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Synthesis and degradability of a novel aliphatic polyester based on L-lactide and sorbitol: 3

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Reaction of L-lactide (LLA) with sorbitol (SB) in the presence of stannous octoate (Sn oct), tetraphenyl tin (TPhT) and several other catalysts gave a series of novel polyesters. Several techniques such as nuclear magnetic resonance (n.m.r.) and Fourier transform infra-red (*FT*i.r.) spectroscopy, gel permeation chromatography (g.p.c.) and differential scanning calorimetry (d.s.c.) were used in order to characterize these polymers. The crystallinity of the polyesters was found to depend on the molar ratio of LLA to SB, i.e. when LLA/SB $> 20/1$ or $> 40/1$ (for Sn oct or TPhT, respectively) the polyesters are semicrystalline (from d.s.c. results) whereas at molar ratios of LLA to SB which are lower than those mentioned above the polymers become amorphous. High SB contents have an adverse effect on the thermal properties (i.e. lower T_g, T_m, and ΔH_m) and the molecular weight distribution (lower M_n and M_w) but they enhance their biodegradability. The latter was tested in terms of enzymatic and alkali hydrolysis. Both total organic carbon (TOC) and g.p.c. measurements confirmed the degradation of the polyesters at different hydrolysis modes.

(Keywords: poly(L-lactide); biodegradability; enzymatic hydrolysis)

INTRODUCTION

Nowadays biodegradable, usually referred to as either erodible, bioabsorbable and resorbable, polymers[1] which have been designed for a predetermined service lifetime have gained in importance in view of their numerous applications in medicine and biology, as well as to their utility in the recycling of polymers[2-4]. Although the use of polylactides (PLLAs) and their copolymers with glycolide as suture materials has been claimed both in early patent literature[5] and in several publications[6-12] none of these have been widely commercialized[1]. Among the many applications of the high lactide-based polymers, vascular grafts[13-15], controlled delivery of drugs[16,17] meshes for dental wound healing[1], implants and sutures for fixation of fractures[18-27], and, very recently for the manufacture of disposable plastic articles[28], are probably the most important. However, PLLA fibres also showed several drawbacks, mainly with regard to their high or low crystallinity[1], a general lack of total absorption at the worst even after 3 years[29] (a recent article[30] confirmed that PLLA degradation occurs within 10 years), inflammatory foreign body reactions (clinical studies on bone tissue of animals[31,32] and their thermal instability, which limits their melt processability[1,33,34]. With a view to solving this problem, several approaches were adopted, such as the use of copolymers, i.e. methyl valerolactone/LA[35,36] or ϵ-caprolactone/LA[34], or aliphatic polycarbonates[37-42], or more recently star lactide polymers[29,33,43-46]. In our previous papers in this series, the novel series of polymers based on LLA/glycerol[47], LLA/aminohydroxyl-1,3-propanediol[48] and LLA/aminopropanediol[48] were synthesized, characterized and tested with regard to their biodegradability. This contribution aims to present the synthesis and characterization of a further new series of polymers based on LLA and sorbitol and to correlate the effect of the introduction of sorbitol to PLLA with the effect of the above-mentioned and previously investigated multifunctional monomers.

EXPERIMENTAL

Reagents

L-Lactide (LLA) from Boehringer (Ingelheim) was purified by recrystallization from dry toluene under a nitrogen atmosphere and then dried for 24 h in vacuum at 30°C. Sorbitol (SB, analytically pure) was purified by recrystallization from ethanol and methanol and then treated with sodium sulfate in order to remove any residual moisture traces. Stannous 2-ethylhexanoate (stannous octoate, Sn oct) and tetraphenyl tin (TPhT) were purchased from Wako Chemicals (Japan) and used without further purification. Triethylaluminium ($AlEt_3$) in toluene solution (15% wt/vol, Tokyo Kasei), titanium tetrabutoxide ($Ti(n\text{-}BuO)_4$) (Wako Chemicals), n-butyllithium in hexane solution (15% wt/vol, Tokyo Kasei)

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*To whom correspondence should be addressed. Present address: School of Agriculture, Department of Food Science, Aristotle University of Thessaloniki, Thessaloniki, Greece and anhydrous iron chloride ($FeCl_3$, Nakarai) were used as catalysts without any further purification. Zinc dibutoxide [$Zn(t\text{-}BuO)_2$] and μ-oxo-aluminium–zinc complex and ($(n\text{-}butoxy)_4Al_2O_2Zn$) were prepared as previously reported[36]. The enzyme used for biodegradation testing was lipase from *Rhizopus arrhizus*, which was purchased from Boehringer, Mannheim.

Synthesis of polymers from L-lactide and sorbitol in the presence of various catalysts

The polymerization of L-lactide (LLA) was carried out in a glass ampoule. Freshly recrystallized LLA and various amounts of sorbitol (SB) were transferred into the ampoule, and the appropriate catalyst was added under a nitrogen atmosphere. The ampoule was sealed in vacuum after purging three times with nitrogen. The ampoule was heated up to 130°C in an oil bath for 120 h. After this time, the ampoule was broken and the products were dissolved in $CHCl_3$, followed by microfiltration through a 0.45 μm pore membrane filter. The polymers whose monomer molar feed (LLA/SB) was higher than 20/1 or 40/1 (for Sn oct and TPHT, respectively) were precipitated dropwise into methanol whereas those with a molar composition lower than these values, i.e. richer in SB, were evaporated to yield low-molecular-weight PLLA. Both high- and low-molecular-weight PLLA were dried in a vacuum dessicator at 50°C for 24 h.

