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Synthesis and Thermal Properties of Linear Amphiphilic Diblock Copolymers of L-Lactide and 2-Dimethylaminoethyl Methacrylate

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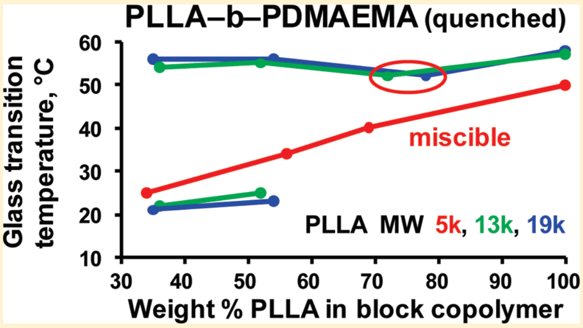
Supporting Information

ABSTRACT: A well-defined series of nine poly(L-lactide)-*b*-(2-dimethylaminoethyl methacrylate) (PLLA-*b*-PDMAEMA) linear diblock copolymers with low polydispersity were prepared by ring-opening polymerization of LLA using 4-isopropylbenzyl alcohol and tin octoate as the initiating system, conversion of the OH-terminated PLLA into Br-terminated macroinitiators (5, 13, and 19 kg/mol), followed by atom transfer radical polymerization of DMAEMA (to obtain one-half, equal, and twice the molecular weight of each PLLA block). Compositional analysis and molecular weight characterization were done using NMR, SEC−LS, TGA, polarimetry, and PDMAEMA quaternization/precipitation to test for residual PLLA homopolymer. DSC investigations indicate that low molecular weight amorphous PLLA or PDMAEMA blocks (less than or equal to ca. 5000 g/mol) are miscible in the second block. Compared to the parent PLLA homopolymers, PLLA crystallization in the block copolymers is significantly retarded, whereas the degree of crystallinity is only mildly affected and melting points are reduced only for the low molecular weight miscible blocks.



INTRODUCTION

Poly(lactic acid) or polylactide (PLA) combines many desirable characteristics, including availability from renewable resources, that make these materials useful for a variety of engineering and biomedical applications. In stereochemical form, the most common being poly(L-lactide) (PLLA), the material is semi-crystalline with a high melting point, conferring good mechanical properties over a wide range of use temperatures. The well-known degradability and biocompatibility of PLA[1] are attractive for applied areas such as tissue engineering[2] and suture design.[3] Moreover, PLA hydrophobicity and biodegradability enable drug-encapsulating and -release capabilities in materials containing this component.[4] As one of the blocks in block copolymer systems, PLA can serve as an easily removable moiety in the design of nanoporous materials and films.[5] The possibility of stereocomplexing PLLA with its D-lactide form, PDLA, further expands the versatility of these materials.[6,7] On the other hand, poly(2-dimethylaminoethyl methacrylate) (PDMAEMA) has received considerable attention due to its hydrophilicity, pH and temperature sensitivity, ease of quaternization, and availability of the functional amine/ammonium moiety for complexation with acidic/anionic substances that make it attractive for wide-ranging applications including as flocculation agents,[8] as biocides,[9], and in gene delivery[10] systems.

In developing these materials and their applications, both PLA and PDMAEMA have been associated with a variety of other polymers in the form of block copolymers, a quintessential route for forming self-assembling meso- and nano-structured materials. PLA has been combined with, for example, poly(caprolactone),[11,12] poly(ethylene oxide),[13,14] polystyrene,[15−17] poly(isopropylacrylamide),[18,19] polyethylene,[20,21] poly(vinylpyrrolidone),[22] and polythiophene[5] and PDMAEMA with, for example, various other polymethacrylates,[23−28] poly(caprolactone),[29,30] poly(ethylene oxide),[31] polystyrene,[32,33] poly(2-vinylpyridine),[34] and poly(ethylene-*co*-butylene).[9] Cationic PDMAEMA has also been adsorbed onto PLA nanoparticles to enhance DNA delivery.[35] The combination of PLA and PDMAEMA into block copolymers has appeared only recently.[36−41] Amphiphilic block copolymer systems such as these have particular interest, since they can form micelles (or gels at higher concentration) in both organic and aqueous media and interact with both polar and nonpolar solutes, providing, for example, an adaptable drug delivery matrix. Combining the amphiphilicity with the individual characteristics of PLA and PDMAEMA in block copolymers potentially make of them highly versatile materials for a large variety of applications, both in solution and in the solid state. For example, stereocomplexes of PLLA-*b*-PDMAEMA with PDLA-*b*-PDMAEMA were prepared for the fabrication of antibacterial

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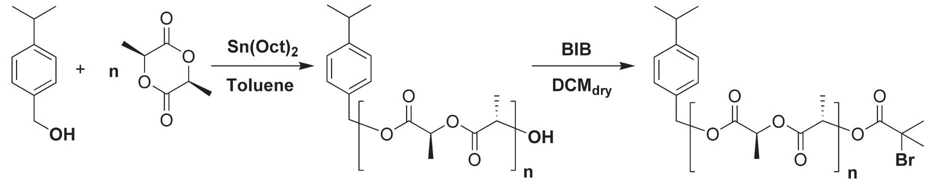
Scheme 1. Synthesis of the PLLA Macroinitiator by ROP Followed by Terminal Group Modification



and hemostatic electrospun fibers[39,40] and dendritic star−block copolymers for controlled drug release applications.[38] As bulk and thin film materials, the microphase-separated structure of these block copolymers can be coupled with the ability to modulate the microstructure and functionality of the material by hydrogen-bonding, ionically complexing or quaternizing the PDMAEMA block with appropriate molecules or by selectively post-degrading or stereocomplexing the PLA (PLLA) block.

In this context, it is of interest to synthesize and characterize PLA−PDMAEMA block copolymers with a wide range of well-controlled block lengths and narrow polydispersity. Among the syntheses described in refs 37−41, one involves such a series, where the PLA block is in the PDLLA form and is restricted to low molecular weight (1.3−3.7 kg/mol).[41] In the present contribution, we describe the synthesis of similar block copolymers, but where the PLA block is in the stereochemical PLLA form and has a much wider molecular weight range (5−20 kg/mol). A three-step synthetic procedure similar to that in refs 39 and 41 was used, involving ring-opening polymerization (ROP) of LLA, followed by appropriate end group conversion to obtain PLLA macroinitiators, and finally by addition of the PDMAEMA block using atom transfer radical polymerization (ATRP). PDMAEMA blocks with molecular weights that are half of, equal to, and twice that of each of the three macroinitiators synthesized were targeted. In addition, we investigated the thermal properties of the well-defined series to observe transition temperatures, the effect of the PDMAEMA block on PLLA crystallization, and the state of phase separation of the blocks, all as a function of block molecular weight. Knowledge of these characteristics is important to efficiently exploit these materials in various applications, particularly in the bulk and as films.

