STEREOCOMPLEX FORMATION IN AB DI-BLOCK COPOLYMERS OF POLY(ε-CAPROLACTONE) (A) AND POLY(LACTIDE) (B)

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Abstract: The thermal properties of two series of AB di-block copolymers of poly(ε-caprolactone) (A) and poly(lactide) (B) and their blends were studied. Each series contained poly(lactide) blocks of opposite chirality. The length of the poly(ε-caprolactone) blocks was not varied (DP = 70), whereas the poly(lactide) blocks were of varying length (DP = 5 - 80). Blends of polymers containing blocks of opposite chirality were prepared by mixing in solution. The melting temperature of the PLA phase was raised by approximately 55 °C in the blends due to stereocomplex formation. The melting temperatures of the crystalline PCL and PLA phases strongly depended on the composition of the block copolymers.

INTRODUCTION

Polymers based on L-lactide and ε-caprolactone are interesting materials for use in biomedical applications such as drug delivery devices (Ref. 1). In this respect the phase behaviour of polymers consisting of a highly crystalline block and a block with a rubbery character is of interest, because the permeability of the individual components for drugs in general differs widely (Ref. 2). This offers the opportunity to generate a desired release profile. The synthesis of block copolymers of poly(L-lactide) and poly(ε-caprolactone) could afford materials with properties to be used in matrices or reservoir devices, like hollow fibres, for drug delivery systems (Ref. 3). Furthermore, such block copolymers can be used as compatibilizers in blends of homopolymers (Ref. 4).
Co-crystallization of enantiomeric poly(lactide)s in a racemic lattice, also called stereocomplex formation, leads to materials with higher melting points and lower critical gelation concentrations in solution compared to the optically pure polymers (Ref. 5). These phenomena have been described extensively (Ref. 6). Stereocomplex formation in block copolymers of poly(L-lactide-*block*-D-lactide) was shown for the first time by our

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group and later by others (Refs. 7,8). The concepts of PCL/PLLA block copolymers and stereocomplex formation in PLA have now been combined by the preparation of binary blends of PCL/PLLA and PCL/PDLA block copolymers.

RESULTS AND DISCUSSION

The polymers were prepared by the sequential polymerization of ε-caprolactone and L- or D-lactide in dichloromethane using $Y_5(\mu\text{-}O)(O^iPr)_{13}$ as an initiator. The lenght of the poly(ε-caprolactone) blocks was not varied (DP = 70), whereas the poly(lactide) blocks were of varying length (DP = 5 - 80). The increasing poly(lactide) content in a series of block copolymers is shown in Fig. 1.

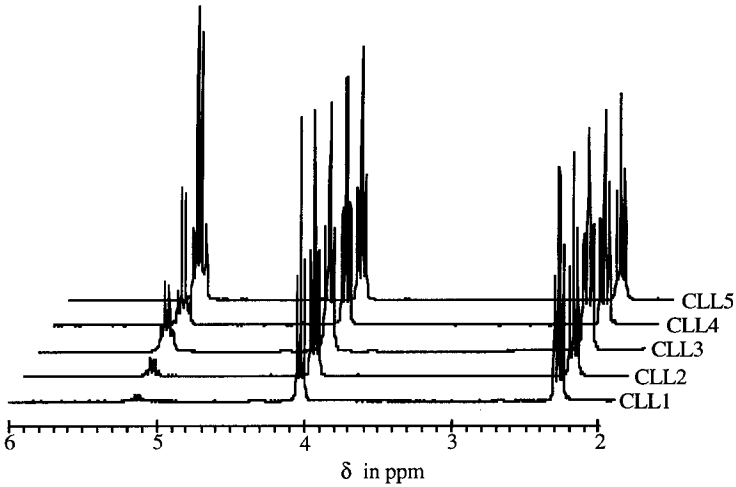

Fig. 1. Detail of ^1H NMR spectra of polymers CLL1 to CLL5 showing increasing amounts of poly(lactide) in the polymers from the signal at δ = 5.15 ppm (methine proton). Other signals at δ = 4.05 and 2.30 are assigned to the α- and ε-methylene group of the poly(ε-caprolactone), respectively.

The synthesis of poly(ε-caprolactone-*b*-L-lactide)s using $Y_5(\mu\text{-}O)(O^iPr)_{13}$ as an initiator was already described in some detail (Ref. 9). Results for poly(ε-caprolactone-*b*-D-lactide)s are very similar, only minor differences in molecular weights were observed and no significant difference in the weight composition of the polymers was found. Racemization of chiral lactyl units or transesterfication reactions between the blocks are

absent in this synthetic method, which has some characteristics of living polymerization. Detailed results of the polymerization reactions are presented in Tab. 1.

