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Block Copolymerization of ε-Caprolactone and Adipic Anhydride Initiated with Aluminum Complex Catalyst

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ABSTRACT

This communication describes a living block copolymerization of ε-caprolactone with adipic, anhydride in the presence of a complex catalyst of $AliBu_3/H_3PO_4/H_2O$. The new copolymer with high molecular weight and narrow molecular weight distribution was achieved in a very short time. It may be potential in medical applications for it is combined with properties of poly(ε-caprolactone) (PCL) and PAA.

Key Words: Block copolymerization; Biodegradable; Poly(ε-caprolactone); Polycondensation.

INTRODUCTION

Following the recognition of polylactide as a successful biomedical polymer, attention was drawn to related polyesters in the search for new biodegradable polymers in similar applications. In the family of polyesters, poly(ε-caprolactone) (PCL) occupies a unique position: it is at the same time biodegradable and miscible with a variety of polymers and it crystallizes very readily.[1] A lack of toxicity and great permeability has

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already found wide use for PCL in medical applications.[1] Poly(ε-caprolactone) degradation proceeds through hydrolysis of backbone ester bonds as well as by enzymatic attack. Hydrolysis, however, proceeds by homogeneous erosion at a much slower rate than polylactide (PLA) and polylactide-*co*-glycolide (PLGA).[2]

Many approaches of varying the PCL properties have been investigated. Above all, there is an interest in accelerating its degradation rate. This problem might be overcome by copolymerization of ε-caprolactone (ε-CL) with other monomers, such as glycolide, lactide, δ-valerolactone, ε-decalactone, and poly(ethylene oxide).[3–6] In this paper, we modify the PCL properties by copolymerizing with adipic anhydride (AA). It is well known that polyanhydrides based on a variety of aromatic and aliphatic diacids have been developed by Langer et al. as bioerodible carrier matrices for controlled drug delivery applications.[7] They are of great interest because they show no evidence of inflammatory reactions, they are hydrolytically unstable, and degraded in vitro, as well as in vivo with the release of nonmutagenic and noncytotoxic by-products.[8]

Polycondensation of mixed anhydrides is the traditional method for the synthesis of polyanhydrides, which has all the drawbacks of a step-growth polymerization.[9] Poly adipic anhydride (PAA) was also prepared by an improved melt polycondensation process.[10] The ring-opening polymerization of alicyclic anhydrides provides a direct access to the related polyanhydrides and is more likely the best way of avoiding all the disadvantages of the traditional polycondensation method. However, the resultant polymers have low molecular weight and broad molecular weight distribution due to the side inter- and intramolecular transacylation reactions, which rapidly disturb the chain propagation.

In the past 10 years, only a few papers reported the living polymerization of ε-CL with alicyclic anhydrides. Ropson et al.[9,11] reported the living polymerization of ε-CL and AA initiated by $Al(O^iPr)_3$. However, they only obtained low molecular weight ($M_n < 58{,}000$) copolymers using more than 40 hr. In this paper, we aim to report preliminary results on the living block copolymerization of ε-CL with AA as initiated by a complex catalyst of triisobutylaluminum together with phosphoric acid and water ($AliBu^3/H^3PO^4/H^2O$). The complex catalyst has proved to be very effective in initiating the ring-opening polymerization of *D,L*-lactide with poly(ethylene glycol).[12] There have been some reports of the polymerization of *DL*-β-butyrolactone and ε-CL by using organometallic catalysts,[13] but these polymerizations generally give rise to broad molecular weight distributions. In this paper, we successfully obtained poly(ε-CL-*b*-AA) copolymer with high weight molecular weight and narrow molecular weight distribution in a very short time.

EXPERIMENTAL

Adipic anhydride was prepared as described previously.[9] ε-Caprolactone (from Aldrich) was dried over calcium hydride for 48 hr at room temperature and then distilled under reduced pressure prior to polymerization. Solvents were dried and purified in the usual manner.

One gram of AA was polymerized in 3.0 mL xylene at 45°C for 3 hr under stirring using 0.01 g $AliBu_3/H_3PO_4/H_2O$ as initiator, in a previously flamed and nitrogen-purged glass reactor. Polymerization was stopped by adding a large volume excess of petroleum ether, and the precipitated PAA was recovered by filtration. Poly(ε-CL-*b*-AA) block copolymer was synthesized by adding the adipic anhydride (AA, 0.5 g) solution into a living PCL, 5.0 g solution under strict anhydrous conditions. After 3 hr, the copolymerization was also terminated by adding a large volume excess of petroleum ether. Then, PAA homopolymer and poly(CL-*b*-AA) copolymer were dissolved in a small volume of chloroform and added with an aqueous EDTA solution to remove the catalyst residues. The polymer solution was washed with distilled water up to neutral pH, concentrated under reduced pressure, and finally precipitated with a large volume of heptane. The resultant polymers were dried at 40°C under vacuum.

