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Polylactic acids produced from l- and dl-lactic acid anhydrosulfite: stereochemical aspects

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Abstract

The polymerisations of l- and dl-lactic acid anhydrosulfite were conducted at room temperature in tetrahydrofuran with butyllithium as initiator. The polyesters obtained were analysed by gel permeation chromatography, both ^{1}H and ^{13}C NMR spectroscopy and also characterised by DSC. In all polymerisations, l-monomers led to highly crystalline isotactic polylactic acid, while dl-monomers produced amorphous polymers with randomly distributed l- and d- lactic acid units.

Keywords: Polylactic acids; Gel permeation chromatography; Polymerisation

1. Introduction

Polylactic acids are of considerable interest as biodegradable polymers in medical applications and also potentially for use as environmentally friendly packaging materials. However, the variety of methods available for their synthesis is limited. It is difficult by direct polycondensation of lactic acid to produce polymers with useful properties and the ring-opening polymerisation of lactide is most frequently initiated by toxic heavy-metal compounds, which have to be removed if the polymers are to be used for medical applications [1].

The polymers normally obtained from the polymerisation of dl-lactide cannot be strictly described as atactic, i.e. comprised of randomly distributed d- and l- monomer units, or *meso* and racemic diads. Polymerisation of the dl- diastereoisomer, or *meso*-, lactide gives a polymer that is predominantly syndiotactic because the incorporation of the *meso* diastereoisomeric structure favours the formation of *racemic* diads in the polymer. Racemic lactide (racemic combinations of d,d- and l,l-lactides) gives a 'predominantly isotactic' polymer (Vert's terminology [2]) because the diads that are generated by l,l- and d,d-repeating units are principally *meso* in nature.

The anionic ring-opening polymerisation of anhydrosulfites was shown to provide an interesting and useful route to polyesters. Poly(lactic acid) is produced by a process over which there is a close control of molecular weight and molecular weight distribution [3,4]. The effects of the configurational structure on the physical, mechanical and biological properties and, consequently, on the rate of degradation are well known in the case of a series of lactic acid stereocopolymers [5,6]. Accordingly, we were interested to investigate the microstructure of polylactic acid produced by the anionic polymerisation of l- and dl-lactic acid anhydrosulfites respectively.

In this present work, we have studied the stereospecificity of the anionic ring-opening polymerisation of lactic acid anhydrosulfite. Gel permeation chromatography, NMR spectroscopy and DSC were used to characterise the polymers.

2. Experimental part

2.1. Materials

Both l- and dl-lactic acids were obtained from Aldrich, as was butyllithium as a solution in hexanes (1.6 M). The initiator was used directly as supplied. THF utilised in the polymerisation was purified and dried according to standard procedures [7].

2.2. Monomer synthesis

l- and dl- lactic acid anhydrosulfites (l- and dl-LAAS) (1) were synthesised according to a multi-stage process that

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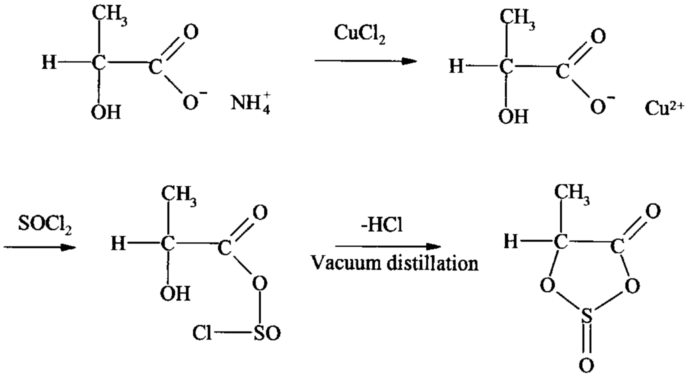

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Scheme 1. Synthesis of anhydrosulfites.

involved the reaction of thionyl chloride with copper(II) lactate as a suspension in dry diethyl ether [8–9]. Ring closure of the intermediate chlorosulfinate, formed in this initial process, to the anhydrosulfite took place during the recovery of the product by distillation under vacuum. The monomers were then purified by reaction with copper(I) oxide, to remove chloride impurities, and further distilled under reduced pressure. The synthesis of the monomers is summarised in Scheme 1.

