Polylactones: 23. Polymerization of *racemic* and *meso* D,L-lactide with various organotin catalysts—stereochemical aspects

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Racemic and *meso* D,L-lactide were polymerized at 90 or 120°C in xylylene or at 120, 150 and 180°C in bulk. Furthermore, copolymerizations of *racemic* D,L-lactide and L,L-lactide were conducted at 180°C in bulk. Tributyltin methoxide (Bu_3SnOMe), dibutyltin dimethoxide ($Bu_2Sn(OMe)_2$) and Sn(II) octoate were used as initiators. Despite high yields only low molecular weights were obtained with both tin methoxides. Sn(II) octoate gave significantly higher molecular weights. The stereosequences were analysed by ^1H and ^{13}C n.m.r. spectroscopy on the basis of tetrad effects. The signal assignments are discussed. Bu_3SnOMe and $Bu_2Sn(OMe)_2$ are effective transesterification catalysts and cause 'back-biting' degradation even at 90°C. In all series of polymerizations initiated with tin methoxides two tendencies are detectable: increasing randomization of the stereosequence with increasing reaction time and with higher reaction temperatures. In contrast, Sn(II) octoate does not cause transesterification at $\leqslant 120°C$ and even at 180°C randomization of the stereosequences is slow.

(Keywords: polylactones; polymerization; catalysis; stereochemistry)

INTRODUCTION

Poly(D,L-lactide) with a more or less random stereosequence is known to be an amorphous, transparent material with a glass transition temperature (T_g) around 50–55°C. It may be useful for the production of biodegradable films and for drug delivery devices. Some properties such as the T_g, solubility or rate of biodegradation may depend on the stereosequence[1–3], yet systematic studies in this direction are still lacking.

In the past 15 years four papers have appeared dealing with n.m.r. spectroscopic stereosequence analyses of poly(D,L-lactide)s prepared by ring-opening polymerization of *racemic* D,L-lactide[1–4]. Only one report describes the polymerization of *meso* D,L-lactide[5]. The poly(D,L-lactide)s were prepared in a very narrow range of reaction conditions and the stereosequence analyses are not convincing. Only quite recently have consistent ^{13}C n.m.r. stereosequence analyses of poly(D,L-lactide)s derived from *racemic* D,L-lactide been reported[4].

The present work is part of a systematic study of poly(D,L-lactide)s prepared under a broad variety of reaction conditions. The purpose of the entire work is three-fold. First, comparison of *racemic* with *meso* D,L-lactide under identical reaction conditions. Second, comparison of various initiators under identical reaction conditions. Third, the evaluation of the influence of the reaction time and temperature on the stereochemical course of all polymerizations. This paper concentrates on two highly effective tin initiators: tributyltin methoxide (Bu_3SnOMe) and Sn(II) octoate. The latter is mentioned in several papers and patents[4,6–12], because it enables the preparation of high molecular weight polylactides without racemization. Bu_3SnOMe was recently reported[13,14] to be an effective transesterification catalyst initiating the polymerization of L-lactide and various lactones at moderate temperatures. A non-ionic insertion mechanism was established for this initiator.

EXPERIMENTAL

Materials

Racemic and *meso* D,L-lactide were donated by Boehring AG (Ingelheim, Germany). They were recrystallized from dry ethyl acetate and dried over P_4O_{10} *in vacuo*. Bu_3SnOMe and dibutyltin dichloride were purchased from Aldrich Co. (St Louis, MO, USA) and distilled *in vacuo*. Tin(II) octoate (2-ethylhexanoate) was purchased from Ventron GmbH (Karlsruhe, Germany) and used without purification. Xylylene was distilled over P_4O_{10} and then over sodium/potassium alloy.

Dibutyltin dimethoxide ($Bu_2Sn(OMe_2)$)

Sodium (0.4 mol) was dissolved in dry methanol (200 ml) and a solution of dibutyltin dichloride (0.2 mol) in methanol (100 ml) was added dropwise. After standing for 12 h the reaction mixture was decanted from sodium chloride, and the product was isolated by distillation *in vacuo*. Yield: 71%; b.p. 126–128°C/0.05 mbar; n_D^{20} 1.4890. Analyses (%): calculated for $C_{10}H_{24}SnO_2$ (295.0), C 40.76, H 8.21; found C 40.96, H 8.35.

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Polymerizations

In solution. Erlenmeyer flasks (50 ml) with ground glass joints were used as reaction vessels, after silanization of the glass walls with dichlorodimethylsilane. A D,L-lactide (30 mmol) was weighed into the reaction vessel, then 25 ml of dry xylylene and 0.6 ml of an 0.5 M initiator solution in xylylene were added. The reaction vessel was closed with a glass stopper and steel spring and immersed in a thermostatically controlled oil bath. Finally, the reaction mixture was diluted with dichloromethane (20–40 ml) and precipitated poly(D,L-lactide) was isolated by filtration, washed with cold methanol and dried at 40°C *in vacuo*.

In bulk. A D,L-lactide (30 mmol) was weighed into a silanized Erlenmeyer flask (25 ml) and heated to 120 or 130°C until the monomer was completely molten. The reaction vessel was then opened for 1 s and 0.6 ml of a 0.5 M initiator solution (in xylylene) was injected by means of a syringe. The reaction vessel was completely immersed into a thermostatically controlled oil bath. The polylactide was worked up as described above.

