Amphiphilic Poly(L-lysine-*b*-caprolactone) Block Copolymers: Synthesis, Characterization, and Solution Properties

Shaheen Motala-Timol,[†] Dhanjay Jhurry,*[,†] Jiawen Zhou,[‡] Archana Bhaw-Luximon,[†] Gaytree Mohun,[†] and Helmut Ritter[‡]

Department of Chemistry, Faculty of Science, University of Mauritius, Réduit, Mauritius, and Institut für Organische Chemie and Makromolekulare Chemie, Heinrich-Heine-Universität, D-40225 Duesseldorf, Germany

Received April 25, 2008; Revised Manuscript Received June 6, 2008

ABSTRACT: We report on the synthesis of poly(L-lysine-*b*-caprolactone) block copolymers via an original and elegant approach whereby Z-L-lysine is first polymerized in the presence of allylamine and the resulting amino-terminated poly(Z-L-lysine) is then used in situ as macroinitiator for the polymerization of ε-caprolactone in the presence of tin(II) octanoate as catalyst. A range of poly(ester-*b*-peptide)s were obtained by varying the ratio of polypeptide to polycaprolactone units. After removal of the Z group of L-lysine units, the copolymers were soluble in water and their solution behavior was examined. They spontaneously form micelle-like objects in solution with sizes around 10 and 70 nm depending on the block lengths of the hydrophilic and hydrophobic sequences. The smaller size particles would adopt a core−shell morphology while the larger particles would be more in line with a vesicle morphology.

1. Introduction

Among the degradable biomaterials,[1a,b] the synthetic polyesters and poly(ether−ester) (polyglycolic, polylactic, polycaprolactone, and polydioxanone) find the widest applications in the medical field presently. While polypeptides derived from *N*-carboxyanhydrides also exhibit interesting biodegradable properties, their applications in the medical field is more limited. This is due primarily to the difficulty in processing these materials. The combination of both ester and amide or peptide linkages in the same polymer chain to derive materials with enhanced biocompatibility and biodegradability as well as better processability has attracted worldwide interest. Such polymeric biomaterials can be classified according to their structures: alternating, graft, and block poly(ester−amide)s. The synthesis of alternating copolymers containing both ester and amide bonds via ring-opening polymerization of morpholine-2,5-dione derivatives has been extensively studied and is reviewed by Okada.[2] In this state-of-the-art review, we shall lay more emphasis on the synthesis of graft and block poly(ester−amide)s from the corresponding cyclic lactones, lactides, and NCAs.

Poly(ester-*graft*-peptide) Copolymers. Nottelet et al.[3] reported on the synthesis of amphiphilic poly(ε-caprolactone)-*g*-poly(L-lysine) degradable copolymers using two distinct methods. In the first one, activated poly(Z-L-lysine) was allowed to react with a macropolycarbanion derived from PCL, leading to graft copolymers containing 36% of ε-caprolactone and 64% of Z-L-lysine units. The second method of obtaining a graft copolymer was based on the anionic ring-opening polymerization of Boc-L-lysine NCA initiated by PCL carbanion. A copolymer containing 45% ε-caprolactone and 55% Z-L-lysine units was thus prepared. Deprotection of the lysine units led to water-soluble copolymers at physiological pH, which formed nanometric micelle-like objects with mean diameters between 60 and 500 nm. Narrow size distribution micelles of poly(lactic-*co*-glycolic acid)-grafted poly(L-lysine)[4] were used as an effective DNA condensation carrier for gene delivery system. The hydrodynamic diameter of PLL-*g*-PLGA micelles in an aqueous solution was ca. 149 nm.

