Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

Synthesis of Potentially Biodegradable Polymers

Zbigniew Jedliński[a]; Piotr Kurcok[a]; Robert W. Lenz[b]
[a] Institute of Polymer Chemistry Polish Academy of Sciences, Zabrze, Poland [b] Polymer Science and Engineering Department, University of Massachusetts, Amherst, Massachusetts, USA

To cite this Article Jedliński, Zbigniew , Kurcok, Piotr and Lenz, Robert W.(1995) 'Synthesis of Potentially Biodegradable Polymers', Journal of Macromolecular Science, Part A, 32: 4, 797 — 810
To link to this Article: DOI: 10.1080/10601329508010290
URL: http://dx.doi.org/10.1080/10601329508010290

J.M.S.—PURE APPL. CHEM., A32(4), pp. 797–810 (1995)

SYNTHESIS OF POTENTIALLY BIODEGRADABLE POLYMERS

ZBIGNIEW JEDLIŃSKI* and PIOTR KURCOK

Institute of Polymer Chemistry
Polish Academy of Sciences
41-800 Zabrze, Poland

ROBERT W. LENZ

Polymer Science and Engineering Department
University of Massachusetts
Amherst, Massachusetts 01003 USA

ABSTRACT

Homopolymers of β-butyrolactone, L-lactide, δ-valerolactone, and methyl methacrylate, as well as their block copolymers, were prepared with simple initiator systems based on alkali metal alkoxides and alkali metal supramolecular complexes. The goal was to synthesize polymeric materials with potential biodegradability.

INTRODUCTION

In past decades a great deal of research has been done on the synthesis of polymers and polymeric materials for long-term service. In particular, many kinds of thermally stable and chemically stable polymeric materials have been developed. Essential contributions to this field were made by Professor Herman Mark, with his remarkable ideas and research carried out by himself and his students, as well as by many other outstanding polymer scientists.

Many of the traditional applications of synthetic polymers are due to their chemical and biological inertness, as some of the earliest studies on the biodegradation of polymers were performed to prevent or to retard polymer degradation by microorganisms, such as bacteria and fungi. Today however, a new field of research has developed, which is concerned with the synthesis of biodegradable polymers. This field of research is growing rapidly because of the strong demand for such polymers as packing materials and, in particular, as biocompatible materials for specific medical applications, such as sutures, surgical implants, and formulations of drugs with controlled-release. Research on these materials continues at an extraordinary pace. One of the important current incentives for the study of biodegradable polymers is, of course, the potential for their easy disposal and biodegradation under natural environmental conditions.

Current attempts to develop biodegradable polymers have focused on the synthesis of new polymers and on the modifications of natural polymers. However, such materials are often too expensive for commercial applications, and, therefore, further studies are needed. One important commercial product is poly(β-hydroxybutyrate-β-hydroxyvalerate) (PHB/V) copolymer, which is produced via fermentation by Zeneca Bio Products in the UK and distributed under the tradename of Biopol.

Other synthetic polyesters obtained via the polymerization of lactones, lactides, cyclic carbonates, etc. are of interest for such application, and in our laboratory a new procedure has been elaborated for the synthesis of biodegradable "tailor-made" polyesters with well-defined mechanical, physical, and chemical properties. In these syntheses anionic initiators are employed, capable of producing homopolymers, block polymers, or graft polymers via "living" polymerization processes. The interdisciplinary approach has been adopted for preparation of such initiators, which are based on the principles of supramolecular chemistry. The utility of such novel initiator systems, containing cation complexing agents as crown ethers, cryptands, and others, is discussed in this report.

SYNTHESIS OF HOMOPOLYMERS VIA RING-OPENING POLYMERIZATION WITH ALKALI METAL ALKOXIDES AS INITIATOR

Poly(β-Hydroxybutyrate) of Various Tacticities Synthesized with Alkali Metal Alkoxides/18-Crown-6 Complexes as Initiators

High molecular weight, stereoregular poly(β-butyrolactone)s have been synthesized with coordinative initiators [1, 2], but anionic polymerization reactions of racemic β-butyrolactone are also convenient methods in the synthesis of poly(β-hydroxybutyrate) with the desired tacticity. Furthermore, the results presented in this report indicate that the anionic polymerization of β-butyrolactone proceeds to almost complete conversion of monomer, both in bulk and in solvent, when alkali metal alkoxide/18-crown-6 complexes are used as initiators. End-group analysis by ^{1}H NMR revealed that, besides carboxylate active species, unsaturated and hydroxyl dead groups are present in the poly(β-butyrolactone) as prepared (Fig. 1) [3].