Thermal analysis

The thermal behaviour of the polyester was studied by using a differential scanning calorimeter (DSC-10A Rigaku, Thermoflex) connected to a charge recorder (Rigaku) and a temperature controller unit (PTC10D, Rigaku). The heating rate was $10°C\,min^{-1}$, with an empty aluminium pan being used as the reference. Indium metal was used for calibration purposes, for both T_m and ΔH_m ($T_{m_{indium}} = 156.7°C$ and $\Delta H_m = 28.36\ J\,g^{-1}$). The glass transition point (T_g) was determined as the middle of the recorded step change in heat capacity, with the melting points (T_{m1}, T_{m2}) being defined as the peaks of the endothermic curve. The second heating took place after the polymer samples had remained in the melt at temperatures $T = (T_m + 10°C)$ for 10 min, and were then subsequently quenched with liquid nitrogen. The advantage of this 'second-heating' process is for obtaining a clear recording of the T_g by increasing the amorphous content of the polymer samples.

Fourier transform infra-red

The *FT* i.r. spectra were recorded with a spectrometer (Nicolett, Model 710–FT-IR) connected with a PC computer (Nicolett) and colour pro plotter (Fujitsu, Model FPG 315-101). The samples were examined as films since they were soluble in $CHCl_3$.

Nuclear magnetic resonance spectroscopy

^1H n.m.r. (200 MHz) and ^{13}C n.m.r. (50 MHz) spectra were recorded on a JEOL-FX200 spectrometer. All spectra were obtained in $CDCl_3$ at room temperature with tetramethylsilane (TMS) as internal standard and according to the following specification: pulse width 30°C, acquisition time 3.276 s, and pulse interval time 1.00 s.

Gel permeation chromatography

The molecular weight distributions (M_n, M_w and polydispersity indices) were measured by g.p.c. (Tosoh, Model HLC-8020) using polystyrene standards. The columns used were TSK gel G4000 HXL and TSK gel G3000 HXL with a limited exclusion molecular weight of 4×10^5. The eluent used was $CHCl_3$ and the flow rate was $0.6\ ml\ min^{-1}$.

Enzymatic hydrolysis

A polyester sample (15 mg) and 2 ml of phosphate buffer (KH_2PO_4/Na_2HPO_4, pH = 7.00) were added to three tubes; 200 units of enzyme were then added to two of the tubes, while the third was used as a blank test. The enzyme used was lipase from *Rhizopus arrhizus*. The enzymatic hydrolysis was carried out at 37°C for 24 and 72 h, respectively. After filtration (0.2 μm membrane filter), a small amount of 1 N hydrochloric acid was dropped in to the filtrate and the total organic carbon (TOC) was measured. The TOC values were the average of two measurements and appropriately corrected by subtracting the blank values.

Enzymatic hydrolysis for studying the degradation products

A polyester sample (100 mg) and 2 ml of phosphate buffer (KH_2PO_4/Na_2HPO_4, pH = 7.00) were added to three tubes; 2000 units of enzyme were then added to two of the tubes, while the third was used as a blank test. The enzyme used was lipase from *Rhizopus arrhizus*. The enzymatic hydrolysis was carried out at 37°C for 120 h, and after this time the suspension was extracted with $CHCl_3$, dried with Na_2SO_4 in order to remove residual

Table 1 Effect of catalyst on the polymerization of L-lactide with sorbitol (100/1 molar feed ratio)

Run	Catalyst[a]	Temperature (°C)	Time (h)	Yield (%)	$M_n \times 10^{-3}$	M_w/M_n
1	TPhT	130	120	99	17 500	1.2
2	Sn oct	130	120	98	16 900	1.7
3	$AlEt_3$	60	120	60	23 500	1.8
4	$ZnEt_2$	60	120	58	26 000	1.5
5	AZ[b]	60	120	69	19 080	1.6
6	$Zn(t\text{-}BuO)_2$	60	120	65	21 300	1.9
7	$Ti(n\text{-}BuO)_4$	60	120	70	17 000	2.2
8	n-BuLi	60	120	70	18 200	2.1
9	$FeCl_3$	60	120	58	8 900	2.5

[a] Amount of catalyst used: 0.3 mol per 100 mol of reactants

[b] AZ = $(n\text{-}BuO)_4\ Al_2O_2Zn$

Table 2 Polymerization of L-lactide with sorbitol (40/1 molar feed ratio) in the presence of various catalysts for 120 h

Catalyst[a]	Temperature (°C)	Yield (%)	LLA/SB[b] (mol%)	M_n[c]	M_w/M_n[c]	T_g[d](°C)	T^d_{m1} (°C)	T^d_{m2} (°C)
TPhT	130	92	45/1	5500	1.1	34	85	–
Sn oct	130	89	34/1	10050	1.7	36	405	–
$AlEt_3$	60	48	63/1	11300	1.6	39	142	130
$ZnEt_2$	60	44	68/1	14500	1.5	44	151	142
AZ[e]	60	55	85/1	19700	1.7	48	157	147
$Zn(t\text{-}BuO)_2$	60	52	74/1	14200	1.4	48	153	144
$Ti(n\text{-}BuO)_4$	60	61	90/1	21850	1.6	50	160	148
n-BuLi	60	63	100/1	24500	2.0	52	163	150
$FeCl_3$	60	45	72/1	16450	1.3	44	452	140
$Al(i\text{-}PrO)_3$	60	42	80/1	16370	1.5	47	154	138
$Mg(OEt)_2$	60	48	125/1	27000	1.5	55	165	151

[a] Amount of catalyst used: 0.3 mol per 100 mol of reactants
[b] Obtained from n.m.r. spectroscopy
[c] Obtained from g.p.c.
[d] Obtained from d.s.c. (2nd run)
[e] AZ = $(n\text{-}BuO)_4\ Al_2O_2Zn$

moisture (from the phosphate buffer), and then with hot CH_3OH. After filtration (removal of Na_2SO_4) the chloroform of CH_3OH was evaporated, and the remaining sample was subjected to n.m.r. spectroscopy and g.p.c. measurements.

