

NOTES

Synthesis of Optically Active Polyesters from Chiral Diols Containing Bis[(*R*)-3-hydroxybutyrate] Units and Aromatic Diacid Chlorides

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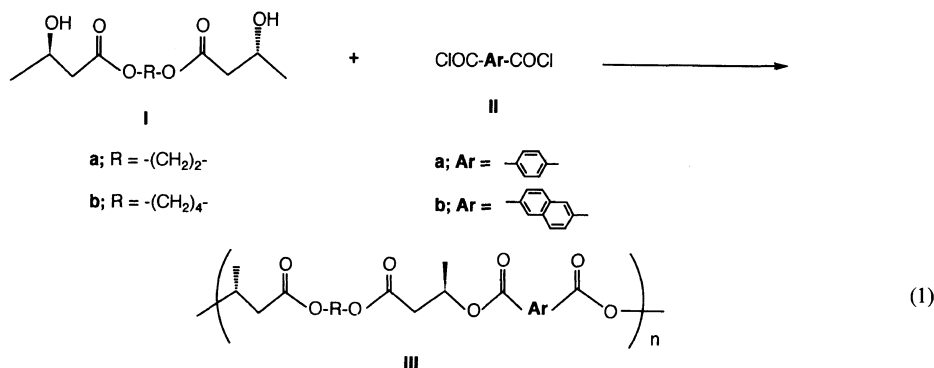
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Polymers containing (*R*)-3-hydroxyalkanoate unit in the main chain have attracted wide attention because of their interesting properties, mainly biodegradability. Among them, poly[(*R*)-3-hydroxyalkanoates] (PHA) are naturally occurring polyesters that can be synthesized by a variety of bacteria¹⁻³ and serve as intracellular carbon and energy reserve materials.¹ Although many polymers containing (*R*)-3-hydroxybutyrate units in the main chain have been synthesized by ring opening polymerization, few examples have been reported on the polycondensation method. The polycondensation for polymers with 3-hy-

droxybutyrate units is an important subject for polymer synthesis because the monomers are easy to dehydrate to produce crotonate. During the course of our study on polymers containing (*R*)-3-hydroxybutyrate units in the main chain by the polycondensation method, we prepared optically active diols symmetrically possessing two (*R*)-3-hydroxybutyrate units. This paper reports the syntheses of optically active diols symmetrically containing (*R*)-3-hydroxybutyrate units and polyesters by polycondensation with aromatic diacid chloride (eq 1).



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EXPERIMENTAL

Measurements

IR spectra were recorded on a JASCO IR-810 spectrophotometer. ^1H NMR spectra were measured on a Bruker AMX 400 spectrometer using tetramethylsilane as the internal standard. Optical rotation measurements were performed on a JASCO DIP-360 spectrometer. Differential scanning calorimetry (DSC) and thermogravimetry (TG) were performed with Shimadzu thermal analyzers DSC-50 and TGA-50, respectively, and measurements were made at a heating rate of $10^\circ\text{C min}^{-1}$ under nitrogen at a flow rate of 50 ml min^{-1} . Weight-average molecular weight (\bar{M}_w) and number-average molecular weight (\bar{M}_n) were obtained by gel permeation chromatography (GPC) on a Hitachi apparatus with polystyrene calibration (eluent, chloroform).

Materials

Terephthaloyl chloride (**IIa**) was purified by distillation under reduced pressure. 2,6-Naphthalenedicarbonyl chloride (**IIb**) was prepared by reaction of 2,6-naphthalenedicarboxylic acid with thionyl chloride, and purified by sublimation. Methylene chloride and pyridine were distilled over phosphorous pentoxide and calcium hydride, respectively.

Monomer Synthesis

Ethylene Bis[(R)-3-hydroxybutyrate] (**Ia**). A solution of ethylene bis(acetoacetate) (**IVa**) (14.5 g, 63.0 mmol) and $\text{Ru}_2\text{Cl}_4((+)\text{BINAP})_2\text{-Et}_3\text{N}$ (0.29 g) in methylene chloride (120 ml) was stirred at 40°C under a hydrogen pressure of 50 kg cm^{-2} for 3 days (BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl).⁴ After the mixture was concentrated, the residue was stirred at 40°C in 2-propanol (100 ml) and methylene chloride (100 ml) with 2 g of active carbon for 2 h. The solution was filtered and the filtrate was concentrated. The product was purified by column chromatography (silica, $\text{CHCl}_3\text{-MeOH} = 15:1-3:1$), followed by dis-

tillation to give 7.21 g (49%) of **Ia**. bp $143\text{--}145^\circ\text{C}/2.5\text{ Torr}$, $[\alpha]_D^{25} -41.8^\circ$ (c 1.01, CHCl_3).

