〈研究論文(學術)〉

생분해성 고분자 폴리에스테르의 합성

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Chemically synthesized polyester for use as biodegradable polymers

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요 약

Poly(3-hydroxybutylate) 및 그들 유도체의 화학적 합성을 위해 γ-butyrolactone(γBL)과 γ-valerolactone (γVL)을 사용 γ-butyrolactone(βBL)과의 개환중합을 시도했다. 공중합체는 5원환 락톤 단위를 포함한 코 폴리에스테르를 BF₃ · OEt₂ 촉매하에서 고상(bulk state)중합에 의해 얻었고, 이러한 방법으로 합성한 코폴 리머의 구조를 ¹H NMR과 ¹³C NMR 분석법으로 결정했다. 그결과 βBL, γBL과 γVL의 첨가비가 증가함에따라 수율은 저하되었고, 또한, γVL의 경우 4HV의 증가가 34~35%가 한계로써, γVL의 첨가비가 0.5(γVL/βVL = 50/ 50)보다 증가 할지라도 안정상태를 유지하였다.

1. Introdution

Because of their excellent biodegradability, aliphatic polyesters such as poly(3-hydroxybutyrate) (P3HB)) have given a bright prospect for the industrial and biomedical applications as biodegradable polymers. These ployesters are usually synthesized by bacterial fermentation process as well as by chemical process based on the ring-opening polymerization of various lactone monomers. In the f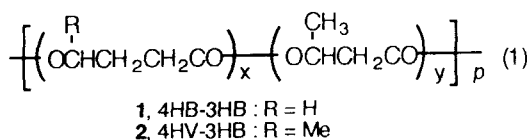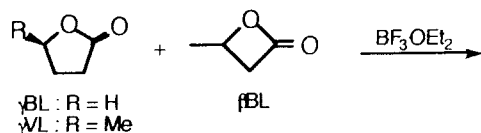ermentation process, however, polymer composition, molecular weight and higher order structure of the polymer are not easily controlled. It has also been pointed out that the processability of the bacterial polymers was too poor to obtain high quality materials. So, development of a new synthetic method for preparing the alopathic polyesters has been desired. In this paper we report on the copolymerization of 4-membered β-butyrolactone(βBL)and a 5-membered γ-butyrolactone (γBL) or γ-valerolactone(γVL) by catalysis of boron trifluoride etherate(BF₃ · OEt₂) to give novel

derivatives of P(3HB) which consist of 3-hydroxy-butyrate(3HB), 4-hydroxybutyrate(4HB), and 4-hydroxyvalerate(4HV) units.

2. Experimental

2.1. Materials

[R]-βBL and [R]-γVL ([α]D= +31.1°) were supplied by Takasago Co. γBL and[RS]-βBL were purchased from Nakarai Tesque. They were puri-fied by distillation on CaH_2 at reduced pressure. $BF_3 \cdot OEt_2$ was purified by distillation. The other reagents were commercially available and were used without further purification.

$$\text{γBL : R = H} \quad \text{βBL} \qquad \text{γVL : R = Me}$$

$$-\left[\left(\underset{|}{O}CHCH_2CH_2CO\right)_x \left(\underset{CH_3}{|}OCHCH_2CO\right)_y\right]_p \quad (1)$$

1, 4HB-3HB : R = H
2, 4HV-3HB : R = Me

2.2. Measurements

^{1}H and ^{13}C NMR spectra (internal reference : 1 vol% solution of TMS in $CDCl_3$) were measured at 200MHz and 50.3MHz, respectively, on a Varian XL-200 spectrometer(Japan). $^{13}C-^1H$ COSY spect-rum was recorded at 300MHz on a GE QE 300MHz instrument. The number-average molecular weight (Mn) and molecular weight distribution(Mw/Mn) were determined by gel permeation chromatogra-phy (GPC). The analyzer was composed of a Shi-mazu LC-10A pump, a Shodex RI DE-31RI detec-tor, a Shimazu C-R7A chromatopac data processor, a Shodex DEGAS KT-16 degassor, and a Sugai R-620 column oven. A Combination of two polysty-rene gel columns of TSK and gel $G4000H_8$(7.5mm I.D ×300mm, each) were used with chloroform

as the eluent at 35℃. The molecular weight was calibrated according to polystyrene standards. The specific optical rotation was measured on a Union PM-101 high-sensitive auto polariscope under an incident beam of sodium D-ray for a sample solu-tion(0.9g/dl) in acetone or chloroform at 25℃.

