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Lipase-catalysed polyester synthesis in 1-butyl-3-methylimidazolium hexafluorophosphate ionic liquid

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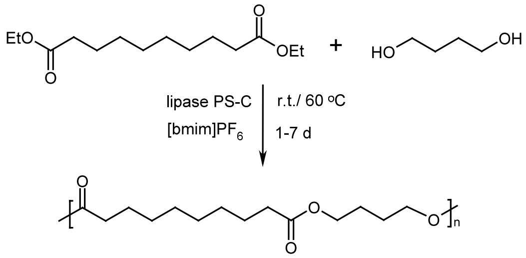
Abstract—1-Butyl-3-methylimidazolium hexafluorophosphate ionic liquid was employed as a reaction medium for lipase-catalysed aliphatic polyester synthesis. Lipase PS-C exhibited excellent catalysis in polycondensation of diethyl octane-1,8-dicarboxylate and 1,4-butanediol at room temperature and at 60°C. A relatively high molecular weight polymer was obtained at 60°C. © 2003 Elsevier Science Ltd. All rights reserved.

The last decade has witnessed a phenomenal development of ionic liquids as potential solvents for several chemical processes. The breakthrough in the know-how of ionic liquids has triggered an intensive exploration of their potential prospects in synthetic organic chemistry. These developments can be attributed to their properties such as negligible vapour pressure, recyclability and high thermal stability, which make them stand aloof from conventional organic solvents. However, the most interesting of them all is our capability to engineer their structure and consequently their properties at will, which enables us to conglomerate the most suitable properties and make them process-compatible.[1,2]

Ionic liquids have been widely employed for synthetic organic reactions.[3–5] In order to establish the compatibility of enzymes with ionic liquids, we carried out the lipase-catalysed transesterification of 2-hydroxymethyl-1,4-benzodioxane.[6] In continuation of our effort to tap the barely explored potential of ionic liquids in enzyme chemistry, we conceptualised lipase-catalysed polyester synthesis via polytransesterification. Polycondensation reactions for polyester synthesis employing lipases have been extensively investigated in conventional organic solvents.[7] However, with a view to circumvent the difficulties associated with conventional organic solvents, we thought it would be worthwhile to replace them by these neoteric solvents. Moreover, we found that 1-butyl-3-methylimidazolium hexafluorophosphate ionic liquid, [bmim]PF_6, unlike most polar organic solvents, despite being polar is highly hydrophobic in nature. This property seems to provide the desired conformational flexibility to an enzyme without drastically altering its catalytically active conformation. This prompted us to attempt enzyme-catalysed polyester synthesis using diethyl octane-1,8-dicarboxylate and 1,4-butanediol as the substrates employing *Pseudomonas cepacia* lipase supported on Celite, PS-C as the biocatalyst in [bmim]PF_6 as the reaction medium (Scheme 1). Initially the reactions were carried out at room temperature and the preliminary results demonstrated excellent catalysis by PS-C lipase in [bmim]PF_6 as solvent. Within 12 h of stirring, the reaction gave solid polyester.



Scheme 1. Lipase PS-C catalysed polyester synthesis using diethyl octane-1,8-dicarboxylate and 1,4-butanediol in [bmim]PF_6 at room temperature or at 60°C.

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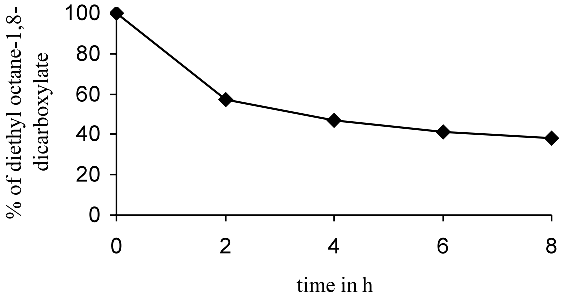

Figure 1. Initial decay of diethyl octane-1,8-dicarboxylate with time in the lipase PS-C catalysed polycondensation of diethyl octane-1,8-dicarboxylate with 1,4-butanediol in [bmim]PF_6 at room temperature.

To establish the initial rate of the enzyme catalysed transesterification in [bmim]PF_6, different experiments were designed. We monitored on GC the decay of diethyl octane-1,8-dicarboxylate as a function of time. The results revealed a high initial rate of transesterification as indicated from the rapid consumption of the monomer (Fig. 1). This signified the rapid assembly of low molecular weight oligomers by sequential condensation of monomers on to the developing chain.

The molecular weight of the polyester obtained was monitored at different intervals of time during the course of polymerisation at room temperature. After 1 day, the reaction furnished a polymer (obtained on precipitation using methanol) possessing an average molecular weight of 2230 as determined by Gel Permeation Chromatography, GPC analysis. We observed that practically no substantial improvement in the molecular weight of the polymer was seen with time thereafter. However, after 7 days there was a marginal decrease in the average molecular weight of the polymer isolated and also the GPC profiles exhibited a gradual increase in low molecular weight oligomers. Thus, it appears that the polyester undergoes lipase-catalysed disproportionation. This is understood from the reactions that were studied for very long periods of time (12–15 days), which gave less high molecular weight polymers after precipitation using methanol.