The tacticity of the poly(β-butyrolactone)s obtained in the presence of various alkoxides has been studied using ^{13}C-NMR spectroscopy (Fig. 2). The results obtained indicate that poly(β-butyrolactone) prepared in the presence either of potassium methoxide- or *tert*-butoxide/18-crown-6 complex possesses stereosequences distribution obeying Bernoullian statistics and are atactic. However, in polymeriza-

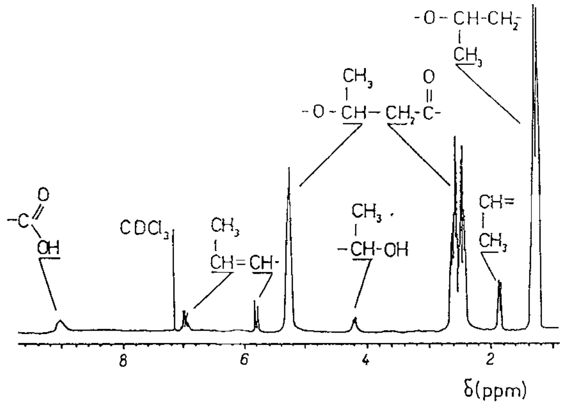

FIG. 1. ^{1}H-NMR of atactic poly(β-butyrolactone) prepared with potassium methoxide/18-crown-6 complex as the initiator.

tion with the optically active potassium (+)*sec*-butoxide/18-crown-6 complex, the product was predominantly syndiotactic poly(β-butyrolactone), in which with syndiotactic fraction was as high as 60%. The results of anionic polymerization of racemic β-butyrolactone initiated with various alkali metal alkoxide/18-crown-6 complexes are presented in Table 1. As shown by the data in Table 1, high molecular poly(β-butyrolactone) with a number-average molecular weight M_n, up to 40,000 and with various tacticities could be obtained via anionic polymerization of racemic β-butyrolactone with alkali metal alkoxide/18-crown-6 complexes as the initiator.

Synthesis of Poly(α-Hydroxy Acids) via Anionic Polymerization of L- and L,D-Lactide Initiated with Potassium Methoxide

The anionic polymerization of optically active L-lactide and racemic L,D-lactide in THF solution at room temperature proceeded fast and with good yields. The analysis of ^{1}H-NMR spectra of polylactides as obtained (Fig. 3) indicate that

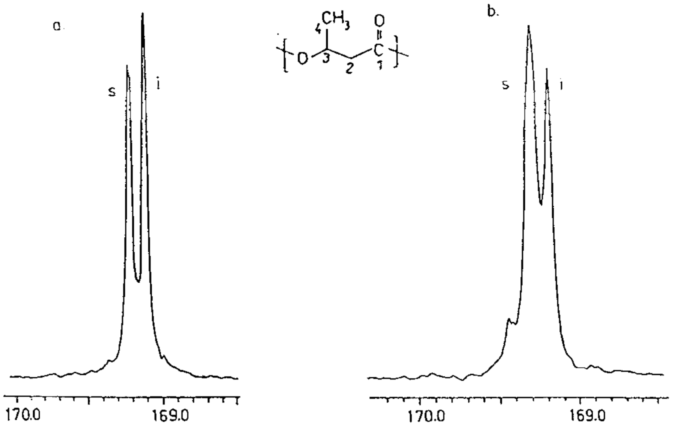

FIG. 2. ^{13}C-NMR (75 MHz) spectra (carbonyl carbon region) of (a) atactic poly(β-butyrolactone) and (b) predominantly syndiotactic poly(β-butyrolactone).