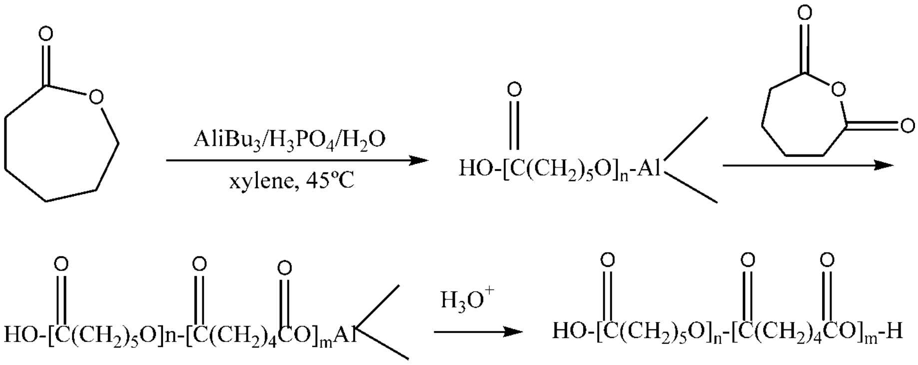
The ^{13}C-NMR and ^{1}H-NMR spectrum of poly(CL-*b*-AA) block copolymer were recorded on a Unit-Inova-200 spectrometer and a Unit-Inova-400 spectrometer at room temperature in $CDCl_3$, respectively. IR spectra were recorded on a Nicolet MX-1 IR spectrometer. Molecular weight and its distribution were determined by GPC using a Water Associates Model ALC/GPC 2410 apparatus operating with THF and calibrated with polystyrene standards. The melting temperatures of polymers were measured by DSC (Perkin–Elmer DSC 7) under a flow of nitrogen at a scanning rate of 10°C/min.

RESULTS AND DISCUSSION

Recently, some papers reported that the AA homopolymerization and block copolymerization of ε-CL and AA initiated by Al tri-sopropoxide ($Al(O^iPr)_3$) in toluene at 20°C.[9] The polymerization procedure was proved to be typically "living." Here, we used a complex catalyst of triisobutylaluminum together with phosphoric acid and water ($AliBu_3/H_3PO_4/H_2O$) to initiate the homopolymerization of AA and copolymerization of ε-CL with AA. To the best of our knowledge, the synthesis of PAA and poly(CL-*b*-AA) initiated by $AliBu_3/H_3PO_4/H_2O$ was first studied in xylene at 45°C.

Indeed, copolymerization of AA is also a good way to overcome the poor solubility of the PAA chains in apolar solvents and the occurrence of side reactions in polar solvents. In this paper, we chose two methods to copolymerize ε-CL with AA. One method was random copolymerization of ε-CL with AA. When a mixture of ε-CL and AA is polymerized in xylene at 45°C under stirring, it has been rapidly observed that insoluble PAA is formed, whereas ε-CL monomer remains unreacted. The result is exactly the same as that observed when ε-CL is polymerized with $Al(O^iPr)_3$.[9] The other method is the sequential copolymerization of ε-CL with AA (shown in Sch. 1). In preliminary block copolymerization experiments, the ε-CL is first polymerized into PCL active chains, and then a AA solution is added to the living system. The reason why we adopt the feed sequence is that reactivity of AA is more active than that of ε-CL in the experiment. After 1 hr, an increase in viscosity and a sudden rise in temperature were observed. At last, it has been observed that the viscous polymer prevented the magnetic stirring from occurring. The yield of the copolymers was in the range of 80–96%, which was determined by comparing the weight of two monomers and resultant copolymers. The conversion of the two monomers being more than 95% was achieved.

