Enzymatic Polymerization of Dicarboxylic Acid and Glycol to Polyester in Solvent-Free System

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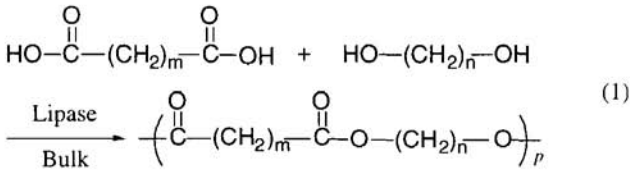
Candida antarctica lipase induced polymerization of a dicarboxylic acid and glycol in a solvent-free system, despite the heterogeneous mixture of the monomers and catalyst. The chain length of the monomers strongly affected the yield and molecular weight of the product polyester.

Recently, polyester syntheses using isolated enzymes as catalyst have received much attention as environmentally benign processes of plastics production under mild reaction conditions.[1-3] So far, various monomer combinations have been reported; a combination of dicarboxylic acids or their esters and glycols,[4-7] oxyacids or their esters,[8] lactones,[8-15] and lactide.[16] In case of the liquid monomers, the polymerization proceeded even without solvent to give the corresponding polyesters. In using the solid monomer, on the other hand, the polymerization was often carried out in organic solvents, probably to avoid the immiscibility of the monomers. Very recently, we have found that polyester synthesis in water was achieved by the lipase-catalyzed polymerization of solid dicarboxylic acids and glycols showing the very low solubility toward water,[17] in which the dehydration took place in the aqueous medium.

Protease-catalyzed peptide synthesis in the solid form of substrates and products was reported to be successfully carried out by the addition of a small amount of organic solvents.[18] This encourages us to perform the enzymatic polyester synthesis from the heterogeneous mixture of monomers in a solvent-free system. Here, we demonstrate the lipase-catalyzed polymerization of dicarboxylic acids and glycols without solvents (Eq. 1).[19] The catalyst lipase and dicarboxylic acids were solid at the polymerization temperature and glycols were solid or liquid depending on the chain length.



(1)

The polymerization was carried out at 60 ℃ by using lipase as catalyst in bulk or diisopropyl ether.[20] At first, enzyme activity was screened by using a combination of sebacic acid and 1,4-butanediol monomers. Lipases used were derived from *Candida antarctica* (lipase CA), *Mucor miehei* (lipase MM), *Pseudomonas cepacia* (lipase PC), *Pseudomonas fluorescens* (lipase PF), and porcine pancreas (PPL),[21] all of which showed high catalytic activities for lactone polymerizations.[9-13] Among these, only lipase CA produced the polymer in bulk as well as diisopropyl ether in the present study. The yield and molecular weight of the polymer (methanol-insoluble part) obtained for 8 h in bulk were 56% and 3800, respectively, which were higher than those obtained in diisopropyl ether (yield = 34%; molecular weight = 2000). Lipases MM and PC afforded the polymer in the organic solvent, however, the polymer formation was not observed in bulk by using the lipase catalysts except lipase CA. These results indicate that lipase CA was highly efficient as catalyst for the polycondensation in the solvent-free system.

Table 1 summarizes results of the polymerization of sebacic acid and 1,4-butanediol catalyzed by lipase CA. The polymerization at 60 ℃ for 2 h produced the polymer with molecular weight of 2700 in 21% yield (entry 1). Beyond 2 h of the reaction time (4, 8, and 24 h), the yield and molecular weight were not so different (entries 2, 4, and 7). These data show that the present polymerization proceeded relatively fast, despite the initial heterogeneous mixture of the substrates. In case of the lower temperature (entry 3), the yield and molecular weight decreased in comparison of those at 60 ℃. The data of the polymerization at 70 ℃ (entry 6) were almost the same as those at 60 ℃. Both monomers were recovered unchanged in the absence of enzyme (control experiment) (entry 5), indicating that the present polymerization proceeded through enzyme catalysis.

