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Novel polylactides with aminopropanediol or aminohydroxymethylpropanediol using stannous octoate as catalyst; synthesis, characterization and study of their biodegradability: 2

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Two series of novel polymers were synthesized by reacting L-lactide (LLA) with aminohydroxymethylpropanediol (AHPD) or aminopropanediol (APD) using stannous octoate as catalyst. Nuclear magnetic resonance, Fourier-transform infra-red spectroscopy, gel permeation chromatography (g.p.c.), differential scanning calorimetry (d.s.c.) and thermogravimetric analysis were employed for the characterization of these polymers. The above-mentioned polymers were semicrystalline (d.s.c. traces) when the molar ratio LLA/AHPD or LLA/APD was higher than 32/1. However, at molar ratios LLA/AHPD or LLA/APD below 32/1, the synthesized polymers were amorphous. D.s.c. and g.p.c. measurements show that, the higher the LLA content in the polymer, the higher the glass transition temperature T_g, melting temperature T_m, enthalpy of melting ΔH_m and number-average molecular weight M_n. The potential biodegradability of these polymers was tested with the aid of enzymatic and alkali hydrolysis. Total organic carbon and g.p.c. measurements showed that high AHPD or APD contents impart to polymers a higher susceptibility to degradation.

(Keywords: poly(L-lactide); propanediols; biodegradability)

INTRODUCTION

Poly(L-lactide)s (PLLA)[1–4], polyglycolide (PGA)[5] and polycaprolactone (PCL)[6–9], and several of their copolymers[10–17], have been widely investigated because of their inherent degradability[18] and compatibility[18,19] and their potential applications as controlled-release devices[20], absorbable sutures[21–24], implants for orthopaedic use[5,17,25], absorbable fibres[26] and most recently for disposable degradable plastic articles[27]. Despite its relatively high cost, PLLA has attracted much research work in view of its multipurpose applications[5,26–28]. Orthopaedic applications require a high *MW* and tensile strength, which, in the case of linear PLLA, also implies high melt viscosity. However, the latter may eventually result in degradation at melt processing[29]. Several previous publications have suggested the use of star-shaped PLLA in order to overcome the above-mentioned problem[28–34]. L-Lactide (LLA) is usually copolymerized with a multifunctional monomer such as pentaerythritol[29,30,32] or glycerol[28,33] in the bulk or in solution[31]. In this paper aminohydroxymethylpropanediol (AHPD) and aminopropanediol (APD) (with four and three functional groups, respectively) were copolymerized with LLA in an attempt to synthesize polymers endowed with biodegradability, but also with a somewhat higher rigidity (probably higher T_g and T_m because of amide bonds) compared to LLA/pentaerythritol polymers[29,32]. Stannous octoate was used as a catalyst in view of both its high efficiency (repeatedly stated in previous publications[1,10,28,29]) and its acceptance by the US FDA as a food additive[29].

EXPERIMENTAL

Synthesis of polymers from L-lactide (LLA) and aminohydroxymethylpropanediol (AHPD) or aminopropanediol (APD) in presence of tin octoate

L-Lactide (LLA) was purified by recrystallization from dried toluene under a nitrogen atmosphere and then dried for 24 h in vacuum at 30°C. 2-Ethylhexanoate tin (stannous octoate, Sn oct) was purchased from Wako Chemicals (Japan) and used without further purification. AHPD and APD were purified by distillation under reduced pressure and treated with sodium sulfate to remove any residual traces of moisture. Polymerization of L-lactide was carried out in a glass ampoule. Freshly recrystallized LLA and various amounts of AHPD or APD were transferred into the ampoule. Sn oct was added under nitrogen atmosphere. The ampoule was sealed in vacuum after three times purging with nitrogen. The ampoule was heated to 130°C in an oil bath for 5 days. After this time had elapsed, the ampoule was broken and

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the products were dissolved in chloroform, followed by microfiltering through a 0.45 μm pore membrane filter. The polymers whose comonomer molar feed was higher than 32/1 (LLA/AHPD) and 24/1 (LLA/APD) were precipitated dropwise into methanol, whereas those with molar composition lower than 32/1 (LLA/AHPD) and 20/1 (LLA/APD), that is richer in AHPD or APD, were evaporated to yield low-molecular-weight PLLA. Both high- and low-molecular-weight PLLA were dried in a vacuum desiccator at 50°C for 24 h.

Thermal analysis

The thermal behaviour of the polymers was studied by using a differential scanning calorimeter (DSC-10A Rigaku, Thermoflex) connected with a chart recorder (Rigaku) and a temperature controller unit (PTC 10D, Rigaku). The heating rate was 10°C $\min^{-1}$ and an empty aluminium pan was used as reference. Indium metal was used for calibration purposes for both T_m and ΔH_m (T_m(indium) = 156.7°C and ΔH_m(indium) = 28.36 J g^{-1}). The glass transition (T_g) was determined as the middle of the recorded step change in heat capacity, and melting points (T_{m1}, T_{m2}) were defined as the peaks of the endotherm curve.

Thermogravimetric analysis (t.g.a.)

T.g.a. measurements were carried out with a Shimadzu model DT-30 TGA at a heating rate of 5°C $\min^{-1}$ under a stream of N_2.

FT*i.r. spectroscopy*

The *FT*i.r. spectra were recorded with a spectrometer (Nicolet, model 710 FT-IR) connected to a PC (Nicolet) and Colour Pro plotter (Fujitsu, model FPG 315–101). The samples were recorded as films since they were soluble in $CHCl_3$.

Nuclear magnetic resonance spectroscopy (n.m.r.)

