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Synthesis and biodegradability of novel copolyesters containg γ-butyrolactone units

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Copolymers were synthesized by ring-opening polymerization of γ-butyrolactone (BL) with cyclicesters. Comonomers used were L-lactide (LLA), glycolide (GL), β-propiolactone (PL), δ-valerolactone (VL) and ε-caprolactone (CL). Tetraphenyl tin was used as an initiator. The copolymerization was carried out in bulk at 140°C for 4 days and the polymers were characterized by ^{1}H n.m.r., ^{13}C n.m.r., g.p.c. and d.s.c. The BL contents of the copolymers varied in the range 0 and 26 mol%. The number average molecular weights were from 1.3×10^3 to 1.5×10^5. When a small amount of the BL unit was introduced into the polymer chain, increased flexibility and excellent biodegradability were imparted to the polymer. However, excess of BL resulted in low molecular weight polymers with substantially low yields. D.s.c. measurements showed that the copolymers had one single endothermic peak at lower temperatures than those of the T_ms of each homopolymer. The BL rich copolymers were shown to be amorphous. The statistical nature of the synthesized copolymers was confirmed with n.m.r. analysis. The copolyesters were hydrolyzed in distilled water at 70°C and their hydrolyzability was found to be affected by the chemical structure and polymer composition. The hydrolyzability of glycolide or lactide copolymers was high in comparison with other copolyesters. The BL-rich copolyesters were easily hydrolyzed. The copolymers were also hydrolyzed with lipases from *Rhizopus arrhizus, R. delemar* and *Candida cylindracea* in phosphate buffer solution (pH 7.0) at 37°C. Copolymers without substituents, such as the poly(BL-*co*-ε-caprolactone)s, were easily enzymatically hydrolyzed. It is noteworthy that the non-enzymatic hydrolysis was not affected by the presence of substituents.

(Keywords: biodegradable polymer; γ-butyrolactone; polyester)

INTRODUCTION

Most synthetic carbon-based polymers are inert toward micro-organisms in the form in which they are initially produced. The long-term properties of synthetic and natural polymers have attracted more interest during recent years as environmental concern has increased[1]. Biodegradable polymers have been studied in an attempt to solve the problems of waste management for conventional plastics[2–12]. Among them, aliphatic polyesters presently constitute the most attractive class of synthetic polymers, both in the terms of their degradability in contact with living tissues or under outdoor conditions and in view of their processing[1,13–17]. A popular method to synthesize them is by ring-opening polymerization of lactones[18–22]. γ-Butyrolactone (BL) is one of the lactones which has not been yet studied in detail mainly because of its poor polymerizability[23–27]. However, the use of BL as a monomer for biodegradable materials has several advantages over other potential candidates. Firstly, its corresponding polymer, poly(4-hydroxybutyrate) (P4HB), is produced by some species of microbes, so the polymer and degraded products are expected to be harmless to the environment[28,29]. Secondly, BL and other aliphatic lactones are suitable comonomers for imparting flexibility to hard polymers such as polyglycolide[30–33]. Furthermore, BL is one of the financially viable monomers among commercially available lactones. As it has already been mentioned above, the polymerization of BL is of great interest both in the fields of research and product development. As for BL, although a restricted number of polymerizations of BL have been reported, high molecular weight copolymers have not yet been synthesized[34–37]. Recently, we have reported the copolymers of BL with L-lactide (LLA)[38]. In that paper, the following two aspects of the polymerization mechanism were reported; dominant homopolymerization of LLA; and transesterification between poly LLA and BL monomer. In the case of BL/LLA, the maximum BL content in the copolymer was 17% and the copolymer was found to be random. As the copolymerization of BL with LA proceeds via transesterification, it is expected that the same mechanism is applicable to other combinations of various monomers with BL. Therefore, copolymerization of BL with several lactones and a cyclic diester was investigated in an attempt to synthesize novel biodegradable and financially viable polymers which could eventually find applications either in medicine or in packaging.

EXPERIMENTAL

Reagents

γ-Butyrolactone (BL) (Wako), ε-caprolactone (CL) (Wako), β-propiolactone (PL) (Grand Labs Inc.) and

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δ-valerolactone (VL) (Aldrich) were purified by distillation under vacuum. L-Lactide (LLA), (Boehringer Ingelheim) was purified by recrystallization from ethyl acetate. Glycolide (GL) (Boehringer Ingelheim) was used without any further purification. Tetraphenyl Tin (Wako) was used as an initiator without purification. The enzymes for the biodegradation tests were lipases from *Rhizopus arrhizus* (Boehringer, Mannheim), *Rhizopus delemar* (Seikagaku kogyo) and *Candida cylindracea* (Boehringer, Mannheim).

Measurements

Infrared spectra were recorded on a Nicolet 710 *FT*-i.r. spectrometer, using film samples casted on a sodium chloride plate from chloroform solutions. ^{1}H n.m.r. (500 MHz) and ^{13}C n.m.r. (125 MHz) spectra were recorded on a JEOL JNM A-500 spectrometer. The spectra were mainly obtained from chloroform-d solutions at room temperature. In the case of glycolide copolymers, the mixed solution of hexafluoro isopropanol/chloroform-d (9/1; v/v) was used. The spectra of water-soluble compounds were obtained from D_2O. Thermal analyses were performed on a Rigaku model-10A differential scanning calorimeter (d.s.c.). Samples of 2–8 mg (weighed into aluminium pans) were measured from −60°C to 200°C at a heating rate of 10°C min^{-1}. Molecular weight distributions were determined with a TOSOH g.p.c. system (HLC-8020) using polystyrene standards. The columns were a TSKgel G4000HXL and a TSKgel G3000HXL with a limited exclusion molecular weight of 4×10^5.

