

Supporting Information

A Strategy for Control of “Random” Copolymerization of Lactide and Glycolide: Application to Synthesis of PEG-*b*-PLGA Block Polymers Having Narrow Dispersity

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Tacticity analysis of PEG-*b*-PLAs. A representative ¹H NMR spectrum of one of the PEG-*b*-PLAs (PEG₅-PL₁₀A) is shown in Figure S1. The tacticity of the PLA block can be judged from

analysis of the methine proton resonances between $\delta = 5.10\text{-}5.25$ ppm.^{1,2} The array of overlapped quartets centered at ca. 5.16 ppm arises from backbone methine protons flanked on both sides by a lactic acid moiety of the same configuration (*isotactic, isotactic* or *i,i*) while the array at ca. 5.21 ppm reflects flanking by one lactic acid moiety of the same and a second of opposite configuration (*isotactic, syndiotactic*, or *i,s*) . Racemic lactide [(±)-1] was used as the monomer for these ROPs. Since each monomer lactide in (±)-1 (**R,R-1** or **S,S-1**) bears two lactic acid moieties of the *same* configuration, there are no individual lactic acid moieties in the PLA that are flanked on both sides by ones of opposite configuration (and thus there are no *syndiotactic, syndiotactic*, or *s,s* relationships). Arrays of similar quartets rather than a single discrete quartet are observed because of small influences on the precise chemical shifts from longer-range, relative configurational relationships. If the rates for homochiral (PLA-R with **R,R-1** or PLA-S with **S,S-1**) vs. heterochiral (PLA-R with **S,S-1** or PLA-S with **R,R-1**) propagation were identical, the intensity of each of the two multiplets at $\delta = 5.16$ and 5.21 (proportional to the $\#i,i$ and $\#i,s$, respectively) would be equal. The average sequence length (SL, the number of adjacent lactic acid moieties of the same configuration) is $[(\#i,i + \#i,s)/(\#i,s/2)]$,³ and in this scenario SL would be 4. Since, instead, the ratio of these resonances is 3, the average SL is 8. Finally, from the SL, one can deduce the reactivity ratio⁴ (r) for homo- vs. heterochiral propagation events; namely, $r = (SL-2)/2^5$ or 3.

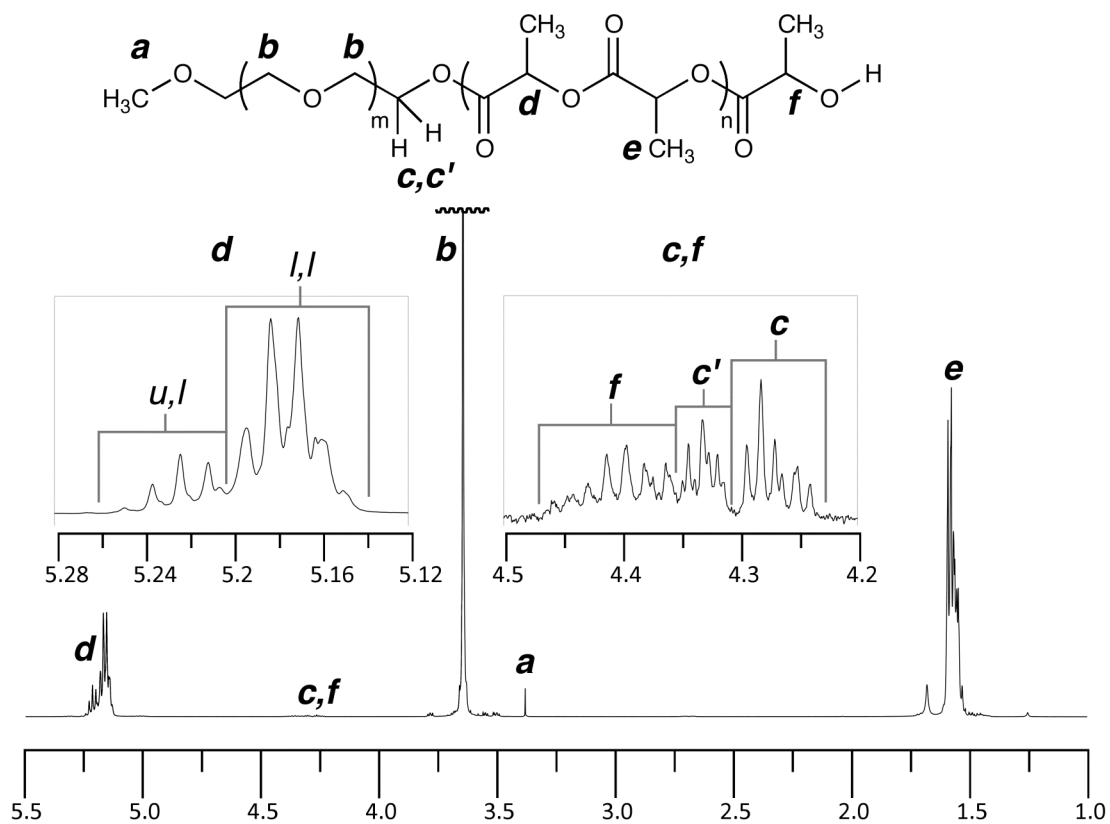


Figure S1. ¹H NMR spectrum of the PEG-*b*-PLA copolymer PEG₅-PL₁₀A (CDCl₃). The ratio of the methine multiplets at ca. δ 5.16 and 5.21 ppm indicates that the DBU catalyst favors the formation of isotactic sequences with a homochiral/heterochiral reactivity ratio of 3 (see text).