Measurements

The inherent viscosities were measured with an automated Ubbelohde viscometer thermostatically controlled at 20°C. The g.p.c. measurements were conducted on a Kontron h.p.l.c. apparatus combined with a Waters differential refractometer (model 410). Dichloromethane was used as eluent at a flow rate of 1 ml min^{-1}. A combination of four Ultrastyrogel® columns was used.

The ^{1}H n.m.r. spectra were obtained on a Bruker AM 360 FT spectrometer in 5 mm o.d. sample tubes. A digital resolution of 16 K data points/4000 Hz spectral width was applied. The ^{13}C n.m.r. spectra were performed on a Bruker MSL 300 FT spectrometer in 10 mm o.d. sample tubes. A digital resolution of 32 K data points/18 000 Hz spectral width was used, a pulse angle of ~30° along with a relaxation delay of 2 s, and 10^3–10^4 transients were accumulated. $CDCl_3$ served as solvent and TMS as internal standard for all ^{1}H and ^{13}C n.m.r. measurements. The quantification of signal intensities was achieved by the Bruker 'Linesim' program. Its reliability was checked in several cases by the cut-and-weigh method using expanded plots.

RESULTS AND DISCUSSION

Polymerizations—preparative aspects

It is well known and quite conceivable that high temperatures favour transesterification. In order to obtain random stereosequences and to study the influence of the reaction temperature, bulk polymerizations were conducted at 120, 150 and 180°C (*Tables 1* and *2*). Low reaction temperatures are of interest to avoid or minimize transesterification. However, the melting point of *racemic* D,L-lactide (124–126°C) prevents bulk polymerizations below 120°C. Therefore, polymerizations at lower temperatures had to be conducted in solution. A comparison of four different high boiling solvents showed that no polymerization occurred in dimethylsulphoxide, dimethylformamide or diethyleneglycol dimethyl ether, whereas xylylene proved to be useful. Thus, xylylene was used throughout this work as the inert reaction medium (*Tables 3–5*).

Unfortunately, *racemic* D,L-lactide is only sparingly soluble in xylylene at temperatures $\leqslant 60$°C. Furthermore, regardless of initiator no polymerization was observed at 60°C within 24 h. Therefore, polymerizations conducted at 90 and 120°C are listed in *Tables 3–5*.

When the yields are compared for *racemic* and *meso* D,L-lactide it is conspicuous that polymerizations of *meso* D,L-lactide give lower yields under all circumstances. As described in future parts of this series the same observation was made for other initiators. Because recrystallized *meso* D,L-lactide with constant melting point was used and because the lower yields are independent of initiator, it is obvious that the higher thermodynamical stability of *meso* D,L-lactide is responsible for this negative result. In the case of L-lactide and *racemic* D,L-lactide both methyl groups are located on the same side of the ring plane. This unfavourable *cis* position favours polymerization compared to the *trans* position of *meso* D,L-lactide.

Comparison of the viscosities demonstrates that Bu_3SnOMe yields low molecular weights regardless of the reaction conditions and despite high yields (*Tables 1* and *3*). Furthermore, the yields decrease with increasing reaction time in series 3–6 and 7–12 in *Table 3* or 1–5, 7–10 and 11–15 in *Table 1*. These findings are best explained by transesterification yielding cyclic oligomers

Table 1 Bulk polymerizations conducted with tributyltin methoxide (M/I = 100:1)

No.	Temp. (°C)	Time (h)	*Racemic* D,L-lactide			*Meso* D,L-lactide		
			Yield	η_{inh}(dl g^{-1})^a	L_i^{b}	Yield (%)	η_{inh}(dl g^{-1})^a	L_i^{b}
1	120	2	91	0.06	3.8	27	0.09	1.4
2	120	4	90	0.07	–	52	0.12	
3	120	8	80	0.23		56	0.22	
4	120	16	72	0.23	–	57	0.16	
5	120	24	70	0.10	2.5	60	0.14	1.8
6	150	2	48	0.09	3.6	59	0.11	1.6
7	150	4	77	0.08	–	60	0.13	
8	150	8	65	0.08		62	0.16	
9	150	16	50	0.11	–	69	0.15	
10	150	24	48	0.08	2.1	66	0.13	2.0
11	180	2	58	0.10	2.5	55	0.10	1.8
12	180	4	45	0.09	–	47	0.12	
13	180	8	43	0.10	–	45	0.10	
14	180	16	42	0.08	–	44	0.10	
15	180	24	40	0.07	2.0	41	0.09	2.0

^{a}Measured at 20°C (2 g l^{-1}, CH_2Cl_2)

^{b}Average length of isotactic blocks, margin of error ±0.2

Table 2 Bulk polymerizations conducted with Sn(II) octoate (M/I = 100:1)

