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Synthesis and thermal properties of poly(ethylene glycol)–poly(ϵ-caprolactone) copolymers

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Three different types of polyester–polyether copolymers were synthesized by PEG initiated ring-opening polymerization of ϵ-caprolactone: an A–B and an A–B–A block copolymer and an $(A)_2$–B star copolymer, where A is a poly(ϵ-caprolactone) (PCL) and B is a poly(ethylene glycol) (PEG) block. The monomer to initiator ratio was varied to obtain copolymers with different PCL block length and weight fraction ranging from 68–85 wt%. These PCL–PEG copolymers were characterized by means of g.p.c., n.m.r., d.s.c. and WAXD.

In all types of copolymer the PCL constituent crystallizes first when cooling from the molten state. This leads to significant undercooling and imperfect crystallization of the PEG block. The mutual influence between PCL and PEG constituents is significantly stronger in the A–B–A block copolymers, having a central PEG block, and in the $(A)_2$–B star copolymers.

The effect of the PCL/PEG ratio on the melting and crystallization behaviour of the copolymers was investigated. The results obtained demonstrate that the thermal properties and morphology are affected significantly by the chain length of the PCL and PEG constituents in the copolymers and by the type of copolymers (sequence of the different blocks). © 1997 Elsevier Science Ltd. All rights reserved.

(Keywords: poly(ethylene glycol)/poly(ϵ-caprolactone) copolymers; melting)

INTRODUCTION

Biodegradable polyesters have received considerable attention over the past two decades. Polymers prepared from glycolide, lactide or ϵ-caprolactone have been used in medical implants to ensure a temporary mechanical or therapeutic function. It has been shown that by appropriate selection of the comonomers a wide variety of materials with a broad range of properties can be obtained[1–5]. More recently, poly(ethylene glycol)–polyester block copolymers have been prepared using a monohydroxy or α,ω-dihydroxy poly(ethylene glycol) as initiator for the polymerization of lactone monomers[6–11]. Such amphiphilic block copolymers exhibit different properties, i.e. permeability, degradability, which may lead to new application possibilities.

Until now, the number of papers dedicated to the morphology and the crystallization (melting) properties of such block copolymers has been limited[12–16]. It was reported before [13–16] that the crystallization properties of an A–B–A type poly(ϵ-caprolactone)–poly(ethylene glycol) triblock copolymer depend on the length of each block and the crystallization temperature. Gan *et al.*[8] studied the isothermal crystallization and melting behaviour of the A–B type poly(ϵ-caprolactone)–poly(ethylene glycol) diblock copolymers. It was established that only the PCL block is crystallizable when the weight fraction of the PEG block is below 20%. Until now no comparative study of crystallization and melting behaviour of A–B and A–B–A type copolymers was made.

As part of an ongoing programme on biodegradable polymers designed for biomedical applications we have prepared three types of poly(ϵ-caprolactone)–poly(ethylene glycol) copolymers of different architecture having comparable total block length of poly(ϵ-caprolactone) (PCL) and poly(ethylene glycol) (PEG): (1) an A–B diblock copolymer; (2) an A–B–A triblock copolymer; and (3) an $(A)_2$–B star copolymer, with A = poly(ϵ-caprolactone) and B = poly(ethylene glycol) (*Figure 1*).

In this paper we briefly describe the synthesis of such copolymers and discuss in more detail the crystallization properties and melting behaviour of the different copolymer systems.

EXPERIMENTAL

Materials

Poly(ethylene glycol) with a molecular weight of 4000 (PEG4000) and monomethoxy-poly(ethylene glycol) with a molecular weight of 5000 (MPEG5000) were obtained from Fluka. All PEG-macroinitiators were dried by an azeotropic distillation in toluene.

ϵ-Caprolactone (from Acros) was purified by vacuum distillation over CaH_2. The fraction collected at 96–98°C (5 mm Hg) was used in all polymerization.