The purified polymers were first analyzed by FTIR. It can be seen that some differences exist between the spectra of poly(CL-*b*-AA) block copolymer (Fig. 1B) and PAA homopolymer (Fig. 1A). The absorption bands at 1810 cm^{-1} and 1730 cm^{-1} are



Scheme 1. Reaction equilibria for poly(CL-*b*-AA) formation.

attributed to anhydride and ester carbonyl for the copolymer. Furthermore, the signal intensity of the two kinds of carbonyl for PAA and poly(CL-*b*-AA) displays a reverse change. The reason may be that ε-CL monomers were copolymerized with AA.

In order to further confirm the formation of poly(CL-*b*-AA) block copolymer, ^{1}H-NMR spectrum is made and shown in Fig. 2. Peaks at 1.39 (c), 1.60 (b), 2.30 (d), and 4.05 ppm (a) are assigned to methylene protons in PCL units, respectively. Peaks at 1.72 (f) and 2.52 ppm (e) are attributed to the methylene protons in PAA units. These results are consistent with that obtained from poly(CL-*b*-AA) block copolymer prepared by the copolymerization of ε-CL and AA initiated by Al(O^{i}Pr)$_3$.[9,11] The same conclusion is also supported by ^{13}C-NMR (Fig. 3). In addition to the typical signals ($\delta = 173.5$ (a), 64.1 (f), 34.0 (b), 28.3 (e), 25.3 (c), and 23.8 ppm(d)) of the PCL chain, the ^{13}C-NMR spectrum shows three additional signals at $\delta = 169.0$ (g), 33.3 (h), and 23.3 (i) ppm. The result is in agreement with that reported previously.[9]

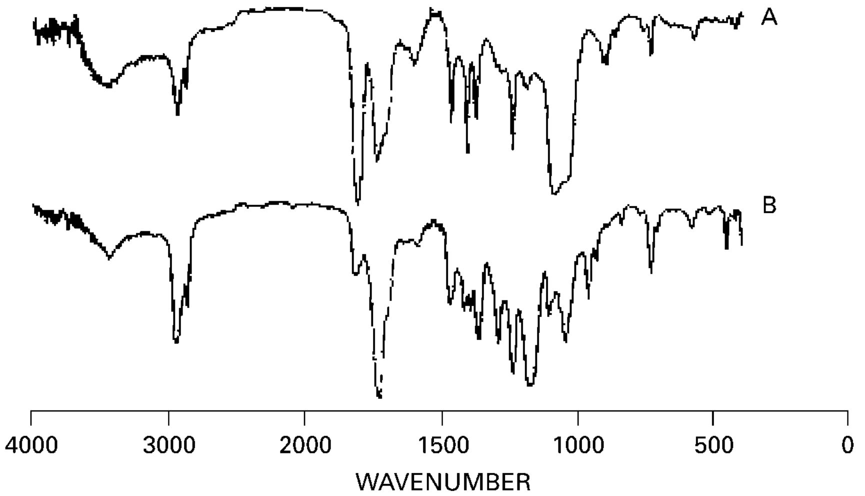


Figure 1. FTIR spectra of PAA homopolymer (A) and poly(CL-*b*-AA) copolymer (B).

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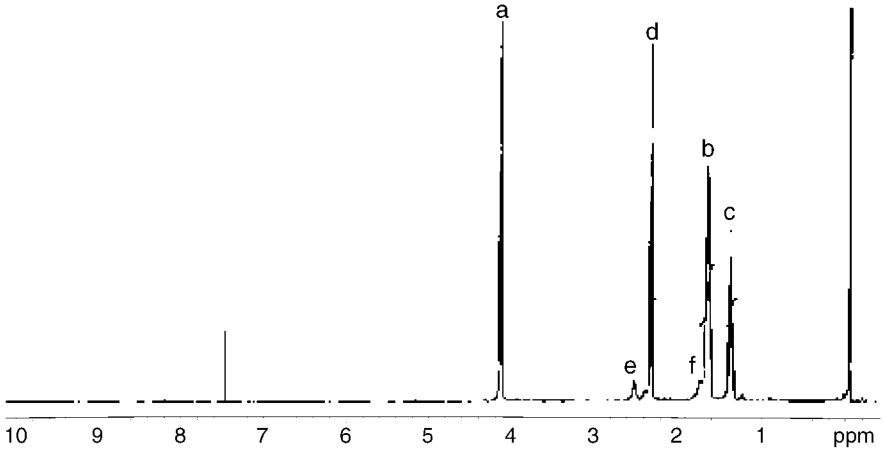

Figure 2. ^{1}H-NMR spectrum of poly(CL-*b*-AA) copolymer.

