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Stereoselective polymerization of racemic DL-lactide in the presence of butyllithium and butylmagnesium. Structural investigations of the polymers

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Abstract

The use of butyllithium and butylmagnesium in the polymerization of racemic lactide leads to the formation of polylactide with a partially disyndiotactic structure. A coefficient of stereoselectivity p_2 which describes the content of disyndiotactic structures appears to be higher for the lithium initiator; however an increase in the concentration of this initiator tends to enhance an intermolecular transesterification process thus leading to the formation of totally random structures in a polylactide chain. In contrast, in the case of butylmagnesium, an increase in the initiator concentration does not induce the intermolecular transesterification processes. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Lactide; Polyesters; Polymer structure

1. Introduction

For many years polylactide has been a well-known biodegradable polymer used in medicine for drug delivery systems or resorbable medical implants [1–3]. A high molecular weight polylactide is prepared by ring opening polymerization from lactide [4–6], which is a cyclic product of condensation of two lactic acid molecules [1]. Owing to the presence of two asymmetric carbon atoms in its structure, lactide has three stereoisomeric forms: SS, RR and RS. An equimolar mixture of RR and SS stereoisomers is referred to as racemic DL-lactide [1,2]. During polymerization of racemic lactide there occurs the addition of RR and SS stereoisomers to the growing chain end. In the case when the stereochemistry of the growing chain end has no influence on the selection of configuration of the monomer molecule being added, then such a process conforms to “pair addition Bernoullian statistics” [7]. The resulting polymer is characterized by a “predominantly isotactic” structure [6,7]. On the contrary, in the case of stereoselective polymerization the following two possibilities may occur:

1. selection of the monomer molecule of the same configuration as that exhibited by the chain end—isotactic polymer is obtained;
2. selection of the monomer molecule of the reverse configuration than that of the chain end—disyndiotactic polymer is formed.

Obviously, the observed stereoselectivity is not complete. In the case of polymerization of racemic DL-lactide in the presence of lithium *t*-butoxide we observed stereoselectivity of the process leading to the formation of the polymer with predominant amount of disyndiotactic segments [8]. For this initiator the coefficient p_2 describing the content of disyndiotactic structures was determined to be 0.76. The presence of syndiotactic structures in poly(DL-lactide) obtained with the use of stannous octoate was reported by Vert [9] and Thakur [10]. The latter author using NMR spectroscopy at the ^{1}H resonance frequency of 500 MHz and ^{13}C resonance frequency of 125 MHz demonstrated a possibility of observation of hexad sequences in the methine region of ^{13}C and ^{1}H (homonuclear decoupled) spectra [10,11]. On the contrary, the analysis of HETCOR (heteronuclear chemical shift correlation) spectra allowed us to assign the iss and ssi tetrads in the methine region of the ^{13}C NMR (75 MHz) spectra [12] as well as to describe the 300 MHz ^{1}H NMR (homonuclear decoupled) spectra on pentad level.

The aim of the present study was to compare the microstructure of poly(DL-lactide) chain obtained in the presence of butyllithium and butylmagnesium, as well as to examine the influence of the initiator concentration on the chain