Stannous(II) octoate (SnOct) (from Sigma Corp.) was used as received. Methylene chloride and pyridine were

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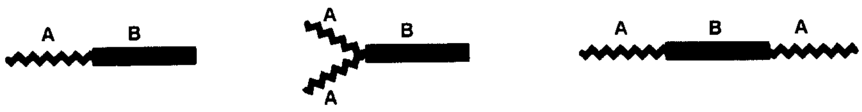

A-B diblock copolymers (A)$_2$-B star copolymers A-B-A triblock copolymers

Figure 1 Different types of poly-ε-caprolactone-poly(ethylene glycol) copolymers

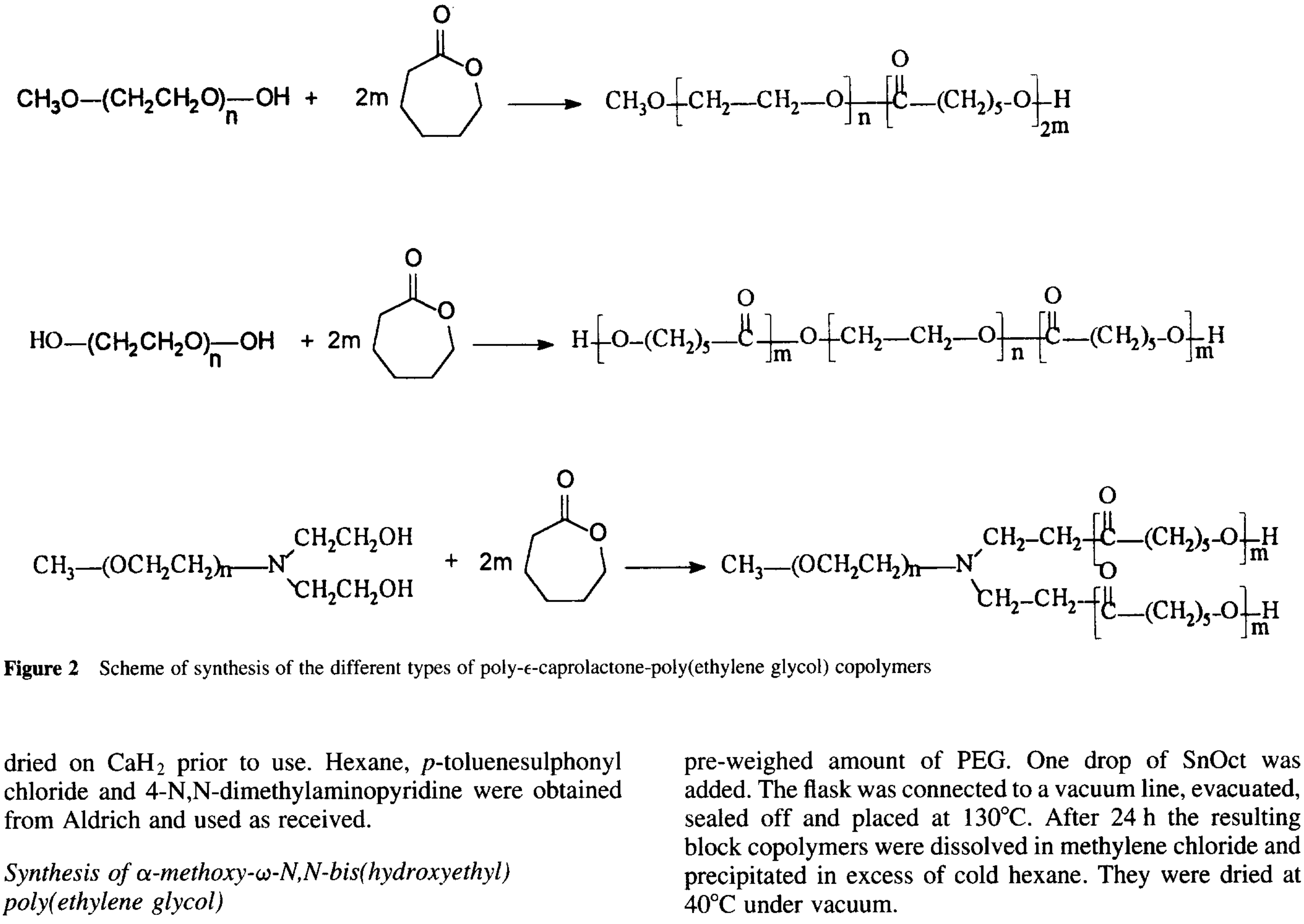

Figure 2 Scheme of synthesis of the different types of poly-ε-caprolactone-poly(ethylene glycol) copolymers

dried on CaH_2 prior to use. Hexane, *p*-toluenesulphonyl chloride and 4-N,N-dimethylaminopyridine were obtained from Aldrich and used as received.