TABLE 1. Anionic Polymerization of Racemic β-Butyrolactone Initiated with Alkali Metal Alkoxide Complex with 18-Crown-6 at 20°C

No.	Potassium alkoxide	Solvent	$[M]_0$ in mol/dm^3	$[I]_0 \times 10^{-2}$ in mol/dm^3	Time in hours	Yield in %	M_n[a]	M_n (GPC)	M_w/M_n
1	MeOK	THF	2.30	6.80	3	98	2,900	3,100	1.08
2	MeOK	THF	3.62	1.02	150	96	30,500	24,000	1.07
3	MeOK	Benzene	1.89	7.40	4	99	2,200	4,100	1.09
4	MeOK	–	12.18	5.23	90	95	20,000	18,100	1.03
5	(+)*sec*-BuOK	–	12.18	29.93	6	98	3,500	3,600	1.10
6	(+)*sec*-BuOK	–	12.18	15.40	10	99	6,800	6,700	1.07
7	*tert*-BuOK	THF	2.5	3.07	10	98	7,000	6,900	1.05
8	*tert*-BuOK	THF	4.5	2.42	48	97	16,000	15,800	1.08
9	*tert*-BuOK	Benzene	3.42	1.73	48	98	17,000	16,900	1.07
10	*tert*-BuOK	–	12.18	4.70	85	99	22,500	21,300	1.08
11	*tert*-BuOK	–	12.18	2.30	170	95	45,000	38,000	1.08

[a] Number-average molecular weight calculated for 100% conversion.

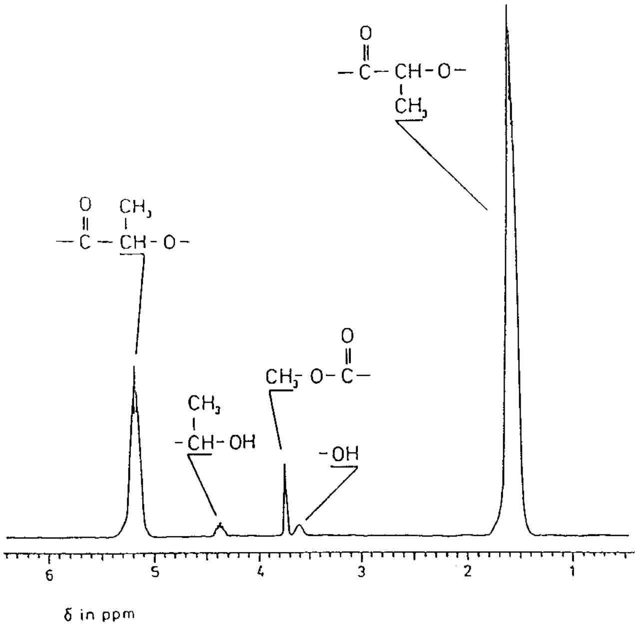

FIG. 3. ^{1}H-NMR spectrum of poly(L-lactide) prepared with potassium methoxide initiator.

the initiator was incorporated into the polymer chain in contrast to previous reports [4]. The results of anionic polymerization of lactides initiated with potassium methoxide are presented in Table 2.

The microstructure of the polymers obtained was studied using ^{13}C-NMR spectroscopy. The spectrum of poly(L-lactide) obtained (Fig. 4) in the region of methine and carbonyl carbons contains peaks corresponding to isotactic tetrads and hexads as well as signals corresponding to other stereosequences, although their intensities are small. Those results indicate that the polymers obtained possessed a high degree of tacticity, and revealed that the anionic polymerization of lactides

TABLE 2. Anionic Polymerization of L- and L,D-Lactide with Potassium Methoxide in THF at 20°C

Lactide	$[M]_0$ in mol/dm^3	$[I]_0 \times 10^2$ in mol/dm^3	Time in minutes	Yield in %	M_{ncalc}[a]	M_n	M_w/M_n
L-	1.31	2.33	10	89	7,640	7,100	1.35
L-	1.66	1.63	15	90	13,300	13,500	1.30
L-	2.07	0.74	135	94	37,500	38,000	1.38
L,D-	0.98	1.86	15	90	6,960	6,500	1.37
L,D-	1.13	1.40	20	96	11,300	11,500	1.36

[a] Calculated molecular weight $M_{ncalc} = 144([M]_0/[I]_0) \times$ conversion.

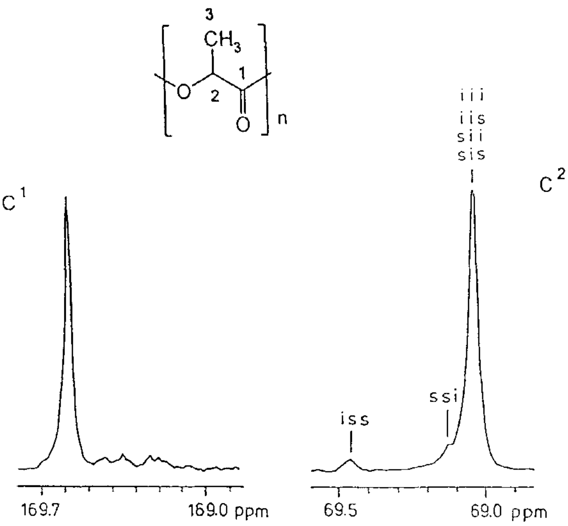

FIG. 4. ^{13}C-NMR (75 MHz) spectrum of poly(L-lactide) (carbonyl and methine region) prepared with potassium methoxide initiator; assignments for tetrads are indicated.

initiated with potassium methoxide led to well-defined polymers. Side reactions, such as racemization and transesterification, were negligible [5].