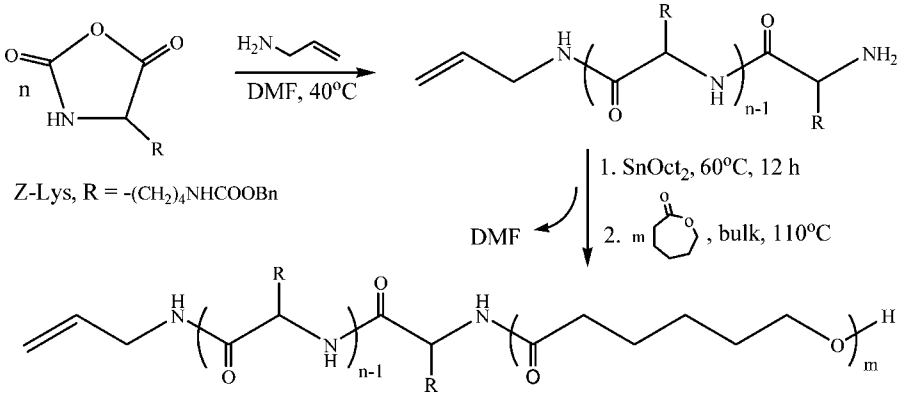
Synthesis of Poly(ester-*block*-peptide). Degée et al.[5] first reported on the synthesis of poly(caprolactone-*b*-polyglutamic acid). They used a multistep strategy to first transform a Br-terminated polycaprolactone into an amino-terminated polycaprolactone, which was used as macroinitiator to polymerize γ-benzylglutamate NCA. The block copolymer with free acid groups was obtained after selective hydrogenation of the benzylglutamate units. Höcker et al.[6] used a quite similar strategy to synthesize poly(L-lactide-*block*-L-amino acid)s. They first synthesized aminopropoxy- or phenylalanine-end-capped poly(L-lactide) which was used as macroinitiator to polymerize alanine, phenylalanine, and leucine NCAs.

Kricheldorf et al.[7] used di-4-aminobenzoyl telechelic poly(caprolactone) as a macroinitiator for the ring-opening polymerization of *N*-carboxyanhydrides, thus obtaining ABA triblock copolymers. The NCA/macroinitiator ratio was varied between 20 and 100. With γ-Bzl-Glu-NCA, mixtures of di- and triblock copolymers were obtained. Rong et al.[8] synthesized poly(ε-caprolactone)-*block*-poly(γ-benzyl-L-glutamic acid) block copolymer using amino organic calcium catalyst. They first polymerized ε-caprolactone (CL) using amino calcium 4-nitrobenzoxide as initiator. Hydrogenation of the resulting 4-nitrophenethoxyl-PCL lead to aminophenethoxyl-PCL. They used the latter as macroinitiator to polymerize γ-benzyl-L-glutamate *N*-carboxyanhydride. Fan et al.[9] synthesized poly(L-lactide)-*block*-poly(L-lysine) copolymer using a similar approach. L-Phe end-capped poly(L-lactide) was used as macroinitiator for the ring-opening polymerization of (Z)-lysine-*N*-carboxyanhydride. The L-Phe-terminated PLLA was prepared through a three-step process by first synthesizing a hydroxyl-terminated PLLA, converting the hydroxyl group to a BOC-L-Phe and finally acid hydrolyzing to a free amino end group. Poly(L-lactide)-*b*-poly(L-lysine) block copolymer was produced after deprotection treatment of PLLA-*b*-PZLys. The preparation of well-defined biodegradable amphiphilic poly(L-lactide)-*b*-dendritic poly(L-lysine)s was more recently reported by Li et al.[10] Boc-protected poly(L-lysine) dendron initiators with hydroxyl end functional groups were used for the ring-opening copolymerization of poly(L-lactide)s catalyzed by (dimethylamino)pyridine. Boc

* To whom correspondence should be addressed.
[†] University of Mauritius.
[‡] Heinrich-Heine-Universität.

10.1021/ma800917c CCC: $40.75
Published on Web 07/02/2008

Scheme 1. Synthetic Pathway to Poly(Z-L-Lys-*b*-CL)



deprotection of the dendron amino groups lead to diblock amphiphilic poly(L-lactide)-*b*-dendritic poly(L-lysine)s bearing lipophilic PLLA and hydrophilic dendritic PLL were finally prepared. Guillaume et al.[11] first prepared mono- or diamino-functionalized PCLs by chemical modification of the corresponding hydroxyl-terminated PCLs and used them as macroinitiators to polymerize γ-benzyl L-glutamate, thus obtaining diblock and triblock poly(ester−peptide)s.

To summarize, most of the published work concerning poly(ester-*b*-peptide) copolymers resort to polymerization of an NCA using an amino-end-capped polyester as macroinitiator. The latter is generally synthesized via a multistep process making use of a range of reagents, which may constitute a barrier to later applications of the polymers in the biomedical sector.