Molecular Weight Determination via SEC/MALS. To assess the accuracy of our determinations of M_n via ^1H NMR spectroscopy, we further analyzed three polymers by SEC/MALS to determine the absolute molecular weight of the samples. The results are summarized in Table S1. The specific refractive index (dn/dc) of a polymer is a concentration-dependent value of the difference in the refractive index of a dilute solution of the polymer and the corresponding pure solvent. If we assume a 100% recovery of the polymeric sample through the SEC column, then the value we measured for the specific refractive index (dn/dc) for the PEG sample was lower than its known value. This results in an M_n value that is higher than expected (i.e., 5K for the mPEG–OH sample, entry 1) or measured (for the block copolymers in entries 2 and 3) via ^1H NMR spectroscopy. Specifically, if we assume 100% recovery in the analysis of the 5K PEG-OH (run as a control), the experimentally determined dn/dc value was only 0.055 mL/g and the calculated M_n was 6.0 K. However, when the reported dn/dc value for poly(ethylene oxide) in THF of 0.068 mL/g was used,⁶ the M_n was determined to be 4.9K—in good agreement with the value reported by the supplier of this commercial sample. Presumably, sample loss during filtration prior to injection and/or during elution from the SEC column is responsible for the need to correct the data in this manner.

Similarly, the observed dn/dc values for both the PEG-*b*-PLA and PEG-*b*-PLGA samples were also lower than expected, resulting, again, in correspondingly high M_n values. In this case, the known dn/dc value in THF for PLA of 0.042 was used,⁶ for either the PLA block or as an approximation for the PLGA block. The weighted average of the dn/dc values for the PEG and polyester blocks were then used to calculate a dn/dc value for the block copolymer.⁷ Using this approach, satisfactory correlation was found between the corrected M_n values found via SEC/MALS and ^1H NMR spectroscopy.

Table S1. Comparison of M_n values obtained via ^1H NMR spectroscopy and SEC/MALS.

Polymer	dn/dc (mL/g) (measured)	M_n^a (MALS)	dn/dc (mL/g) (literature)	M_n^b (MALS/corrected)	M_n (^1H NMR)
PEG ₅ -OH	0.055	6.0 K	0.068	4.9 K ^b	5.0 K
PEG ₅ -PL ₁₀ A	0.042	19.0 K	0.051	15.5 K ^c	14.5 K
PEG ₅ -PL ₅ G ₅ A	0.031	24.2 K	0.051	14.7 K ^c	14.2 K

^a M_n value assuming 100% recovery of the polymer sample during the SEC analysis.

^b M_n value using the reported dn/dc value for PEG (0.068).⁶ ^c M_n value using a weighted average (0.33/0.67) for the reported dn/dc values for PEG (0.068) and PLA (0.042).

References for Supporting Information

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- ² Thillaye du Boullay, O.; Marchal, E.; Martin-Vaca, B.; Cossio, F. P.; Bourissou, D. An activated equivalent of lactide toward organocatalytic ring-opening polymerization. *J. Am. Chem. Soc.* **2006**, *128*, 16442–16443.
- ³ Each run of *i,i* moieties is terminated at each of its ends by a *i,s* moiety; there are two *i,s* moieties per run; and the number of runs is one half the number of *i,s* moieties. The average sequence length in any sample is the total number of lactic acid units ($\#i,i + \#i,s$) divided by the total number of runs ($\#i,s/2$).
- ⁴ Hiemenz, P. C.; Lodge, T. P. Copolymers, microstructure, and stereoregularity. In *Polymer Chemistry*, 2nd Ed.; Taylor & Francis Group, LLC: Boca Raton, **2007**, *1*; 165–216.
- ⁵ The reactivity ratio for a growing chain whose reactive terminal carbinol center has the *R* configuration is $r_{\text{PLA-R}} = (\text{SL}-2)/(2*[\mathbf{R,R-1}]/[\mathbf{S,S-1}])$. Likewise, $r_{\text{PLA-S}} = (\text{SL}-2)/(2*[\mathbf{S,S-1}]/[\mathbf{R,R-1}])$. Since $(\pm)\text{-1}$ was used here, $[\mathbf{S,S-1}]/[\mathbf{R,R-1}] = 1$ and $r_{\text{PLA-R}} = r_{\text{PLA-S}} = r = (\text{SL}-2)/2$.
- ⁶ Bandrup, J.; Immergut, E. H.; Grulke, E. A.; Abe, A.; Bloch, D. R. *Polymer Handbook*, 4th Edition, John Wiley & Sons, Inc. New York, 1999.
- ⁷ Medrano, R.; Laguna, M. T. R.; Saiz, E.; Tarazona, M. P. Analysis of Copolymers of Styrene and Methyl Methacrylate using Size Exclusion Chromatography with Multiple Detection. *Phys. Chem. Chem. Phys.* **2003**, *5*, 151–157.