Synthesis and Self-Assembly Properties of Peptide−Polylactide Block Copolymers

Sylvain Caillol,[§] Sébastien Lecommandoux,*[,†] Anne-Françoise Mingotaud,*[,⊥] Michèle Schappacher,[†] Alain Soum,[†] N. Bryson,[‡] and R. Meyrueix[‡]

Laboratoire de Chimie des Polymères Organiques, UMR CNRS 5629, ENSCPB, 16 Av. Pey Berland, 33600 Pessac, France, and Flamel Technologies, Parc Club du Moulin à Vent, 33 Av. Dr Georges Lévy, 69693 Vénissieux Cedex, France

Received July 23, 2002; Revised Manuscript Received October 21, 2002

ABSTRACT: Poly(L-lactide-*b*-γ-benzyl glutamate) copolymers with various block lengths were synthesized by sequential ring-opening polymerization of L-lactide and *N*-carboxyanhydride of γ-benzyl glutamate. The copolymers were characterized by SEC and NMR spectrometry. DSC and SAXS data suggested that the copolymers were phase-separated in domains containing either crystalline PLLA or liquid-crystalline columnar hexagonal morphology of PBLG. When varying the temperature, reversible local order−order transition could be observed on these diblock copolymers.

Introduction

The progress made in controlling polymerization processes has led to the development of well-defined architectures. Among these, block copolymers, although known for a long period, have nowadays been formed with a variety of monomers. This has allowed the development of physical chemistry studies that have shown the possibility of new self-assemblies. Two main types of block copolymers have been studied, namely coil−coil or rod−coil copolymers. The last ones represent a special class of block copolymers that have attracted increasing attention during the past 5−10 years.[1] The interest in rod−coil block copolymers is due to their unconventional phase behavior in comparison with the common "coil−coil" type diblock copolymers, i.e., block copolymers that consist of two chemically dissimilar amorphous segments. Coil−coil block copolymers have been intensively investigated, both experimentally and theoretically, and their phase behavior and properties are therefore nowadays reasonably understood.[2] The anomalous phase behavior of rod−coil block copolymers is due to the rigidity of one of the segments, which has at least two important consequences. First of all, the self-assembly of rod−coil block copolymers is determined not only by phase separation but also by the crystallization of the rod segments. The competition between these two processes can lead to the formation of unconventional phase-separated morphologies. A second important consequence of the rigid character of one of the blocks is a stiffness asymmetry over the molecule, which leads to an increase in the Flory−Huggins χ parameter in comparison with the "common" coil−coil block copolymers. Because of their relatively large Flory−Huggins χ parameter, rod−coil diblock copolymers can undergo phase separation at much lower molecular weights than coil−coil type block copolymers. This feature has driven to a large part the numerous efforts in this area that focus on the use of rod−coil type diblock copolymers as building blocks for the generation of self-assembled nanostructured materials with length scales that cannot be accessed with coil−coil block copolymers. In contrast to the traditional mesogens,[3] which typically comprise the rigid segment of rod−coil block copolymers, an α-helical peptide has more conformational freedom and may be transformed from a rigid rod into for example a random coil or a sheet structure composed of β-strands. In addition to a higher degree of conformational freedom of the rod−segment, a second feature that distinguishes such peptide-based diblock copolymers from most other rod−coil block copolymers is the possibility for intermolecular hydrogen-bonding interactions. In contrast to the unspecific $\pi-\pi$ and hydrophobic interactions that drive the self-assembly of most other rod−coil block copolymers, hydrogen-bonding interactions are more specific and directional, which may allow a more accurate control over the self-assembly process. Nevertheless, only few have presented the use of peptide-based copolymers.[4] In one case, Klok and Lecommandoux have shown that oligomers of poly(styrene-*b*-γ-benzyl glutamate) were able to form thermotropic liquid-crystalline phases. The supramolecular organization depended both on the relative block lengths and on the conformation of the peptide segment.

In this study, we report on the synthesis of analogous peptide-based block copolymers, such as poly(L-lactide-*b*-γ-benzyl glutamate). Very little research activity has been focused on block copolymers consisting of polypeptides and biodegradable polyesters.[5,6] Poly(L-lactide) is a well-known polymer used in medical applications because of its degradability in living environments.[7] Its combination with peptide blocks modifies the stability of the copolymer because enzymatic degradation is required to hydrolyze the peptide bonds. Furthermore, its semicrystallinity enables the formation of crystallites which can have a great influence on the self-assembly properties of the rod−coil block copolymer. Indeed, Ober et al.[8] described the complexity for the self-assembly of rod−coil type molecules from an isotropic melt or solution, depending on whether the glass transition of

---

[†] Laboratoire de Chimie des Polymères Organiques.

[‡] Flamel Technologies.

