Macromolecules **1996,** *29,* 804−806

Ring-Opening Copolymerization of (*R*)-*β*-Butyrolactone with Cyclic Carbonates: New Biodegradable Poly(ester carbonate)s

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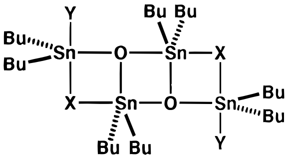
Received September 8, 1995
Revised Manuscript Received November 16, 1995

Introduction. A wide variety of different types of microorganisms are known to produce poly[(*R*)-3-hydroxyalkanoate]s (PHAs) as intracellular energy and carbon storage materials.[1] The PHAs produced by a fermentation process are limited to only a few copolyesters such as P[(*R*)-3-hydroxybutyrate-*co*-(*R*)-3HA] and P[(*R*)-3-hydroxybutyrante-*co*-4-hydroxybutyrate], since no microorganism can synthesize PHAs which contain 5-, 6-, or more hydroxy-substituted alkanoate units.

We reported on the ring-opening copolymerization of (*R*)-*β*-butyrolactone ((*R*)-*β*-BL) with several lactones using distannoxane complexes (**1**) as new catalysts to obtain a new series of biodegradable PHAs[2−6] which are difficult to obtain by a fermentation method. Further, we reported on the preparation of a biodegradable poly(ester ether) by the ring-opening copolymerization of (*R*)-*β*-BL and (*R*)-3-methyl-4-oxa-6-hexanolide.[7]



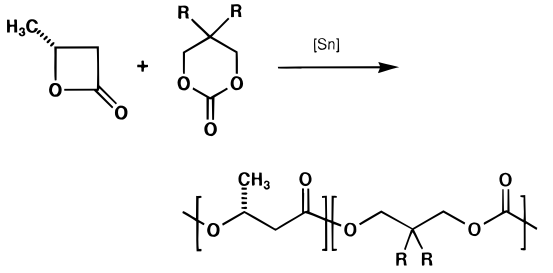
1a : X= OEt, Y= Cl
1b : X= OH, Y= NCS
1c : X= OH, Y= Cl
1d : X= Cl, Y= Cl

1

On the other hand, ring-opening polymerization of cyclic carbonates and copolymerization of cyclic carbonates with other monomers are known.[8] For example, since polyglycolide was stiff and relatively inflexible, poly(glycolide-*co*-trimethylene carbonate) was developed by copolymerization of glycolide with trimethylene carbonate as flexible, strong, and absorbable monofilament sutures.[8h] However, it has not been reported that copolymers of (*R*)-*β*-BL with cyclic carbonates should be more flexible than bacterial poly(3-hydroxybutyrate) (PHB).

Our interests are in the scope and limitation of the chemical synthesis of novel biodegradable PHAs. We have tried ring-opening copolymerization of (*R*)-*β*-BL with cyclic carbonates (trimethylene carbonate (TMC) and 2,2-dimethyltrimethylene carbonate (DMC)) to obtain a new series of polymers containing (*R*)-3-hydroxybutyrate units. In this paper we report on the synthesis of poly(ester carbonate)s and their biodegradability (eq 1).

Experimental Section. (*R*)-*β*-Butyrolactone[9] ((*R*)-*β*-BL, 92% ee) was prepared using the literature method, dried over CaH_2, and distilled under reduced pressure. Distannoxanes **1a**,[4,10] **1b**,[11] **1c**,[10] and **1d**[10] were prepared using literature methods and dried in vacuo at 80 °C for 20 h. Cyclic carbonates were prepared using a literature method[8a] and recrystallized from dry ethyl acetate. P[(*R*)-3HB] was obtained by the ring-opening polymerization of (*R*)-*β*-BL.[2] Bacterial P(3-hydroxybutyrate-*co*-11% 3-hydroxyvalerate) (P(3HB-*co*-11% 3HV), M_n 246 000, $M_w/M_n = 2.1$) was purchased from Aldrich Chemical Co. Molecular weights of the polymers were determined by GPC using a polystyrene calibration. Chloroform was used as the eluent at a flow rate of 1.0 mL/min. ^1H NMR spectra were recorded on a Bruker AM-400 spectrometer at 400 MHz. ^1H NMR chemical shifts in parts per million (ppm) are reported downfield from 0.00 ppm using tetramethylsilane (TMS) as an internal reference. The parameters for the polymer spectra are as follows: ca. 1% wt/wt polymer in $CDCl_3$, temperature 300 K, pulse width 45°, 32K data points, relaxation delay 2.5 s, and 8−16 transients. Differential scanning calorimetric (DSC) studies of polymers were carried out on a Shimadzu thermal analysis system in a temperature range of −80 to +200 °C at heating and cooling rates of 10 °C/min. The melting temperature (T_m) was taken as a peak temperature of the melting endotherm (first run). The glass transition temperature (T_g) was taken as the inflection point of a specific heat increment at the glass transition (second run).