Tab. 1. Results of block copolymerization of ε-caprolactone (C) and L-lactide (LL) or D-lactide (DL) in dichloromethane using yttrium isopropoxide as a catalyst

No.	$\bar{M}_{n,calc}$[a] *10^{-3} (g/mol)	$\bar{M}_{n,NMR}$[b] *10^{-3} (g/mol)	$\bar{M}_{n,GPC}$[c] *10^{-3} (g/mol)	$\bar{M}_w/\bar{M}_n$
CLL1	7.3	9.8	11.4	1.20
CLL2	7.9	11.3	12.8	1.18
CLL3	10.1	12.6	13.2	1.25
CLL4	12.7	15.7	15.2	1.27
CLL5	19.2	18.8	18.4	1.26
CDL1	7.3	8.7	11.5	1.27
CDL2	7.9	9.5	12.6	1.22
CDL3	10.1	11.1	14.7	1.23
CDL4	12.7	14.5	17.3	1.23
CDL5	19.2	19.5	22.5	1.19

a) $\bar{M}_{n,calc}$ was calculated assuming that all isopropoxide groups are active in initiation and was corrected for monomer conversion (Ref. 9)

b) as determined by ^{1}H-NMR end group analysis

c) as determined by GPC analysis using the universal calibration principle

Binary blends of these polymers were prepared by combining equimolar amounts of polymers with similar composition in a 1:1 ratio in chloroform solution. After precipitation in diethyl ether the thermal properties of the blends and of the synthesized block copolymers were determined by DSC. Melting temperatures and melting enthalpies are presented in Tab. 2. Glass transition temperatures are not detected because the T_g of poly(L-lactide) coincides with the melting peak of poly(ε-caprolactone) and the T_g of poly(ε-caprolactone) is below the temperature range studied. As can be expected for a block copolymer, two melting peaks, each for one polymer phase, are detected. The data for each pair of L- and D- polymers are very similar, and small differences may reflect slight differences in composition or are within the accuracy of the measurement.

Tab. 2. Composition, melting temperatures and melting enthalpies of block copolymers CLL1 to CLL5[a)]

No.	PLA (wt.-%)	$T_{m,PCL}$ (°C)	$T_{m,PLA}$ (°C)	ΔH_{PCL} (J/g)	ΔH_{PLA} (J/g)
CLL1	11	70	-	114	-
CLL2	22	64	-	132	-
CLL3	45	62	129	125	27
CLL4	59	64	143	101	46
CLL5	72	57	154	85	58
CDL1	11	63	-	130	-
CDL2	21	64	-	130	-
CDL3	42	63	128	108	36
CDL4	58	57	145	105	55
CDL5	74	53	154	65	58
SC1	11	67	-	116	-
SC2	22	63	-	123	-
SC3	44	59	180	118	55
SC4	59	58	203	115	73
SC5	73	56	212	63	81

[a)] properties bearing a PLA subscript relate to the poly(lactide) phase, a PCL subscript relates to the poly(ε-caprolactone) phase

Crystallization of the PCL phase occurs in all polymers studied in contrast with the crystallization of the PLA phase, which does not occur in polymers containing less than 40 wt.-% PLA, which in this case corresponds to about 40 lactyl units. In block copolymers of poly(ethylene glycol) and poly(lactide) of comparable molecular weight the minimum poly(L-lactide) block length for crystallization was found to be around 40 lactyl units as well (Ref. 10). The polymers which contain a crystalline PLA phase, show increasing melting temperatures and melting enthalpies with increasing PLA content, but the melting temperatures of the poly(L-lactide) block in the polymers having the highest $\bar{M}_n$ (CLL5 and CDL5) (155 °C) are still considerably lower than that of the corresponding homopolymer (170 °C). This could indicate imperfect crystallization or formation of smaller crystallites due to incorporation of poly(ε-caprolactone) segments or amorphous poly(lactide) regions in the lattice.

The DSC traces of the blends differ largely from those of the separate block copolymers. Second heating curves of polymers with a crystalline PLA phase are presented in Fig. 2.

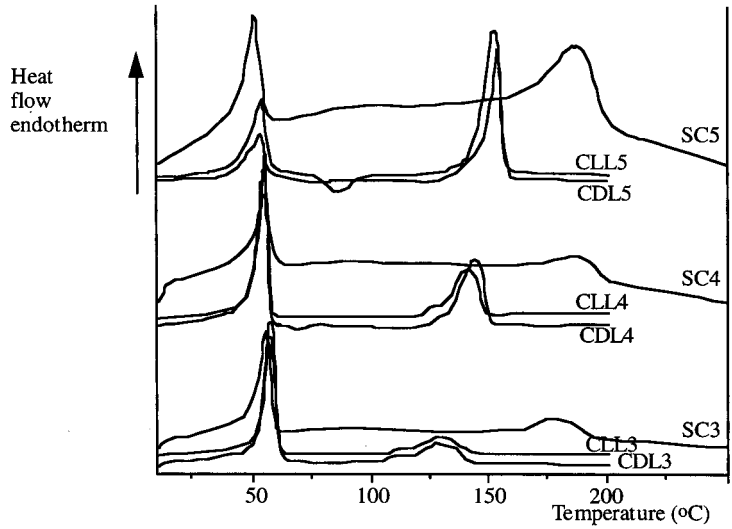

Fig. 2. Thermal properties of blends and block copolymers having a crystalline PLA phase.