Synthesis of α-methoxy-ω-N,N-bis(hydroxyethyl) poly(ethylene glycol)

α-Methoxy-ω-N,N-bis(hydroxyethyl) poly(ethylene glycol) was synthesized as follows: 15 g of MPEG5000 (3 mmol) was dissolved in a mixture of methylene chloride and pyridine (20 ml, 1:1). 15 mg 4-N,N-dimethylaminopyridine (DMAP) was added to the solution which was then cooled to 0°C. *p*-Toluenesulphonyl chloride (tosylchloride) (16 mmol, 3 g) dissolved in methylene chloride was added dropwise. This reaction mixture was left overnight on a ice bath. Then 30 ml HCl (36%), 50 g ice and 30 ml methylene chloride were added. The organic layer was washed respectively with cold HCl (3 N), NaCl and $NaHCO_3$. The product was then dried over $MgSO_4$. The resulting α-methyl-ω-tosyl-PEG was added to an excess of diethanolamine (30 ml) and stirred for 4 h at 90°C. The mixture was then cooled to room temperature by adding 30 ml of water. The water phase was extracted with methylene chloride and dried over $MgSO_4$. The resulting polymer was dissolved in CH_2Cl_2 and purified by precipitation in diethylether.

Polymerisation procedure

The reaction mixtures were prepared by introducing under a nitrogen atmosphere a known volume of caprolactone monomer into a silanised flask containing a pre-weighed amount of PEG. One drop of SnOct was added. The flask was connected to a vacuum line, evacuated, sealed off and placed at 130°C. After 24 h the resulting block copolymers were dissolved in methylene chloride and precipitated in excess of cold hexane. They were dried at 40°C under vacuum.

Characterisation

The copolymers were characterized by gel permeation chromatography (g.p.c.) (Millipore-Waters GPC instrument) with chloroform as an eluent and a Plgel 5μ Mixed-D column; PEG-standards were used for calibration.

^{1}H-NMR spectra of the copolymers in deuterated chloroform solutions were recorded using a Brucker 360 MHz spectrometer with tetramethylsilane as internal standard. The molecular weight values and PCL/PEG ratios of the different type of copolymers were evaluated from ^{1}H-NMR spectra and compared with the corresponding values obtained by g.p.c.

Differential scanning calorimetry was carried out using a DSC-7 (Perkin Elmer) under a dynamic atmosphere of N_2.

A Philips model PW-1820 X-ray diffractometer employing Ni-filtered Cu, K_α radiation was used for obtaining wide angle X-ray diffraction (WAXD) patterns of the polymers at room temperature. The scan rate was 0.01° 2θ/s.

RESULTS AND DISCUSSION

Block copolymers are easily prepared by adding ε-caprolactone to poly(ethylene glycol) in the presence

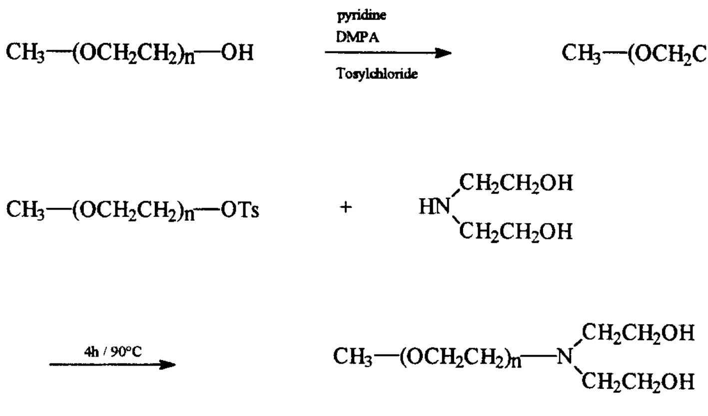

Figure 3 Scheme of synthesis of α-methoxy-ω-N,N-bis(hydroxyethyl) poly(ethylene glycol)

Table 1 Composition and molecular weight of PCL–PEG block copolymers (A = PCL; B = PEG)