For our part, our main objective is to synthesize amphiphilic poly(ester−amide) block copolymers. In this paper, we present a direct sequential method to synthesize block copolymers consisting of L-lysine and caprolactone units using an amino-end-capped poly(Z-lysine) as macroinitiator to polymerize ε-caprolactone. First, Z-L-lysine is polymerized in the presence of allylamine, and the resulting amino-terminated poly(Z-L-lysine) is then used in situ as macroinitiator for the polymerization of ε-caprolactone in the presence of FDA-approved tin(II) octanoate as catalyst.

2. Experimental Section

Materials. Solvents were purchased from Aldrich Chemicals or Fisher and were subjected to purification prior to use in (co)polymerization of NCAs. DMF was dried over calcium sulfate for 72 h, followed by distillation under reduced pressure. The middle fraction was collected and stored over 4 Å molecular sieves under an argon atmosphere. Allylamine was dried over sodium and distilled under reduced pressure. Tin(II) octanoate was distilled under reduced pressure and stored under argon. All other reagents were purchased from Acros, Fluka, and Aldrich Chemicals and used without further purification.

Measurements. ^{1}H and ^{13}C NMR spectra were recorded on a 250 MHz Bruker Electrospin spectrometer at the University of Mauritius. Infrared spectra were recorded on a Thermo Nicolet Avatar spectrometer. Size exclusion chromatography analysis of polymer samples was performed using a Polymer Standards Systems apparatus with a refractive index detector. A PSS Suprema column was used for characterization under aqueous conditions while a PSS Gram Linear column was used with 0.1 M LiBr in DMF as eluent. Calibration was done using poly(ethylene oxide) and polystyrene standards.

The size distribution of the copolymer particles was determined by dynamic light scattering using a Malvern Instruments Zetasizer Nano ZS with a He−Ne laser (633 nm, 4 mW). Solutions of the block copolymers were prepared in distilled water and in phosphate buffer (PBS, pH = 7.4) and filtered using a 0.45 μm PET filter. The concentrations vary between 0.1 and 5 mg/mL. Measurements were carried out at 25 °C, and data were analyzed by the supplied Malvern Instruments software DTS v5.02.

Synthesis of Z-L-Lys NCA. Synthesis of ε-carbobenzoxy-L-lysine *N*-carboxyanhydride (Z-L-Lys NCA). ε-Carbobenzoxy-L-lysine (8.0 g, 28 mmol) was added to 200 mL of THF and stirred at 50 °C. Triphosgene (2.83 g, 9.5 mmol), dissolved in THF (50 mL), was added dropwise over a period of 1 h. The reaction was left to proceed for a further 2 h under nitrogen flux until a clear solution was obtained. The solution was filtered, concentrated, and poured into hexane. The crude white precipitate was recrystallized twice in THF/hexane mixtures. Yield $\approx$ 70%.

Polymerization of Z-L-Lys NCA. All polymerizations were carried out in Schlenk tubes under argon. The Z-L-Lys NCA (2.5 mmol) was first dissolved in DMF. The calculated amount of initiator, depending on the [monomer]/[initiator] ratio, was subsequently added. The reaction was allowed to proceed at 40 °C until all the monomer was consumed, as monitored by IR spectroscopy. DMF was removed under vacuum, and the crude polymer was analyzed by NMR and SEC.

Polymerization of ε-Caprolactone. A typical polymerization is here described: $SnOct_2$ (1 mg, 2.5×10^{-3} mmol) was added to a solution of poly(NCA Z-Lys) (0.6 g, 2.3 mmol) in DMF (3 mL). The solution was stirred at 50 °C for 20 h, and DMF was then slowly evaporated under vacuum. ε-Caprolactone (0.22 g, 1.96×10^{-3} mmol) was then added under N_2. Polymerization of ε-CL was monitored by ^{1}H NMR. The reaction was stopped when monomer signals were no longer observed. The crude polymer was precipitated in methanol and dried under vacuum. The white precipitate was then precipitated thrice in THF. The filtrates and the final residue were dried under vacuum and characterized by NMR and SEC.

Deprotection of the Z Groups of Poly(Z-L-Lys-*b*-CL) Copolymer. The amine groups of poly(NCA-z-Lys-*b*-CL) copolymers were regenerated by hydrolysis of the Z groups in TFA using a 33 wt % hydrobromic acid solution in glacial acetic acid. Different experimental methods were used to obtain complete deprotection of Z groups without degradation of polyester chains.