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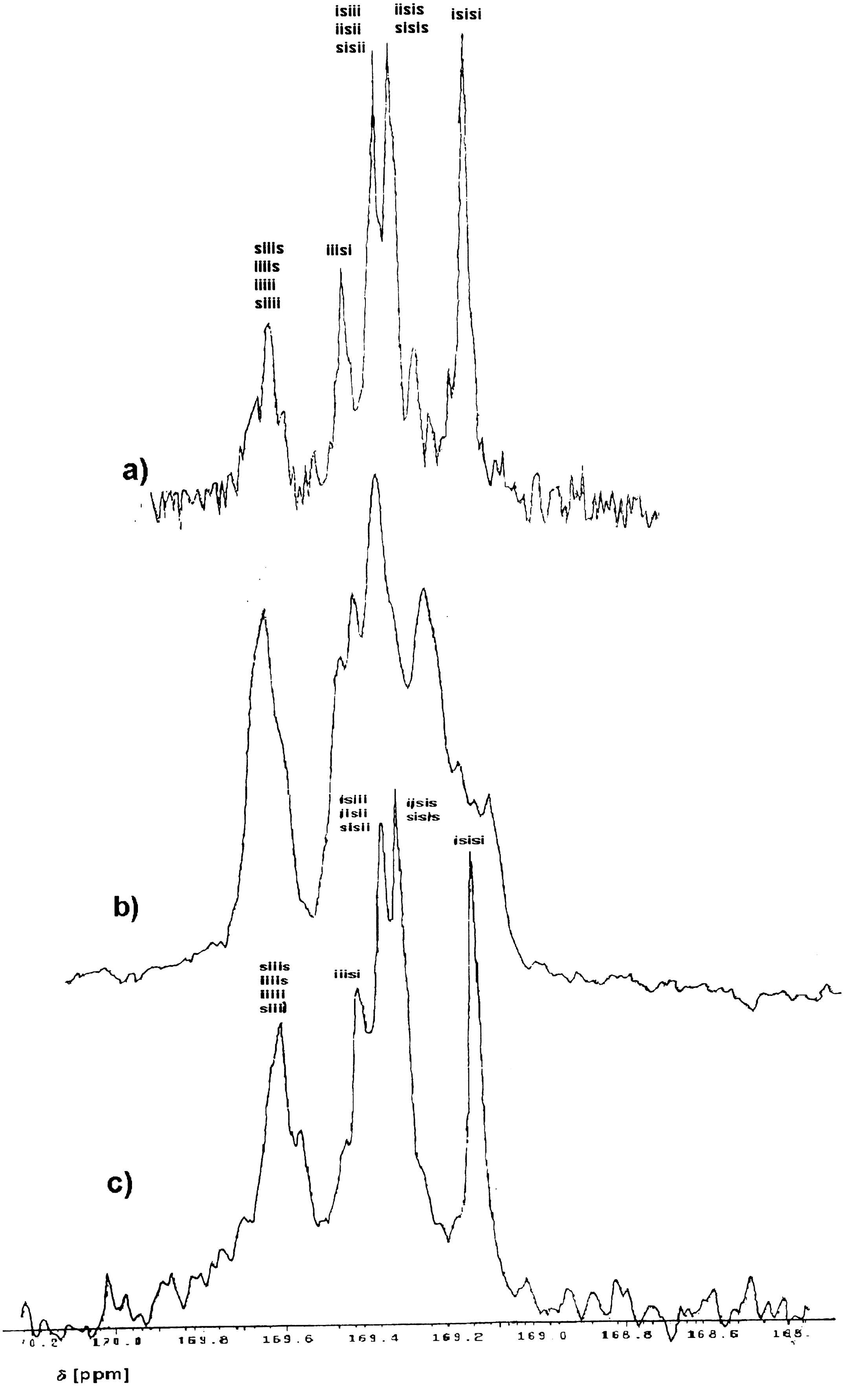
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170.0
169.8
169.6
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169.2
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168.
δ [ppm]

Table 1
The results on polymerization of racemic DL-lactide in tetrahydrofuran at 20°C (time of polymerization 40 min., concentration of monomer 1 mol/dl)

No.	Initiator	I/M[a]	Y^b (%)	$M_n \times 10^{3\,c}$	D^d
1	BuLi	1/400	60	45	1.6
2	BuLi	1/200	79	20	1.6
3	BuLi	1/100	81	18	1.8
4	BuLi	1/50	93	7	3.2
5	Bu_2Mg	1/400	75	23	1.5
6	Bu_2Mg	1/200	75	19	1.6
7	Bu_2Mg	1/100	80	7	1.7
8	Bu_2Mg	1/50	94	4	3.1

[a] I/M—initiator/monomer ratio.
[b] Y—yield.
[c] M_n—molecular weight.
[d] $D = M_w/M_n$—polydispersity.

microstructure and the related phenomena of intermolecular transesterification. Butyllithium was applied earlier by Kricheldorf to polymerize L-lactide [13]. Kricheldorf also used butylmagnesium to the polymerization of racemic and meso DL-lactide [14]. In the case of polymerization of racemic DL-lactide the average length of isotactic blocks of the obtained polymer was $L_i = {\sim}3.4$ indicating the deviation from Bernoullian statistics ($L_i = 4$). We decided to perform a more detailed study based on the recent achievements in the interpretation of the NMR spectra [10–12].

