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Crosslinked poly(L-lactide) and poly(ε-caprolactone)

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Several methods of introducing crosslinks into poly(L-lactide) (PLLA) were studied. Electron beam irradiation was not effective in crosslinking PLLA, and, moreover, caused severe polymer degradation and embrittlement of the material. Peroxide crosslinking of PLLA with dicumyl peroxide (DCP), however, resulted in gelation. At high peroxide concentrations (13–25 wt%) and high curing temperatures (192°C), a gel fraction equal to 1 could be determined gravimetrically. Peroxide crosslinking with DCP caused chemical modification of the PLLA polymer chain, with the decomposition products having a plasticizing effect on the resulting network. For the *in situ* crosslinking, a tetrafunctional monomer, 5,5′-bis(oxepane-2-one) (5,5′-BO), was synthesized and used in the copolymerization with ε-caprolactone and L-lactide. Differential scanning calorimetry (d.s.c.) and swelling experiments showed that network formation did take place. A pronounced difference in reactivity between the L-lactide and the 5,5′-BO crosslinker was observed, with this difference in reactivity being found to be comparable to the difference between L-lactide and ε-caprolactone. Swelling experiments carried out with crosslinked PLLA showed that incorporation of this crosslinker into the polymer network increased at higher polymerization temperatures and longer polymerization times. When 1 mol% of crosslinker was used in the copolymerization with L-lactide, a significant increase in the impact and tensile strength was obtained when compared to uncrosslinked PLLA. Copyright © 1996 Elsevier Science Ltd.

(Keywords: crosslinking; poly(L-lactide); poly(ε-caprolactone))

INTRODUCTION

A number of ways have been reported to influence the physical properties of polylactones, such as variation of the (co)polymer composition, the polymerization conditions and/or the processing conditions. In this way, polymers ranging from fully amorphous to semicrystalline rubbers or glassy materials with either a low or an extremely high molecular weight have been obtained. The crosslinking of homo- and copolymers of linear polylactones would add an extra possibility to the ways of modifying the physical and mechanical properties of these materials.

By introducing crosslinks into polylactones physical properties such as the crystallinity, the melting point and the glass transition temperature will be influenced. The characteristics of the degradation by hydrolysis of these biodegradable polymers will in turn also be influenced. Certain mechanical properties, such as the creep resistance and high-temperature dimensional stability, are in general improved by crosslinking. These properties are very important in (biomedical) applications, especially when amorphous rubbers are to be used. Furthermore, the modulus, tensile strength and impact strength of the polymer will be affected by crosslinking, either directly or indirectly.

In this present study three methods of introducing crosslinks into polylactones were investigated. First, the capability of high-energy electrons in crosslinking poly(L-lactide) was studied. This type of radiation has been used for the crosslinking of a great number of polymers. In relation to the biomedical applications of polylactones this method is particularly interesting because of its possible additional application in sterilization procedures[1].

As was the case with high-energy electron beam irradiation, peroxide crosslinking was shown to be effective with numerous polymers. Because of the good results achieved with poly(ε-caprolactone)[2] this appeared to be a promising method for the crosslinking of other polylactones.

A different method to those previously described, where linear polymer chains are crosslinked to form a network, is copolymerization of the lactone monomers with a multifunctional monomer. Up until now this method of crosslinking has only been studied for amorphous polylactones with a low glass transition temperature[3,4]. For this present study we have synthesized a new bis-lactone, namely γ,γ'-bis(ε-caprolactone) or 5,5′-bis(oxepane-2-one) (in short 5,5′-BO) and used it for the preparation of poly(L-lactide) and poly(ε-caprolactone) networks.

EXPERIMENTAL

Chemicals

L-Lactide (LLA) (Purac/Biochem, Gorinchem, The Netherlands) was recrystallized from sodium-dried,

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freshly distilled toluene. ε-Caprolactone (ε-Cl) (Janssen Chimica, Beerse, Belgium) was dried and distilled over calcium hydride at reduced pressure prior to use. All other chemicals were used as received.

Synthesis of bis(4-cyclohexanone)

Bis(4-cyclohexanone) was prepared according to the (slightly modified) procedure of Wilds *et al.*[5]. In this, 20 g of finely powdered bis(4-cyclohexanol) (a gift from DSM Research, Geleen, The Netherlands) was suspended in 120 ml of glacial acetic acid (Janssen Chimica, Beerse, Belgium). The suspension was cooled to 10°C and a solution of 24 g of chromium (VI) oxide (Janssen Chimica, Beerse, Belgium) in 20 ml of water and 120 ml of glacial acetic acid was added over a period of 30 min, with the temperature of the reaction mixture being kept between 10 and 20°C. After stirring for another 2 h at 15°C, a mixture of 30 ml of formic acid (Merck-Schuchardt, Darmstadt, Germany) and 70 ml of water was added and the temperature was raised to 45°C. After the evolution of carbon dioxide had practically ceased (due to oxidation of the formic acid by the excess of chromium (VI) oxide) the reaction mixture was concentrated to a partly solidified syrup by using a rotary evaporator under reduced pressure. The syrup was dissolved in 400 ml of hydrochloric acid (10%) and extracted 4 times with 100 ml of chloroform. The combined organic layers were washed twice with 100 ml of hydrochloric acid (5%), passed through a paper filter to remove insoluble particles and then washed once with 100 ml of a saturated sodium bicarbonate solution. After filtration, the solution was dried overnight with sodium sulfate. The yield of the crude diketone was 15.1 g (77 mol%, m.p. 113°C). The nuclear magnetic resonance (n.m.r.) spectrum showed only small amounts of impurities. Recrystallization from carbon tetrachloride yielded a product with two distinct melting points, i.e. at 109 and 117°C (lit. 113.5–115.5°C)[5], as measured by d.s.c. ^{1}H n.m.r. ($CDCl_3$), δ (ppm): 2.398–2.208 (m, 4 H), 2.080–1.977 (m, 2 H), 1.740–1.600 (m, 1 H), 1.545–1.363 (m, 2 H).