Typically, a few drops (1 mL) of TFA were added to poly(NCA-Z-Lys-*b*-CL) (0.25 g) to dissolve the copolymer, and $CHCl_3$ was then added until a slight cloudiness was observed. A solution of HBr in glacial acetic acid (2.5 or 5 times excess with respect to polypeptide) was added to the copolymer solution, and the mixture was slowly stirred for the required time at room temperature. The reaction mixture was then poured into an excess of cold diethyl ether. The precipitate was filtered and washed twice with diethyl ether and was then dried under vacuum.

3. Results and Discussion

As discussed in the Introduction, the main strategy developed by researchers in synthesizing poly(ester-*b*-peptide) block copolymers is to use an amino-end-capped polyester to poly-

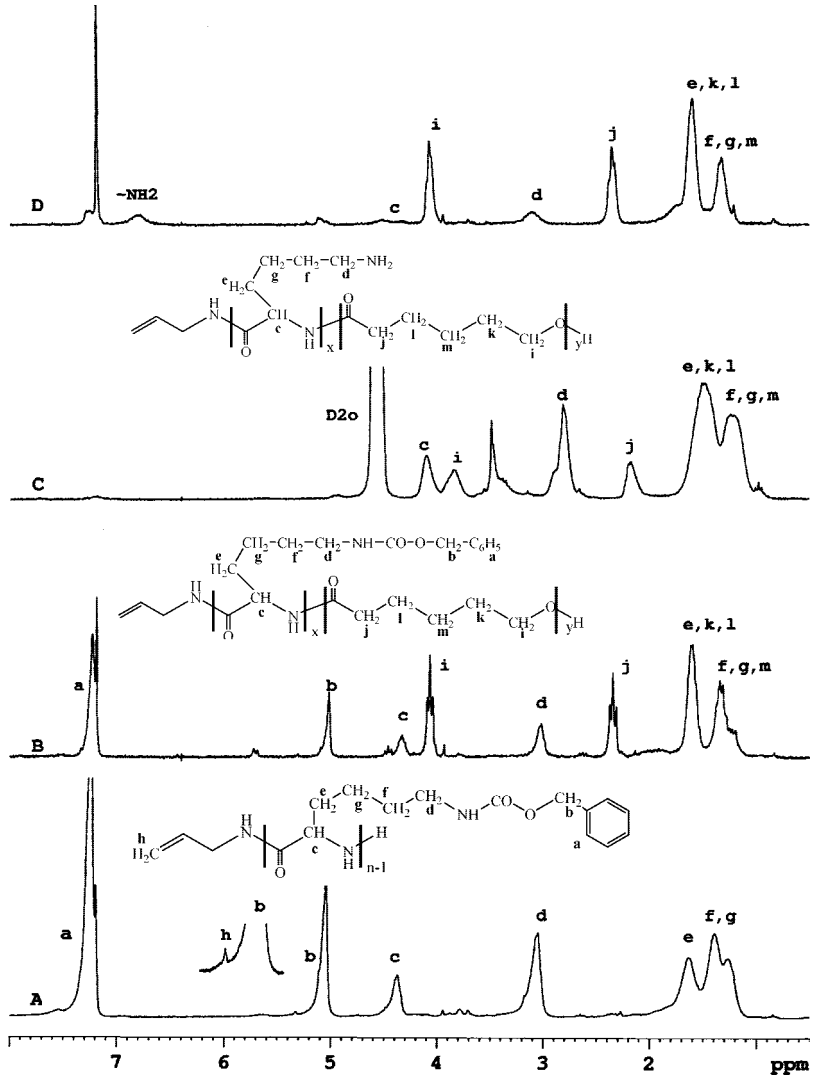


Figure 1. . ^{1}H NMR spectra of (A) poly(Z-L-Lys) in $CDCl_3$/TFA, (B) poly(Z-L-Lys-*b*-CL) in $CDCl_3$/TFA, (C) poly(L-Lys-*b*-CL) in D_2O, and (D) poly(L-Lys-*b*-CL) in $CDCl_3$/TFA.