Alkali hydrolysis (10% NaOH wt/vol, 80°C)-weight loss experiments

In view of the friability of our polyester and their inadequate strength, no films could be formed. Therefore, bars of the following dimensions (40 mm length, 7 mm width and 2.0 mm thickness) were moulded and immersed in alkali solutions (10% NaOH wt/vol) at 80°C. The weight losses of the samples were followed by weighing every day, with the results given being the average of three measurements.

RESULTS AND DISCUSSION

Various coordinated catalysts, including both anionic and cationic ones were used in order to find the optimum conditions for the polymerization of LLA with SB (100/1 molar feed ratio (*Table 1*)). All of the catalysts give reasonably high yields (58–99%), reaching their maximum yields of 98 and 99% when using Sn oct and TPhT, respectively. It is noteworthy that the use of coordinated catalysts such as triethylaluminium, zinc dibutoxide, μ-oxo-aluminium–zinc complex and titanium tetrabutoxide at 60°C resulted in yields only up to 70%, which are considerably lower than those obtained by using Sn oct and TPhT, in contrast to the results reported in a previous publication on the copolymerization of LLA with β-methyl-δ-valerolactone[36]. The use of anionic or cationic catalysts (n-BuLi and $FeCl_3$, respectively) also resulted in similar yields (70 and 58%) to those obtained with the coordinated catalysts. The synthesized polymers were white in colour, apart from the one obtained by using $FeCl_3$, which was dark brown.

Table 2 gives the results of polymerization of LLA with SB at a different molar feed ratio in the presence of several catalysts. The highest yields, i.e. 92 and 89% are still obtained with TPhT and Sn oct and the n.m.r. spectroscopic analysis (as will be explained later) shows a rather satisfactory agreement between the molar feed ratio and the determined molar ratios in the final products. However, both the g.p.c. and d.s.c. results show that the polymers which are rich in LLA, obtained by using the rest of the catalysts, have both higher molecular weights and glass transitions and melting points, due to the formation of longer LLA–LLA chains. Therefore by comparing *Tables 1* and *2* it could be concluded that both Sn oct and TPhT promote to a far greater extent, the reaction of LLA with SB, whereas the remaining catalysts mainly initiate the formation of long LLA chains with only a minimum contribution of the SB units.

The effect of reaction time on the polymerization of LLA with SB (40/1 molar feed ratio) in the presence of Sn oct and TPhT is shown in *Table 3*. After 120 h the maximum yield is obtained and products rich in SB were synthesized. However, a further prolongation of the reaction time (> 168 h) resulted in dark coloured products, probably due to oxidation of the occurrence of side and/or depolymerization reactions.

A further series of experiments were conducted in order to find out the optimum amount of catalyst required since this is of great importance for many applications of biomedical polymers where a minimum amount of catalyst is needed. *Table 4* provides an overview of our results, and shows that the addition of 0.3 mol% of catalyst is essential for reaching high yields, and simultaneously, higher M_n, T_g and T_m values. However, if higher catalyst contents are used, the molecular weights and the thermal parameters (T_g, T_m) decrease, presumably because employment of more catalyst initiates the formation of more propagation centres, thus resulting in the formation of many more, but shorter, polymeric chains.

Zhang *et al.* have recently published an excellent review[49] on the currently suggested mechanisms concerning the catalytic action of Sn oct in the polymerization of LLA. In several earlier publications it was suggested that Sn oct and stannous hydroxide can readily react with compounds containing hydroxyl groups (e.g. SB), thus forming stannous alkoxide (equations (1) and (2))[50]. Furthermore, the hydrolysis of Sn oct, because of traces of absorbed moisture, can result in several

Table 3 Polymerization of L-lactide with sorbitol (40/1 molar feed ratio) using TPhT and Sn oct for various polymerization times at 130°C

Catalyst[a]	Time (h)	Yield (%)	LLA/SB[b] (mol%)	M_n^c	M_w/M_n^c	T_g^d (°C)	T_m^d(°C)
Sn oct	3	8	150/1	1 000	1.8	−7	–
Sn oct	6	11	135/1	1 350	1.9	−4	–
Sn oct	9	16	122/1	1 600	1.9	0	–
Sn oct	12	24	115/1	2 150	1.7	3	41
Sn oct	24	43	96/1	2 800	1.7	10	47
Sn oct	36	59	84/1	3 850	1.6	15	52
Sn oct	48	67	67/1	5 300	1.8	19	60
Sn oct	72	75	55/1	7 100	1.5	25	73
Sn oct	96	80	49/1	9 300	1.6	34	90
Sn oct	120	89	34/1	10 050	1.7	36	105
Sn oct	168	86	35/1	10 000	1.7	36	106
TPhT	3	5	166/1	800	2.0	−10	–
TPhT	6	9	154/1	1 100	2.1	−8	–
TPhT	9	14	137/1	1 300	1.9	−4	–
TPhT	12	20	124/1	1 650	1.8	−1	35
TPhT	24	33	107/1	1 850	1.6	5	38
TPhT	36	45	98/1	2 300	1.9	10	43
TPhT	48	56	79/1	3 550	1.5	16	50
TPhT	72	70	63/1	4 200	1.3	21	58
TPhT	96	87	52/1	4 850	1.2	27	70
TPhT	120	92	45/1	5 500	1.1	34	85
TPhT	168	90	44/1	5 600	1.1	33	86

[a] Amount of catalyst used: 0.3 mol per 100 mol of reactants
[b] Obtained from n.m.r. spectroscopy
[c] Obtained from g.p.c.
[d] Obtained from d.s.c. (2nd run)

Table 4 Polymerization of L-lactide with sorbitol (40%/1 molar feed ratio) using various amounts of catalysts (TPhT and Sn oct) for 120 h at 130°C