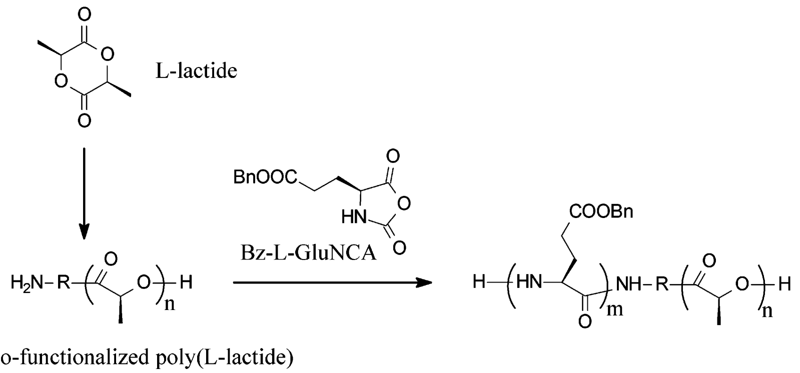
[§] Present address: RHODIA RECHERCHES CRA/STP, 52 rue de la Haie Coq, F-93308 Aubervilliers, France.

[⊥] Present address: Laboratoire des IMRCP, UMR CNRS 5623, Université Paul Sabatier, 118 route de Narbonne, 31062 Toulouse Cedex 4, France.

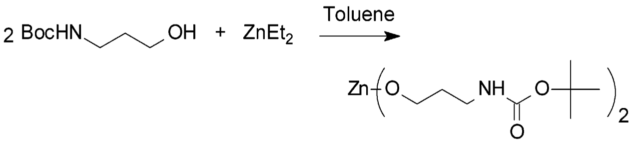
* To whom correspondence should be addressed: e-mail afmingo@chimie.ups-tlse.fr; s.lecommandoux@enscpb.fr.

10.1021/ma021187c CCC: $25.00

Scheme 1. Strategy for the Synthesis of Block Copolymers



Scheme 2. Structure of the Initiator of Lactide Polymerization



the coil or the (liquid) crystallization of the rod appeared first. In the system studied, poly(L-lactide-*b*-γ-benzyl glutamate), where the poly(L-lactide) block is semicrystalline, the situation is even more complicated.

We thus decided to study the self-assembly properties of this kind of copolymers, depending on the relative segment length as well as the temperature and the thermal history of the material.

Experimental Part

Reagents. L-Lactide was purchased from Aldrich, washed twice with diethyl ether, dried under high vacuum, and stored in a glovebox at −30 °C. Bz-L-GluNCA was synthesized according to the method of Daly[9] and stored in a glovebox at −30 °C. The absence of residual chloride was checked by DSC from the position and the shape of the melting endotherm. Indeed, when traces of chloride are present, this peak becomes highly asymmetric, and the melting temperature is much lower than the theoretical one, namely 93−94 °C. In our case, the peak was found around 90−91 °C and was symmetric. The initiator of the L-lactide polymerization (Scheme 2) was synthesized according to the method of Gotsche[6] and was used immediately. Toluene (Atlantic labo) was distilled over CaH_2 and stored over Na mirror. Methylene chloride (Atlantic labo) was distilled over $MgSO_4$. Anhydrous trifluoroacetic acid (Sigma) was used as received.

Polymerization of L-Lactide. All experiments were carried out under nitrogen in flame-dried glass apparatus sealed with Rotaflo taps. Polylactide was obtained by ring-opening polymerization of L-lactide initiated by zinc *tert*-butoxycarbonylaminopropoxide according to the method of Gotsche.[6] L-Lactide (1.5 g, 10.4 mmol) was weighed in a glovebox and introduced in the flask. Freshly distilled toluene (8 mL, $[\text{lactide}]_0 = 1$ M) was added by trap-to-trap distillation. The solution was heated to 80 °C and the initiator introduced by cannula transfer (0.2 g in 2 mL, 0.52 mmol). The solution was stirred at 80 °C for 1 h. 0.6 mL of acetic acid (10 vol % in toluene) was added to terminate the polymerization. The solvent was evaporated, and the polymer was dissolved in CH_2Cl_2 and precipitated in cold MeOH. The solution was centrifuged at −5 °C, 10 000 rpm for 1 h to recover the polymer.

Deprotection of Amino-polylactide. 1 g of polylactide was introduced in a flask fitted with a gas outlet. Freshly distilled methylene chloride (12 mL) was added, followed by a large excess of anhydrous trifluoroacetic acid (2 mL). The solution was stirred at ambient temperature for 30 min, after which time all solvents were evaporated. The polymer was redissolved in methylene chloride, and the solution was washed with aqueous $NaHCO_3$ (5%) and water and finally dried over $MgSO_4$. After filtration and evaporation of the solvent, the polymer was recovered in 95% yield.

Polymerization of Bz-L-GluNCA. Bz-L-GluNCA (2.8 g, 10.6 mmol) was weighed in a glovebox and introduced in a flame-dried flask equipped with a drying tube. The initiator (3 mg of propylamine or 1 g of amino-functionalized polylactide) was dissolved in dry CH_2Cl_2 (respectively 5 or 15 mL) and added via cannula. The solution was stirred for 3 h at room temperature. Copolymers were recovered by precipitation in cold methanol and dried under high vacuum.