2.3. Polymerisation

All polymerisation experiments were conducted under argon at 25°C.

The solvent THF (10 ml) was first injected into the polymerisation vessel, followed by the desired quantity of initiator. Shortly afterwards, 0.04 mole of purified monomer (l- or dl-LAAS) was added to the vessel by syringe. All injections were effected through Suba seal stoppers. The mixture was then further agitated for 6 mins during which time polymerisation took place with accompanying evolution of sulfur dioxide. After this time approximately 5 ml of methanol was added to the system to terminate the polymerisation

At the end of the polymerisation, the solvent was removed from the reaction products by evaporation, except when the monomer was the mixture of the dl enantiomers. In that case, a precipitation of the polymer in hexane was found to be necessary. The product was then filtered and dried in a desiccator for 5 h.

2.4. Characterisation of polymers

^{1}H and ^{13}C NMR spectra were obtained in CDCl$_3$ with tetramethylsilane as an internal standard using a Bruker 300 MHz FT-NMR Spectrometer. Molar masses were estimated by size exclusion chromatography, in THF or CHCl$_3$ solution at room temperature according to a calibration curve obtained using polystyrene standard samples. The thermal behaviour of polymers was studied using a Polymer Laboratories Thermal Sciences PL-DSC differential scanning calorimetre.

Table 1
Polymerisation of l and dl-LAAS with butyllithium in THF at 25°C

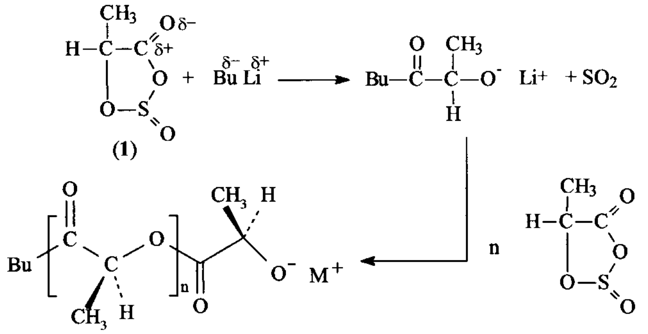
Monomer	$[M]/[I]$	$\bar{M}_n/10^3$gmol^{-1}	$\bar{M}_w/10^3$gmol^{-1}	$\bar{M}_w/\bar{M}_n$
l-LAAS	100	15.0	26.8	1.8
dl-LAAS	95	7.3	8.0	1.1

3. Results and discussion

3.1. Preparative aspects

The results presented in this article concern the anionic polymerisation in THF solution of l- and dl-lactic acid anhydrosulfites initiated by butyllithium at ambient temperature.

Whether the monomer was derived from the pure enantiomer or was from a dl-mixture appeared to have a profound effect on the molecular weight and the breadth of the molecular weight distribution of the poly(lactic acid) produced. l-LAAS was found to yield higher molecular weight polymers than dl-LAAS when the monomers were polymerized under similar reaction conditions, as shown in Table 1. Additionally, when the monomer was the pure enantiomer, the polymer (l-PLAAS) produced was highly crystalline and not soluble in THF. Precipitation of the polymer occurred during polymerisation, whereas the polymerisation of dl-LAAS produced an amorphous polymer which remained soluble in the polymerisation solvent. It would appear that the polymerisation of dl-LAAS is a conventional anionic living polymerisation of a cyclic monomer with the rate of initiation being fast compared to the rate of propagation and almost complete consumption of the initiator takes place. However, the polymerisation of the pure enantiomer is complicated by the insolubility of the polymer. It would appear that the initiation of the polymerisation is incomplete because the number average molecular weight is greater than expected for efficient initiation and,



Scheme 2. Mechanism for the anionic polymerisation of lactic acid anhydrosulfite.

because the polymer is insoluble in the solvent, the probability of consistent propagation sequences is low.

