Poly(ω-pentadecalactone)-b-poly(L-lactide) Block Copolymers via Organic-Catalyzed Ring Opening Polymerization and Potential Applications

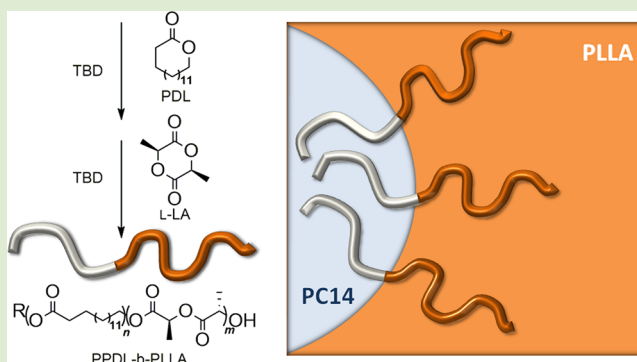Richard Todd,*,[†] Sarah Tempelaar,[†] Giada Lo Re,[†] Stephen Spinella,[†,‡] Scott A. McCallum,[‡] Richard A. Gross,[‡] Jean-Marie Raquez,[†] and Philippe Dubois*,[†]

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ⓢ *Supporting Information*

ABSTRACT: Poly(pentadecalactone)-b-poly(L-lactide) (PPDL-b-PLLA) diblock copolymers were prepared via the organic catalyzed ring-opening polymerization (ROP) of L-lactide (L-LA) from PPDL macroinitiators using either 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD). Synthesis of PLLA blocks targeting degrees of polymerization (DP) up to 500 were found to yield diblock copolymers with crystalline PPDL and PLLA segments when TBD was used as the catalyst. The synthesis was further improved in a one-pot, two-step process using the same TBD catalyst for the synthesis of both segments. The application of these diblock copolymers as a compatibilizing agents resulted in homogenization of a biobased PLLA/poly(ω-hydroxytetradecanoate) (90:10) blend upon a melt-process, yielding enhanced material properties.

Biodegradable polymers are important materials that have found use in various applications from biomedical to packaging and rapid prototyping. Polyesters make up a large proportion of these materials, and among these, poly(lactide) (PLA) is most dominant.[1−3] While biobased and highly stiff, the brittleness and poor hydrolytic stability of PLA limits its potential uses and necessitates the use of additives/fillers to rival most petroleum-based polymers. In contrast, polyesters derived from the 16-membered macrolactone ω-pentadecalactone (PDL) display ductility and toughness that resemble linear low density polyethylene. Poly(pentadecalactone) (PPDL) owes its increased tensile properties to its long methylene sequences and its strength to the crystalline structure. Both its crystallinity and hydrophobicity contribute to the low susceptibility of PPDL to hydrolytic degradation.[4,5] The synthesis of PPDL-b-PLA diblock copolymers could afford materials that incorporate the beneficial properties of both component parts.

Preparation of polyesters from lactones through ring-opening polymerization (ROP) is the preferred synthetic method when good control over the polymer microstructure is required. Although well-studied for highly strained cyclic esters, only few studies report the successful ROP of macrolactones. So far, most studies make use of lipase[4−9] or metal-based catalysts,[10−16] with only Bouyahyi et al. and Pascual et al. having recently described the limited use of organic catalysts.[17−20] Unsurprisingly, only a few examples of block copolymers incorporating PPDL exist due to complications by unwanted side reactions during synthesis.[7,17,21,22] For example, the desired high degree of control for block copolymer synthesis is not obtained in enzymatic ROP due to transesterification and water initiation. PPDL grown from a hydroxyl-terminated poly-(butadiene) macroinitiator required fractionation to remove water-initiated chains.[21] Duchateau and co-workers emphasized the difficulty using organic catalysts (e.g., 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD)) when attempting the synthesis of PPDL-b-poly(caprolactone) (PCL) block copolymers.[17] Random copolymers resulted despite the sequential addition of monomers, highlighting the presence of rapid intra- and intermolecular transesterification. Only when metal catalysts were used were PPDL-b-PCL block copolymers synthesized with a high degree of control.[13,17] The combination of PPDL and PLA in a block copolymer structure has to date not been reported. In comparison to PCL, the use of PLA is further complicated by the ease with which the crystallinity/microstructure can be lost during synthesis.
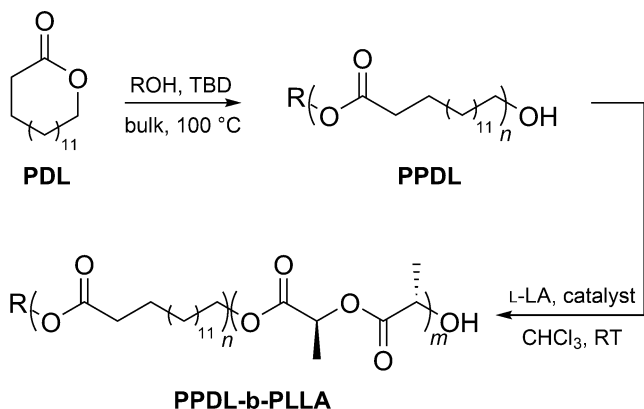
To avoid the use of metal-based catalysts, herein PPDL-*b*-PLLA syntheses were carried out using organic catalysts (Scheme 1). ROP of PDL was first carried out in bulk at 100

