Poly(L-lactide) crosslinked with spiro-bis-dimethylene-carbonate

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Poly(L-lactide) and other poly(lactones) can be crosslinked by ring opening polymerization of the corresponding cyclic esters in the presence of a tetrafunctional bicyclic biscarbonate. Spiro-bis-dimethylene-carbonate was synthesized from pentaerythritol and diethylene-carbonate and used to prepare polyester networks for use in biomedical applications. Bulk copolymerization of L-lactide with only small amounts of this crosslinker leads to networks with very high gel percentages of up to 100%. The initial crystallinity of these crosslinked poly(L-lactides), as well as the melting temperature, is very much reduced when compared with the homo poly(L-lactide). The degradation of the polymer *in vivo* is therefore expected to be enhanced and more benign at longer durations. Tensile strength and impact resistance are also greatly influenced by copolymerization with spiro-bis-dimethylene-carbonate. Much tougher and stronger materials can be obtained in this way. These favourable properties allow the material to be used in the preparation of degradable implants such as fracture fixation devices.

INTRODUCTION

The synthesis and properties of poly(L-lactide) homo- and copolymers have received considerable attention recently[1-3]. The hydrolysability to non-toxic degradation products makes these materials suitable for use in resorbable surgical implants. A great number of degradable biomedical products have already been developed and are commercially available; examples are Maxon, Dexon, Vicryl and PDS, while new materials, designs and applications are continuously being explored[4-7].

Poly(L-lactide) (PLLA), as-polymerized, was found to be a strong and tough material, to be used in plates and screws for the fixation of bone fractures in maxillofacial surgery. As the devices are degradable in the body, problems related to the use of metallic devices could be by-passed[8]. After *in vitro* degradation tests and animal *in vivo* experiments on sheep and dogs[9-11], a number of patients were operated upon[12]. Fixation of the zygomatic fracture with poly(L-lactide) plates and screws was successful in all cases and healing took place without complications. However, complete resorption of the polymer still had not taken place within a period of more than three years[13]. At this stage of the degradation large amounts of needle-like PLLA debris were found internalized within fibrocytic cells and, to a lesser degree, in lysosomes of giant cells and macrophages. These needle-like remains, with a minimal thickness of 22 nm and lengths of 1–3 μm, were highly crystalline (a heat of fusion of 96 J g^{-1}), had a molecular weight of 5000 g mol^{-1} and a degree of

dispersion of 1.17. A lamellar fold length of 22 nm corresponds to a molecular weight of 5500. This suggests that upon breakdown of the poly(L-lactide) the large and very slow degrading lamellar crystallites remain after the amorphous regions have long been hydrolysed. Etching of poly(lactide) single crystals gives comparable results[14].

The intermittent swelling that was observed at this stage of the resorption[13] may also be related to the spiked nature of the PLLA implant fragments which could puncture and damage the cell membrane. We have therefore set out not only to increase the rate of mass loss after the implant disintegrates, but also to reduce the amount of crystalline material and to reduce the lateral and longitudinal dimensions of the crystalline lamellae in the polymer. An accompanying increase in mechanical properties would enhance the safety of the fracture fixation devices. Copolymers of L-lactide with glycolide[15], ε-caprolactone and trimethylene-carbonate (TMC) have been prepared[16]. Glycolide leads to copolymers with a very rapid loss of mechanical strength and only initially an increased rate of mass loss. Copolymerization of L-lactide with more than 5 mol% of ε-caprolactone or trimethylene-carbonate significantly reduces the tensile strength and modulus of the copolymers.

A more effective way of influencing thermal properties without necessarily deteriorating the mechanical properties is by crosslinking the poly(L-lactide) chains. In poly(ε-caprolactone) copolymers, crosslinked in bulk with a tetrafunctional bis-ε-caprolactone[17], the rate of (enzymatic) degradation and the modulus could be controlled by varying the crosslink density. In our laboratory, another bis-ε-caprolactone was synthesized and copolymerized with L-lactide[18]. It was found that at low polymerization

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temperatures, the much lower reactivity of the ε-caprolactone unit in comparison with L-lactide[19] leads to inhomogeneous crosslinking. Because trimethylene carbonate is more reactive than ε-caprolactone in the ring opening copolymerization with lactide[16], a bis-TMC crosslinker should perform more satisfactorily. Spiro-bis-dimethylene-carbonate, which was synthesized and used in the crosslinking of poly(carbonates)[20], is now copolymerized with L-lactide and other lactones. As the products of hydrolytic degradation, carbon dioxide and pentaerythritol, are soluble in water and are also non-toxic[21], these compounds can be applied in biodegradable implants. The structural formulae of the cyclic monomers are given in *Figure 1*.

The preparation of spiro-bis-dimethylene-carbonate (spiro-bis-DMC) and the crosslinking of lactones by copolymerization with it are discussed. The effect of crosslinking on the swelling and thermal properties of poly(L-lactide), as well as on the mechanical properties will be illustrated.

MATERIALS AND METHODS

Spiro-bis-dimethylene-carbonate synthesis

Spiro-bis-DMC was prepared according to the patent literature[20]. Pentaerythritol (12.5 g) was finely powdered and brought into a three-necked flask containing a sevenfold excess of diethylene-carbonate (75.9 g) and 0.1 wt% potassium carbonate as a catalyst. By heating in an oil bath at 120°C, ethanol was slowly distilled off, while at the same time pentaerythritol dissolved. After the calculated amount of ethanol had been distilled off, the excess diethylene-carbonate was removed by gradually increasing the temperature to 150°C. The soluble polycondensate thus formed was dissolved in dichloromethane from which the catalyst was removed by washing with 2 n HCl and water.