Copolymerizations

The copolymerization of BL with a lactone was carried out in bulk. Comonomers and tetraphenyl tin (0.3 mol% *versus* total monomers) were charged on a dried ampoule. After degassing, the ampoule was sealed under vacuum and heated at 140°C for 4 days. They were allowed to cool down to room temperature and the contents were dissolved in chloroform after the addition of a few drops of methanol to stop the polymerization. Crude polymer was obtained as a precipitate in excess methanol, and was purified by repeated precipitations. A series of copolymers with different compositions were synthesized by changing the feed molar ratio of BL/lactone from 0/100 to 80/20. The molar compositions of the copolymers and the sequence distributions of the comonomer units were determined from ^{1}H n.m.r. and ^{13}C n.m.r. spectra. In the case of BL/GL, GL and its homopolymer were found to be insoluble in chloroform and in most common solvents. However, the copolymer containing BL unit is soluble in some solvents, for example, chloroform, dimethylsulfoxide and hexafluoro isopropanol (HFIP). Therefore, the solvent-soluble parts were characterized by n.m.r. and d.s.c.

Biodegradation tests

Biodegradability was evaluated both by enzymatic and non-enzymatic hydrolysis tests[39]. In the case of enzymatic hydrolysis, 25 mg of polymer samples were coated over a fixed area to each of the three tubes and 2 ml of phosphate buffer (KH_2PO_4/Na_2HPO_4, pH 7.0) were added to the tubes. Then 200 U of a lipase were added to the tubes with the exception of one for a control test. The hydrolysis was carried out at 37°C for 24 h. After filtration (0.2 μm membrane filter), a small amount of 1 N HCl was added to the filtrate in order to acidify the solution and to remove CO_2 from it. The total organic carbon concentration (TOC) was measured in duplicate. The TOC data were averaged and corrected appropriately by taking into account the blank levels. In the case of non-enzymatic hydrolysis, 25 mg of polymer samples were added to each of three tubes. The first two tubes were used for accelerated hydrolysis tests at 70°C and the third one for a blank test at room temperature. TOC values were measured and averaged from the recorded data of the first two tubes after having subtracted the blank levels.

RESULTS AND DISCUSSION

Characterization of the copolymers

The obtained polymers were characterized by i.r., n.m.r., g.p.c. and d.s.c. The i.r. spectra of the poly(BL-*co*-CL)s showed a shifted band in the C=O stretch region (1736 cm^{-1}) compared to that of polyCL (1729 cm^{-1}). The ^{1}H n.m.r. and ^{13}C n.m.r. spectra of poly(BL-*co*-CL) and their assignment are shown in *Figure 1*(a) and (b). Protons from (C=O)–O–CH_2 were observed at 4.10 and 4.06 ppm. The former was from the BL unit and the latter was assigned to CL. Protons from O–(C=O)–CH_2 were at 2.38 ppm (BL) and 2.31 ppm (CL). However, no signals derived from diad hetero sequences such as BL–CL or CL–BL were observed throughout the entire spectrum. On the contrary, in the ^{13}C n.m.r. spectrum, five strong signals (64.16, 34.13, 28.36, 25.54 and 24.59 ppm) and a carbonyl carbon at 173.56 ppm were observed and assigned to CL units, whereas three minor signals (63.34, 30.79 and 24.09 ppm) and a carbonyl carbon at 172.85 ppm were assigned to BL units. Furthermore, most of them were split to a major and a minor peak, which suggests the existence of diad homo and diad hetero sequences. Consequently, the major signals of CL were from the diad homo sequence (CL–CL) because of the agreement with peaks of PCL and the others should be most likely due to diad hetero sequences (CL–BL and BL–CL). Since the major signals of BL were of similar intensity to the minor ones of CL, it is fair to claim that the major ones of BL were from the diad hetero sequences (CL–BL and BL–CL) and the minor ones of BL should be due to the diad homo sequence (BL–BL). According to the above assignment, the obtained polymer was found to be a random copolymer. The average block length was calculated from the intensity of signals [see equation (1)], that is, $\overline{BL} = 1.1$ and $\overline{CL} = 6.0$ which means single BL units were scattered along the CL polymer chain. It was shown that the ratio of $\overline{BL}/\overline{CL}$ was well matched to that of the copolymer composition, BL/CL = 16/84. In any case, the values of $\overline{BL}$ were almost 1, so there appears to be very few BL–BL sequences in the copolymer chain.

$$\text{Average block length} = I_{\text{homo}}/I_{\text{hetero}} + 1 \qquad (1)$$

In the case of the other copolymers, the recorded ^{13}C n.m.r. signals due to the hetero sequence were as follows: PL/BL (63.77 ppm (BL, γ-CH_2, hetero), 63.53 ppm (BL, γ-CH_2, homo), 60.08 ppm (PL, β-CH_2, homo), 59.84 ppm (PL, β-CH_2, hetero), 33.66 ppm (PL, α-CH_2, hetero), 33.58 ppm (PL, α-CH_2, homo), 30.51 ppm (BL, α-CH_2, hetero), 30.30 ppm (BL, α-CH_2, homo); VL/BL (64.09 ppm (VL, δ-CH_2, hetero), 63.93 ppm (VL, δ-CH_2, homo), 63.41 ppm (BL, γ-CH_2, hetero), 63.37 ppm (BL, γ-CH_2, homo), 33.70 ppm (VL, α-CH_2, homo), 33.63 ppm (VL, α-CH_2, hetero), 30.74 ppm (BL, α-CH_2, hetero), 30.70 ppm (BL, α-CH_2, homo); LLA/BL (see Ref. [38]); GL/BL (see another section).