Scheme 1. Synthesis of PPDL-*b*-PLLA Block Copolymers

°C using TBD and 1-phenylethanol as the catalyst and initiator, respectively, yielding PPDL (81−90%) with no evidence of water initiation that could be subsequently used as a macroinitiator for further L-LA polymerizations.[17]

PPDL-*b*-PLLA block copolymer formations were investigated using either 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or TBD as the organic catalysts (1 or 0.5 equiv, respectively, to alcohol initiator). PDL polymerizations are generally performed in bulk or toluene at elevated temperatures as PPDL is only sparingly soluble. However, these conditions favor rapid transesterification of PLA in the presence of DBU and TBD. To avoid transesterification from occurring, block formations were carried out at room temperature in solution at concentrations that allowed for the easy dissolution of both L-LA and the PPDL macroinitiator. This is in contrast to the method adopted by Duchateau and co-workers who attempted the formation of PPDL-*b*-PCL block copolymers in bulk at 100 °C using TBD.[17] At an L-LA concentration of 0.35 M in chloroform, macroinitiators with molecular weights up to 82 300 g/mol could be dissolved. Under these conditions, high L-LA conversions were achieved (84−98%) with both catalysts (Table 1). Similar molecular weights were found for the resulting diblock copolymers when the same [M]/[I] ratios were used during polymerizations, irrespective of the catalyst employed, although DBU resulted in slightly lower polymer

Table 1. PPDL-*b*-PLLA Block Copolymers[a]

| cat.	cat/ROH/LLA	time (min)	conv.[c] (%)	$M_n{}^d$ (g/mol)	$Đ_M{}^d$
DBU	1:1:25	10	92	21200	1.40
DBU	1:1:50	45	91	27130	1.26
DBU	1:1:100	360	98	41020	1.16
DBU	1:1:250	1440	95	68730	1.09
DBU	1:1:500	2940	84	102910	1.06
DBU	1:1[b]:250	1380	93	112100	1.35
TBD	0.5:1:25	0.5	98	20400	1.54
TBD	0.5:1:100	10	98	37740	1.28
TBD	0.5:1:500	60	88	107910	1.11

[a]Conditions: [LLA] = 0.35 M, 25 °C, ROH = PPDL$_{27}$ (M_n = 12000 g/mol, $Đ_M$ = 2.00). [b]ROH = PPDL$_{130}$ (M_n = 82000 g/mol, $Đ_M$ = 1.79). [c]Determined by ^{1}H NMR. [d]Determined by chloroform GPC analysis.

dispersities ($Đ_M$). As expected, the polymerizations catalyzed by TBD proceeded considerably faster than those employing DBU. Increasing the size of the PLA block resulted in a corresponding increase in molecular weight and a reduction in polymer dispersity from $Đ_M$ = 2.00 for the PPDL homopolymer down to $Đ_M$ = 1.06−1.11 for diblocks with long PLA segments (Figure S1, Supporting Information (SI)). Diblock copolymers with degrees of polymerization (DP) between 25 and 50 had no obvious shift in molecular weight from the macroinitiator by GPC.

^{1}H NMR spectra of all PPDL-*b*-PLLA diblock copolymers do not display the methylene resonance at the hydroxyl chain end, which is observed in the PPDL homopolymer (at 3.64 ppm, see SI), suggesting complete initiation from the macroinitiator (Figure 1). Instead, a resonance at 4.34 ppm corresponding to the formed PLA end group is found with integral values that are in good agreement with those of the α-chain end, confirming a lack of PLA homopolymer.[23,24] Further evidence that PPDL-*b*-PLLA diblock copolymers were successfully synthesized was obtained by ^{13}C and DOSY NMR experiments. The DOSY NMR spectrum (Figure S2, SI) confirms the presence of a copolymer structure between the PPDL and PLA as well as the absence of any homopolymer (PLA or PPDL). The ^{13}C NMR spectra (Figure 2) reveal only two resonances between 160 and 180 ppm, one of the PPDL carbonyl and the other of the PLA carbonyl. The lack of further responses within this region shows that transesterification during ROP has been minimal and with the combined NMR analyses provides complete proof of PPDL-*b*-PLLA diblock copolymer formation.