No	Copolymer	Molecular weight, Mn (g.p.c.)	Molecular weight, Mn (n.m.r.)	Mn of PCL and PEO blocks (GPC)	PCL/PEG, wt% (GPC)	PCL/PEG, wt% (NMR)
1.	A–B	25553	20918	PCL$_{20500}$–MeO–PEG$_{5000}$	80/20	76/24
2.	(A)$_2$–B	16856	19510	(CH$_2$CH$_2$–PCL$_{6000}$)$_2$N–MeO–PEG$_{5000}$	70/30	74/26
3.	(A)$_2$–B	23350	23947	(CH$_2$CH$_2$–PCL$_{9000}$)$_2$N–MeO–PEG$_{5000}$	78/22	79/21
4.	A–B–A	12554	12070	PCL$_{4300}$–PEG$_{4000}$–PCL$_{4300}$	68/32	67/33
5.	A–B–A	22153	21620	PCL$_{9000}$–PEG$_{4000}$–PCL$_{9000}$	82/18	81/19
6.	A–B–A	26072	21440	PCL$_{11000}$–PEG$_{4000}$–PCL$_{11000}$	85/15	81/19

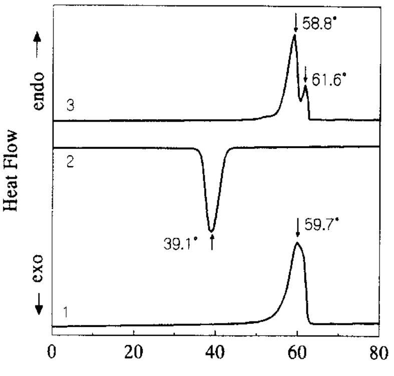

Figure 4 D.s.c. curves of PEG (MW = 4000); 1-1st heating; 2-cooling; 3-2nd heating. Heating and cooling rate 10°C/min

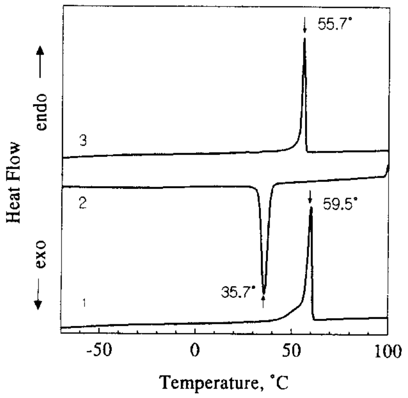

Figure 5 D.s.c. curves of PCL (MW = 8000); 1-1st heating; 2-cooling; 3-2nd heating. Heating and cooling rate 10°C/min

of stannous octoate as catalyst. The polymerization is carried out in bulk at 130°C for 24 h. Starting from different types of PEG-initiators, it is possible to obtain diblock, triblock or star copolymers (*Figure 2*). A monomethoxy-PEG is used as an initiator to obtain a diblock copolymer (A–B type). Triblock copolymers (A–B–A type) are formed by ring opening polymerization of ε-caprolactone with bifunctional HO-PEG-OH. A star (A)$_2$–B type copolymer is obtained with α-methoxy-ω-N,N-bis(hydroxyethyl) PEG. This type of initiator is synthesized by conversion of α-methyl-ω-hydroxy-PEG into α-methyl-ω-tosyl-PEG which is then allowed to react with an excess of diethanolamine (*Figure 3*). The concentration of ε-caprolactone monomer was varied to obtain copolymers with different PCL block length. GPC analysis confirmed quantitative reaction of PEG. The PEG weight fraction in copolymers is varied from 15 to 32%. A good agreement between the PCL/PEG weight ratio as calculated from g.p.c. and n.m.r. analysis is observed in *Table 1*.

The melting and crystallization behaviour of PCL–PEG copolymers with the different molecular architecture is investigated by d.s.c. PEG and PCL homopolymers are also included for comparison. *Figures 4–7* show the characteristic d.s.c. curves of the homopolymers and the PCL–PEG copolymers. All samples are first heated above the melting temperature, then allowed to crystallize by cooling at a rate of 10°C/min and finally heated at 10°C/min to 100°C.

PEG and PCL homopolymers

Figure 4 shows the d.s.c. curves for PEG with molecular weight Mn = 4000. This polymer has a monomodal peak of first melting (T_m = 59.7°C) and crystallization (T_c = 39.1°C). The endotherm of second melting is bimodal with peak maxima at 58.8°C and 61.6°C. Different endothermic peaks of PEG can be attributed to the melting of PEG lamellae with a different fold number[17].