After drying with Na_2SO_4, the depolymerization catalyst stannous octoate (0.1 wt%) was added and mixed in the solution. Dichloromethane was removed by evaporation, and the polycondensate was turned into a network by further distilling off diethylene-carbonate at

150°C and a pressure of 10 mmHg. The insoluble network was crushed and placed in a sublimation apparatus. At a temperature of 240°C and 0.003 mmHg spiro-bis-dimethylene-carbonate slowly sublimated. The total yield was ca. 50%.

Spiro-bis-DMC is insoluble in ordinary organic solvents, and was purified by washing with dichloromethane. The synthesized product was characterized by *F T*i.r. analysis (KBr disc) on a Mattson GL6021 spectrometer and ^{1}H- and ^{13}C n.m.r. spectra were recorded in deuterated dimethylsulphoxide (DMSO $\delta = 2.50$ ppm) on a Varian 300-NMR spectrometer. Mass spectra were obtained on an AEI MS9 mass spectrometer operated at 70 eV and 110°C.

Elemental analysis of the purified spiro-bis-DMC resulted in the following values for C: 44.60% and H: 4.31%. (Theoretical values are C: 44.69%, H: 4.38% and O: 50.91%.)

Polymerization

L-lactide and D,L-lactide (CCA/PURAC BIOCHEM, the Netherlands), ε-caprolactone (Janssen, Belgium) and trimethylene-carbonate (TMC) (synthesized from propanediol and diethylene-carbonate[22]) were purified according to standard procedures[1,16,19].

All copolymerizations of spiro-bis-DMC with lactones (20–30 g) were carried out *in vacuo* in the monomer melt at 110°C, unless mentioned otherwise. The polymerization time was seven days and the catalyst (1×10^{-4} mole/mole of monomer) stannous octoate (Sigma, USA) was used without further purification.

Characterization of crosslinked poly(L-lactide)

Swelling experiments on crosslinked poly(L-lactide) were carried out at room temperature (22°C). The degree of swelling was measured by weighing network samples before and after a swelling period of two days. Equilibrium swelling was usually reached within 24 hours. The swelling volume was calculated using the following densities: chloroform 1473 kg m^{-3} and poly(L-lactide) 1248 kg m^{-3} (see ref. 14).

Gel percentages were determined gravimetrically after drying the swollen gels for a period of two days at ambient conditions, followed by a seven-day drying period *in vacuo* at 100°C.

Thermal characterization was carried out by differential scanning calorimetry on a calibrated Perkin-Elmer DSC-7. Samples of 5–10 mg were heated at a scanning rate of 10°C min^{-1}.

Tensile strength was measured on an Instron 4301 tensile tester at room temperature. Specimens $4 \times 6 \times 50$ mm^3 were machined from the crosslinked poly(L-lactide) and subjected to tensile testing. The distance between the clamps was 25 mm and the testing speed was 10 mm min^{-1}.

Impact testing was performed on unnotched specimens of crosslinked material, machined to $2 \times 10 \times 15$ mm^3 according to DIN 53453 (Dynstat). A 1 J hammer was employed.

Membrane osmometry measurements of poly(L-lactide) in chloroform were performed on a Knauer membrane osmometer equipped with a regenerated cellulose membrane. The concentrations of the solutions were in the range of 1–10 kg m^{-3}. The Flory–Huggins interaction parameter χ was determined from the second virial coefficient[23].
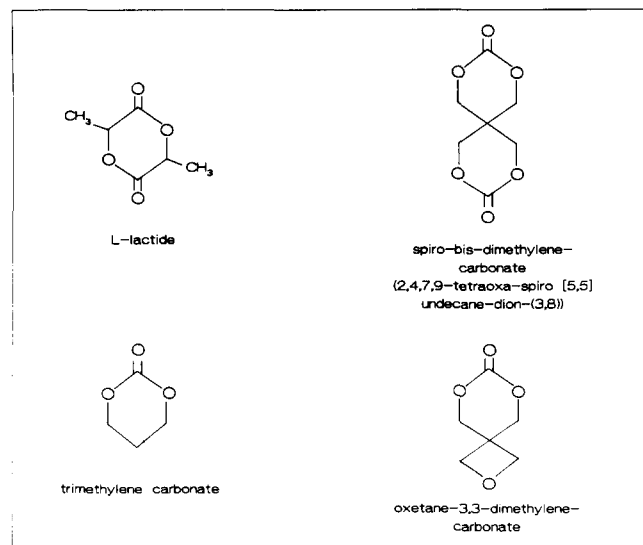

Figure 1 Structural formulae of cyclic esters and carbonates used in the preparation of networks by ring opening copolymerization

Viscosity average molecular weights of poly(L-lactide) were determined at 25°C in chloroform using the relation: $[\eta] = 5.45 \times 10^{-4} M_v^{0.73}$.

RESULTS AND DISCUSSION

Spiro-bis-dimethylene-carbonate synthesis

The synthesis of spiro-bis-dimethylene-carbonate (*Figure 1*) as described by Krimm and Buysch[20] is laborious but successful. Starting from pentaerythritol and diethylene-carbonate a bicyclic biscarbonate can be prepared in a three-step process. In principle, a polycondensate network of pentaerythritol and diethylene-carbonate is prepared which, upon depolymerization, gives spiro-bis-dimethylene-carbonate.

First, a soluble polycondensate of pentaerythritol and a large excess of diethylene-carbonate is prepared by transesterification in the presence of K_2CO_3. Ethanol is distilled off. In order to obtain the bicyclic biscarbonate in the depolymerization stage, it is necessary to remove the strong transesterification catalyst and replace it with a less active one such as stannous octoate. This removal is effectively done by washing the polycondensate solution in dichloromethane with acid solutions.

