

SHORT COMMUNICATIONS

## Enzymatic Synthesis of Polyesters in Ionic Liquids

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Recently, room-temperature ionic liquids have received much attention as green designer solvents.<sup>1</sup> They are good solvents for a wide range of organic and inorganic materials and have high thermal stability. Furthermore, these ionic liquids are recognized environmentally benign owing to their no detectable vapor pressure. So far, ionic liquids have been used as solvents for a number of chemical reactions such as Diels–Alder reaction, Suzuki coupling, and dimerization of butadiene.<sup>1–4</sup> A variety of structure and function of ionic liquids will control activity, selectivity and stability of catalysis in their use as solvent, yielding production of useful and functional materials. As for polymerizations in ionic liquids, olefin polymerization,<sup>5</sup> oxidative polymerization of benzene to poly(*p*-phenylene),<sup>6</sup> and copper (I)-mediated living radical polymerization of methyl methacrylate<sup>7</sup> were reported.

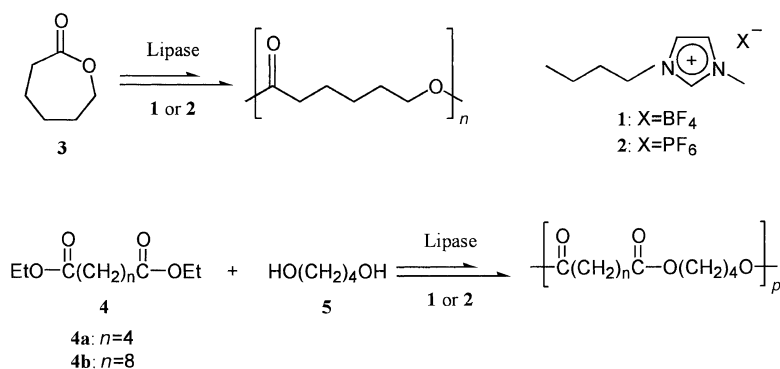
Lipase-catalyzed polymerizations provide an environmentally friendly methodology of biodegradable polyester syntheses owing to non-toxic enzyme catalyst and mild reaction conditions.<sup>8–15</sup> Various monomer combinations have been developed for enzymatic synthesis of polyesters. Lipase catalysis induced enantio- and regioselective polymerizations to give functional polyesters, most of which are very difficult to synthe-

size by conventional chemical catalysts.

Very recently, biotransformations in ionic liquids have been reported.<sup>16–20</sup> Efficient synthesis of esters and amides was achieved using *Candida antarctica* lipase (lipase CA) as catalyst in ionic liquids,<sup>17</sup> and this enzyme showed high enantioselectivity of acylation in these media.<sup>18–20</sup> In this study, we have examined lipase-catalyzed synthesis of polyesters in ionic liquids (Scheme 1). This is the first example of the enzymatic polymerization in ionic liquids to our best knowledge.

### RESULTS AND DISCUSSION

In the present study, 1-butyl-3-methylimidazolium tetrafluoroborate (**1**) and butylmethylimidazolium hexafluorophosphate (**2**) were used. In both solvents, it was reported that lipase CA showed high catalytic activity for transesterification.<sup>17–20</sup> At first, the ring-opening polymerization of  $\epsilon$ -caprolactone (**3**) was carried out using lipase CA as catalyst in **1** or **2** at 60°C. Previously, we found highly efficient catalysis of lipase CA for the polyester production.<sup>21</sup> Polymerization results are summarized in Table I. The monomer conversion and molecular weight of polymers were deter-



Scheme 1.

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**Table I.** Enzymatic Ring-Opening Polymerization of  $\epsilon$ -Caprolactone (**3**)<sup>a</sup>

Entry	Solvent <sup>b</sup>	Time h	Conv. <sup>c</sup> %	$M_n^d$	$M_w/M_n^d$
1	<b>1</b> (0.42)	24	24	470	6.3
2	<b>1</b> (0.42)	72	54	850	6.7
3	<b>1</b> (0.42)	168	74	1200	5.5
4	<b>1</b> (1.05)	24	23	<300	–
5	<b>1</b> (1.05)	72	44	450	7.3
6	<b>1</b> (1.05)	168	97	4200	2.7
7	<b>2</b> (0.42)	24	35	510	4.1
8	<b>2</b> (1.05)	24	51	430	3.0
9	<b>2</b> (1.05)	72	62	540	4.2

<sup>a</sup>Polymerization using lipase CA catalyst (50 mg) in ionic liquid at 60°C. <sup>b</sup>In parenthesis, volume of ionic liquid (mL). <sup>c</sup>Determined by <sup>1</sup>H NMR. <sup>d</sup>Determined by SEC.