Catalyst	Amount of catalyst[a]	Yield (%)	LLA/SB[b] (mol%)	M_n^c	M_w/M_n^c	T_g^d (°C)	T_m^d (°C)
Sn oct	0.01	25	90/1	3 900	2.0	30	88
Sn oct	0.03	43	70/1	5 100	1.8	31	93
Sn oct	0.08	59	62/1	6 900	1.5	33	96
Sn oct	0.15	70	54/1	8 700	1.9	34	98
Sn oct	0.30	98	34/1	10 050	1.7	36	105
Sn oct	0.60	97	32/1	10 100	1.6	35	104
Sn oct	1.00	99	30/1	9 200	1.9	30	100
Sn oct	2.00	98	25/1	8 000	1.5	24	91
TPhT	0.01	28	76/1	1 500	1.3	22	71
TPhT	0.03	40	65/1	2 300	1.5	24	75
TPhT	0.08	63	58/1	3 600	1.2	28	78
TPhT	0.15	76	52/1	4 700	1.3	30	82
TPhT	0.30	99	45/1	5 500	1.1	34	85
TPhT	0.60	98	37/1	5 200	1.2	31	79
TPhT	1.00	97	32/1	4 800	1.4	26	75
TPhT	2.00	99	26/1	3 800	1.2	23	69

[a] In mol per 100 mol of reactants
[b] Obtained from n.m.r. spectroscopy
[c] Obtained from g.p.c.
[d] Obtained from d.s.c.

derivatives possessing high catalytic activity (see equation (3))[51,52]. Therefore it was proposed [49] that the true initiator in the polymerization reaction might be the stannous alkoxide, and consequently a coordination mechanism, which is shown in *Figure 1*, is likely to occur[53].

However, according to the mechanistic scheme proposed by Nijenhuis *et al.* The hydroxyl groups (contained in Sn oct) act as the true catalysing agents by the fact that they carry out a nucleophilic attack upon the carbonyl carbon in the cationic complex of the Sn oct

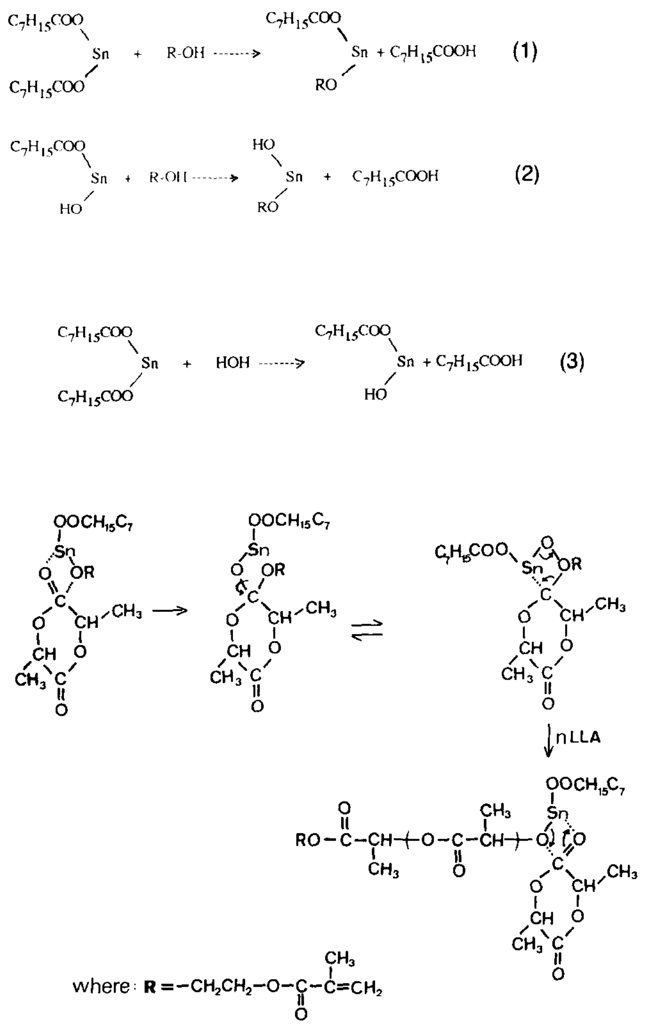

Figure 1 Polymerization mechanism of LLA with SB using stannous alkoxide as the catalyst

and LLA which has been stabilized by resonance[54]. Therefore, this mechanism could be described in terms of a Lewis acid catalysed alcoholysis[52,54]. Although according to equations (1)–(3), any presence of alcohol is expected to result in the formation of higher amounts of stannous alkoxide initiator and presumably faster polymerization rates our results (*Table 5*) show that in the case of SB this is not true. In fact, the higher the SB content, then the lower the molecular weights and the slower the polymerization rates, as has been already reported in several publications on LLA/pentaerythritol (PET)[33,44], LLA/glycerol[47] and LLA/aminohydroxylpropanediol[48]. Among the reasons that could explain the discrepancies mentioned above we could refer to impurities persisting in the LLA (even after its purification), such as lactic and lactoyl lactic acid and 2-ethylhexanoic acid (in Sn oct), which have an adverse effect on the propagation of the polymerization due mainly to transfer reactions[49,54]. The occurrence of transesterification reactions in conjunction with the effect of crystallinity and probably stereochemical inhibitions (i.e. SB) can further complicate our understanding of this particular mechanism and the application of a simple mechanistic scheme. Use of TPhT instead of Sn oct resulted in lower molecular weights for the polylactides rich in SB and in higher values for those rich in LLA (*Table 5*).

Figure 2 shows an idealized scheme where all the functional groups of SB (6-OH) react with LLA, thus forming the core of a star-shaped polymer.

Table 5 gives the yields obtained in the polymer syntheses, either after precipitation with CH_3OH (from $CHCl_3$) or evaporation of $CHCl_3$ after filtration for (SB poor and rich polymers, respectively) and the LLA/SB (molar ratio) results obtained from n.m.r. spectroscopic measurements.

