Supplementary Material (ESI) for:

Stereoselective and Controlled Polymerization of D,L-Lactide Using Indium(III) Trichloride

Agostino Pietrangelo, Marc A. Hillmyer*, and William B. Tolman*

Department of Chemistry, University of Minnesota, 207 Pleasant Street SE, Minneapolis, Minnesota. 55455, USA.

Experimental

General Methods and Materials. Indium trichloride, benzyl alcohol, and deuterated solvents were purchased from Aldrich and used as received. Triethylamine was purchased from Acros and distilled from calcium hydride. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride and degassed 3x using freeze-pump-thaw techniques. Toluene was distilled from sodium and benzophenone and degassed using freeze-pump-thaw techniques. D,L-Lactide (Purac) was purified by recrystallization from toluene followed by repeated vacuum sublimations (2x). *Meso*-Lactide was obtained from NatureWorks and purified by recrystallization from isopropanol (2x), then toluene (2x), and dried under high vacuum for 48 h. All reagents were stored in a dinitrogen-filled MBraun UNIIab glovebox. All reactions were carried out under a dinitrogen atmosphere unless otherwise reported.

Physical Methods. All ¹H NMR homonuclear coupled and decoupled spectra were collected on a Varian VXR-500 spectrometer and calibrated to the residual protonated solvent at δ 7.24 for deuterated chloroform (CDCl₃). Molecular weights (M_n and M_w) and polydispersity indices (M_w/M_n) were determined by size exclusion chromatography (SEC). SEC was performed using a Hewlett-Packard 1100 series liquid chromatograph with chloroform as the mobile phase at 35 °C. The chromatograph was equipped with 3 Varian PLgel Mixed C Columns, and a PLgel 5 µm guard column. Output was detected with an HP1047A differential refractive index detector using an eluent flow rate of 1 mL/min and a 50 µL injection loop. Molecular weights were determined from a 10-point calibration curve created using polystyrene standards purchased from Polymer Laboratories.

<u>General Procedure for Synthesis of PLA.</u> All experiments were carried out in an inert atmosphere using dry solvents and reagents unless otherwise noted. Polymerizations were performed using 1.0 M monomer solutions (in CH_2Cl_2) prior to addition of BnOH and NEt₃. A typical procedure for the polymerization of *meso-* and D,L-lactide is as follows: Under an inert atmosphere, the appropriate amount of initiator (0.276 M BnOH in CH_2Cl_2) was added to a stirring suspension of $InCl_3$ in a 1.0 M monomer solution. After 10 minutes of stirring, triethylamine (0.276 M, in CH_2Cl_2) was added (2 mol. equiv. with respect to BnOH) after which the indium salt began to dissolve. Once the reaction reached near complete conversion (96–99% conversion), the polymer was precipitated out of solution upon dropwise addition to cold wet methanol (0 °C, 20 mL of methanol/ 1.38 mL of reaction solution). The polymer was isolated and dried under high vacuum for 48 h.

Procedure for *in situ* **Observation of D,L-LA Polymerization.** Polymerization was monitored using ¹H NMR spectroscopy. In a scintillation vial, 100 μ L of BnOH stock solution (0.276 M in CH₂Cl₂) and 200 μ L of NEt₃ stock solution (0.276 M in CH₂Cl₂) were added to a suspension of InCl₃ (6.6 mg, 0.0298 mmol) in a D,L-LA (406 mg, 2.82 mmol) solution (CD₂Cl₂, 2.76 mL). Once the suspension dissolved, an aliquot was placed into an NMR tube and placed in the probe (21 °C). Data from a selected run is shown in Figure S1.



Figure S1. Illustrative kinetic data for D,L-LA polymerization with a fit to the equation for first order decay, giving $k_{obs} = 2.3 \times 10^{-4} \text{ s}^{-1}$. A second run gave $k_{obs} = 3.0 \times 10^{-4} \text{ s}^{-1}$, yielding an average value of 2.7 x 10^{-4} s^{-1} that is cited in the text.



Figure S2. ¹H NMR spectra (500 MHz, CDCl₃) of the PLA methine resonances with selective decoupling of the methyl resonances (Entries, 2,6-8, Table 1). Experimental integration values were determined using a literature procedure.¹ Below the spectra is a table showing the predicted Bernoullian integration percentages for a given P_r .