EXPERIMENTAL SECTION

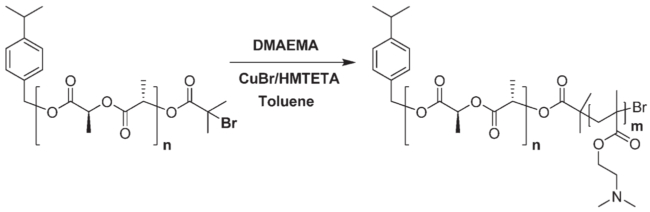
Techniques. ^{1}H NMR spectra were recorded at room temperature on a Bruker Avance 400 MHz spectrometer using CDCl$_3$ (Aldrich) solutions containing 0.03% of tetramethylsilane (TMS) as an internal standard. Sequential size exclusion chromatography (SEC) and light scattering (LS) data of the PLLA homopolymers and block copolymers were obtained using a Waters 510 HPLC pump, PLgel columns (Polymer Laboratories) with 5-μm pore sizes (50 × 7.5, 300 × 7.5 and 600 × 7.5 mm), a Wyatt EOS refractive index (RI) detector and a Wyatt QUELS LS detector. Tetrahydrofuran (THF) with 2−5% v/v of triethylamine (TEA) was used as the mobile phase, at a flow rate of 1 mL/min. The performance of the SEC−LS system was verified using polystyrene standards. The data were collected and processed using the ASTRA software package. Dn/dc measurements of the homopolymers and six representative copolymers (not necessarily those presented in this manuscript) were determined to a precision of ±0.001 mL/g for a series of five solutions per sample with precise concentrations ranging between 1 and 5 mg/mL, using the Wyatt EOS RI detector (operating at 691 nm) and a flow rate of 0.2 mL/min. The d*n*/d*c* values for PLLA and PDMAEMA in THF (with 2−3% TEA) were found to be 0.048 and 0.084 mL/g, respectively. The relationship between d*n*/d*c* and block composition including the homopolymers was found to be linear, as it should be,[42] and was used to interpolate the d*n*/d*c* values for the subsequent copolymers synthesized. The specific optical rotatory powers, [α_L], of the PLLA macroinitiators and representative block copolymers were measured at room temperature in chloroform solution at a concentration of ca. 1 g/dL, using a PerkinElmer 341 polarimeter operating at 589 nm.

Thermogravimetric analysis (TGA) was performed with a TA Instruments Hi-Res TGA 2950 analyzer under nitrogen flow at a heating rate of 10 °C/min. Differential scanning calorimetry (DSC) measurements were acquired with a TA Instruments Q1000 DSC, using standard aluminum pans, an indium standard for calibration, and nitrogen as the purge gas. Scan details are given in the Supporting Information. Melting/crystallization temperatures were determined by their peak values. Glass transition temperatures of the homopolymer were identified by the inflection points in the heating thermograms. For the copolymers, where baselines, especially between two T_g's, were often difficult if not impossible to determine, T_g's were identified by the peak values in the first derivative curves.

Materials. L-Lactide (LLA), obtained from Aldrich, was recrystallized twice from anhydrous ethyl acetate (distilled over P_2O_5 prior to use) and stored under dry nitrogen prior to use. Stannous 2-ethylhexanoate [tin octoate, Sn(Oct)$_2$],[43−45] 4-isopropylbenzyl alcohol (iPBA), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA), 2-bromoisobutyryl bromide (BIB), triethylamine, and 2-dimethylaminoethyl methacrylate (DMAEMA),[45] all supplied by Aldrich, were used as received. 2-Hydroxyethyl-2-bromoisobutyrate (HEBIB) was prepared following a procedure described in ref 29 [^{1}H NMR: δ_H, *ppm* 1.96 (s, 2CH$_3$), 2.42 (br. s, OH), 3.81−3.93 (m, CH$_2$OH), 4.26−4.34 (m, OCH$_2$)]. Copper(I) bromide (Aldrich) was dispersed in boiling glacial acetic acid under vigorous stirring for a few hours, then filtered, washed successively with ethanol and ether, and dried under reduced pressure at 60 °C. The assembled reaction system (flask, magnetic stirrer, 3-way adapter) was thoroughly dried/deoxygenated by repeated evacuate (10 mTorr)−heat (250 °C)−refill (dry N$_2$) cycles prior to synthesis.

Synthesis of Bromine-Terminated Poly(L-lactic acid), PLLA−Br. PLLA−Br macroinitiators were synthesized as shown in Scheme 1, using a procedure similar to those described previously for ring-opening polymerization of LLA[46,47] to give PLLA−OH, followed by terminal group modification using BIB.[9,39] The polymerization took place in concentrated solution (ca. 3 M in toluene) at 120 °C using iPBA as initiator and tin octoate as catalyst [5:1 iPBA:Sn(Oct)$_2$]. Specifically, 2−3 g of LLA were charged into the prepared flask and three vacuum−nitrogen cycles were carried out. Calculated amounts of freshly prepared solutions of tin octoate (0.44 M in toluene) and iPBA (0.06 M in toluene), followed by 8 mL of dry toluene, were then added through a septum via a syringe under nitrogen flow. Finally, the system was closed under positive nitrogen pressure, and polymerization proceeded under stirring at 120 °C. The degree of conversion was monitored by NMR analysis of reaction mixture aliquots, and polymerization was stopped at ca. 95% conversion by cooling to room temperature. The solidified reaction mixture was dispersed in 30 mL of methanol, then poured into 200 mL of methanol containing 1 mL of concentrated HCl to remove the Sn residue. The white solid was collected by filtration, washed with methanol, dried, redissolved in 10 mL of dry dichloromethane or chloroform, and precipitated dropwise into 300 mL of methanol containing 1 mL of concentrated HCl. The fibrous precipitate was collected by filtration, washed with methanol and dried in vacuo at 30 °C for 72 h. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H, ppm 1.24 (d, J = 6.8 Hz, 2

Scheme 2. Synthesis of PLLA-*b*-PDMAEMA Block Copolymers Following Standard ATRP Procedures



CH_3, initiator fragment), 1.58 (d, $J = 7.2$ Hz, CH_3, PLLA), 5.16 (q, $J = 7.2$ Hz, CH, PLLA).