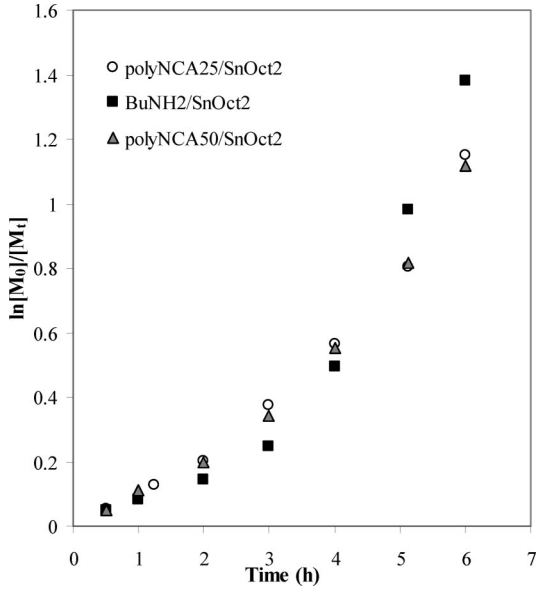


Figure 2. Semilogarithmic plots of conversion vs time for the polymerization of ε-CL at 110 °C using the amine/$SnOct_2$ as initiator/catalyst system at [ε-CL]/[amine initiator] = 50.

Table 1. SEC Molar Mass of Copolymers

sample	M_n[c]	M_n^{SEC} [d]	M_w/M_n^{SEC}
P(Z-L-Lys)$_{28}$[a]	7 300	20 200	1.38
P(Z-L-Lys)$_{28}$[a]-PCL$_{50}$[b]	13 000	35 800	1.27
deprotected P(Z-L-Lys)$_{28}$[e]-PCL$_{50}$[b]	9 700[f]	39 800	1.04
P(Z-L-Lys)$_{28}$[a]-PCL$_{112}$[b]	20 100	35 600	1.25
P(Z-L-Lys)$_{47}$[a]	12 300	19 500	1.33
P(Z-L-Lys)$_{47}$[a]-PCL$_{47}$[b]	17 700	31 800	1.40
deprotected PNCA$_{47}$-PCL$_{47}$[e]	13 100[f]	37 700	1.03
		12 400	1.40
P(Z-L-Lys)$_{47}$-PCL$_{94}$[a]	23 000	34 900	1.90
P(Z-L-Lys)$_{100}$	26 200	14 900	1.47
P(Z-L-Lys)$_{100}$-PCL$_{200}$	49 000	37 000	2.30

[a] DP_n(Z-L-Lys) determined by ^{1}H NMR by comparing the intensity of the allylic amine to that of *O*-benzyl protons, for lower molar mass polypeptides. [b] DP_n of CL in copolymer determined by ^{1}H NMR by comparing the ratio of the methine proton of poly(Z-L-Lys) and the methylene protons of PCL. [c] Molar mass of copolymer = [DP_n(Z-L-Lys) × M_r(Z-L-Lys)] + [DP_n(CL) × M_r(CL)]. [d] Determined by SEC in DMF/LiBr, using polystyrene standards. [e] % deprotection of (Z-L-Lys) determined by ^{1}H NMR. [f] Molar mass = [DP_n(L-Lys) × M_r(L-Lys) + DP_n(Z-L-Lys) × M_r(Z-L-Lys)] + [DP_n(CL) × M_r(CL)].

merize an NCA. We propose an original method which consists of first generating an amino-terminated polypeptide via polymerization of an NCA in the presence of a primary amine and using the latter as macroinitiator in combination with tin(II) octanoate for the ring-opening polymerization of ε-caprolactone (Scheme 1). This is based on previous work reported by our