2.3 Copolymerization of βBL with γBL or γVL.

Both of the monomers were charged in a glass reactor at a predetermined feed ratio, and 1mol% of a catalyst was added to it. The reaction system was kept stirred at room temperature under a nit-rogen atmosphere for 7days it gives a very viscous product. It was then dissolved in a chloroform, reprecipitated into 10ml of an diethyl ether/n-he-xane(1 : 1 in volume)mixture, and dried in vacuo.

3. Results and Discussion

3.1 Copolymerization of βBL and γBL

The Copolymerization of [RS]-βBL and δBL was examined by various catalysts, cationic, anionic and coordinated. The Copolymerization took place only by catalysis of $BF_3 \cdot OEta_2$ in a bulk mixture of the monomers at room temperature(Eq.(1)). The ^{1}H NMR spectrum of the copolymer obtained at a γBL to βBL feed ratio of 1 : 1 showed the signals due to the methylene groups 4HB units at δ172.5— 173ppm. These results suggested the formation of P(3HB-co-4HB). Typical results of the copoly-merization are summarized in Table 1. With inc-reasing the feed ratio of γBL, the copolymers com-position yield decreased less than 24% at high γBL to βBL ratios. The molecular weight was in the range of 1700-3700 in the present conditions.

Figure 1 shows the monomer-copolymer compo-sition curves, where the open and closed marks denote the plots at high(>50%)and low(ca. 10%) conversions, respectively. This shows that both the copolymer compositions were comparable with each other. The curves approximately agreed with an

Table 1. Results of copolymerization of γBL and βBL with $BF_3 \cdot OEt_2$ as a catalysts[a]

Run No.	Feed ratio γBL/βBL	Unit ratio[b] 4HV/3HB	Yield (%)	$Mn \times 10^{3c}$	Mw/Mn[c]
1	10/90	10.4/89.6	88.7	2.91	1.63
2	20/80	17.6/82.4	88.2	2.00	1.30
3	35/65	29.2/70.8	91.3	2.56	1.60
4	50/50	39.0/61.0	66.3	2.80	1.41
5	65/35	43.4/56.6	55.4	3.64	1.67
6	80/20	47.5/52.5	25.1	1.77	1.28
7	90/10	56.1/43.9	24.3	1.81	1.70

[a]Polymerized in bulk by 1.0mol% of $BF_3 \cdot OEt_2$ under nitrogen at room temperature for 7days.
[b]Determined by ^1H NMR.
[c]Determined by GPC(chloroform eluent).

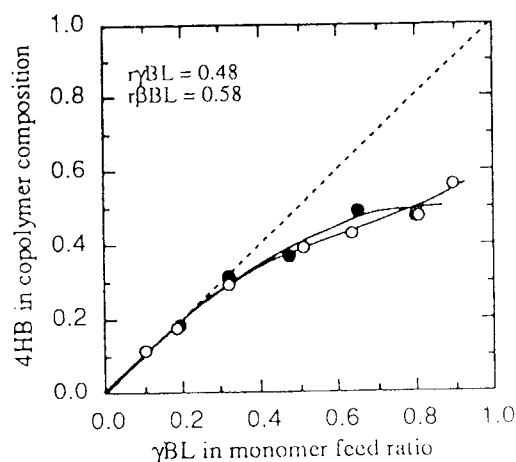

Fig. 1 Monomer-copolymer compositior curves for the bulk copolymerization of βBL and γBL by $BF_3 \cdot OEt_2$ under N_2 at room temperature.
● low conversion(ca 10%)
○ high conversion(>50%)

azeotrope line at the γBL ratio below 0.3, but deviated from the line at the higher γBL ratio. This result suggested a tendency that a random copolymer was produced at the lower γBL ratio and that the 4HB composition decreased at the higher γBL ratio. The monomer reactivity ratios were calculated

by Lewis-Mayo method. The values obtained were 0.58(rβBL) and 0.48(rγBL), respectively. Analysis of the expanded carbonyl signals revealed that these chemically synthesized copolymers have higher compositions of the alternating diad of 4HB-3HB than the corresponding copolymers that were biologically synthesized by Doi et al[10].

The copolymerization of γBL and [R]-βBL was also carried out to give the identical results. The copolymer obtained at an [R]-βBL feed ratio of 0.8 was subjected to methanolysis under acidic conditions[11]. The specific rotations of this reaction product was found to be almost the methanolysis product of a monomer mixture of [R]-βBL and γBL in the same ratio with copolymer composition. It was therefore considered that the stereochemistry of the βBL was preserved during the copolymerization.

Analysis of ^1H-^1H COSY NMR spectrum revealed that the copolymer possesses a secondary hydroxyl group in its terminal. This finding suggested that the propagating species of the hydroxyl group on which the monomers are added successively.

