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Synthesis of block copolymers of ε-caprolactone and lactide in the presence of lithium *t*-butoxide

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SUMMARY

High molecular mass copolymers with microphase separation can be obtained in block copolymerization of ε-caprolactone with L,L- and D,L-lactide carried out in the presence of lithium t-butoxide. A kind of solvent applied strongly affects the molecular mass and polydispersity index of obtained copolymers.

INTRODUCTION

Copolymers of lactide and ε-caprolactone are known to provide valuable materials for controlled release of drugs (1). They combine a good biodegradability with an excellent permeability of the copolymers to drugs (2).

In the literature there are some reports on the syntheses of block copolymers of lactide and ε-caprolactone carried out in the presence of aluminium compounds (3) or Al-Zn initiators (4) at 90°C. However in practice it is not possible to completely remove the heavy metals contained in the copolymers.

For the synthesis of the copolymers not containing any traces of heavy metals we used lithium t-butoxide as an initiator.

Lithium t-butoxide is known to initiate a homopolymerization of ε-caprolactone (5). The polymerization proceeds at room temperature and practically does not involve any intramolecular transesterification reaction (back-biting).

EXPERIMENTAL PART

Monomers: L,L and L,D lactide (Boehringer, Ingelheim, Germany) was purified by distillation in vacuum and several recrystalizations from ethyl acetate; ε-caprolactone (Fluka,

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Buchs, Switzerland) was distilled under dry argon.

Initiator: The commercial grade lithium tert-butoxide (Fluka, Buchs, Switzerland) was used.

Polymerization procedure: The copolymerization of lactide with ε-caprolactone was carried out in a closed flask equipped with a magnetic stirrer and dry argon supply. A solvent, monomers and initiator were added to the flask by means of syringe. At the first step a solution of an initiator was introduced into a 1.4 M solution of ε-caprolactone in benzene or tetrahydrofuran. After 6-7 minutes a lactide solution of the same concentration was added. Polymerization was conducted for 40 minutes, than the reaction mixture was poured into n-hexane to precipitate the polymer. In order to remove residual amounts of the monomers the polymer was purified by dissolving in THF and precipitated into methanol. The obtained products was dried in vacuum at 50°C.

Measurements: Molecular masses of the resulting copolymers were determined by means of the liquid chromatography method using ALC/GPC 3M Waters apparatus. THF was used as eluent, polystyrene standards served for calibration.

The GPC experiments were conducted in THF solution at 35°C (flow rate 1 ml/min.) using a Spectra Physics SP 8800 gel permeation chromatograph equipped with RI detector. The configuration of columns consisited two styrogel-packed columns 500 and 1000 A (Polymer Laboratories). M_n and M_w/M_n were estimated according to the PS calibration curve.

The C-13 NMR spectra of the copolymers were recorded in $CDCl_3$ at a resonance frequency of 75 MHz on a Varian VXR-300 spectrometer using TMS as an internal standard (temperature 30°C).

Thermal properties of the copolymers were determined by differential scanning calorymetry using a DSC Du Pont 1090 B apparatus calibrated with gallium and indium.

RESULTS AND DISCUSSION

The experimental data on the block copolymerization of lactide with ε-caprolactone are presented in Table 1.

Table 1.

No	monomer	solvent	[M]/[I] $\times 10^{-2}$	N_L	Y [%]	M_n $\times 10^{-3}$	M_n/M_C	M_w/M_n
1.	ε-CL	benzene	4.5	-	100	134	2.54	1.1
2.	ε-CL+L,L-lactide	benzene	4.5	0.48	98	145	2.5	1.2
3.	ε-CL+L,L-lactide	benzene	6.0	0.46	96	185	2.47	1.2
4.	ε-CL	H_4-furan	4.5	-	98	52	1.0	1.6
5.	ε-CL+L,L-lactide	H_4-furan	2.0	0.49	96	27	1.1	1.7
6.	ε-CL+L,L-lactide	H_4-furan	4.5	0.50	97	56	1.0	1.7
7.	ε-CL+D,L-lactide	H_4-furan	2.5	0.45	95	34	1.1	1.7
8.	ε-CL+D,L-lactide	H_4-furan	4.5	0.45	95	62	1.1	1.7

[M]/[I]- monomer to initiator mole ratio
N_L- molar fraction of lactide in copolymer
Y- mole conversion
M_C- calculated stechiometric molecular mass

A kind of the solvent applied strongly affects a molecular mass and a polydispersity index of the obtained copolymer. In the case of benzene the molecular masses are almost two times higher than those calculated for a 'living' polymer, assuming a complete conversion of an initiator. The polydispersity indices (M_w/M_n) are close to 1. A typical plot of a distribution of molecular masses is displayed in Figure 1.

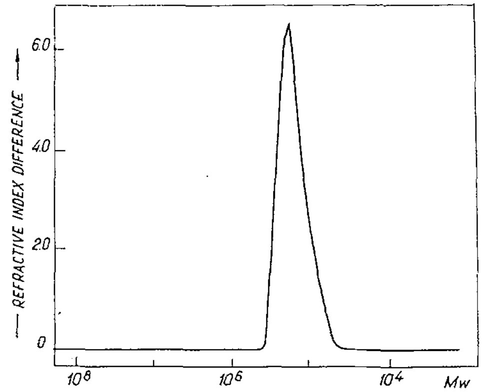

Figure 1. Molecular mass distribution of the L,L-lactide-ε-caprolactone block copolymer (M_w=170385; M_n=144679; M_w/M_n=1.18)

Similarly, unexpectedly high values of molecular masses were previously reported by Morton and Wu (5) in the case of a homopolymerization of ε-caprolactone in benzene in the presence of lithium t-butoxide. The observed increase of molecular masses in the block copolymerization carried out in benzene is presumably due to an association of the initiator in a medium of low polarity. On the other hand, molecular masses of the copolymers obtained in THF as a solvent are close to theoretically calculated ones, the polydispersity indices being however rather large.