IR (Neat): 3440, 2970, 1730, 1460, 1410, 1380, 1300, 1260, 1180, 1130, 1080 cm^{-1} .

^1H NMR (CDCl_3): 1.24 (d, $J=6.3\text{ Hz}$, 6H), 2.45 (dd, $J=16.3\text{ Hz}$, $J=8.5\text{ Hz}$, 2H), 2.53 (dd, $J=16.3\text{ Hz}$, $J=3.7\text{ Hz}$, 2H), 2.95 (br s, 2H), 4.17–4.25 (m, 2H), 4.35 (s, 4H) ppm.

Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_6$: C, 51.27%; H, 7.74%. Found: C, 51.33%; H, 7.85%.

Diol **Ib** was synthesized from **IVb** in 45% yield as described for **Ia**. bp $164\text{--}166^\circ\text{C}/3.6\text{ Torr}$, $[\alpha]_D^{25} -40.9^\circ$ (c 1.06, CHCl_3).

IR (Neat): 3440, 2970, 1730, 1460, 1400, 1300, 1180, 1130, 1090 cm^{-1} . ^1H NMR (CDCl_3): 1.24 (d, $J=6.3\text{ Hz}$, 6H), 1.68–1.77 (m, 4H), 2.40 (dd, $J=16.3\text{ Hz}$, $J=8.6\text{ Hz}$, 2H), 2.50 (dd, $J=16.3\text{ Hz}$, $J=3.7\text{ Hz}$, 2H), 2.88 (br s, 2H), 4.10–4.25 (m, 6H) ppm.

Anal. Calcd for $\text{C}_{12}\text{H}_{22}\text{O}_6$: C, 54.95%; H, 8.45%. Found: C, 55.12%; H, 8.33%.

Determination of Optical Purity. Symmetric diol **Ia** was converted into methyl (*R*)-3-hydroxybutyrate **V** by methanolysis with sulfuric acid. bp $75\text{--}76^\circ\text{C}/16.1\text{ Torr}$, $[\alpha]_D^{25} -46.1^\circ$ (c 1.10, CHCl_3). lit.⁵ $[\alpha]_D -47.6^\circ$ (c CHCl_3).

^1H NMR (CDCl_3): 1.23 (d, $J=6.5\text{ Hz}$, 3H), 2.43 (dd, $J=16.4\text{ Hz}$, $J=8.6\text{ Hz}$, 1H), 2.50 (dd, $J=16.5\text{ Hz}$, $J=3.6\text{ Hz}$, 1H), 2.95 (d, $J=3.8\text{ Hz}$, 1H), 3.72 (s, 3H), 4.16–4.25 (m, 1H) ppm.

Enantiomeric excess (e.e.) of **V** from **Ia** was 98.6% as determined by HPLC analysis (Cosmosil, $0.46 \times 25\text{ cm}$, flow rate 1.0 ml min^{-1} ; eluent, 9:1 hexane-ether; detection, 254 nm) of its (*R*)-MTPA ester (MTPA = α -methoxy- α -trifluoromethylphenylacetyl).

Diol **Ib** was also converted to **V** ($[\alpha]_D^{25} -46.4^\circ$ (c 1.02, CHCl_3)) and e.e. of **V** from **Ib** was determined as 97.6% as described above.

Polymerization

A typical polymerization is as follows.

Polyester IIIa. To a mixture of **Ia** (2.34 g, 10.0 mmol) and pyridine (1.74 g, 22.0 mmol) in

methylene chloride (10 ml) was added portion-wise terephthaloyl chloride **IIa** (2.03 g, 10.0 mmol) at room temperature. The mixture was refluxed for 7 h under nitrogen and poured into 100 ml of methanol. The methanol-insoluble polymer was collected and washed with hot methanol. Drying under reduced pressure gave 2.55 g (70%) of polymer **IIIa**.

IR (CHCl₃): 3030, 3000, 1740, 1720, 1460, 1390, 1280, 1220, 1190, 1125, 1105, 1060, 1020 cm⁻¹.