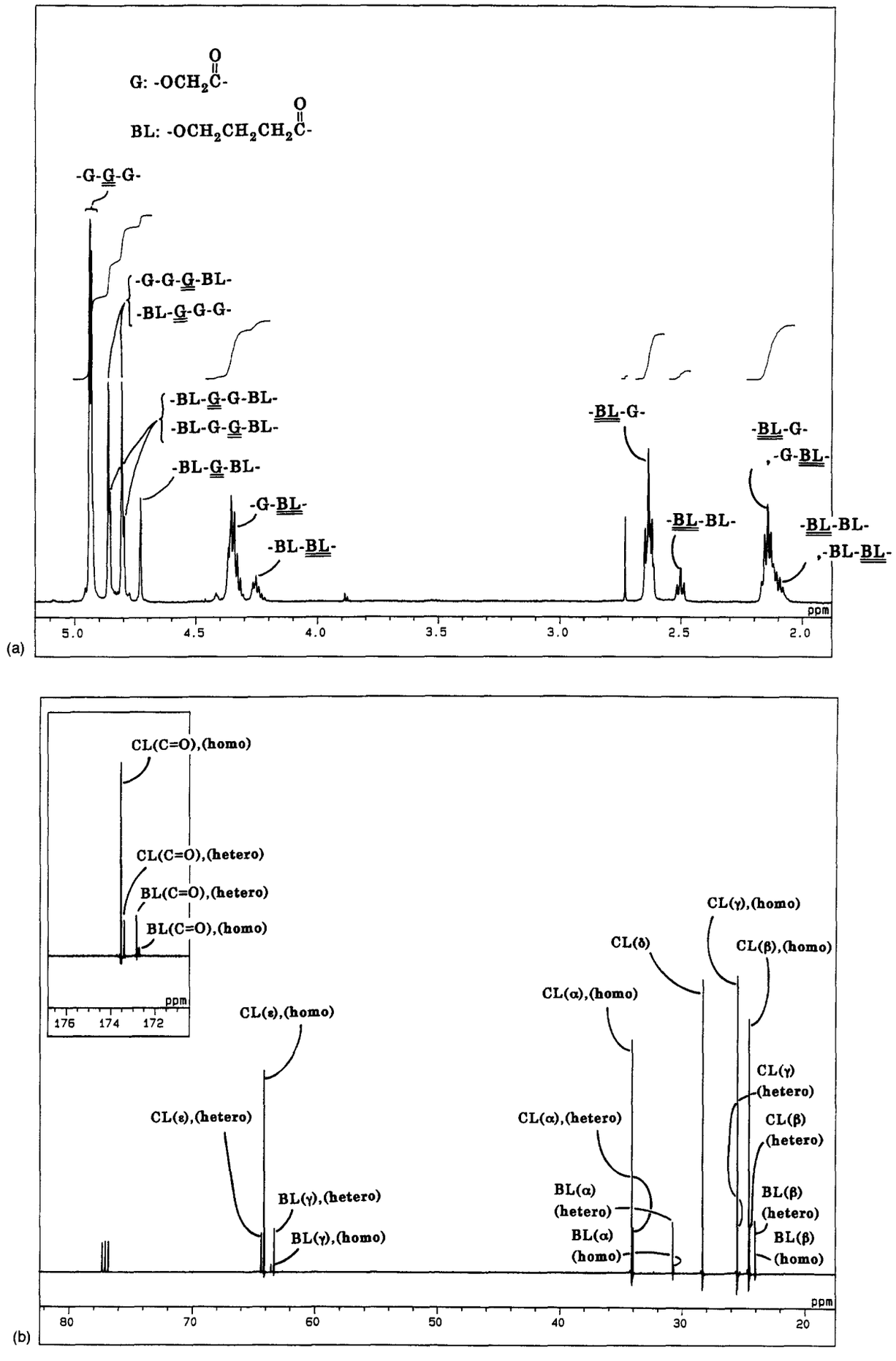

Figure 1 ^{1}H and ^{13}C n.m.r. spectra of the copolyester (BL/CL = 16/84) measured in $CDCl_3$ at room temperature: (a) 500 MHz ^{1}H n.m.r.; (b) 125 MHz ^{13}C n.m.r.

The number average molecular weights ranged from 1.3×10^3 to 1.5×10^5, depending on the comonomer combination and composition. Generally speaking, introduction of BL units caused a decrease in the molecular weight, although the molecular weight distribution itself was not affected at all. Most glycolide copolymers did not dissolve in chloroform, the g.p.c. elusion solvent, so no data concerning their molecular weight distribution could be obtained.

D.s.c. results showed only one endothermic peak of lower T_m than those of both homopolymers, which supports our hypothesis that these copolymers are random. The values of T_g were not strongly affected by polymer composition in each series.

Copolymerization of BL with lactones

The obtained polymers, except for glycolide copolymers, are soluble in chloroform. Similar protocol for polymer synthesis and characterization were carried out in most cases. The glycolide based copolymers are mentioned in the next section. *Table 1* shows the copolymerization results of BL with CL. The BL contents in the precipitated copolymer were proportional to the feed ratio. 80% of the BL feed ratio results in 16% of BL in the copolymer. In the case of a high BL feed ratio, the yield was less than 20% and unreacted BL monomer was recovered.

BL-poor copolymers had high molecular weights, whereas when the BL contents in the copolymer exceeded 12% the molecular weights exhibited a remarkable decrease. This trend can be explained by taking into account the fact that the concentration of the catalyst *versus* the amount of reacted monomers increases proportionally to an increase in the feed BL ratio because of decreasing BL monomer conversion. The T_m lowered from 58°C of poly CL as the BL contents increased.

The copolymerization results of BL with VL are shown in *Table 2* and they present several similarities to the ones obtained from the copolymerization of BL with CL. Rich in BL feed ratio resulted in rich BL copolymer composition, for example, the BL composition was 15% for a 65% BL feed ratio. The relationships between feed ratio and polymer composition, yield and T_m followed the same trend as the ones obtained from CL copolymerization.

In the case of PL, the copolymerization results were different from those mentioned above (*Table 3*), because the molecular weights were rather low, even below 2×10^3.

Table 1 Copolymerization of γ-butyrolactone (BL) with ε-caprolactone (CL) using tetraphenyl tin at various feed ratios[a]

Feed (mol%) BL/CL	Yield (%)	Polym. comp. BL/CL	M_n ($\times 10^3$)	M_w/M_n	T_m (°C)	T_g (°C)
10/90	86	3/97	145	1.9	58	− 71
20/80	80	6/94	116	1.7	58	− 71
30/70	73	8/92	123	1.5	55	− 72
40/60	65	10/90	94.5	1.6	56	− 76
50/50	51	12/88	83.3	1.8	55	− 73
65/35	34	14/86	56.4	1.4	51	− 69
80/20	16	16/84	29.5	1.4	49	− 70

[a]Copolymerization conditions: catalyst tetraphenyl tin (0.3 mol%), 140°C, 96 h.