Characterizations. The average molecular weight of polylactide was determined by SEC analysis in THF (flow rate 1.0 mL/min) on a Varian apparatus equipped with a refractive index detector and a TSK column pack (HXLG 4000, HLX 3000, HLX 2000) and using a polystyrene calibration curve. The values were corrected by a factor 0.57 first introduced by Penczek.[10] The validity of this factor was verified by vapor pressure osmometry on some polylactide samples. The molecular weight of the copolymers was determined by ^{1}H NMR in TFA-*d* from the ratio of lactide units vs glutamate units. SEC analysis in DMF was carried out using the same type of columns (flow rate 0.7 mL/min).

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 200 spectrometer at 200.15 and 50.32 MHz, respectively.

Differential scanning calorimetry analyses (DSC) were recorded on a Perkin-Elmer apparatus (DSC7) at a rate of 30 °C/min under nitrogen. DSC calibration was performed with indium, and the transition temperatures were determined at the midpoint between upper and lower intersection of the baseline with the tangent to the transition step.

MALDI−TOF MS experiments were carried out on a TOF-SPEC apparatus (Micromass) equipped with a pulsed N_2 laser (337 nm, 4 ns pulse width) and time delayed extracted ion source. Spectra were recorded in the positive ion mode using the reflectron mode and an accelerating voltage of 20 kV.

Small-angle X-ray scattering was performed with Cu Kα radiation from an 18 kW rotating anode X-ray generator. A flat pyrolytic graphite (002) monochromator delivered a 0.5 × 0.5 mm^2 spot on the sample. The scattered radiation was collected on a 2D imaging plate system. The instrumental resolution in the reciprocal space was $\Delta q = 2.5$ mm^2 Å^{-1} fwhm (full width at half-maximum) in both vertical and horizontal directions. The measured q range was 0.01 Å$^{-1} < q < 1.6$ Å^{-1}.

Results and Discussion

The synthesis of poly(L-lactide-*b*-γ-benzyl glutamate) was based on a method first described by Höcker[6] in 1995. The main point was the synthesis of a polylactide end-functionalized with a primary amine group (Scheme 1), which is a well-known initiator of the polymerization of *N*-carboxyanhydrides (NCAs). Thus, it allowed the sequential polymerization of Bz-L-GluNCA in a second step to yield the copolymer.

Scheme 3. Synthesis of Amino-Functionalized Polylactide

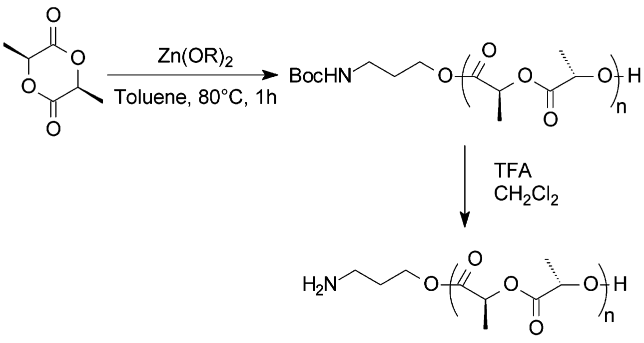


Table 1. Molecular Weight Characterization of Homopolylactides

polymer	$\bar{M}_{n,th}$[a]	$\bar{M}_n$[b] (corr SEC)	$I = \bar{M}_w/\bar{M}_n$	$\bar{M}_n$ (VPO)	$\bar{M}_n$[c] (^{1}H NMR)	f[d]
PLLA$_{10}$	1440	1600	1.2		1500	1.1
PLLA$_{15}$	2160	2100	1.2		2000	1.0
PLLA$_{20}$	2500	2280	1.5	2800	2400	0.95
PLLA$_{25}$	3600	3700	1.2		3500	1.0
PLLA$_{40}$	5760	5800	1.4		5700	1.0

[a] $\bar{M}_{n,th} = [M]_0/(2[Zn(OR)_2]_0) \times$ yield $\times$ 144. [b] $\bar{M}_n = \bar{M}_{n,SEC} \times 0.57$. [c] Calculated from the ratio between signals c and g (see Figure 2). [d] $f = \bar{M}_{n,corr}/\bar{M}_{n,NMR}$.

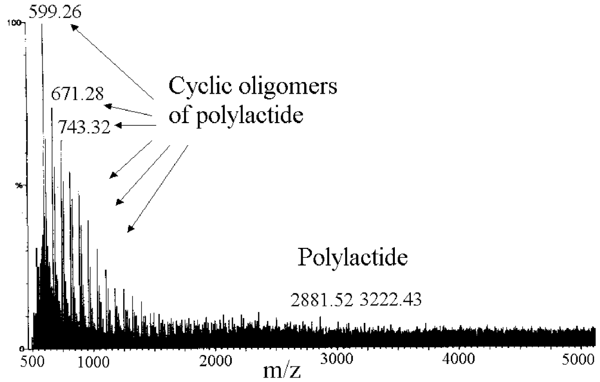


Figure 1. MALDI spectrum of methanol fraction of PLLA.