3.2 Copolymerization of βBL and [R]-βVL

Table 2 shows the typical results of the copoly-

Table 2. Results of copolymerization of γVL and βBL with BF$_3$ · OEt$_2$ as a catalysts[a]

Run No.	Feed ratio γVL/βBL	Unit ratio[b] 4HV/3HB	Yield (%)	Mn×10^{-3c}	Mw/Mn[c]	$[\alpha]_0^{25d}$
1	10/90	11.5/88.5	85.6	2.80	1.65	3.1
2	20/80	22.1/77.9	73.3	3.55	1.62	6.6
3	30/70	26.3/73.7	94.7	2.02	1.64	6.7
4	33/67	24.4/75.6	54.8	3.77	1.54	—[e]
5	50/50	33.9/66.1	57.2	4.25	1.61	7.9
6	70/30	32.2/67.8	42.2	2.21	1.60	7.3
7	80/20	34.4/65.6	18.4	1.18	1.47	10.1
8	90/10	33.3/66.7	9.4	0.84	1.28	7.4

[a]Polymerized in bulk by 1.0mol% of BF$_3$ · OEt$_2$ under nitrogen at room temperature for 7days. [b]Determined by ^{1}H NMR. [c]Determined by GPC(chloroform eluent). [d]In acetone(0.9g/dl). [e][R,S]-γVL monomer was used.

merization at different feed ratios. Similarly to the former examples, the copolymer yield decreased with increasing the [R]-γVL to βBL feed ratio. The copolymer composition of 4HV increased to 34-40% and leveled off even if the γVL ratio was increased more than 0.5.

Figure 2 shows a typical ^{1}H NMR spectrum of the copolymer which was obtained by the catalysis of BF$_3$ · OEt$_2$ at a [R]-γVL to [RS]-βBL feed ratio of 1 : 1, as compared with that of the homo-PHB synthesized by [RS]-βBL with a ZnEt$_2$-H$_2$O catalyst[12,13]. The signals due to 4HV unit can be clearly detected at δ1.23, 1.86, 2.32 and 4.93 ppm besides the two signals due to 3HB units. Their signal assignments are involved in this Figure.

Figure 3 shows the ^{13}C NMR spectrum of the same coplymer together with the signal assignments. While the carbon signals due to 3HB unit are shown at δ20, 30, 70 and 172ppm. The methyl carbon signals of both 3HB and 4HV units were superimposed, but separated by ^{13}C-^{1}H COSY spectroscopy. These results supported the formation of P(3 HB-co-4HV), that has never been produced by fermentation.
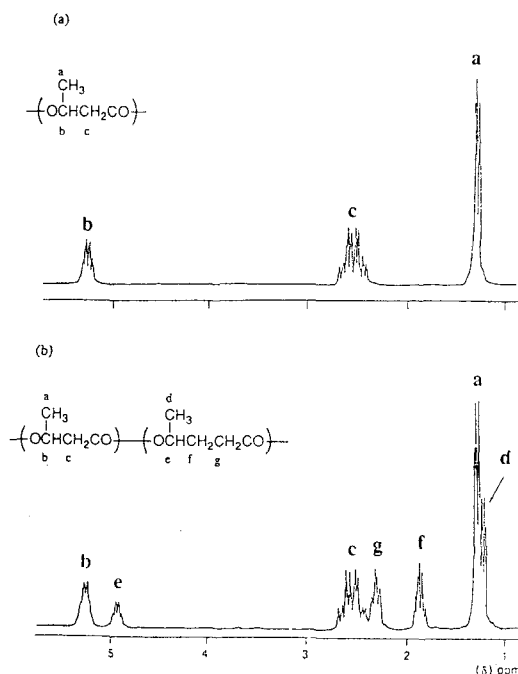

Fig. 2 ^{1}H NMR spectrum of (a) P([RS]-3 HB) and (b) the chemically synthesized P(3HB-co-4HV).

Figure 4 shows the monomer-copolymer composition curves. The curves at low(closed) and high (open) conversions were different at high γVL
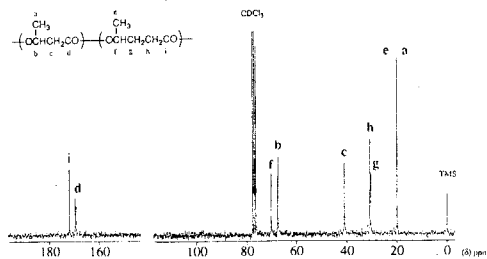
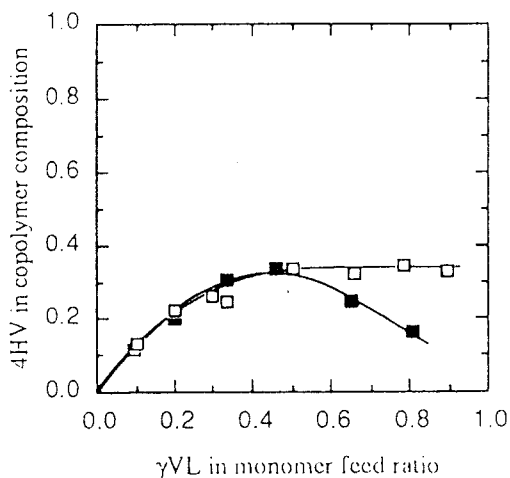Fig. 3 ^{13}C NMR spectrum of the chemically synthesized P(3HB-co-4HV) (at a γVL to BBL feed ratio of 1 : 1)