			Racemic D,L-lactide			*Meso* D,L-lactide		
No.	Temp. (°C)	Time (h)	Yield (%)	η_{inh}(dl g^{-1})[a]	L_i[b]	Yield (%)	η_{inh}(dl g^{-1})[a]	L_i[b]
1	120	2	99	0.41	3.2	12	0.25	1.3
2	120	4	99	0.44	3.2	85	0.44	1.3
3	120	8	99	0.46	3.2	90	0.50	1.3
4	120	16	99	0.58	3.2	80	0.19	1.3
5	120	24	99	0.52	3.2	78	0.13	1.4
6	150	2	92	0.30	2.9	98	0.10	1.4
7	150	4	90	0.37	2.9	79	0.39	1.4
8	150	8	99	0.35	2.9	72	0.47	1.4
9	150	16	99	0.36	2.7	65	0.28	1.6
10	150	24	76	0.33	2.8	61	0.21	1.5
11	180	2	88	0.70	2.8	99	0.13	1.5
12	180	4	93	0.61	2.8	91	0.28	1.5
13	180	8	12	0.20	2.5	10	0.17	1.8
14	180	16	0	–	–	0	–	–

[a] Measured at 20°C (2 g l^{-1}, CH_2Cl_2)
[b] Average length of isotactic blocks

Table 3 Polymerizations conducted in xylylene with tributyltin methoxide (M/I = 100:1)

			Racemic D,L-lactide			*Meso* D,L-lactide		
No.	Temp. (°C)	Time (h)	Yield (%)	η_{inh}(dl g^{-1})[a]	L_i[b]	Yield (%)	η_{inh}(dl g^{-1})[a]	L_i[b]
1	90	4	40	0.06	3.6	–	–	
2	90	8	63	0.06		–	–	
3	90	16	85	0.06	4.2	–	–	
4	90	24	72	0.07		–	–	
5	90	32	69	0.06		0	–	
6	90	48	68	0.08	3.6	0	–	
7	120	4	73	0.12	3.8	0	–	
8	120	8	69	0.03		0	–	
9	120	16	66	0.06	4-0	0	–	
10	120	24	56	0.06		0	–	
11	120	32	55	0.06		0	–	
12	120	48	54	0.06	2.9	18	0.13	1.4

[a] Measured at 20°C (2 g l^{-1}, CH_2Cl_2)
[b] Average length of isotactic blocks, margin of error ±0.2

Table 4 Polymerizations conducted at 120°C with dibutyltin dimethoxide (M/I = 100:1) in xylylene or in bulk

			Racemic D,L-lactide		*Meso* D,L-lactide	
No.	Reaction medium	Time (°C)	Yield (%)	η_{inh}(dl g^{-1})[a]	Yield (%)	η_{inh}(dl g^{-1})[a]
1	Xylylene	15	47	0.06	0	–
2	Xylylene	24	44[b]	0.06[b]	32	0.10
3	Bulk	2	0	–	–	–
4	Bulk	4	42	0.06	0	–
5	Bulk	8	60	0.06	0	–
6	Bulk	16	77	0.06	26	0.03[d]
7	Bulk	24	96	0.07	86	0.07
8	Bulk	36	98	0.06	–	–
9	Bulk	48	99[c]	0.03[c]	78	0.06

[a] Measured at 20°C (2 g l^{-1}, CH_2Cl_2)
[b] $L_i = 3.8$
[c] $L_i = 3.7$
[d] $L_i = 1.4$

Table 5 Polymerizations conducted in xylylene with Sn(II) octoate (M/I = 100:1)

No.	Temp. (°C)	Time (h)	*Racemic* D,L-lactide			*Meso* D,L-lactide		
			Yield (%)	η_{inh}(dl g^{-1})^a	L_i^{b}	Yield (%)	η_{inh}(dl g^{-1})^a	L_i^{b}
1	90	4	0	–	–	53	0.35	1.3
2	90	8	60	0.04	3.3	60	0.37	–
3	90	16	75	0.38	–	66	0.39	–
4	90	24	97	0.48	–	85	0.51	–
5	90	48	93	0.31	3.1	74	0.40	1.3
6	120	4	80	0.56	3.2	85	0.54	1.3
7	120	8	90	0.61	–	68	0.44	–
8	120	16	93	0.34	–	64	0.40	–
9	120	24	95	0.32	–	62	0.38	–
10	120	48	99	0.30	3.1	46	0.17	1.4

[a] Measured at 20°C (2 g l^{-1}, CH_2Cl_2)
[b] Average length of isotactic blocks

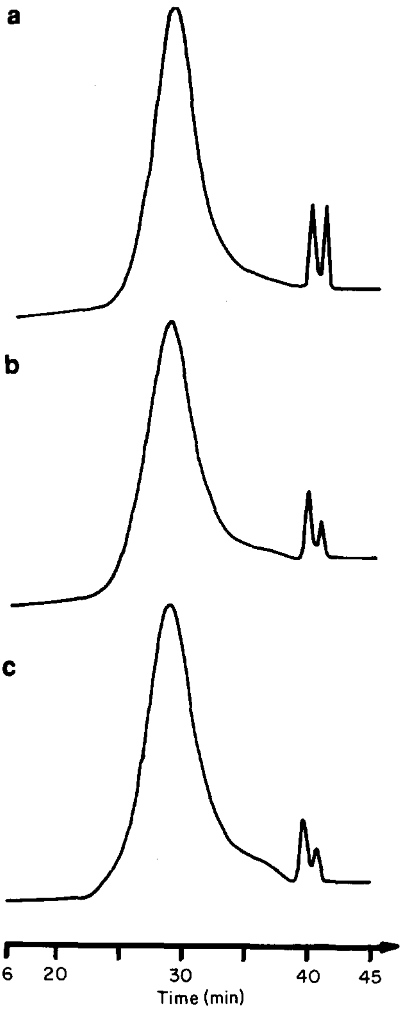

Figure 1 G.p.c. measurements of reaction mixtures obtained from *racemic* D,L-lactide with Bu_3SnOMe in bulk at 120°C after: (a) 2 h; (b) 8 h; (c) 24 h