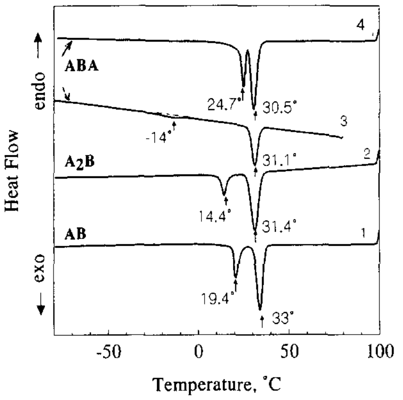

Figure 6 DSC curves at cooling of PCL-PEG copolymers, 10°C/min: 1-A-B (PCL-PEG, MW = 20 500-5000); 2-(A)$_2$-B [(PCL)$_2$-PEG, MW = (9000)$_2$-5000]; 3 and 4-A-B-A [PCL-PEG-PCL, MW = 9000-4000-9000 (curve 3) and 4300-4000-4300 (curve 4)]

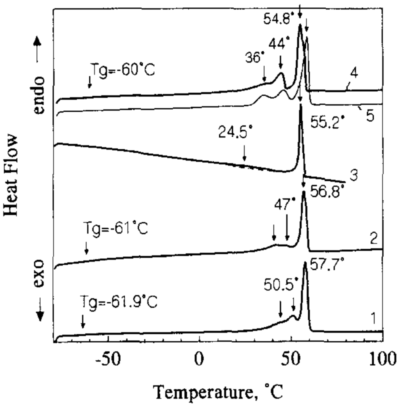

Figure 7 D.s.c. curves at second heating (curves 1-4) and first heating (curve 5) of PCL-PEG copolymers, 10°C/min: 1-AB (PCL-PEG, MW = 20 500-5000); 2-(A)$_2$-B [(PCL)$_2$-PEG, MW = (9000)$_2$-5000]; 3-5-A-B-A [PCL-PEG-PCL, MW = 9000-4000-9000 (curve 3) and 4300-4000-4300 (curve 4, 5)]

The d.s.c. curves of PCL with molecular weight Mn = 8000 show single melting and crystallization peaks ($T_{\mathrm{m(1st\ heating)}} = 59.5$°C, $T_{\mathrm{m(2nd\ heating)}} = 55.7$°C and $T_c = 35.7$°C) (*Figure 5*).

The difference between the second melting and the crystallization temperatures (which we define as an apparent undercooling $\Delta T = T_m - T_c$), under the conditions of the d.s.c. experiment, is about 20°C for both homopolymers. It must be noted that both polymers have a comparable melting temperature (about 60°C) and glass transition temperature (about −61°C).

PEG–PCL block copolymers

The d.s.c. curves obtained at cooling the A–B, A–B–A block copolymers and the star (A)$_2$–B block copolymer are presented in *Figure 6*. They display two distinct exotherms that correspond to the crystallization of each constituent block. Two approaches are used to determine which of the constituent blocks, PCL or PEG, crystallizes first at cooling from the melt: (1) calculation of the crystallinity α_c from the enthalpy of crystallization with respect to the PCL and PEG content; (2) WAXD analysis. The results of the α_c calculation and WAXD (the WAXD results will be discussed in more detail below) show that the first exothermic peak ($T_c = 30$–33°C) can be attributed to the crystallization of the PCL blocks. The second exotherm (range − 14° to 25°C) corresponds to the crystallization of the PEG constituent. This data demonstrates that microphase separation (segregation) take place in all three types of copolymers. In spite of the fact that the PCL and PEG constituents are covalently coupled, they are both able to crystallize and form two separate micro domains (crystal–amorphous phases).

Figure 6 allows comparison of the d.s.c. curves at cooling of the A–B (curve 1), (A)$_2$–B (curve 2) and A–B–A (curve 3) copolymers which have approximately the same PCL/PEG ratio. The crystallization temperature T_c of the PCL block (first exotherm) decreases with decreasing molecular weight of the PCL block as expected. The T_c of the PEG block (second exotherm) depends on the type of copolymer and decreases in the sequence A–B > (A)$_2$–B > A–B–A. Curve 4 in *Figure 6* represents the crystallization of an A–B–A type block copolymer with the same length of the PEG block (Mn = 4000) as in curve 3, but with shorter PCL block (Mn = 4300). In this case, the PEG crystallization temperature is significantly higher and more pronounced in comparison with the PEG exotherm in curve 3.

The heating curves (*Figure 7*) show more than two endotherms. The higher temperature endotherm from 55–58°C can be attributed to melting of the PCL crystal phase. The low temperature peaks in the range of 25–50°C correspond to the melting of the PEG crystal phase. The bimodal melting peak observed for PEG is again most likely due to the existence of folded-chain lamellae with different fold numbers [17].