γVL in monomer feed ratio

Fig. 4 Monomer-copolymer compositior curves for the bulk copolymerization of βBL and γVL by BF₃ • OEt₂ under N₂ at room temperature.
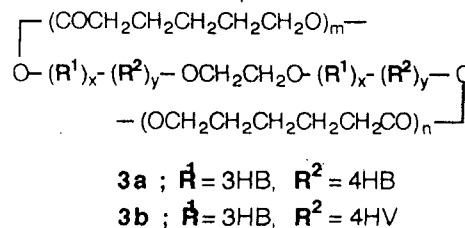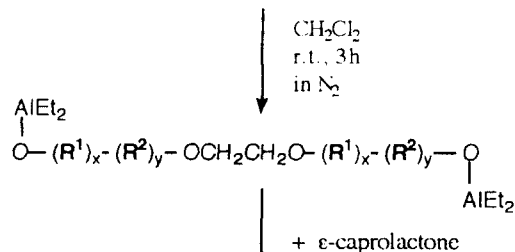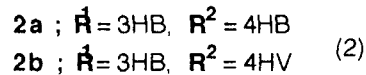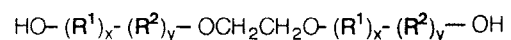■ low conversion(ca 10%)
☐ high conversion(> 50%)

to βBL feed ratio. Since the copolymerization of γVL is thought to be highly induced after the polymerization of βBL proceeded in some degree,γVL any react much faster with the propagating species with an enough chain length than with short initiating species which is still unknown.

3.3 Copolymerization in the presence of hydroxyl compounds

The copolymerization of βBL with γVL was

carried out in the presence of lauryl alcohol(LA) and ethylene glycol(EG)[14]. The ^{1}H NMR spectra of the resultant copolymers showed the presence of the terminal lauryl ester group and the internal (oxyethylene)oxy unit, respectively. This result is another support for the polymerization mechanism that the hydroxyl terminal reacts with the monomers activated by the catalyst.

Since the copolymer prepared in the presence of EG has a struture shown in the Eq. (2),it can be utilized a telechelic polymer. In the present study, 2a and 2b were reacted with e-caprolactone by the action of triethylalminym catalyst to give the triblock copolymers 3a and 3b[15].

$$HO-(R^1)_x-(R^2)_y-OCH_2CH_2O-(R^1)_x-(R^2)_y-OH$$

2a ; R^1 = 3HB, R^2 = 4HB
2b ; R^1 = 3HB, R^2 = 4HV   (2)

$$\downarrow \quad \begin{array}{l} CH_2Cl_2 \\ r.t., 3h \\ in\ N_2 \end{array}$$

AlEt₂
|
$$O-(R^1)_x-(R^2)_y-OCH_2CH_2O-(R^1)_x-(R^2)_y-O$$
|
AlEt₂

$$\downarrow \quad + \text{ e-caprolactone}$$

$$\begin{array}{l} -(COCH_2CH_2CH_2CH_2CH_2O)_m- \\ O-(R^1)_x-(R^2)_y-OCH_2CH_2O-(R^1)_x-(R^2)_y-O \\ -(OCH_2CH_2CH_2CH_2CH_2CO)_n- \end{array}$$

3a ; R^1 = 3HB, R^2 = 4HB
3b ; R^1 = 3HB, R^2 = 4HV

4. conclusions

It was found that the 5-membered lactones such as γBL and γVL can be copolymerized with a 4-membered lactone βBL with BF³ • OEt² as a catalyst. The stereochemistry of both the monomers was retained in the copolymer, but their molecular weight did not become large enough at the present reaction of the hydroxyl terminal and the monomers, the copolymer prepared in the presence of

such a diol as EG was found to be a telecheilic polymer with hydroxyl terminals for preparing various block copolymers. Therefore, the copolymerization conditions should be improved in order to obtain high polymers, and telechelic copolymers with highly-regulated structure.

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