

Configurational structures of lactic acid stereocopolymers as determined by $^{13}\text{C}\{-^1\text{H}\}$ n.m.r.

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Investigations are made of the $^{13}\text{C}\{-^1\text{H}\}$ n.m.r. spectra of a series of poly(lactic acid) stereocopolymers obtained by different means, i.e. ring-opening polymerization of L-, *rac*- and *meso*-lactides initiated by powdered Zn, or copolymerization of L- and *rac*-lactides in different proportions, or condensation polymerization of *rac*-lactic acid. Resonances arising from the stereosensitivity of the carbonyl carbon atoms have been resolved using the resolution enhancement technique. The fine structures thus obtained are discussed in terms of configurational sequences. Comparison is made of the peak intensities with theoretical stereosequence distributions obtained when assuming single and pair additions of repeating units according to the Bernoullian statistics. Neither of the models for triad, tetrad and pentad stereosequences agrees with the area of the experimental lines. It is shown that redistribution of stereosequences in poly(lactic acid) occurs because of *transesterification* at the ester bonds in the melt. The final stereosequence distribution in the polymers obtained by ring-opening polymerization of lactides is discussed in relation to the pair-addition mechanism and to the redistribution due to *transesterification* reactions.

Keywords Poly(lactic acid); stereocopolymers; carbon 13 nuclear magnetic resonance; stereosequence redistribution; biodegradable; *transesterification*

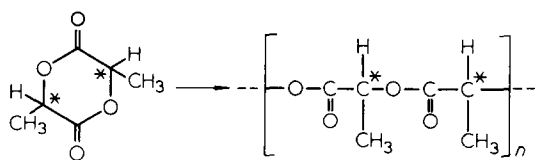
INTRODUCTION

Racemic and optically active lactic acids can undergo condensation polymerization to yield polymers of low molecular weight which are not suitable for applications as plastics or fibres¹. In contrast, the cyclic diesters, or diastereoisomeric lactides, derived from L- and D-lactic acid enantiomers can polymerize by ring-opening polymerization to high polymers of different configurational structures depending on the diastereoisomeric composition of the feed^{2,3}. Though casting and spinning of poly(lactic acid) were claimed⁴, thermal sensitivity and hydrolytic de-esterification has so far precluded real applications as industrial polyester. The recognition of the potentiality of lactic acid polymers for biomedical applications as resorbable materials has renewed the interest for the preparation of this type of polyester⁵, and especially for stereocopolymers (i.e. copolymers composed of L- and D-lactic acid repeating units)⁶. Though the configurational dependence of

physical and biological properties of lactic acid polymers has already been mentioned⁵⁻⁸, it is only recently that tensile strength, biodegradability and enantiomeric purity of lactic acid stereocopolymers have been quantitatively related⁹.

In particular, we have shown that poly(L-lactic acid) can be prepared and processed to give ready-for implantation endproducts with a previously unknown resistance to degradation in the biological milieu⁹. Because the introduction of D units within the poly-L chains was initially considered in attempts to control and to adjust mechanical properties and bioresorption rate of poly(lactic acid), attention is now being given to the characterization of the chain structures of resulting stereocopolymers. Enantiomeric purity in the polymer chains is a coarse parameter which does not necessarily reflect the configurational structure of stereocopolymers. This statement is of special value in the case of lactic acid stereocopolymers because of a particular mechanism of chain growth. Indeed the configuration-respecting

polymerization of cyclic L and D,L lactides has been shown to proceed primarily through pair addition of lactic acid repeating units which yields polydimers¹⁰:



The resulting stereocopolymers have been shown to contain the monomeric units in the same proportion as that of the monomer mixture, which implies that the reactivities of the optically and racemic monomers are the same³.

However, it has been suggested that the occurrence of transesterification reactions involving ester bonds and active species might affect the stereosequence distributions resulting from the polymerization reaction alone¹⁰.

Attempts to characterize the sequences of D- and L-lactic units precisely and to show the occurrence of transesterification by n.m.r. techniques have been reported. Lillie and Schulz¹¹ did not succeed conclusively in selectively fitting the fine structures of ¹H and ¹³C n.m.r. spectra to theoretical distributions given by models based on Bernoullian statistics for single and pair addition of lactic repeating units in growing chains. Schindler and Harper¹² found a good agreement of respective line intensities observed in the dyad, triad and tetrad sensitive regions of ¹H n.m.r. spectra with values calculated for a Bernoullian-type polymerization of dimers. However, these authors were unable to decide about the occurrence of transesterification. They concluded that the frequencies of such reactions is too low to generate additional stereosequences in amounts detectable by ¹H n.m.r.