Table 5 Percentage yields and n.m.r. spectroscopic evaluation of the LLA/SB polymer molar ratios for the bulk polymerization of LLA/SB at 130°C for 96 h

LLA/SB[a]	Catalyst[b]	Separation techique[c]	Yield (%)	LLA/SB[d]	M_n^e	M_w^e
100/0	Sn oct	A	99	–	42 000	81 000
200/1	Sn oct	A	98	–	33 350	40 100
100/1	Sn oct	A	98	110/1	16 900	29 000
70/1	Sn oct	A	95	82/1	12 200	21 400
40/1	Sn oct	A	89	34/1	10 050	17 200
20/1	Sn ocr	B	88	20/1	3 400	4 600
12/1	Sn oct	B	87	9/1	2 600	3 850
6/1	Sn oct	B	84	7/1	2 700	4 050
100/0	TPhT	A	100	–	47 000	160 000
200/1	TPhT	A	98	–	25 600	31 000
100/1	TPhT	A	99	92/1	17 500	21 300
70/1	TPhT	A	96	69/1	7 00	10 400
40/1	TPhT	A	92	45/1	5 500	6 200
20/1	TPhT	B	86	18/1	4 350	5 700
12/1	TPhT	B	82	10/1	2 200	3 850
6/1	TPhT	B	80	8/1	2 000	3 100

[a] Feed molar ratio of monomers
[b] Amount of catalyst used: 0.3 mol per 100 mol of reactants
[c] A, extraction with $CHCl_3$ and precipitation with CH_3OH; B, evaporation of $CHCl_3$ after filtration
[d] Polymer molar ratio, obtained from n.m.r. spectroscopy
[e] Obtained from g.p.c.

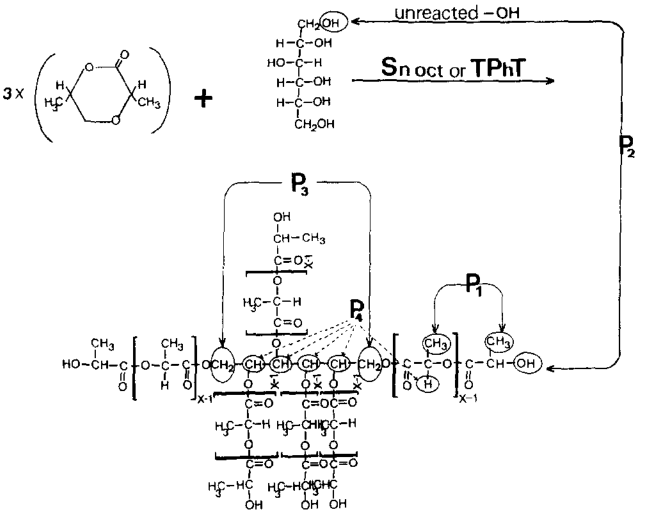

Figure 2 Idealized reaction mechanism scheme for the LLA/SB polycondensation reaction

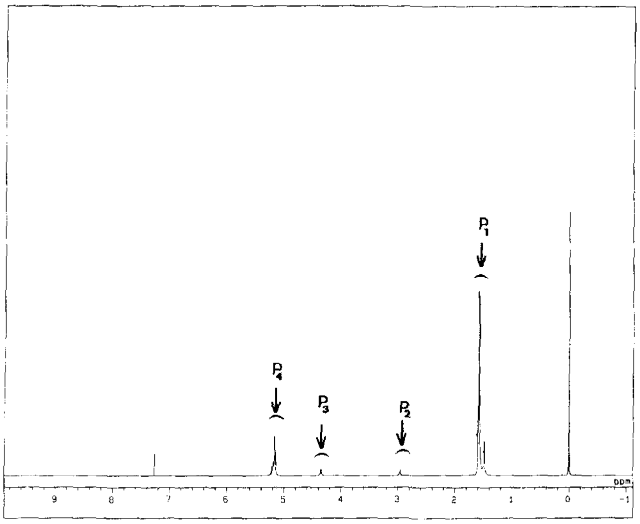

Figure 3 ^{1}H n.m.r. spectrum of LLA/SB (12/1 molar ratio) polyester in $CDCl_3$

The use of relatively high concentrations of SB and catalyst was aimed at synthesizing polymers of low molecular weight for easier and more precise characterization[33,44]. A temperature of polymerization of 130°C was chosen because at higher temperatures the reaction products were decomposed whereas at lower temperatures completion of the reaction (conversion polymer > 95%) proved to be a very lengthy process[33,44,48]. The polymers with high sorbitol content (similar to our previously studied star-shaped polymers[38]) were associated with lower polymer yields.

The presence of unreacted –OH groups in these polyesters was deducted from the *FT*i.r. spectra. The absorption band at 1750 cm^{-1} supports the formation of –O–C = O ester bonds. It was found that the intensity of the hydroxyl absorption increases in proportion to the sorbitol content in the polymer, as was also the case for LLA/glycerol polyesters[48].

In the n.m.r. spectra signals for methyl and methine protons were identified (at 1.4 and 5.1 ppm, respectively), as reported in previous publications on linear and star-shaped PLLA[41–44]. However, several other peaks were also present which are likely to be attributed to the reaction of SB with LLA. The peak occurring at 3.6 ppm could possibly be assigned to the sorbitol. Furthermore, the peak at 3.2 ppm could be an –OH group, due to its relative mobility (3.0–4.0 ppm). A typical n.m.r. spectrum for the LLA/SB (12/1 molar ratio) polyester is given in *Figure 3* (see *Figure 2* for assignments).