Since the microstructure of the PLLA block can be affected by transesterification and/or epimerization during ROP, thermal characterizations of the block copolymers were carried out (DSC, TGA). It is worth noting that polymerizations were always stopped before full conversion to avoid the occurrence of transesterification.[25,26] Generally, the block copolymers displayed melting points for both their PPDL and PLLA segments (Figure S3, SI) proving the block copolymer structure is not disrupted by transesterification and the PLLA segment is unaffected by epimerization.[27] However, in the case of the DBU-catalyzed polymerization with [M]/[I] = 500, the long reaction time (49 h) required to reach high monomer conversion provides an extended time period wherein significant epimerization occurs. This was evidenced by its DSC result in which no melting point is observed for the PLLA block. Furthermore, the ^{13}C NMR spectrum points to the occurrence of transesterification (Figure S4, SI). This result indicates that, even though TBD is a stronger base, the considerably shorter polymerization times result in a lack of significant epimerization or transesterification with no/little disturbance to the diblock structure and should, therefore, be the preferred choice of organic catalyst in PPDL-*b*-PLLA diblock copolymer synthesis.

Confirmation that the synthesis of stereopure PPDL-*b*-PLLA diblock copolymers is possible using TBD for both blocks led to the exploration and further improvement in system scalability. Instead of performing the synthesis of each block in a separate pot, we developed a one-pot, two-step process that takes advantage of the different kinetics of the PDL and L-LA ring-opening polymerizations. The one-pot process avoids the purification and extensive drying of the PPDL macroinitiator and reuses the organic catalyst in the second step. The first step was performed in bulk at 100 °C, before a solution of L-LA in dry CHCl$_3$ was added at room temperature immediately
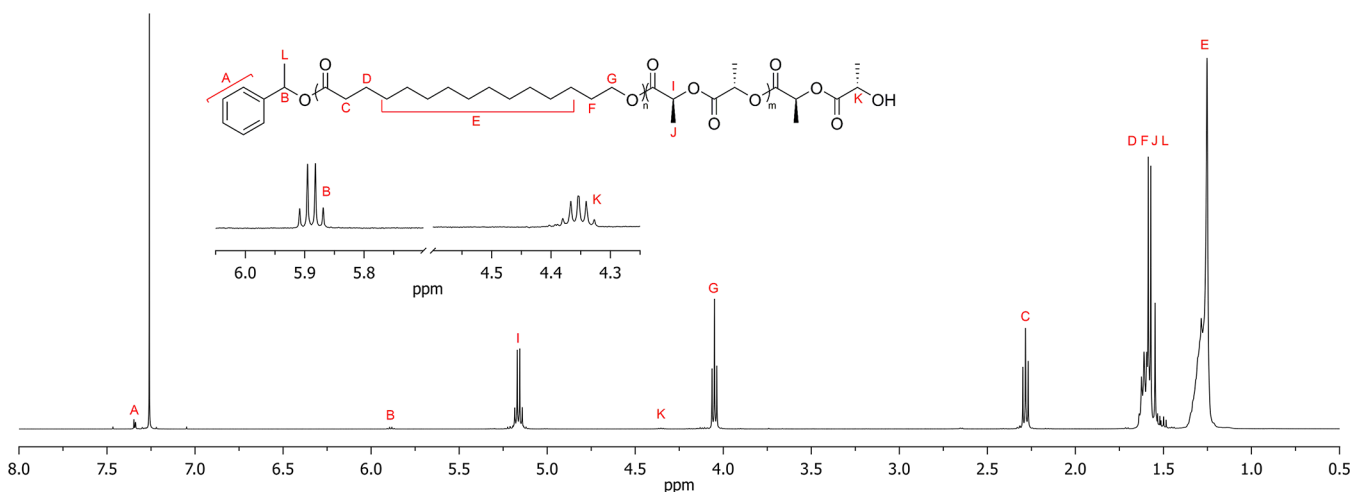
**Figure 1.** ^{1}H NMR spectrum of PPDL-*b*-PLLA diblock copolymer in CDCl$_3$ at 500 MHz.
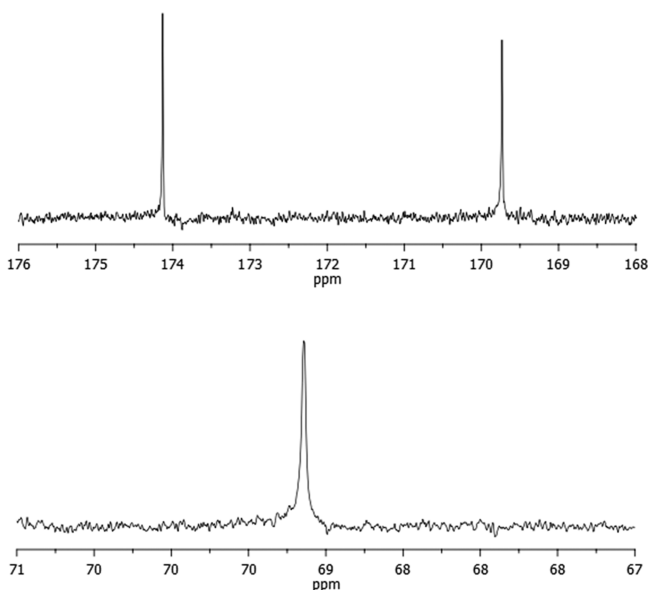
Figure 2. ^{13}C NMR spectrum of a PPDL-*b*-PLLA block copolymer magnified in the carbonyl region (168−176 ppm) and the PLLA methine region (67−72 ppm).