In this paper, we present ¹³C n.m.r. spectra of a series of lactic acid stereocopolymers including compounds with the same enantiomeric composition and different configurational structures. Comparisons are made between line intensities and calculated L and D repeating unit distributions for both the single and the pair addition Bernoullian mechanisms of chain growth. The discrepancies are discussed in relation to stereosensitivity of the carbonyl resonance and to redistribution due to transesterification reactions.

EXPERIMENTAL

Materials

The lactic acid stereocopolymers were prepared simultaneously by polymerizing suitable mixtures of L- and *rac*-lactides (m.p. = 96° and 125°C respectively) in bulk in the presence of 500 ppm of powdered Zn, with the various sealed flasks placed on a rotating wheel in an oven set at 140°C. After cooling, the flasks were opened and the residual monomers were separated by precipitation of the stereocopolymers from 10% chloroform solutions with suitable amounts of methanol.

The sample of atactic optically inactive poly(lactic acid) (PLA 50_{at}) was obtained by fractionation of the crude low molecular weight polymer which resulted from the condensation polymerization of D,L-lactic acid in the presence of ZnO, water being removed by distillation.

Meso-lactide was separated from the filtrate of recrystallized crude *rac*-lactide. The filtrate was concentrated to dryness. The solid was recrystallized twice from ethyl ether and finally vacuum distilled onto a cold wall. *Meso*-lactide thus obtained (m.p. = 42°C) still contained a small amount of *rac*-lactide as shown by n.m.r.

Measurements

Optical rotatory power of optically active lactic acid stereocopolymers was measured with a FICA 'Spectropol I' spectropolarimeter thermostatted at 25°C.

Molecular weights were evaluated from g.p.c. chromatograms obtained with a Waters apparatus equipped with μ -styragel columns. $\bar{M}_{g.p.c.}$ are given with reference to polystyrene standards.

Melting points of semicrystalline materials were determined with a Dupont 900 apparatus.

¹³C n.m.r. spectra, decoupled from protons, were recorded at 20.11 MHz on a Bruker WP 80 spectrometer. The high-field spectra were obtained at 62.86 MHz on a Bruker WH 250 spectrometer. The different polymers were dissolved in CDCl₃ and the ¹³C resonance of the solvent was taken as secondary internal reference with $\delta_{CDCl_3} = 76.91$ ppm compared to TMS. The temperature was 28°C and the spectra were usually obtained with 10 000 to 20 000 scans.

Methods

Resolution enhancement for spectra obtained at 20.11 MHz was achieved using the difference between the experimental decay (FID) and the decay obtained by multiplying the FID by both the usual exponential factor and 0.85. The resulting differential decay was then Fourier-transformed. For the high-field spectra, the resolution enhancement was carried out by multiplying the FID by a weighted binomial exponential function $\exp(-at - bt^2)$ according to the method proposed by Lindon and Ferridge¹³. Only the carbonyl region has been successfully resolved.

RESULTS AND DISCUSSION

Lactic acid stereocopolymers

Lactic acid stereocopolymers obtained by ring-opening polymerization of lactide can have particular configurational structures not only because of the pair-addition mechanism as mentioned above, but also because of the diastereoisomeric nature of the 'dimeric' monomer. Indeed, the cyclic diester, or lactide, of lactic acid exists as four different compounds, the L,L and D,D antipodes (L- and D-lactides respectively), the D,L diastereoisomer or *meso*-lactide, and the D,D+L,L solid racemic combination of L- and D-lactides (*rac*-lactide) depending on the L and D configuration of the lactic moieties forming the cyclic molecules (Table 1)¹⁴.

As many of the initiators of the ring-opening polymerization of lactides are configuration-respecting^{2,3}, in the absence of transesterification reactions, the pair-addition mechanism of chain growth provides a means to synthesize macromolecules with various configurational structures, or tacticity, from suitable mixtures of the different lactides. For example, L-lactide leads to a highly crystalline poly(L-lactic acid) isotactic polymer¹⁵ while *rac*-lactide should give