Synthesis of Amino-Functionalized Poly(L-lactide). Amino-functionalized poly(L-lactide) was synthesized according to the method of Höcker[6] through ring-opening polymerization of L-lactide with a zinc alkoxide (Scheme 2) bearing a protected amine group. This initiator was obtained from the reaction between diethylzinc and Boc-aminopropanol and was used immediately after the synthesis. The polymerization of L-lactide was performed at 80 °C in toluene for 1 h (Scheme 3). The characteristics of the synthesized polymers are reported in Table 1.

Monomer conversions were high (around 95%), but yields in recovered polymer ranged between 80 and 95%. This was explained by the existence of low molecular weight polylactide that is slightly soluble in cold methanol and also by the presence of cyclic oligomers due to backbiting reactions. This was confirmed by MALDI mass spectra of the soluble part in methanol (Figure 1). These intramolecular reactions were quite limited in this case, representing approximately 5% of the total polymer.

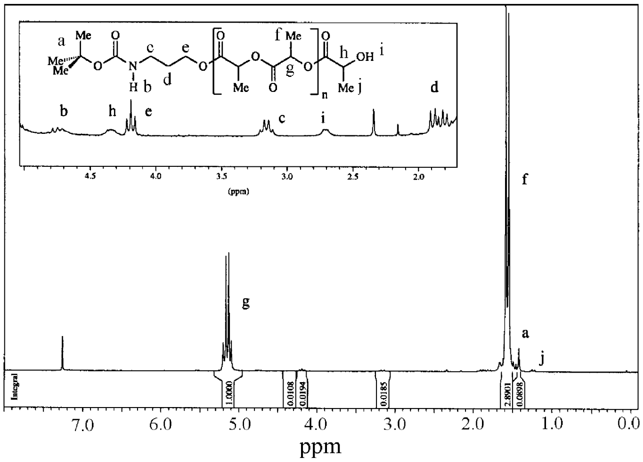


Figure 2. ^{1}H NMR spectrum of polylactide bearing $-$NHBoc end group in CDCl$_3$.

The functionality of the polymer was determined by comparing the molecular weight obtained by SEC and that determined by ^{1}H NMR using the signals c or e of the end group and that of lactide units g (Figure 2). In all cases, the functionality was found close to 1, meaning that all polymer chains were functionalized with the amine group. This was also confirmed by MALDI mass spectrometry (Figure 3) which revealed only one type of polymer corresponding to the expecting end group. In the presented example, a partial deprotection of the amine group occurred, leading to a mixture of PLLA$-$NHBoc and PLLA$-$NH$_2$ species.

Compared to the method of Höcker, it was possible to reduce the polymerization time from 12 to 1 h after a kinetic follow-up of the process, which showed that the monomer was already consumed at this point. This led to a better control of side reactions that are known to happen during this type of polymerization. Also, adding the monomer to the solution of initiator allowed us to reduce the polydispersity index from 1.5 (addition of initiator to monomer) to 1.2, thus leading to a better control of the polymer chain length.

The next step consisted in deprotecting the amine group of the poly(L-lactide). This was realized by reacting it with anhydrous trifluoroacetic acid (TFA). This reaction (Scheme 3) deprotected all primary amine functions at the end of the polymer, without lowering the molar mass nor increasing I, as shown by the SEC chromatograms (Table 2). This was also confirmed by ^{1}H NMR (Figure 4). The signal corresponding to the Boc group at 1.4 ppm completely disappeared, and that of $-$CH$_2-$N shifted from 3.15 to 2.78 ppm. The ratio between this peak and that of lactide units remained also constant after the deprotection. It could be expected that the loss of the Boc group should lead to a decrease in the molar mass of the corresponding value (i.e., 100). Even if some samples showed this small decrease, this cannot be considered as significant, since modifying the end group can also modify the interactions between the polymer chain and the solvent.

Block Copolymerization. The amine group of the polylactide polymer was then used to initiate the ring-opening polymerization of benzyl glutamate NCA (Scheme 1). The second block was synthesized in 3 h at room temperature in dichloromethane. The characteristics of the copolymers are detailed in Table 3. The polymers described in this table are not those derived from the samples of Table 2, but are new samples made in the same conditions, to have increased quantities of copolymers. The chain length was varied between 10 and 40 lactide units and between 20 and 100 for