Table 2 Copolymerization of γ-butyrolactone (BL) with δ-valerolactone (VL) using tetraphenyl tin at various feed ratios[a]

Feed (mol%) BV/VL	Yield (%)	Polym. comp. BV/VL	M_n ($\times 10^3$)	M_w/M_n	T_m (°C)	T_g (°C)
0/100	86	0/100	75.3	1.4	58	—
10/90	81	3/97	52.2	1.4	58	—
20/80	69	5/95	47.1	1.3	52	—
30/70	61	8/92	46.4	1.3	53	—
40/60	49	10/90	42.6	1.3	50	− 36
50/50	38	12/88	31.2	1.4	50	− 48
65/35	12	15/85	18.6	1.5	44	—

[a]Copolymerization conditions: catalyst tetraphenyl tin (0.3 mol%), 140°C, 96 h.

Table 3 Copolymerization of γ-butyrolactone (BL) with β-propiolactone (PL) using tetraphenyl tin at various feed ratios[a]

Feed (mol%) BL/PL	Yield (%)	Polym. comp. BL/BP	M_n ($\times 10^3$)	M_w/M_n	T_m (°C)	T_g (°C)
0/100	87	0/100	1.7	1.6	67	− 42
10/90	75	4/96	2.1	1.6	66	− 35
20/80	60	8/92	2.2	1.6	58	− 38
30/70	69	13/87	2.1	1.7	45	− 57
40/60	61	15/85	1.3	2.1	—	− 57
50/50	55	18/82	1.8	1.9	42	− 61
80/20	9	23/77	1.6	1.8	40	− 52

[a]Copolymerization conditions: catalyst tetraphenyl tin (0.3 mol%), 140°C, 96 h.

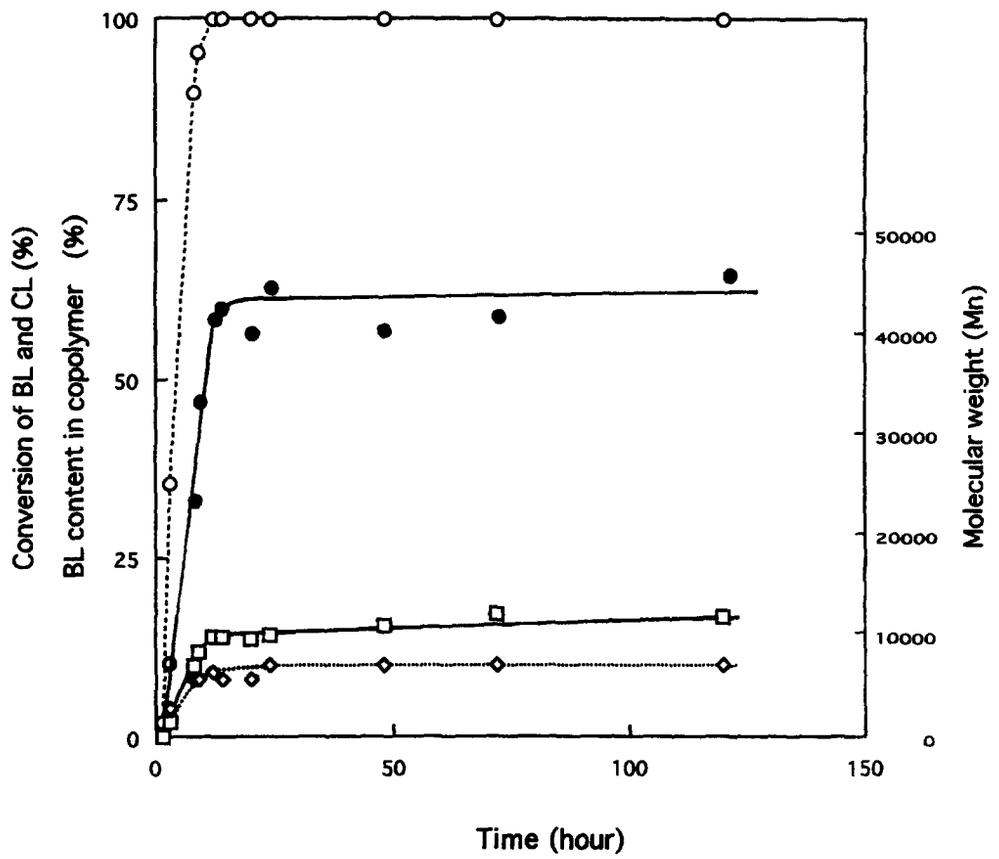

Figure 2 Polymerization profile of γ-butyrolactone and ε-caprolactone (BL/CL = 50/50) at 120°C with 0.3 mol% Ph_4Sn. (○) Conversion of CL; (□) conversion of BL; (◇) BL content in the copolymer; (●) number average molecular weight

Tetraphenyl tin appears not to catalyze PL effectively, although the reason has not been clarified yet. The molecular weights calculated from end group analysis of ^1H n.m.r. (1700 and 1900 for BL/PL = 0/100 and BL/PL = 23/77, respectively) were in good agreement with the GPC results. The obtained copolymers were BL rich (up to 23%) in comparison with CL or VL copolymers.

Figure 2 shows the relationships of the conversions of both comonomers (BL and CL) *versus* the polymerization time from n.m.r. analysis. As shown from *Figure 2*, CL conversion was considerably higher than BL conversion, although the time required for both comonomer conversion curves to reach equilibrium were almost equal. This implies that the transesterification rate is as fast as the propagation rate because the polymerization of BL is highly dependent upon the transesterification reaction.

Copolymerization of BL with glycolide

The structure of GL homopolymer is quite rigid because GL is composed of an ester group and a single methylene group. Therefore, its T_m is recorded at high temperature and its processing is not an easy task. Furthermore, GL and its homopolymer are insoluble to any common organic solvents. Thus, the copolymerization is expected to extend the applications of the polymer by improving its processing and solublization. The obtained copolymer was separated into soluble and insoluble parts to chloroform, DMSO or HFIP (*Table 4*). Although usage of several organic solvents for fractionation of copolymers could have resulted in differences of average molecular weights of the fractionated polymers, the end group analysis by ^1H n.m.r. did not support this speculation. Furthermore, the insoluble parts are rather GL rich (GL content in copolymers is more than 95%), so fractionation was mainly geared by polymer composition than by molecular weight.