The crystallization and melting temperature of the PCL block in PCL–PEG copolymers is similar to that of PCL homopolymer. The PEG crystallization and melting temperature in A–B–A block copolymers and (A)$_2$–B type copolymers is considerably lower than those of the PEG homopolymers. The shift of T_c and T_m of PEG block is more pronounced when the PCL block length increases (*Figures 6 and 7*, curves 3 and 4).

Therefore, the PCL constituent which crystallizes first disturbs the crystallization of the PEG block. This mutual influence between PCL and PEG chains that are covalently linked is stronger in the A–B–A triblock and (A)$_2$–B star copolymers compared to the A–B diblock copolymers. In the latter case the freedom (mobility) of the terminal PEG block is higher and consequently the restriction of crystallization is smaller (*Figures 6 and 7*, curves 1).

The apparent undercooling ΔT of the PCL blocks in all three types of copolymers is about 25°C which is similar to that of the PCL homopolymer. In all copolymers studied, the apparent undercooling ΔT of the PEG constituent is significantly higher than that of the PEG homopolymer. This explains why the DSC curves of cooling display more distinct exotherms of crystallization than the endotherms of melting.

The apparent undercooling ΔT of the PEG constituent in the different types of copolymers with similar weight content of ethylene oxide and caprolactone monomeric unit increases from 30°C to 38°C in the following order: A–B → (A)$_2$–B → A–B–A (*Figures 6 and 7*, curves 1–3). The PEG crystallization and melting temperature decreases in the same order.

The crystallinity of the PCL and PEG microdomain phases is calculated from the d.s.c. curves. The results are presented in *Table 2*. It can seen that the crystallinity α_c of the PCL constituent in the same type of copolymers slightly decreases when the molecular weight of PCL is

Table 2 D.s.c. crystallinity (α_c) of PEG–PCL block copolymers

No	Copolymer		1st heatingα_c (%)		Coolingα_c (%)		2nd heatingα_c (%)	
	A = PCL; B = PEG	PCL/PEG(wt%)	PCL	PEG	PCL	PEG	PCL	PEG
1	A-B 20500-5000	80/20	61.8	87.8	45	52.6	50	51
2	$(A)_2$-B $(6000)_2$-5000	70/30	63.4	84.6	52.7	43.4	50	63
3	$(A)_2$-B $(9000)_2$-5000	78/22	53.4	80.2	46.5	33	46.5	58
4	A-B-A 4300-4000-4300	68/32	62	63.6	50	51.3	49	64.3
5	A-B-A 9000-4000-9000	82/18	56	—	49	15.3	45.4	19.5
6	PEG-4000	/100	—	95	—	86.4	—	90
7	PCL-4000	100/	71	—	56	—	58	—
8	PCL-8000	100/	73	—	52	—	51	—
9	PCL-30000	100/	71	—	50	—	48	—

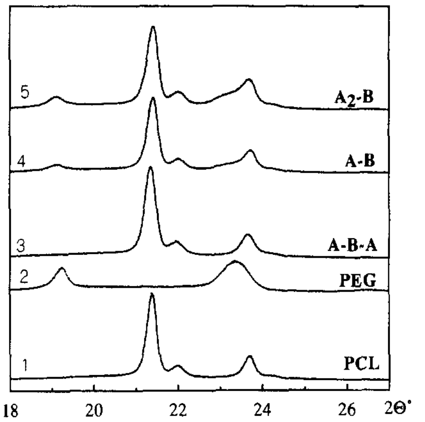

Figure 8 WAXD of PCL (curve 1), PEG (curve 2) and PCL-PEG copolymers: A-B-A PCL-PEG-PCL, MW = 9000-4000-9000 (curve 3); A-B (PCL-PEG, MW = 20500-5000) (curve 4); $(A)_2$-B [$(PCL)_2$-PEG, MW = $(9000)_2$-5000]. Room temperature

increased. However the crystallinity of the PEG constituent in the PCL–PEG copolymers is much lower than the crystallinity of the PEG homopolymer. For the A–B–A type copolymers it can be seen that α_c for PEG decreases significantly with increasing length of the PCL block.

In order to support the conclusions derived from d.s.c., WAXD studies of the A–B, A–B–A and $(A)_2$–B copolymer were carried out. All samples were obtained by compressing moulding and underwent crystallization by cooling.