^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 from chloroform-d solutions at room temperature with tetramethylsilane (TMS) as internal standard and according to the following specifications: pulse width, 30°; acquisition time, 3.276 s; pulse interval time, 1.00 s.

Gel permeation chromatography (g.p.c.)

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

Enzymatic hydrolysis

Experimental details. 15 mg of polyester samples 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 added to two tubes and the third was for 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 onto the filtrate and TOC (total organic carbon) was measured. The TOC values were the average of two measurements and corrected appropriately by subtracting the blank levels.

Enzymatic hydrolysis for studying the degradation products. 100 mg of polyester sample 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 added to two tubes and the third was for a blank test. The enzyme used was lipase from *R. arrhizus*. The enzymatic hydrolysis was carried out at 37°C for 120 h. After the end of enzymatic hydrolysis the suspension was extracted first with $CHCl_3$ (and dried with Na_2SO_4 in order to remove residual moisture from the phosphate buffer) and the $CHCl_3$-insoluble part was treated with dimethylsulfoxide (DMSO). After filtration (removal of Na_2SO_4) the chloroform or DMSO was evaporated and the remaining samples were used for n.m.r. and g.p.c. measurements.

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

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

RESULTS AND DISCUSSION

The general schemes for the conversion of LLA and APD or AHPD to polymer are given in *Figures 1* and *2*, respectively.

The yields of polymer syntheses after precipitation with CH_3OH or evaporation of $CHCl_3$ (for AHPD/APD-poor and -rich polymers respectively), the n.m.r. determination of the LLA/AHPD or LLA/APD molar ratio in the polymer, and the M_n, M_w and n ($= M_w/M_n$) from the g.p.c. measurements are given in *Tables 1* and *2*.

Relatively high amounts of AHPD or APD and catalyst (Sn oct) were used for the purpose of obtaining low-molecular-weight polymers appropriate for both n.m.r. analysis and biodegradability experiments. Since our preliminary experiments showed that below 110°C no polymerization occurred whereas above 160°C the reaction proceeded at a non-controllable rate (browning of products due to decomposition), the temperature of 130°C was selected similar to previous publications[28,29,32] on LLA/glycerol or pentaerythritol. The polymer yields *versus* the AHPD or APD feed ratios were found to be in direct proportion, showing that AHPD or APD contents are always associated with lower polymer yields.

Apart from a broad absorption at ca. 3500 cm^{-1} indicating the presence of –OH groups, the *FT*i.r. spectra of these polymers show absorption bands at 1750 cm^{-1} and 1640, 1620 cm^{-1} thus confirming the formation of ester and amide bonds. *Figure 3* shows a representative *FT*i.r. trace of polymer LLA/AHPD, 8/1 (mol/mol) where all the above-mentioned absorptions can be identified.

The n.m.r. spectra analysis of our polymers shows the presence of resonance signals at 1.4 and 5.1 ppm, which were attributed to methyl and methine protons,