After end-capping the hydroxyl end groups of PLLA–OH by BIB following a literature procedure,[39] the resulting PLLA–Br were dried in vacuo at 30 °C for at least 72 h. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H, ppm 1.24 (d, $J = 6.8$ Hz, 2 CH_3, initiator fragment), 1.58 (d, $J = 7.2$ Hz, CH_3, PLLA), 1.95 (s, CH_3, BIB end group), 1.98 (s, CH_3, BIB end group), 5.16 (q, $J = 7.2$ Hz, CH, PLLA).

Synthesis of Poly(L-lactic acid)-*b*-poly(2-dimethylaminoethyl methacrylate), PLLA-*b*-PDMAEMA (Scheme 2). Macroinitiated atom-transfer radical polymerization (ATRP) of DMAEMA is well described in the literature,[9,29,37] with variations in the detailed procedures such as in the choice of ligand or in the structure of the terminal Br-containing moiety. The procedure we used has been optimized for obtaining copolymers with a low polydispersity as follows. PLLA–Br (0.5 g), 1 equiv of CuBr and 4 equiv of HMTETA were charged into the reaction flask and deoxygenated by three vacuum–nitrogen cycles. After addition of 3.5–4.5 mL (more for the longer PLLA macroinitiators) of dry deoxygenated toluene, the mixture was stirred at 40 °C and further heated if necessary to achieve dissolution (as was the case for the longer PLLAs), until a clear light-green solution was formed. Finally, the required amount of DMAEMA was introduced via a syringe, the system was closed under positive nitrogen pressure, and then polymerization proceeded under stirring at 70 °C for the required time (maximum of 81 h). For the longer PLLA macroinitiators, polymerization was carried out initially at higher temperature, notably at ca. 90 °C for ca. 2 h, to avoid solution cloudiness, and 70 °C for the remaining time.

Polymerization was stopped at an estimated DMAEMA conversion of 97–98%, monitored by NMR, by cooling to room temperature and diluting with ca. 40 mL of THF. The solution was then passed through a short silica column to remove the copper residue, followed by flushing of the column with 40 mL of THF. The resulting light-yellow solution was evaporated to dryness, and the product was redissolved in 10 mL of dichloromethane, and precipitated dropwise into hexane. Sticky flakes were isolated by filtration, washed with hexane and dried in vacuo at 30 °C for at least 72 h. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H, ppm 0.80–1.12 (m, CH_3, PDMAEMA), 1.58 (d, $J = 7.2$ Hz, CH_3, PLLA), 1.65–2.15 (m, CH_2, PDMAEMA), 2.20–2.35 (m, $N(CH_3)_2$, PDMAEMA), 2.50–2.65 (m, NCH_2, PDMAEMA), 3.95–4.20 (m, OCH_2, PDMAEMA), 5.16 (q, $J = 7.2$ Hz, CH, PLLA).

A PDMAEMA homopolymer was synthesized by ATRP following the procedure described in ref 9, but using HEBIB as the initiator. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H, ppm 0.81–1.11 (m, CH_3), 1.71–2.07 (m, CH_2), 2.23–2.33 (m, $N(CH_3)_2$), 2.50–2.63 (m, NCH_2), 3.96–4.15 (m, OCH_2). SEC–LS in THF (with added 2% v/v TEA): M_n = 15 800 g/mol, M_w/M_n = 1.21.

The nomenclature of the homopolymers and copolymers are given in terms of number-average molecular weights, as in PLLA_{xk}–PDMAEMA_{yk}, where x and y refer to the molecular weight rounded off to the nearest thousand (k). The copolymers will also be referred to frequently as xk–yk.

RESULTS AND DISCUSSION

Synthesis and Characterization of the PLLA Macroinitiators. The targeted range of the PLLA–Br macroinitiators synthesized was limited to about 20 kg/mol in the present series, in order to be able to proceed with ATRP under optimal conditions; i.e., in concentrated solution without unduly high viscosity. ROP was conducted in concentrated solution as a compromise between the best conditions for obtaining narrow PDI (in dilute solution) and reasonable reactions times (fastest for bulk ROP). Moreover, 4-isopropylbenzyl alcohol was chosen as the ROP initiator to optimize molecular weight determination by ^{1}H NMR, particularly for the longer PLLA chain lengths targeted. This initiator provides a PLLA terminal moiety giving a well-defined and isolated 6-proton signal at 1.24 ppm [$-C_6H_4-CH(C\boldsymbol{H}_3)_2$; c in Figure 1] for comparison with the polymer chain methine signal at 5.16 ppm [$-OC(=O)-C\boldsymbol{H}(CH_3)-$; a in Figure 1]. This affords up to a 6-fold improvement in NMR molecular weight determination, compared to using the very weak and concentration-dependent signal of the terminal methine protons of PLLA–OH (4.35 ppm, $-O-C(=O)-C\boldsymbol{H}(CH_3)-OH$, d in Figure 1).[37,48] End-capping with BIB introduces another well-defined and isolated 6-proton signal at 1.96 ppm [$O-C(=O)-C(C\boldsymbol{H}_3)_2-Br$; e in Figure 1]. This allows comparison of the integrals of the signals at 1.24 ppm from the initiator moiety and at 1.96 ppm from the BIB moiety to determine the completeness of terminal group modification, which is also more accurate than relying on the disappearance of the signal at 4.34 ppm.

The NMR-determined M_n's of the synthesized PLLAs are given in Table 1. They correspond well to the theoretical M_n's determined from the monomer/initiator feed ratios. The differences observed between the PLLA–OH and corresponding PLLA–Br are within experimental uncertainty. For further comparison and to determine polydispersity indices, SEC–LS experiments were performed in THF containing 2–3% v/v TEA (TEA added for consistency with the block copolymer conditions). The SEC–LS M_n values correspond well to the NMR-determined M_n values. The PDIs are relatively narrow, between 1.1 and 1.3. As also shown in Table 1, the specific optical rotatory powers, $[\alpha_L]$, of the different PLLA–OH and PLLA–Br were all in the range of $-150 \pm 5°$, compared to literature values for PLLA considered as optically pure that range from -145 to $-160°$,[6,39,46,49,50] This indicates that the optical purity of the macroinitiators is very high, certainly better than 90%. The high optical purity was supported by ^{13}C and ^{1}H homonuclear decoupling NMR experiments that show no evidence of racemization in either OH- or Br-terminated PLLA (see Supporting Information).