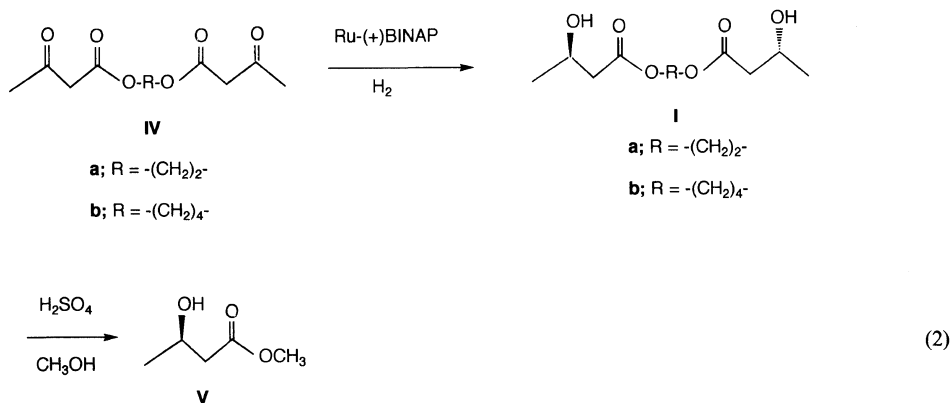
¹H NMR (CDCl₃): 1.42 (d, *J* = 6.3 Hz, 6H), 2.62 (dd, *J* = 15.6 Hz, *J* = 5.5 Hz, 2H), 2.78 (dd, *J* = 15.6 Hz, *J* = 7.5 Hz, 2H), 4.22 (m, 4H), 5.51 (sextet, *J* = 6.2 Hz, 2H), 8.05 (s, 4H) ppm.

Anal. Calcd for C₁₈H₂₀O₈: C, 59.34%; H, 5.53%. Found: C, 59.02%; H, 5.43%.

RESULTS AND DISCUSSION

Monomer Synthesis

New optically active diols **I**, symmetrically possessing (*R*)-3-hydroxybutyrate units, were synthesized as shown in eq 2. Ethylene bis(acetoacetate) **IVa** and tetramethylene bis(acetoacetate) **IVb**, prepared from the corresponding diols and methyl acetoacetate by transesterification, were transformed to **Ia** and **Ib**, respectively, by Ru-(+)-BINAP-catalyzed asymmetric hydrogenation.⁴ To examine configurations and optical purities of generated asymmetric carbons, diols **I** were converted to methyl 3-hydroxybutyrate **V** by methanolysis. Enantiomeric excess of **V** from **Ia** and **Ib** was 98.6% and 97.6%, respectively, both with *R* configuration.



Polymer Synthesis and Characterization

Optically active diols **I** were subjected to polycondensation. Recently, we reported the successful synthesis of optically active polyesters from chiral 1,3-diols and aromatic diacid chlorides in the presence of pyridine as an accelerator of the reaction and hydrogen chloride acceptor.⁶ The same procedure was used in this study. Diols **I** were reacted with aromatic diacid chlorides **II** in refluxing methylene chloride in the presence of pyridine. Figure 1 illustrates the relationship between the reaction period and molecular weight measured by GPC analysis of the reaction mixture when

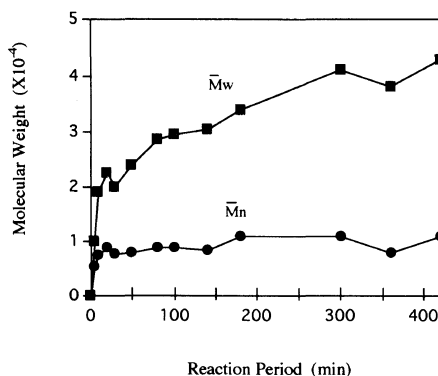


Figure 1. Relationship between reaction period and molecular weight measured by GPC analysis of the reaction mixture for the polymerization of **Ia** and **IIa**.