The melting point of the PLA phase is increased by approximately 55 °C independent of the composition of the polymers. The sharp increase in melting temperature has been shown to be related to the crystallization of PLA blocks in a racemic lattice, or stereocomplex formation (Ref. 5). The phase behaviour of the PCL phase seems to be unaffected by the stereocomplex formation. Also, the critical PLA blocklength for (co)crystallization seems to be unchanged in the blends. Interestingly, the stereocomplex formation has an effect on the melting enthalpy of the PLA phase in contrast with blends of PLLA and PDLA (Ref. 11). It is not clear whether the increase in melting enthalpy in the stereocomplexes in this case indicates a higher degree of crystallinity or a higher ΔH_∞, because there is considerable scatter in the literature values of ΔH_∞ for PLLA and racemic PLA crystallites. If the crystallinity is increased in these blends, this is probably due to the multi-phase character of the materials allowing a more extensive crystallization by more efficient packing of the racemic crystallites forcing out the second phase.

EXPERIMENTAL PART

Reagents: L(-)-lactide and D(+)-lactide (Purac Biochem b.v., the Netherlands) were used as received. ε-Caprolactone (Merck-Schuchardt, Darmstadt, Germany) was dried over calciumhydride and distilled prior to use. Yttrium isopropoxide (Aldrich, Brussels, Belgium) was washed with toluene and filtered to remove insolubles and dried for 48 h at 35 °C *in vacuo* and stored in a dry-box under nitrogen. Toluene was distilled from sodium benzofenonketyl and dichloromethane was distilled from calciumhydride prior to use. All manipulations were carried out in an inert nitrogen or argon atmosphere.

Block copolymerizations of ε-caprolactone and lactide: Polymerizations were carried out in a Braun 150 GI dry-box. To a solution of 4.28 g (37.5 mmol) ε-caprolactone in 40 mL of dichloromethane 5.0 mL of a 0.05 M solution of yttrium isopropoxide in toluene was added, corresponding to a mole ratio of monomer to initiator ([M]/[I]) of 150. Polymerization commenced at once and after 4 minutes a sample was taken for characterization of prepolymer followed by the addition of an appropriate amount of a 0.1 M solution of lactide in dichloromethane. The conversion of lactide in time was followed by ^{1}H-NMR spectroscopy. To limit the reaction time the polymerization was quenched at 75 % conversion by the addition of an equal volume of a 0.1 HCl solution. The organic phase was collected, solvents were removed under reduced pressure and the product was dried (70 °C) *in vacuo*. The white solid obtained was dissolved in chloroform and precipitated in a 10 fold excess of cold methanol and dried again.

Blend preparation: A chloroform solution containing equal amounts of PLLA/PCL and PDLA/PCL polymers (10 wt.-%) was stirred for 72 hours. The mixture was precipitated in a ten fold excess of well stirred diethyl ether and dried overnight *in vacuo*.

Characterization: The number-average degree of polymerization of ε-caprolactone and L-lactide or D-lactide was determined by ^{1}H-NMR end group analysis. ^{1}H-NMR spectra were recorded on a Bruker AC 250 operating at 250 MHz (^{1}H) or 62.5 MHz (^{13}C). Gel permeation chromatography (GPC) was used to determine molecular weights and molecular weight distributions ($\bar{M}_w/\bar{M}_n$). GPC measurements were carried out with THF as the eluent (2.0 mL/min) using a Waters 510 pump, a HP 1050 autosampler, four Waters μStyragel columns (10^5, 10^4, 10^3, 5 x 10^2) in series, a Waters 410 differential refractometer, and a Viscotek Viscometer Detector H502. The columns were calibrated with poly(styrene) standards using the universal calibration technique. Thermal analysis of polymers was carried out with a Perkin-Elmer DSC7 differential scanning calorimeter calibrated with pure indium. The polymers were heated from - 20 °C to 200 °C

(homopolymers) or 250 °C (blends) at a heating rate of 20 °C/min, annealed for 1 minute and slowly cooled to -20 °C, whereafter a second heating curve was recorded.

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