Synthesis of 5,5′-bis(oxepane-2-one) (5,5′-BO)

The Baeyer–Villiger rearrangement of the bis(4-cyclohexanone) was carried out according to the method of Kirschke[6]. A solution of 30 g of urea hydrogen peroxide ($CO(NH_2)_2.H_2O_2$, 35 wt% H_2O_2) (Janssen Chimica, Beerse, Belgium) in 150 ml of formic acid was kept at 20°C for 2 h. Then 15.1 g of bis-(4-cyclohexanone) was added over a period of 5–10 min, during which time the temperature of the reaction mixture increased to 32°C. After 2 h at 30°C, 200 ml of water were added to the mixture, and it was then extracted 4 times with 100 ml of chloroform. After passing through a paper filter the combined organic layers were then washed with 100 ml of a saturated sodium bicarbonate solution and dried overnight with sodium sulfate. The yield of crude product was 10.1 g. Flash chromatography, according to the method of Still *et al.*[7], was used for purification. A column (4 cm in diameter, 22 cm in length) of silica gel 60 (40–63 μm) (Merck-Schuchardt, Darmstadt, Germany) was used with an eluent consisting of chloroform/ether/methanol (54/40/6, vol%). All solvents were distilled prior to use. The yield of the pure 5,5′-bis(oxepane-2-one) product was 8.0 g (overall yield 35 mol%). ^{1}H n.m.r. ($CDCl_3$), δ (ppm): 4.292 (dd, 0.5 H, $J = 12.8$, $J = 5.9$), 4.290 (dd, 0.5 H, $J = 12.8$, $J = 4.8$), 4.121 (dd, 1 H, $J = 12.8$, $J = 9.3$), 2.725–2.500 (m, 2 H), 1.900–1.698 (m, 2 H), 1.650–1.280 (m, 3 H). Melting point 174°C. Elemental analysis, found: C 63.58, H 8.04%; calculated: C 63.70, H 8.02%.

Polymerization

Bulk polymerizations were carried out with 10 to 30 g of monomer in vacuum sealed (0.1 Pa) silanized glass ampoules at specified polymerization temperatures and times. Micropolymerizations (30 mg) were performed in large volume stainless steel pans (Perkin-Elmer) sealed with silicon rubber O-rings punched from rubber sheets and carried out in a Perkin-Elmer DSC-7 calorimeter. Polymerization scans were performed at a scan speed of 2°C min^{-1}, over the temperature range from 20 to 235°C. The monomer to catalyst mole ratio in all of these d.s.c. polymerizations was 250 : 1.

Electron beam irradiation of poly(L-lactide)

PLLA was compression moulded in stainless steel moulds at 210°C and subsequently quenched. After moulding, the molecular weight (M_v) was 3.3×10^5 and the heat of fusion (ΔH_f) was 5.4 J g^{-1}. Polymer bars ($4 \times 6 \times 50\ mm^3$) were glued on to an aluminium cylinder, and the latter was then irradiated in a nitrogen atmosphere at room temperature with 3 MeV electrons by means of a Van de Graaff generator[8,9]. During irradiation the cylinder was rotated in order to ensure a homogeneous distribution of the radiation.

Dicumyl peroxide (DCP) crosslinking of poly(L-lactide)

Chloroform solutions of PLLA/DCP mixtures were dried in a Petri dish for 14 h at 40°C and a final pressure of 50×10^2 Pa. Strips of the resulting film were cured under vacuum in an oven at predetermined times and temperatures. Samples were swollen in chloroform for 1 day in order to determine the degree of swelling and the gel content.

Characterization

The thermal properties of the polymers were studied with a calibrated Perkin-Elmer DSC-7 machine; polymer samples of ca. 10 mg in weight were heated at a scan speed of 10°C min^{-1}.

Swelling experiments were performed in chloroform at room temperature. Samples of 50 to 100 mg in weight were swollen in 50 ml of chloroform for 2 weeks. The degree of swelling (q) was calculated from the weight of the swollen samples (m_s) and the weight of the dry samples (m_d), and the specific densities of the solvent (ρ_s) (1.473 g cm^{-3} for chloroform) and amorphous polymer (ρ_p) (1.248 g cm^{-3} for poly(L-lactide)[10] and 1.094 g cm^{-3} for poly(ε-caprolactone)[11]) by using the following relationship:

$$q = 1 + \rho_p[(m_s)/(m_d \times \rho_s) - 1/\rho_s] \qquad (1)$$

N.m.r. spectra of 1% (wt/vol) solutions in $CDCl_3$ were recorded on a 300 MHz Varian VXR-300 spectrometer. Scanning electron micrographs were taken from gold coated samples with an ISI-DS 130 scanning electron microscope, operating at 40 kV.

An Instron (4301) tensile tester equipped with various load cells (100 N, 5000 N) was used to determine the mechanical properties of the materials. Tensile tests were performed at room temperature with a cross-head speed of 10 mm min^{-1} and a gauge length of 25 mm (strain rate $6.67 \times 10^{-3}\ \text{s}^{-1}$). Impact testing was performed according to DIN 53453 (Dynstat) using unnotched specimens which were machined from the bulk polymers to dimensions of $2 \times 10 \times 15\ \text{mm}^3$.