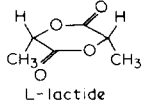
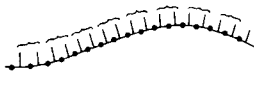
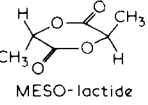
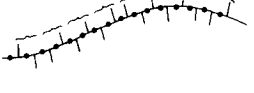
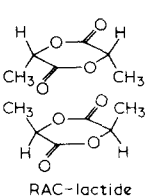
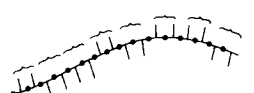
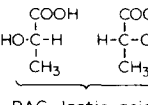
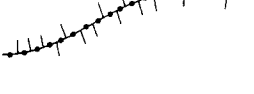
predominantly isotactic, as *meso* dyads are favoured by L,L and D,D 'dimeric' repeating units, and *meso*-lactide should give predominantly syndiotactic as *rac* dyads are favoured by the *meso* diastereoisomeric structure (Table 1). In contrast, the step-growth polymerization of racemic lactic acid definitely yields an atactic polymer, i.e. a polymer with randomly distributed L- and D-lactic units (Table 1). It is noteworthy that the last three stereocopolymers in Table 1 are optically inactive, as they are composed of 50–50 L- and D-lactic repeating units, but have completely different stereosequence distributions.

Based on the preceding remarks, the various stereocopolymers listed in Table 2 were prepared. All the stereocopolymers obtained by ring-opening polymer-

ization of lactides were polymerized using powdered Zn as initiator so as to be the same as compounds prepared for biomedical uses⁹.

Polymerization times necessary to have highly viscous or solid polymers in the reaction flasks decreased as the enantiomeric purity of the feed decreased. After separation of the residual monomers and of the low molecular weight compounds by dissolution/precipitation, optical rotary power, molecular weights and melting points were measured. As shown in Table 2, the ratios $[\alpha]_D^{25}$ PLA X / $[\alpha]_D^{25}$ PLA 100 correspond to the excess of L units in the feeds, thus confirming that the polymerization rates of L- and D,L-lactides are the same³. The molecular weights of the various poly(lactides) are comparable as deduced by g.p.c. with reference to polystyrene standards. The melting points of the semicrystalline stereocopolymers decrease as the content of D units increases, as already noted³. PLA X with X < 87.5 are amorphous.

Table 1 Theoretical configurational structures of the simplest lactic acid stereocopolymers (PLA) in the absence of transesterification reactions

Monomer	Mode of polymerization	Configurational structure
 L-lactide	ROP ^a	
 MESO-lactide	ROP	
 RAC-lactide	ROP	
 RAC-lactic-acid	SGP ^b	

^a ROP = Ring-opening polymerization

^b SGP = Step-growth polymerization

General features of $^{13}\text{C}\{-^1\text{H}\}$ n.m.r. spectra of lactic acid stereocopolymers

At 20.11 MHz, all the stereocopolymers give similar spectra composed of three lines located at $\delta = 16.4$, 68.8 and 169.1 ppm as shown in Figure 1 for PLA 75. These three lines correspond to the methyl, the methine and the carbonyl carbon atoms respectively. It has previously been reported that all lines observed in the $^{13}\text{C}\{-^1\text{H}\}$ n.m.r. spectra of SnCl_4 -initiated polymers show fine structure¹¹. For our stereocopolymers, the attempts to detect fine structure due to stereosensitivity in the methyl and the methine peak failed. On the contrary, expansion

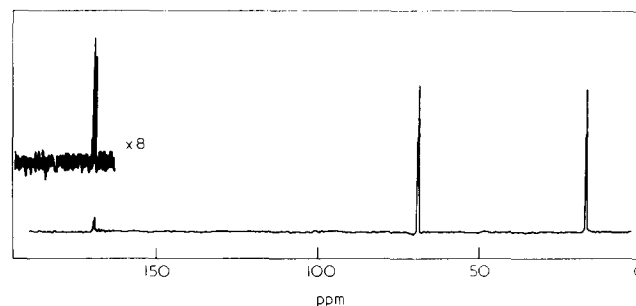


Figure 1 ^{13}C n.m.r. spectra (20.11 MHz) of PLA 75 (10000 scans)

Table 2 Characteristics of the lactic acid stereocopolymers PLA X^a

X in PLA X	Lactides in the feed (%)			Polymerization time (h)	$[\alpha]_D^{25b}$ (deg)	M_{gpc} ($\times 10^{-4}$)	M.p. ^c (°C)	$\frac{[\alpha]_{\text{PLA X}}}{[\alpha]_{\text{PLA 100}}}$ (%)
	L	<i>rac</i>	<i>meso</i>					
100	100	—	—	480	-156	11	173	100
98	96	4	—	672	-150	9	160	96
96	92	8	—	744	-142	11	145	91
92	84	16	—	744	-127	10	124	81.5
87.5	75	25	—	168	-119	—	am. ^d	76.3
75	50	50	—	168	-75	10.5	am.	48
62.5	25	75	—	168	-37	—	am.	23.7
50 _i	—	100	—	96	0	11	am.	—
50 _s	—	—	100	96	0	—	am.	—
50 _a ^e	—	—	—	—	0	0.2	am.	—