In this table, the GL contents of the copolymers are indicated as glycolic acid unit (G), which is a half-unit of GL, and the feed ratio is represented by both the molar and

Table 4 Copolymerization of γ-butyrolactone (BL) with glycolide (GL) using tetraphenyl tin at various feed ratios[a]

Feed (mol%) (eq%) BL/GL (BL/G)	Soluble part				Insoluble part
	Yield (%)	Polym. comp. BL/G	T_m (°C)	T_g (°C)	Yield (%)
10/90 (5/95)	23 (HFIP soluble)	3/97	214	18	66
20/80 (11/89)	62 (HFIP soluble)	4/96	212	22	22
30/70 (18/82)	64 (HFIP soluble)	7/93	207	14	8
40/60 (25/75)	58 (HFIP soluble)	11/89	207	—	5
65/35 (48/52)	36 (DMSO soluble)	21/79	92–137	—	4
80/20 (67/33)	26 ($CHCl_3$ soluble)	26/74	76–112	—	3

[a]Copolymerization conditions: catalyst tetraphenyl tin (0.3 mol%), 140°C, 96 h.

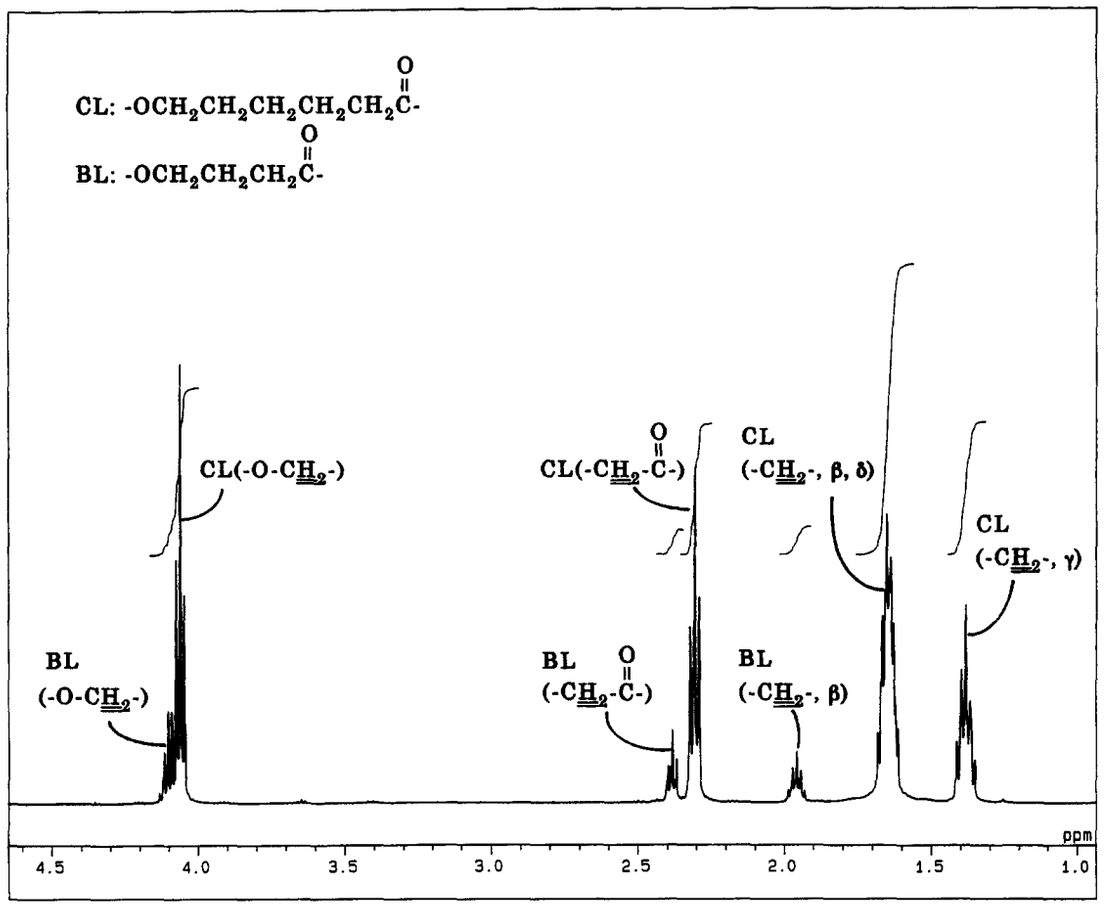

Figure 3 ^{1}H n.m.r spectrum of the copolyester (BL/G = 26/74) measured in $CDCl_3$ at room temperature (500 MHz)

the equimolar ratio. The polymerized products of 80 mol% of BL feed ratio were separated by chloroform. The soluble part was found to contain 26% of BL in the copolymer, which suggests that the obtained products are copolymers and not a mixture of both homopolymers because homopolyGL is insoluble in chloroform. Furthermore, the DSC curve revealed its melting point at a considerably lower temperature (76–112°C), compared to polyGL, and did not show any endothermic peaks at the temperature corresponding to the T_m of polyGL. This suggests that the –G–G– sequence in the copolymer should not be that long. In the case of 65 mol% of BL feed ratio, the crude polymer, although not soluble to chloroform, was soluble to DMSO. The composition ratio of the soluble part was 21/79 of BL/G. The copolymer solubility to chloroform threshold depends on the BL content (range 21–26% BL). The T_m was higher than that of 26% BL copolymer. If the BL feed ratio is less than 65 mol%, the obtained polymer was not soluble either to chloroform or DMSO, so its separation was feasible only by using HFIP. The soluble part contained less than 11% BL. Whereas the border of soluble–insoluble (solubility threshold) is from 11 to 21% of BL. The T_ms of the HFIP soluble part were close to that of polyGL. The yield of the soluble part decreased with a decrease in BL feed ratio and this tendency is the opposite shown by the other BL/lactone polymers. The poor solubility of GL rich copolymer seems to have greatly affected the copolymer composition, that is the yield of the insoluble part increased with a decrease in BL feed ratio and the total amount of both yields increased with a decrease in BL feed. The ^{1}H n.m.r. spectrum of the poly(BL-*co*-GL), (BL/G = 26/74) was recorded by using $CDCl_3$ as a solvent (*Figure 3*). The α-methylene protons in G unit were observed at 4.94–4.73 ppm as singlets assigned to triad or tetrad sequences; –G–G–G–, 4.94, 4.93 ppm; –G–G–G–BL–, –BL–G–G–G–, 4.86, 4.81 ppm; –BL–G–G–BL–, –BL–G–G–BL–, 4.86, 4.80 ppm; –BL–G–BL–, 4.73 ppm. Although glycolide is a cyclic dimer of glycolicacid, a single 'G' unit such as –BL–G–BL– was observed in the copolymer. Therefore, it could be assumed that a transesterification reaction might have occurred during the polymerization. In a similar reaction, reported for the copolymerization of BL with LLA, the same reaction conditions and catalyst and a similar comonomer (LLA) to GL were used[38]. In that experiment, the transesterification proceeded between PLLA and BL monomer, because the polymerization of LLA was considerably faster.