The viscosity-average molecular weight (M_v) was determined with an Ubbelohde viscometer (type Oa, ASTM D-445). From the intrinsic viscosity ($[\eta]$) of the PLLA solutions in chloroform at 25°C, M_v was determined by using the following[12]:

$$[\eta] = 5.45 \times 10^{-4} \times M_v^{0.73} \qquad (2)$$

RESULTS AND DISCUSSION

Electron beam irradiation of poly(L-lactide)

Ionizing radiation such as gamma rays or electron beam irradiation is increasingly used for the sterilization of medical devices[1,12]. It would be interesting to investigate whether this type of (readily available) radiation can be used to crosslink PLLA and so modify the physical properties of the polymer. The effects on several biomedical (semicrystalline) polymers have previously been described[13–16] and from these results it can be expected that the crystallinity of PLLA will strongly influence the effect of the irradiation. It was found that irradiation of non-crystalline polyethylene[17] and poly(tetramethylene sebacate)[18] in the molten state results in a high crosslinking efficiency, while the molecular weight and the mechanical properties after irradiation of semicrystalline fibres such as polydioxanone, poly(L-lactide), polyglycolide and poly(β-hydroxybutyrate) decrease as a result of irradiation. It is believed that in these semicrystalline polymers the scissioning of the taut-tie molecules dominates the effect of the crosslinking. For this reason, crosslinking by electron beam irradiation in our experiments was performed on almost amorphous, quenched, poly(L-lactide) (see *Table 1*).

When a dose rate of $0.38\ \text{Mrad}\ \text{s}^{-1}$ is used the heat evolved caused the polymer to melt. The irradiated material was also found to contain large voids. Neither of these phenomena was observed when a lower dose rate of $0.038\ \text{Mrad}\ \text{s}^{-1}$ was used. It has been reported that the evolution of gaseous degradation products in combination with a high sample temperature can cause the formation of voids in several other polymers[19]. The production of gases in the polymer matrix will cause the formation of high-stress concentrations and strained areas[19], thus resulting in embrittlement of the material. This was observed for all of our irradiated PLLA samples.

Polylactides show a strong decrease in the molecular weight at a low ^{60}Co γ-irradiation dose (<30 Mrad)[15,20]. A previously estimated 'gel-dose' of 97 Mrad[15] was not confirmed by our results; here we used a very high dose rate and a polymer sample with a very high molecular weight. All of our irradiated PLLA samples were completely soluble, and gel formation, and therefore crosslinking, could not be observed. The ester bonds in saturated aliphatic polyesters[18] and also in poly(methyl methacrylate) (PMMA)[19] have been shown to be susceptible to degradation upon irradiation. It was suggested that for aliphatic polyesters the ratio of the backbone carbon atoms to the backbone ester groups should at least be equal to 3 in order for gel formation by irradiation to be possible[18]; for PLLA this ratio is equal to 2.

All in all the previous data indicate that high-energy irradiation is not a suitable technique for obtaining crosslinked PLLA and thus influence the physical properties of the polymer. Care should also be taken when using this type of irradiation for sterilization purposes because of the large detrimental effects on the mechanical and the chemical properties of PLLA, even at a low dose and dose rate.

Poly(L-lactide) crosslinking with dicumyl peroxide (DCP)

DCP has been shown to be a very effective crosslinking agent for a great number of polymers, among which is poly(ε-caprolactone)[2]. Preliminary experiments showed that in PLLA/DCP mixtures gel formation could be observed with DCP concentrations of 5 wt% at curing

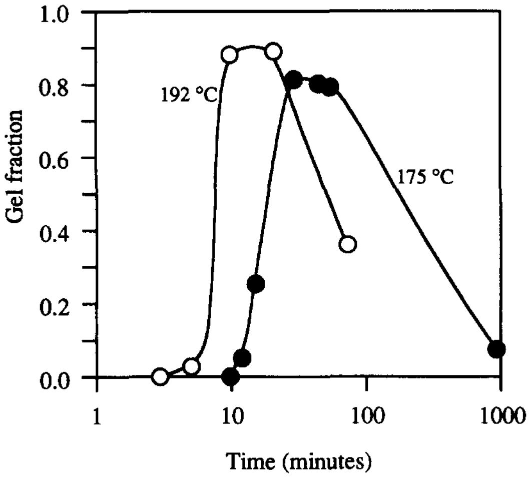

Figure 1 Gel fraction of crosslinked PLLA as a function of curing time at 192°C (5.25 wt% DCP) and 175°C (5.39 wt% DCP)

Table 1 Electron beam irradiation of poly(L-lactide)

Irradiation dose (Mrad)	Dose rate ($\text{Mrad}\ \text{s}^{-1}$)	M_v	Observations
0.0	0.0	3.3×10^5	Strong; transparent; homogeneous
5.0	0.38	4.7×10^4	Very brittle; contains large voids
50.0	0.38	–	Very brittle; contains large voids
100.0	0.38	–	Very brittle, contains large voids
5.0	0.038	5.1×10^4	Brittle; homogeneous
15.0	0.038	–	Very brittle; homogeneous

temperatures of ca. 170°C. *Figure 1* shows the dependence of gel formation on the curing temperature. At a curing temperature of 192°C a maximum gel fraction of 0.9 is obtained, while at 175°C the maximum gel fraction found is 0.8. As a result of the thermal instability of PLLA at these crosslinking temperatures, chain scissioning will also occur[21], causing the gel fraction to decrease at longer reaction times.

The ratio of chain scissioning and crosslinking can be determined by using the Charlesby–Pinner equation, adapted for chemical crosslinking, as follows[22,23]:

$$S + S^{0.5} = p/q + 1/(M_w \times [I] \times E) \qquad (3)$$

In this equation, S is the sol fraction, p and q are the fractions of the repeat units of the polymer undergoing scission and crosslinking, respectively, M_w is the weight-average molecular weight of the polymer, [I] is the decomposed peroxide concentration in moles per gram of polymer, and E is the crosslinking efficiency.

The results obtained in this work are shown in Charlesby–Pinner plots[24] (*Figure 2*). The intercept, p/q, is 0.64 at 175°C and 0.30 at 192°C, indicating that chain scission occurs under these conditions. It is important to keep in mind that at least part of the chain scissioning results from the thermal instability of the polymer. This will also influence the slope, which is given by $(M_w \times [I] \times E)^{-1}$.

