

## Synthesis of Aliphatic Polyester by Insertion of Glycols into Polyanhydrides Using Lipase Catalyst

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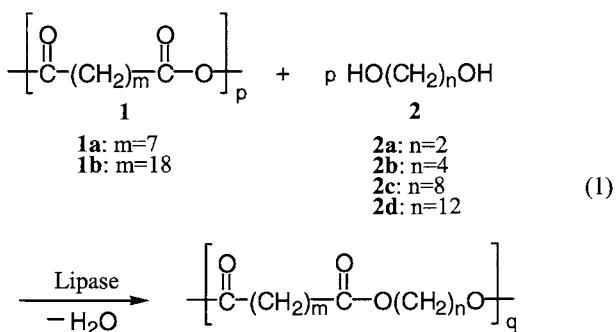
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Polyester synthesis was carried out by insertion-dehydration of glycols into polyanhydrides using *Candida antarctica* lipase as catalyst. The insertion of 1,8-octanediol into poly(azelaic anhydride) took place under mild reaction conditions to give the corresponding polyester with molecular weight of several thousands.

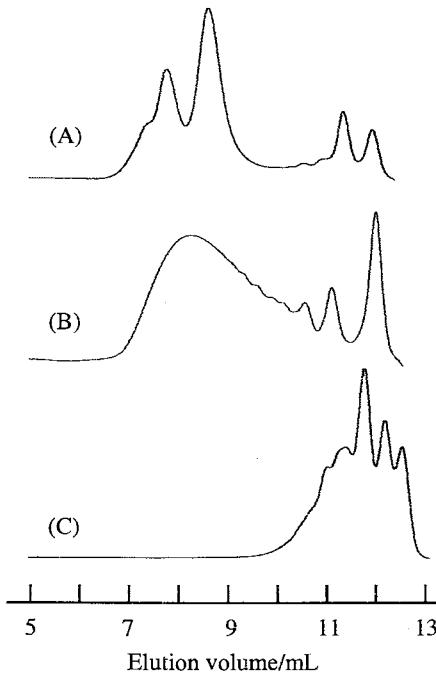
Recently, there has been much interest in polyester syntheses catalyzed by isolated enzymes as environmentally benign processes of plastics production under mild reaction conditions.<sup>1-3</sup> So far, various monomer combinations have been reported; a combination of dicarboxylic acids or their esters and glycols,<sup>4,5</sup> oxyacids or their esters,<sup>6</sup> lactones,<sup>6-10</sup> and lactide.<sup>11</sup>

We have reported that the polymerization of succinic anhydride and  $\alpha,\omega$ -glycols using *Pseudomonas fluorescens* lipase as catalyst proceeded at room temperature.<sup>12</sup> This means that anhydride derivatives can be good candidates as starting materials for enzymatic synthesis of polyesters.

Polyanhydrides exhibit biodegradability<sup>13</sup> and some of them are industrially manufactured as crosslinking agent for epoxy resins. This study deals with polyester synthesis by insertion of  $\alpha,\omega$ -glycols into polyanhydrides using lipase as catalyst (Eq. 1). The enzyme catalysis induced the polyester synthesis under mild reaction. Relevant to this study, a chemical insertion of oxirane derivatives into polyanhydrides was recently reported; however, the severe conditions such as high temperature (100 °C) and long reaction time (24 h) are required to complete the reaction and the polymer structure was limited as 1,2-glycol unit.<sup>14</sup>



In this study, *Candida antarctica* lipase (lipase CA) was used as catalyst, which showed very high catalytic activity toward ring-opening polymerization of lactones<sup>15</sup> and polycondensation of dicarboxylic acids or their esters with glycols.<sup>16,17</sup> At first, the insertion reaction of 1,8-octanediol (**2c**) into poly(azelaic anhydride) (**1a**) was carried out at 60 °C in toluene for 4 h.<sup>18</sup> **1a** is of technical grade and has a multimodal peak pattern in the size exclusion chromatography (SEC) chart (Figure 1(A)). Peak-top molecular weight values of



**Figure 1.** SEC traces of (A) **1a**, (B) the polymer obtained from **1a** and **2c** using lipase CA catalyst in toluene at 60 °C for 4 h, and (C) the product without the enzyme.

two peaks in the region of low elution volume (6-9 mL) were  $1.7 \times 10^4$  and  $6.7 \times 10^3$ .