Distillation of the excess diethylene-carbonate at low pressures (10 mmHg) and 150°C results in the formation of an insoluble network. Depolymerization of the network at high vacuum and 240°C leads to slow sublimation of spiro-bis-dimethylene-carbonate, a white crystalline material.

If, in the first step, K_2CO_3 is replaced by stannous octoate, the transesterification does not take place at all. The presence of K_2CO_3 in the depolymerization step, however, is undesired, as the decarboxylation which then occurs will mainly lead to the formation of side products such as oxetane-3,3-dimethylene-carbonate (*Figure 1*).

Purification of spiro-bis-DMC is done by washing with dichloromethane, which is a good solvent for oxetane-3,3-dimethylene-carbonate and a very poor one for spiro-bis-DMC.

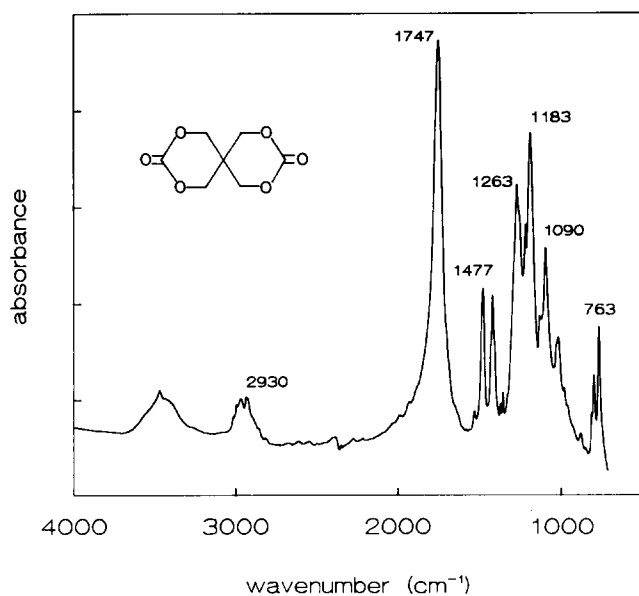*Figure 2* shows the unsmoothed infra-red spectrum of the resulting spiro-bis-DMC. Most obvious is the strong
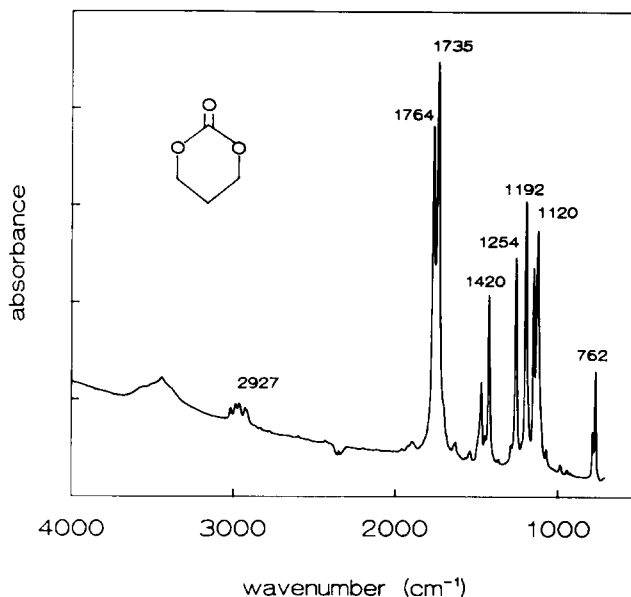

Figure 3 The *FT*i.r. spectrum of trimethylene-carbonate (KBr disc)

absorption band due to the C=O stretch vibration that can be discerned at 1747 cm^{-1}. The C–O stretch vibration of the ester group gives strong bands at 1090, 1183 and 1263 cm^{-1}. C–H stretching shows characteristic bands at 2930 and 3000 cm^{-1}, while C–H in-plane bending gives rise to absorption bands at 1416 and 1477 cm^{-1}. The band at 763 may also be due to –CH$_2$– vibrations. The characteristic oxetane band at 980 cm^{-1} is not present. The spectrum shows very close resemblance to the i.r. spectrum of trimethylene-carbonate, which is shown in *Figure 3*.

All corresponding stretching and bending vibrations can be found in the TMC spectrum, although the bands are shifted to some extent. The characteristic peaks due to the C=O can be found at 1764 and 1735 cm^{-1}, C–H stretching and bending gives rise to absorptions at 3000, 2927, 1475, 1420 and 762 cm^{-1}. The C–O stretch vibration absorption bands can be found at 1254, 1192 and 1120 cm^{-1}.

^{1}H n.m.r. in deuterated DMSO shows a single peak at 4.42 ppm, and ^{13}C n.m.r. shows the presence of a carbonyl carbon atom absorbing at 154.1 ppm.

It was observed that a small fraction of the synthesized spiro-bis-DMC did not dissolve in DMSO, but only swelled. Thermal polymerization during the sublimation of spiro-bis-DMC might have taken place, resulting in the formation of small amounts of polycarbonate network.

Mass spectrometry confirmed the presence of m/e values of 188.1, corresponding to the molecular weight of spiro-bis-dimethylene-carbonate, but also showed intensities at higher m/e values, perhaps related to fragments of crosslinked or polymerized structures. D.s.c. scans did not reveal an endothermic melting peak below the decomposition temperature of 260°C.

In analogy to the copolymerization of lactones and cyclic carbonates in bulk with stannous octoate, the prepared and purified spiro-bis-DMC was copolymerized with several cyclic esters. The results of these first experiments are presented in *Table 1*.