Figure 2 presents the C-13 NMR spectra of the obtained copolymers.

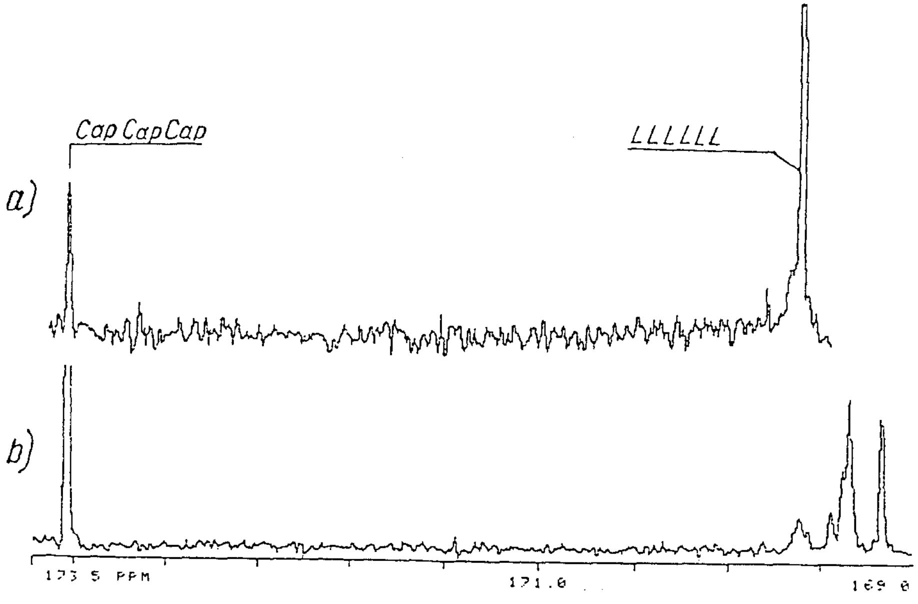

Fig.2. C-13 NMR (75 MHz) spectra of lactide-ε-caprolactone block copolymers. 169 ppm - spectral range of carbonyl carbons of lactide blocks, 173.5 ppm - spectral range of carbonyl carbons of caproyl blocks; a) copolymer with L,L-lactide b) copolymer with D,L-lactide.

The presented spectra are characteristic for a diblock copolymer. Within the spectral range of carbonyl carbons only the signals arising from caproyl (σ=173.49 ppm) and lactydyl (σ=169.57 ppm) blocks are visible. The absence of any signals in the range of 169.6-173.4 ppm indicates that there is no intermolecular transesterification between caproyl and lactydyl fragments of the copolymer chains (6).

The signals due to carbonyl carbons of lactydyl segment of the D,L lactide containing copolymers reveal only the presence of 11 hexads resulting from a usual addition between enantiomeric pairs of lactide molecules (4).

The observations presented above indicate a very limited degree of transesterification proceeding particularly in THF due to a high polarity of this solvent. It manifests by a large distribution of molecular masses of the copolymers obtained in this solvent.

A typical DSC curve of the obtained copolymers is presented in Figure 3.

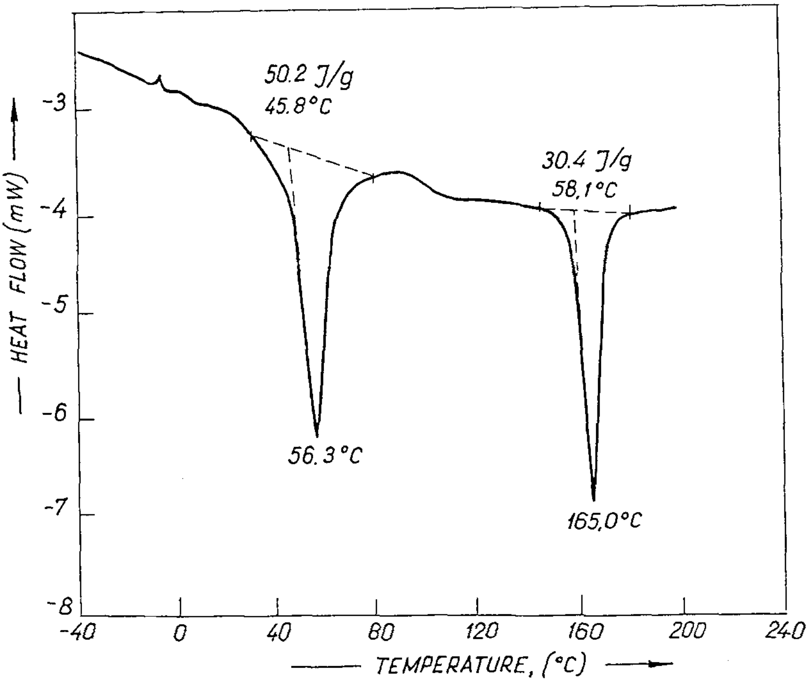

Fig.3. DSC thermogram of L,L lactide-ε-caprolactone block copolymer.

For a copolymer with a moderately high molecular mass, the melting endotherms due to crystalline domains of ε-caprolactone (56°C) and L,L-lactide blocks (165°C) are clearly seen.

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