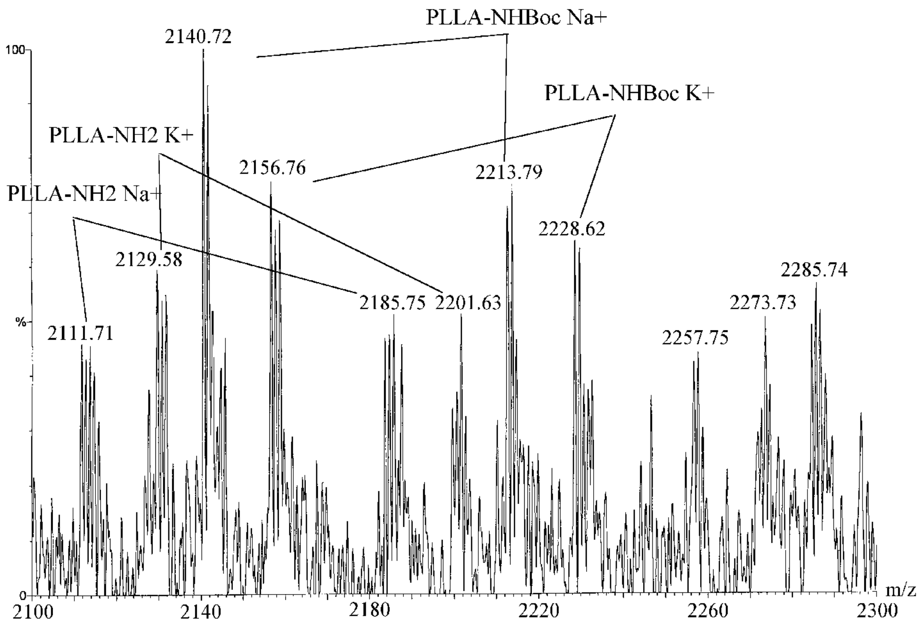


Figure 3. MALDI spectrum of polylactide bearing −NHBoc end group.

Table 2. Effect of the Deprotection of the Amine Group on PLLA Characteristics

polymer	$\bar{M}_n$[a] (before)	$I = \bar{M}_w/\bar{M}_n$ (before)	$\bar{M}_n$[a] (after)	$I = \bar{M}_w/\bar{M}_n$ (after)
$PLLA_{10}$	1600	1.2	1600	1.2
$PLLA_{15}$	2100	1.2	2000	1.2
$PLLA_{20}$	2280	1.5	2280	1.5
$PLLA_{25}$	3700	1.2	3550	1.3
$PLLA_{40}$	5800	1.4	5700	1.4

[a] Corrected SEC molecular weight.

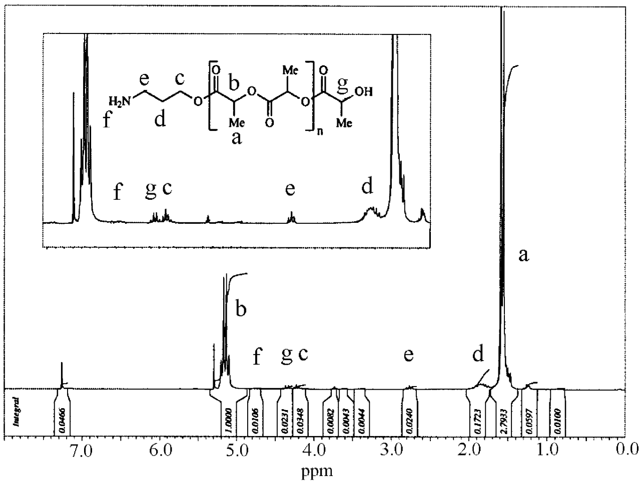


Figure 4. ^1H NMR spectrum of PLLA−NH_2 in $CDCl_3$.

γ-benzyl L-glutamate units. The molecular weight of the copolymers was calculated from ^1H NMR in deuterated TFA which does not lead to any association of the polypeptide part (Figure 5).

Block copolymers poly(lactide-*b*-γ-benzyl glutamate) were also characterized by ^{13}C NMR spectrometry (Figure 6) and SEC in DMF (Figure 7). However, this method could not be used to determine the molecular weight or the polydispersity indices, since self-assembly can exist. Indeed, for some samples, molecular weights of several millions were calculated by SEC whereas NMR data and solubility properties could not fit with such values. Nevertheless, it confirmed the total reaction of the polylactide precursor, contrary to Höcker's method. Indeed, in their case, an average of 30% polylactide precursor was found remaining after the polymerization of NCA. In our case apparently, the good functionality of the precursor as well as the reduced time of polymerization allowed us to eliminate this problem.

DSC and SAXS experiments were then performed to evidence the phase separation and elucidate the supramolecular organization of the peptide-based diblock copolymers. DSC was first used to analyze the specific transitions of the two blocks. A representative DSC trace for these PLLA-*b*-PBLG diblock copolymers is shown in Figure 8 for $PLLA_{25}$-*b*-$PBLG_{50}$. The presence of the polylactide block in the copolymer was reflected in a glass transition (T_g) around 50 °C and a melting temperature (T_m) at 160 °C, in agreement with literature data.[11] The presence of the PBLG block was identified by a small peak with a typical low enthalpic change observed around 100 °C (T_{LC}). This observed transition was irreversible and only occurred during the first heating run; it was attributed to an irreversible change from a 7/2 to an 18/5 α-helical conformation.[4d,12] Depending on the length of each block, these transitions were more or less important but were always detectable. At higher temperature, no other transition could be observed for PBLG which is well-known to degrade before isotropization.[4] Although these DSC data were not conclusive evidence of an ordered block copolymer with nanoscopic domains of PLLA and PBLG, the presence of the characteristic transitions of the two blocks supported a phase-separated morphology.

In an effort to further characterize the morphology of these block copolymers, small-angle X-ray scattering (SAXS) experiments were performed. Figure 9 shows the one-dimensional SAXS data obtained at 100 °C for three representative diblocks $PLLA_{15}$-*b*-$PBLG_{100}$, $PLLA_{20}$-*b*-$PBLG_{40}$, and $PLLA_{40}$-*b*-$PBLG_{20}$, corresponding respectively to a volume fraction of PBLG equal to 91%, 76%, and 44%. The wave vector *q* range explored was ranging from 0.2 to 1.5 $Å^{-1}$.