^a X = percentage of L units; subscripts a, i and s stand for atactic and predominantly isotactic or syndiotactic respectively

^b In CHCl_3 , C = 0.861 g/100 cm³

^c Temperature of the ATD peak

^d Amorphous as controlled by X-rays

^e Derived from racemic lactic acid by condensation polymerization and fractionation

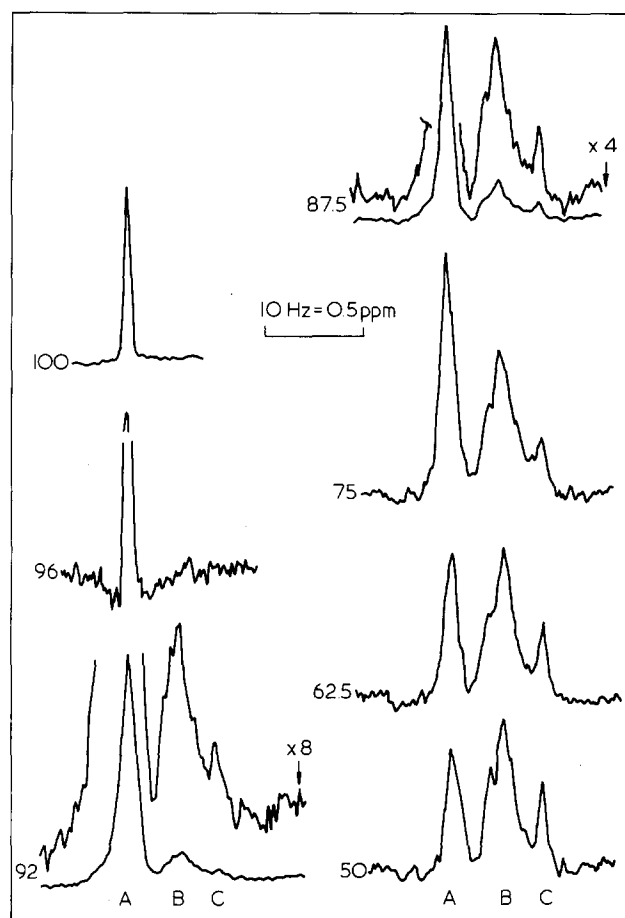


Figure 2 ^{13}C n.m.r. spectra (20.11 MHz) of the carbonyl groups of lactic acid stereopolymers for various enantiomeric compositions obtained by mixing L-lactide and *rac*-lactide in suitable amounts in the feed

and line narrowing of the C=O region by the resolution enhancement technique led to patterns composed of several lines whose respective intensities depended on the nature and enantiomeric composition of the stereopolymers, as shown in Figure 2.

As expected for an isotactic polymer, only one peak was observed downfield in the PLA 100 pattern. PLA 98 gave a one-peak spectrum also, thus showing that a very small amount of D units in poly-L chains can be undetected by ^{13}C n.m.r. if high-sensitivity investigations are not carried out. For PLA 96, the major peak corresponding to the PLA 100 is still present but a very weak line appears upfield. This new peak grows at the expense of the major one when going to PLA 92. Furthermore, shoulders appear on both sides. From PLA 87.5 to PLA 50_i, the trend is confirmed as the spectrum evolves progressively, with a decrease of the low-field peak and an increase of the high-field part.

Considering the different compounds, the C=O spectrum of the PLA stereopolymers can be divided in three regions labelled A, B and C with the low-field peak A and the high-field peak C. A is a single peak which corresponds to the unique peak observed for isotactic PLA 100. Region B is a multiplet which is included between peaks A and C. The presence of three peaks in lactic acid stereopolymers has already been observed in 25.2 MHz ^{13}C - $\{^1\text{H}\}$ n.m.r. spectra¹¹ but relative areas were not measured accurately. In the spectrum of the poly(*rac*-lactide) (PLA 50_i type) the relative areas turned out to be 1:2:1 and were tentatively assigned to lines corresponding to random triads i, (hi,hs) and s. The percentage of the relative intensities of the three regions of spectra shown in Figure 2 are gathered in Table 3. These intensities were measured by the spectrometer using the

Table 3 Comparison between experimental relative intensities of the various regions in the C=O ^{13}C n.m.r. patterns of PLA X stereopolymers shown in Figure 2 and triad, tetrad and pentad relative intensities calculated according to the pair-addition Bernoullian mechanism