Entr	y 5 P _r = 0.94		0.447	0.028	0.029	0.050 0.446					
Entr	y 4 P _r = 0.93			-		4					
Entr	Entry 3 $P_r = 0.94$ 0.055 0.039/0.031/0.443										
Entr	y 2 P _r = 0.94	0.442	0.038	0.0	34/0.046	2					
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5.24	5.22	5.20	5.18 ppm ^{5.}	16 5.1	14 5.12	5.10					
*											
\mathbf{P}_r	rmr	rmm	mmr	mmm	mrm						
0.86	0.370	0.060	0.060	0.080	0.430	* Predicted Bernoullian					
0.87	0.378	0.057	0.057	0.073	0.435	Integration percentages for					
0.88	0.38/	0.053	0.053	0.06/	0.440	a given P_r					
0.89	0.390	0.048	0.048	0.001	0.445						
0.90	0.403	0.043	0.043	0.033	0.450						
0.91	0.423	0.041 0.037	0.041 0.037	0.047	0.460						
0.92	0.432	0.033	0.033	0.045	0 465						
0.94	0.442	0.028	0.028	0.032	0.470						
0.95	0.451	0.024	0.024	0.026	0.475						
0.96	0.461	0.019	0.019	0.021	0.480						
0.97	0.470	0.015	0.015	0.015	0.485						

Figure S3. ¹H NMR spectra (500 MHz, CDCl₃) of the PLA methine resonances with selective decoupling of the methyl resonances (Entries 1-5, Table 1). Experimental integration values were determined using a literature procedure.¹ Below the spectra is a table showing the predicted Bernoullian integration percentages for a given P_r .



Figure S4. Plot of observed M_n versus equivalence of converted monomer at time t.

Table S1. Poly	merization of D	,L-LA usin	g $InCl_3$ (6	o mg) and	excess Bn0	OH (see	Figure
S4).							

Entry	[BnOH] ₀ ^a /	[D,L-LA] ₀ /	t	%	M_n	PDI ^c	P_r^{d}	Yield
-	$[InCl_3]_0$	$[BnOH]_0$	(h)	conv. ^b	(kg mol ⁻¹) ^c			(%)
3	1	203	5	96	39.9	1.06	0.94	75
9	1.12	161	5	96	29.4	1.06	0.94	82
10	1.45	134	5	97	22.2	1.08	0.94	79
11	1.57	115	5	98	21.5	1.08	0.94	83
12	1.80	101	5	96	18.8	1.07	0.93	79
13	2.21	80	5	98	15.5	1.07	0.93	72
14	2.73	67	5	98	12.8	1.07	0.92	76
15	3.29	57	5	98	11.1	1.07	0.91	75
16	3.76	50	5	98	9.8	1.09	0.91	61

^a Benzyl alcohol and 2 mol. equiv. of triethylamine. ^b Determined by ¹H NMR spectroscopy. ^c Determined by SEC (relative to polystyrene in CHCl₃). ^d See ref. 1.

Entry	$[InCl_3]_0/$	$[D,L-LA]_0/$	T	t (b)	M_n	PDI⁵
			(\mathbf{C})	(11)	(kg mor)	
17	1	100	25	5	23.8	1.08
18	2	100	25	5	24.7	1.13
19	3	100	25	46	24.4	1.19

Table S2 Polymerization of D,L-LA ([D,L-LA] $_0 \approx 1$ M, CH₂Cl₂) using excess InCl₃.

^aBenzyl alcohol and 2 mol. equiv. of triethylamine. ^bDetermined by SEC (relative to polystyrene in CHCl₃).

Table S3 Polymerization of meso-LA using InCl₃ (6 mg).

Entry	[InCl ₃] ₀ /	[D,L-LA] ₀ /	Т	t	%	M_n	PDI ^c	P_r^{d}
-	[BnOH] ₀ ^a	$[BnOH]_0$	(°C)	(h)	conv. ^b	$(\text{kg mol}^{-1})^{c}$		
9	1	100	0	30	100	23.2	1.10	0.62
10	1	100	25	5	100	22.4	1.07	0.56
11 ^e	1	50	70	5	100	13.9	1.31	0.44

^aBenzyl alcohol and 2 mol. equiv. of triethylamine. ^bDetermined by ¹H NMR spectroscopy. ^c Determined by SEC (relative to polystyrene in CHCl₃). ^d See ref. 1. ^e Solvent free.

¹ B. M. Chamberlain, M. Cheng, D. R. Moore, T. M. Ovitt, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2001, *123*, 3229.