Cumulated advantages of enzymatic and carbene chemistry for the non-organometallic synthesis of (co)polyester

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Experimental procedures

Chemicals. ε-Caprolactone (CL) was purchased from Aldrich, distilled over CaH_2 and stored over molecular sieves. Novozyme 435 (**E**) was obtained from Novozymes A/S, Denmark. L-Lactide (LA) was obtained from Purac, recrystallized from toluene three times prior to use and stored in a glovebox. Benzyl alcohol and toluene were distilled over CaH_2. Carbon disulfide (Acros) was dried on molecular sieves (4Å) for 12 hours. The carbene catalyst 1,3,4-Triphenyl-4,5-dihydro-*1H*-1,2,4-triazol-5-ylidene (*Wanzlick*-type carbene) was obtained from its commercially available methoxy-precursor following a procedure of Enders.[1] Thermolysis of its methanol adduct (Acros) under vacuum at 90 °C for 12 hours yielded the carbene catalyst by α-elimination of methanol.

Characterization. Gel permeation chromatography was performed in tetrahydrofuran on a Waters chromatograph equipped with four 5 μm Waters columns (300 mm × 7.7 mm) connected in series with increasing pore size (10, 100, 1000, 10^5, 10^6 Å). Polystyrene samples of known molecular weight were used as calibration standards. A Waters 410 differential refracometer and 996 photodiode array detector were employed. THF was used as eluent with a flow rate of 1.0 ml/min. All samples were diluted to 1.0 mg/ml in THF and filtrated using 0.2 μm syringe filters. ^{1}H- and ^{13}C-NMR spectroscopies were performed using a VARIAN 400 NMR at 20 °C. Samples were diluted in $CDCl_3$ to 30-50 mg/ml. Data were processed using VNMR-software.

General procedure for Novozym 435 polymerization of ε-caprolactone. Table 1, Entry 1-1. In a flame-dried and purged round bottom flask, a stock solution of benzyl alcohol (0.5 ml, 4.8 mmol) and toluene (25.5 ml) was prepared ($[I]_0$ = 0.18 M). In a second flamed-dried and purged flask, 0.02 g Novozym 435 (**E**) (10 wt.% with respect to monomer) was dried with a stirring bar under vacuum at 40 °C overnight. The reaction was started by adding 0.2 g ε-caprolactone (1.8 mmol) and 0.19 ml stock solution (3.5×10^{-5} mol) under nitrogen flow to the enzyme. The mixture was kept stirring at 90 °C for 6 hours, followed by the precipitation in cold methanol (yield: 70 %).

General procedure for carbene polymerization of lactide
Table 1, Entry 4. In a glove-box, 0.2 g of L-lactide (1.4 mmol) was charged in a flame-dried and purged round bottom flask containing 9 mg of 5-methoxy-1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene previously dried under vacuum for 12 hours at 90°C to generate the 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene active carbene (**C**). Outside of the glove-box, 0.15 ml of an initiator stock solution of benzyl alcohol (0.5 ml, 4.8 mmol) in toluene (25.5 ml) was added (2.79×10^{-5} mol) under nitrogen by using a dried and purged syringe. After 6 hours at 90 °C, the polymerization was quenched by addition of dried CS_2 (0.4 ml, 6.9 mmol) and the

medium was precipitated in excess of cold methanol (~20 ml). The recovered polymer was dried until constant weight and analyzed by SEC and NMR analysis. Yield = 82%

General procedure for ε-caprolactone/L-Lactide copolymerization. Table 2, Entry 2-3. In a flame-dried and purged round bottom flask, a stock solution of benzyl alcohol (0.5 ml, 4.8 mmol) and toluene (25.5 ml) was prepared ($[I]_0$ = 0.18 M). In a second flame-dried and purged round bottom flask, 0.18 g of Novozym 435 (10 wt % of monomers) was dried under vacuum for 12 hours at 40 °C. At room temperature, 1 ml of ε-caprolactone (7.0 mmol) and 1.5 ml of the initiator stock solution were added under nitrogen (2.79 x 10^{-4} mol). The mixture was then kept stirring at 60 °C for 6 hours. Then, the mixture was added by a purged capillary to a mixture of 92 mg of 5-methoxy-1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene and 1 g of L-lactide (6.9 mmol) in a previously purged and dried round bottom flask. The copolymerization was then initiated by increasing the temperature to 90 °C. After 6 hours, the solution was filtered and precipitated in excess of cold methanol. The recovered polymer was dried until constant weight and analyzed by SEC and NMR analysis (yield: 62 %).

Table 1: PCL-PLA block polymers with different compositions obtained in a one pot polymerization.

Entry	DP_{CL}		DP_{LA}		Mn (g/mol)[a]	
	Targeted	Exp.[b]	Targeted	Exp.[b]	PCL[c]	PCL-*b*-PLA
1	15	13	35	38	4,150	9,020
2	25	26	25	25	7,070	10,540
3	35	37	15	13	8,180	9,870

[a] Determined by SEC in THF with polystyrene standards. [b] Determined by ^{1}H-NMR analysis : $DP_{CL} = [I_{4.1}/(I_{3.65}+2I_{4.35})]$; $DP_{LA} = [I_{5.1}/(I_{3.65}+2I_{4.35})]$. [c] Samples taken out before LA polymerization.

(1) D. Enders, K. Breuer, G. Raabe, J. Runnink, J. H. Teles, J.-P. Melder, K. Ebel, S. Brode, *Angew. Chem.* 1995, **107**, 1119.