**Table II.** Enzymatic Polycondensation of Diesters (**4**) and 1,4-Butanediol (**5**)<sup>a</sup>

Entry	Diester	Solvent	Pressure mmHg	Time h	Conv. <sup>b</sup> %	$M_n^c$	$M_w/M_n^c$
1	<b>4a</b>	<b>1</b>	60	24	85	840	2.9
2	<b>4a</b>	<b>1</b>	60	72	91	1500	3.4
3	<b>4a</b>	<b>1</b>	760	24	50	350	1.4
4	<b>4a</b>	<b>2</b>	60	24	86	860	1.9
5	<b>4a</b>	<b>2</b>	60	72	95	1200	2.8
6	<b>4b</b>	<b>1</b>	60	24	82	1100	2.2

<sup>a</sup>Polymerization using lipase CA catalyst (50 mg) in ionic liquid (5 fold volume of monomers) at 60°C.

<sup>b</sup>Determined by <sup>1</sup>H NMR. <sup>c</sup>Determined by SEC.

mined by <sup>1</sup>H NMR and size exclusion chromatography (SEC), respectively.

In using **1** as solvent, the monomer was almost quantitatively consumed under the selected conditions to give the corresponding polyester with molecular weight of several thousands (entry 6). The solvent amount affected the polymerization behaviors; on the other hand, only oligomeric products were formed in using **2** in less than 3 days (entries 7–9).

Lipase CA-catalyzed polycondensation of dicarboxylic acid diesters (**4**) and 1,4-butanediol (**5**) was examined (Table II). In the polymerization of diethyl adipate (**4a**) and **5** under ambient pressure, the monomer conversion and polymer molecular weight were low (entry 3). In the enzymatic synthesis of polyesters from dialkyl ester monomer, the polymerization was often carried out under reduced pressure in order to remove the alcohol formed during the reaction.<sup>22</sup> The ionic liquids show no volatility; and hence, the polymerization can be performed under reduced pressure. The monomer conversion and molecular weight of the polymer in the polymerization under reduced pressure improved in comparison with those under the ambient conditions (entry 1). The polymerization behaviors in **1** were relatively close to those in **2**. The polymerization of diethyl sebacate (**4b**) and **5** also proceeded in **1** in the presence of lipase CA (entry 6).

## CONCLUSIONS

Lipase-catalyzed polymerization to polyesters has been first achieved in ionic liquids **1** and **2**. For the lactone polymerization, **1** was suitable for the production of higher molecular weight polymer. In the polymerization of diethyl esters and 1,4-butanediol, the reaction under the reduced pressure improved the monomer conversion and polymer molecular weight.

Very recently, we briefly reported that the lipase-catalyzed synthesis<sup>23</sup> and degradation<sup>24</sup> of polyesters took place in supercritical carbon dioxide. Furthermore, we have achieved the direct dehydration polymerization of dicarboxylic acids and glycols in water<sup>25,26</sup> and first proposed a new concept “dehydration in water” in organic chemistry. Our preliminary results on the enzymatic polymerization and degradation in environmentally benign solvents, ionic liquid, supercritical carbon dioxide and water, will be highly significant as basic research for development of an environmentally benign process of plastics production and degradation, providing an example system of *green polymer chemistry*.<sup>13,15,27</sup> Further investigations on the enzymatic polymerization in ionic liquids are under way in our laboratory.

## EXPERIMENTAL

Ionic liquids **1** and **2** were synthesized according to the literature.<sup>28</sup> Lipase CA was kindly donated by Novozymes Japan Ltd. Other reagents and solvents are commercially available and used as received.

A typical run was as follows (entry 6 in Table I). A mixture of **1** (1.05 mL), **3** (0.228 g, 2.0 mmol), and lipase CA (50 mg) was placed in a dried test tube under argon. The mixture kept at 60°C under moderate stirring. After 168 h, the residual monomer and resulting polymer were extracted with toluene (3 mL) three times. The solvent was removed under reduced pressure and dried *in vacuo*. The residue was dissolved in a small amount of tetrahydrofuran and the solution was analyzed by SEC for the determination of the polymer molecular weight.

SEC analysis was carried out by using a Tosoh SC8020 apparatus equipped with refractive index (RI) detector at 40°C under the following conditions: TSKgel G3000 H<sub>HR</sub> column and tetrahydrofuran eluent at a flow rate of 1.0 mL min<sup>-1</sup>. The calibration curves were obtained using polystyrene standards. <sup>1</sup>H NMR spectra were recorded on a Bruker DPX400 spectrometer.

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