Lipase-Catalyzed Ring-Opening Polymerization of Cyclic Diesters

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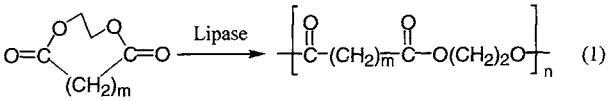
Ring-opening polymerization of cyclic diesters, ethylene dodecanedioate and ethylene tridecanedioate, took place using lipases as a catalyst under mild reaction conditions to give the corresponding polyesters with molecular weight of several thousands. Enzymatic polymerizability of these new monomers was compared with that of lactones.

Recently, polyester syntheses catalyzed by isolated enzymes have received much attention as environmentally benign synthetic processes of biodegradable plastics under mild reaction conditions.[1-4] Hitherto, polyesters were enzymatically synthesized from various monomer combinations,[5-16] and among them, the enzymatic polymerization of lactones has been extensively studied.[9-16]

Ring strain of macrocyclic lactones (macrolides) is very small, therefore, they showed lower anionic polymerizability than ε-caprolactone (ε-CL, a 7-membered lactone). On the other hand, the polymerization of the macrolides proceeded much faster than that of ε-CL using *Pseudomonas* family lipases as catalyst.[11,16] This is probably because lipase catalyst recognizes the macrolides more strongly than ε-CL.

Various lactones (cyclic monoesters) have been found to be polymerized by chemical and enzyme catalysts. However, there were only a few reports on the polymerization of cyclic diesters: systematic study on the copolymerization of ethylene dodecanedioate (**1a**) (a 16-membered diester) or ethylene tridecanedioate (**1b**) (a 17-membered diester) with β-butyrolactone by tin catalyst[17] and demonstration of one example of 1,4,7-trioxa-cyclotridecane-8,13-dione polymerization catalyzed by lipase.[18] In this study, we have first used **1a** and **1b** as a new monomer for the enzymatic polymerization and compared their polymerizability with that of lactones (Eq. 1).



(1)

1a: m=10
1b: m=11

Commercially available lipases of different origin were used as catalyst: lipases derived from *Candida antarctica* (lipase CA), *Pseudomonas cepacia* (lipase PC), *Pseudomonas fluorescens* (lipase PF), and porcine pancreas (PPL). These lipases showed high catalytic activity toward ring-opening polymerization of lactones.[9-16] The polymerization of **1** was performed in bulk under an argon atmosphere. The molecular weight of polymers obtained was determined by size exclusion chromatography (SEC).

Polymerization results are summarized in Table 1. As to the polymerization at 60 °C for 6 or 24 h, lipase CA was the most active as catalyst for both monomers; the monomer conversion was the largest (entries 2 and 10). *Pseudomonas* family lipases (lipases PC and PF) showed relatively high catalytic activity (entries 3, 4, 13, and 15), whereas the polymerization catalyzed by PPL proceeded much slower to give the polymer of lower molecular weight (entries 5 and 16). In the polymerization

Table 1. Ring-opening polymerization of cyclic diesters using various lipase catalysts[a]

Entry	Monomer	Catalyst	Temp./°C	Time/h	Conv./% [b]	M_n/x10^{-3} [b]	M_w/M_n [b]
1	**1a**	Lipase CA	60	1	51	2.4	1.8
2	**1a**	Lipase CA	60	6	97	4.1	2.4
3	**1a**	Lipase PC	60	6	72	2.7	2.0
4	**1a**	Lipase PF	60	6	64	2.6	1.9
5	**1a**	PPL	60	24	15	1.8	1.5
6	**1a**	---[c]	60	24	0		
7	**1b**	Lipase CA	45	24	77	2.5	2.3
8	**1b**	Lipase CA	60	1	60	3.6	1.9
9	**1b**	Lipase CA	60	6	91	3.5	2.3
10	**1b**	Lipase CA	60	24	92	2.8	1.9
11	**1b**	Lipase CA	75	24	96	4.1	2.2
12	**1b**	Lipase PC	45	24	75	1.8	1.9
13	**1b**	Lipase PC	60	6	75	3.9	2.1
14	**1b**	Lipase PF	45	24	54	2.0	2.0
15	**1b**	Lipase PF	60	6	83	3.5	2.0
16	**1b**	PPL	60	24	17	1.5	1.1
17	**1b**	---[c]	60	24	0		

[a]Polymerization of cyclic diester (1.0 mmol) using lipase catalyst (50 mg) in bulk under an argon atmosphere. [b]Determined by SEC using chloroform eluent. [c]Without enzyme.

Table 2. Comparison of enzymatic polymerizability between lactones and cyclic diesters[a]

	Lipase CA				Lipase PC			
Monomer	Time/h	Conv./% [b]	M_n/x10^{-3} [b]	M_w/M_n [b]	Time/h	Conv./% [b]	M_n/x10^{-3} [b]	M_w/M_n [b]
1a	1	51	2.4	1.8	6	72	2.7	2.0
1b	1	60	3.6	1.9	6	75	3.9	2.1
ε-CL	1	87	4.1	2.4	6	<3		
DDL	1	17	4.9	2.0	6	24	3.9	1.9

[a]Polymerization of monomer (1.0 mmol) using lipase catalyst (50 mg) in bulk under an argon atmosphere. [b]Determined by SEC using chloroform eluent.

without lipase (control experiment), the monomer was recovered unchanged (entries 6 and 17), indicating that the present polymerization took place via the lipase catalysis.