Compound	Region		
	I_A/I_{total} (%)	I_B/I_{total} (%)	I_C/I_{total} (%)
PLA 100	100 ^a (100, 100, 100) ^{b,c}	0 ^a (0, 0, 0) ^{d,c}	0 ^a (0, 0, 0) ^{e,c}
PLA 98	100 (96, 95.0, 94.1)	0 (2, 4, 4.9)	0 (2, 1, 1)
PLA 96	91 (92.3, 90.4, 88.5)	8 (3.9, 7.7, 9.6)	1 (3.8, 1.9, 1.9)
PLA 92	81 (85.3, 81.6, 77.9)	16 (7.4, 14.7, 18.4)	3 (7.4, 3.7, 3.7)
PLA 87.5	71 (78.1, 72.6, 67.2)	24 (11.0, 21.95, 27.35)	5 (10.9, 5.45, 5.45)
PLA 75	47 (62.5, 53.1, 43.75)	44 (18.75, 37.5, 46.85)	9 (18.75, 9.4, 9.4)
PLA 62.5	32 (53.1, 41.4, 29.7)	56 (23.5, 43.9, 58.6)	12 (23.4, 11.7, 11.7)
PLA 50 _i	27 (50, 37.5, 25)	59 (25, 50, 62.5)	14 (25, 12.5, 12.5)

^a Experimental data

^b In brackets are given the calculated relative intensities of isotactic triad ($100(p^2 + q^2)$), tetrad ($100(p^2 + q^2 + p^3 + q^3)/2$) and pentad ($100(p^3 + q^3)$) respectively, with $p = L/(L + D)$ and $q = D/(L + D)$ ¹²

^c Underlined: the best fit corresponding to pentad stereosensitivity for experimental data

^d In brackets are given the calculated relative intensities of the rest of the spectra in terms of triads, tetrads and pentads respectively, as deduced by difference according to $I_B/I_{\text{total}} = 100 - (I_A \text{ calc} + I_C \text{ calc})$

^e In brackets are given the calculated relative intensities of a stereosequence of the lower probability triad ($100pq$), tetrad ($100pq/2$) and pentad ($100pq/2$), respectively

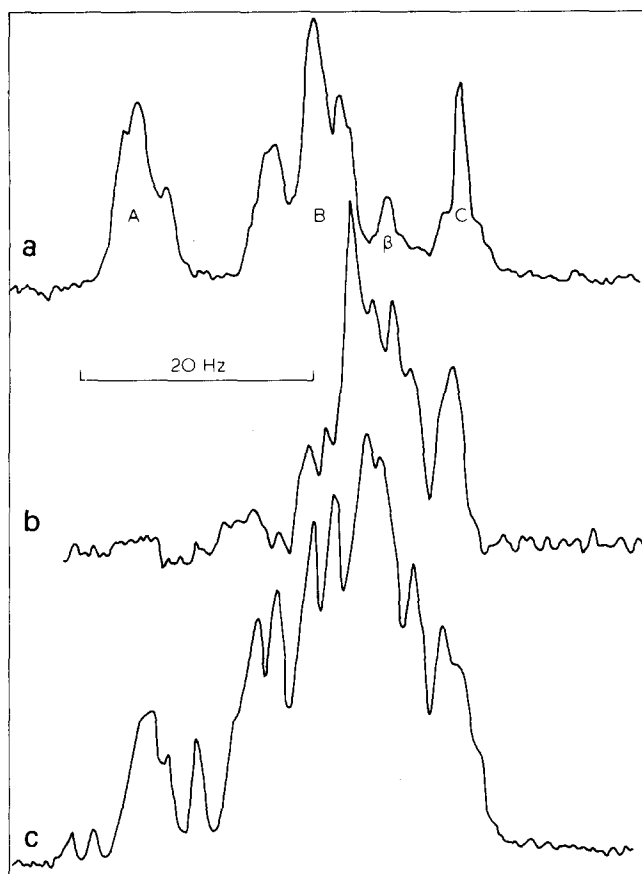


Figure 3 High-field ^{13}C n.m.r. spectra (62.86 MHz) of the carbonyl groups for lactic acid stereopolymers with 50–50 L and D units but different stereosequence distributions: (a) PLA 50_i (predominantly isotactic); (b) PLA 50_s (predominantly syndiotactic); (c) PLA 50_a (atactic). (The respective positions of the three spectra are given tentatively)

classical step-like curve, and by curve weighting. Both methods gave similar results within a 3% error range.