SYNTHESIS OF BLOCK POLYMERS VIA RING-OPENING POLYMERIZATION

δ-Valerolactone–L-Lactide Block Copolymers Obtained via Anionic Polymerization Initiated with Potassium Methoxide

The highly crystalline poly(α-hydroxyester)s obtained via lactide polymerization show poor water permeability and poor compatibility with soft tissue. This problem was overcome by block copolymerization of either glycolide or L-lactide with ε-caprolactone to yield polymers with good permeability and compatibility [6].

Previously, alkali metal alkoxides were found to act as initiators for the polymerization of L-lactide [5] and δ-valerolactone [7]. The polymerization of both monomers and the synthesis of their AB copolymers is demonstrated in this report. First, δ-valerolactone prepolymer was obtained by anionic polymerization initiated with potassium methoxide. This prepolymerization yielded "living" poly-δ-valerolactone with the expected molecular weight. When a THF solution of L-lactide was introduced into δ-valerolactone prepolymer solution, further reaction proceeded spontaneously, and after 15 minutes the L-lactide was almost entirely consumed, producing block copolymer as evidenced by GPC. The absence of peaks for possible cyclic oligomers in the GPC chromatogram of the reaction mixture suggests that no backbiting reaction took place in this process [8].

The ^1H-NMR spectrum of low molecular weight block copolymer obtained is presented in Fig. 5, and the results obtained for the block copolymerization reac-

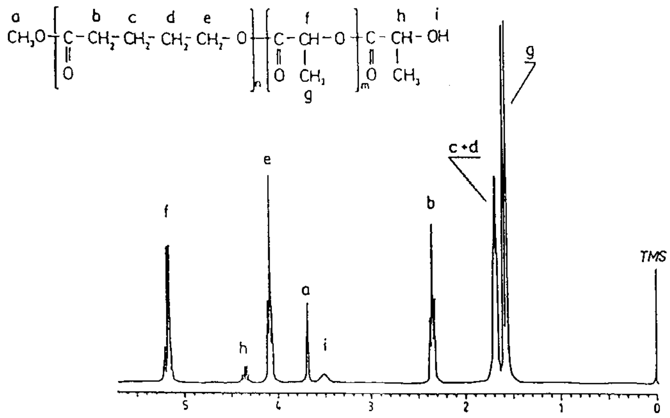

FIG. 5. ^{1}H-NMR (300 MHz) spectrum of poly(δ-valerolactone-*block*-L-lactide) prepared with potassium methoxide initiator (M_n = 3200, VPO; composition VL:LL = 55:45).

tions in THF at various ratios of δ-valerolactone prepolymer to L-lactide monomer are presented in Table 3.

The results in Table 3 indicate that poly-δ-valerolactone–poly-L-lactide block copolymers with the expected molecular weights were obtained with good yields, and the block copolymer compositions (i.e., content of δ-valerolactone and L-lactide segments) were close to the calculated values. Typical DSC traces for poly(δ-valerolactone-*block*-L-lactide) copolymers with different compositions are shown in Fig. 6. Two melting endotherms (Fig. 6, Curve b) are characteristic for block copolymers with a lactide content in the range between 43 and 62 mol%, which indicates that microphase separation of crystalline domains occurred in these poly(δ-valerolactone-*block*-L-lactide)s.