Synthesis and Molecular Weight Characterization of the PLLA-*b*-PDMAEMA Copolymers. Because PLLA–Br is not soluble in DMAEMA, the synthesis of PLLA-*b*-PDMAEMA was carried out in toluene solution. DMAEMA polymerization was initiated from the PLLA–Br block using the CuBr/HMTETA ATRP catalyst, generally at 70 °C. However, since PLLA solubility in toluene decreases with increasing molecular weight, the solutions of PLLA–Br of molecular weights greater than 10 000 g/mol were diluted and polymerization took place initially at 90 °C. In the course of polymerization, the temperature was reduced to the usual polymerization temperature (70 °C), the good solubility of the PDMAEMA block in toluene maintaining the copolymer in solution.

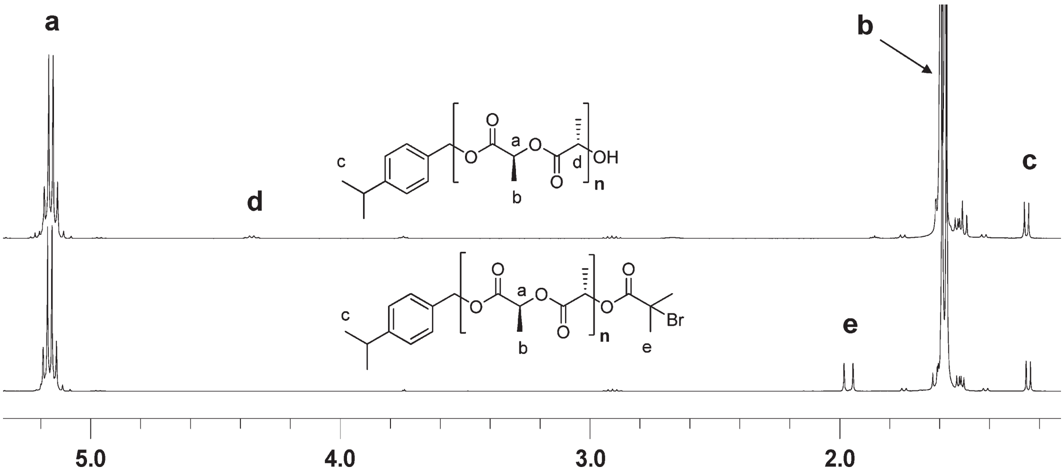


Figure 1. ^{1}H NMR spectra of PLLA$_{5k}$−OH (upper) and PLLA$_{5k}$−Br (lower).

Table 1. Molecular Weight Characteristics and Optical Rotatory Powers of the PLLA Homopolymers and Macroinitiators Synthesized

sample[a]	M_n(theor[b]), g/mol	M_n(NMR[c]), g/mol	M_n(SEC−LS[d]), g/mol	PDI(SEC−LS[d])	$[\alpha_L]$[e], deg
PLLA$_{5k}$−OH	4900	4600	4600	1.11	−152
PLLA$_{13k}$−OH	11 600	11 600	13 000	1.19	−155
PLLA$_{19k}$−OH	17 300	19 000	19 800	1.14	−156
PLLA$_{5k}$−Br	5100	4900	5200	1.09	−147
PLLA$_{13k}$−Br	11 700	13 800	13 200	1.32	−153
PLLA$_{19k}$−Br	17 400	18 900	19 500	1.20	−145

[a] The subscript in the sample nomenclature indicates the average molecular weight (rounded off to the nearest 1k) of the four M_n values from the NMR and SEC−LS measurements considering both the OH and Br forms. [b] Theoretical assuming 95% conversion, $M_n = [([LLA]_0/[I]_0) \times 144) \times 0.95] + M_{initiator}$ (+ M_{BIB}). [c] Estimated by comparing the integrals of the PLLA methine protons (5.16 ppm) and the methyl protons of the initiator fragment (1.24 ppm), and adding $M_{initiator}$ and/or M_{BIB}. [d] Determined in THF with 2% (v/v) TEA, dn/dc = 0.048 mL/g. [e] Measured at room temperature.

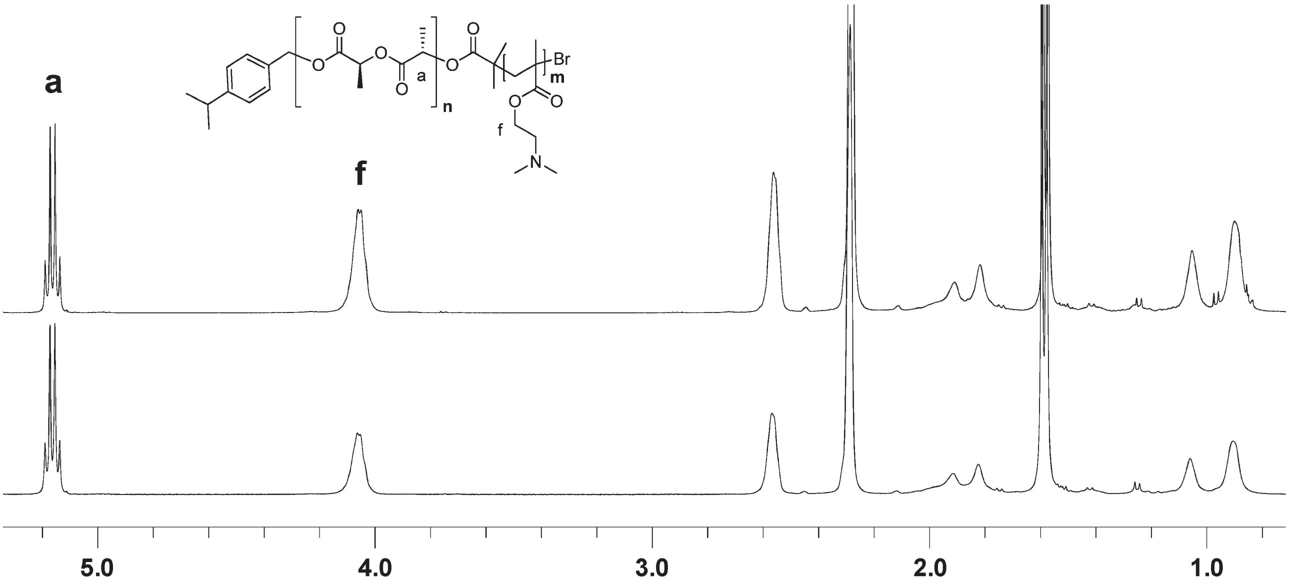


Figure 2. ^{1}H NMR spectra of PLLA-*b*-PDMAEMA [13k−12k (lower) and 13k−23k (upper)].

