Synthesis of Functional Polycarbonates by Lipase-Catalyzed Ring-Opening Polymerization

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Summary: Poly(5-benzyloxy-trimethylene carbonate) (PBTMC), a new functional polycarbonate was synthesized by enzymatic ring-opening polymerization in bulk at 150°C using Porcine pancreas lipase (PPL) or Candida rugosa lipase (CL) as catalyst. Influences of different polymerization conditions such as the source of enzyme, enzyme concentration and polymerization time on the molecular weight and yield were studied. The results showed that PPL exhibited higher activity than CL. Both higher molecular weight(*Mn*, 18953) and yield(98%) could be obtained by the use of PPL as catalyst. ^{1}H NMR spectrum showed no decarboxylation occurrence during the ring-opening polymerization.

Keywords: enzymes; lipase; poly(5-benzyloxy-trimethylene carbonate); polycarbonates; ring-opening polymerization

Introduction

Biodegradable and bioresorbable nontoxic polymers having pendent functional groups are of particular importance in the biomedical fields. Functional groups can be used to regulate the properties of the polymers, such as hydrophilicity, permeability, bioresorption as well as mechanical properties. Particularly, they also provide an opportunity for attaching drugs or bioactive components to make these polymers suitable for use in medical and surgical applications [1~3]. Aliphatic polycarbonates represent one family of bioresorbable materials that have been engineered for biomedical applications [4]. Recently, increasing efforts have been devoted to the synthesis of polycarbonates having pendent functional groups [5,6]. In our previous paper, we reported the synthesis of a new functional cyclic carbonate BTMC(5-benzyloxy-trimethylene carbonate) and its polymer PBTMC[poly(BTMC)] catalyzed by metallic catalysts [7]. After deprotection of benzyl group by catalytic hydrogenation, the corresponding polymers exhibited much better degradation property due to their pendent hydroxyl group. In view of the

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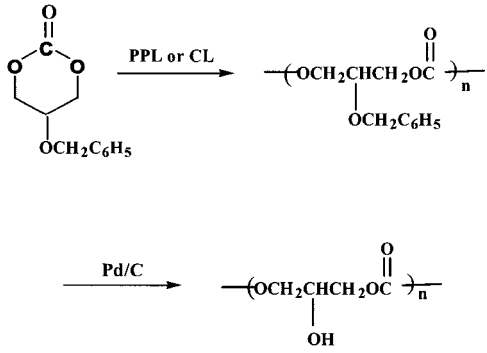
possible toxicity that may be caused by the remaining of trace metal compounds in the biomaterials products, we have attempted to use enzymes instead of metallic catalysts for the preparation of biomedical polymers, such as PBTMC in this study.



Scheme 1. Enzymatic ring-opening polymerization of BTMC.

Results

BTMC was successfully ring-opening polymerized by PPL or CL to yield corresponding polymer PBTMC with molecular weight(*Mn*) up to 18953. The ^{1}H NMR spectra of PBTMC showed no decarboxylation occurrence during the polymerization process. It was found that BTMC was thermally oligomerized at 150°C for 24h without any catalyst. However, both the molecular weight and yield were much more lower than that of the polymers obtained in the presence of PPL or CL. It demonstrated that the PPL and CL actually catalyzed the polymerization. It is known that $Sn(OCt)_2$ is the most widely used catalyst for the preparation of biomedical polymers such as polylactide and polycarbonates because it is a highly efficient commercial catalyst and is nontoxic. Compared with $Sn(OCt)_2$, PPL exhibited even higher catalytic activity in the ring-opening polymerization of BTMC[7]. The results of the ring-opening polymerization of BTMC with/without lipase(PPL or CL) are shown in Table 1.

The lipase concentration affected the molecular weight significantly both in the case of PPL and CL. It seems that a suitable enzyme concentration could help to obtain the higher molecular weight and yield. At the same time, molecular weight and yield of the polycarbonate was markedly influenced by the polymerization time. Experimental data (Table 1) show that the

optimal polymerization time for the synthesis of PBTMC catalyzed by PPL is 8 hrs. Elongation of the reaction time would lead to an decrease of both molecular weight and yield. The similar result could be observed in the case of CL. This is probably due to that PPL and CL not only could catalyze the polymerization of BTMC, but also catalyze the degradation of PBTMC (Figure 1). The thermal properties of PBTMC was examined by DSC. The glass-transition temperature (*Tg*) of the PBTMC obtained (Table 1.entry 16) is –0.03°C. No melt-transition temperature (*Tm*) could be detected at the temperature range (-100~200°C). It suggested that PBTMC might be amorphous.

Table 1. Ring-opening polymerization of BTMC in bulk at 150°C.

Entry	Enzyme	Conc. (mg/2.5mmol)	Time (h)	Mn	Dp	Yield (wt.-%)
1	CL	0.35	48	4591	1.90	73
2	CL	1.5	48	5537	1.90	82
3	CL	3.4	48	4380	1.60	70
4	CL	5.2	48	3505	1.87	67
5	CL	1.5	4	9460	2.08	88
6	CL	1.5	8	9833	2.21	93
7	CL	1.5	16	11645	1.59	87
8	CL	1.5	24	8796	2.63	87
9	CL	1.5	72	5202	2.13	82
10	PPL	1.0	48	4257	1.40	36
11	PPL	1.9	48	4668	1.63	63
12	PPL	3.1	48	6745	1.73	59
13	PPL	4.6	48	3019	1.57	58
14	PPL	5.2	48	2239	3.40	54
15	PPL	3.1	4	12376	3.81	92
16	PPL	3.1	8	18953	2.28	98
17	PPL	3.1	16	10741	1.68	90
18	PPL	3.1	24	9284	2.71	77
19	PPL	3.1	72	6232	2.32	66
20[a]	-	-	24	1500	1.6	24

[a)]Blank test: the polymerization was carried out without any catalysts.

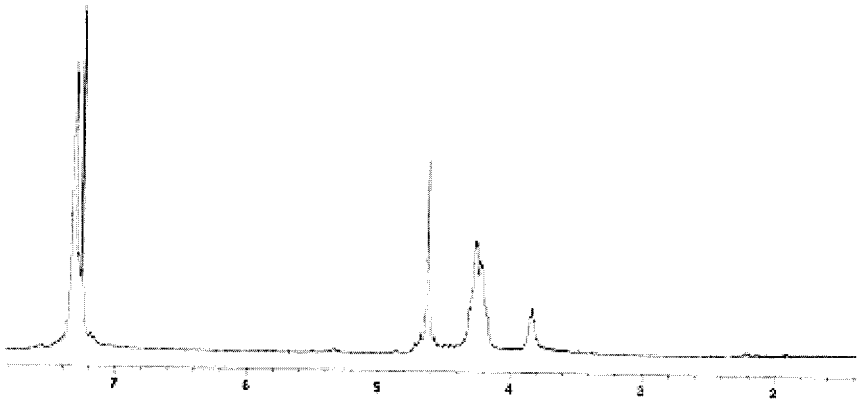


Figure 1. ^{1}H NMR spectrum of PBTMC.

Conclusion

Cyclic carbonate BTMC was readily polymerized in the presence of PPL or CL at 150°C. PPL exhibited better activity than CL with respect to the yield and *Mn* of the resultant polycarbonates. The polymerization catalyzed by PPL at 3.1mg/2.5mmol monomers concentration for 8h could result in higher Mn(18953) and better yield(98%). The ^{1}H NMR spectrum showed no decarboxylation occurrence during the ring-opening polymerization.

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