initiating the second step. Although full PDL conversion is not achieved in the first step, the reduced temperature and the considerably higher activity of LA in solution polymerization compared to PDL results in the formation of a diblock copolymer.

We envisage that one important application of PPDL-*b*-PLLA diblock copolymers is as compatibilization agents employed in the blending of commercial PLLA with polymers with a high carbon content. It was therefore investigated whether enhanced compatibilization between PLLA and renewable poly(ω-hydroxytetradecanoate) (PC14) could be obtained with their use. PC14 is a polymer structurally similar to PPDL, albeit with one less methylene unit in each repeat unit, and is derived from ω-hydroxytetradecanoic acid.[28] While PDL is petroleum-based, ω-hydroxyfatty acids can be prepared via a practical biotechnological route, as demonstrated in 2010.[29] A PPDL-*b*-PLLA diblock copolymer with similar molecular weight segments (PPDL$_{55}$-*b*-PLLA$_{99}$) was tested as a compatibilizing agent for a PLLA/PC14 (90:10) blend

prepared by a melt-process using 4% of diblock copolymer. A lower content in PC14 was investigated in this preliminary study to readily highlight the presence of dispersed PC14 domains within the continuous PLLA matrix. SEM images of the blends obtained with and without the addition of 4% diblock copolymer display stark differences. A complete separation of the PC14 phase from the PLLA majority phase is observed without the use of the diblock, whereas the addition of the diblock yields a finely homogenized surface (Figure 3).
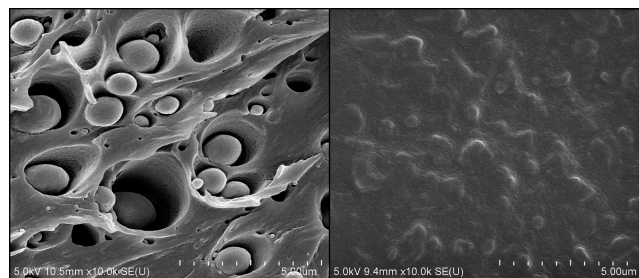
Figure 3. SEM images of a PLLA/PC14 (90:10) blend (left) and a PLLA/PC14/PPDL-*b*-PLLA (90:10:4) blend (right).

The improved affinity between the two polymeric phases also resulted in an improvement of the material properties. A significant increase in storage modulus from 7790 to 12160 MPa was recorded at room temperature by dynamic mechanical thermal analysis (Figure S5, SI).

In conclusion, the synthesis of PPDL-*b*-PLLA block copolymers was reported for the first time. Although PPDL-based block copolymers have previously not been obtained via ROP using organic catalysts, we were able to prepare well-defined, crystalline blocks through ROP using TBD in solution. This process could be fine-tuned to a one-pot, two-step process wherein the catalyst is reused and isolation and drying of the PPDL intermediate is avoided. Furthermore, these block copolymers proved to be excellent compatibilizers in PLLA/PC14 blends yielding a material with improved properties and a high biobased content.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures, as well as NMR spectra, GPC, DSC, and TGA data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Hollister, S. J. Nat. Mater. **2005**, 4 (7), 518−524.

(2) Ikada, Y.; Tsuji, H. Macromol. Rapid Commun. **2000**, 21 (3), 117−132.