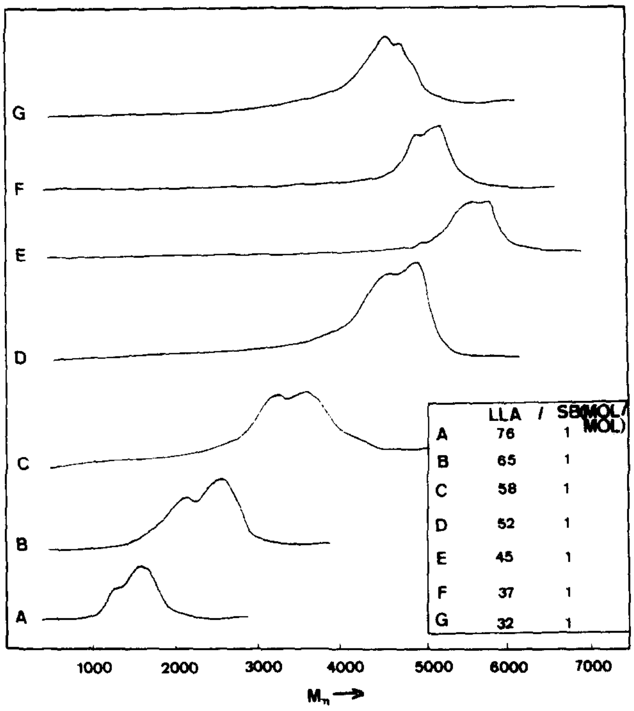

Figure 4 Some representative bimodal g.p.c. curves of LLA/SB polymers obtained by using TPhT as the catalyst

A system of three equations was suggested for determining the LLA/SB molar ratios in these polymers:

$$3x = P_1 \tag{4}$$

$$4y = P_3 \tag{5}$$

$$x + 4y = P_4 \tag{6}$$

where P_1, P_3 and P_4 are equal to the integration intensities and (x/y) represent the LLA/SB molar ratio. By referring to the n.m.r. spectrum in *Figure 3* LLA/SB (12/1, comonomer molar feed ratio):

$$3x = 89.3,\ x = 29.277 \tag{7}$$

$$4y = 14.7,\ y = 3.675 \tag{8}$$

$$x + 4y = 36.1 \tag{9}$$

By dividing equation (7) by equation (8) we obtain $x/y = 8.1/1$ (molar ratio) and then by substituting the value of x (29.77) in equation (9) the value of y is again found ($y = 2.98$). Therefore by taking the average value of y, i.e. $(3.675 + 2.98)/2 = 3.33$, and dividing x by this value of y we find $x/y = 29.77/3.33 = 9$.

Although a detailed description of the exact polymerization mechanism is not available for the reasons already stated, it is generally believed that two polymerization routes are possible, with the first being initiated by the alcohol (SB in this case) and the second via the catalyst[55–58].

The g.p.c. curves of the LLA/SB polyesters are monomodal and bimodal, for the catalysts Sn oct and

Table 6 Glass transitions (T_g), crystallization temperatures (T_{cr}), melting points (T_{m1}, T_{m2}), heats of fusion (ΔH_m) and percentage crystallinities (X_c) of the polyesters, obtained from d.s.c. measurements

		T_g (°C)		T_{cr} (°C)	T_{m1} (°C)		T_{m2} (°C)		ΔH_m (J/g^{-1})		X_c^c (%)	
LLA/SB[a]	Catalyst[b]	1st Run	2nd Run	2nd Run	1st Run	2nd Run	1st Run	2nd Run	1st Run	2nd Run	1st Run	2nd Run
100/0	Sn oct	–	57	107	176	178	–	–	60.2	58.0	64.3	61.9
200/1	Sn oct	57	58	122	169	168	–	161	57.0	54.8	60.9	58.5
100/1	Sn oct	55	55	111	166	164	–	153	53.9	52.1	57.6	55.7
70/1	Sn oct	47	48	107	155	154	–	145	48.5	46.0	51.8	49.1
40/1	Sn oct	34	36	–	105	95	–	–	32.4	–	34.6	–
20/1	Sn oct	25	26	–	78	–	–	–	12.8	–	13.7	–
12/1	Sn oct	5	7	–	–	–	–	–	–	–	–	–
6/1	Sn oct	−10	−13	–	–	–	–	–	–	–	–	–
100/0	TPhT	–	58	104	177	176	–	–	58.7	56.2	62.7	60.0
200/1	TPhT	60	58	118	163	162	–	154	55.3	53.4	59.1	57.0
100/1	TPhT	53	54	121	150	148	–	142	51.8	50.3	55.3	53.7
70/1	TPhT	44	45	82	138	138	–	–	46.2	42.0	49.3	44.9
40/1	TPhT	22	34	–	85	–	–	–	21.1	–	22.5	–
20/1	TPhT	11	12	–	–	–	–	–	–	–	–	–
12/1	TPhT	4	5	–	–	–	–	—	–	–	–	–
6/1	TPhT	−8	−10	–	–	–	–	–	–	—	–	–

[a] Feed molar ratio of monomers

[b] Amount of catalyst used: 0.3 mol per 100 mol of reactants

[c] The percentage crystallinity was calculated from the heat of fusion of PLLA where ΔH_m of 100% crystalline PLLA = 93.7 J g^{-1} (ref. 59)

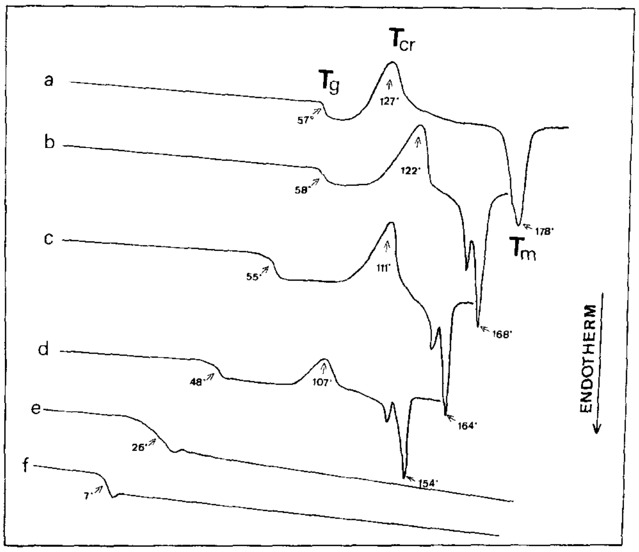

Figure 5 D.s.c. (second run) curves of LLA/SB polyester, synthesized by using Sn oct as the catalyst, for different monomer feed molar ratios: (a) 100/0; (b) 200/1; (c) 100/1; (d) 70/1; (e) 20/1; (f) 12/1

