in Figure 4. In contrast, there was only single broad ester carbonyl absorption band for the random copolymers [5].

Table 1 Melt and solution sequential copolymerizations of ε-CL and L-LA initiated with Bu_2Mg[a]

Sample	CL conv.[b]	M_{PCL}[c]	M_{n1}[d]	PDI[d]	CL/LA in feed[e]	CL/LA in product[f]	LA conv.[g]	M_{PLA}[h]	M_{n2}[h]	PDI[i]
M1	0.98	4500	7100	1.57	0.75/0.25	0.80/0.20	0.75	1400	9700	2.31
M2	0.92	4200	6900	1.53	0.50/0.50	0.54/0.46	0.80	4500	12800	2.23
S1	0.90	5200	8300	1.35	0.75/0.25	0.78/0.22	0.78	1900	10800	1.89
S2	0.96	4800	10400	1.42	0.50/0.50	0.60/0.40	0.65	5000	15800	1.88

[a] Molar ratio of monomer ε-CL to initiator=50;
[b] Conversion of monomer ε-CL measured by ^{1}H NMR;
[c] Calculated by the ratio end group to polymer chain in ^{1}H NMR;
[d] Prepolymer molecular weight measured by GPC using THF as an eluent at 40°C.
[e] Molar ratio in the comonomers feed;
[f] Molar composition in the copolymer measured by ^{1}H NMR;
[g] Conversion of monomer L-LA measured by ^{1}H NMR;
[h] Calculated from M_{PCL} and the CL/LA ratio determined by ^{1}H NMR;
[i] Copolymer molecular weight measured by GPC using THF as an eluent at 40°C.



Scheme 1 A possible mechanism for sequential copolymerization of ε-CL and L-LA with Bu_2Mg as initiator

Furthermore, the melting and crystallization behaviors of the block copolymers were investigated by DSC and XRD. Figure 5 showed that the sample M2 exhibited two

melting endothermic peaks (T_m) during heating and two crystallization exothermal peaks (T_c) during cooling. The results indicated that both PCL and PLLA blocks can be crystallized and form two different crystal domains. In other words, the microphase separation took place in the block copolymers.

It is seen in Figure 6 that the XRD patterns of the copolymers are approximately the superposition of both the PCL and PLLA homopolymer peaks. There are two separated crystalline microdomains due to the PCL and PLLA blocks in these block copolymers, respectively, in agreement with the DSC results.

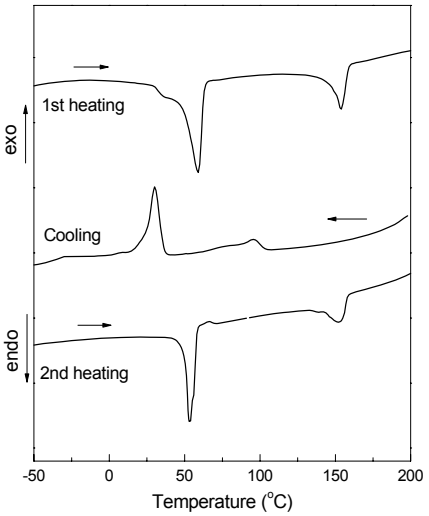


Figure 5 Typical DSC curves of PCL-PLLA block copolymer (Sample M2)

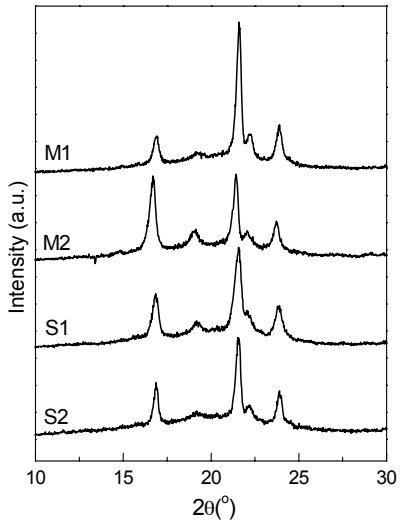


Figure 6 XRD patterns of the PCL-PLLA block copolymers (Samples in Table 1)

Conclusions

In conclusion, we synthesized successfully poly(ε-caprolactone)-poly(L-lactide) block copolymers by melt or solution sequential copolymerization of ε-caprolactone and L-lactide with Bu_2Mg as initiator. The ^{1}H-NMR, ^{13}C-NMR, GPC and FT-IR measurements confirmed the formation of block structure of copolymers. DSC and XRD results indicated that the microphase separation took place in the block copolymers.

References

[1] Platel, R. H., Hodgson, L. M., Williams, C. K., Polym Rev 2008, 48, 11.
[2] Okada, M., Prog Polym Sci 2002, 27, 87.
[3] Vanhoorne, P., Dubois, P., Jerome, R., et al, Macromolecules 1992, 25, 37.
[4] In't Veld, P.J.A., Velner, E.M., Van de Witte, P., et al, J Polym Sci Part A: Polym Chem 1997, 35, 219.
[5] Qian, H.T., Bei, J.Z., Wang, S.G., Polym Degrad Stabi 2000, 68, 423.
[6] Fan, L., Xiong, Y.B., Xu, H., et al, Eur Polym J 2005, 41, 1647.
[7] Contreras, J., Davila, D., Polym. Int. 2006, 55, 1049.
[8] Piao, L.H., Sun, J.R., Zhong, Z.Y., et al, J. Appl Polym Sci 2006, 102, 2654.
[9] Nalampang, K., Molloy, R., Punyodom, W., Polym Adv Technol 2007, 18, 240.
[10] Palard, I., Schappacher, M., Soum, A., Guillaume, S.M., Polym Int 2006, 55, 1132.
[11] Palard, I., Soum A, Guillaume, S.M., Macromolecules 2005, 38, 6888.
[12] Huang, M.H., Coudane, J., Li, S.M., et al, J Polym Sci Part A: Polym Chem 2005, 43, 4196.
[13] Li, F., Li, S.M., Vert, M., Macromol Biosci 2005, 5, 1125.
[14] Lemmouchi, Y., Perry, M.C., Amass, A.J., et al, J Polym Sci Part A: Polym Chem 2007, 45, 3975.
[15] Zhong, Z.Y., Dijkstra, P.J., Birg, C., et al, Macromolecules 2001, 34, 3863.
[16] Zhang, L., Nederberg, F., Pratt, R.C., et al, Macromolecules 2007, 40, 4154.
[17] Kricheldorf, H.R., Lee, S.R., Polymer 1995, 36, 2995.
[18] Kasperczyk, J., Bero, M., Polymer 2000, 41, 391.
[19] Dobrzynski, P., Kasperczyk, J., Jelonek, K., et al, J Biomed Mater Res A 2006, 79A, 865.
[20] Wei, Z.Y., Liu, L., Qi, M., Eur Polym J 2007, 43, 1210.
[21] Bero, M., Kasperczyk, J., Adamus, G., Makromol Chem 1993, 194, 907.
[22] Bero, M., Kasperczyk, J., Makromol Chem 1993, 194, 913.
[23] Shelton, R. J., Agostini, D. E., Lando, J. B., J Polym Sci A-1 1971, 9, 2789.