TABLE 3. Preparation of Block Copolymers of δ-Valerolactone (VL) and L-Lactide (LL) with Potassium Methoxide in THF at 20°C[a]

Sample no.	Mole ratio of monomers in reaction mixture, VL:LL	Yield in %	M_n of prepolymer[c]	Polymer composition (mole ratio of units), VL:LL	M_{ncalc}[b] of copolymer	M_{nGPC}[c] of copolymer	M_w/M_n[c] of copolymer
1	80:20	98	12,700	81:19	17,160	16,200	1.39
2	58:42	99	12,200	57:43	24,900	23,500	1.40
3	51:49	98	11,600	55:50	25,000	23,900	1.41
4	39:61	97	8,000	38:62	25,200	24,500	1.45
5	20:80	99	3,500	19:81	23,600	22,100	1.40

[a] The conversion of δ-valerolactone in the polymerization was higher than 99% after 5–10 minutes.

[b] Calculated for 100% conversion.

[c] Determined by GPC in THF.

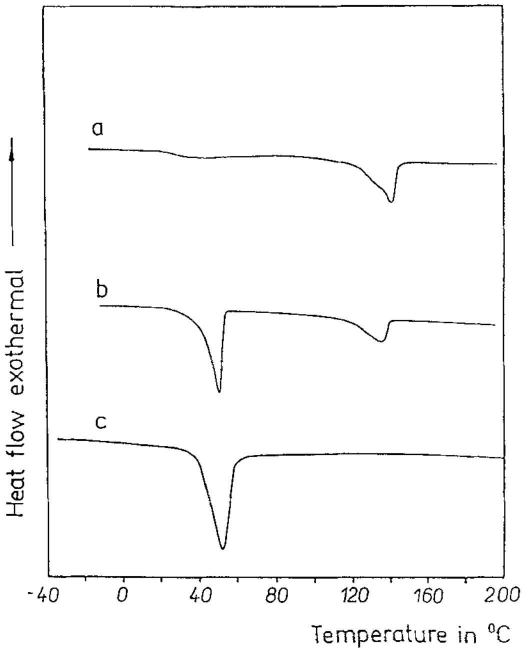

FIG. 6. Typical DSC curves for original samples of block copolymers (a) VL:LL = 19:81, (b) VL:LL = 57.43, and (c) VL:LL = 81:19.

Synthesis of Poly(L-Lactide-*block*-Oxyethylene-*block*-L-Lactide) via Anionic Polymerization

The low hydrophilicity of poly-L-lactides decreases their compatibility with soft tissues and lowers their biodegradability [9]. This problem may be overcome by introducing hydrophilic segments into the polylactide chain, and in the present studies oxyethylene-L-lactide triblock ABA copolymers were synthesized. Sodium salts of poly(ethylene glycol)s were employed as macroinitiators for the anionic polymerization of L-lactide in THF at room temperature for this purpose.

It was found that the polymerization reaction proceeded rapidly, and after addition of the macroinitiator, the lactide monomer was almost entirely consumed in a short time. The block structure of the product obtained was confirmed by GPC and also by selective extraction experiments [10].

The results of ^{1}H-NMR measurements show that the polymerization of L-lactide initiated by the sodium salts of poly(ethylene glycol)s as macroinitiator yielded ABA-type block copolymers (Fig. 7).

The presence of a $-CH(CH_3)OH$ end group in the poly(L-lactide-*block*-oxyethylene-*block*-L-lactide) indicates that, similarly to the L-lactide polymerization initiated with potassium methoxide [5], the reaction proceeds via acyl—oxygen bond cleavage and that alcoholate anions were responsible for propagation. The results of the block polymerizations are presented in Table 4.

The results of water absorption experiments presented in Fig. 8 indicate clearly that the equilibrium water content in the poly(L-lactide-*block*-oxyethylene-*block*-L-

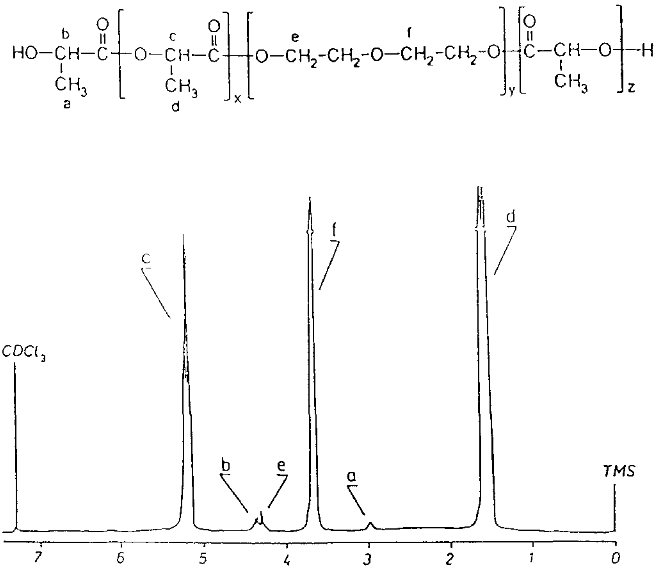

FIG. 7. ^{1}H-NMR (300 MHz) spectrum of poly(L-lactide-*block*-oxyethylene-*block*-L-lactide) prepared with sodium poly(ethylene glycol)ate initiator (M_n = 4800; composition EO:LA = 60:40).