Reaction feeds for each PLLA macroinitiator were calculated to target three block copolymers compositions, namely 0.5:1, 1:1 and 2:1 PLLA:PDMAEMA weight ratio, corresponding to approximately 1:1, 2:1 and 4:1 LLA:DMAEMA molar ratio. The experimental block molar ratios obtained were determined from ^{1}H NMR spectra (Figure 2) by comparison of the integrals

Table 2. Molecular Weight Characterization of the PLLA-*b*-PDMAEMA Copolymers Synthesized

sample	PLLA M_n (g/mol)/DP_n[a]	PDMAEMA M_n (g/mol)/DP_n[b]	Total (SEC−LS) M_n (g/mol)/PDI[c]
5k−2k	4800/63	2200/14	8100/1.10
5k−4k	4800/63	3800/24	9600/1.13
5k−10k	4800/63	9500/60	16900/1.15
13k−5k	12900/175	5000/32	18600/1.18
13k−12k	12900/175	12100/77	26000/1.16
13k−23k	12900/175	22900/146	38300/1.20
19k−5k	19300/264	5400/34	20500/1.20
19k−17k	19300/264	16600/106	37300/1.11
19k−35k	19300/264	35100/223	54200/1.19

[a] The M_n value given is the average of the four M_n values determined by NMR and SEC−LS for PLLA−OH and PLLA−Br (Table 1). DP_n: degree of polymerization. [b] Determined by NMR by comparison of the integrals for the PLLA *a* and PDMAEMA *f* signals (see Figure 2). [c] Determined by SEC−LS in THF with 3% (v/v) TEA; d*n*/d*c* values used are 0.055 (19k−5k), 0.058 (5k−2k, 13k−5k), 0.068 (5k−4k, 13k−12k, 19k−17k) and 0.073 (5k−10k, 13k−23k, 19k−35k).

Table 3. Composition of PLLA-*b*-PDMAEMA Determined by TGA Compared with NMR

sample	wt % PDMAEMA, NMR[a]	wt % residue at 375 °C, TGA	wt % PDMAEMA, TGA[b]
$PDMAEMA_{16k}$		46	100
5k−2k	31	10	22
5k−4k	44	19	41
5k−10k	66	33	72
13k−5k	28	14	30
13k−12k	48	26	56
13k−23k	64	31	67
19k−5k	22	11	24
19k−17k	46	25	54
19k−35k	65	32	69

[a] Calculated from the NMR-determined block ratios; experimental uncertainty estimated as ±2 wt %. [b] wt % PDMAEMA = wt % residue ($PLLA_{xk}$−$PDMAEMA_{yk}$) × 100%/wt % residue (PDMAEMA homopolymer); experimental uncertainty estimated as ±5 wt % at best.

of the PLLA methine signals at 5.16 ppm [$-OC(=O)-C\boldsymbol{H}(CH_3)-$, *a* in Figure 2] with the integrals of the PDMAEMA signal at 4.06 ppm [$-C(=O)-O-C\boldsymbol{H_2}-CH_2-$, *f* in Figure 2]. The molecular weights, based on the block molar ratios and on the average of the four NMR and SEC−LS molecular weight values for the PLLA−OH/Br in Table 1, are given in Table 2, and generally correspond well to the targeted values (only $PLLA_{19k}$−$PDMAEMA_{5k}$ has a PDMAEMA block that is about half of what was targeted). The SEC elugrams of the block copolymers are monomodal, with no shoulder on the low molecular weight side, thus showing no evidence of unreacted macroinitiator. The molecular weights obtained by SEC−LS correspond well to the sum of the M_n for the individual blocks (Table 2). The low PDI's, between 1.1 and 1.2, are indicative of well-controlled polymerization. Specific optical rotatory power measurements of three copolymers, adjusted to the PLLA content, gave values of −145°, −148°, and −147° for 5k−4k, 13k−12k, and 19k−17k, respectively, indicating essentially no change in the purity of the PLLA block compared to the parent homopolymer/macroinitiator.

To further confirm the absence of homopolymer impurity in the block copolymers, particularly of the initial (PLLA) block,[51,52] the PDMAEMA block of an aliquot of the block copolymer was quaternized by methyl iodide in dichloromethane (DCM). This procedure results in a gel (except for low PDMAEMA content, such as in samples 5k−2k, 13k−5k, and 19k−5k), which can be broken up mechanically or by ultrasound to obtain insoluble and filterable block copolymer. The filtrate, which would contain any PLLA homopolymer that might be present, is then evaporated, weighed, and analyzed by NMR using $CDCl_3$. Samples 5k−10k, 13k−23k, and 19k−35k were tested in this way, and no trace of PLLA homopolymer was found in any of them, thus confirming successful chain extension. It may be added that elemental analysis of the quaternized block copolymers corresponded to the composition based on the molecular weight determination above.

TGA thermograms of several PLLA-*b*-PDMAEMA block copolymers compared with the two homopolymers are shown in the Supporting Information. PLLA degrades in a single step in the 280−360 °C region, whereas PDMAEMA degrades in two steps, the first in the 250−325 °C region, and the second in the 375−425 °C region. With the two blocks degrading in distinct temperature regions separated by a pseudo-plateau, TGA can be used to roughly estimate the relative block composition by determining the wt % sample remaining in the block copolymers at 375 °C, where the PLLA block is completely degraded, relative to the wt % sample remaining in the PDMAEMA homopolymer at 375 °C. The resulting estimations are given in Table 3 and correspond satisfactorily to the ^1H NMR data.