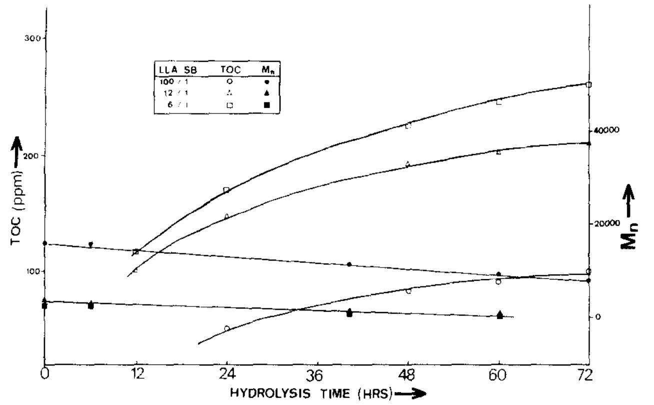

Figure 6 TOC and M_n (from g.p.c.) values *versus* exposure time to enzymatic hydrolysis for several LLA/SB polyester synthesized by using Sn oct as the catalyst

TPhT, respectively. Previous publications referring to LLA/PET[33,44] and LLA/glycerol polymers[48] (using Sn oct) are in agreement with these results and confirm the occurrence of one sole polymerization mechanism. It should be mentioned, however, that the bimodal g.p.c. traces shown in *Figure 4* (using TPhT as the catalyst are an indication of the presence of two mechanisms[48]. In addition, *Table 5* also gives the g.p.c. results (i.e. M_n and M_w obtained for these two novel series of LLA/SB polymers.

The thermal properties of the polyester (obtained from d.s.c.) are presented in *Table 6*. The glass transitions (T_g), crystallization temperatures (T_g), melting peaks (T_m), heats of fusion (ΔH_m) and percentage crystallinities (X_c, calculated from 100% crystalline PLLA) all show a decrease proportional to the increase in SB content.

Figure 5 shows some representative d.s.c. (second run) curves for the LLA/SB polyesters. Apart from curve a, the remaining curves b–f show a double-melting type of behaviour, probably because of the existence of two distinct crystalline morphologies or as a consequence of a complex interplay between melting and recrystallization[60–63].

The novel polyesters were tested both with regard to their enzymatic and alkali hydrolysis behaviour. *Table 7* gives values for the total organic carbon (TOC) for the soluble products and the percentage weight losses of the polyesters as a function of time after enzymatic and alkali hydrolysis treatment respectively. In addition, the susceptibility of several of the polyesters (LLA/SB: 6/1, 12/1, 100/1 feed molar ratio) to degradation was tested

Table 7 Results of enzymatic hydrolysis (*R. arrhizus*) of LLA/SB polyesters in phosphate buffer (15 mg of polyester in 2 ml of KH_2PO_4/Na_2HPO_4, pH = 7.0) expressed as TOC (ppm) and percentage weight loss (% wt against alkali hydrolysis (10% wt/vol NaOH, 80°C) against hydrolysis time

		TOC (ppm)		Weight loss (%)				
LLA/SB[a]	Catalyst[b]	1 day	3 days	2 h	5 h	12 h	24 h	48 h
100/0	Sn oct	3	7	1.2	2.6	5.3	9.2	14.7
200/1	Sn oct	15	30	1.7	3.5	7.0	11.4	19.0
100/1	Sn oct	30	50	1.6	4.8	8.8	13.5	18.3
70/1	Sn oct	50	90	3.5	6.6	13.0	21.4	35.7
40/1	Sn oct	100	150	5.2	7.4	15.6	36.5	51.0
20/1	Sn oct	120	180	8.3	12.9	23.1	37.2	57.5
12/1	Sn oct	150	210	9.5	15.7	29.4	52.0	61.8
6/1	Sn oct	170	260	11.0	21.4	38.0	59.3	67.4
100/0	TPhT	2	5	1.0	2.1	4.3	6.9	11.7
200/1	TPhT	20	40	2.1	3.9	8.2	12.5	21.8
100/1	TPhT	40	70	3.0	5.7	9.0	14.8	23.4
70/1	TPhT	65	100	4.2	8.0	14.5	23.2	40.0
40/1	TPhT	110	170	6.0	9.5	19.4	31.0	54.6
20/1	TPhT	130	210	8.5	14.0	25.6	40.8	59.0
12/1	TPhT	150	240	10.0	17.1	30.4	56.2	63.5
6/1	TPhT	180	290	11.4	22.5	40.2	61.0	69.3

[a] Feed molar ratio of monomers
[b] Amount of catalyst used: 0.3 mol per 100 mol of reactants

Table 8 Results of alkali hydrolysis (10% wt/vol NaOH, 80°C) of the LLA/SB polyesters expressed as percentage crystallinity (from d.s.c.) and molecular weight (from g.p.c.) against hydrolysis time