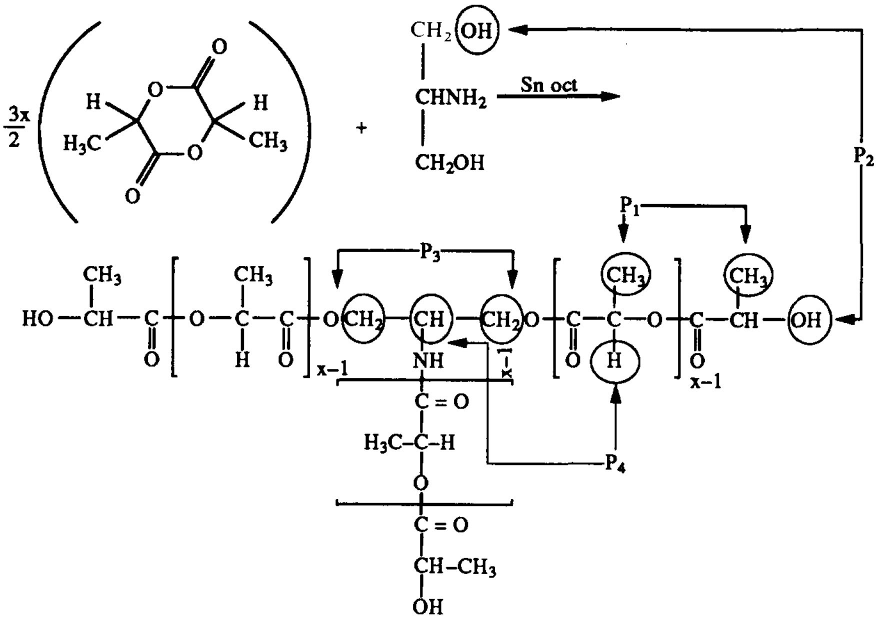


Figure 1 Reaction scheme of LLA/APD polycondensation polymers

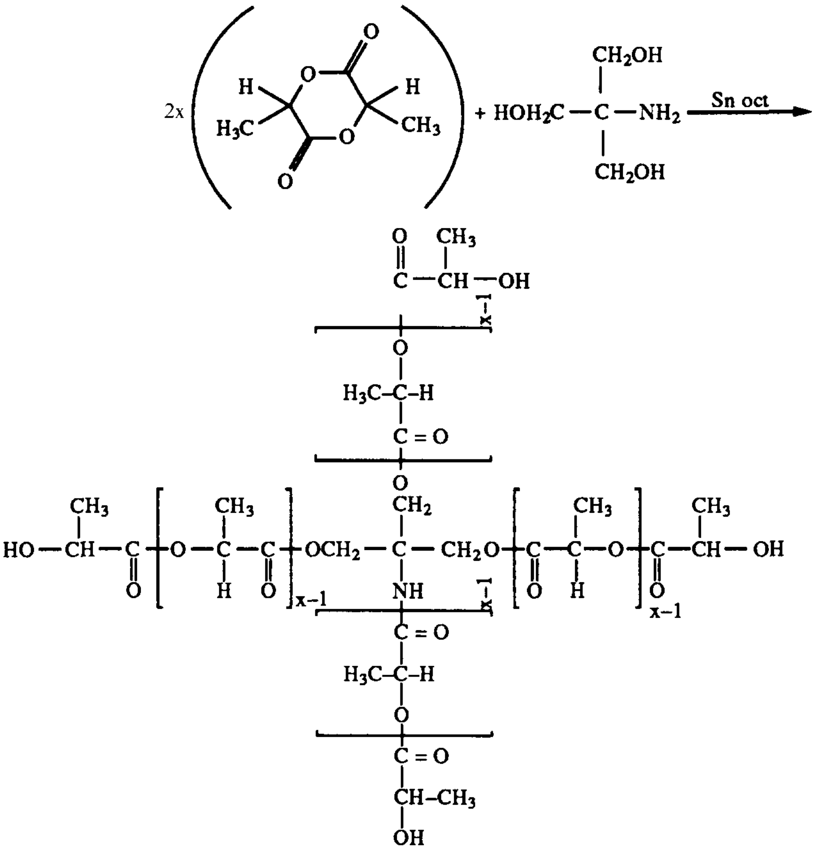


Figure 2 Reaction scheme of LLA/AHPD polycondensation polymers

respectively, similarly to previous publications for both linear[35] and star-shaped[29,32,36] PLLA. However, several other peaks were also identified and attributed to the incorporation of AHPD or APD, respectively. The peak at 4.2 ppm, for example, is believed to belong to the methylene groups of AHPD/APD in view of its proportional decrease in resonance intensity with an increase in the LLA/AHPD or LLA/APD molar ratio. Furthermore, the assignment of the peak at 2.8 ppm to the presence of a secondary –OH group at the chain end and/or an unreacted –OH group of AHPD or APD is also supported by the relative mobility concerning its position (2.4–3.6 ppm).

Figures 4 and *5* show representative n.m.r. traces for

Table 1 Percentage yields, n.m.r. evaluation of LLA/AHPD molar ratio in the polymer (synthesized using tin octoate at 130°C for 120 h) and determination of number- and weight-average molecular weights (M_n, M_w) and polydispersity indices (n) from g.p.c. measurements

Monomers LLA/AHPD (feed molar ratio)	After extraction ($CHCl_3$) and precipitation (CH_3OH)	Yield (%)	N.m.r. LLA/AHPD (polymer molar ratio)	G.p.c. M_n	G.p.c. M_w	G.p.c. n ($=M_w/M_n$)
100/0	+	100	–	42000	81000	1.9
256/1	+	99	–	11800	21600	1.8
128/1	+	99	120/1	9500	15700	1.7
96/1	+	96	80/1	8900	14100	1.6
64/1	+	95	56/1	7200	9400	1.3
48/1	+	96	45/1	5300	7400	1.4
40/1	+	92	36/1	4750	6900	1.5
32/1	+	91	28/1	2600	3900	1.5
24/1	after evaporation ($CHCl_3$)	93	25/1	1700	2800	1.6
16/1	+	84	16/1	1100	1700	1.5
8/1	+	82	10/1	800	1100	1.4
4/1	+	82	6/1	610	980	1.6

Table 2 Percentage yields, n.m.r. evaluation of LLA/APD molar ratio in the polymer (synthesized using tin octoate at 130°C for 120 h) and determination of number- and weight-average molecular weights (M_n, M_w) and polydispersity indices (n) from g.p.c. measurements

Monomers LLA/APD (feed molar ratio)	After extraction ($CHCl_3$) and precipitation (CH_3OH)	Yield (%)	N.m.r. LLA/APD (polymer molar ratio)	G.p.c. M_n	G.p.c. M_w	G.p.c. n ($=M_w/M_n$)
100/0	+	100	–	42000	81000	1.9
256/1	+	98	–	23900	57100	2.4
192/1	+	99	–	16000	33600	2.1
128/1	+	97	–	15300	29800	2.0
96/1	+	95	100/1	10400	18100	1.7
64/1	+	94	72/1	6500	11500	1.8
48/1	+	94	55/1	5250	6770	1.3
32/1	+	91	36/1	4970	6500	1.3
24/1	after evaporation ($CHCl_3$)	90	27/1	4200	5500	1.3
18/1	+	86	19/1	2020	2970	1.5
12/1	+	85	14/1	1000	1460	1.5
6/1	+	81	6/1	790	1170	1.5
3/1	+	80	4/1	470	800	1.4

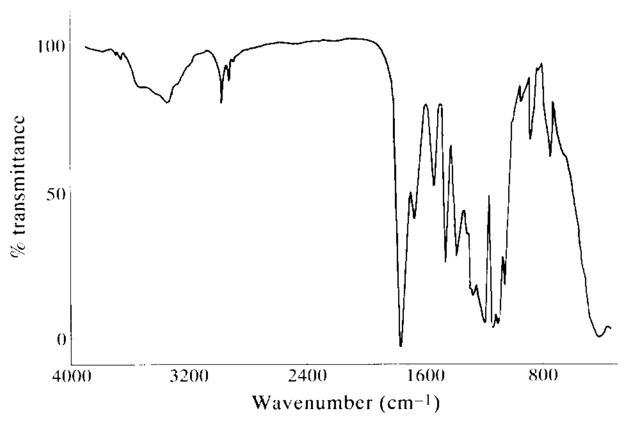


Figure 3 *FT*i.r. spectrum of LLA/AHPD, 8/1 (mol/mol) polymer

LLA/APD, 18/1 (mol/mol) and LLA/AHPD, 24/1 (mol/mol). *Figure 1* shows the peak assignments for LLA/APD polymers.