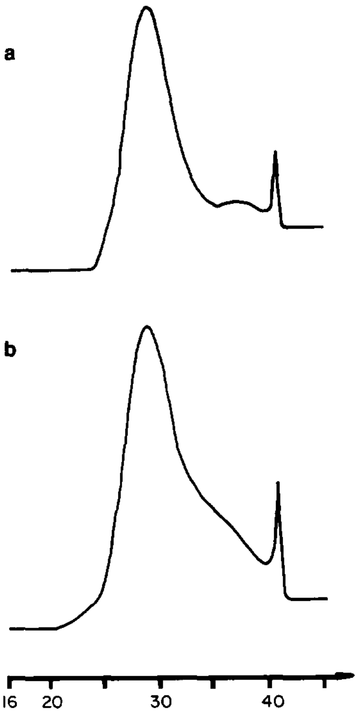

Figure 2 G.p.c. measurements of reaction mixtures obtained from *racemic* D,L-lactide with Sn(II) octoate in bulk at 180°C after: (a) 2 h; (b) 8 h

by 'back-biting' degradation. This interpretation is confirmed by the following observations. G.p.c. measurements display broad molecular weight distributions with a considerable fraction of low molecular weight components (*Figure 1*). The molar fraction of oligomers increases with increasing reaction times. Similar results were obtained for the polymerization of ε-caprolactone[13]. A comparison of various initiators has shown that Bu_3SnOMe and in particular $Bu_2Sn(OMe)_2$ (*Table 4*) were the best transesterification catalysts. At 100°C in solution poly(ε-caprolactone) was rapidly degraded to cyclic oligomers[13].

In contrast to both tin methoxides, Sn(II) octoate yields high molecular weight polyesters (*Tables 2* and *5*). Both yields and viscosities indicate slow 'back-biting' degradation for polymerizations of *meso* D,L-lactide at 150°C (6–10 in *Table 2*) and rapid degradation for both monomers at 180°C (11–14 in *Table 2*). G.p.c. measurements illustrate the broadening of the molecular weight distribution at 180°C with increasing time (*Figure 2*). These results demonstrate that Sn(II) octoate is a much poorer transesterification catalyst than the butyltin meth-

Table 6 Bernoullian probabilities of dyads and tetrads of poly(D,L-lactide)s prepared from *racemic* D,L-lactide with and without addition of L,L-lactide (*Figures 1* and *2*)

Sequence	Formula used[a]	Probability for variable molar fractions of L:x			
		100	0.80	0.60	0.50
Dyads					
i	$(1+x^2+z^2)/2$	1.00	0.84	0.76	0.75
s	xz	0	0.16	0.24	0.25
Tetrads					
iii	$(x^3+z^3+x^2+z^2)/2$	1.00	0.60	0.40	0.375
isi	$(2xz)/2$	0	0.16	0.24	0.250
iis	$(x^2z+z^2x)/2$	0	0.08	0.12	0.125
sii	$(x^2z+z^2x)/2$	0	0.08	0.12	0.125
sis	$(x^2z+z^2)/2$	0	0.08	0.12	0.125
sss	–	0	0	0	0

[a] $x=[\text{L}]/([\text{L}]+[\text{D}])$; $z=[\text{D}]/([\text{L}]+[\text{D}])$

Table 7 Bernoullian probabilities of dyads and tetrads of poly(D,L-lactide)s prepared from *meso* D,L-lactide

Sequence	Formula used[a,b]	Probability
dyads		
i	xz	0.25
s	$(1+x^2+z^2)/2$	0.75
Tetrads		
iii	–	0
isi	$(x^2z+z^2x)/2$	0.125
sis	$(2xz)/2$	0.250
ssi	$(x^2z+z^2x)/2$	0.125
iss	$(x^2z+z^2x)/2$	0.125
sss	$(x^3+z^3+x^2+z^2)/2$	0.375

[a] $x=[\text{L}]/([\text{L}]+[\text{D}])$; $z=[\text{D}]/([\text{L}]+[\text{D}])$

[b] These formulae cannot be used to calculate dyad or tetrad probabilities for mixtures of L,L-lactide and *meso* D,L-lactide

oxides. The analyses of stereosequences support this conclusion.

N.m.r. spectroscopic methods

The isolated poly(D,L-lactide)s were characterized on the basis of 360 MHz ^{1}H n.m.r. and 75.4 MHz ^{13}C n.m.r. spectra. A comparison of all signals suggested that the methine proton and the methine carbon are best suited for stereosequence analyses. Because the resolution of ^{13}C n.m.r. signals was better than that of ^{1}H n.m.r. signals assignments were first conducted with ^{13}C n.m.r. measurements, and the results then compared with ^{1}H n.m.r. spectra. In order to simplify the ^{1}H n.m.r. spectra proton–proton coupling was eliminated by homonuclear decoupling.

$$p_{\text{sequ.}}=\frac{n!}{m!(n-m!)}x^m z^{n-m} \qquad (1)$$

where $p_{\text{sequ.}}$ is the probability of an individual stereosequence (e.g. dyad, triad, tetrad, etc.), n is the number of monomers, m is the number of isotactic dyads, $(n-m)$ is the number of syndiotactic dyads, and $x=[\text{L}]/([\text{L}]+[\text{D}])$ and $z=[\text{D}]/([\text{L}]+[\text{D}])$ are the molar fractions of L or D units.