DSC Characterization of PLLA−OH/Br. DSC data for the PLLA homopolymers and macroinitiators are given in Table 4, and will serve as reference for the thermal analysis of the block copolymers. It may also be noted that, despite the growing importance of this polymer, there is limited thermal data as a function of PLLA molecular weight in the available literature (although there is extensive data for certain molecular weights, particularly regarding crystallization phenomena, as noted below), which is further reason to describe the tendencies observed. Since there are no significant differences in the data for the PLLA−OH/Br pairs, unless otherwise noted, what follows will refer to both as PLLA. The melting temperature of the highest molecular weight PLLA ($PLLA_{19k}$) is 172 °C, which is in the range expected for optically pure medium-to-high molecular weight PLLA (e.g., 167−169 °C for $PLLA_{10-20k}$;[6,46] 170−176 °C for $PLLA_{40-220k}$;[53] 175 °C for $PLLA_{200k}$ with 1.5% D-lactide content following 15 h of isothermal crystallization at 145 °C[54]). It is slightly lower for $PLLA_{13k}$ (although higher than the 161 °C reported in ref 53 for a $PLLA_{15k}$) and is significantly lower for $PLLA_{5k}$, in accordance with the well-known dependence of T_m on molecular weight. It may also be mentioned that the melting peaks are dominated by a single sharp peak, often accompanied by a shoulder or smaller peak a few degrees lower (see Figure 3). The appearance of two (or more) melting peaks, depending on molecular weight and thermal history, has been reported frequently for PLLA, and its origin has been ascribed to melting−recrystallization and/or to two different crystalline forms, α (highly ordered and more stable) and α′ (relatively disordered and less stable).[53,55−57] The heats of fusion obtained by integrating both peaks are ca. 60 J/g for all samples in all conditions measured (nascent, after controlled cooling at rates of

Table 4. DSC Characterization of the PLLA Homopolymers and PLLA-*b*-PDMAEMA Copolymers Synthesized

sample[a]	W_{PLLA}[b] %	T_g (ΔC_p),[c,d] °C ($J \cdot g^{-1} \cdot K^{-1}$)	T_g (ΔC_p),[c,e] °C ($J \cdot g^{-1} \cdot K^{-1}$)	T_m, °C	ΔH_m^{total}, J/g (% cryst)[f]
$PLLA_{5k}$−OH	100		48 (0.58)	151 (155[g])	60 (66)
$PLLA_{5k}$−Br	100		50 (0.56)	154	64 (70)
$PLLA_{13k}$−OH	100		57 (0.57)	164 (168[g])	59 (65)
$PLLA_{13k}$−Br	100		57 (0.58)	168	57 (63)
$PLLA_{19k}$−OH	100		57 (0.57)	171	57 (63)
$PLLA_{19k}$−Br	100		58 (0.59)	172	58 (64)
5k−2k (cr)	69	27 (0.19)		144 (148[h])	37 (59)
5k−2k (am)	69		40 (0.54)		
5k−4k (cr)	56	21 (0.20)		144 (149[h])	30 (59)
5k−4k (am)	56		35 (0.48)		
5k−10k (cr)	34	20 (0.16)		140 (146[h])	15 (49)
5k−10k (am)	34	26 (0.35)			
13k−5k (cr)	72		40 (0.19)	166 (168[h])	37 (57)
13k−5k (am)	72		52 (0.47)[i]		
13k−12k (cr)	52	22 (0.1)		165 (167[h])	24 (51)
13k−12k (am)	52	25 (0.1)	55 (0.20)		
13k−23k (cr)	36	20 (0.17)		163 (165[h])	18 (55)
13k−23k (am)	36	22 (0.20)	54 (0.14)		
19k−5k (cr)	78		45 (0.22)	167 (169[h])	43 (61)
19k−5k (am)	78		52 (0.50)[i]		
19k−17k (cr)	54	20 (0.10)		167 (169[h])	26 (53)
19k−17k (am)	54	23 (0.09)	56 (0.23)		
19k−35k (cr)	35	20 (0.18)	58 (0.07)	167 (169[h])	16 (50)
19k−35k (am)	35	21 (0.19)	56 (0.15)		

[a] The notations "cr" and "am" refer to crystallized samples (annealed at 100 °C for 1 h) and amorphous samples (no crystallization observed in the preceding 10 °C/min cooling scan from the melt), respectively. [b] $W_{PLLA} = [M_{n(PLLA)} \times 100\%]/[M_{n(PLLA)} + M_{n(PDMAEMA)}]$, using the M_n values given in Table 2. [c] The T_g's were determined from inflection points for PLLA (20 °C/min curves, quenched samples) and from first derivative maxima for the copolymers (10 °C/min curves, average of two scans per point). ΔCp's were estimated from the heating curves. [d] PDMAEMA or PDMAEMA-rich phase. [e] PLLA or PLLA-rich phase. [f] For the copolymers, obtained from 10 °C/min heating curves of samples previously annealed at 100 °C for 1 h (two experiments). The ΔH_m^{total} values are relative to the total copolymer weight. The % cryst (= % crystallinity) is relative to the PLLA weight fraction: $[(\Delta H_m/W_{PLLA})/\Delta H_{m(\text{ideal PLLA cryst})}] \times 100\%$, where $\Delta H_{m(\text{ideal PLLA cryst})} = 91$ J/g.[54] [g] First heating scan only. [h] Maximum T_m observed (usually in the first heating scan, often also in the second heating scan). [i] The first derivative peak showed pronounced asymmetry on the low temperature side.

5 and 10 °C/min, and after cold crystallization of melt-quenched samples). This indicates a degree of crystallinity of ca. 65%, when referenced to 91 J/g for 100% crystalline PLLA.[54,58,59] On cooling from the melt (at rates of −5 and −10 °C/min), crystallization occurs at peak values between 110 and 90 °C (with a weak tendency to increase in temperature with increase in molecular weight) in all PLLA samples. Cold crystallization in quenched samples (as well as in $PLLA_{13k}$−Br under all thermal histories tested, even if already partially crystallized, and in nascent $PLLA_{13k}$−OH and $PLLA_{19k}$) occurs in this same temperature range. Crystallization peaks are usually relatively sharp (both in cooling curves and in cold crystallization), with associated enthalpies (37−45 J/g) that are somewhat lower than for melting. Finally, the T_g's of quenched samples were determined to be 57 °C for $PLLA_{13k}$ and $PLLA_{19k}$ and 49 °C for $PLLA_{5k}$ (Figure 3). Given the T_g of 59 °C measured for amorphous $PLLA_{200k}$,[54] it can be concluded that only $PLLA_{5k}$ in the present series is in the sharply molecular weight dependent T_g range, similar to the T_m dependence. The ΔCp's are 0.58 ± 0.01 $J \cdot g^{-1} \cdot K^{-1}$, very close to the value of 0.61 $J \cdot g^{-1} \cdot K^{-1}$ reported in ref 54 for a completely amorphous sample.