3.2. Stereochemical aspects

The stereostructure of the polymer was dependent on the monomer used in this type of polymerisation. When the monomer used was derived from l-lactic acid, the polymer was isotactic in nature. The ^{13}C NMR spectrum of the polymer showed that there was only a single peak associated with each type of carbon atom so that for instance the carbonyl (C=O) carbon atoms showed only one peak at 169.60 ppm. There was no sign of any other absorbance associated with carbonyl carbon atoms and accordingly the polymer could be considered to be stereoregular.

This information is in support of the fact that the syntheses of both the monomer and the polymer do not involve racemization of the asymmetric carbon atom. Accordingly a proton is not abstracted from the methine carbon of the monomer either during the synthesis of the monomer or during the initiation or propagation stages of the polymerisation, unlike some polymerisations of d,d or l,l lactide [12].

As illustrated in Scheme 2, the butyl anion is believed to attack the carbonyl-carbon atom in the monomer molecule with acyl-oxygen bond scission and formation of the butyl end group. The alcoholate obtained is thought to be the active propagating species which is regenerated after addition of each subsequent monomer molecule. Other work has shown that alcoholates are active initiators in such polymerisations.

Polymerisation of the monomer prepared from the dl lactic acid was equally interesting. First of all the monomer (dl-lactic acid anhydrosulfite) had a ^{1}H NMR spectrum identical to that of the corresponding l isomer. This was not unexpected because the stereochemistry of the (CH) and (CH_3) will not depend on the chirality of the molecule in this case. However, on polymerisation, the monomer produced a