In the course of the ring opening polymerization, spiro-bis-DMC will be incorporated into the growing

Figure 2 The *FT*i.r. spectrum of spiro-bis-DMC (KBr disc)

Table 1 Crosslinking of lactones and cyclic carbonates with spiro-bis-dimethylene-carbonate in bulk with stannous octoate as catalyst. All formed copolymers were insoluble in chloroform

Cyclic ester	spiro-bis-DMC (mol%)	Temperature (°C)	Characteristics
L-lactide	2.0	150	glass
L-lactide	4.3	110	semi-crystalline
L-lactide	1.7	110	semi-crystalline
D,L-lactide	2.0	130	glass
ε-caprolactone	1.9	110	tough, semi-crystalline
L-lactide/TMC 50/50	1.0	110	tough, low crystalline
L-lactide/TMC 98/2	1.0	110	semi-crystalline

poly(lactone) chain and thus form tetrafunctional crosslinks. Since the resulting polymers were all insoluble in chloroform, and the gel percentages were 95% or higher, it may be established that spiro-bis-DMC is an adequate crosslinker for lactones as well as for cyclic carbonates. The small amounts of insoluble but swollen spiro-bis-DMC may still contribute to the crosslinking reaction due to the occurrence of transesterification reactions.

By copolymerizing different lactones and cyclic carbonates in this manner a range of materials with varying thermal and mechanical properties can be prepared which are suitable for use in a variety of biomedical applications.

When used in load bearing devices such as bone plates and screws, the materials need to be strong, rigid, and tough. Polymerization and crosslinking of D,L-lactide results in an amorphous, glassy material with low impact strength. Polymers based on ε-caprolactone or trimethylene-carbonate have glass transition temperatures below room temperature and, unless heavily crosslinked, are perhaps more suited for the preparation of (surgical) membranes, drug delivery systems, nerve guides or artificial blood vessels. Poly(L-lactide) is more suited for the preparation of orthopaedic implants. The effect of crosslinking of L-lactide with spiro-bis-DMC was therefore studied in more detail.

Swelling of crosslinked poly(L-lactide)

When L-lactide is copolymerized with spiro-bis-DMC at a relatively low polymerization temperature of 110°C very efficient crosslinking takes place as can be deduced from *Figure 4*. In this figure the gel percentage is given as a function of the amount of crosslinker used. Even for the lowest concentrations of spiro-bis-DMC very high gel percentages are obtained. The homo-polymerization of L-lactide by the method described results in the formation of very high molecular weight PLLA. Molecular weights of up to 1×10^6 were synthesized[1]. A building-in of only a small amount of tetrafunctional comonomer will then result in almost complete gel formation. From the very high gel percentages at the lowest crosslinker concentrations it follows that spiro-bis-DMC is indeed a very successful crosslinker for L-lactide.

The degrees of swelling from the swelling experiments in chloroform are shown in *Figure 5*. The decrease in the degree of swelling, q, with an increase in crosslinker concentration follows the expected behaviour. As the crosslink density increases, the molecular weight between crosslinks (M_c) decreases, allowing for less swelling of the network to take place in good solvents. At spiro-bis-DMC concentrations higher than 2 mol% no further decrease
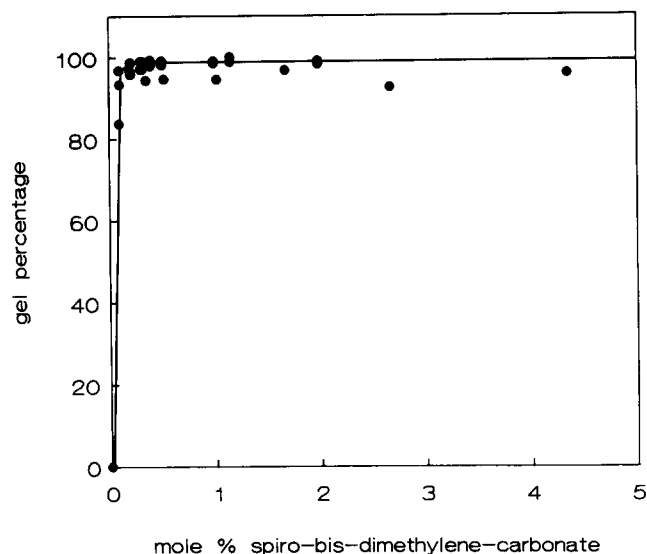
Figure 4 The gel percentage of PLLA networks crosslinked in bulk with spiro-bis-DMC, as a function of crosslink density
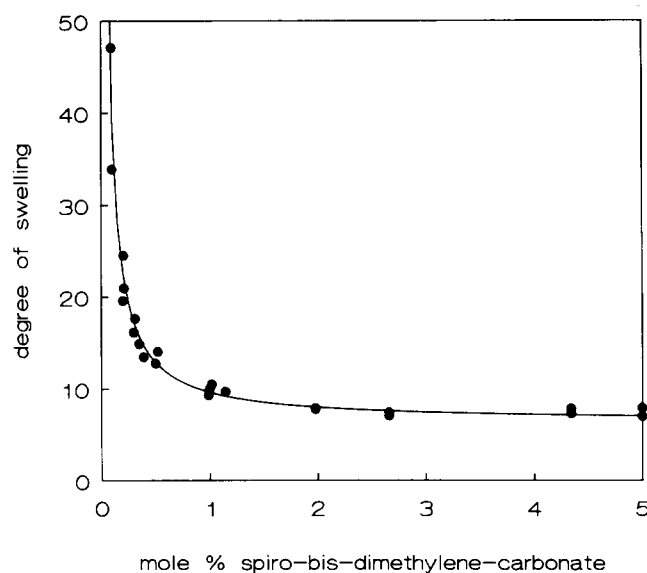
Figure 5 The degree of equilibrium swelling in chloroform of PLLA crosslinked with spiro-bis-DMC *versus* the crosslinker concentration

in the degree of swelling can be observed, which may indicate the limit of solubility of spiro-bis-DMC in molten L-lactide.