The following three equations were suggested for the determination of the LLA/APD or LLA/AHPD molar ratio of the polymers according to the n.m.r. assignment:

$$3x=(P_1) \tag{1}$$

$$x+y=(P_4) \tag{2}$$

$$4y=(P_3) \tag{3}$$

where (P_1), (P_4) and (P_3) are equal to the integration intensities and x/y is the LLA/APD molar ratio. As an example we could refer to LLA/APD, 18/1 (comonomer molar feed ratio):

$$3x=22.3 \Rightarrow x=7.433 \tag{4}$$

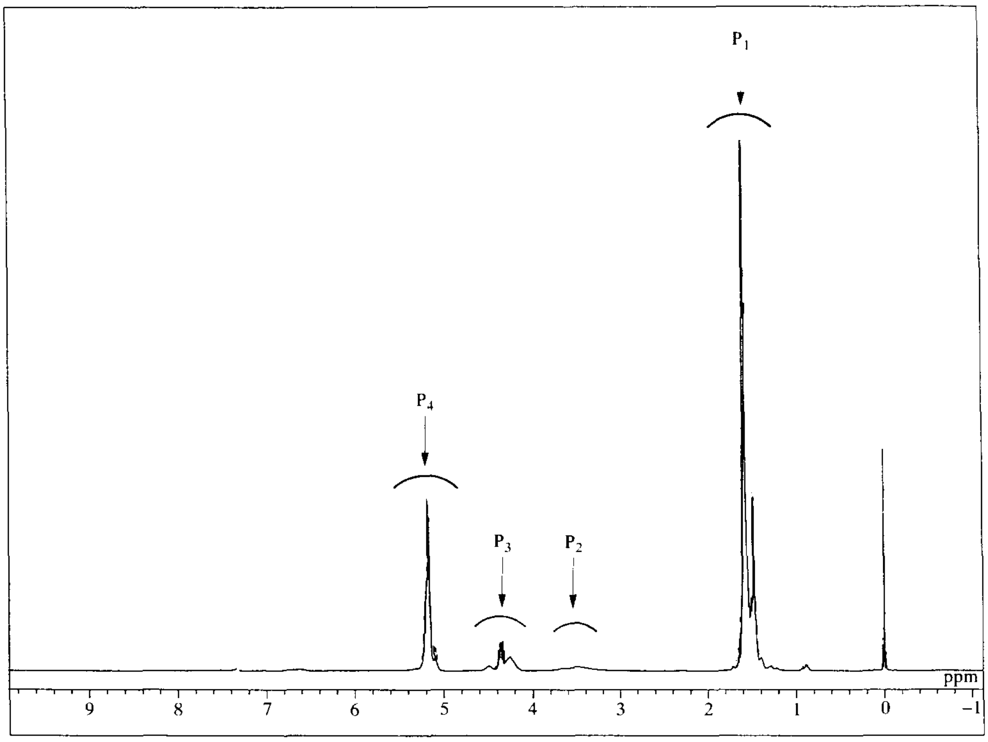


Figure 4 ^{1}H n.m.r. spectrum of LLA/APD, 18/1 (mol/mol) polymer

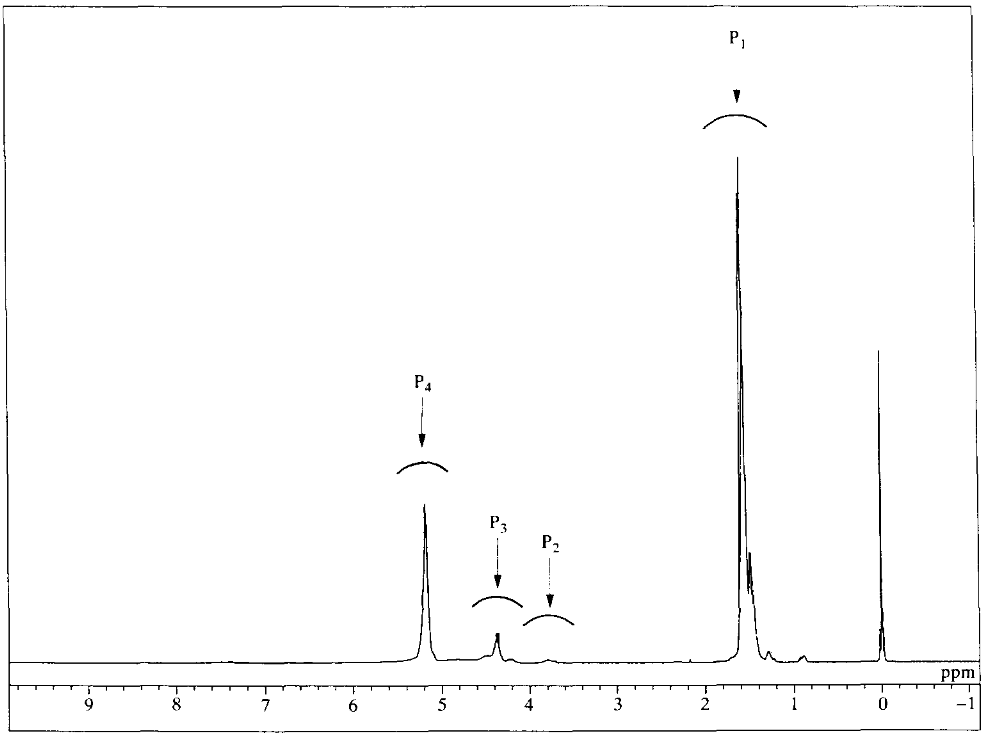


Figure 5 ^{1}H n.m.r. spectrum of LLA/AHPD, 24/1 (mol/mol) polymer

$$x+y=6.35 \Rightarrow x=6.00 \quad (5)$$

$$4y=1.4 \Rightarrow y=0.35 \quad (6)$$

By taking the average of the x values found from equations (4) and (5), we get $x=6.75$. Hence:

$$\frac{x}{y}=\frac{6.75}{0.35}=\frac{19}{1}$$

The g.p.c. traces for both LLA/AHPD and LLA/APD polymers (synthesized using Sn oct as catalyst) give monodisperse curves, thus excluding the possibility that more than one mechanism is in action. Since this is in agreement with previous publications where Sn oct was used as catalyst for the LLA/pentaerythritol[29] and LLA/glycerol[28] systems, it is fair to suggest that the initiation of the polymerization occurs via the hydroxyl groups of the multifunctional component (AHPD or APD) similarly to the polymerization of ε-caprolactone in the presence of alcohol[37].

At this instance it should be mentioned that the PLLAs (synthesized with LLA/APD in the presence of Sn oct) are viscous liquids at LLA/APD$<$24/1 (mol/mol) whereas they become solids for LLA/APD$\geqslant$24/1 (mol/mol). Similarly the LLA/AHPD polymers are viscous liquids for LLA/AHPD$<$32/1 and solids for LLA/AHPD$\geqslant$32/1 (mol/mol).

Tables 3 and *4* summarize the thermal properties of these novel polymers such as their glass transitions (T_g), crystallization temperatures (T_{cr}), melting peaks (T_m), heats of fusion (ΔH_m) and percentage crystallinities (X_c) obtained from d.s.c. analysis.

