

Table I. Enzyme screen for polycondensation of **1a** and **2d**^a

Entry	Catalyst	Yield ^b	M_n^c	M_w/M_n^c
		%		
1	Lipase CA	74	5500	1.6
2	Lipase CC	0		
3	Lipase MM	40	2600	1.2
4	Lipase PC	13	2000	1.1
5	Lipase PF	36	2900	1.5
6	PPL	0		
7	— ^d	0		

^a Polymerization of **1a** and **2d** (each 1.0 mmol) using lipase catalyst (100 mg) in heptane (5.0 mL) at 60°C for 48 h. ^b Methanol-insoluble part. ^c Determined by SEC. ^d Control experiment.

The other is synthesis of poly(1,6-hexanediyl isophthalate) and poly(1,6-hexanediyl terephthalate) from the corresponding dimethyl esters by using lipase catalyst, which involved a nitrogen bubbling procedure for the removal of methanol formed during the polymerization.³²

RESULTS AND DISCUSSION

In this study, four monomers containing an aromatic moiety, divinyl isophthalate (**1a**), divinyl terephthalate (**1b**), divinyl *p*-phenylene diacetate (**1c**), and *p*-xylylene glycol (**2a**), were used as new monomer of enzymatic polymerizations.

Enzymatic Polymerization of Divinyl Isophthalate and α,ω -Alkylene Glycols

The polymerization of divinyl isophthalate (**1a**) with 1,6-hexanediol (**2d**) was carried out by using six lipases of different origin as catalyst in heptane at 60°C for 48 h (Table I). The catalysts used were lipases derived from *Candida antarctica* (lipase CA), *Candida cylindracea* (lipase CC), *Mucor miehei* (lipase MM), *Pseudomonas cepacia* (lipase PC), *Pseudomonas fluorescens* (lipase PF), and porcine pancreas (PPL), which showed high catalytic activity for the lactone polymerizations.^{8,13–17} Lipases CA and MM are granular immobilized enzymes and the others are crude powdery ones. In most cases, the monomer was quantitatively consumed, however, the yield was not high due to the loss of the oligomers during the purification procedure. The molecular weight of the polymer was estimated by size exclusion chromatographic (SEC) analysis using tetrahydrofuran (THF) eluent.

Active were lipases CA, MM, PC, and PF for the present polymerization, which also efficiently catalyzed the polymerization of divinyl sebacate (**1d**) and 1,4-butanediol (**2c**).³⁰ On the other hand, no polymeric materials were obtained in using lipase CC and PPL. Lipase CA showed the highest catalytic activity; the yield and molecular weight of the polymer were the largest (entry 1). In the polymerization without enzyme (control experiment), the monomers were recovered unchanged (entry 7). These results indicate that the present polymerization proceeded through the enzyme catalysis and the polymerization behaviors depended on the lipase origin. In the subsequent experiments, therefore, lipase

Table II. Enzymatic polymerization of **1a** and **2**^a

Entry	Glycol	Solvent	Temper- ature	Yield ^b	M_n^c	M_w/M_n^c
			°C	%		
1	2b	Heptane	60	0		
2	2c	Heptane	60	60	1500	1.2
3	2d	Acetonitrile	60	0		
4	2d	Cyclohexane	60	72	5300	1.8
5	2d	Heptane	45	42	2500	1.5
6	2d	Heptane	60	74	5500	1.6
7	2d	Heptane	75	66	4200	1.8
8	2d	Isooctane	60	73	4400	1.7
9	2d	Tetrahydrofuran	60	0		
10	2d	Toluene	60	71	2000	1.4
11	2e	Heptane	60	54	7200	2.1

^a Polymerization of **1a** and **2** (each 1.0 mmol) using lipase CA catalyst (100 mg) in organic solvent (5.0 mL) for 48 h. ^b Methanol-insoluble part. ^c Determined by SEC.

CA is mainly used as catalyst.

The polymer structure was confirmed by ¹H and ¹³C NMR spectroscopies. In all cases, the desired product was obtained and peaks due to the units of the vinyl polymer from **1** were not detected. Besides the main peaks, there were small peaks due to α -methylene moiety of the terminal hydroxyl group: a triplet peak at δ 3.7 in ¹H NMR spectrum and a peak at δ 62 in that of ¹³C NMR. Peaks of the vinyl ester were not observed, suggesting that the hydrolysis of the terminal vinyl ester occurred during the polymerization.