2. Experimental

2.1. Materials

Monomer—racemic DL-lactide (Purac) was recrystallized several times from ethyl acetate.

Solvent—tetrahydrofuran (Aldrich) was dried over sodium/potassium alloy and kept under dry argon atmosphere.

Initiators—the commercial grade butyllithium and butylmagnesium (Aldrich) were used.

2.2. Polymerization procedure

Polymerization of racemic DL-lactide was carried out in a closed glass reactor equipped with a magnetic stirrer and dry argon supply. A solution of initiator in hexane was introduced by a syringe into a 1 M solution of DL-lactide in tetrahydrofuran. The polymerization was conducted for 30 min, and stopped by adding methyl iodide into the reaction mixture. Then the reactor content was poured into cold methanol in order to precipitate the polymer. The precipitated

Table 2
Tetrads and hexads intensities of lines in ^{13}C NMR spectra of poly(rac-lactide) obtained by BuLi and Bu_2Mg as initiators (I/M—initiator to monomer mole ratio)

Initiator (or structure)	Tetrad intensities (%)					Hexad intensities (%)						p_2[a]	L_i[b]	T[c]
	ssi	sss	isi	iss	sis + iis + sii + iii	siiis + iiiis + iiiii + siiii	iiisi	isiii + iisii + sisii	iisis + sisis	isisi	Remaining 21 hexads with ss structure			
Predominantly isotactic	0	0	25.0	0	75.0	37.5	12.5	25.0	12.5	12.5	0	0.5	4	0
Atactic	12.5	12.5	12.5	12.5	50.0	12.5	3.125	9.375	6.25	3.125	65.625	–	–	1
Completely disyndiotactic	0	0	50.0	0	50.0	0	0	0	50.0	50.0	0	1	2	0
BuLi (I/M = 1/400)	0	0	36.0	0	64.0	18.0	10.0	20.0	26.0	26.0	0	0.72	2.77	0
BuLi (I/M = 1/200)	0	0	36.0	0	64.0	18.0	10.0	19.0	27.0	26.0	0	0.72	2.77	0
BuLi (I/M = 1/100)	10.0	8.0	14.0	11.0	57.0	–	–	–	–	–	–	–	–	0.94
BuLi (I/M = 1/50)	10.0	9.0	14.0	11.0	56.0	–	–	–	–	–	–	–	–	0.94
Bu_2Mg (I/M = 1/400)	0	0	31.5	0	68.5	25.3	11.7	23.3	19.8	19.9	0	0.63	3.17	0
Bu_2Mg (I/M = 1/100)	0	0	31.5	0	68.5	25.3	11.7	23.4	19.8	19.8	0	0.63	3.17	0
Bu_2Mg (I/M = 1/50)	0	0	31.0	0	69.0	26.2	11.8	23.5	19.3	19.2	0	0.62	3.23	0

[a] p_2—coefficient of stereoselectivity calculated from the equations presented in Ref. [8].
[b] $L_i = 2/p_2$-average length of L-lactyl units [9].
[c] $T = (isi_0 - isi)/(isi_0 - 0.125)$—transesterification coefficient [9].

Fig. 1. 75 MHz ^{13}C NMR spectra of racemic polylactide-carbonyl carbon region: (a) BuLi as the initiator [I]/[M] = 1/400; (b) BuLi as the initiator [I]/[M] = 1/100; (c) Bu_2Mg as the initiator [I]/[M] = 1/100.