TABLE 4. Anionic Polymerization of L-Lactide (LL) Initiated with Sodium Poly(Ethylene Glycol)ates (PEO) in THF at 20°C[a]

Sample no.	Mole ratio of EO to LL in the reaction mixture	Yield in %	Copolymer composition (mole ratio of units EO:LL)	Number-average molecular weight of block copolymer	
				M_{ncalc}[b]	M_n[c]
1	26:74	93	30:70	81,000	70,000
2	32:68	94	33:67	64,500	62,000
3	37:63	91	38:62	53,200	51,400
4	49:51	95	52:48	35,200	32,600
5	60:40	90	62:38	26,000	24,300

[a] M_n(VPO) of PEO used to obtain the macroinitiator was 8100. The polymerization time was equal to 5 minutes.

[b] Calculated for 100% conversion.

[c] Estimated from ^{1}H-NMR.

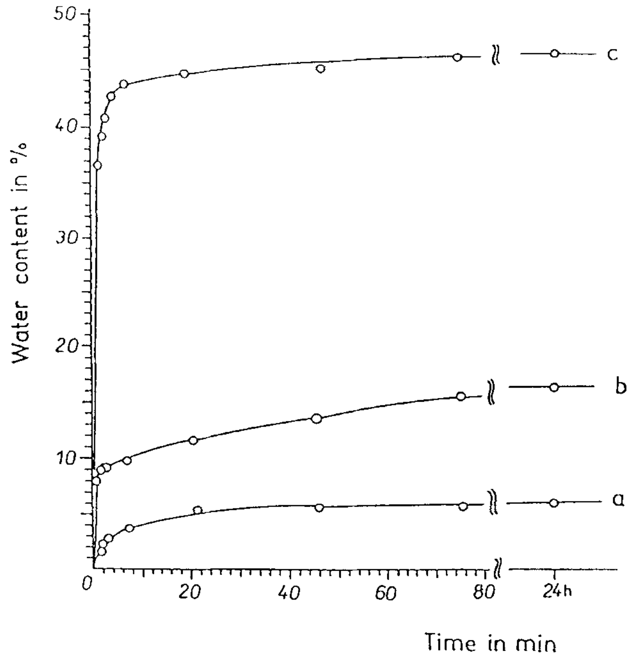

FIG. 8. Water absorption vs time curves for block polymers with compositions (a) EO:LA = 38:62, (b) EO:LA = 52:48, and (c) EO:LA = 70:30. For poly-L-lactide (M_n = 27,000), an equilibrium water content of 3% was determined.

lactide)s is considerably higher than that for poly(L-lactide), and the water content increased with increasing content of oxyethylene units in the block polymers obtained (Fig. 8).

The thermal properties of the block polymers obtained are presented in Table 5. The results in Table 5 indicate that some degree of crystallinity was present in the

TABLE 5. Thermal Properties of Poly(L-Lactide-*block*-Oxyethylene-*block*-L-Lactide)s[a]

Sample no.	Copolymer composition (mole ratio of units EO:LL)	M_n	T_g[b] in °C	T_m[b] in °C	ΔH_m[b] in J/g	ΔH_{cryst}[b] in J/g
1	30:70	70,000	20	153	38.3	30.1
2	33:67	62,000	29	151	32.8	25.3
3	38:62	52,400	18	145	31.2	23.0
4	52:48	32,600	9	137	18.6	18.6
5	62:38	24,300	−12	38	51.9	—

[a] Heating rate 10°C/min.

[b] T_g, T_m, ΔH_m, and ΔH_{cryst} were determined for original samples.