(1)

P[(*R*)-3HB-*co*-carbonate]
2a-2f: R= H, **4a-4e**: R= CH_3

Ring-Opening Copolymerization. A mixture of (*R*)-*β*-BL (3.10 g, 36.0 mmol), trimethylene carbonate (TMC) (0.41 g, 4.0 mmol), and 1-ethoxy-3-chlorotetrabutyldistannoxane (**1a**) (11.2 mg, 10^{-2} mmol) was heated in a 20-mL Schlenk tube at 80 °C for 18 h. The resulting mixture was dissolved in chloroform and then added to a mixture of diethyl ether and hexane (the volume ratio being 1:3) to afford a white solid of P[(*R*)-3HB-*co*-TMC]; yield 2.98 g (85%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.18−1.40 (m, 3H, CH_3 for the 3HB unit), 1.95−2.08 (m, 2H, $-CH_2-\mathbf{CH_2}-CH_2-$ for the trimethylene glycol unit), 2.40−2.75 (m, 2H, CH_2 for the 3HB unit), 4.12−4.28 (m, 4H, $-\mathbf{CH_2}-CH_2-\mathbf{CH_2}-$ for the trimethylene glycol unit), 5.06−5.32 (m, 1H, CH for the 3HB unit). Other reactions were carried out in a similar manner.[12]

Biodegradation Test. Biodegradation tests of P(3HB-*co*-11% 3HV) and poly(ester carbonate) films were carried out at 25 °C in a 500 ppm activated sludge (pH 7.2).[13] The standard activated sludge was purchased from the Chemicals Inspection and Testing Institute, Japan. P(3HB-*co*-11% 3HV), P(TMC), and poly(ester carbonate) films were prepared by solvent-casting techniques from chloroform solutions of the polymers using glass Petri dishes as casting surfaces. The polymer films (initial weights, 20.1−41.6 mg; initial film dimensions, 10 × 10 mm^2 and 0.17−0.30 mm thick) were placed in 100-mL bottles. The reaction was started by the addition of 50 mL of an aqueous solution of the activated sludge, and then the mixture was incubated at 25 ± 0.1 °C with shaking for 4 weeks. Samples were collected once a week, washed with water, and dried to constant weight in vacuo.

Results and Discussion. A new series of poly(ester carbonate)s (P[(*R*)-3HB-*co*-TMC], **2**; P(3HB-*co*-TMC), **3**; and P[(*R*)-3HB-*co*-DMC], **4**) was obtained in the pres-

0024-9297/96/2229-0804$12.00/0

Table 1. Polymerization of (*R*)-β-BL with Cyclic Carbonates[a]

entry	cat.	monomer (molar ratio of feed)	polymer (obsd molar ratio)[b]	T_m, °C	T_g, °C	mol wt[c]		yield, %
						M_w	M_n	
1	**1a**	(*R*)-β-BL	P(3HB)[d]	163	5.3	424 000	178 000	99
2	**1a**	(*R*)-β-BL/TMC (90/10)	**2a** (90/10)	126	0.0	210 000	110 000	85
3[f]	**1b**	(90/10)	**2b** (89/11)	119	−0.1	126 000	50 000	89
4	**1c**	(90/10)	**2c** (90/10)	133	−0.1	155 000	72 000	96
5	**1d**	(90/10)	**2d** (94/6)	133	−1.2	165 000	73 000	85
6	**1a**	(50/50)	**2e** (50/50)	n.d.[e]	−9.1	130 000	72 000	98
7	**1a**	(20/80)	**2f** (21/79)	n.d.[e]	−15.8	150 000	78 000	98
8	**1a**	β-BL/TMC (90/10)	**3** (94/6)	59	2.3	240 000	130 000	87
9[f]	**1a**	(*R*)-β-BL/DMC (95/5)	**4a** (96/4)	138	1.5	204 000	138 000	89
10[f]	**1a**	(90/10)	**4b** (91/9)	124	1.8	193 000	131 000	93
11[f]	**1a**	(80/20)	**4c** (82/18)	115	1.6	180 000	119 000	90
12[f]	**1a**	(50/50)	**4d** (48/52)	n.d.[e]	4.0	213 000	151 000	71
13[f]	**1a**	(20/80)	**4e** (21/79)	48	3.2	243 000	165 000	96
14	**1b**	TMC	P(TMC), **5**	40	−23.9	170 000	99 000	100
15	**1a**[g]	DMC	P(DMC), **6**	118	n.d.[e] (27)[h]	176 000	110 000	95

[a] Polymerization conditions: catalyst **1** = 1.0×10^{-2} mmol, monomers = 40 mmol, 80 °C, 18 h. [b] Determined by ^{1}H NMR analysis. [c] Determined by GPC analysis, calibrated with a polystyrene standard. [d] Obtained by the ring-opening polymerization of (*R*)-β-BL. See ref 2. [e] Not detected. [f] 100 °C. [g] Catalyst **1a** = 2.0×10^{-2} mmol was used. [h] See ref 8i.