Analysis of the swelling behaviour of polymer networks in low molecular weight solvents allows the determination of the molecular weight between crosslinks[24-26]. The

Flory–Huggins interaction parameter, χ, for the polymer–solvent system then needs to be known. An estimate of χ for high molecular weight poly(L-lactide) in chloroform was obtained from the second virial coefficient in membrane osmometry measurements[23,24,27].

$$A_2 = (1/2 - \chi)\frac{\bar{v}^2}{V_1}J(X) \qquad (1)$$

Here A_2 is the second virial coefficient, $\bar{v}$ is the specific volume of the polymer and V_1 is the molar volume of the solvent. $J(X)$ is a quantity which is dependent on the molecular weight, the nature of the solvent and the temperature. At the Θ-temperature, $\chi = 1/2$ and $J(X)$ becomes equal to unity. $J(X)$ and A_2 are inversely dependent on the molecular weight[24,27,28]. As the measurements were carried out on very high molecular weight polymers, this molecular weight dependence is neglected and $J(X)$ is taken to be 1. Also, bearing in mind that A_2 and χ are dependent on the polymer concentration[23], the determination of χ from the initial slope in the osmotic pressure data (*Figure 6*) is only an approximation, and the resulting values should therefore be used with caution.

At these high molecular weights, the determination of the number average molecular weight of PLLA is not very accurate. Although in agreement with the viscosity measurements, the molecular weights were found to be very high. *Table 2* shows several values of χ determined this way at different temperatures and with PLLA of different molecular weights, resulting in an average value of 0.20 for PLLA in chloroform at room temperature.

When the effect of constraints on junction fluctuations in a real network on the elastic contribution to the chemical potential of the diluent in a swollen network is taken into account[29,30], the following formula for the molecular weight between crosslinks (M_c (cj)) of a perfect tetrafunctional network crosslinked in the undiluted state can be deduced:

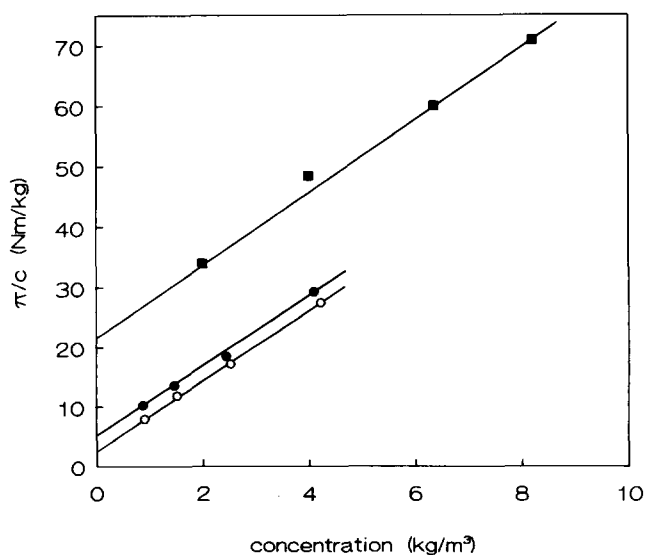$$M_c\ (\text{cj}) = \frac{1/2\rho V_1 v_2^{1/3}(1 + K)}{-\ln(1 - v_2) + v_2 + \chi v_2^2} \qquad (2)$$

Figure 6 Plot of π/c against concentration for a number of high molecular weight poly(L-lactide) samples in chloroform. $\bigcirc M_v = 922 \times 10^3$, $\bullet M_v = 498 \times 10^3$, $\blacksquare M_v = 111 \times 10^3$

Table 2 Determination of the Flory–Huggins χ-parameter for high molecular weight poly(L-lactide) in chloroform by membrane osmometry

M_v ($\times 10^{-3}$)	M_n ($\times 10^{-3}$)	Temperature (°C)	$A_2 \times 10^{-3}$ (mol m^3 kg^{-2})	χ
103	111 ± 5	21.5	2.57	0.18 ± 0.02
–	266 ± 20	21.5	2.77	0.15 ± 0.01
770	875 ± 110	21.5	2.12	0.22 ± 0.02
–	470 ± 50	26.5	2.26	0.22 ± 0.01
303	498 ± 50	26.5	2.36	0.20 ± 0.01
380	395 ± 200	26.5	2.26	0.21 ± 0.01
883	922 ± 100	26.5	2.39	0.20 ± 0.01
380	515 ± 80	37.0	1.90	0.26 ± 0.02
440	303 ± 20	37.0	1.85	0.27 ± 0.03
675	614 ± 90	37.0	1.99	0.25 ± 0.02

Here, v_2 is the volume fraction of polymer in the swollen network (the reciprocal of the degree of swelling), χ is the Flory–Huggins interaction parameter, ρ is the density of the network (taken to be $1248\ \text{kg m}^{-3}$) and V_1 is the molar volume of the swelling medium, chloroform ($81.06 \times 10^{-3}\ \text{dm}^3\ \text{mol}^{-1}$).

$(1 + K)$ characterizes the extent to which the deformation in swelling approaches the affine limit[31]. The function K is dependent on the degree of swelling, and also on two network parameters, κ and p, which specify, respectively, the severity of the constraints on the crosslinks from neighbouring chains and the dependence of the crosslink fluctuations on the strain. To a first approximation $\kappa = 20$ and $p = 2$ are reasonable estimates[29]. In the limit of affine deformation, $\kappa = \infty$. In the case of phantom behaviour $\kappa = 0$ and $(1 + K)$ equals 1 for all v_2.