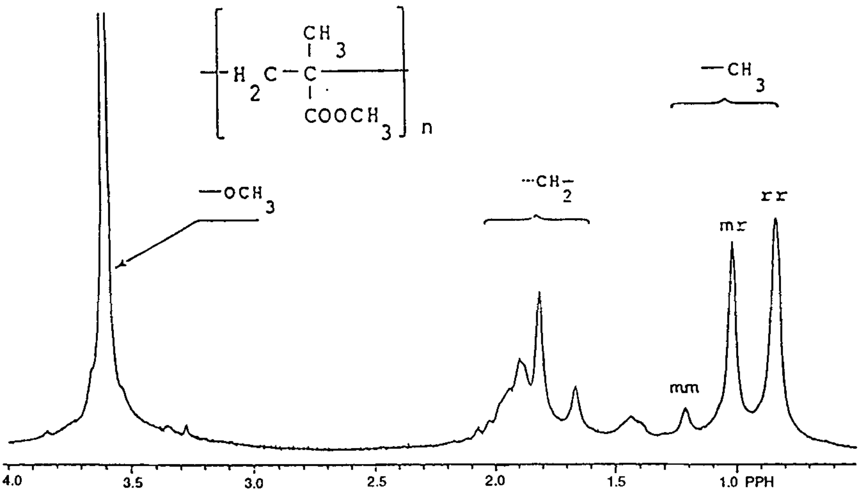

FIG. 9. ^{1}H-NMR spectrum of PMMA polymer prepared with supramolecular complex of sodium–potassium alloy as initiator in THF at 25°C.

block copolymers. The glass transition and the melting temperatures of the block copolymers depended on polymer composition and decreased when the oxyethylene unit content in the block copolymer was increased.

SYNTHESIS OF POLYMERS AND COPOLYMERS OF METHYL METHACRYLATE WITH ALKALI METAL SUPRAMOLECULAR COMPLEXES AS INITIATOR

Commercial poly(methyl methacrylate) is produced by radical polymerization, but it is also possible to synthesize stereoregular poly(methyl methacrylate)s. They are of better thermal stability than ordinary polymers obtained via radical

TABLE 6. Homopolymerization of MMA in THF Initiated by Na^-/K^+, 18-Crown-6 Complex at 25°C. Initiator Concentration 0.03 mol/L

Sample no.	Yield, %	$10^{-3} M_{n,exp}$	M_w/M_n	Microstructure i	h	s
1	100	18.0	1.3	8	37	55
2	100	36.0	1.6	9	36	55
3	100	37.7	2.5	10	37	53
4	100	33.6	2.2	9	39	52
5	100	37.7	2.5	10	37	53
6	100	66.1	2.6	9	38	53
7	98	106.0	3.2	8	38	54

TABLE 7. Properties of Block Polymers of MMA and δVL in THF Initiated by Na^-/K^+, 18-Crown-6 Complex at 25°C. Initiator Concentration 0.03 mol/L

Sample no.	Yield, %	$10^{-3} M_{n,exp}$	M_w/M_n	Polymer composition, % δVL[a]	T_g,[b] °C	T_m, °C	ΔH_m, J/g
1	85	33.5	2.4	14	115	51	3.8
2	85	34.0	2.3	48	–	62	43.6
3	87	36.5	2.1	68	–	54	47.8
4	91	24.3	2.5	83	–	63	61.6
5	93	30.2	2.4	91	–	60	66.1

[a] Estimated from ^{1}H-NMR.

[b] T_g for atactic PMMA = 105°C; T_g for syndiotactic PMMA = 125°C.

polymerization. In addition, coordinative and various anionic initiators [11–14] have been used to prepare stereoregular polymers in order to improve the thermal stability of methyl methacrylate polymers.

In our work, initiators based on solutions of modified alkali metal supramolecular complexes were employed. The first attempts to use alkali metal solutions as initiators for methyl methacrylate polymerization were made by a French group [15–17]. From the results of our previous work [18], and after some modifications

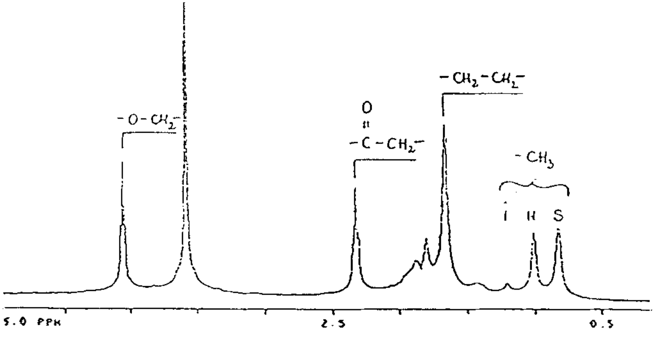

FIG. 10. ^{1}H-NMR spectrum of block polymer prepared with supramolecular complex of sodium-potassium alloy as initiator in THF at 25°C (M_n = 32,400; composition MMA: VL = 54:46).

were carried out, very effective catalysts were prepared which work perfectly even at room temperature.