Both the ^{1}H and ^{13}C n.m.r. methine signals of most poly(D,L-lactide)s display five peaks indicating a tetrad sensitivity of both signals. Therefore their stereosequences were analysed on the basis of tetrad peaks. In order to simplify the calculation of tetrad probabilities, Bernoulli statistics [equation (1)] was used as a mathematical basis. A random stereosequence consists of eight tetrads with probability of 0.125 each.

For the polymerization of *racemic* or *meso* D,L-lactide only five tetrads are expected provided that transesterification and racemization are absent. The probabilities of these tetrads calculated from equation (1) for a non-stereospecific polymerization are listed in *Tables 6* and *7*. Copolyesters containing a variable fraction of L,L-lactide were also included (*Table 6*). The peak assignments are based on four sources of information:

1. Comparison of ^{1}H and ^{13}C n.m.r. spectra.
2. Comparison of poly(D,L-lactide)s prepared from *racemic* and *meso* D,L-lactide in the absence of transesterification and racemization of monomers or monomeric units (polymerization at low temperatures).
3. Evaluation of perfectly random stereosequences obtained by rapid transesterification (e.g. at 180°C).
4. Evaluation of copolylactides prepared by copolymerization of L,L-lactide with *racemic* D,L-lactide (*Figures 3–6*).

This is a much broader basis of information than that used by other authors for their stereosequence analysis of poly(D,L-lactide)s[1–5]. Nonetheless a clear-cut differentiation between sii and iis (or ssi and iss) peaks was not feasible. Fortunately, both tetrads possess identical probabilities under the given experimental conditions and thus the lacking differentiation does not affect the interpretation of the experimental results.

The signal assignments used in this work are shown in *Figures 3–10*. The assignments of the ^{13}C n.m.r. signals agree with those of Bero *et al.*[5].

For the characterization of stereosequences the average length of an isotactic block ($L_i=L_{\text{LL}}, L_{\text{DD}}$) is a useful term. It may be calculated from dyad or tetrad probabilities according to equation (2). Values of 4.0 for a Bernoullian-type polymerization of *racemic* D,L-lactide, 1.3 for *meso* D,L-lactide and 2.0 for a random stereosequence are obtained. The evaluation of L_i from peak intensities (I)

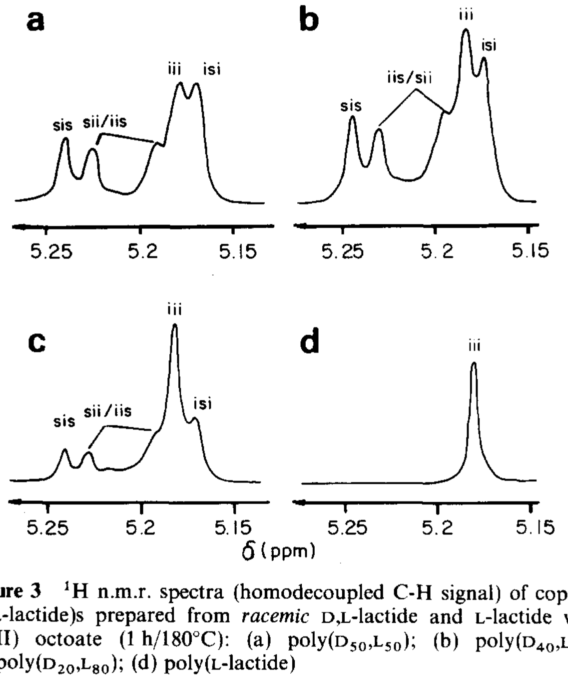

Figure 3 ^{1}H n.m.r. spectra (homodecoupled C-H signal) of copoly(D,L-lactide)s prepared from *racemic* D,L-lactide and L-lactide with Sn(II) octoate (1 h/180°C): (a) poly(D_{50},L_{50}); (b) poly(D_{40},L_{60}); (c) poly(D_{20},L_{80}); (d) poly(L-lactide)

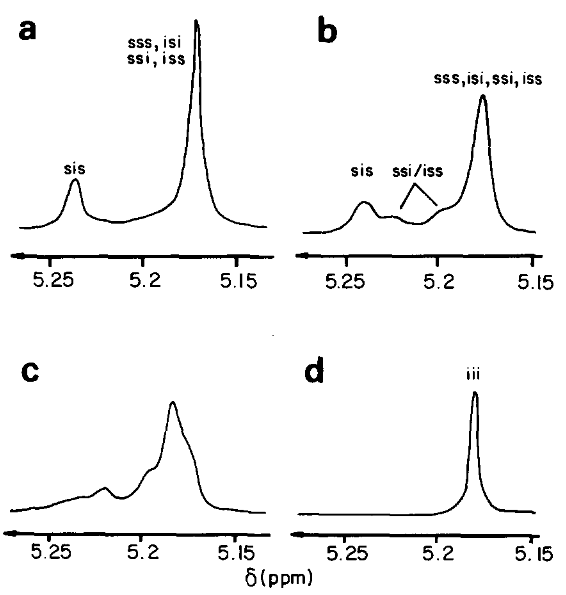

Figure 4 ^{1}H n.m.r. spectra (homodecoupled C-H signal) of copoly(D,L-lactide)s prepared from *meso* D,L-lactide and L-lactide with Sn(II) octoate (1 h/180°C): (a) poly(D_{50},L_{50}); (b) poly(D_{40},L_{60}); (c) poly(D_{20},L_{80}); (d) poly(L-lactide)