With HFIP/$CDCl_3$ (9/1 v/v) as a solvent, all the signals were slightly shifted to a higher magnetic field (0.03–0.06 ppm, ^{1}H n.m.r.) but no changes in the intensity and coupling pattern were observed.

Hydrolysis

The biodegradability of the synthesized copolymers was studied both by non-enzymatic hydrolysis at 70°C and by enzymatic hydrolysis, using lipases, at 37°C. The hydrolyzability of the copolyesters was evaluated by measuring the TOC values which provide irrefutable evidence of the amount of hydrolyzed water-soluble products. Furthermore, the hydrolyzability was calculated by dividing the experimental TOC values by the theoretical

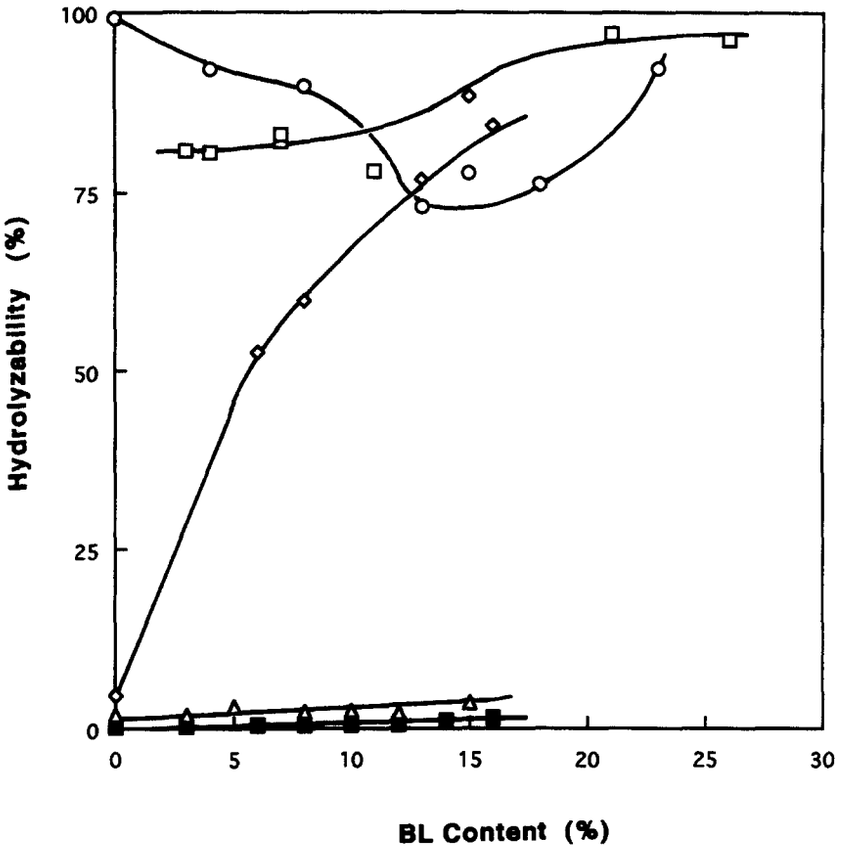

Figure 4 Accelerated hydrolysis of a series of poly(BL-*co*-lactone)s in distilled water at 70°C for a week *versus* polymer composition. (○) Poly(BL-*co*-PL)s; (□) poly(BL-*co*-GL)s; (◇) poly(BL-*co*-LA)s; (△) poly(BL-*co*-VL)s; and (■) poly(BL-*co*-CL)s

TOC as follows*:

$$\text{Hydrolyzability } (\%) = \text{TOC}_{\text{exp.}}/\text{TOC}_{\text{theor.}} \times 100$$

$$\text{TOC}_{\text{theor.}} \text{ (ppm)} = \frac{75\{n+(4-n)v\}}{(15+7n)+7(4-n)v} \times 1000$$

v : BL content in copolymer ($0 \leq v \leq 1$)

where n means the carbon number of the other comonomer unit, not the BL unit, of BL/lactone polymers. For example, in the case of poly(BL-*co*-GL), n equals 2.

Figure 4 shows the results of non-enzymatic test for 7 days. Poly(BL-*co*-GL)s and poly(BL-*co*-LLA)s, containing α-hydroxycarboxylic acid units, were readily hydrolyzed. However, poly(BL-*co*-CL)s or poly(BL-*co*-VL)s, composed of long methylene chains, were only sparingly hydrolyzed. Except for PL, the biodegradability augmented with an increase in BL copolymer content even in the cases of the CL/BL or the VL/BL copolymers. This could be explained in terms of lower crystallinity values induced by the presence of BL. The hydrolyzability of the PL copolymer was considerably high and was not dependent upon the BL copolymer content. These results could be understood in the light of self-catalyzed hydrolysis occurring at high temperature by carboxyl as an end group. This hypothesis is favoured by the fact that the PL copolymers have low molecular weights (less than 3000) in conjunction with the high concentration of carboxyl group indicated by the ^{1}H n.m.r. spectra.