		Crystallinity (%)		6 h		40 h	
LLA/SB[a]	Catalyst[b]	6h	48h	M_n	M_w	M_n	M_w
100/0	Sn oct	61.6	57.0	41 500	83 000	40 000	85 600
200/1	Sn oct	62.3	53.5	32 200	42 000	25 800	47 400
100/1	Sn oct	59.8	51.0	15 600	31 500	11 000	32 000
70/1	Sn oct	54.2	38.9	10 100	23 200	7 300	22 800
40/1	Sn oct	39.6	19.7	8 800	19 500	6 400	18 700
20/1	Sn oct	23.0	6.2	3 100	4 900	2 200	4 500
12/1	Sn oct	–	–	2 300	4 000	1 400	3 900
6/1	Sn oct	–	–	2 200	4 200	1 200	3 600
100/0	TPhT	61.0	55.1	45 700	170 000	43 000	174 000
200/1	TPhT	58.7	47.3	14 400	33 400	11 500	34 200
100/1	TPhT	55.2	38.4	6 900	13 500	5 200	12 800
70/1	TPhT	55.2	30.0	6 250	11 300	4 400	10 900
40/1	TPhT	34.5	8.7	4 850	6 600	3 500	6 850
20/1	TPhT	6.1	–	3 780	6 200	2 650	5 800
12/1	TPhT	–	–	1 950	4 300	1 060	3 950
6/1	TPhT	–	–	1 800	3 350	970	3 200

[a] Feed molar ratio of monomers
[b] Amount of catalyst used: 0.3 mol per 100 mol of reactants

by recording the changes in TOC and M_n against their exposure time to lipase (*R. arrhizus*). From *Figure 6* it can be seen that TOC values lie on an exponential curve whereas the M_n values decrease with time thus giving straight lines.

The n.m.r. spectra shown in *Figure 7* are recorded for the polyester LLA/SB= 20/1, before and after enzymatic hydrolysis (5 days). *Figure 7b*$_1$ shows the oligomer of LLA where the -OH peak (3.3 ppm), representing the end-groups of PLLA, becomes proportionally bigger when compared to the rest of the peaks. The residue which is insoluble in $CHCl_3$, but soluble in H_2O, appears to be SB if we compare its spectrum (*Figure 7b*$_2$) to that of pure sorbitol[64].

The percentage crystallinities (X_c) and values for the molecular weights (M_n, M_w) were determined from d.s.c. and g.p.c. measurements, and the results are presented as a function of the exposure time to alkali hydrolysis in *Table 8*. The most dramatic decreases in the percentage crystallinities occur for LLA/SB (20/1) (Sn oct) and

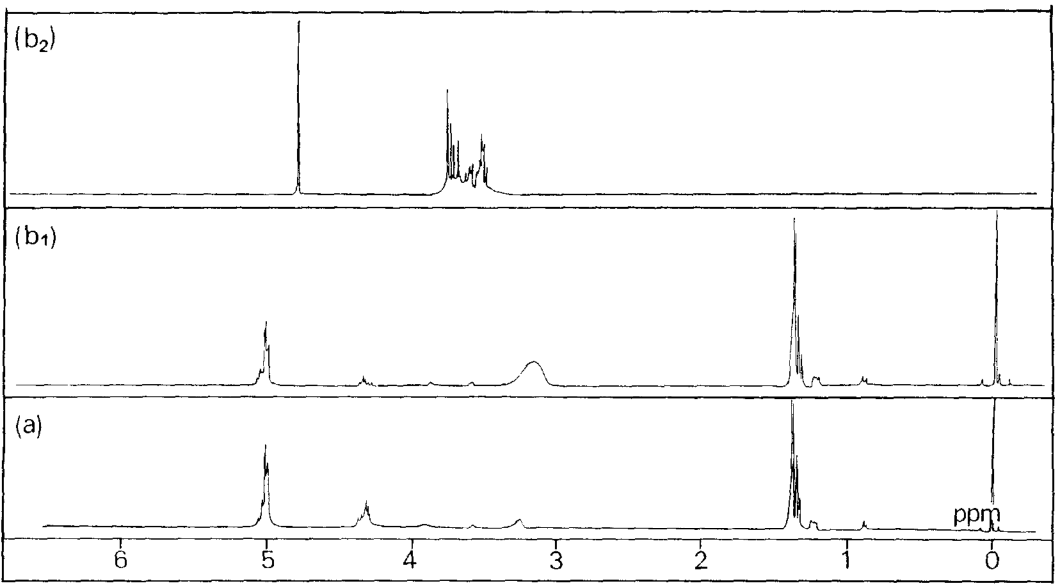

Figure 7 ^{1}H n.m.r. spectra of LLA/SB (20/1, molar ratio) polyester (a) before and (b) after exposure for 5 days to enzymatic hydrolysis; b_1 represents the fraction soluble in $CDCl_3$ (oligomeric PLLA) and b_2 the fraction soluble in D_2O (SB), after hydrolysis

LLB/SB (40/1) (TPhT), where decreases which were almost equal to 80% of the original contents were observed. G.p.c. measurements showed a significant decrease in the M_n values of the polyesters only after hydrolysis for a period of 40 h. At an initial stage (after 5 h hydrolysis) the M_n values did not show any substantial changes, but the M_w values appeared to become greater with exposure time, thus showing higher polydispersity indices (M_w/M_n). In the absence of any evidence for crosslinking (i.e. solubility experiments) and in view of our degradation results it may be suggested that the labile hydrolysable bonds are the SB/LLA, and obviously a higher content of these bonds results in enhanced susceptibility to degradation, as previously observed for several other systems containing LLA and various multifunctional monomers[47,48].

CONCLUSIONS

Two series of biodegradable polyesters, based on L-lactide and sorbitol, were synthesized using various catalysts for comparison purposes, and then characterized. At a later stage, stannous octoate and tetraphenyl tin were selected as catalysts for a more detailed study of the polymerization of LLA. The bimodal curves obtained from g.p.c. and d.s.c. studies in the case of the TPhT-initiated polymerization constitute an indirect indication of the occurrence of two initiation mechanisms. Both enzymatic and alkali hydrolysis experiments confirmed the degradability of these LLA/SB polyesters. The polyesters with high SB contents were associated with low crystallinities and were therefore found to be most susceptible to degradation.

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