Although chain scissioning occurs, a gel fraction of 1 can still be determined when higher DCP concentrations of 13 to 25 wt% are used. This is the result of side reactions occurring during the crosslinking process. At these very high DCP crosslinker concentrations, the combination of a polymer radical with a peroxy or methyl radical during crosslinking is possible[25]. This chemical modification of the polymer chain increases the weight of the crosslinked fraction and as a result the gravimetrically determined gel fraction will be too high. The presence of aromatic rings in the extracted polymer which had been crosslinked by using these high DCP concentrations was demonstrated by infra-red (i.r.) spectroscopic analysis of the PLLA network.

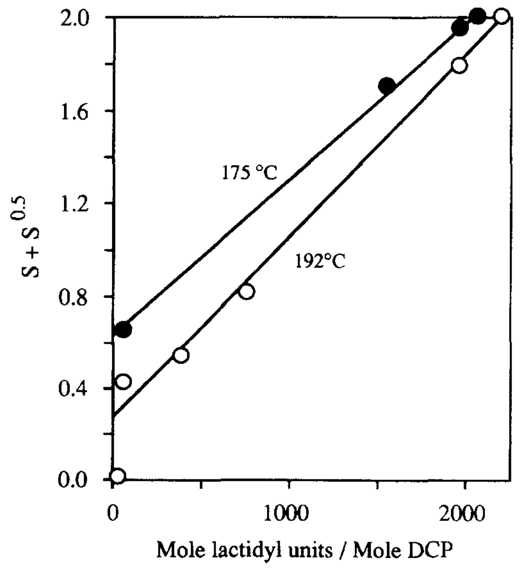

Figure 2 Charlesby–Pinner plots of the crosslinking of PLLA with DCP at 175°C for 40 min and at 192°C for 20 min

PLLA which had been crosslinked by using 25 wt% DCP at 192°C for 20 min was found to be a ductile material with a tensile strength of 18 MPa and an elongation at break of 190%. For untreated PLLA these values are close to 60 MPa and 8%. Calorimetric measurements showed a glass transition temperature of 17°C, a peak melting temperature of 147°C, and a heat of fusion of 9 J g^{-1}. Normally these values are close to 57°C, 180°C and 50 J g^{-1}, respectively, for solvent-cast PLLA. The decrease in the glass transition temperature can be attributed to the plasticizing effect of the low-molecular-weight decomposition and degradation products. The decrease of the melting temperature and the very low heat of fusion is a combined plasticizing and crosslinking effect.

Peroxide crosslinking of PLLA appears to be a suitable method for affecting the thermal as well as the mechanical properties of the polymer. However, regarding the potential biomedical applications of these materials, the method has two disadvantages. First, it was shown by i.r. spectroscopy that the PLLA polymer chain was chemically modified during crosslinking, possibly resulting in undefined degradation products during hydrolysis[26]. Secondly, because of the toxicity of many of the DCP decomposition products, e.g. acetophenone, α-methylstyrene and 2-phenyl-2-hydroxypropane[27], the final crosslinked materials will need to be thoroughly extracted. This should not be very difficult in the case of films and fibres, but might be a problem with larger and more bulky devices.

Micropolymerizations of L*-lactide, ε-caprolactone and 5,5′-bis(oxepane-2-one)*

A crosslinking method that is basically different from the previously mentioned methods is the *in situ* formation of a crosslinked polymer during polymerization of the monomers. For this purpose a tetrafunctional monomer, 5,5′-bis(oxepane-2-one) (5,5′-BO), which can be thought of as two ε-caprolactone rings joined together, was prepared and used in copolymerization with L-lactide and ε-caprolactone.

The first step in the synthesis was the oxidation of bis(4-cyclohexanol) for which several routes were evaluated. The use of pyridinium dichromate (PDC)[28] or pyridinium chlorochromate (PCC)[29] resulted in low yields of an impure product. Oxidation of the diol in a chloroform/water two-phase system by using sodium dichromate as an oxidizing agent[30] gave high yields of raw material (80–90 mol%), which unfortunately contained large amounts of non-specified impurities. Other routes using sodium dichromate or chromium(VI)oxide in butanone[31] gave yields which did not exceed 55 mol%. The most favourable route was found to be the oxidation of bis(4-cyclohexanol) by chromium trioxide in acetic acid[5] which resulted in a relatively pure bis(4-cyclohexanone) in a 77 mol% yield. The yield may depend on the diastereomeric composition of the starting diol because of the difference in reactivity of the equatorial and axial hydroxyl functionalities[5,32]. The crude bis(4-cyclohexanone) which was obtained in this manner, was subjected without further purification to a Baeyer–Villiger oxidation to form the bislactone.

The oxidation of ketones can be carried out with a great number of reagents, among which are peracids[33], hydrogen peroxide[34] or a hydrogen peroxide/carboxylic acid reagent[35]. An alternative route makes use of a solution of urea hydrogen peroxide in formic acid. In this way the handling of hazardous and unstable chemicals such as concentrated hydrogen peroxide or concentrated peracids is avoided. This reagent has been shown to be safe and capable of oxidizing cyclohexanone and substituted cyclohexanones to give product yields higher than 90 mol%[6]. In our case, oxidation with a urea hydrogen peroxide solution in formic acid resulted in a 57 mol% yield of the crude product (5,5′-BO).

Axial and equatorial methylene proton resonances in the ^{1}H n.m.r. spectrum close to 4.2 ppm showed two distinct absorptions of the equatorial hydrogen, indicating the formation of a mixture of *d*-, *l*- and *meso*-stereoisomers of 5,5′-BO. The mixture of diastereoisomers accounts for the broad melting range (150 to 174°C) and the lack of optical activity of the product.