DSC Characterization of PLLA-*b*-PDMAEMA. DSC thermograms of representative copolymers are illustrated in Figure 3 and the results of the DSC analysis are compiled in Table 4. It was observed, first of all, that no crystallization was detected by DSC in any of the samples during cooling scans from the melt for scan speeds as low as 5 °C/min, in contrast to the PLLA homopolymers, which is ascribed to the PDMAEMA block significantly slowing down the rate of crystallization. Subsequent cold crystallization was similarly affected, with its occurrence and extent decreasing with increase in scan rate and in relative PDMAEMA block length (details given in the Supporting Information). Cold crystallization temperatures range from ca. 95 to 135 °C, tending to increase somewhat with increasing PLLA block molecular weight and scan rate (see Supporting Information for further details). The cold crystallization peaks are usually fairly sharp, but sometimes broad, particularly in the presence of the longest PDMAEMA blocks and when occurring at higher temperatures.

The degree of crystallinity in the block copolymers (given in Table 4 for samples annealed for 1 h at 100 °C) relative to that in PLLA tends to decrease mildly with increase in relative PDMAEMA block length. For example, after 1 h of annealing at 100 °C, the degree of crystallinity of the PLLA component ranges from 50 to 60% for the various block copolymers (compared to ca. 65% for PLLA), usually near the lower and upper end of the range for the longest and shortest relative PDMAEMA block lengths, respectively. The reduction in the degree of crystallinity

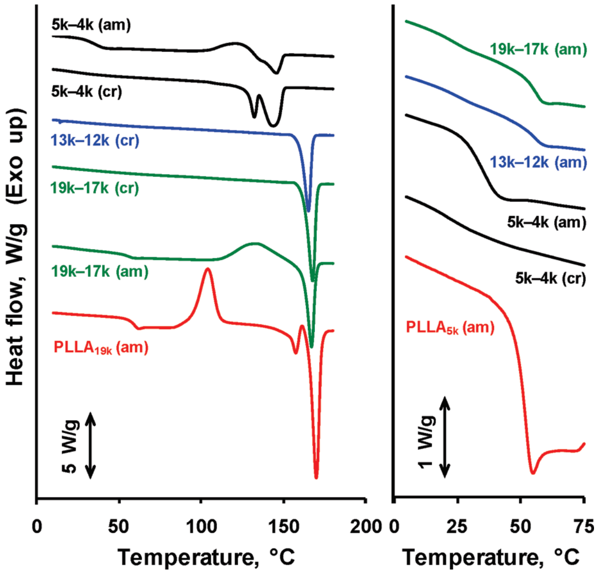


Figure 3. DSC thermograms of representative PLLA-*b*-PDMAEMA copolymers and PLLA homopolymers, scanned at 10 °C/min (except PLLA, scanned at 20 °C/min); "am" indicates samples that are initially amorphous (following a cooling scan of −10 °C/min for the *x*k−*y*k and following quenching for PLLA$_{xk}$) and "cr" indicates samples that are initially crystallized (following 1 h of annealing at 100 °C).

of individual copolymers compared to the corresponding parent PLLA homopolymer ranges from 2−3% (19k−5k, the copolymer with the least PDMAEMA content) to ca. 20% (5k−10k). For longer annealing times (tested at 120 °C for 24 h on one representative block copolymer, 19k−17k, and parent homopolymer, PLLA$_{19k}$), the degree of crystallinity is increased but remains significantly lower in the copolymer compared to the homopolymer, 63 vs 77%.

For well-crystallized samples (i.e., after annealing or after significant cold crystallization), it is observed that the DSC melting peaks of the 19k−*y*k and 13k−*y*k series are essentially monomodal and sharp, with peak values ranging from 163 to 169 °C (2−3 °C higher in the initial scan than in the two scans following annealing, as well as 1−4 °C higher for the 19k−*y*k series compared to the 13k−*y*k series scanned under the same conditions). In some cases (especially in the 13k−*y*k series), the sharp, intense peak is accompanied by a slight shoulder or weak, sharp peak located a few degrees lower. Only the 20 °C/min curves of 13k−5k and 19k−5k show two closely spaced, similar intensity peaks. Overall, both the form and the melting temperatures in these two copolymer series are similar to what is observed in the corresponding parent homopolymers. In contrast, the 5k−*y*k series shows more complex melting, generally composed of at least two melting peaks, a sharp lower temperature one and a broader higher temperature one, their maxima typically separated by 10−15 °C. The melting endotherms in this series span the temperature range of ca. 110−150 °C, much lower than for the other two series due, first of all, to the low PLLA molecular weight. In addition, compared to the PLLA$_{5k}$ parent polymer, the melting region in the 5k−*y*k copolymers is both more complex and reduced in temperature by ca. 10 °C (comparing peak values). This, as will be shown below, can be related to the miscibility of the low molecular weight blocks. It may be added, for completeness, that a broad and very weak exotherm just before the melting peak was sometimes observed in the heating curves of the copolymers, particularly (but not always and not only) in the heating curves of the annealed samples, observed also by others in PLLA homopolymers and possibly related to additional crystallization or recrystallization.[53,54a,57]

Analysis of the T_g's of the block copolymers can provide information about block miscibility. For this purpose, we examined in detail the T_g region in the 10 °C/min heating thermograms, obtained both after 10 °C/min cooling (completely amorphous samples) and after 1 h annealing at 100 °C (semicrystalline samples), with each of the two thermal histories repeated twice. The T_g data, given in Table 4, were determined from the maxima in the first derivative curves, which was found to provide the most reliable values. It may be mentioned that the T_g's determined from the 20 °C/min curves (first derivative maxima, one scan per sample) were usually 1−3 °C higher than in the corresponding PLLA homopolymers (which were scanned, in the completely amorphous state, at only this heating rate), and also that the T_g of the minor phase in these curves was often less obvious than in the curves scanned at lower rates.