At 100 °C, according to the DSC results discussed above, the PLLA and PBLG blocks should be respec-

Table 3. Molecular Weight Characteristics of the PLLA-*b*-PBLG Block Copolymers

	PLLA			PBLG	
sample	$\bar{M}_{n(theo)}$ (g/mol)	^{1}H NMR $\bar{M}_{n(exp)}$ (g/mol)	corrected SEC $\bar{M}_{n(exp)}$ (g/mol)	$\bar{M}_{n(theo)}$ (g/mol)	^{1}H NMR $\bar{M}_{n(exp)}$ (g/mol)
PLLA$_{20}$-*b*-PBLG$_{40}$	2880	2900	2800	8 760	8 800
PLLA$_{40}$-*b*-PBLG$_{20}$	5760	5700	5800	4 380	4 400
PLLA$_{25}$-*b*-PBLG$_{50}$	3600	3500	3700	10 950	11 000
PLLA$_{15}$-*b*-PBLG$_{100}$	2160	2000	2100	21 900	21 700
PLLA$_{10}$-*b*-PBLG$_{80}$	1440	1500	1600	17 520	17 700

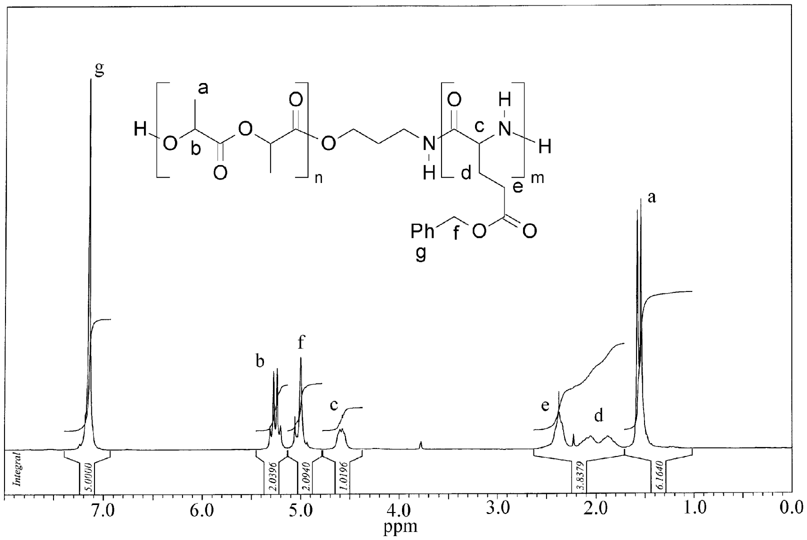


Figure 5. ^{1}H NMR spectrum of the block copolymer PLLA-*b*-PBLG in TFA-*d*.

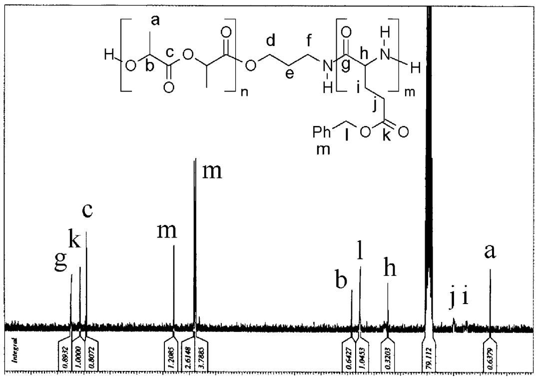


Figure 6. ^{13}C NMR spectrum of the block copolymer PLLA-*b*-PBLG in DMSO-*d*.

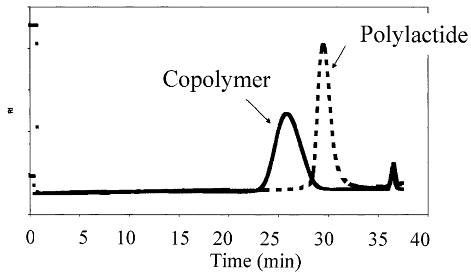


Figure 7. Overlay of size exclusion chromatograms of PLLA and a block copolymer.

tively in its crystalline and liquid-crystalline phase. For the block copolymer with the highest PBLG content (PLLA$_{15}$-*b*-PBLG$_{100}$), a set of Bragg peaks at low scattering angles ($q = 0.45$, 0.78, and 0.90 Å^{-1}) with a ratio of 1:3$^{1/2}$:2 is observed, corresponding to a columnar hexagonal organization of the peptide α-helices with a lattice parameter of ~16 Å, which fits with the intermolecular distance between neighboring poly(γ-benzyl L-glutamate) chains. This set of characteristic peaks could be observed for all copolymers. However, their intensity decreased with the ratio of PBLG in the block copolymer, and in the meantime, one more scattering peak appeared at low q values (0.32 Å^{-1}). As previously demonstrated by infrared spectroscopy experiments,[4d] decreasing the length of the peptide chain leads to a destabilization of the α-helical secondary structure. Thus, the Bragg peak at $q = \sim 0.32$ Å^{-1} in the SAXS pattern results from a change in the peptide chain organization to a lamellar organization with a β-sheet secondary structure. The corresponding d spacing (~20 Å) represented the width of a lamellae. This traduces a coexistence of layered and columnar hexagonal structure within phase-separated domains of peptide blocks as previously reported.[4d] At high scattering angles, another set of three Bragg peaks ($q = 1.02$, 1.15, and