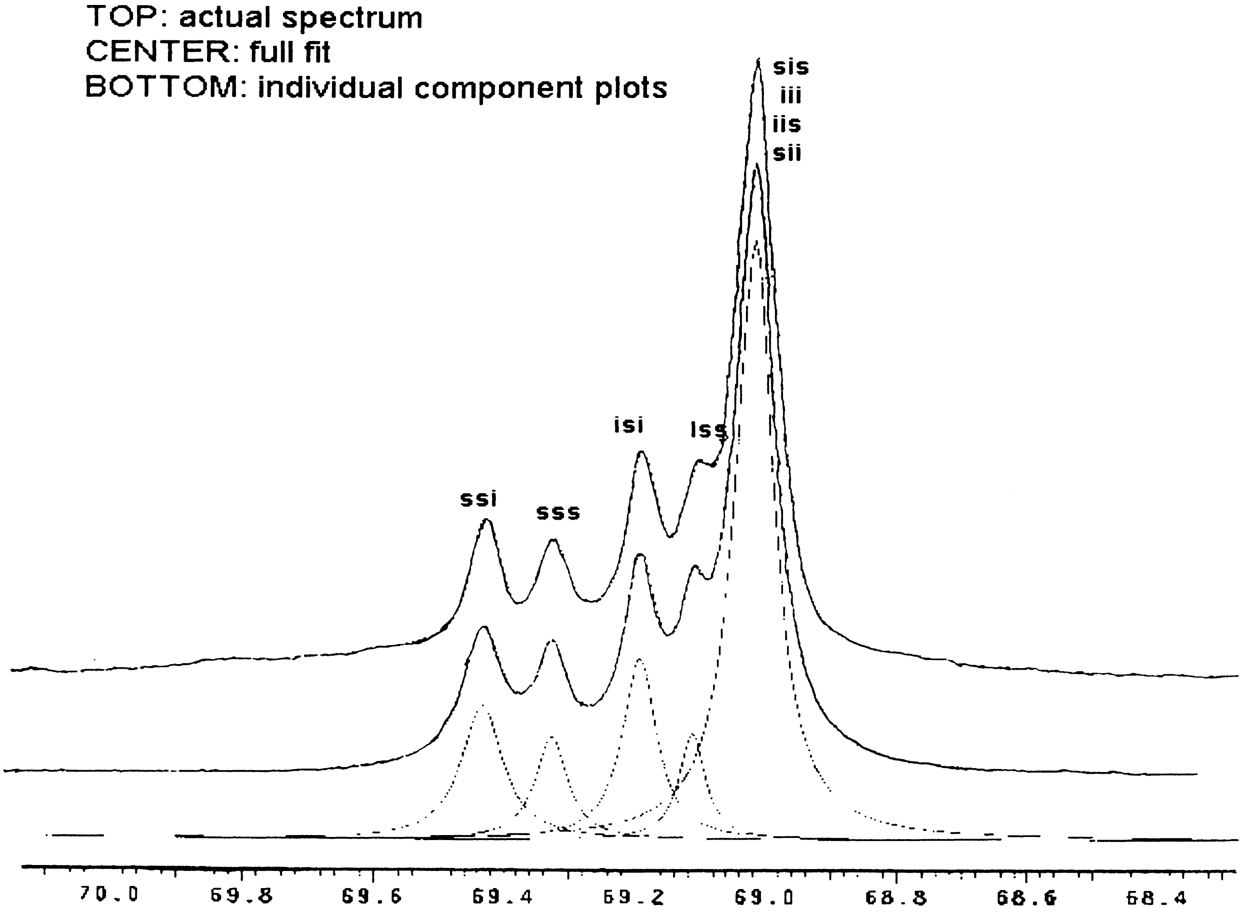

Fig. 2. 75 MHz ^{13}C NMR spectra of racemic polylactide-methine carbon region—obtained in the presence of BuLi as the initiator; [I]/[M] = 1/100.

polymer was washed with methanol and dried under vacuum at 50°C.