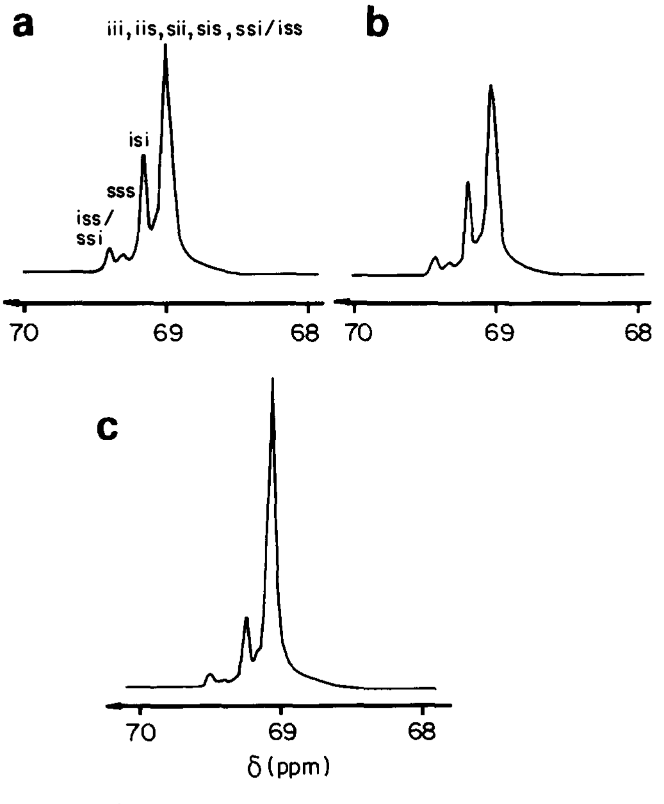

Figure 5 ^{13}C n.m.r. spectra (CH group) of copoly(D,L-lactide)s prepared from *racemic* D,L-lactide and L-lactide with Sn(II) octoate (1 h/180°C): (a) poly(D_{50},L_{50}); (b) poly(D_{40},L_{60}); (c) poly(D_{20},L_{80})

of experimental n.m.r. spectra is based on equation (3). The intensities of poorly resolved peaks were determined by means of computer simulation and checked by the cut-and-weigh method.

$$L_i = \frac{p_i}{p_s} + 1 = \frac{p_{iii}+p_{iis}+p_{isi}+p_{iss}}{p_{sss}+p_{ssi}+p_{sis}+p_{sii}} = 1 \qquad (2)$$

where $L_i = L_{LL}$ or L_{DD}, the average length of isotactic

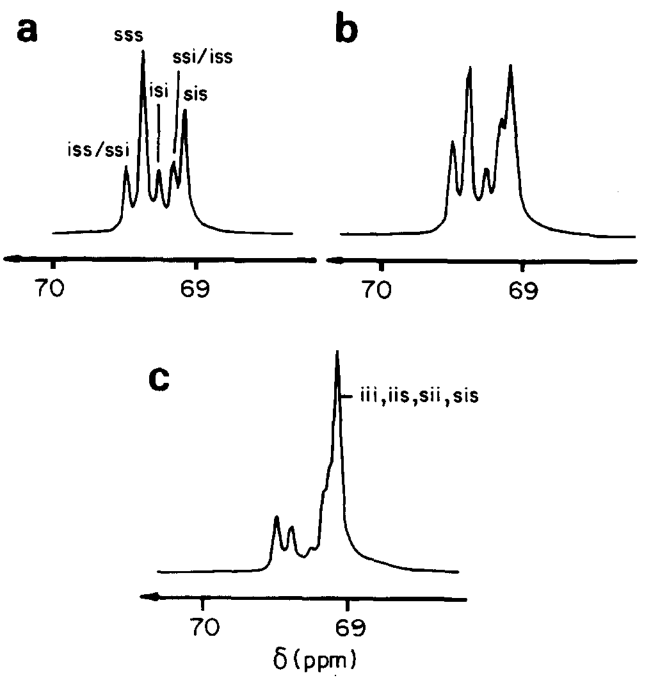

Figure 6 ^{13}C n.m.r. spectra (CH group) of copoly(D,L-lactide)s prepared from *meso* D,L-lactide and L-lactide with Sn(II) octoate (1 h/180°C): (a) poly(D_{50},L_{50}); (b) poly(D_{40},L_{60}); (c) poly(D_{20},L_{80})