The ^{1}H-NMR (300 MHz) spectrum of PMMA prepared with these initiators is shown (Fig. 9), and the properties of the resulting polymers are summarized in Table 6. A high content of syndiotactic triads has been observed in polymers exhibiting molecular weights M_n up to 100,000.

The copolymerization of methyl methacrylate with δ-valerolactone (δVL) initiated by "living" PMMA proceeds fast and produces block polymers exhibiting unimodal molecular weight distribution (Table 7). Results of selective extraction and ^{1}H-NMR spectra confirm the block structure of these polymers (Fig. 10), and the properties of the block polymers as obtained are summarized in the Table 7.

CONCLUSIONS

In the search for inexpensive methods of preparation of potentially biodegradable polymeric materials, simple initiator systems for cyclic monomers and methyl methacrylate, including alkali metal alkoxides with crown ethers as complexing agents and alkali metal supramolecular complexes, were investigated. The homo and block copolymers of β-butyrolactone, L-lactide, δ-valerolactone, and methyl methacrylate prepared with these initiators exhibited interesting physical properties and are expected to show biodegradability. Structure–property relationships for these materials were studied.

ACKNOWLEDGMENTS

The financial support from US-Polish M Skłodowska-Curie Joint Fund, Grant PAN/NSF-91-60, and from National State Committee for Scientific Research, Grant KBN 2 0867 9101, is acknowledged.

REFERENCES

[1] R. A. Goss, Y. Zhang, G. Konrad, and R. W. Lenz, *Macromolecules, 21*, 2657 (1988).

[2] J. E. Kemnitzer, S. P. McCarthy, and A. Gross, *Ibid., 26*, 1221 (1993).

[3] P. Kurcok, Z. Jedliński, and M. Kowalczuk, *Ibid., 25*, 2017 (1992).

[4] H. R. Kricheldorf and I. Kreiser-Saunders, *Makromol. Chem., 191*, 1057 (1990).

[5] Z. Jedliński, W. Wałach, P. Kurcok, and G. Adamus, *Ibid., 192*, 2051 (1991).

[6] C. X. Song and X. D. Feng, *Macromolecules, 17*, 2764 (1984).

[7] K. Ito, M. Tomida, and Y. Yamashita, *Polym. Bull. (Berlin), 8*, 569 (1979).

[8] P. Kurcok, J. Penczek, J. Franek, and Z. Jedliński, *Macromolecules, 25*, 2285 (1992).

[9] R. A. Miller, J. M. Brady, and D. E. Cutright, *J. Biomed. Mater. Res., 11*, 711 (1977).

[10] Z. Jedliński, P. Kurcok, W. Wałach, H. Janeczek, and I. Radecka, *Makromol. Chem.*, *194*, 1681 (1993).

[11] S. K. Varshney, R. Jerome, P. Bayard, C. Jacobs, R. Fayt, and P. Teyssie, *Macromolecules, 25*, 4457 (1992).

[12] M. V. Beylen, S. Bywater, G. Smets, M. Szwarc, and D. J. Worsfold, *Adv. Polym. Sci.*, *86*, 87 (1988).

[13] B. Masar, P. Vlcek, J. Kriz, and J. Kovarova, *Macromol. Chem. Phys.*, *195*, 289 (1994).

[14] M. Kuroki, S. Nashimoto, T. Aida, and S. Inoue, *Macromolecules, 21*, 3114 (1988).

[15] S. Alev, F. Schué, and B. Kaempf, *J. Polym. Sci., Polym. Lett. Ed.*, *13*, 397 (1975).

[16] S. Alev, A. Collet, M. Viguier, and F. Schué, *J. Polym. Sci., Polym. Chem. Ed.*, *18*, 1155 (1980).

[17] M. Viguier, M. Abadie, B. Kaempf, and F. Schué, *Eur. Polym. J.*, *13*, 213 (1977).

[18] Z. Jedliński, A. Stolarzewicz, Z. Grobelny, and M. Szwarc, *J. Phys. Chem.*, *88*, 6094 (1984).