Table 1. Lipase-catalyzed polymerization of sebacic acid and 1,4-butanediol in solvent-free system[a]

Entry	Time/h	Temp./℃	Yield/%[b]	M_n/x10^{-3}[c]	M_w/M_n[c]
1	2	60	21	2.7	1.2
2	4	60	59	3.0	1.3
3	8	50	28	2.3	1.2
4	8	60	56	3.8	1.3
5[d]	8	60	0		
6	8	70	55	3.3	1.5
7	24	60	63	3.4	1.3

[a]Polymerization of monomers (2.0 mmol each) using lipase CA catalyst (100 mg) under argon. At the polymerization temperature, sebacic acid was solid and 1,4-butanediol was liquid. [b]Methanol-insoluble part. [c]Determined by SEC using tetrahydrofuran eluent. [d]Without catalyst.

The polymerization was performed using other alkylene dioic acids and glycols with different chain length in the presence of lipase CA (Table 2). In the case of hydrophilic dicarboxylic acids, succinic and adipic acids, the polymer yield was low (entries 1 and 2). The polymerization using ethylene glycol also gave the polymer in a lower yield (entry 3) than that by 1,4-butanediol. These data indicate that the hydrophilic monomer was not preferable to the present polymerization.

The yield and molecular weight of the polymer from 1,14-tetradecanedioic acid and 1,4-butanediol (entry 8) were lower than those using sebacic acid as diacid monomer. In using sebacic acid as diacid monomer in the polymerization at 60 ℃, 1,8-octanediol afforded the highest yield among the glycols examined (entry 5). From these data, the combination of the monomers with appropriate hydrophobicity was favored for the polymer formation.

No polymer formation was observed in the polymerization

Table 2. Lipase-catalyzed polymerization of dicarboxylic acids and glycols with different chain length in solvent-free system[a]

Entry	Monomers[b] m	n	Yield/%[c]	M_n/x10^{-3}[d]	M_w/M_n[d]
1	2 (S)	4 (L)	3	1.7	1.5
2	4 (S)	4 (L)	8	2.9	1.2
3	8 (S)	2 (L)	20	1.7	1.2
4	8 (S)	4 (L)	56	3.8	1.3
5	8 (S)	8 (L-S)[e]	73	3.8	1.5
6	8 (S)	12 (S)	0		
7[f]	8 (S)	12 (S)	87	4.8	1.7
8	12 (S)	4 (L)	42	1.9	1.3

[a]Polymerization of monomers (2.0 mmol each) using lipase CA catalyst (100 mg) at 60 °C for 8 h under argon. [b]In parenthesis, the state of monomers at the polymerization temperature; S: solid, L: liquid. [c]Methanol-insoluble part. [d]Determined by SEC using tetrahydrofuran eluent. [e]Melting point of 1,8-octanediol: 59-61 °C. [f]Polymerization temperature: 70 °C.

of sebacic acid and 1,12-dodecanediol at 60 °C (entry 6), in which both monomers were solid under the polymerization conditions; melting points of sebacic acid and 1,12-dodecanediol are 135 and 82 °C, respectively. Interestingly, the polymerization at 70 °C produced the polymer in a high yield (entry 7), although the reaction temperature was below the melting point of both monomers. This may be because 1,12-dodecanediol is mobile for the occurrence of the polymerization at the temperature close to its melting point.

In conclusion, the enzymatic polymerization of the dicarboxylic acid and glycol proceeded in a solvent-free system to produce the polyester despite the initial heterogeneous mixture of the substrates. The polymerization behaviors strongly depended on the chain length of both monomers, i.e., on the hydrophobicity of the monomers. The polymerization in solvent-free system afforded aliphatic polyesters from various monomer combinations by using a naturally-occuring lipase enzyme as catalyst without organic solvents under mild reaction conditions. Therefore, the present enzymatic polymerization has a large potential as an environmentally friendly synthetic process of polymeric materials.

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20 A typical run was as follows (entry 4 in Table 1). A mixture of 0.41 g (2.0 mmol) of sebacic acid, 0.18 g of 1,4-butanediol, and 0.10 g of lipase CA were placed in a dried tube under argon and sealed. The tube was kept under gentle stirring at 60 °C for 8 h. A small amount of chloroform was added to the mixture and the part of the organic solution was separated by filtration. The filtrate was poured into a large amount of methanol. The resulting precipitates were collected by centrifugation, followed by drying in vacuo to give 0.29 g of the polymer (yield 56%).
21 Lipases CA and MM are immobilized enzymes on polymer beads, which were donated by Novo Nordisk Bioindustry, Ltd. Other lipases were powdery enzymes. Lipases PC and PF were gifts from Amano Pharmaceutical Co. and PPL was purchased from Sigma Chemical Co.