Regioselective Polymerization of Sorbitol and Divinyl Sebacate Using Lipase Catalyst

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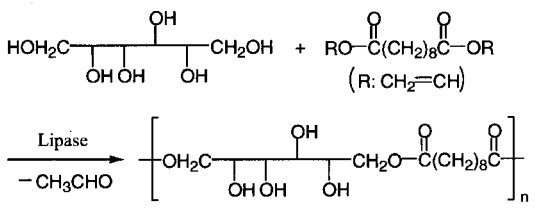
A sugar-containing polyester was synthesized by the polymerization of sorbitol and divinyl sebacate using *Candida antarctica* lipase as catalyst in acetonitrile. NMR analysis showed that sorbitol was regioselectively acylated at 1- and 6-positions.

Lipase-catalyzed polymerizations provide an environmentally friendly methodology of polyester syntheses owing to nontoxic nature of enzyme and mild reaction conditions.[1–7] Various monomer combinations have been developed for enzymatic synthesis of polyesters; dicarboxylic acids or their derivatives/glycols, oxyacids, oxyacid esters, lactones, and lactides.

We reported that divinyl dicarboxylates were effective monomers for the enzymatic polymerization.[8,9] The lipase-catalyzed polycondensation of divinyl adipate with glycols took place under mild conditions to produce polyesters with molecular weight of higher than ten thousands, however, the polymer formation was not observed from adipic acid or diethyl adipate under the similar reaction conditions. Lipase induced the regioselective polymerization of divinyl sebacate and glycerol to give a soluble polymer of relatively high molecular weight and NMR analysis showed that 1,3-diglyceride was a main unit and the branching unit (triglyceride) was contained in the resulting polymer.[10]

Synthetic sugar-containing polymers with well-defined structure have much potential for biocompatible and biodegradable polymeric materials. However, tedious blocking/deblocking steps are often required for their synthesis, since sugars contain multiple hydroxyl functionalities. Protease catalyzed the regioselective polymerization of sucrose and activated diacid derivatives to give the polymer having ester linkages at the C6 and C1' positions on the sucrose, in which much amount of the catalyst load (1 g of protease per 1 mmol of substrate) and long reaction time (7–25 days) are required.[11,12]

This study deals with enzymatic synthesis of a sugar-based polyester by a regioselective polymerization of sorbitol and divinyl sebacate (Eq 1). This is the first example using a sugar alcohol as monomer of the enzymatic polymerizations.



(1)

In this study, lipase derived from *Candida antarctica* was used as catalyst, which showed high catalytic activity toward ring-opening polymerization of lactones,[13–15] polycondensation of divinyl esters and glycols,[9] and polycarbonate synthesis from diethyl carbonate.[16] First, the polymerization was carried out in acetonitrile at 60 °C for 72 h.[17] The polymer (water-insoluble part) was obtained in 64% and the number-average molecular weight and its index of the polymer, determined by size exclusion chromatography (SEC), were 9.8×10^3 and 2.1, respectively. The polymer was soluble in *N*,*N*-dimethylformamide and dimethyl sulfoxide, and insoluble in acetone, chloroform, methanol, toluene, and water.

The polymer structure was confirmed by ^{1}H and ^{13}C NMR spectroscopies. ^{1}H NMR spectrum shows broad multiplet peaks at δ 3.2–4.9 due to protons derived from sorbitol moiety, a broad peak at δ 2.3 ascribed to $CH_2C(=O)O$, a broad peak at δ 1.6 due to $CH_2CH_2C(=O)O$, and a broad peak at δ 1.3 ascribed to $CH_2CH_2CH_2CH_2C(=O)O$. In the ^{13}C NMR chart, observed were two peaks between δ 173.6 and 175.0 due to carbonyl carbon of sebacate, peaks between δ 66.2–71.5 due to methylene and methine carbons from sorbitol, a peak at δ 34.0 ascribed to $CH_2C(=O)O$, a peak at δ 29.1 due to $CH_2CH_2CH_2CH_2C(=O)O$, and a peak at δ 24.9 ascribed to $CH_2CH_2C(=O)O$. These data indicate the formation of the polymer consisting of sorbitol and sebacate moieties.