Calculation of the molecular weight between crosslinks for the affine and phantom limits of the model (M_c (aff) and M_c (ph)) is done by using the formulae[24,25]:

$$M_c(\text{aff}) = \frac{\rho V_1 v_2^{1/3}(1 - 1/2v_2^{2/3})}{-\ln(1 - v_2) + v_2 + \chi v_2^2} \qquad (3)$$

$$M_c(\text{ph}) = \frac{\rho V_1 v_2^{1/3}}{-\ln(1 - v_2) + v_2 + \chi v_2^2} \qquad (4)$$

These values may be compared with the ones expected from the amounts of spiro-bis-DMC that were copolymerized with L-lactide. The theoretical molecular weight between crosslinks that can be expected from the chemical composition of the copolymers is:

$$M_c\ (\text{chem}) = \frac{(\text{mol\% L-lactide})144}{2(\text{mol\% spiro-bis-DMC})} \qquad (5)$$

assuming complete conversion of both reactants.

The results of these calculations are given in *Figure 7*. For spiro-bis-DMC concentrations in L-lactide below 2 mol%, the expected (theoretical) molecular weight between crosslinks falls within the values delineated by the affine and phantom limits. In particular, in the range of 0.1 to 1.2 mol%, the swelling behaviour can satisfactorily be described by the constrained junction theory. At the lowest crosslinker concentrations, the uncertainty is large in the values of both the degree of swelling and the expected molecular weight between crosslinks. This result implies that, taking experimental error into consideration, random and homogeneous crosslinking takes place at spiro-bis-DMC concentrations in the L-lactide melt below a value of 2 mol%. Larger amounts of spiro-bis-DMC do not dissolve in L-lactide.
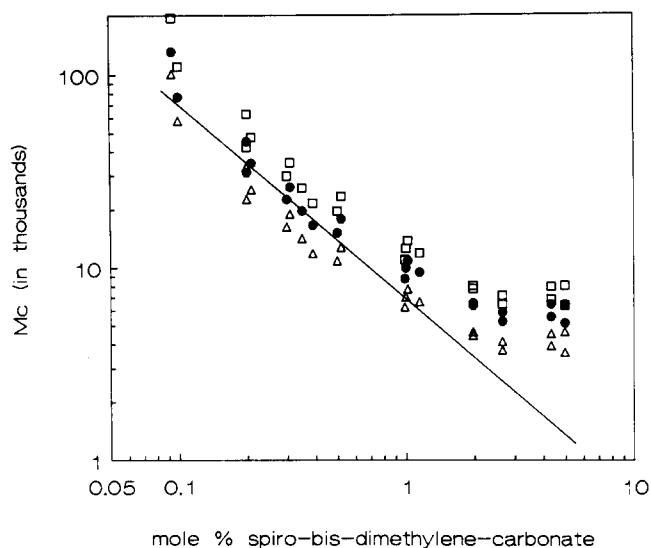
Figure 7 The molecular weight between crosslinks for poly(L-lactide) crosslinked with spiro-bis-DMC as a function of crosslinker concentration. M_c is determined from the swelling data in chloroform by the constrained junction theory (●), affine- (□) and phantom- (△) network behaviour. The drawn line is calculated from the chemical composition
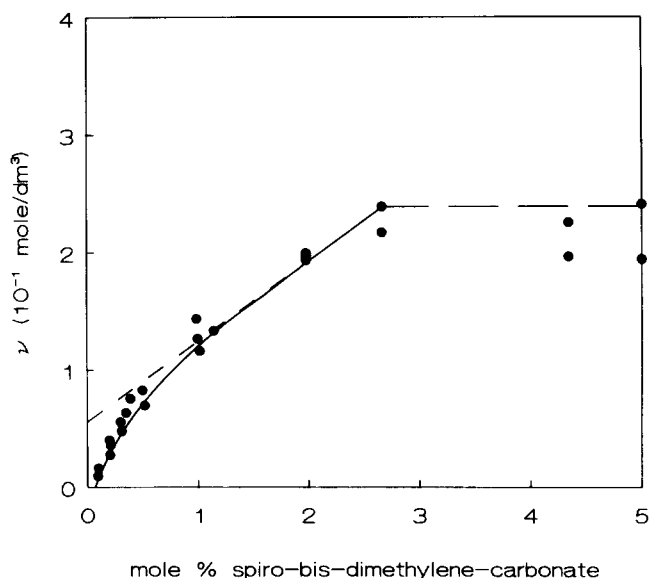

Figure 8 The effective network chain density v as a function of spiro-bis-DMC concentration. By extrapolating the linear part of the curve to zero crosslinker concentration, the molecular weight between entanglements of the as-polymerized uncrosslinked poly(L-lactide) can be estimated

When the effective network chain density, $v = \rho/M_c$, is plotted as a function of crosslinker concentration, shown in *Figure 8*, the onset of gelation can be determined. By extrapolation of the curve to zero effective network chain density, a gel point of 0.06 mol% spiro-bis-DMC in L-lactide can be determined. This extremely low value indicates once more the very powerful crosslinking capability of the bicyclic biscarbonate.

Furthermore, the maximum contribution of entanglements to the elastic behaviour of the network can be obtained by extrapolating the linear portion of the plot to the zero degree of crosslinking[32,33]. From the intercept

on the v axis, an effective network chain density of 0.57×10^{-1} mol l^{-1} is found. This value corresponds to a molecular weight between entanglements (M_e) of 22 000 in as-polymerized PLLA. The affine and phantom limits of the model lead to values for the molecular weight between entanglements of respectively 29 700 and 15 000.