In previous studies, it was shown that 2,2-bis(oxepane-2-one-4-yl)propane, a bislactone similar to 5,5′-BO, can copolymerize (form a network) with various other lactones[3,26]. However, it was not clear if 5,5′-BO would be able to homopolymerize or copolymerize with lactones. It was shown that in the case of bislactams minor changes in chemical structure can have a large effect on the crosslink efficiency in homo- and copolymerizations with ε-caprolactam[31,36,37]. To examine the readiness with which 5,5′-BO polymerizes, a number of micropolymerizations were carried out during a slow d.s.c. scan. The results are shown in *Figures 3* and *4* and *Table 2*. *Figure 3* shows the d.s.c. traces of the homopolymerization of ε-caprolactone and its copolymerization with 5,5′-BO (10 mol%). Curve 1 is the polymerization exotherm of ε-caprolactone and curve 2 is the thermogram of the resulting polymer; the latter clearly shows a low-temperature T_g (with an enthalpy relaxation peak) and a melting endotherm, both with values characteristic of poly(ε-caprolactone). N.m.r. spectroscopic analysis of this sample showed an ε-caprolactone conversion in excess of 99 mol%. The copolymerization with 10 mol% 5,5′-BO, which is shown by curve 3, resulted in a polymer with a higher T_g value and a lower T_m and heat of fusion ΔH_f (*Table 2*). These changes are indicative of the formation of a crosslinked polymer. This was also confirmed by the fact that the polymer obtained did not dissolve, but only swelled in chloroform. N.m.r. spectroscopic analysis of the sol fraction of the polymer showed minute amounts of ε-caprolactone, poly(ε-caprolactone) and 5,5′-BO.

The results of the homopolymerization of L-lactide and the copolymerization with 10 mol% 5,5′-BO are shown in *Figure 4*. The sharp peak in curve 1 is the melting endotherm of L-lactide, which is immediately followed by a polymerization exotherm. The thermogram of the resulting poly(L-lactide) is shown in curve 2. The polymer has T_g and T_m values which are characteristic of low-molecular-weight PLLA[38] (an M_n close to 10^4). Curve 3 shows the copolymerization of L-lactide with 10 mol% 5,5′-BO. The L-lactide melting endotherm has shifted to a lower temperature as a result of the melting-point depression due to the presence of 5,5′-BO. In curve 4 it can be seen that the resulting copolymer does not show a melting endotherm, which could be the result of the formation of a network. In addition, the polymer did not dissolve in chloroform, but was found to swell and break up into small gel particles.

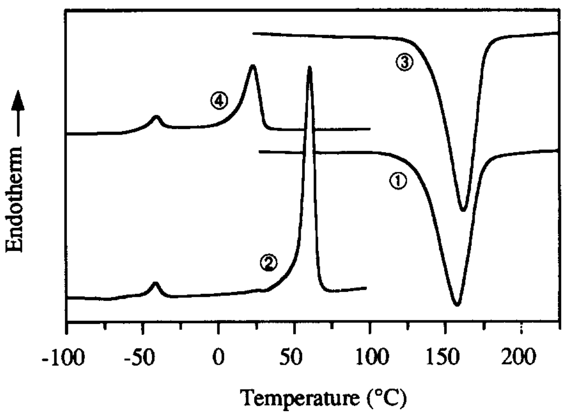

Figure 3 D.s.c. polymerization thermogram of ε-caprolactone (1) and the thermogram of the resulting poly(ε-caprolactone) (2). Curve 3 represents the polymerization of an ε-caprolactone/5,5′-BO mixture (mole ratio = 9/1), with the thermogram of the resulting network shown by curve 4

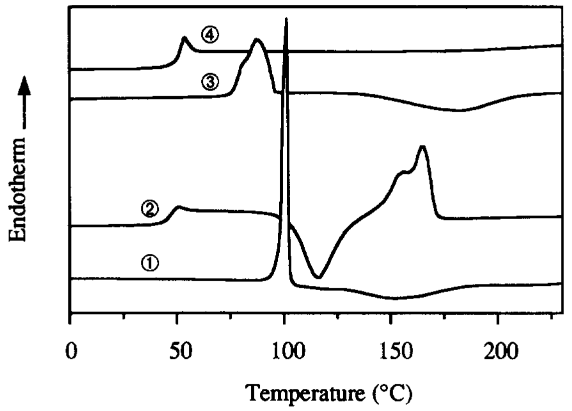

Figure 4 D.s.c. polymerization thermogram of L-lactide (1) and the thermogram of the resulting poly(L-lactide) (2). The polymerization thermogram of an L-lactide/5,5′-BO mixture (mole ratio = 9/1) and the thermogram of the resulting network are shown by curves 3 and 4, respectively

Table 2 Results obtained from the micropolymerizations shown in *Figures 3* and *4*

	ε-Cl	ε-Cl/5,5′-BO	LLA	LLA/5,5′-BO	5,5′-BO
T_p[a] (°C)	161	168	152	181	182
ΔH_p[b] (J g^{-1})	−154	−155	−100[c]	−124	–[d]
T_g[e] (°C)	−64	−57	47	51	94
ΔH_f[f] (J g^{-1})	85	33	25	0	0
T_m[g] (°C)	64	24	165	–	–

[a] Peak temperature of the polymerization exotherm

[b] Heat of polymerization

[c] Value not very accurate due to significant polymerization during melting of the monomer

[d] Not determined

[e] Glass transition temperature of the formed polymer

[f] Heat of fusion of the formed polymer

[g] Peak melting temperature of the formed polymer

In the case of the homopolymerizations of L-lactide, as well as that of 5,5′-BO, no accurate heat of polymerization could be determined because of the overlap of the monomer melting endotherm and the polymerization exotherm. As a result of the relatively high catalyst concentration, significant polymerization had taken place during the melting of the monomer.

The d.s.c. scan of the homopolymer of 5,5′-BO showed an extremely broad T_g, ranging from 35 to 130°C, which indicated a very large variation in the molecular weights between the crosslinks. When using even higher catalyst concentrations, and reaction temperatures up to 250°C, a network could be obtained without a d.s.c.-detectable T_g, which is a strong indication for a very high crosslink density[39]. These results show that 5,5′-BO can homopolymerize and can also function as a crosslinking agent in the copolymerization with ε-caprolactone and L-lactide.

