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Enzymatic Ring-Opening Polymerization of Lactones Catalyzed by Lipase

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Enzymatic ring-opening polymerization of lactones was achieved by using lipase as catalyst. The polymerization of ε-caprolactone by *Pseudomonas fluorescens* lipase at 60 ℃ in bulk for 10 days afforded a polyester with average molecular weight of 7.0×10^3. From ^1H and ^{13}C NMR analysis, the polymer possesses the terminal structure of a carboxylic acid group at one end and a hydroxyl group at the other.

Organic reactions by enzyme catalysts have been extensively studied because of high substrate specificity and enantioselectivity.[1] By utilizing such specific properties of enzymes, a polymerization catalyzed by enzymes (*enzymatic polymerization*) has much potential for synthesis of new functional polymers. However, there have been a few reports on enzymatic polymerizations, and moreover, the enzymatic catalysis has not been utilized fully in the polymerization chemistry.[2] Recently, cellulose was successfully synthesized for the first time via a non-biosynthetic path by enzymatic polymerization of β-D-cellobiosyl fluoride monomer using cellulase as catalyst.[3] Further, we reported a new type of enzymatic polymerization; an oxidation polymerization of *o*-phenylenediamine catalyzed by horseradish peroxidase produced a polymer consisting of iminophenylene unit,[4] which is unable to be obtained by a conventional oxidation polymerization. Almost all the enzymatic polymerizations hitherto reported were of polycondensation type. In this study, we have broadened the scope of *enzymatic polymerization* to ring-opening polymerization of lactones by lipase catalyst.[5]

The polymerization of lactones was carried out in bulk for 10 days. In this study, ε-caprolactone (ε-CL) and δ-valerolactone (δ-VL) were employed as a monomer and lipase enzymes used were derived from *Pseudomonas fluorescens* (lipase P), *Candida cylindracea* (lipase B), and porcine pancreas (PPL). Polymerizations gave a corresponding ring-opened type polyester from ε-CL and δ-VL, respectively (Table 1). All the enzymes examined were effective for the polymerization of ε-CL. Among them, lipase P afforded the

polyester of higher molecular weight in a better yield.

The effect of the temperature on the polymerization of ε-CL was examined (Entries 1 and 4-6). The higher the polymerization temperature, the higher the monomer conversion and the molecular weight of the polymer. Lipase P was also effective for the polymerization of δ-VL (Entries 7 and 8). The rate of the monomer conversion was larger than that of ε-CL, however the molecular weight of the polymer was lower.

Table 1. Enzymatic polymerzation of lactones catalyzed by lipase[a)]

Entry	Lactone	Enzyme	Temp (°C)	Conv. (%)	M_n[b)] (x10^{-3})	M_w/M_n[b)]
1	ε-CL	lipase P	60	85	7.0	2.2
2	ε-CL	lipase B	60	75	3.3	2.5
3	ε-CL	PPL	60	69	2.5	1.9
4	ε-CL	lipase P	30	8	1.1	1.4
5	ε-CL	lipase P	45	40	3.4	2.5
6	ε-CL	lipase P	75	92	7.7	2.4
7	δ-VL	lipase P	45	95	1.6	2.4
8	δ-VL	lipase P	60	95	1.9	3.0

a) Polymerization of lactone (1 mmol) by lipase (50 mg) in bulk for 10 days. b) Determined by GPC.

In order to examine the structure of terminal groups, ^{13}C and ^{1}H NMR analysis of the polymer (Entry 1) was performed. ^{13}C NMR spectrum of poly(ε-CL) shows three small characteristic peaks besides main peaks due to the carbons of poly(ε-CL); peaks at δ 177, 32, and 62 ascribable to the carbon of carboxylic acid group, the carbon adjacent to the carboxylic acid group, and the α-carbon of hydroxyl group, respectively. In the ^{1}H NMR spectrum, a small triplet peak at δ 3.5 due to the α-methylene protons of the hydroxyl group is observed in addition to the main peaks of poly(ε-CL). From the integrated area of the peaks due to the α-methylene protons of the hydroxyl group and to $C(=O)OCH_2C$ (δ 4.0) of the polymer main-chain, the molecular weight of the polymer was calculated as $7.1x10^3$, which is close to that determined by GPC. These data support the terminal structure of the polymer having a carboxylic acid group at one end and a hydroxyl group at the other.

Further investigations including the mechanism of the present polymerization are now in progress.

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