It is this rather unentangled structure which is responsible for the excellent drawability of as-polymerized PLLA filaments[34]. The draw ratio was found to depend on the filament machining temperature. Draw ratios of $\lambda = 12$ to $\lambda = 18.5$ were achieved under optimal circumstances. Without the occurrence of chain slippage and scissioning, the maximum allowable extension of the entanglement network, λ_{max}, may be calculated from the ratio of the contour length of the chain between entanglements (L_e) and the root mean square end-to-end distance of a chain with molar mass M_e ($\langle R_0^2 \rangle^{1/2}$) (see refs 24, 35):

$$\lambda_{max} = \frac{L_e}{\langle R_0^2 \rangle^{1/2}} = \frac{fn^{1/2}}{C_\infty^{1/2}} \tag{6}$$

When a single L-lactyl residue is considered as a virtual bond, the length and mass of the repeating units are known[36]. The factor f takes into account the projection of the virtual bond along the length of the extended polymer chain and depends on the value of the angles between repeating bond vectors. n is the number of these repeating virtual bonds in the polymer chain. From the angles between the virtual bonds[36], the projection factor f can be calculated to be 0.963. The value of the characteristic ratio C_∞ is 2.0 for poly(L-lactide)[36].

Assuming no chain slippage occurs, a maximum draw ratio of $\lambda = 11.9$ can be calculated from the value for M_e, found by extrapolation of v, which is close to the observed maximum draw ratio. In comparison, melt spun PLLA fibres could only be drawn to a maximum draw ratio of 8 (see ref. 34), indicating a much more entangled structure.

For a crosslinked polymer, the maximum draw ratio will be determined by the crosslink density as well as by the density of (trapped) entanglements. Summation of the crosslink and entanglement densities of PLLA crosslinked at 110°C with 0.19 mol% spiro-bis-DMC and calculation of the molecular weight between crosslinks, either chemical or physical, leads to a value of 13 900. The maximum draw ratio calculated is then 9.4. It was found that cylindrical specimens of this material could be drawn on a hot plate at 200°C to a maximum draw ratio 10.0. Again, this value is in very good agreement with the one calculated. The tensile strength of these drawn rods was quite high; values of 660 MPa were found for specimens with a diameter of 0.24 mm. Specimens crosslinked with 0.10 mol% spiro-bis-DMC could be hot drawn even further to $\lambda = 13.4–14.0$, resulting in a tensile strength of 750 to 800 MPa. The calculated maximum allowable draw ratio in this case is 10.4.

Thermal and mechanical properties of crosslinked poly(L-lactide)

Incorporation of foreign units into a crystallizable polymer chain will impede crystallization. Exclusion of the comonomer unit from the crystals reduces crystallite dimensions, melting temperature and overall crystallinity. Copolymerization of L-lactide with ε-caprolactone, trimethylene-carbonate and glycolide results in poly(lactides) with much lower crystallinity and melting temperatures. Copolymerization with a

tetrafunctional monomer forming crosslinks, will have a much larger effect on thermal and mechanical properties. Not only are foreign units built into the stereoregular chain, but the mobility and the accessible chain conformations are greatly hampered, resulting in a considerable melting point depression.

The influence of the amount of biscarbonate crosslinker on the heat of fusion and the melting temperature of as-polymerized PLLA networks is presented in *Figure 9*. The molecular weight of the chains between crosslinks determines the length of crystallizable L-lactide sequences. An increase in crosslink density has a pronounced effect on thermal behaviour. Copolymerization of less than 2 mol% crosslinker already gives quite low melting temperatures and a marked decrease in the heat of fusion. Such a large effect is not seen when L-lactide is copolymerized with other cyclic esters, except with D-lactide which will be dealt with separately. These low crystallinities will increase the rate of mass loss upon degradation and at the same time decrease the dimensions of the remaining crystalline debris and prevent the formation of needle-like structures.

Copolymerization with more than 2 mol% spiro-bis-DMC does not seem to depress further the melting temperature and heat of fusion, which is in agreement with the earlier observations that higher concentrations will not be incorporated into the network.

Network formation of poly(L-lactide) also has a positive influence on the tensile properties of the materials. The tensile strength as a function of crosslink density is given in *Figure 10*. It is shown that as the crosslink density increases, the tensile strength increases and reaches a limiting value of 70 MPa. High molecular weights lead to materials with the highest tensile and impact strengths in amorphous polymers, due to an increase in interconnectivity[37]. In this case crystallinity, as well as chemical crosslinking, accounts for the interconnectivity of the network, which leads to these high values of tensile strength. It was also found that, macroscopically, these bulk synthesized specimens were very homogeneous. As heterogeneities, such as voids formed during crystallization of the polymer, give rise to
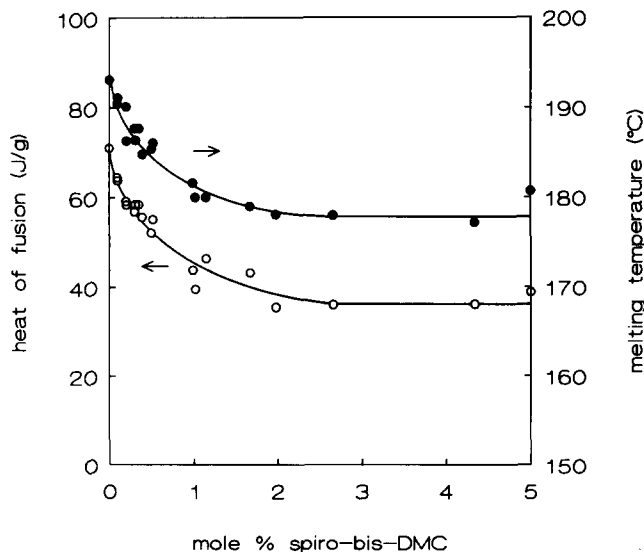