Table 2 also shows that the use of 5,5′-BO in the copolymerization with L-lactide and ε-caprolactone causes the T_p to shift to higher temperatures (by 29.7 and 7.0°C, respectively), most likely as a result of the lower polymerizability of 5,5′-BO. Apparently there is a large difference in polymerizability between 5,5′-BO and L-lactide, and only a small difference with ε-caprolactone. Because of the chemical similarity between ε-caprolactone and 5,5′-BO and the previously observed difference in reactivity between ε-caprolactone and L-lactide[40,41], this is to be expected.

Bulk polymerizations of ε-caprolactone with 5,5′-bis(oxepane-2-one)

Because of the similar reactivity of 5,5′-BO and ε-caprolactone these two monomers seem to be a good model system for studying the effect of crosslinking on the thermal properties of the resulting polymer network. Chemically, the crosslinked polymer resembles poly(ε-caprolactone) which has been bridged at the 5-position of the monomer. The results of a series of bulk copolymerizations are shown in *Table 3*. None of the copolymers were soluble in chloroform, indicating that the synthesized copolymers were actually crosslinked and that the observed effects on the physical properties were not just comonomer effects.

Crosslinking of a semicrystalline polymer will hinder crystallization, which will result in a decrease of the lamellar thickness, smaller crystallites and less crystalline material. These effects will be enhanced when the concentration of crosslinks is increased. The decrease in melting point and ΔH_f as a function of the crosslink concentration is shown in *Figure 5*. Here it can be seen that in order to eliminate crystallization at room temperature (20°C), or at body temperature (37°C), a crosslink concentration of, respectively, 10 and 4.6 mol% is needed.

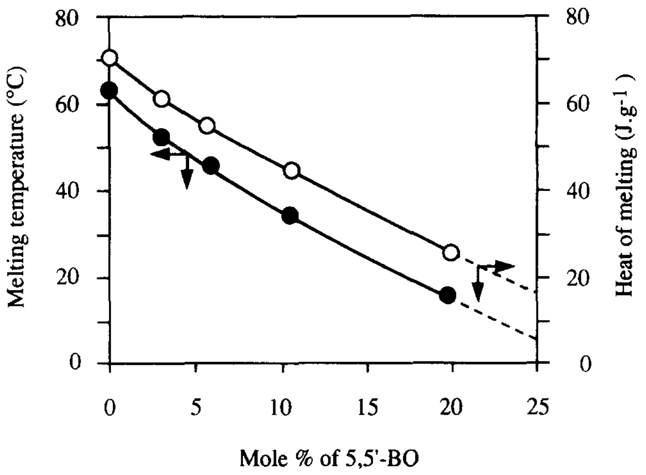

Figure 5 The peak melting temperature and the heat of fusion of poly(ε-caprolactone) which has been crosslinked with 5,5′-BO at 135°C as a function of crosslinker concentration

Table 3 Copolymerization of ε-caprolactone with 5,5′-BO[a]

5,5′-BO (mol%)	T_m (°C)	ΔH_f (J g^{-1})	T_g (°C)	ΔC_p[b] (J g^{-1} °C^{-1})
0.0	63	71	−64	0.39
1.5	52	61	−65	0.28
3.0	46	55	−64	0.33
5.6	35	45	−62	0.32
11.0	16	26	−62	0.62
20.0	–	–	−53	0.49

[a] Reactions carried out at 135°C for 90 h with a monomer to catalyst ratio of 2000 : 1; thermal history of all samples is identical (1 min at 100°C)

[b] Refers to amorphous material; corrections have been made for amount of crystalline material present

As can be seen in *Table 3* the T_g of poly(ε-caprolactone) does not seem to be influenced by crosslink concentration up to a value of 11 mol%. In a semicrystalline polymer such as poly(ε-caprolactone) the T_g is not only influenced by chemical crosslinks[42,43], but also by physical crosslinks such as crystallites[44]. The increase in chemical crosslinks will tend to increase the T_g. However, the decrease in crystallinity (the number of physical crosslinks) will have the opposite effect on T_g. Under the given conditions the net result is that T_g does not change significantly up to a crosslinker concentration of 11 mol%. The T_g of pure, amorphous poly(ε-caprolactone) is −71°C[44], meaning that the polymer samples with 11 and 20 mol% crosslinker show an increase of 9 and 18°C, respectively, in the T_g due to crosslinking. (The sample with 11 mol% 5,5′-BO is fully amorphous when quenched.)

The magnitude of ΔC_p is influenced by the length of the network chains between the crosslinks, whether they are chemical or physical crosslinks, and as a result ΔC_p will decrease with increasing concentration of crosslinks[39,45]. This can be observed in *Table 3* for the samples which have been crosslinked with 11 and 20 mol% 5,5′-BO. Both samples are completely amorphous, with the sample with the highest crosslink concentration having a lower ΔC_p. As is the case with the behaviour of T_g, the decrease of crystallinity with an increasing concentration of 5,5′-BO makes the behaviour of ΔC_p in semicrystalline crosslinked poly(ε-caprolactone) very complicated. The values for ΔC_p in *Table 3* have been corrected for the amount of crystalline material present, assuming $\Delta H_f = 139.5\,\mathrm{J\,g^{-1}}$ for 100% crystalline poly(ε-caprolactone)[46].