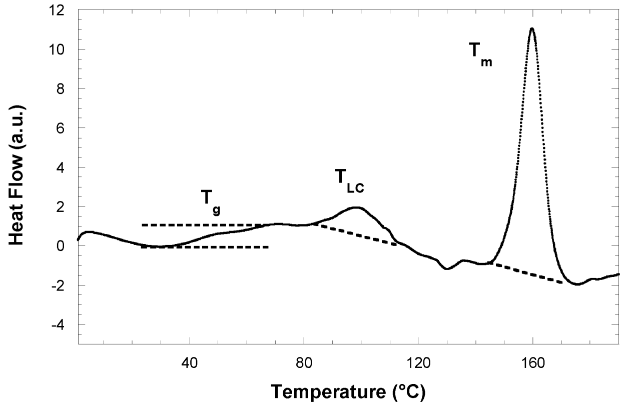


Figure 8. DSC trace obtained for PLLA$_{25}$-*b*-PBLG$_{50}$ diblock copolymer.

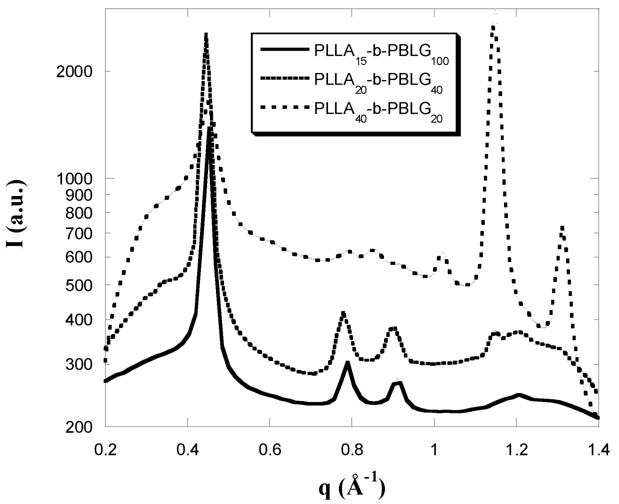


Figure 9. One-dimensional SAXS data obtained at 100 °C for $PLLA_{15}$-*b*-$PBLG_{100}$, $PLLA_{20}$-*b*-$PBLG_{40}$, and $PLLA_{40}$-*b*-$PBLG_{20}$ diblock copolymers.

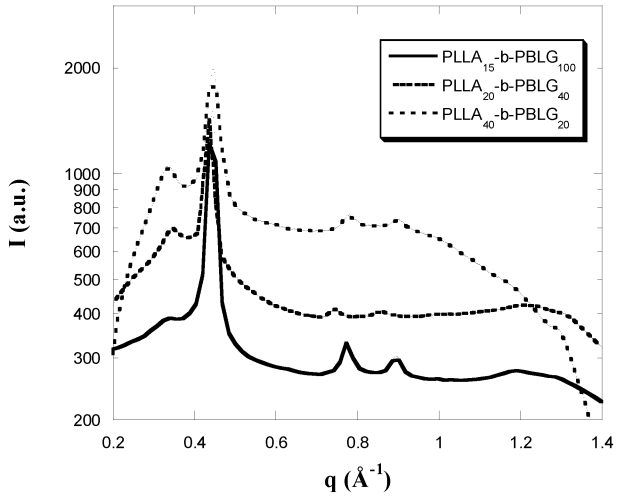


Figure 10. One-dimensional SAXS data obtained at 200 °C for $PLLA_{15}$-*b*-$PBLG_{100}$, $PLLA_{20}$-*b*-$PBLG_{40}$, and $PLLA_{40}$-*b*-$PBLG_{20}$ diblock copolymers.

1.31 $Å^{-1}$) could be observed, particularly for block copolymers with high PLLA content, corresponding to its crystalline organization. Like for PBLG, the intensity of these characteristic scattering peaks assigned to PLLA decreases with its content in the block copolymers. All these results are supporting evidence of a phase segregation of the block copolymers and were in good agreement with the DSC data. The fact that the two blocks present their characteristic organization as “pure compounds” reflects that the system is phase-separated. Nevertheless, the absence of additional scattering peaks at low *q* values reflects a lack of organization of the phase-separated domains. Moreover, depending on temperature, one could observe different order−order transitions. Figure 10 shows the one-dimensional SAXS patterns obtained for $PLLA_{15}$-*b*-$PBLG_{100}$, $PLLA_{20}$-*b*-$PBLG_{40}$, and $PLLA_{40}$-*b*-$PBLG_{20}$ diblock copolymers at 200 °C. These SAXS data indicate the coexistence of a columnar hexagonal arrangement of α-helical peptides with a lamellar assembly of *β*-sheet type peptide chains as previously reported on PBLG-based diblock copolymers.[4c,d] At this temperature, the PLLA domains are “liquid”: we thus have phase-separated domains of PBLG with coexisting columnar and layered structure, in disordered domains of PLLA. When cooling below 150 °C, crystallization of PLLA could be observed, revealing the reversibility of the melting transition. These results evidence that the degree of order within the phase-separated domains can be tailored and thus the resulting properties of the materials.