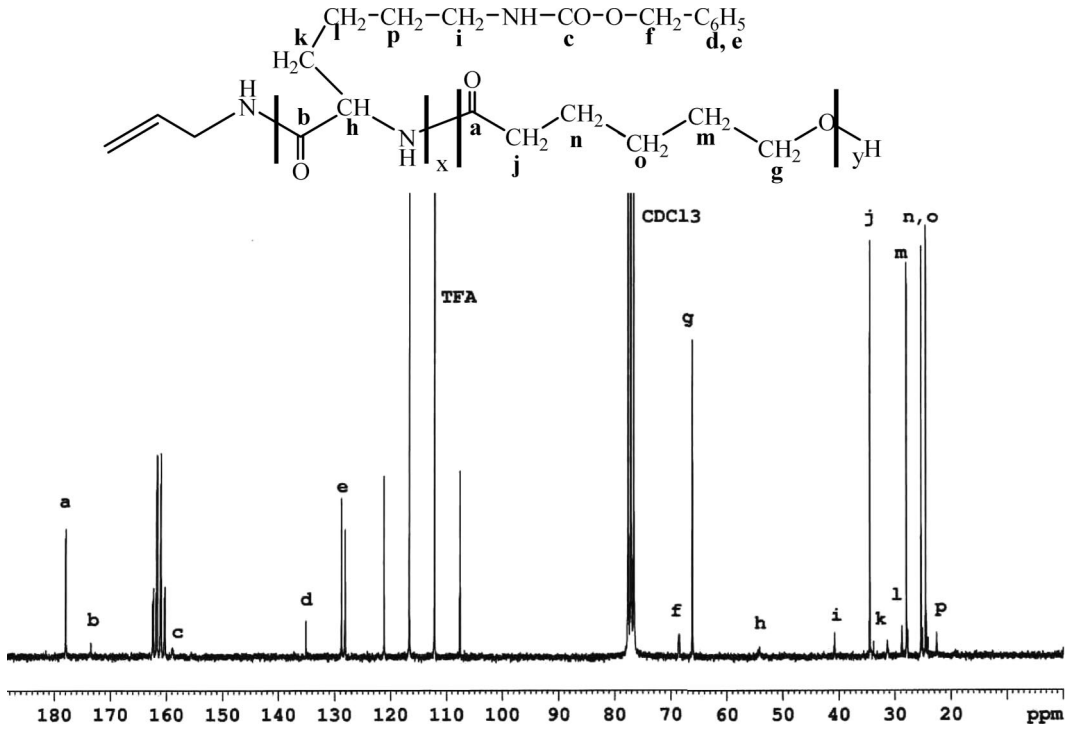


Figure 3. ^{13}C NMR spectrum of poly(Z-L-Lys-*b*-CL) copolymer in $CDCl_3$/TFA.

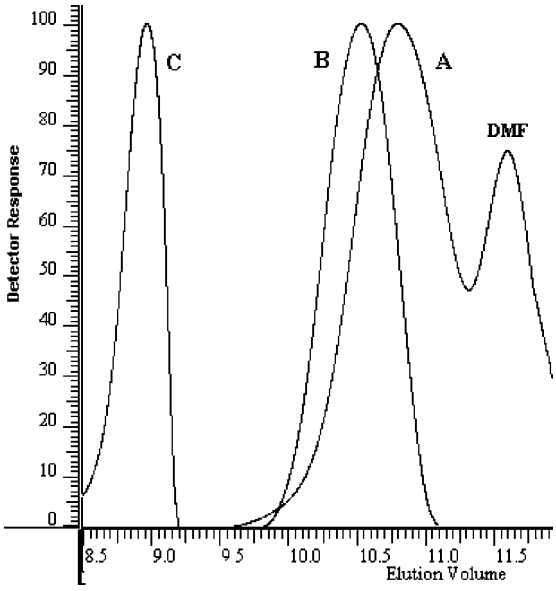


Figure 4. SEC traces (DMF/LiBr as eluent) of (A) poly(Z-L-Lys), (B) poly(Z-L-Lys-*b*-CL) copolymer after precipitation in THF, and (C) poly(L-Lys-*b*-CL) copolymer after removal of Z group.

Table 2. Deprotection of Z-Groups in Block Copolymers Poly(Z-L-Lys-*b*-CL) Using HBr/Acetic Acid Mixture[b]

poly (Z-Lys): PCL	DP_n poly (Z-Lys)/ PCL	poly(Lys)-*b*-PCL (after deprotection)[a]	% deprotection (^1H NMR)	solubility in H_2O
1:1	50−50	1:1	90	soluble
1:2	25−100	1: 1	100	soluble

[a] ^1H NMR in D_2O. [b] Experimental conditions: TFA/$CHCl_3$, excess HBr/AcOH, 2 h.