Bulk polymerizations of L-lactide with 5,5′-bis(oxepane-2-one)

The crosslinking of L-lactide with 5,5′-BO was studied at two polymerization temperatures, namely 110 and

Table 4 Crosslinking of L-lactide with 5,5′-BO, with reactions being carried out at 110°C for 230 h[a]

5,5′-BO (mol%)	T_m (°C)	ΔH_f ($J\,g^{-1}$)	T_{g1} (°C)	T_{g2} (°C)	ΔC_p[b] ($J\,g^{-1}\,°C^{-1}$)
0.00	195	77	–	–	–
0.10	194	85	62	–	0.09
0.20	196	82	59	–	0.09
0.35	192	81	59	–	0.09
0.50	192	74	53	64	0.10
1.00	190	60	54	64	0.16
1.50	187	57	54	61	0.18

[a] Monomer to catalyst ratio of 5000 : 1
[b] Not corrected for amount of crystalline material in sample

Table 5 Crosslinking of L-lactide with 5,5′-BO, with reactions being carried out at 130°C for 72 h[a]

5,5′-BO (mol%)	T_m (°C)	ΔH_f ($J\,g^{-1}$)	T_g (°C)	ΔC_p[b] ($J\,g^{-1}\,°C^{-1}$)
0.00	197	94	–	–
0.10	196	88	58	0.08
0.20	193	84	58	0.09
0.35	195	81	57	0.09
0.50	194	81	55	0.10
1.00	192	64	56	0.16
1.50	187	50	54	0.17

[a] Monomer to catalyst ratio of 5000 : 1
[b] Not corrected for amount of crystalline material in sample

130°C. The thermal properties of these materials are shown in *Tables 4* and *5*. The two different polymerization conditions do not result in large differences in the peak melting temperature and heat of fusion of the networks that are obtained. A pronounced effect, however, is the double glass transition found in the samples synthesized at 110°C with 5,5′-BO concentrations of 0.5 mol% and higher. This indicates that the amorphous fraction of the polymer is made up of two distinct amorphous phases, i.e. one with a relatively high T_g and another phase with a relatively low T_g. It is most likely that this difference in T_g is related to differing concentrations of crosslinks in the two amorphous phases as a result of reactivity differences between L-lactide and 5,5′-BO. The trend in the changes of T_m and ΔH_f are similar to those of crosslinked poly(ε-caprolactone). At higher crosslinker concentrations, the melting temperature T_m decreases, as does the total amount of crystalline material, with this being reflected by the decrease in ΔH_f. The decrease in T_g with increasing crosslinker concentrations also reflects the decrease of the total amount of physical and chemical crosslinks, as previously discussed for crosslinked poly(ε-caprolactone). However, ΔC_p could not be corrected for the amount of crystalline material as no accurate value of the heat of fusion of 100% crystalline PLLA is known[47]. Because of this, no correlation can be made between the change in crystallinity and the change in ΔC_p.

Polymerization carried out at these two different temperatures results in small but significant differences in the degree of swelling of the PLLA networks that are obtained, as is shown in *Table 6*. In the sol fractions of PLLA that are crosslinked with 5,5′-BO at these temperatures the presence of minute amounts of L-lactide, PLLA and 5,5′-BO could be demonstrated by n.m.r. spectroscopy. The amounts present, however, were too small to accurately determine the concentrations of the components. This shows that although the crosslinker is present in small amounts, its lower reactivity inhibits full incorporation into the polymer. At higher polymerization temperatures the incorporation of the crosslinker is more efficient. This is shown in *Table 6* where an increase in the polymerization temperature results in a lower degree of swelling, thus indicating an increase in the concentration of crosslinks. The molecular weight of the polymeric sol fraction, determined by gel permeation chromatography (g.p.c.), reflects the decreasing molecular weight between the crosslinks with increasing polymerization temperatures. For a 5,5′-BO concentration of 1 mol% the M_n of the sol fraction of the obtained PLLA network is 114 000 at 110°C and 34 000 at 130°C. It can be anticipated that the sol fraction of the polymer will be branched to some extent, with this meaning that the M_n values determined by g.p.c. will deviate from the true

Table 6 Degree of swelling in chloroform of crosslinked PLLA polymerized under different conditions

5,5′-BO (mol%)	Degree of swelling: PLLA 1[a]	Degree of swelling: PLLA 2[b]
0.10	274	135
0.20	127	91
0.35	83	71
0.50	–[c]	45
1.00	25	20
1.50	16	13
3.00	–[c]	10

[a] Polymerized at 110°C for 230 h
[b] Polymerized at 130°C for 72 h
[c] Not determined

Table 7 Degree of swelling in chloroform of crosslinked PLLA polymerized at 130°C for 72 h and 120 h

5,5′-BO (mol%)	Degree of swelling: 72 h	Degree of swelling: 120 h	Gel fraction: 72 h	Gel fraction: 120 h
0.10	135	122	72.4	87.2
0.20	91	62	96.0	97.3
0.35	71	33	97.2	99.6

Table 8 Impact and tensile strengths of PLLA crosslinked in bulk with 5,5′-BO under different conditions

5,5′-BO (mol%)	PLLA 1[a]: Impact strength ($kJ\,m^{-2}$)	PLLA 1[a]: Tensile strength (MPa)	PLLA 2[b]: Impact strength ($kJ\,m^{-2}$)	PLLA 2[b]: Tensile strength (MPa)
0.00	14	55	5	28
0.10	18	54	11	45
0.20	10	54	14	49
0.35	11	52	16	2
0.50	23	58	–[c]	–[c]
1.00	24	61	14	56
1.50	14	62	16	–[c]
3.00	5	47	6	48

[a] Polymerized at 110°C for 230 h
[b] Polymerized at 130 °C for 72 h
[c] Not determined

molecular weight of the sol fraction. Because of such a large difference in the molecular weights of the sol fractions, however, we assume that there are much lower molecular weights between the crosslinks at higher polymerization temperatures.

The decrease of the degree of swelling and the increase of the gel fraction with increasing polymerization times, shown in *Table 7*, are the results of two mechanisms. First, the conversion of crosslinker will increase at longer reaction times. Secondly, partly reacted crosslinker will further react through transesterification reactions, which further increase the concentration of crosslinks. The values for the degree of swelling and the gel fraction shown in *Table 7* also reflect the difference in reactivity of 5,5′-BO and L-lactide, which was already evident from the d.s.c. experiments.