In order to examine the microstructure of the polymer, the ^{13}C NMR peaks between δ 66.2–71.5 were assigned by using 2D NMR techniques, H–H correlation spectroscopy (COSY) and heteronuclear multiple quantum coherence (HMQC), in comparison with those of sorbitol. The polymer consisted exclusively of the acylated unit of sorbitol at 1- and 6-positions (Figure 1), indicating that the regioselectivity was perfectly controlled through the enzyme catalysis.

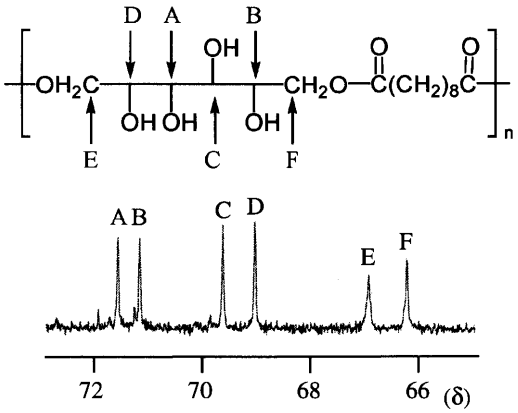


Figure 1. Expanded ^{13}C NMR of the polymer obtained from sorbitol and divinyl sebacate.

Effects of the temperature on the polymer yield and molecular weight are shown in Figure 2. The yield increased as a function of the temperature and the polymerization at 80 °C

gave the polymer with molecular weight of higher than 1×10^4. The highest yield was observed at 20 °C, however, the molecular weight was low. The temperature scarcely affected the molecular weight distribution. The polymerization also proceeded in other polar solvents such as acetone, *t*-amyl alcohol, and 1,4-dioxane. In the polymerization in bulk, the polymer yield was very low (10%).

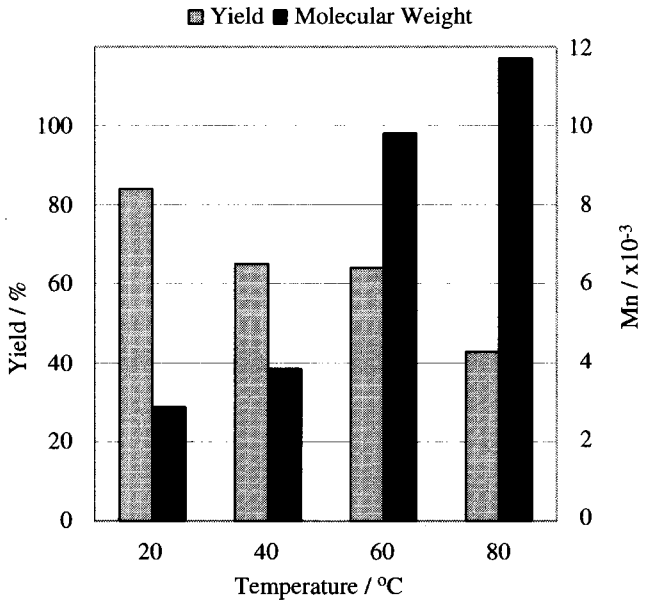


Figure 2. Effects of temperature on the polymer yield and molecular weight in the lipase-catalyzed polymerization of sorbitol and divinyl sebacate in acetonitrile.

In conclusion, the lipase-catalyzed polymerization of sorbitol and divinyl sebacate regioselectively proceeded to produce the polyester having a sorbitol unit in the main chain. In our laboratory, it has been successfully applied to the regioselective polymerization of other sugar alcohols such as mannitol and *meso*-erythritol with divinyl sebacate by lipase catalyst to give the sugar-containing polyesters. Further investigations on the lipase-catalyzed synthesis of polyesters from various sugar derivatives are now under way in our laboratory.

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17 A mixture of 55 mg of sorbitol (0.30 mmol), 77 mg of divinyl sebacate (0.30 mmol), and 100 mg of lipase in 2 mL of acetonitrile was placed in a dried tube under argon and sealed. The tube was kept under gentle stirring at 60 °C. After 72 h, 10 mL of dimethyl sulfoxide was added and the part of the organic solution was separated by filtration. The filtrate was concentrated under reduced pressure and the residue was washed with water, followed by drying in vacuo to give 67 mg of the polymer (yield 64%).