In the SEC chart of the resulting product obtained by using lipase CA as catalyst (before purification) (Figure 1(B)), a large peak of the polymer as well as several oligomer peaks were observed. In the IR spectrum, a characteristic peak ascribed to the carbonyl vibration of acid anhydride of **1a** at  $1822\text{ cm}^{-1}$  completely disappeared and a characteristic strong peak due to the  $\text{C}=\text{O}$  vibration of ester group newly appeared at  $1734\text{ cm}^{-1}$ . In the  $^1\text{H}$  NMR spectrum, observed were a large triplet peak at  $\delta$  4.1 due to  $\text{CH}_2\text{OC(=O)}$  and a very small triplet peak at  $\delta$  3.7 ascribed to  $\alpha$ -methylene protons of alcohol. These data indicate that the insertion took place quantitatively to give the corresponding polyester. By reprecipitation procedure (tetrahydrofuran (THF) as good solvent; methanol as poor solvent), the polymer was isolated in 54% yield. The number-average molecular weight and its index were 5800 and 1.6, respectively.

In case of the reaction without lipase (control experiment), peaks were found only in the oligomer region (molecular weight less than 1000) of the SEC chart (Figure 1(C)). There were three strong peaks at 1741 and 1707  $\text{cm}^{-1}$  in the IR spectrum, which were ascribed to the carbonyl vibration of

**Table 1.** Polyester synthesis by insertion of glycols into polyanhydrides using lipase catalyst<sup>a</sup>

Entry	Polyanhydride	Glycol	Temp./°C	Solvent	Yield/% <sup>b</sup>	$M_n/x10^{-3}$ <sup>c</sup>	$M_w/M_n$ <sup>c</sup>
1	<b>1a</b>	<b>2a</b>	60	Bulk	21 <sup>d</sup>	1.2	1.2
2	<b>1a</b>	<b>2b</b>	60	Bulk	25 <sup>d</sup>	1.7	1.3
3	<b>1a</b>	<b>2c</b>	30	Toluene	39	3.4	1.3
4	<b>1a</b>	<b>2c</b>	45	Toluene	39	5.9	1.4
5	<b>1a</b>	<b>2c</b>	60	Bulk	58	5.9	1.5
6	<b>1a</b>	<b>2c</b>	60	Toluene	54	5.8	1.6
7 <sup>e</sup>	<b>1a</b>	<b>2c</b>	60	Toluene	0		
8	<b>1a</b>	<b>2d</b>	60	Bulk	24	3.9	1.4
9	<b>1a</b>	<b>2d</b>	60	Toluene	81	5.0	1.7
10	<b>1b</b>	<b>2c</b>	60	Bulk	82	6.2	1.3

<sup>a</sup>Insertion of monomers (2.0 mmol each) using lipase catalyst (50 mg) for 4 h under argon. <sup>b</sup>Methanol-insoluble part. <sup>c</sup>Determined by SEC using THF eluent. <sup>d</sup>Methanol/water (50:50 vol%)-insoluble part. <sup>e</sup>Without catalyst.

ester and carboxylic acid moieties, respectively. These data imply that the thermal reaction of acid anhydride and alcohol occurred, resulting in the formation of the ester and carboxylic acid groups. Methanol-insoluble part was not formed without the enzyme.

The above results clearly showed that the lipase catalysis afforded the polyester from combination of a polyanhydride and a glycol. Under the similar reaction conditions, the polymerization of azelaic acid and 1,8-octanediol produced the polymer with lower molecular weight ( $M_n=4210$ ) in a lower yield (36%), suggesting that the polyanhydride was superior to the corresponding diacid monomer as starting material for the enzymatic synthesis of polyesters.

Polymerization results are summarized in Table 1. The insertion proceeded even at 30 °C (entry 3), although the yield and molecular weight were lower than those at 60 °C (entry 6). The polymerization of **1a** and **2c** also proceeded in bulk (entry 5) and the polymerization behavior was similar to that in toluene.

The effects of the chain length of the monomers were examined. As for the bulk polymerization of **1a** with glycols (**2**) of different chain length in bulk, **2c** afforded the highest yield and molecular weight. In case of **2d**, the yield greatly improved by use of the toluene solvent (entry 9). The combination of poly(eicosanedioic anhydride) (**1b**) (mol. wt. =  $1.6 \times 10^3$ ) and **2c** produced the polymer in a high yield (entry 10).

In conclusion, the reaction of polyanhydrides and glycols took place in the presence of lipase catalyst under mild reaction conditions to give the aliphatic polyesters. The polyanhydride was superior to the corresponding diacid monomer as monomer of the lipase-catalyzed polymerization. Further investigations on the synthesis of functional polyesters from polyanhydrides are now under way in our laboratory.

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- 18 A typical run was as follows (entry 6 in Table 1). A mixture of 0.34 g (2.0 mmol of monomer unit), 0.29 g of 1,8-octanediol (2.0 mmol), and 0.050 g of lipase CA in 10 mL of toluene were placed in a dried tube under argon and sealed. The tube was kept under gentle stirring at 60 °C. After 4 h, the part of the organic solution was separated by filtration. The filtrate was concentrated under reduced pressure and the residue was poured into a large amount of methanol. The resulting precipitates were collected by centrifugation, followed by drying in vacuo to give 0.33 g of the polymer (yield 54%).