As is well known¹⁶, stereosensitivity to triads, tetrads and pentads should give 4, 8 and 16 components, respectively, for the case of a Bernoullian single addition of D- and L-lactic end units during chain growth. In contrast, patterns with 3, 5 and 7 lines, respectively, should be observed in the case of a Bernoullian D,D and L,L pair addition, as already pointed by Schindler and Harper¹².

Assuming that A and C peaks are single lines and that B includes all the other lines, theoretical relative intensities have been calculated for triads, tetrads and pentads in the case of a Bernoullian pair-addition mechanism and are given in Table 2. The comparison between experimental and theoretical relative intensities shows that the best fit is apparently obtained for a pentad stereosensitivity, a result in contradiction with the triad stereosensitivity previously suggested¹¹.

In order to clear up the level of the C=O stereosensitivity, the spectra of optically inactive PLA 50_i, PLA 50_s and PLA 50_a were investigated at 62.86 MHz (Figure 3). These three polymers have the same basic configurational composition (L=D) but different stereosequence distributions, with that of PLA 50_a corresponding to Bernoullian single-addition statistics. Because chemical shifts are concentration-dependent and configuration-dependent, and because the amounts of PLA 50_s and PLA 50_a were small, it has been impossible

to compare the line positions with enough accuracy to correlate the various resonances between the three high-resolution spectra. However, several points can be emphasized from a qualitative viewpoint. First of all, the three patterns are different and those of PLA 50_i and PLA 50_s are composed of a much smaller number of lines than PLA 50_a. These two points are in favour of the pair-addition mechanism for PLA 50_i and PLA 50_s.

Secondly, the number of lines observed for PLA 50_a can reasonably be considered to be in the range of 16, taking into account all observable lines and shoulders, except both weak lines downfield which can be tentatively assigned to the carbonyl of chain extremities as PLA 50_a has low molecular weights.

Pentad stereosensitivity has already been suggested for highly resolved ^{13}C - $\{^1\text{H}\}$ n.m.r. spectra of poly(lactide). However, it was for poly(lactide) of the PLA 50_i type at 25.2 MHz,¹¹ i.e. for a compound which shows less than 16 lines in our case, even though the frequency was 62.86 MHz (Figure 3a). In any case, the 16 lines observed in the PLA 50_a pattern (Figure 3c) favours pentad stereosensitivity at 62.86 MHz for our lactic acid stereopolymers. Accordingly, the PLA 50_i and PLA 50_s patterns (Figures 3a and 3b) should display seven lines, corresponding to the seven allowed pentads¹², if chain growth occurs through pair addition of repeating units. However, taking into account line and shoulders, as done for PLA 50_a, spectra of Figures 3a and b show contributions of more than seven pentads. The presence of more than seven lines shows that forbidden pentads are present and, thus, is inconsistent with the pure pair-addition mechanism. It is of value to note that the presence of ~10% of *rac*-lactide in the *meso*-lactide precursor of PLA 50_s, as shown by n.m.r., might explain the presence of the forbidden pentads in small proportions. However, this restriction is worthless in the case of PLA 50_i which was prepared from highly configurationally pure *rac*-lactide. In that case, the presence of forbidden pentads is well exemplified by the β line in the spectrum in Figure 3a. Indeed, the relative intensity of this line ($\approx 6.5\%$) is meaningless in regard to the theoretical triad, tetrad and pentad distributions as none corresponds to such a low intensity in the pair-addition mechanism.

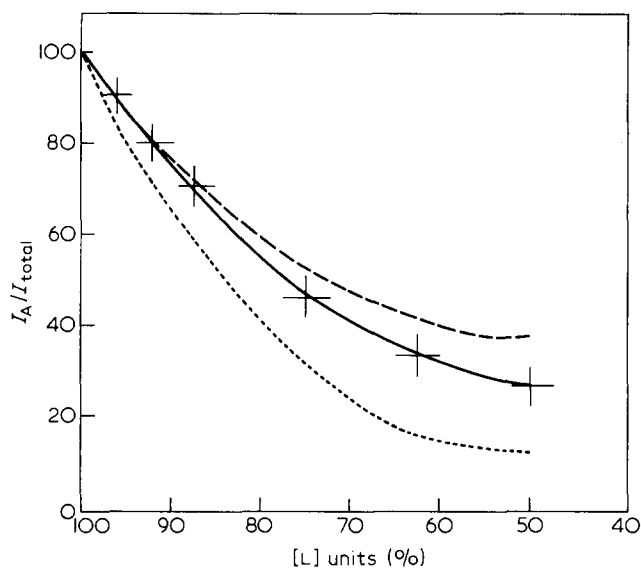
Finally, pentad stereosensitivity at 62.86 MHz, as has been deduced from the spectrum of PLA 50_a, is inconsistent with pentad stereosensitivity deduced from the relative line intensities at 22.51 MHz (Figure 2 and Table 2), a frequency which gives much lower resolution and, especially, no structure in the downfield peak A. Therefore, we are forced to conclude that the 22.51 MHz C=O patterns, shown in Figure 2, reflect tetrad stereosensitivity and that the downfield A peak, observed for all the stereopolymers in Figure 2, can be assigned to isotactic tetrads mmm. This peak, which is well isolated in 22.51 MHz spectra, was used to investigate further the discrepancies between the experimental C=O patterns (Figure 2 and Table 2) and the theoretical tetrad distributions for single- and pair-addition mechanisms (Table 4).