Almost all the d.s.c. first-run traces for LLA/AHPD and LLA/APD polymers gave monodisperse curves whereas in the second run two distinct peaks appeared and on some occasions this second peak was in the form of a 'shoulder' as indicated in *Tables 3* and *4*. Therefore the monodispersity of d.s.c. (first-run) and g.p.c. curves confirms the occurrence of one single polymerization mechanism whereas the bimodality of second-run d.s.c. traces should be attributed to the formation of different spherulite morphologies and sizes, as previously confirmed with SEM measurements[38,39], and probably differences in molecular weights as well[38].

The t.g.a. measurements of the polymers (*Tables 3* and *4*) are expressed in terms of 'initial' ($T_{d,0}$) and 'half' decomposition ($T_{d,1/2}$) temperature[40]. $T_{d,0}$ is defined as the inclination point of the loss weight/temperature curve and $T_{d,1/2}$ as the temperature at which the loss of weight of the polymer during pyrolysis reaches 50% of its final value. Despite the fact that $T_{d,0}$ decreased on increasing the ratio of AHPD or APD, $T_{d,1/2}$ occasionally followed a different tendency; that is, the polymers rich in AHPD or APD showed a degradation pattern consisting of two stages, similarly to that reported in publications on

Table 3 Glass transitions (T_g), crystallization temperatures (T_{cr}), melting points (T_{m1}, T_{m2}), heats of fusion (ΔH_m), percentage crystallinities (X_c), initial decomposition ($T_{d,0}$) and half decomposition temperatures ($T_{d,1/2}$) of LLA/AHPD polymers

Monomers LLA/AHPD (feed molar ratio)	T_g (°C)		T_{cr} (°C)	T_{m1} (°C)		T_{m2} (°C)		ΔH_m (J g^{-1})		X_c (%)		T.g.a.	
	1st run	2nd run	2nd run	1st run	2nd run	1st run	2nd run	1st run	2nd run	1st run	2nd run	$T_{d,0}$ (°C)	$T_{d,1/2}$ (°C)
100/0	61	60	118	177	175	–	–	65.8	63.0	70.2	67.2	241.1	300.5
256/1	46	46	100	157	156	126	144	61.6	59.3	65.7	63.2	240.7	303.8
128/1	42	42	92	148	145	120	133	55.4	53.1	59.1	56.7	239.9	307.9
96/1	41	40	85	146	143	125	135	52.3	50.0	55.8	53.4	239.5	314.6
64/1	38	37	79	132	133	127(sh)	125	40.2	37.5	42.9	40.0	235.0	317.0
48/1	33	31	–	120	–	108	–	30.5	27.3	32.6	29.1	231.6	320.3
40/1	25	27	–	94	–	60(sh)	–	19.9	18.6	21.2	19.9	229.7	322.7
32/1	20	24	–	91	–	60	–	14.7	11.4	15.7	12.2	227.8	323.5
24/1	12	14	–	88	–	–	–	10.8	9.2	11.5	9.8	225.6	320.0
16/1	5	8	–	–	–	–	–	–	–	–	–	217.0	317.5
8/1	−15	−22	–	–	–	–	–	–	–	–	–	208.4	313.2
4/1	−20	−25	–	–	–	–	–	–	–	–	–	195.7	310.8