Enzymatic hydrolysis was carried out with three kinds of lipases derived from *R. arrhizus*, *R. delemar* and *Candida cylindracea* (*Figures 5–7*). All the data were corrected by subtraction of both blank values: an enzyme blank level and a polymer blank level. The polymer blank level corresponds to non-enzymatic hydrolyzability at 37°C, and its level was rather negligible. It suggests that the hydrolyzability of the copolymers hardly proceeds at 37°C in contrast to 70°C. In most cases, the copolymers were found to be readily hydrolyzed with a lipase. Although each homopolymer on their own and the copolymers containing a small amount of

* The average (A) of copolymer which contain $v \times 100$ (%) of BL is represented as follows:

$$A = v(C_4H_6O_2) + (1-v)(C_nH_{2(n-1)}O_2) = C_{n+(4-n)v}H_{2(n-1)+2(4-n)v}O_2$$

Therefore, the weight percentage (W) of carbon in the copolymer is

$$W = 12\{n+(4-n)v\}/[12\{n+(4-n)v\} + 1 \times \{2(n-1)+2(4-n)v\} + 16 \times 2] \times 100$$

$$= \{6n+6(4-n)v\}/\{(15+7n)+7(4-n)v\} \times 100$$

The sample used was 25 mg and the solution volume was 2 ml, so the theoretical TOC value is calculated as follows:

$$TOC_{\text{theor.}} = 25(W/100) \times (1000/2) = 75\{n+(4-n)v\}/\{(15+7\text{n})+7(4-n)v\} \times 1000$$

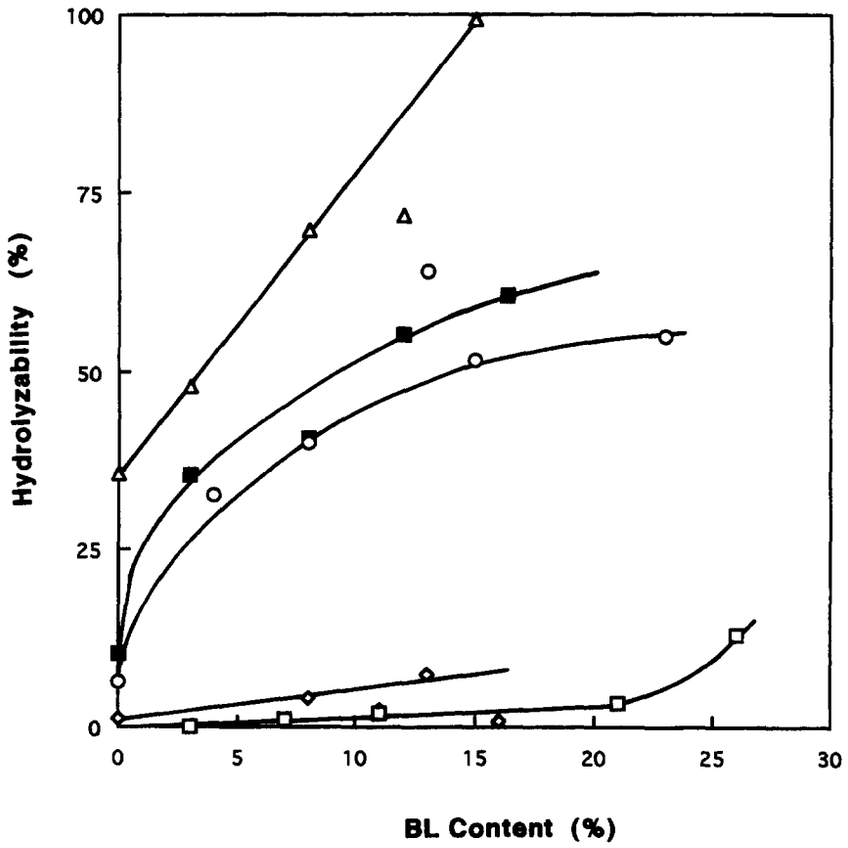

Figure 5 Enzymatic hydrolysis of a series of poly(BL-*co*-lactone)s using 200 U of lipase from *Rhizopus arrhizus*. (○) Poly(BL-*co*-PL)s; (□) poly(BL-*co*-GL)s; (◇) poly(BL-*co*-LA)s; (△) poly(BL-*co*-VL)s; and (■) poly(BL-*co*-CL)s. Conditions: 37°C; 24 h; phosphate buffer (pH 7.0), 2 ml; sample 25 mg coated on tube with fixed area

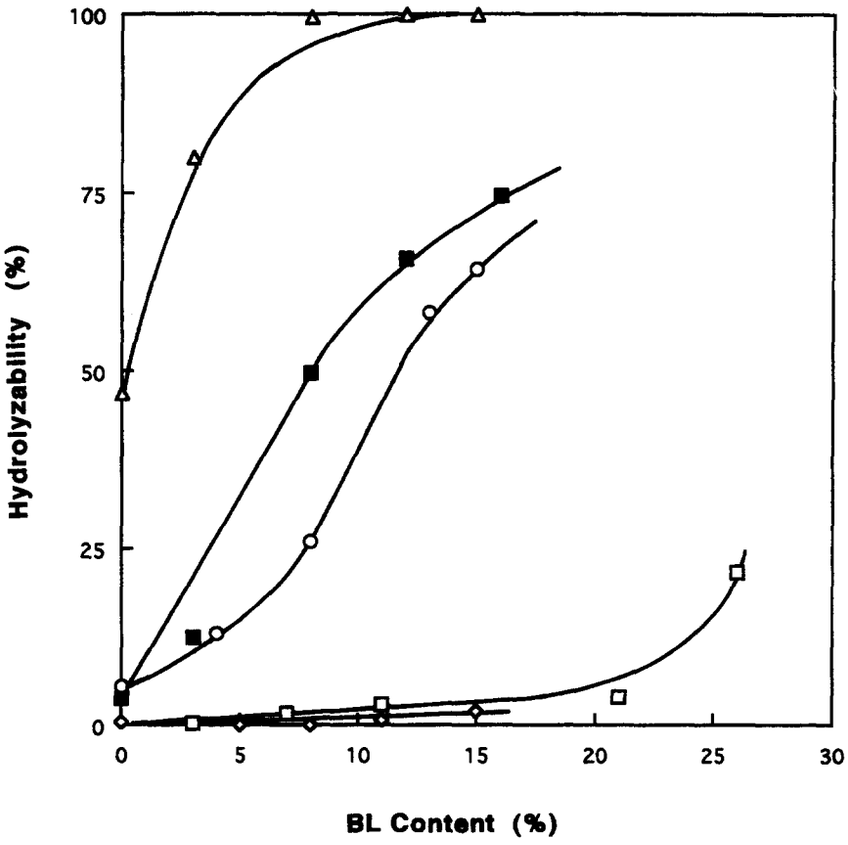

Figure 6 Enzymatic hydrolysis of a series of poly(BL-*co*-lactone)s using 200 U of lipase from *Rhizopus delemar*. (○) Poly(BL-*co*-PL)s; (□) poly(BL-*co*-GL)s; (◇) poly(BL-*co*-LA)s; (△) poly(BL-*co*-VL)s; and (■) poly(BL-*co*-CL)s. Conditions: 37°C; 24 h; phosphate buffer (pH 7.0), 2 ml; sample 25 mg coated on tube with fixed area