Comparison between experimental and calculated data

Figure 4 shows the comparison, for the various PLA X stereopolymers, between the mmm tetrad experimental weight, in regard to the all C=O pattern, and the corresponding theoretical weights calculated according

Table 4 Relative intensities (%) of ^{13}C n.m.r. lines corresponding to the various tetrads in lactic acid stereopolymers (PLA X) as deduced from Bernoullian statistics applied to pair addition (lactide ring-opening polymerization) and single addition (lactic acid condensation) mechanisms of chain growth

Tetrad	General equation ^a	Pair addition							Single addition	
		X (%)							General equation	X (%) 50 _a
		100	92	87.5	75	62.5	50 _i	50 _s ^b		
mmm	$(p^2 + q^2 + p^3 + q^3)/2$	100	81.6	72.7	53.1	41.4	37.5	0	$p^4 + q^4$	12.5
mrm	pq	0	7.4	10.9	18.7	23.4	25	12.5	$2p^2q^2$	12.5
mrr	$pq/2$	0	3.7	5.5	9.4	11.7	12.5	0	$p^3q + pq^3$	12.5
rrm	$pq/2$	0	3.7	5.5	9.4	11.7	12.5	0	$p^3q + pq^3$	12.5
rrr	$pq/2$	0	3.7	5.5	9.4	11.7	12.5	25	$2p^2q^2$	12.5
rrm	0	0	0	0	0	0	0	12.5	$p^3q + pq^3$	12.5
mrr	0	0	0	0	0	0	0	12.5	$p^3q + pq^3$	12.5
rrr	0	0	0	0	0	0	0	37.5	$2p^2q^2$	12.5

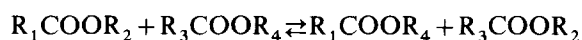
^a $p = L/(L + D)$; $q = D/(L + D)$
^b $b_{mrm} = rrm = mrr = p^2/2$; $rrr = p^2$; $rrr = (2p^2 + 2p^3)/2$

Figure 4 Comparison of the experimental variation of the I_A/I_{total} ratio and the theoretical variation as deduced from the tetrad distributions given by the single- and pair-addition Bernoullian mechanisms: ···· (pure single addition); - - - - (pure pair addition); + (experimental points)

to the Bernoullian single- and pair-addition statistics. The experimental data lie between the two theoretical curves for all the stereopolymers considered, especially those with a high content of D units.

In an attempt to account for the discrepancies, the occurrence of configurational rearrangement due to transesterification reactions was then considered.

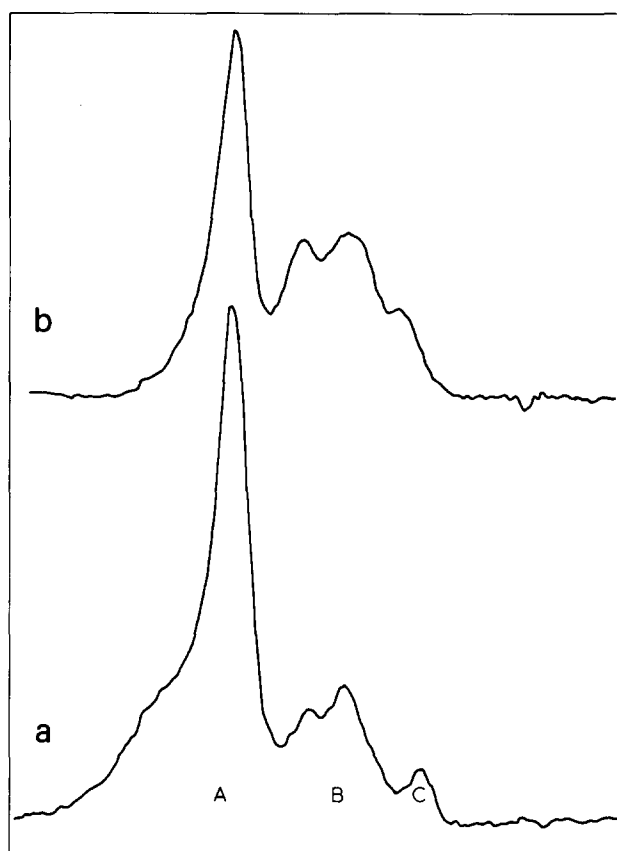
Experimental evidence for transesterification reactions at the ester bonds