Table 4 Glass transitions (T_g), crystallization temperatures (T_{cr}), melting points (T_{m1}, T_{m2}), heats of fusion (ΔH_m), percentage crystallinities (X_c), initial decomposition ($T_{d,0}$) and half decomposition temperatures ($T_{d,1/2}$) of LLA/APD polymers

Monomers LLA/APD (feed molar ratio)	T_g (°C)		T_{cr} (°C)	T_{m1} (°C)		T_{m2} (°C)		ΔH_m (J g^{-1})		X_c (%)		T.g.a.	
	1st run	2nd run	2nd run	1st run	2nd run	1st run	2nd run	1st run	2nd run	1st run	2nd run	$T_{d,0}$ (°C)	$T_{d,1/2}$ (°C)
100/0	61	60	118	177	175	–	–	65.8	63.0	70.2	67.2	241.1	300.5
256/1	55	53	111	164	163	–	153	63.2	59.7	67.5	63.7	240.0	304.6
192/1	52	50	102	162	161	–	150	61.4	56.0	65.5	59.8	238.8	309.4
128/1	48	49	98	161	159	–	–	59.8	52.5	63.8	56.0	238.2	316.2
96/1	43	45	96	145	143	–	130	56.7	50.1	60.5	53.5	237.6	318.7
64/1	39	43	90	141	138	135	119	44.0	38.5	47.0	41.1	233.2	323.8
48/1	36	38	87	132	132	118(sh)	128	33.7	27.3	36.0	29.1	230.7	325.9
32/1	30	32	–	131	129	122	122	24.2	19.2	25.8	20.5	228.9	327.3
24/1	22	21	–	110	–	–	–	11.4	7.8	12.2	8.3	226.0	324.5
18/1	7	14	–	–	–	–	–	–	–	–	–	224.8	321.6
12/1	−17	−16	–	–	–	–	–	–	–	–	–	212.5	317.5
6/1	−24	−22	–	–	–	–	–	–	–	–	–	207.3	314.2
3/1	−30	−28	–	–	–	–	–	–	–	–	–	196.8	312.0

Table 5 Results of enzymatic hydrolysis using lipase (*Rhizopus arrhizus*) in phosphate buffer (15 mg of polymer in 2 ml of buffer KH_2PO_4/Na_2HPO_4, pH 7.0) expressed in TOC (ppm) and percentage weight losses (wt%) against alkali hydrolysis (10% NaOH w/v, 80°C) time for LLA/AHPD polymers

Monomers LLA/AHPD (feed molar ratio)	TOC (ppm)		Weight loss (%)				
	1 day	3 days	2 h	5 h	10 h	20 h	40 h
100/0	3	7	1.0	2.2	3.8	6.1	10.5
256/1	15	25	1.4	3.0	5.4	7.6	12.8
128/1	40	70	1.8	3.9	6.9	9.4	15.5
96/1	60	80	2.1	4.4	7.2	12.6	17.9
64/1	70	90	2.6	4.9	7.4	15.8	26.0
48/1	90	120	3.5	5.8	8.8	18.4	32.5
40/1	90	110	3.7	6.3	9.4	20.0	34.1
32/1	110	140	4.6	7.2	12.0	21.7	35.4
24/1	125	160	5.8	9.1	16.4	27.0	46.4
16/1	140	190	6.7	10.0	18.2	31.6	51.8
8/1	160	200	9.1	17.2	23.9	46.4	66.5
4/1	170	220	11.3	18.5	32.5	54.0	74.1

Table 6 Results of enzymatic hydrolysis using lipase (*Rhizopus arrhizus*) in phosphate buffer (15 mg of polymer in 2 ml of buffer KH_2PO_4/Na_2HPO_4, pH 7.0) expressed in TOC (ppm) and percentage weight losses (wt%) against alkali hydrolysis (10% NaOH w/v, 80°C) time for LLA/APD polymers

Monomers LLA/APD (feed molar ratio)	TOC (ppm)		Weight loss (%)				
	1 day	3 days	2 h	5 h	10 h	20 h	40 h
100/0	3	7	1.0	2.2	3.8	6.1	10.5
256/1	10	20	1.2	2.5	4.7	6.9	11.4
192/1	20	30	1.4	2.8	5.3	7.5	12.0
128/1	35	50	1.5	3.0	5.8	8.0	13.8
96/1	40	60	1.7	3.3	6.0	9.1	17.0
64/1	40	70	2.0	3.9	6.8	13.0	21.5
48/1	60	90	3.2	4.7	8.4	16.7	30.8
32/1	70	100	4.0	6.5	10.7	20.2	34.6
24/1	75	120	5.3	8.0	14.9	25.3	43.2
18/1	90	140	6.0	9.1	16.0	28.5	47.5
12/1	90	150	7.2	10.5	19.2	35.7	55.0
6/1	110	170	8.0	14.8	25.6	43.0	62.7
3/1	125	190	8.9	17.2	30.0	50.8	70.8

LLA/glycerol polymers[28], LLA/sorbitol[36] and annealed nylon-6,6 samples[41]. This two-stage decomposition pattern should be attributed as previously to post-condensation/crosslinking reactions mainly induced by the presence –OH (either AHPD/APD or chain ends of LLA)[36] or to lesser extent by $-NH_2$ (AHPD or APD).

The biodegradability of these novel polymers was assessed in terms of their susceptibility to enzymatic hydrolysis. *Tables 5* and *6* give the TOC (total organic carbon, soluble products) results for the two series of polymers after the samples were exposed to hydrolysis for 24 and 72 h, respectively.