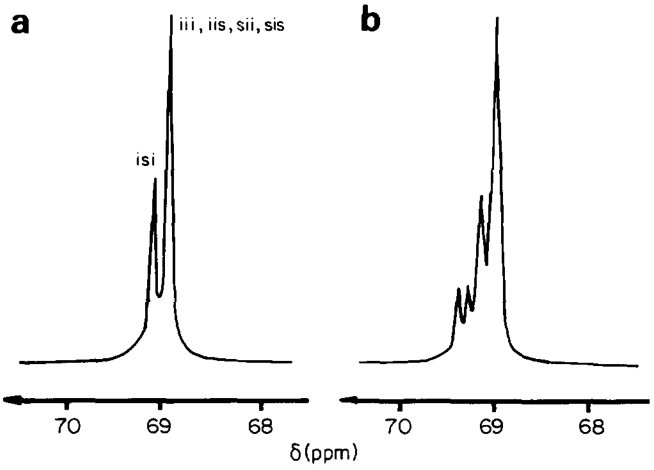

Figure 7 ^{13}C n.m.r. spectra (CH group) of poly(D,L-lactide)s prepared from *racemic* D,L-lactide with Bu_3SnOMe in xylylene at 120°C after: (a) 4 h; (b) 48 h

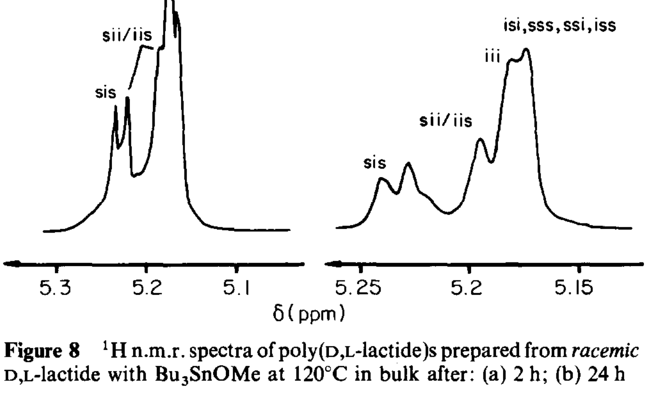

Figure 8 ^{1}H n.m.r. spectra of poly(D,L-lactide)s prepared from *racemic* D,L-lactide with Bu_3SnOMe at 120°C in bulk after: (a) 2 h; (b) 24 h

blocks.

$$L_i=\frac{3I_{iii}+2I_{isi}+2I_{sii}+2I_{iis}+I_{sis}+I_{ssi}+I_{iss}}{I_{isi}+I_{iis}+I_{sii}+2I_{sis}+2I_{ssi}+2I_{iss}+3I_{sss}}+1 \quad (3)$$

Stereochemical aspects

In the present work two stereochemical aspects were of particular interest: the extent of stereospecificity, in particular the formation of long isotactic blocks; and the influence of transesterification on the stereosequences.

For the evaluation of stereospecificity the L_i values [equations (2) and (3)] were taken as a crude measure. For a Bernoullian-type polymerization of *racemic* D,L-lactide a value of 4.0 is expected and for *meso* D,L-lactide a value of 1.3 (a margin of error of ± 0.2 must be taken into account due to insufficient resolution of the tetrad peaks).

The results listed in *Tables 1–5* clearly indicate that a stereospecific polymerization of *racemic* D,L-lactide favouring isotactic blocks never occurred, because L_i vaues >4.0 were never found. L_i values <3.8 may either result from a stereospecificity favouring an alternating incorporation of L,L- and D,D-monomers or it might result from transesterification and (possibly at 180°C) racemization of monomers and monomeric units. The g.p.c. measurements (*Figures 1* and *2*) and the n.m.r. sequence analyses discussed below suggest that transesterification is mainly responsible for the lower L_i values.

However L_i values in the range of 3.1–3.3 were found for Sn(II) octoate initiated polymerizations at 90 and 120°C after short reaction times (2–8 h) (1–6 in *Tables 2* and *5*). Under these reaction conditions transesterification is absent, and thus, the low L_i values obviously indicate a syndiotactic stereospecificity. The absence of transesterification is confirmed by the finding that *meso* D,L-lactide yields L_i values of 1.3 under the same reaction conditions.

In the case of *meso* D,L-lactide the absence of L_i values <1.2 indicates that a stereospecificity favouring syndiotactic blocks did not exist. L_i values >1.4 were observed for *meso* D,L-lactide under conditions yielding L_i values <3.8 in the case of *racemic* D,L-lactide. This finding is a strong argument for concluding that initially Bernoullian-type stereosequences were modified by transesterification under these reaction conditions. It has been previously demonstrated[9,15] that Bu_3SnOMe and Sn(II) octoate initiated polymerizations of L,L-lactide proceed without racemization even at 180°C when the reaction time is short ($\leqslant 12$ h). Thus, it is obvious that the influence of racemization of monomers and monomeric units on the results listed in *Tables 1–5* is negligible.