The average molecular weight of the polymer obtained at room temperature was limited to around 2270. Thus, the results demonstrate that the reaction reaches an equilibrium whereafter the average molecular weight of the product did not increase even after a prolonged incubation time. The mechanism of such enzymic acyl-transfer reactions is well understood.[8] In such a reversible system, the equilibrium shifts towards the right if the ethanol is removed as soon as it is produced in the reaction mixture. The supported PS-C lipase that we employed is robust enough to withstand temperatures around 60°C and is known to exhibit comparable or even better activity at these temperatures. The ionic liquid, [bmim]PF_6 has an infinitesimally small vapour pressure so it can be conveniently employed above ambient temperatures without any loss due to evaporation, which is not possible in the case of volatile organic solvents. The polymerisation was then carried out at 60°C so that the ethanol formed is driven out during the course of the reaction. As expected, the molecular weight of the polymer so obtained improved substantially from 2270 at room temperature to 5400 at 60°C. The results of polymerisation at room temperature and 60°C at different time intervals are summarised in Table 1. In control experiments carried out under identical conditions of time, temperature, concentration and ionic liquid as a medium, no reaction was observed in the absence of enzyme.

An interesting feature that we noticed in the PS-C catalysed polymerisation in [bmim]PF_6 is that the polymeric material obtained after precipitation using methanol, exhibited remarkable polydispersity values, as reflected from the results (Table 1). This can probably be attributed to the insolubility of the polymer formed in the ionic liquid after it exceeds a certain molecular weight limit. Further investigations concerning this problem are in progress in our laboratory. If it is experimentally proved that this is the reason for such polydispersity values, then ionic liquids can broaden the avenues in this area of research. This is due to the fact that the ionic liquids can be tailored and their solvating ability can be streamlined by structural manipulations as required, i.e. with respect to the polymeric material desired.

In conclusion, the present method serves as a green process in entirity since it involves the use of both an environmentally benign biocatalyst as well as reaction medium for the synthesis of aliphatic polyesters.

Experimental

In a typical experimental procedure, to 2 mL of [bmim]PF_6 ionic liquid, diethyl octane-1,8-dicarboxylate (2 mmol, 0.516 g), 1,4-butanediol (2 mmol, 0.180 g)

Table 1. Lipase PS-C catalysed polyester synthesis using diethyl octane-1,8-dicarboxylate and 1,4-butanediol in [bmim]PF_6 at room temperature and at 60°C

Entry	Time in days	Temperature (°C)	M_n[a]	M_w[a]	M_w/M_n[a]
1	1	Rt	2130	2230	1.04
2	2	Rt	2120	2250	1.06
3	3	Rt	2150	2270	1.05
4	7	Rt	2075	2150	1.03
5	7	60	4300	5400	1.26

[a] Determined by GPC of the polymeric material obtained after precipitation using methanol.

and lipase PS-C (30 mg, activity 30 units/mg) were added and the mixture stirred at room temperature or at 60°C (with a $CaCl_2$ drying tube). After stirring for periods ranging from 1 to 7 days as mentioned in the text, the resultant polymer was extracted with ether (3×10 mL). The combined organic extracts were concentrated under reduced pressure. The resulting material was subjected to precipitation using methanol. The polymeric material so obtained was analysed by GPC in $CHCl_3$. The linear polyester structure was confirmed by ^{13}C and ^{1}H NMR analysis.

Gel permeation chromatography (GPC) was performed on a Thermo Quest instrument equipped with a refractive index detector at room temperature. $CHCl_3$ was used as an eluant at a flow rate of 1 mL min^{-1} for the analysis. The molecular mass averages were computed using PSS WinGPC software, and calibrated against the commercial polystyrene standards.

Gas chromatography (GC). The extent of transesterification in the initial phases of polymerisation was monitored in terms of decay of diethyl octane-1,8-dicarboxylate on GC. A Nucon 5700 chromatograph equipped with FID was employed for the analysis. The detector temperature was maintained at 280°C. The column was programmed with an initial temperature of 100°C and was increased thereafter to 270°C at a rate of 10°C min^{-1}. The column used was liquid phase ov-17 (length 6′).

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References

1. Review: Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3772.
2. Cole, A. C.; Jensen, J. L.; Ntai, I.; Tran, K. L. T.; Weaver, K. J.; Forbes, D. C.; Davis, J. H., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 5962.
3. Review: Welton, T. *Chem. Rev.* **1999**, *99*, 2071.
4. Review: Sheldon, R. *Chem. Commun.* **2001**, 2399.
5. (a) Harjani, J. R.; Nara, S. J.; Salunkhe, M. M. *Tetrahedron Lett.* **2001**, *42*, 1979; (b) Nara, S. J.; Harjani, J. R.; Salunkhe, M. M. *J. Org. Chem.* **2001**, *66*, 8616; (c) Potdar, M. K.; Mohile, S. S.; Salunkhe, M. M. *Tetrahedron Lett.* **2001**, *42*, 9285; (d) Harjani, J. R.; Nara, S. J.; Salunkhe, M. M. *Tetrahedron Lett.* **2002**, *43*, 1127.
6. Nara, S. J.; Harjani, J. R.; Salunkhe, M. M. *Tetrahedron Lett.* **2002**, *43*, 2979.
7. Review: Gross, R. A.; Kumar, A.; Kalra, B. *Chem. Rev.* **2001**, *101*, 2097.
8. Faber, K.; Riva, S. *Synthesis* **1992**, *10*, 895.