Although the primary step in biodegradation of a polymeric substrate may result in the formation of one or more organic compound products, often with no formation of CO_2 in the process, the ultimate biodegradation of a molecule requires that the organic carbon trapped in its structure should be mineralized into CO_2:

$$\text{organic C, H, O} \rightarrow CO_2 + H_2O$$

Despite the fact that this approach provides direct reliable information on complete biodegradation, we should bear in mind that it does not work with co-metabolism where a complete mineralization of substrate does not usually take place[42].

The degradation rates of polymers were investigated with regard to TOC and M_n (g.p.c.) changes *versus* their exposure time to lipase (*Rhizopus arrhizus*). Typical curves of TOC and M_n values of LLA/AHPD polymers 3/1, 12/1, 24/1 and 128/1 (expressed in mol/mol) against enzymatic hydrolysis time are shown in *Figure 6*. It is obvious that, although TOC values increase, the M_n value displays only slight decrease because of limited cleavage of hydrolysable bonds. Finally, the n.m.r. spectrum of polymer LLA/APD, 12/1 (mol/mol) (*Figures 7a* and *7b*) before and after its enzymatic hydrolysis (5 days) showed the appearance of a distinct new peak at 3.0 (–OH, end-group of PLLA) and proportionally stronger peak at 5 ppm (–OH of APD)[43], which confirm the degradation of the polymer by releasing APD (peaks between 2.0 and 3.5 ppm, *Figures 7b*$_1$ and *b*$_2$)[43].

Tables 7 and *8* give the weight-loss percentages of the LLA/AHPD and LLA/APD polymers after their alkali

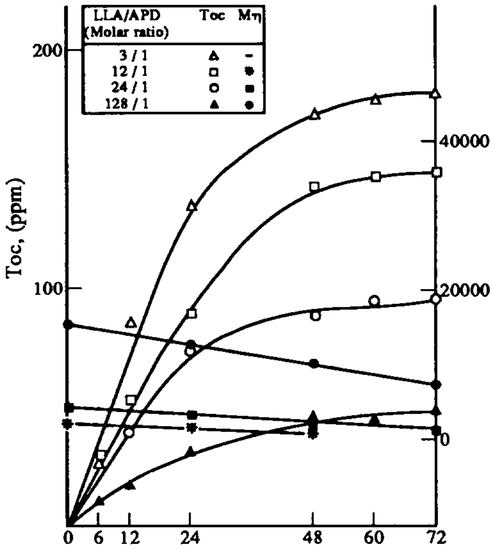


Figure 6 TOC and M_n (g.p.c.) values *versus* exposure time to enzymatic hydrolysis for several LLA/APD polymers

Table 7 Alkali hydrolysis (10% NaOH w/v, 80°C) of LLA/AHPD polymers: percentage crystallinities (X_c) and molecular-weight distribution (M_n, M_w) from d.s.c. and g.p.c. measurements against their hydrolysis time

Monomers LLA/AHPD (feed molar ratio)	X_c (%)		5 h		40 h	
	5 h	40 h	M_n	M_w	M_n	M_w
100/0	75.1	56.5	41500	83800	40500	84000
256/1	70.0	49.2	11000	23000	9000	21600
128/1	62.4	44.0	8450	17600	7200	16800
96/1	60.1	37.5	7600	16500	6100	15700
64/1	54.5	32.3	6050	11200	4800	11400
48/1	40.8	24.9	4100	8150	3000	8900
40/1	30.6	15.0	3580	7700	2850	8450
32/1	23.4	10.2	1860	4600	1400	5100
24/1	17.0	6.8	1340	3500	980	3300
16/1	4.3	–	920	2250	790	2460
8/1	–	–	600	1400	[a]	[a]
4/1	–	–	[a]	[a]	[a]	[a]

[a] No reliable determination of M_n, M_w (g.p.c.) was possible due to overlapping of solvent peak ($CHCl_3$) with that of the monomer/oligomer