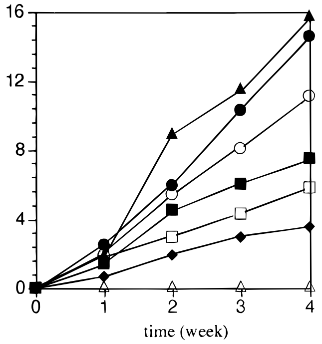


Figure 1. Biodegradation profiles on solution-cast films of poly(ester carbonate)s and P(3HB-*co*-11% 3HV) samples in aqueous solution of standard activated sludge at 25 °C: (■) **2a**; (●) **2e**; (▲) **2f**; (◆) **3**; (□) **4a**; (△) P(TMC); **5**, (○) P(3HB-*co*-11% 3HV).

ence of a catalytic amount of distannoxane complexes (**1**) (Table 1).

The copolymerization of (*R*)-β-BL with TMC catalyzed by 1-ethoxy-3-chlorotetrabutyldistannoxane was faster than that catalyzed by the other distannoxanes (**1b**−**1d**). Single T_g values were observed for all poly(ester carbonate)s. Single melting endotherms were observed for polymers, except **2e**, **2f**, and **4d**. The GPC traces of all polymers were unimodal. In general, ^{1}H and ^{13}C NMR spectra of block copolymer P[(*R*)-3HB]-*b*-PTMC show the signals for the segments of P[(*R*)-3HB] and PTMC homopolymers. However, ^{1}H and ^{13}C NMR spectra of P[(*R*)-3HB-*co*-TMC], **2e**, showed a structure different from that of the block copolymer. Therefore, all poly(ester carbonate)s are considered to be random copolymers. The observed molar ratio of 3HB, TMC, and DMC units in the polymers was almost the same as in the feed ratio (entries 2−13).

The T_g values of the polymers **2a**−**2f** are directly related to the content in 3HB units. By increasing the TMC content, polymers with lower T_g values are obtained (entries 2−7 and 13). In spite of the fact that the 3HB content of the polymers **4a**−**4e** decreases from 96 to 21%, the T_g value of the polymers does not change remarkably, 1.5−4.0 °C (entries 9−13). We did not obtain the T_g value of P(DMC). The T_g value of the copolymer (P[(*R*)-3HB-*co*-6HH]) decreases with increasing content of 6HH units and approaches −67 °C of polycaprolactone (P(6HH)).[14] A similar phenomenon was observed for P[(*R*)-β-BL-*co*-(*R*)-MOHEL] obtained by copolymerization of (*R*)-β-BL with (*R*)-3-methyl-4-oxa-6-hexanolide ((*R*)-MOHEL).[7] From the relationship between the T_g value of copolymers **4a**−**4e** and the content of 3HB units, it is considered that the T_g value of P(DMC) is about 5 °C. Keul et al. reported 27 °C for the T_g value of P(DMC).[8i]

The biodegradability of the polymers was assessed using solution-cast films at 25 °C in aqueous solutions of a standard activated sludge. It was confirmed that no erosion occurs at 25 °C. The weight loss of the polymers was measured after 4 weeks.

The weight loss profiles of **2a**, **2e**, **2f**, **3**, **4a**, **5**, and P(3HB-*co*-11% 3HV) films are presented as a function of degradation time in Figure 1. Poly(ester carbonate)s **2a** and **4a** with over 90 mol % (*R*)-3HB units show slightly smaller weight losses than P(3HB-*co*-11% 3HV). Polymer **3** with racemic 3HB units shows biodegradability. To our surpise, in spite of the fact that P(TMC) did not show biodegradability, polymers **2f** and **2e** with 79 and 50 mol % TMC units, respectively, show larger weight losses than P(3HB-*co*-11% 3HV). These high degradabilities are considered to be related to the crystallinities of **2f** and **2e**; further examination is required though.

Conclusion. The reaction of the (*R*)-β-butyrolactone with cyclic carbonates catalyzed by distannoxane complexes gives a new series of poly(ester carbonate)s, composed of (*R*)-3-hydroxybutyrate. All poly(ester carbonate) films show degradability by a standard activated sludge.

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(12) ^{1}H NMR data for P[(*R*)-3HB-*co*-DMC] are as follows: δ 0.93−1.01 (m, 6H, CH_3 for the DMC unit), 1.20−1.38 (m, 3H, CH_3 for the 3HB unit) 2.40−2.75 (m, 2H, CH_2 for the 3HB unit), 3.86−4.02 (m, 4H, CH_2 for the DMC unit), 5.05−5.33 (m, 1H, CH for the 3HB unit).

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MA951345I