Effects of the polymerization conditions were systematically investigated in the polymerization of divinyl isophthalate and 1,6-hexanediol using lipase CA catalyst (Table II). At first, the polymerization was carried out in various anhydrous organic solvents at 60°C. Hydrocarbons, cyclohexane, heptane, and isooctane, provided the polymer with molecular weight of *ca.* 5×10^3 in good yields (entries 4, 6, and 8), indicating hydrophobic solvents were suitable for the present polymerization. Similar results were obtained in the enzymatic synthesis of aliphatic polyesters from divinyl esters.³⁰ The polymerization in toluene afforded the polymer in a moderate yield, however, the molecular weight of the resulting polymer was relatively low (entry 10). It is to be noted that toluene afforded no polymeric materials from a combination of **1d** and **2c**.³⁰ No polymers were obtained in acetonitrile and THF (entries 3 and 9). This may be due to the inactivation of the enzyme in polar organic solvents.

Polymerization temperature also affected the polymerization results. In the temperature range from 45°C to 75°C (entries 5–7), yield and molecular weight of the polymer were the highest at 60°C (entry 6). These data are in contrast with those in the polymerization of **1d** and **2c**; the polymerization at 45°C afforded the best results.³⁰ This may be due to the difference of the enzymatic reactivity between divinyl esters of aromatic and aliphatic diacids.

Next, effects of the chain length in α,ω -alkylene glycols (**2b–2e**) were examined. The polymerization of ethylene glycol (**2b**) with **1a** did not produce the polymer (entry 1). From 1,4-butanediol (**2c**), 1,6-hexanediol (**2d**), and

Table III. Lipase CA-catalyzed polycondensation of **1b** and **2**^a

Entry	Glycol	Yield ^b	M_n^c	M_w/M_n^c
		%		
1	2b	<5		
2	2c	34 ^d	1100	1.1
3	2d	72	2300	1.3
4	2e	58	2000	1.3

^a Polymerization of **1b** and **2** (each 1.0 mmol) using lipase CA catalyst (100 mg) in diisopropyl ether (5.0 mL) at 60°C for 48 h. ^b Methanol-insoluble part. ^c Determined by SEC. ^d Diethyl ether-insoluble part.

Table IV. Lipase CA-catalyzed polycondensation of **1c** and **2**^a

Entry	Glycol	Yield ^b	M_n^c	M_w/M_n^c
		%		
1	2b	34	1800	1.2
2	2c	43	4400	1.4
3	2d	44	6000	1.4
4	2e	54	5800	1.8

^a Polymerization of **1c** and **2** (each 1.0 mmol) using lipase CA catalyst (100 mg) in heptane (5.0 mL) at 60°C for 48 h. ^b Methanol-insoluble part. ^c Determined by SEC.

1,10-decanediol (**2e**), the polymer formation was observed. The polymer yield was the highest in using **2d** (entry 6) and **2e** afforded the highest molecular weight (entry 11).

Enzymatic Synthesis of Polyesters from Other Aromatic Monomers

Terephthalic acid divinyl ester (**1b**) was also polymerized under the similar reaction conditions of **1a** (Table III). From a combination of **1b** and **2b**, the polymer yield was very low (entry 1), whereas the polymer was obtained from other glycols in moderate yields. The polymer yield was the highest in using **2d** as glycol monomer. A similar tendency was observed in the polymerization using **1a** (Table II). The polymer molecular weight was lower than that from **1a**. This is due to the lower solubility of the polymer having the para-substituted diester structure than that with the meta-substituted structure. Polymer structure was confirmed by ¹H NMR spectroscopy. Besides main peaks of the polyester, there was a characteristic triplet peak at δ 3.7 due to the α -methylene protons of the terminal hydroxy group. No peaks due to the vinyl ester group were detected.

The polymerization of divinyl *p*-phenylene diacetate (**1c**) with glycols proceeded in the presence of lipase CA (Table IV). The polymerization of **1c** and ethylene glycol (**2b**) afforded the polymer with relatively low molecular weight (entry 1), on the other hand, the polymer from **2b** was not obtained in using aromatic diacid divinyl esters (**1a** and **1b**). The larger the methylene chain length of **2**, the higher the polymer yield. In using **2d** as glycol monomer, the highest molecular weight was achieved (entry 3).