Nevertheless, there is no clear evidence of peaks at lower scattering angles which could reveal the morphology of these phase-separated structures. These observations reveal a low degree of organization at the phase-separation scale, as opposed to a high degree of order combining liquid-crystal and crystalline domains at small scale. As previously reported,[8] the phase separation process in rod−coil type molecules can be very complex and especially depends on both the glass-transition temperature of the coil block and the isotropization temperature of the rod segment. The situation in PLLA-*b*-PBLG diblock copolymers is even more complicated due to the fact that these molecules are composed of a rod block and a semicrystalline polymer as the second segment. The fact that the isotropization of PLLA occurs in a liquid crystal medium with a high viscosity (due to the PBLG block) impairs the ability of the system to organize with temperature variation or annealing. Some attempts were carried out in this direction without any success. The other possibility to obtain ordered phase-separated domains would be to adjust the solvent evaporation rate. We are currently exploring this area.

Conclusion

We have described in the present paper a method for the synthesis of a novel set of PLLA-*b*-PBLG diblock copolymers. The synthesis of a well-defined amino-functionalized PLLA allowed us to perform in a second step the polymerization of Bz-L-GluNCA. The block copolymers were obtained as pure products with no trace of residual PLLA. They have been characterized by SEC and NMR which confirmed their expected structure and molecular weight.

In addition, DSC and SAXS data suggest that the copolymers are phase-separated in domains containing crystalline PLLA and liquid-crystal columnar hexagonal morphology of PBLG. When increasing the temperature, liquid-crystalline domains of PBLG are evidenced in an isotropic liquid of PLLA. This reversible local order−order transition might have a great influence on the phase-separated structure of these block copolymers and would particularly allow order−order phase transitions at high temperatures. Attempts to manage this phenomenon are currently in progress.

Acknowledgment. Authors are grateful to Dr. M. F. Achard (Centre de Recherche Paul Pascal, CNRS, UPR 8641, Pessac, France) for her contribution to the SAXS experiments and E. Ibarboure (LCPO, ENSCPB) for his help in the DSC measurements.

References and Notes

(1) For some recent reviews, see e.g.: (a) Lee, M.; Cho, B.-K.; Zin, W.-C. *Chem. Rev.* **2001**, *101*, 3869. (b) Klok, H.-A.; Lecommandoux, S. *Adv. Mater.* **2001**, *13*, 1217 and references therein.

(2) For some reviews, see e.g.: (a) Förster, S.; Plantenberg, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 688. (b) Fredrickson, G. H.; Bates, F. S. *Annu. Rev. Mater. Sci.* **1996**, *26*, 501.

(3) For some recent publications, see e.g.: (a) Stupp, S. I.; LeBonheur, V.; Walker, K.; Li, L. S.; Huggins, K. E.; Keser, M.; Amstutz, A. *Science* **1997**, *276*, 384. (b) Lee, M.; Cho, B.-K.; Kim, H.; Zin, W.-C. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 638. (c) Jenekhe, S. A.; Chen, X. L. *Science* **1999**, *283*, 372.

(4) (a) Gallot, B. *Prog. Polym. Sci.* **1996**, *21*, 1035. (b) Cornelissen, J. J. L. M.; Fischer, M.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. *Science* **1998**, *280*, 1427. (c) Klok, H.-A.; Langenwalter, J. F.; Lecommandoux, S. *Macromolecules* **2000**, *33*, 7819. (d) Lecommandoux, S.; Achard, M.-F.; Langenwalter, J. F.; Klok, H.-A. *Macromolecules* **2001**, *34*, 9100. (e) Schlaad, H.; Kukula, H.; Smarsly, B.; Antonietti, M.; Pakula, T. *Polymer* **2002**, *43*, 5321.

(5) Kricheldorf, H. R.; Hauser, K. *Biomacromolecules* **2001**, *2*, 1110.

(6) Gotsche, M.; Keul, H.; Höcker, H. *Macromol. Chem. Phys.* **1995**, *196*, 3891.

(7) Domb, A. J. *Handbook of Biodegradable Polymers*; Harwood Academic Publishers: New York, 1995.

(8) Mao, G.; Ober, C. K. *Acta Polym.* **1997**, *48*, 405.

(9) Daly, W. H.; Poché, D. *Tetrahedron Lett.* **1988**, *29*, 5859.

(10) Duda, A.; Penczek, S. *Macromolecules* **1998**, *31*, 2114.

(11) Engelberg, I.; Kohn, J. *Biomaterials* **1991**, *12*, 292.

(12) Watanabe, J.; Uematsu, I. *Polymer* **1984**, *25*, 1711.

MA021187C