(3) Gupta, A. P.; Kumar, V. Eur. Polym. J. **2007**, 43 (10), 4053−4074.

(4) Focarete, M. L.; Scandola, M.; Kumar, A.; Gross, R. A. J. Polym. Sci., Part B: Polym. Phys. **2001**, 39 (15), 1721−1729.

(5) van der Meulen, I.; de Geus, M.; Antheunis, H.; Deumens, R.; Joosten, E. A. J.; Koning, C. E.; Heise, A. Biomacromolecules **2008**, 9 (12), 3404−3410.

(6) Kumar, A.; Gross, R. A. J. Am. Chem. Soc. **2000**, 122 (48), 11767−11770.

(7) Kumar, A.; Kalra, B.; Dekhterman, A.; Gross, R. A. Macromolecules **2000**, 33 (17), 6303−6309.

(8) Jiang, Z.; Azim, H.; Gross, R. A.; Focarete, M. L.; Scandola, M. Biomacromolecules **2007**, 8 (7), 2262−2269.

(9) Vaida, C.; Keul, H.; Moeller, M. Green Chem. **2011**, 13 (4), 889−899.

(10) Zhong, Z.; Dijkstra, P. J.; Feijen, J. Macromol. Chem. Phys. **2000**, 201 (12), 1329−1333.

(11) Nakayama, Y.; Watanabe, N.; Kusaba, K.; Sasaki, K.; Cai, Z.; Shiono, T.; Tsutsumi, C. J. Appl. Polym. Sci. **2011**, 121 (4), 2098−2103.

(12) Pepels, M. P. F.; Bouyahyi, M.; Heise, A.; Duchateau, R. Macromolecules **2013**, 46 (11), 4324−4334.

(13) Bouyahyi, M.; Duchateau, R. Macromolecules **2014**, 47 (2), 517−524.

(14) Pepels, M. P. F.; Souljé, P.; Peters, R.; Duchateau, R. Macromolecules **2014**, 47 (16), 5542−5550.

(15) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. Polym. Chem. **2014**, 5 (8), 2691−2694.

(16) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. Macromolecules **2015**, 48 (4), 950−958.

(17) Bouyahyi, M.; Pepels, M. P. F.; Heise, A.; Duchateau, R. Macromolecules **2012**, 45 (8), 3356−3366.

(18) Pascual, A.; Leiza, J. R.; Mecerreyes, D. Eur. Polym. J. **2013**, 49 (6), 1601−1609.

(19) Pascual, A.; Sardon, H.; Veloso, A.; Ruipérez, F.; Mecerreyes, D. ACS Macro Lett. **2014**, 3 (9), 849−853.

(20) Pascual, A.; Sardón, H.; Ruipérez, F.; Gracia, R.; Sudam, P.; Veloso, A.; Mecerreyes, D. J. Polym. Sci., Part A: Polym. Chem. **2015**, 53, 552−561.

(21) Kumar, A.; Gross, R. A.; Wang, Y.; Hillmyer, M. A. Macromolecules **2002**, 35 (20), 7606−7611.

(22) Jasinska-Walc, L.; Hansen, M. R.; Dudenko, D.; Rozanski, A.; Bouyahyi, M.; Wagner, M.; Graf, R.; Duchateau, R. Polym. Chem. **2014**, 5, 3306−3310.

(23) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Waymouth, R. M.; Hedrick, J. L. J. Am. Chem. Soc. **2005**, 127 (40), 13798−13799.

(24) Todd, R.; Rubio, G.; Hall, D. J.; Tempelaar, S.; Dove, A. P. Chem. Sci. **2013**, 4, 1092−1097.

(25) Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. Macromolecules **2006**, 39 (25), 8574−8583.

(26) Comparison of ¹³C NMR data of block copolymer recovered after 10 min and after 24 h of TBD catalyzed polymerization (both >90% L-LA conversion) reveals the occurrence of transesterification in the latter case (Figure S13, SI).

(27) Removal of catalyst using acidic resin prevents transesterification post-polymerization: Lo Re, G.; Benali, S.; Habibi, Y.; Raquez, J.; Dubois, P. Eur. Polym. J. **2014**, 54, 138−150.

(28) Liu, C.; Liu, F.; Cai, J.; Xie, W.; Long, T. E.; Turner, S. R.; Lyons, A.; Gross, R. A. Biomacromolecules **2011**, 12, 3291−3298.

(29) Lu, W.; Ness, J. E.; Xie, W.; Zhang, X.; Minshull, J.; Gross, R. A. J. Am. Chem. Soc. **2010**, 132, 15451−15455.