Effects of temperature were examined using **1b** monomer. The polymerization proceeded even at 45 °C using lipase CA, PC or PF catalyst. The polymerization rate and molecular weight were lower than those at 60 °C. In the lipase CA-catalyzed polymerization of **1b** at 60 °C, the molecular weight initially increased with time, and afterwards, the molecular weight decreased (entries 8-10). This may be because the hydrolysis of the polymer chain also took place during the polymerization. A similar behavior was observed in the lipase CA-catalyzed polymerization of ε-CL.[19]

The enzymatic polymerizability of **1** was compared with that of ε-CL or 12-dodecanolide (a 13-membered lactone, DDL) (Table 2). Both lactones polymerized in the presence of lipase and their polymerizability depended on the lipase origin; in using lipase CA as catalyst, ε-CL polymerized much faster than DDL, whereas the reverse tendency was observed in the case of lipase PC.

When lipase CA was used as catalyst, the reactivity of **1** was in the middle of ε-CL and DDL. Interestingly, the conversion of **1** using lipase PC as catalyst was much larger than that of the monocyclic lactones under the similar conditions. These data indicate that the cyclic diester monomers showed high enzymatic polymerizability and the lipase origin greatly affected the polymerization behaviors.

The structure of the polymer from **1** was the same as that from dicarboxylic acids (or their derivatives) and ethylene glycol. We have reported that divinyl esters of dicarboxylic acids were reactive monomers for the enzymatic polycondensation,[6,20] however, the polymer yield was low in the combination of the divinyl ester and ethylene glycol.[20] This may be due to the low enzymatic reactivity of ethylene glycol and/or the low solubility of ethylene glycol toward the medium. On the other hand, the present cyclic diesters were enzymatically converted into the corresponding polyesters in high yields under the mild reaction conditions, suggesting that **1** was superior to the combination of the divinyl ester and ethylene glycol for the enzymatic synthesis of polyesters.

In conclusion, cyclic diesters, ethylene dodecanedioate and ethylene tridecanedioate, were polymerized through the lipase catalysis to give the corresponding polyesters in high yields. Further investigations on the enzymatic synthesis of polyesters from other cyclic diesters are now under way in our laboratory.

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References and Notes

1 S. Kobayashi, S. Shoda, and H. Uyama, "Catalysis in Precision Polymerization," ed by S. Kobayashi, John Wiley & Sons, Chichester (1997), Chap. 8.
2 S. Kobayashi, S. Shoda, and H. Uyama, *Adv. Polym. Sci.*, **121**, 1 (1995).
3 R. A. Gross, D. L. Kaplan, and G. Swift, *ACS Symp. Ser.*, **684** (1998).
4 S. Kobayashi and H. Uyama, "Materials Science and Technology - Synthesis of Polymers," ed by A.-D. Schlüter, Wiley-VCH, Weinheim (1998), Chap. 16.
5 J. S. Wallace and C. J. Morrow, *J. Polym. Sci., Polym. Chem. Ed.*, **27**, 2553 (1989).
6 H. Uyama and S. Kobayashi, *Chem. Lett.*, **1994**, 1687.
7 S. Kobayashi and H. Uyama, *Makromol. Chem., Rapid Commun.*, **14**, 841 (1993).
8 H. Uyama, K. Inada, and S. Kobayashi, *Chem. Lett.*, **1998**, 1285.
9 D. Knani, A. L., Gutman, and D. H. Kohn, *J. Polym. Sci., Polym. Chem. Ed.*, **31**, 1221 (1993).
10 H. Uyama and S. Kobayashi, *Chem. Lett.*, **1993**, 1149.
11 H. Uyama, K. Takeya, N. Hoshi, and S. Kobayashi, *Macromolecules*, **28**, 7046 (1995).
12 R. T. MacDonald, S. K. Pulapura, Y. Y. Svirkin, R. A. Gross, D. L. Kaplan, J. A. Akkara, G. Swift, and S. Wolk, *Macromolecules*, **28**, 73 (1995).
13 W. Wie, J. Li, D. Chen, and P. G. Wang, *Macromolecules*, **30**, 6997 (1997).
14 H. Uyama, S. Suda, H. Kikuchi, and S. Kobayashi, *Chem. Lett.*, **1997**, 1109.
15 K. S. Bisht, Y. Y. Svirkin, L. A. Henderson, R. A. Gross, D. L. Kaplan, and G. Swift, *Macromolecules*, **30**, 7735 (1997).
16 S. Kobayashi, H. Uyama, S. Namekawa, and H. Hayakawa, *Macromolecules*, **31**, 5655 (1998).
17 Y. Hori, H. Hongo, and T. Hagiwara, *Macromolecules*, **32**, 3537 (1999).
18 F. Binns and A. Taylor, *Tetrahedron*, **47**, 12929 (1995).
19 S. Kobayashi, K. Takeya, S. Suda, and H. Uyama, *Macromol. Chem. Phys.*, **199**, 1729 (1998).
20 H. Uyama, S. Yaguchi, and S. Kobayashi, *J. Polym. Sci., Polym. Chem. Ed.*, **37**, 2737 (1999).