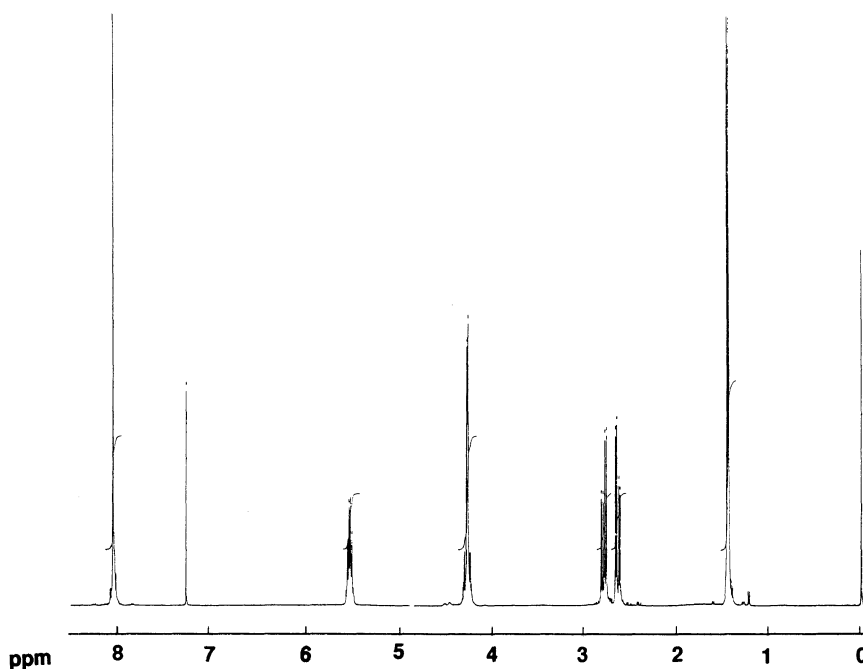


Figure 2. ^1H NMR spectrum of polymer **IIIa** measured in CDCl_3 .

Table I. Synthesis of optically active polyesters

Monomer			Polymer			
Diol	Diacid chloride	Code	Yield	\bar{M}_n^a	\bar{M}_w^a	\bar{M}_w/\bar{M}_n^a
			%	($\times 10^{-4}$)	($\times 10^{-4}$)	
Ia	IIa	IIIa	70	1.4	4.5	3.2
Ia	IIb	IIIb	71	1.1	1.7	1.5
Ib	IIa	IIIc	69	3.9	5.0	1.4
Ib	IIb	IIIc	65	1.6	2.7	1.7

^a Determined by GPC with polystyrene calibration.

Ia and **IIa** were polymerized. Molecular weight increased rapidly in the first 30 min and was almost saturated after 1 h. Figure 2 shows the ^1H NMR spectrum of polymer **IIIa**. Methyne protons moved to 5.5 ppm from 4.2 ppm and a singlet for aromatic protons was newly observed at 8.05 ppm. No peak of crotonate olefin, generated by dehydration reaction, was observed in the ^1H NMR of polyester **IIIa**. The results of polycondensation are summarized in

Table I. Yields of the polymers were 65–71%. \bar{M}_n determined by GPC were 11000–39000 based on standard polystyrenes and \bar{M}_w/\bar{M}_n were 1.4–3.2.

The polymers had negative optical rotation from -55 to -220 degrees as shown in Table II. Thermal characterization of the polymers was carried out by differential scanning calorimetry (DSC) and thermogravimetry (TG). Glass transition temperatures (T_g) were ob-

Table II. Optical rotation and thermal behavior of polyesters

Polymer	$[\alpha]_D^a$ degree	T_g^b °C	T_d^c °C	T_{10}^d °C
IIIa	-62	26	288	301
IIIb	-220	35	286	301
IIIc	-55	1	284	301
III d	-126	25	285	307

^a Measured in chloroform at 25°C.

^b Determined by DSC in nitrogen at a heating rate of 10°C min⁻¹.

^c T_d is the initial decomposition temperature measured by TG in nitrogen at a heating rate of 10°C min⁻¹.

^d T_{10} is the temperature of 10% weight loss, measured by TG in nitrogen at a heating rate of 10°C min⁻¹.

served from 1 to 35°C. T_g s of the polymers from **IIb** were lower than those from **IIa** because of increased flexibility of the longer methylene chain in **III**. TG measurements showed that all the polymers started to decompose at around 285°C and 10% weight loss temperatures ranged from 301 to 307°C. These results are

listed in Table II.

In conclusion, optically active polyesters possessing (*R*)-3-hydroxybutyrate units in the main chain were successfully synthesized by the polycondensation of newly prepared optically active diols and aromatic diacid chlorides. Further investigation of the biodegradability of the polymers is in progress.

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