Another approach to synthesize aromatic polyesters is use of aromatic diols as monomer. However, lipase-catalyzed polymerization of divinyl sebacate with dihy-

Table V. Lipase CA-catalyzed polycondensation of **1d** and **2a**^a

Entry	Catalyst	Yield ^b	M_n^c	M_w/M_n^c
		%		
1	Lipase CA	41	6200	1.7
2	Lipase MM	61	2600	1.3
3	Lipase PC	74	4000	1.5
4	Lipase PF	72	4200	1.5

^a Polymerization of **1c** and **2** (each 2.0 mmol) using lipase CA catalyst (100 mg) in heptane (5.0 mL) at 75°C for 48 h. ^b Methanol-insoluble part. ^c Determined by SEC.

droxybenzenes, catechol, resorcinol, and hydroquinone, did not take place. Thus, *p*-xylylene glycol (**2a**) was employed as new monomer in the lipase-catalyzed polymerization of **1d** (Table V). Lipases showing the high catalytic activity for the polymerization of **1a** and **2d** (Table I) also afforded the polymer from a combination of **1d** and **2a**. In using *Pseudomonas* family lipases (lipases PC and PF), the polymer yield was high (entries 3 and 4). The polymerization catalyzed by lipase CA produced the polymer of the highest molecular weight (entry 1).

CONCLUSION

Facile synthesis of polyesters having aromatic moiety in the main chain was achieved by the lipase-catalyzed polymerization of divinyl esters and glycols. The aromatic polyesters were synthesized by using new monomers of divinyl isophthalate, divinyl terephthalate, divinyl *p*-phenylene diacetate, and *p*-xylylene glycol under mild reaction conditions. In most cases, *Candida antarctica* lipase showed the high catalytic activity for the present polymerization to give the polymers with the molecular weight of several thousands.

Further investigations on enzymatic synthesis of polyesters from other vinyl ester monomers are under way in our laboratory.

EXPERIMENTAL

Materials

Divinyl sebacate (**1d**) was kindly donated by Shin-etsu Chemical Co. Lipases CA and MM were gifts from Novo Nordisk Bioindustry, Ltd. Lipase CC and PPL were purchased from Biocatalysts, Ltd. and Sigma Chemical Co., respectively. Lipases PC and PF were donated by Amano Pharmaceutical Co. These enzyme catalysts were used as received. Liquid monomers and polymerization solvents were stored over freshly activated type 4 molecular sieves. Other reagents were used without further purification.

Preparation of Divinyl Isophthalate³³

A mixture of isophthalic acid (15 g, 90 mmol), vinyl acetate (39 g, 450 mmol), palladium (II) acetate (1.0 g, 4.5 mmol), and potassium acetate (0.88 g, 9.0 mmol) was dissolved in 60 mL of *N,N*-dimethylformamide (DMF). The mixture was stirred at 45°C for 24 h under argon. The reaction mixture was filtrated through Celite, followed by concentration of the filtrate under reduced

pressure. The product was purified by sublimation at 80°C under 400 Pa, yielding 8.2 g of divinyl isophthalate (yield 42%). ^1H NMR (CDCl_3) δ 4.8 and 5.2 (d, $\text{CH}_2=\text{CHO}$ -, 4H), 7.5 (q, $\text{CH}_2=\text{CHO}$ -, 2H), 7.6, 8.3, 8.8 (Ar, 4H).

Terephthalic acid and *p*-phenylene diacetic acid divinyl esters were synthesized by the similar procedure.

Lipase-Catalyzed Polymerization of Dicarboxylic Acid Divinyl Esters and Glycols

A typical run was as follows (entry 1 in Table I). Divinyl isophthalate (0.22 g, 1.0 mmol) and 1,6-hexanediol (0.12 g, 1.0 mmol) in 5.0 mL of heptane were placed in a dried test tube. Lipase CA (100 mg) was added and the mixture was gently stirred at 60°C. After 48 h, 30 mL of chloroform was added to the reaction mixture. The lipase was removed by filtration and the filtrate was concentrated by evaporation under reduced pressure. A small amount of chloroform was added to the residue and the solution was poured into a large amount of methanol. The resulting precipitates were separated by filtration, following by drying *in vacuo* to give the polymer (0.18 g, 74% yield). ^1H NMR (CDCl_3) δ 1.5 (b, $\text{OCH}_2\text{CH}_2\text{CH}_2$, 4H), 1.8 (b, OCH_2CH_2 , 4H), 4.3 (b, OCH_2 , 4H), 7.5, 8.1, 8.6 (Ar, 4H).

^1H NMR of polymer from **1b** and **2c** (CDCl_3) δ 1.5 (b, $\text{OCH}_2\text{CH}_2\text{CH}_2$, 4H), 1.8 (b, OCH_2CH_2 , 4H), 4.3 (b, OCH_2 , 4H), 8.1 (b, Ar, 4H).

Measurements

SEC analysis was carried out using a Tosoh SC8010 apparatus with a refractive index (RI) detector under the following conditions: TSKgel G3000H_{HR} column and THF eluent at a flow rate of 1.0 mL min⁻¹. The calibration curves for SEC analysis were obtained using polystyrene standards. NMR spectra were recorded on a 270 MHz JEOL JNM-EX270J spectrometer.

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