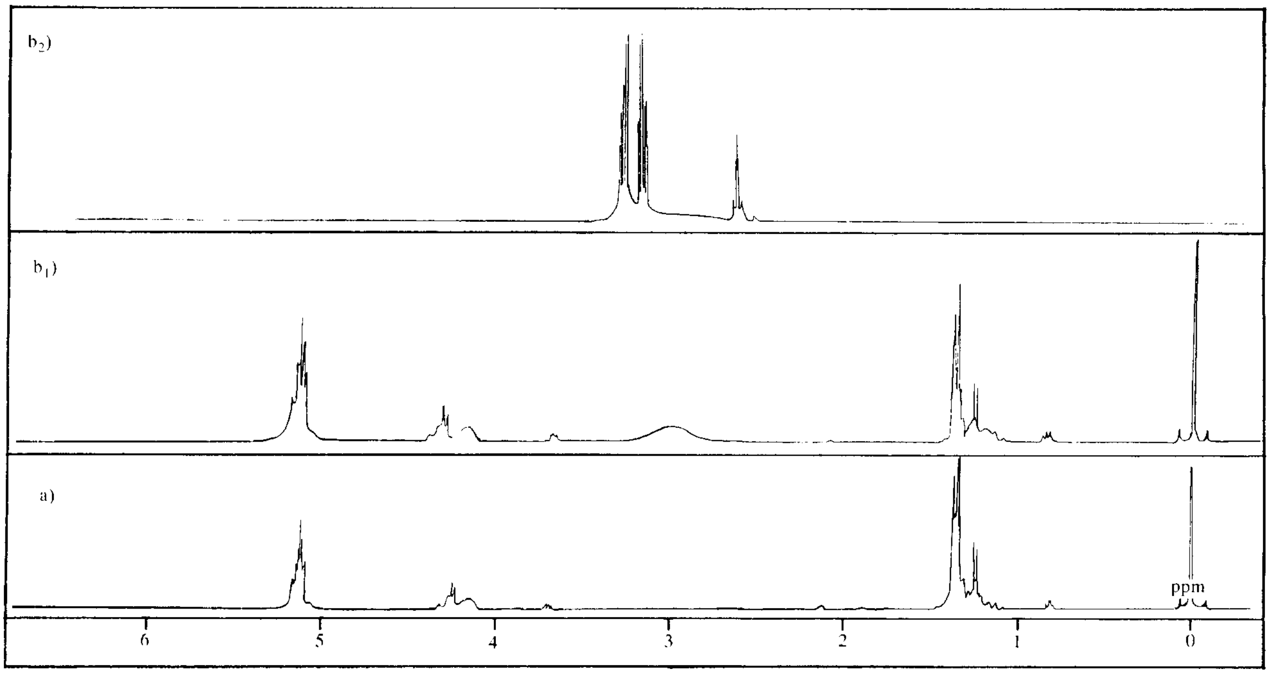


Figure 7 ^{1}H n.m.r. of LLA/APD, 12/1 (mol/mol) before (a) and after (b) exposure for 5 days to enzymatic hydrolysis; b_1 stands for the soluble in $CHCl_3$ ($CDCl_3$ for n.m.r.) PLLA fraction and b_2 stands for the soluble in DMSO (DMSO-d_6 for n.m.r.) APD fraction after enzymatic hydrolysis

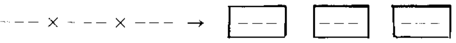
Table 8 Alkali hydrolysis (10% NaOH w/v, 80°C) of LLA/APD polymers: percentage crystallinities (X_c) and molecular-weight distribution (M_n, M_w) from d.s.c. and g.p.c. measurements against their hydrolysis time

Monomers LLA/APD (feed molar ratio)	X_c (%) 5 h	X_c (%) 40 h	5 h M_n	5 h M_w	40 h M_n	40 h M_w
100/0	75.1	56.5	41500	83800	40500	84000
256/1	71.7	52.0	22100	58200	21100	57900
192/1	68.9	49.3	14800	34300	12000	35000
128/1	66.2	47.4	14100	30400	11400	33200
96/1	64.0	43.2	8500	16900	7200	19200
64/1	53.5	37.6	5400	12700	4500	14600
48/1	42.3	29.5	4300	8200	3350	9400
32/1	31.0	15.3	4000	7900	2700	8650
24/1	28.5	9.9	3150	6380	2200	7100
18/1	6.2	–	1640	3550	1100	3960
12/1	–	–	840	1770	620	2150
6/1	–	–	630	1520	[a]	[a]
3/1	–	–	[a]	[a]	[a]	[a]

[a] No reliable determination of M_n, M_w (g.p.c.) was possible due to overlapping of solvent peak ($CHCl_3$) with that of the monomer/oligomer

hydrolysis (10% NaOH w/v, 80°C) against time. High AHPD or APD contents resulted in high weight-loss rates, which were, in their turn, directly proportional to the exposure time of polymers to alkali hydrolysis. The percentage crystallinities (X_c) and the molecular-weight distributions (M_n, M_w) were investigated with d.s.c. and g.p.c. measurements, before and after the hydrolysis of polymers (*Table 8*).

An increase in X_c of polymers against time of alkali hydrolysis shows that, at least at an early stage, the amorphous regions of the LLA/AHPD or APD are far more susceptible to hydrolysis, and thus their gradual removal by degradation results in higher X_c values. The g.p.c. measurements indicated slightly higher M_n and M_w after 5 h whereas a drastic decrease occurred (reaching as low as 40–50% of the initial values) after 40 h. This decrease in molecular-weight distribution of polymers after 40 h hydrolysis should be attributed to cleavage of the main backbone chain, which is the third step after the removal of the amorphous regions (first) and probable disruption of side chains (second)[44]. Since degradation does not occur only at the surface but through the entire mass of the LLA/AHPD or LLA/APD polymer, in view of its impregnation by alkali solution, it could be described as 'homogeneous'. Despite the presence of multifunctional monomers such as AHPD and APD, which theoretically could act as a crosslinking agent, solubility experiments with $CHCl_3$ did not confirm any crosslinking. Therefore it could be suggested that the degradation mechanistic scheme is promoted by the cleavage of labile bonds along the polymer backbone, which eventually result in even lower weights and occasionally water-soluble products as follows:



where × stands for the labile backbone bonds.

Since an increase in AHPD or APD content of the LLA/AHPD or APD copolymers promoted higher degradation rates, the × parts should probably be the bonds between LLA–APD or –AHPD units, as shown in *Figures 1* and *2*, respectively.

CONCLUSIONS

Two novel series of biodegradable polymers were synthesized based on LLA/AHPD and LLA/APD using Sn oct as catalyst. G.p.c. and d.s.c. usually showed monodisperse g.p.c. curves for the Sn oct, thus indicating the occurrence of one single polymerization mechanism. The susceptibility of polymers to biodegradation was tested by means of enzymatic hydrolysis (TOC measurements) *versus* their exposure time. High AHPD or

APD content and low percentage crystallinity (d.s.c.) substantially promoted the degradation of the novel polymers. Alkali hydrolysis tests showed substantial weight losses and lower molecular weights because of bond cleavage along the main chain for the polymers rich in AHPD or APD.

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