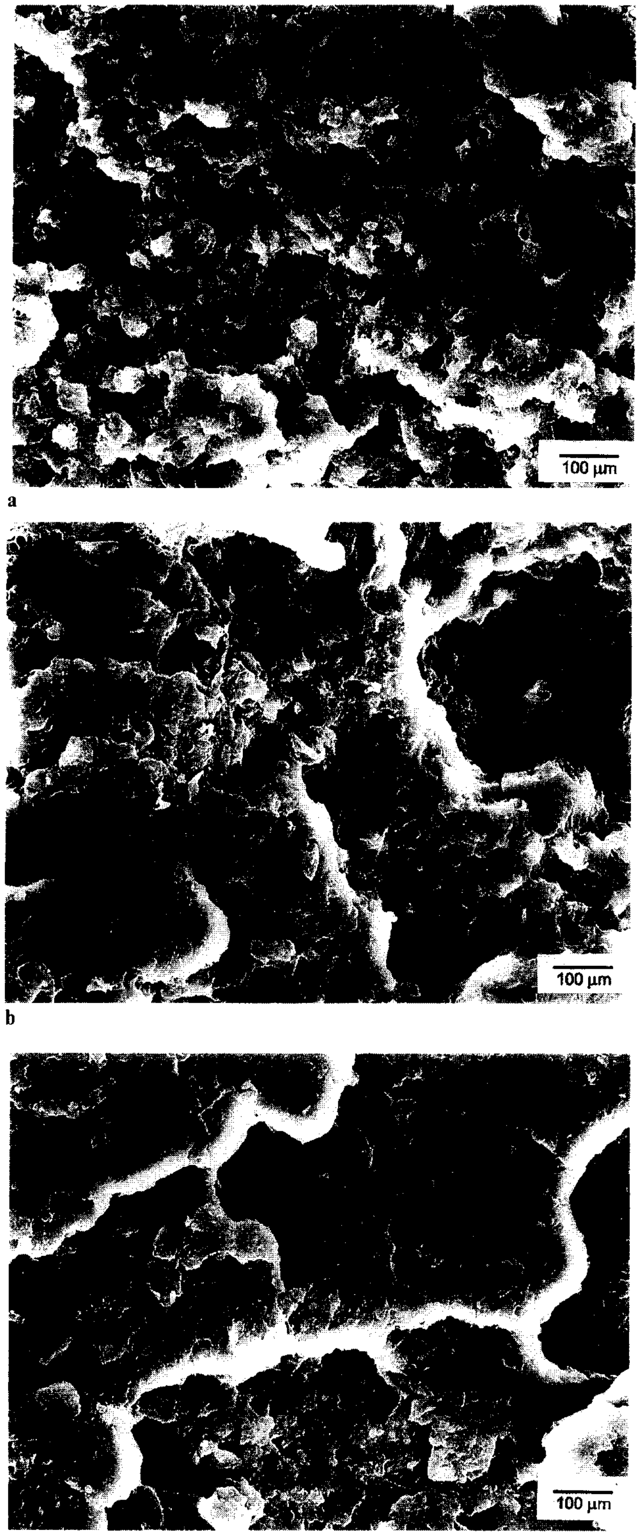

Figure 6 Fracture surfaces of PLLA with different amounts of crosslinker: (a) 0.5; (b) 1.0; (c) 1.5 mol% (samples polymerized at 110°C for 230 h). It can be seen that the fracture surface changes from a granular to a more glass-like structure

The mechanical properties of linear and crosslinked bulk-polymerized PLLA are shown in *Table 8*. Although the differences are not very large there is an increase in the mechanical properties of PLLA networks containing close to 1 mol% 5,5′-BO. For the polymerization at 130°C, crosslinking significantly increases the mechanical properties, compared to linear PLLA. At crosslinker concentrations higher than 1.50 mol%, the mechanical properties deteriorate sharply due to the presence of cracks in the polymer that have appeared during the polymerizations.

The slightly improved mechanical properties at 1 mol% of crosslinker are accompanied by a decrease in crystallinity and an increase in ΔC_p (*Tables 4* and *5*). The fracture surface of the materials changes from a granular surface to a more smooth, glass-like fracture surface as shown in *Figure 6*. The improvement in mechanical properties is most likely to result from the loss of sharp grain boundaries and a broadening of the crystalline–amorphous interphase[48]. When the crystallinity is increased again by longer annealing times, or longer polymerization times, we observed significant deterioration of tensile and impact strengths. An increase in crystallinity will result in sharper grain boundaries and this induces internal stresses which will lower the energy necessary for crack growth.

These results suggest that the optimum mechanical properties of these materials can be obtained at low polymerization temperatures and at as short as possible polymerization times with a crosslinker concentration close to 1 mol%.

CONCLUSIONS

Electron beam irradiation of amorphous PLLA did not result in crosslinking of the polymer. During irradiation there was a strong decrease in the molecular weight. This was also observed for a number of other polyesters with a relatively high concentration of ester groups in the backbone. The embrittlement of the polymer, which is observed in all of the irradiated PLLA samples, is most likely to be a combined result of the molecular weight decrease and the formation of gaseous degradation products in the polymer matrix. It would be interesting to see if these problems can be overcome by using poly(ε-caprolactone) or its copolymers. These polymers have a lower concentration of ester groups in the backbone and lower glass transition temperatures.

Peroxide crosslinking with DCP proved to be effective in the crosslinking of PLLA. The crosslinking resulted in a ductile material. During the crosslinking some chain scission occurred as a result of the high curing temperatures. Use of peroxides with lower decomposition temperatures than DCP should decrease the rate of chain scission and increase the gel fraction in relation to the peroxide concentration used. In addition, the use of an aliphatic peroxide could partly solve the problem of the possibly toxic decomposition products which are formed when using an aromatic peroxide such as DCP.

The tetrafunctional 5,5′-bis(oxepane-2-one) is an excellent crosslinker for lactones. The mechanical properties of as-polymerized PLLA, i.e. the impact and tensile strengths, improve when L-lactide is crosslinked with 1 mol% 5,5′-BO. When the PLLA is annealed at 130°C, the crystallinity increases and the mechanical properties deteriorate. Incorporation of the crosslinker into the polymer network increases at higher polymerization temperatures. Optimal mechanical properties of crosslinked PLLA are obtained at relatively low polymerization temperatures and short polymerization times.

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