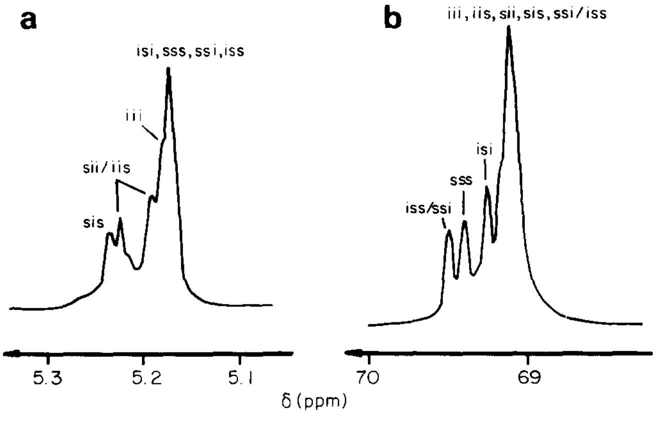

Figure 9 ^{1}H n.m.r. spectrum (a) and ^{13}C n.m.r. spectrum (b) of a poly(D,L-lactide) prepared with Bu_3SnOMe in bulk (24 h/150°C)

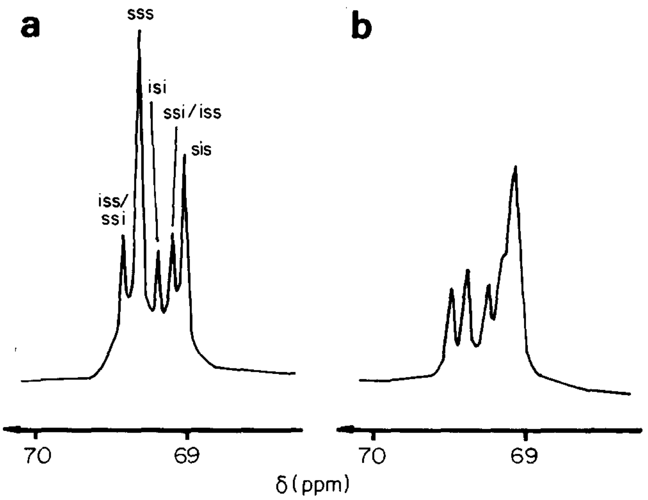

Figure 10 ^{1}H n.m.r. spectra of poly(D,L-lactide)s prepared from *meso* D,L-lactide with Sn(II) octoate in bulk: (a) 8 h/120°C; (b) 8 h/180°C

For the detection of transesterification two sources of information are available: the L_i values and the presence or absence of transesterification-dependent tetrads. Intensive transesterification causes randomization of the stereosequences with the consequence that the L_i values tend to 2.0. A random stereosequence consists of eight tetrads, whereas a Bernoullian-type polymerization of *racemic* or *meso* D,L-lactide only generates five tetrads (*Tables 6* and *7*). The three tetrads lacking in a Bernoullian chain of *racemic* D,L-lactide are ssi, iss and sss. They are best detected in the ^{13}C n.m.r. spectra. In contrast the iis, sii and iii tetrads lacking in the Bernoullian chain of *meso* D,L-lactide are easier to identify (and quantify) in the ^{1}H n.m.r. spectra, when they are generated by transesterification.

When Bu_3SnOMe or $Bu_2Sn(OMe)_2$ were used as initiators the following results were obtained. Transesterification is almost absent at 90°C in xylylene (*Table 3*). However, transesterification is clearly detectable at 120°C regardless of whether polymerizations were conducted in xylylene (*Figure 7*) or in bulk (*Figure 8*). Yet even after 48 h (12, *Table 3*) transesterification was not sufficiently effective to bring about a perfectly random stereosequence (*Figure 7b*). At 150°C (6–10, *Table 1*) transesterification is rapid enough to yield a nearly random stereosequence within 24 h (*Figure 9*). The completion of the transesterification equilibrium is confirmed by four observations. First, the L_i value approaches the theoretical value of 2.0 (10 in *Table 1*). Second, the L_i value and the n.m.r. spectra obtained from polymerized *meso* D,L-lactide are nearly identical with those obtained from *racemic* D,L-lactide. Third, L_i values of 2.0 and identical n.m.r. spectra were also obtained after 24 h at 180°C and the resulting spectra are nearly identical with those found at 150°C after 24 h. Furthermore, Sn(II) octoate and other initiators yield almost identical spectra for *racemic* and *meso* D,L-lactide polymerized at 180°C for several hours.

In the case of Sn(II) octoate tranesterification is considerably slower. At 150°C it is detectable, but even after 24 h the stereosequences are still far from randomness. At 180°C transesterification is poor but detectable after 1 h (*Figures 3a–6a*). After 8 h at 180°C, randomization is nearly complete. The effect of temperature is illustrated by *Figures 10a* and *b* and the influence of reaction time by comparison of *Figures 6a* and *10b*. On the basis of the present results it is evident that Sn(II) octoate is best suited for polymerizations of *racemic* or *meso* D,L-lactide with control of transesterification.

CONCLUSIONS

The comparison of ^{1}H and ^{13}C n.m.r. spectra of poly(D,L-lactide)s prepared from *racemic* D,L-lactide and *meso* D,L-lactide allowed a consistent assignment and interpretation of the tetrad patterns in both kinds of n.m.r. spectra. When *racemic* D,L-lactide and *meso* D,L-lactide were polymerized with various tin catalysts at the lowest possible temperature (i.e. 90°C in solution) a Bernoullian-type stereocopolymerization was found in most cases. A stereospecificity favouring long isotactic blocks could not be detected. Increasing temperatures favour transesterification, and thus, randomization of the stereosequences.

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