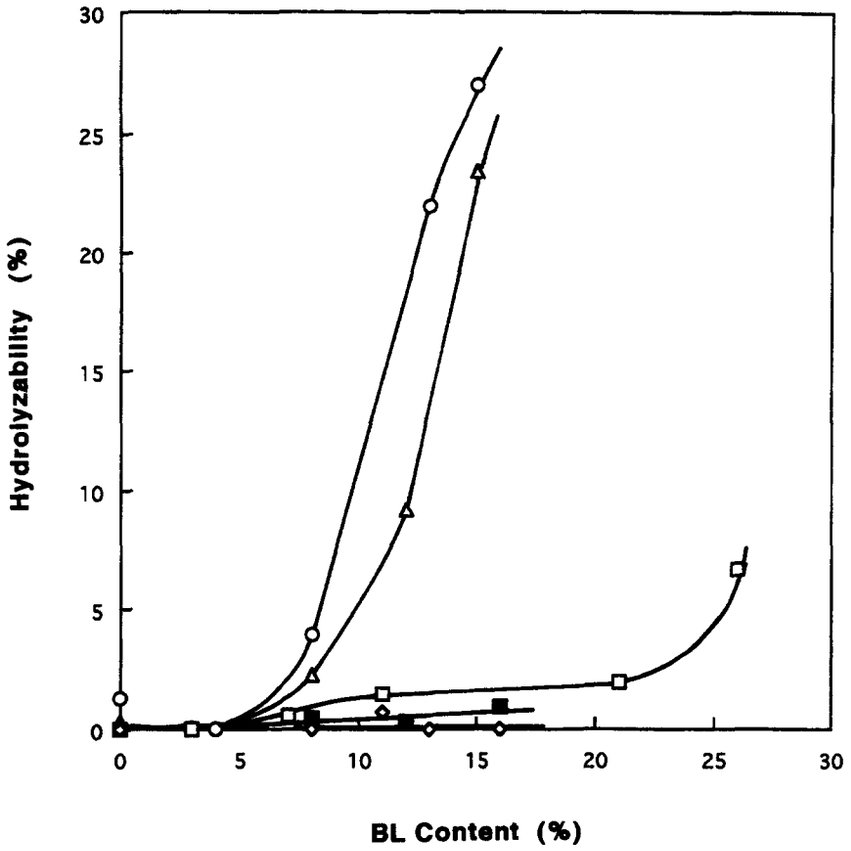

Figure 7 Enzymatic hydrolysis of a series of poly(BL-*co*-lactone)s using 200 U of lipase from *Candida cylindracea*. (○) Poly(BL-*co*-PL)s; (□) poly(BL-*co*-GL)s; (◇) poly(BL-*co*-LA)s; (△) poly(BL-*co*-VL)s; and (■) poly(BL-*co*-CL)s. Conditions: 37°C; 24 h; phosphate buffer (pH 7.0), 2 ml; sample 25 mg coated on tube with fixed area

BL (less than 5%) have a low hydrolyzability, whenever BL exceeded 5% the hydrolyzability of the copolymer augmented proportionally to the increase in BL content, similar to the results of the above-described non-enzymatic hydrolysis. However, the copolymer degradation rate was rather different for enzymatic and non-enzymatic hydrolysis: for enzymatic hydrolysis, CL, VL, PL copolymers ≫ LLA, GL copolymers; and for non-enzymatic hydrolysis, LLA, GL copolymers ≫ CL, VL, PL copolymers. That is, in the case of enzymatic hydrolysis, the copolymers containing α-hydroxycarboxylic acid units such as G were slowly degraded, whereas the flexible copolymers of VL, CL or PL were readily hydrolyzed. The hydrolysis rates with the lipases from *R. arrhizus* and *R. delemar* were rather similar to each other. The order of the copolymers on degradability was VL, CL and PL. LLA and GL copolymers were only very slightly degraded. The hydrolytic action, exhibited by both lipases, resulted in a similar biodegradable polymer percentage, probably because both fungi belong to the same species. In the case of *Candida cylindracea*, the lipase activity to the copolymers was not at all eflective (*Figure 7*). The biodegradability of CL, in particular, was substantially suppressed compared to VL or PL copolymers.

Although the effect of molecular weight has not yet been elucidated, in the case of PL/BL copolymers, low molecular weight is thought to promote the non-enzymatic hydrolysis. Furthermore, BL-rich polymers have a much lower molecular weight which may increase those copolymers' hydrolysis rate. Since samples for biodegradation testing were prepared under the same condition, crystallinity itself appears to affect biodegradability to a much lesser extent compared to other factors, such as the type of monomers or the copolymer composition. These novel copolymers are anticipated to show high susceptibility to environmental degradation.

CONCLUSION

Several series of novel statistical amorphous copolymers based on LLA, GL, PL, VL and CL were synthesized and characterized with ^{1}H n.m.r., ^{13}C n.m.r., d.s.c. and g.p.c. Introduction of BL monomer in the polymeric chain resulted in enhanced flexibility and biodegradability. The latter was tested both with enzymatic (lipases) and non-enzymatic hydrolysis (H_2O, 70°C). It is anticipated that, once a further improvement in the properties of the copolymers is attained by optimizing the synthesis conditions, these novel copolymers will constitute an 'attractive' alternative for medical and packaging applications where cost reduction of monomers is highly desirable.

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