Figure 8 presents WAXD results at room temperature for the different types of PCL–PEG block copolymers with similar weight fraction of the PCL and PEG constituents. The PEG block concentration was varied from 18–22 wt%. In the A–B–A type block copolymer, with a PEG constituent as a central block, only the crystal patterns typical for the PCL crystal phase are observed (*Figure 8*, curve 3). According to the d.s.c. heating curve (*Figure 7*, curve 3) the PEG constituent is in the molten state at room temperature. It was observed that the crystal patterns corresponding to PEG crystallites appears when the concentration of the PEG constituent, in an A–B–A type copolymer, increases to 32 wt% (data not shown).

In the A–B and $(A)_2$–B copolymers both PCL and PEG blocks can crystallize and form separate crystal phases. Such copolymers show in WAXD a superposition of the PEG and PCL crystal patterns (*Figure 8*, curves 1, 2, 4 and 5).

The results from WAXD are in a good agreement with the d.s.c. results and confirm the hypothesis of lower crystallization ability of the PEG constituent in A–B–A type block copolymers with the studied composition.

CONCLUSIONS

Three different types of PCL–PEG copolymers [A–B and A–B–A block copolymers and $(A)_2$_B star copolymer] are synthesized by PEG-initiated ring-opening polymerization of ε-caprolactone. The architecture of the copolymers is controlled by the chemical structure of the PEG macroinitiators. The concentration of the PCL block constituent is varied from 68–85 wt%.

It is established that at constant PCL/PEG ratio, the block sequence in the PCL–PEG copolymers determines the crystallization and melting behaviour. In the three different types of PCL–PEG copolymers, included in this study, the PCL constituent crystallizes first and fixes the total structure leading to imperfect crystallization of the PEG constituent.

The apparent undercooling at crystallization of the PEG segment in the copolymers with comparable PCL/PEG ratio increases in the following order: A–B → $(A)_2$–B → A–B–A. The crystallinity of the PEG phase in the copolymers decreases in the same sequence.

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REFERENCES

1. Engelbert, I. and Kohn, J., *Biomaterials*, 1991, **12**, 292.
2. Lewis, D. H., *Controlled Release of Bioactive Agents from Lactide/Glycolide*, in *Biodegradable Polymers as Drug Delivery Systems*, ed. M. Chasin and R. Langer, New York, 1990, p. 1.
3. Kricheldorf, H. R. and Kreiser-Saunders, I., *Macromol. Symp.*, 1996, **103**, 85.
4. Pitt, C. G., *Poly(ε-Caprolactone) and its Copolymers*, in *Biodegradable Polymers as Drug Delivery Systems*, ed. M. Chasin and R. Langer, New York, 1990, p. 71.
5. Holland, S. J., Tighe, B. J. and Gould, P. L., *J. Contr. Rel.*, 1986, **4**, 155.
6. Rashkov, Il. I., Espartero, J. L., Manolova, N. and Vert, M., *Macromolecules*, 1996, **29**, 57.
7. Cerrai, P., Guerra, G. D., Lelli, L. and Tricoli, M., *J. Mat. Sci.: Mat. in Med.*, 1994, **5**, 33.
8. Gan, Z. H., Jiang, B. Z. and Zhang, J., *J. Appl. Polym. Sci.*, 1996, **59**(6), 961.
9. Youxin, L. and Kissel, T., *J. Contr. Rel.*, 1993, **27**, 247.
10. Jedlinski, Z., Kurcok, P., Walach, W., Janeczek, H. and Radecka, I., *Makromol. Chem.*, 1993, **194**, 1681.

11. Kricheldorf, H. R. and Meier-Haack, J., *Makromol. Chem.*, 1993, **194**, 715.
12. Perret, R. and Skoulios, A., *Die Makromolekuare Chemie*, 1972, **156**, 143.
13. Perret, R. and Skoulios, A., *Die Makromolekuare Chemie*, 1972, **162**, 163.
14. Perret, R. and Skoulios, A., *Die Makromolekuare Chemie*, 1972, **162**, 147.
15. Cerrai, P., Tricoli, M. and Andruzzi, F., *Polymer*, 1989, **30**, 338.
16. Nojima, S., Ono, M. and Ashida, T., *Polymer Journal*, 1992, **24**(11), 1271.
17. Wunderlich, B., *Macromolecular Physics, Crystal Nucleation, Growth, Annealing*, Vol. 2, Academic Press, New York, 1976, p. 218.