The four copolymers, 13k−*y*k (*y* = 12k, 23k) and 19k−*y*k (*y* = 17k, 35k), in their amorphous state, show two well-separated T_g's, the higher one associated with a PLLA or PLLA-rich phase and the lower one with a PDMAEMA or PDMAEMA-rich phase. The higher T_g is essentially identical to that of the PLLA parent homopolymers (taking into account the higher scan rate for the latter), indicative of complete immiscibility of the PDMAEMA block in the PLLA block. The lower T_g, at 23 ± 2 °C, is somewhat higher than the T_g of 17 °C measured for the PDMAEMA$_{16k}$ homopolymer (18 °C reported in ref 60 for PDMAEMA$_{100k}$), suggesting slight miscibility of PLLA in PDMAEMA, particularly for 13k−12k, the lowest total molecular weight copolymer of the four, with its T_g of 25 °C. In the corresponding semi-crystalline samples, this T_g lies at 20 °C (22 °C for 13k−12k), which is still a little higher than that of the PDMAEMA homopolymer. Although T_g determinations by DSC are typically assumed to have a precision of ±2 °C, the observation that a 50/50 (w/w) blend of PLLA$_{13k}$−Br and PDMAEMA also displays a T_g of 20 °C compared to 17 °C for the PDMAEMA homopolymer (both tested in a sequence of seven DSC scans up to 180 °C) suggests that very slight miscibility of PLLA in PDMAEMA remains in the crystallized samples, possibly arising in particular from the lowest PLLA molecular weight fraction. The PLLA T_g is difficult to detect in the phase-separated block copolymers when the PLLA block is semi-crystalline (there is just a slight baseline deviation in the first derivative curves over a relatively wide temperature range, except for 19k−35k, where its value is the same as for PLLA$_{19k}$), due, of course, to the much lower fraction of amorphous PLLA (in the blend, its value is the same as for PLLA$_{13k}$ alone).

In contrast to the above four copolymers showing two distinct T_g's, only one T_g is detectable in the two copolymers of the same two series having the shortest PDMAEMA block length (13k−5k and 19k−5k). In the completely amorphous samples, the T_g value of these two copolymers is 5 °C lower than in the parent PLLA homopolymers. This suggests that the absence of a second (lower) T_g is not due to the low PDMAEMA content rendering the T_g difficult to detect, but rather to the miscibility of the short PDMAEMA block (5k) in the amorphous PLLA phase. This miscibility is confirmed by the observation of a much lower T_g in the semi-crystalline samples (40−45 °C), where the amorphous phase is now composed of a much

Table 5. T_g Values Predicted by the Fox Equation, Compared with the Measured T_g's, for the Miscible PLLA-*b*-PDMAEMA Block Copolymers in their Completely Amorphous and Semi-Crystalline States

copolymer	sample state[a]	PLLA fraction (amorphous), %[b]	predicted T_g °C	measured T_g °C
5k−2k	am	69	38	40
5k−2k	cr	48	31	27
5k−4k	am	56	33	35
5k−4k	cr	34	27	21
5k−10k	am	34	27	26
5k−10k	cr	20	23	20
13k−5k	am	72	45	52
13k−5k	cr	52	36	40
19k−5k	am	78	47	52
19k−5k	cr	58	39	45

[a] The sample states are identified by "am" for completely amorphous samples and "cr" for semi-crystalline samples. The measured T_g's are taken from Table 4. The calculated T_g's were determined using 17 °C for PDMAEMA in all cases, 48 °C for PLLA$_{5k}$, and 57 °C for PLLA$_{13k}$ and PLLA$_{19k}$. [b] The PLLA fraction of the amorphous part in the semi-crystalline samples was determined using the degree of crystallinity reported in Table 4.

greater PDMAEMA fraction compared to the non-crystallized samples.

Miscibility is also evident when both blocks are short (5k−*y*k series). The completely amorphous samples, in particular, show single well-defined T_g's at values that are intermediate to the corresponding homopolymer values, approximately weighted according to the block composition. The T_g's are much lower in the presence of PLLA crystallization, but it is clear that for the 5k−2k copolymer, with its T_g of 27 °C, the amorphous fraction of PLLA still forms a miscible phase with PDMAEMA. This is probably also true for the semi-crystalline 5k−4k copolymer ($T_g = 21$ °C), considering that the T_g of the corresponding low molecular weight PDMAEMA homopolymer may be expected to be significantly lower than 20 °C. For the 5k−10k copolymer, PLLA crystallization reduces the T_g to 20 °C, indicating minimal solubility of PLLA in PDMAEMA, as discussed above for the 12k to 35k PDMAEMA blocks.

For a more quantitative evaluation, predicted T_g's for miscible phases were calculated using the Fox equation,

$$1/T_g = w_A/T_{gA} + w_B/T_{gB}$$

where w_A and w_B represent the weight fractions of A (PLLA) and B (PDMAEMA) and T_{gA} and T_{gB} their glass transition temperatures in K (assuming a molecular weight-independent T_g of 17 °C for PDMAEMA). It can be observed from Table 5 that the measured T_g's compare satisfactorily with the predicted T_g's and are certainly consistent with the blocks being essentially completely miscible in the amorphous state when one or both of them are of low molecular weight (up to at least 5k).

CONCLUSIONS

A series of well-defined linear poly(L-lactide)/poly(2-dimethylaminoethyl methacrylate) (PLLA-*b*-PDMAEMA) diblock copolymers with narrow polydispersity were successfully prepared by ring-opening polymerization of L-lactide, end group conversion of the PLLA homopolymers to suitable macroinitiators, followed by addition of the PDMAEMA block by atom transfer radical polymerization. This method allows the synthesis of low to high molecular weight PLLA-*b*-PDMAEMA. In this work, three PLLA block lengths, with molecular weights ranging from 5000 and 20 000 g/mol (shown to span the range from molecular weight dependent to essentially independent T_g's and T_m's), were each coupled with three PDMAEMA block lengths corresponding to approximately equal to, half of, and one-quarter of PLLA in molar ratio. DSC analysis indicates that low molecular weight blocks of ca. 5000 g/mol and less are miscible in the amorphous phase, including in the presence of PLLA crystallinity, as shown by T_g's that are intermediate to those of the corresponding homopolymers and by the significant decrease in the melting point of the PLLA crystalline phase. With increase in PDMAEMA block length, the degree of crystallinity of the PLLA block tends to decrease mildly, whereas the kinetics of crystallization are significantly reduced.

ASSOCIATED CONTENT

Ⓢ Supporting Information. TGA thermograms, SEC elugrams, DSC details, and ^{13}C and ^{1}H homonuclear decoupled NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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