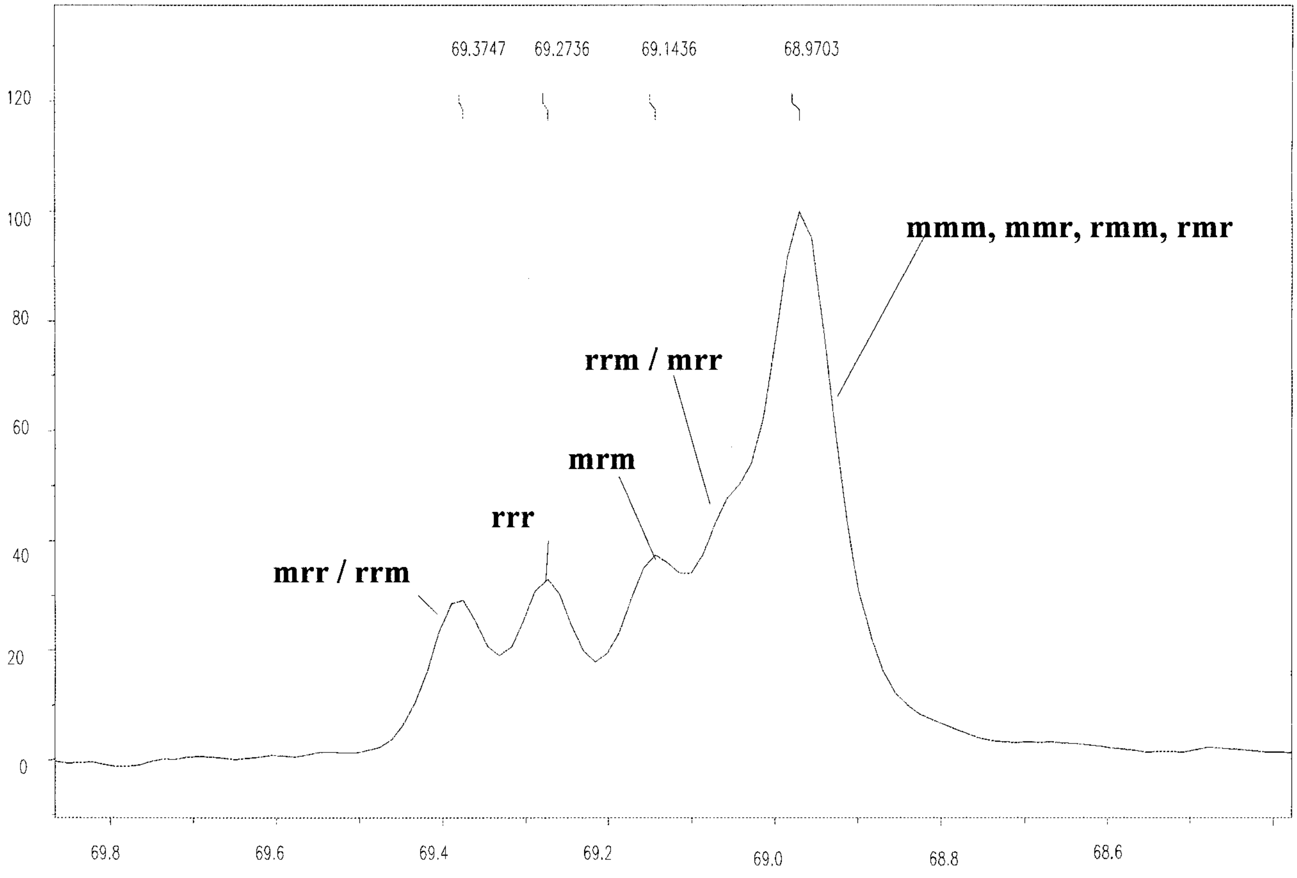


Fig. 1. Methine carbon signals in the ^{13}C NMR spectrum of dl-PLAAS.

Table 2
^{13}C NMR data of the methine carbon of dl-PLAAS

δ ppm	Relative peak intensity	Assignment
68.97	0.519	mmm, mmr, rmm, rmr
–	≅ 0.104	rrm / mrr
69.14	0.143	mrm
69.27	0.130	rrr
69.38	0.104	mrr / rrm

completely different type of product. Polymerisation of dl-lactic acid anhydrosulfite yielded atactic polylactic acid.

Close examination of the methine region of the ^{13}C NMR spectrum shows a fine structure of 5 lines, as shown in Fig. 1. This fine structure corresponds to resonances of the stereoirregular portions of the chains which arise from sensitivity to longer stereochemical sequences than triad (referring to α-carbons).

On the basis of work by Jedlinski [10,11] and Kricheldorf [12–15] on poly(dl-lactide) initiated with several catalysts, it was possible to make the different assignments for the methine carbon signals. They demonstrated that the methine carbon of poly(dl-lactide) was sensitive to tetrads and the signal obtained for dl-PLAAS exhibited a pattern similar to some signals they have reported. They differed slightly in the intensities of the various peaks. Therefore, the stereosequences of dl-PLAAS were analysed by NMR on the basis of tetrad effects and the structures of polymers obtained were described by the single-addition Bernouillian statistics. In this case, the following eight tetrads would be formed in the polymer chains, mmm, mmr, rmm, mrm, rmr, rrm, mrr, rrr with equal probability if no stereoselection occurred. The different assignments are presented in Fig. 1. Beside the lines of the tetrad characteristic for an isotactic tetrad mmm, the mmr, rmm and rmr tetrads were also present and this was in agreement with the fact that the methine carbon signal of l-PLAAS coincided with the main methine signal of dl-PLAAS.

The intensities of the tetrad peaks of the methine carbon atom are listed in Table 2. The intensity of one of the tetrad peaks could not be determined accurately because of its poor resolution. Nevertheless, as the intensity of the main methine peak was equal to the intensity of the other four peaks, dl-PLAAS appeared to be truly atactic with d- and l-lactic units randomly distributed in the polymer chains. The expansion of the carbonyl peak of dl-PLAAS in Fig. 2, which is tetrad stereosensitive, confirmed the atacticity of the polymer. The intensity of the peak in the region