group concerning the polymerization of ε-caprolactone by means of mono- or difunctional amine initiators (butylamine, ethanolamine, ethylenediamine) coupled with tin(II) octanoate.[12–14] We showed that a complex is initially formed between the amine

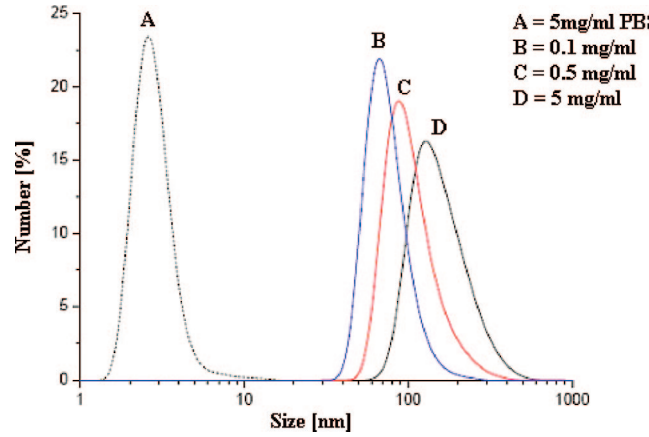


Figure 5. Studies of size distributions of poly(lysine-*b*-caprolactone) (poly(Z-Lys) to PCL 1:1) block copolymer solutions in distilled water (full lines) [*c*: 0.1−5 mg/mL] and PBS [*c*: 5 mg/mL] (dotted lines) using dynamic light scattering.

and the tin(II) salt, and polymerization of ε-caprolactone then proceeds by a coordination−insertion mechanism.

Synthesis of Poly(Z-L-lysine) from Z-lysine NCA. A series of poly(Z-L-lysine) were synthesized using allylamine in DMF at various monomer-to-initiator (M/I) ratios 25, 50, and 100. The reaction was monitored by FTIR to confirm 100% conversion to polymer. The disappearance of the specific absorption bands of NCA at 1860 and 1770 cm^{-1} and the appearance of the polypeptide absorption band at 1650 cm^{-1} confirmed complete polymerization. The polymerization of an NCA in the presence of a primary amine is well established and proceeds via a nucleophilic attack of the amine onto the carbonyl group adjacent to the methine carbon (position 5), leading finally to an amino-terminated polypeptide. The presence of the allyl group at one chain end at 5.2 ppm could be observed by ^1H NMR (Figure 1) for the lower molar mass poly(Z-Lys) obtained at M/I 25 and 50. Its intensity was compared with that of the *O*-benzyl protons (OCH_2) at 5.14 ppm to calculate the degree of polymerization. The DP_n values obtained by ^1H NMR were

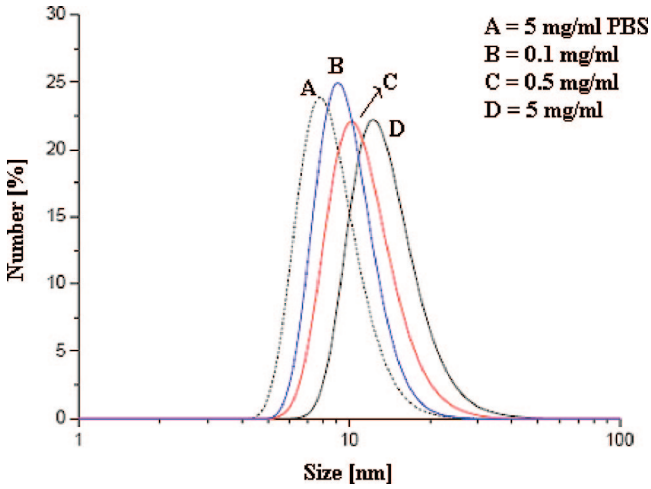


Figure 6. Studies of size distributions of poly(lysine-*b*-caprolactone) (poly(Z-Lys) to PCL 1:4) block copolymer solutions in distilled water (full lines) [*c*: 0.1−5 mg/mL] and PBS [*c*: 5 mg/mL] (dotted lines) using dynamic light scattering.

quite close to those expected according to the experimental M/I ratios. For instance, DP_n of 28 and 47 were obtained when the M/I = 25 and 50, respectively. The DP_n values could not be determined for higher molar mass polypeptides as the allyl signals were not visible in the NMR spectra.