From the GPC curve in Fig. 4(b), it can be seen that only a single peak exists, which suggests that the monodispersion of molecular weight and absence of any detectable amount of homopolymers of PAA and PCL. The GPC curve of PCL block initiated by the aluminum complex catalyst for 1 hr was shown in Fig. 4a. The poly(CL-*b*-AA) copolymer with high weight molecular weight ($M_w = 76\,k$) and narrrow molecular weight distributions ($M_w/M_n = 1.48$) was achieved. This indicates that no trans esterification and/or backbiting reactions occurred during the copolymerization.[14]

The DSC curve for the poly(CL-*b*-AA) copolymer is shown in Fig. 5. The DSC data were recorded for the second heating run from 25 to 80°C. As seen from Fig. 5, the analysis of the PAA homopolymer (curve A) displays a melting temperature ($T_m = 63.8°C$) which is slightly lower than that reported previously.[15] The curve B for

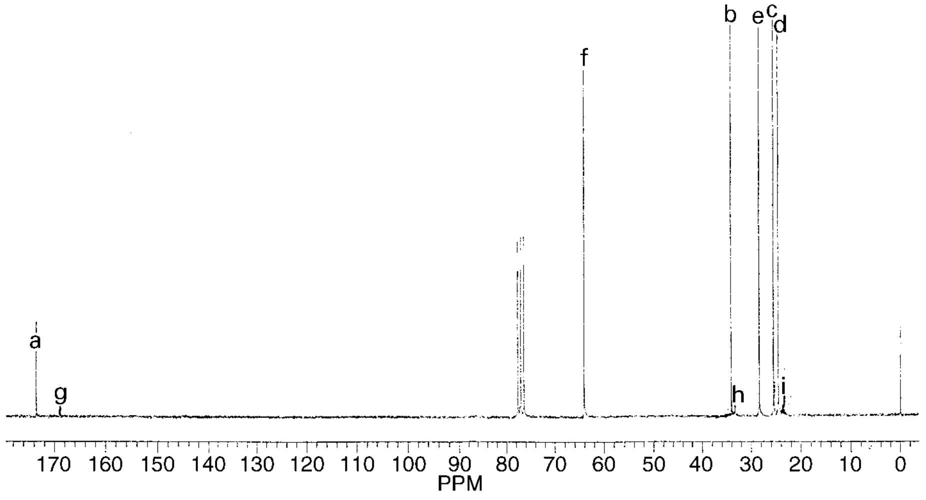

Figure 3. ^{13}C-NMR spectrum of poly(CL-*b*-AA) copolymer.