Figure 10 The tensile strength of PLLA networks as a function of spiro-bis-DMC concentration
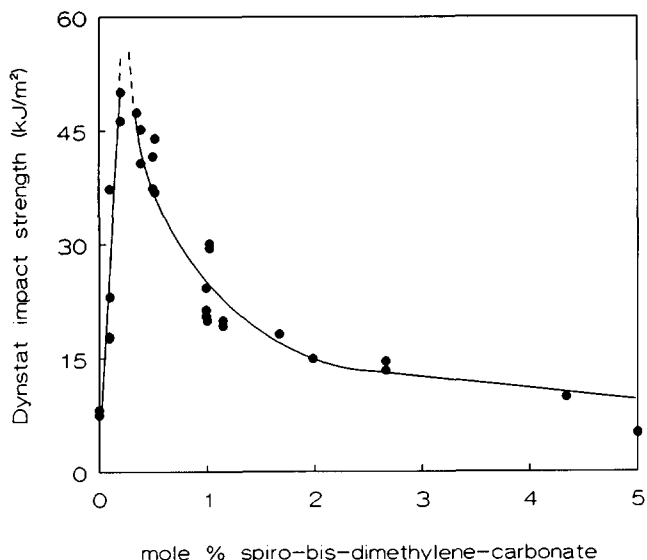
Figure 11 The unnotched Dynstat impact strength as a function of spiro-bis-DMC concentration. Samples crosslinked with 0.20, 0.30 and 0.31 mol% crosslinker (not shown in the figure) did not fracture during impact testing

stress concentrations which may initiate growing cracks, this sample homogeneity is also a very important factor.

Specimen homogeneity is also a prerequisite for impact resistant materials. Shown in *Figure 11* is the influence of spiro-bis-DMC concentration on unnotched Dynstat impact strength. A sharp maximum in material toughness at 0.2–0.3 mol% can be observed. Samples crosslinked with 0.204, 0.300 and 0.311 mol% of spiro-bis-DMC (not shown in the figure) did not fracture in the impact test.

Two effects may play a determining role in the formation of an impact resistant structure. On the one hand, chain interconnectivity is increased upon cross-linking; on the other, crystallinity and crystal size are simultaneously reduced. Increasing the chain length reduces the effect of natural or artificial flaws as stress concentrators[39] by hindering crack propagation.

Figure 9 The heat of fusion (○) and the melting temperature (●) of PLLA networks crosslinked with spiro-bis-DMC as a function of crosslink density
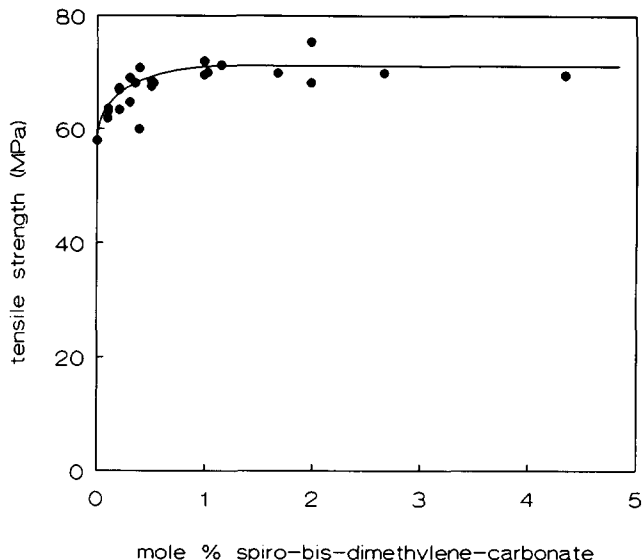
The morphology of semi-crystalline polymers has a large effect on the mode of sample failure[39,40]. A finer spherulitic matrix greatly enhances ductility, yield strength and impact strength[40].

Although the as-polymerized structure of crystalline PLLA synthesized with stannous octoate at these relatively low temperatures does not seem to be spherulitic[41], crosslinking does reduce the dimensions of the structures formed and so increases the impact strength. Amorphous poly(lactides), either copolymers of D- and L-lactide or quenched poly(L-lactide), have much lower impact strengths and slightly higher (brittle) tensile strengths than as-polymerized PLLA (65 MPa *versus* 60 MPa). Consequently, incorporation of too much crosslinker will lead to low crystallinities and again to brittle materials. The crystalline domains may be pictured as stress concentrators which, throughout the sample, lower the yield stress and allow plastic flow and deformation to take place before the material reaches its brittle breaking stress[38]. A similar sharp maximum in the impact strength was also found for copolymers of L-lactide and TMC[42].

It is evident that these findings require more attention. In a future paper the effects of morphology, crystallinity and thermal behaviour on impact strength of poly(lactides) will be dealt with in more detail.

CONCLUSIONS

Spiro-bis-dimethylene-carbonate proves to be an effective crosslinker not only for cyclic carbonates but for lactones as well. It can be used for the preparation of a wide range of materials ranging from crosslinked rubbers to strong and tough semi-crystalline poly(L-lactide) networks. Because the hydrolytic degradation products of spiro-bis-DMC are non-toxic, it can be used in biomedical applications.

The high gel percentages of up to 100% and the extremely low gel point of 0.06 mol% in L-lactide are indicative of the ease with which this crosslinker is copolymerized with L-lactide.

The molecular weights between crosslinks determined from swelling experiments were in accordance with those expected from the charged amounts of tetrafunctional comonomer, indicating that homogeneous crosslinking had taken place at concentrations below 2 mol% of spiro-bis-DMC.

A large melting point depression and significant reduction of the heat of fusion are attained upon crosslinking. The high values of the tensile and impact strengths offer new possibilities for degradable devices where strength and toughness are required such as in orthopaedic pins, nails and bone plates and screws.

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