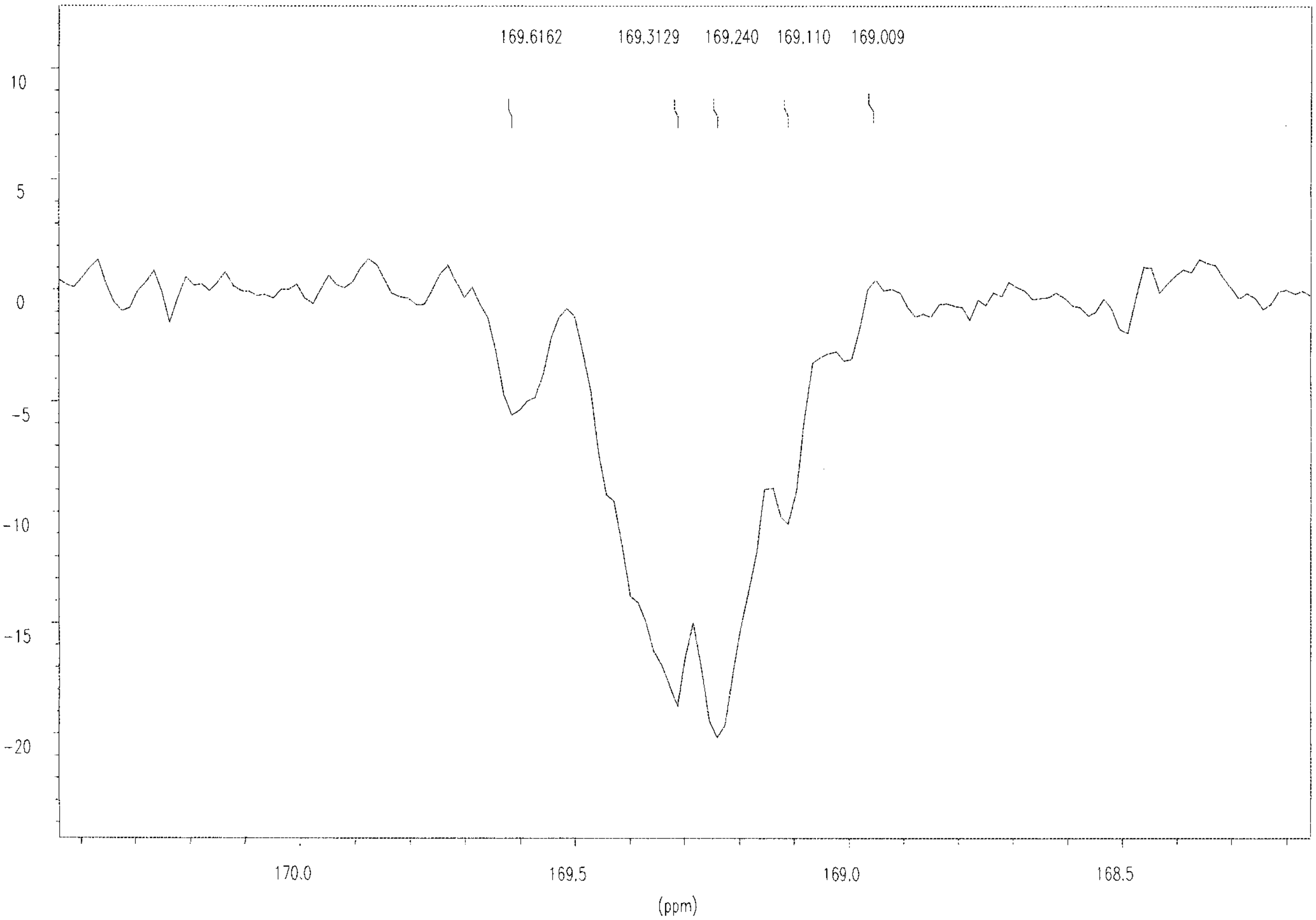
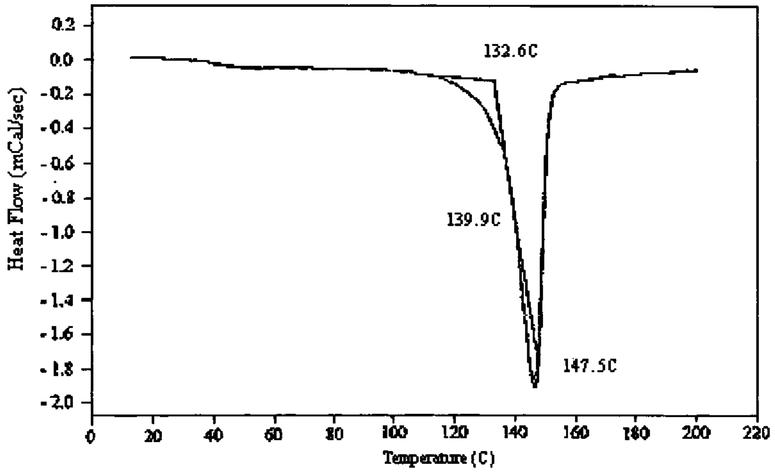
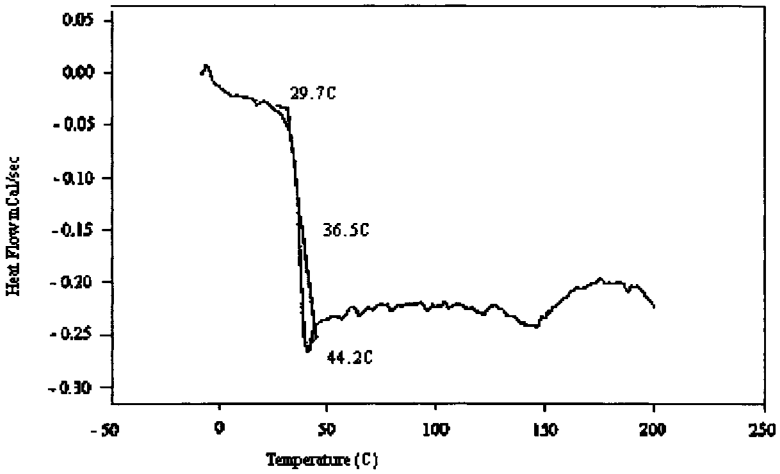