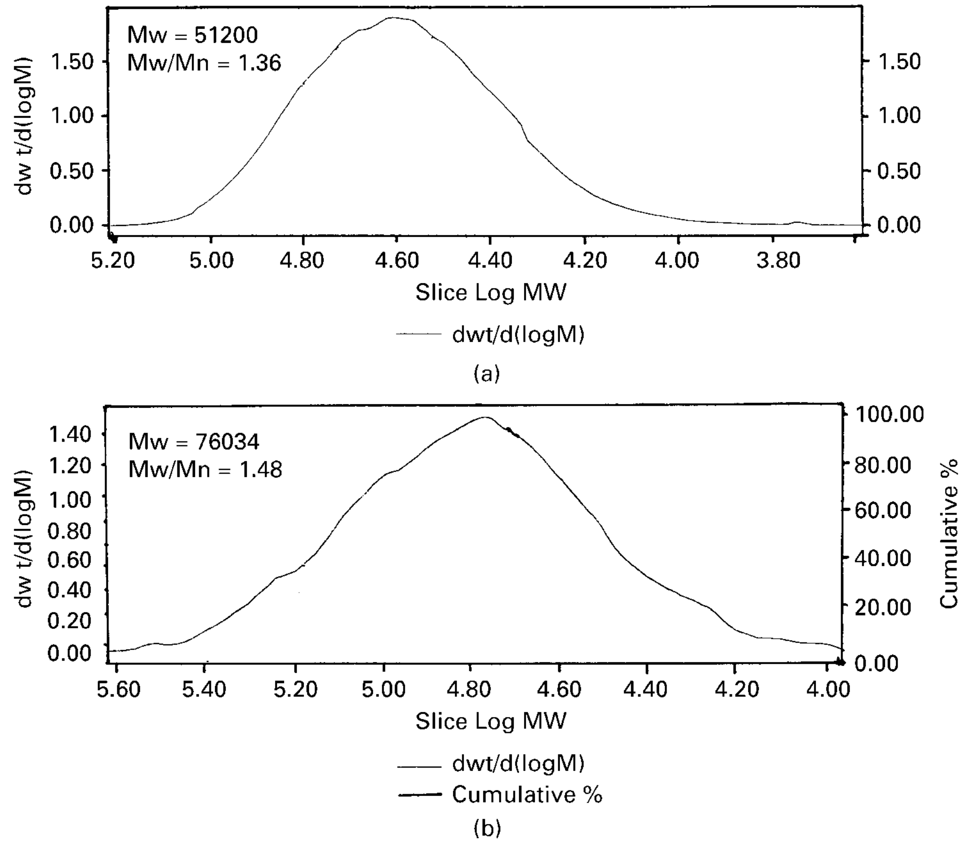

Figure 4. GPC curves of the PCL block (a) and the final poly(CL-*b*-AA) copolymer (b).

poly(CL-*b*-AA) copolymer exhibits two melting temperatures for the crystalline PCL block (56°C) and the PAA block (61°C), respectively, which is also indicative of the formation of the copolymer and the complete immiscibility of the two components.

CONCLUSION

This study has clearly shown that ε-CL can be copolymerized with AA in the presence of the complex catalyst of tri-sobutylaluminum together with phosphoric acid and water as initiator. Furthermore, we can obtain more than 95% yield of poly(CL-*b*-AA) block copolymer with high molecular weight and narrow molecular weight distriution in a very short time. The living polymerization mechanism of AA is also the same as that reported for ε-CL and lactides in the use of Al(O^{i}Pr)$_3$ as initiator. The block copolymer of ε-CL and AA can be synthesized in a controlled way. The aluminum complex catalyst is very effective to initiate the hopolymerization of AA and block copolymerization of AA with ε-CL.

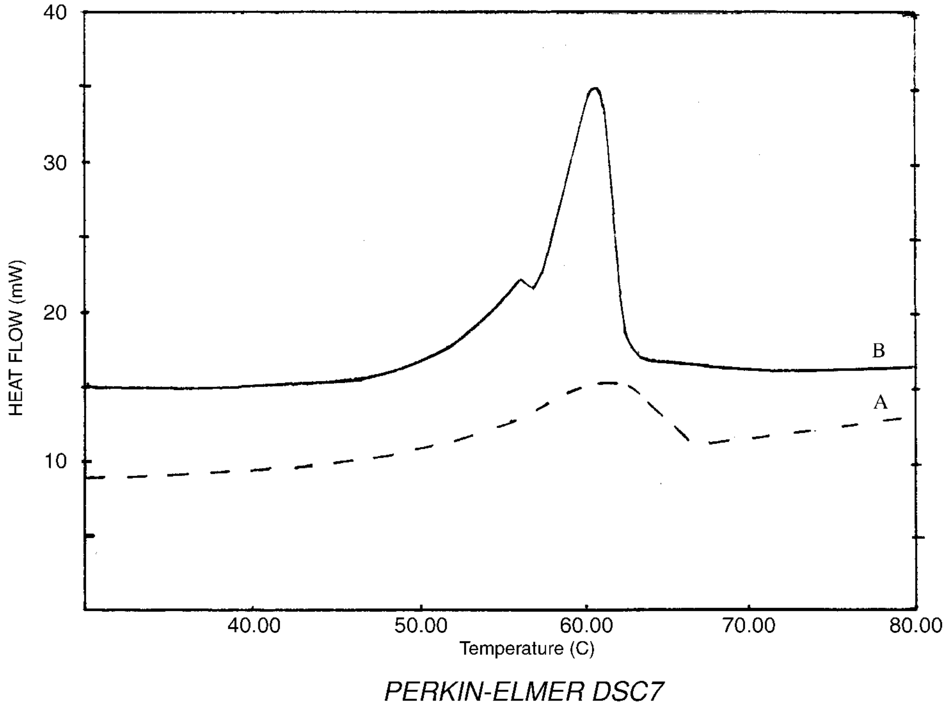

Figure 5. Typical DSC heating curves of PAA homopolymer (A) and poly (CL-*b*-AA) copolymer (B).

However, it is clear that more detailed investigations are necessary to clarify the mechanism of the polymerization process, the mechanistic and kinetic characteristics of the ring-opening polymerization promoted by aluminum alkyl.

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