Stereosequence redistribution because of transesterification reactions involving ester bonds and active species is possible¹⁰. On the other hand, rearrangements between esters according to the following reactions:



has been recognized in organic chemistry^{17,18}.

If such transesterification reactions occur at the ester bonds of PLA stereopolymers in the melt, then highly crystalline isotactic PLA 100 should become amorphous


Figure 5 ^{13}C n.m.r. spectra (20.11 MHz) of the carbonyl groups of an equimolar mixture of PLA 100 and PLA 50_i: (a) just after the mixing; (b) after 3 days at 140°C

if heated in the presence of a stereopolymer rich in D units.

Figure 5 shows the C=O patterns of 50-50 mixture of PLA 100 and of PLA 50_i, i.e. for an artificially made PLA 75, immediately after mixing, and after heating at 140°C for 3 days (the temperature and polymerization time for the ring-opening polymerization of *rac*-lactide). Just after mixing, the spectrum is a superposition of each component, as expected. It is valuable to note that the isotactic tetrad did not come out at the same chemical shift for PLA 100 and PLA 50_i, as shown by the low-field shoulder on the PLA 100 peak. This slight difference shows the configuration dependence of the C=O spectrum mentioned above. After 3 days of heating, the spectrum was severely modified. The central B region

increased at the expense of the initial PLA 100 A peak, while the shoulder and the C peak due to PLA 50_i both disappeared. These modifications prove the rearrangements of chiral units and the occurrence of *transesterification* reactions at the ester bonds. The mixture of the starting polymers was thus transformed to a PLA 75 stereocopolymer. This transformation was confirmed by the total solubility of the polymeric mass in acetone, a non-solvent for the starting PLA 100. However, the PLA 75 obtained differed from the PLA 75 prepared by polymerization of the suitable mixture of L- and *rac*-lactides (*Table 1*) insofar as configurational structure is concerned. Our findings definitely show the occurrence of *transesterification* redistributions between preformed macromolecules. It is likely that similar rearrangements occur during the ring-opening polymerization of lactides under our experimental conditions. It is of value to notice that the resulting configurational rearrangements do not proceed up to complete randomization since compounds like PLA 50_i have been obtained reproducibly with 26–29% for the weight of peak A at 22.51 MHz.

As there is no information available on the rate constants and the respective contributions of both the propagation and the *transesterification* reactions, attempts have been made to take into account the configurational rearrangements on the basis of statistical considerations. So far, all the attempts have failed.

CONCLUSIONS

In this work, we have shown that the C=O carbon atoms of lactic acid stereopolymers are sensitive to tetrads at 22.51 MHz and to pentads at 62.86 MHz when the resolution enhancement technique is used. We have confirmed that the mechanism of ring-opening polymerization of lactides consists primarily in a pair addition of repeating units. However, we have shown that the configurational structures of the polymers prepared in the melt are more complicated because of *transesterification* redistributions at the ester bonds under our experimental conditions. These redistributions seem to be limited since we have not so far succeeded in our attempts to randomize the D and the L unit distributions completely. This limitation might be due to the configuration dependence of these reactions. Evidence for such configuration dependence of *transesterification* reactions is not yet available. However, the much longer averaged polymerization time required for the polymerization of L-lactide-rich feeds in regard to *rac*-

lactide-rich feeds (*Table 1*) may be regarded as a good sign, especially as the polymerization of lactides is not configuration dependent. Other chemical reactions, such as the attack of polymer chain ester bonds by active centres, might contribute to the configurational rearrangements and might be configuration dependent too. Much further work is needed to check these hypotheses. The enhanced resolution technique makes ¹³C-¹H} n.m.r. a convenient method and should permit a deeper investigation of the structural and chemical particularities of poly(lactides) prepared under different conditions.

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