Fig. 2. Carbonyl signals in the ^{13}C NMR spectrum of dl-PLAAS.



Differential scanning calorimetry of poly-L-lactic acid



Differential scanning calorimetry of poly-D,L-lactic acid

Fig. 3. Differential Scanning Calorimetry of poly(l-lactic acid) and poly(dl-lactic acid).

associated with isotactic triads predominates in this spectrum but it also includes other triads such as mmr, and rmm. The application of Bernoullian statistics predicts that the overall intensity of the peak in this region should be 0.5 for atactic polymer. It is therefore reasonable to speculate that during the propagation reaction the polymerisation is not stereoselective. There is no stereochemical relation between the incoming monomer molecule and the structure of the terminal unit in the polymer chain.

3.3. Macroscopic properties

The structures of polylactic acids revealed by analysis of the ^{1}H and ^{13}C NMR spectra were in agreement with the DSC traces of the two polymers shown in Fig. 3. The stereoregular polymer l-PLAAS exhibited an endothermic melting transition in the range 140°C–150°C and so was highly crystalline whereas the atactic polylactic acid, dl-PLAAS, showed only a glass transition at 35°C. This observation was in agreement with the fact that the highly crystalline l-PLAAS was hardly soluble in THF unlike the amorphous dl-PLAAS which was readily soluble. These observations are in agreement with the stereostructures of the respective polymers. It is reasonable to presume therefore that it is possible to synthesise specific structures from monomer mixtures.

4. Conclusion

l-LAAS led to a highly crystalline, purely isotactic poly(l-lactic acid) while dl-LAAS produced an amorphous polymer with randomly distributed d- and l-lactic units. The dl-polymer structure was determined by Bernouillian statistics and turned out to be truly atactic whereas polylactic acid derived from the polymerisation of racemic lactide gave rise to pairwise incorporation of the monomer into the polymer chain.

This gave two indications. On one hand, the formation of l (or dl)-LAAS from l (or dl)-lactic acid did not involve inversion of configuration and this configuration was retained in the ring-opening polymerisation. However, this polymerisation was not stereoselective.

Acknowledgements

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