2.3. Measurements

The molecular weights and polydispersity indexes were determined by means of liquid chromatography method using a Waters ALC/GPC 3M apparatus (tetrahydrofuran (THF) as an eluent, polystyrene standards) and by GPC on a Spectra Physics SP 8800 chromatograph (THF as an eluent, flow rate 1 ml min^{-1}, Styragel columns 104, 103 and 500 Å, Shoedex SE 61 detector).

The ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Varian Unity Inova spectrometer in 5 mm sample tubes using chloroform-*d* as a solvent and TMS as an internal standard; 1.8 s (^{1}H) and 3.7 s (^{13}C) acquisition time, 9 μs pulse width, 3 s pulse delay, digital resolution 64 K, spectral width 4000 Hz (^{1}H) and 16 500 (^{13}C), 64 scans for proton spectra and 10 000 scans for carbon spectra.

3. Results and discussion

The results of our study on the polymerization of DL-lactide are summarized in Table 1. The data indicate that polymerization proceeding in THF is rapid as compared to that conducted by Kricheldorf [13] for L-lactide in aromatic solvents. The molecular weights of the polymer obtained in the presence of butyllithium are higher than those of the polymer prepared with butylmagnesium under the same conditions. They are also higher than assumed. Polydispersity of the obtained copolymers increases in order of increasing concentration of the initiator. Microstructure of the copolymers was studied by NMR spectroscopy.

Table 2 presents the intensities of the ^{13}C NMR lines arising from tetrads and hexads of polylactides obtained in the presence of butyllithium and butylmagnesium as the initiators. In the spectra of polylactide obtained in the presence of BuLi at low initiator concentrations, $c_i \leq 1/200$, no lines due to tetrads and hexads containing the ss sequences are present (Fig. 1(a)). However, the intensities of the lines arising from alternating …isis… sequences (Table 2) are considerably enhanced as compared with those found in the chain with a “predominantly isotactic” structure. The calculated coefficient of stereoselectivity p_2, which reflects the content of disyndiotactic structures in the polymer chain is 0.72, whereas the average length of

L-lactyl units $L_i = 2.77$. The values of p_2 higher than 0.5 with L_i below 4 and transesterification coefficient T equal to 0 indicate a highly disyndiotactic structure of the obtained polymer and no intermolecular transesterification which would lead to the formation of ss structures. An increase in the concentration of initiator induces some additional lines in the NMR spectra, which correspond to n-ads containing the ss structures (Fig. 1(b)). The latter are well visible in the spectra of completely atactic polylactide, which is produced by polycondensation of racemic lactic acid or by polymerization conducted in the presence of the initiators which tend to induce a strong transesterification of polylactide chain (e.g. $ZnCl_2$ [6]). The analysis of intensities of the lines due to tetrads, and the calculated transesterification coefficient $T = 0.88$ (Table 2) indicate a strong intermolecular transesterification of polylactide chain, leading in consequence to the formation of the polymer, the structure of which is close to that of the atactic polymer.

Also when applying Bu_2Mg as the initiator, intensities of the lines due to isi tetrads and isisi hexads are higher as compared with those found in the polymer with a "predominantly isotactic" structure (Fig. 1(c), Table 2). A value of the coefficient of stereoselectivity p_2 is higher than 0.5, being however lower than the respective value found for polylactide obtained in the presence of lithium initiator at low concentrations of the initiator.

By contrast, in the polymerization of racemic lactide in the presence of Bu_2Mg no significant influence of the initiator concentration on the structure of the chain of the obtained polylactide was observed. Regardless of the concentration of the initiator used in the polymerization, no lines due to tetrads and hexads containing the ss structures are visible in the NMR spectra (Table 2).

Moreover, any changes in the polymerization temperature within the range of −15 to 80°C exerted negligibly small effect on the chain microstructure of the polymer obtained in the presence of Bu_2Mg. These observations indicate that intermolecular transesterification processes do not occur (Fig. 2).

The results of more detailed examination on the polymerization of DL-lactide in the presence of lithium compounds will be presented in a successive report.

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