Synthesis of Block Copolymers: Poly(Z-L-lysine-*b*-caprolactone). Amino-terminated poly(Z-L-lysine) of different lengths (DP_n = 25, 50) was used without prior purification as macroinitiator in the presence of tin(II) octanoate to polymerize ε-caprolactone in bulk. At the end of the Z-L-lysine NCA polymerization, tin(II) octanoate was added and allowed to stir while the solvent (DMF) was evaporated. The kinetics of polymerization was monitored by IR spectroscopy, and the semilogarithmic plots show that the polymerization of ε-caprolactone in presence of the amino-poly(Z-lysine)/Sn(II) octanoate system is very comparable to that initiated by the butylamine/tin(II) octanoate system. The semilogarithmic plots exhibit a slight upward curvature in the initial stage attributed to a slow initiation and become linear when initiation is complete (Figure 2). At higher conversions (>60%), the rate of polymerization appears to be lower with the polypeptide/tin(II) octanoate system on account of a much higher viscosity of the medium.

^{1}H NMR of the crude samples confirmed the presence of poly(Z-L-lysine) and PCL sequences. The ratio of Z-L-lysine units to caprolactone units was determined by comparison of the proton intensities at 4.36 and 4.00 ppm corresponding respectively to the C*H* of the poly(Z-Lys) and to the methylene CH_2O of PCL (Table 1). It may be argued that some PCL homopolymer might also be formed during the bulk polymerization of caprolactone. The crude samples were therefore extracted thrice with THF and copolymer compositions compared before and after extraction. The yield of copolymer after extraction was quantitative (over 90%), and no significant change in composition of the two blocks was observed. This result firmly establishes the formation of a true block copolymer. The filtrate resulting from the extraction was also analyzed by ^{1}H NMR and showed the presence of both polymer segments due probably to low molar mass copolymer chains.

As expected for a block copolymer, two distinct signals were observed in the ^{13}C NMR spectrum (Figure 3) at 173.7 and 178.8 ppm, which were assigned to the carbonyl groups of P(Z-Lys) and PCL, respectively.

A range of copolymers having varying lengths of polypeptide and polycaprolactone segments were thus synthesized and characterized by SEC, as listed in Table 1. All copolymers exhibit monomodal distributions, and the chromatograms are shifted toward higher molar mass as compared to the initial polypeptide, which is good evidence of the formation of copolymers (Figure 4). The SEC molar masses of polypeptide and copolymers as determined from polystyrene standards were found to be much higher than the calculated values. Copolymers with shorter caprolactone block lengths (DP_n(CL) = 25, 50) have narrower polydispersities ($M_w/M_n \leq 1.4$) as compared to those with longer CL chains. This indicated that the ROP of CL at higher CL/PP ratio is less controlled. The SEC trace of the deprotected copolymer, P(L-Lys-*b*-CL), was monomodal, and a shift to higher molar mass as compared to the P(Z-Lys-*b*-CL) copolymer was observed.

Deprotection of L-Lysine Units of Copolymers. The Z protecting group of the lysine units of some copolymers were hydrolyzed in TFA/$CHCl_3$ using a mixture of hydrobromic acid and glacial acetic acid. The experimental conditions were adjusted to achieve maximum deprotection without hydrolysis of the PCL chains. Deprotected copolymers listed in Table 2 were all soluble in water. The deprotection yield was determined from ^{1}H NMR spectra recorded in D_2O by comparing the intensities of the aromatic protons of the copolymer at 7.2 ppm before and after hydrolysis (Figure 1C). It is noteworthy that the ^{1}H NMR of poly(Z-L-Lys-*b*-CL) run in $CDCl_3$/TFA solution (Figure 1D) shows a higher ratio of PCL to poly(lysine) due probably to masking of the latter because of micelle formation.

Solution Properties of Poly(lysine-*b*-caprolactone) Block Copolymers. Poly(caprolactone) is a hydrophobic polyester, but a poly(lysine-*b*-caprolactone) block copolymer containing 20% L-lysine units is already water-soluble. In order to analyze the behavior of the copolymers in solution, the particle size distributions in water and in PBS were determined by dynamic light scattering, as shown in Figures 5 and 6. PBS as a solvent was chosen to mimic physiological conditions. The presence of salts screens electrostatic intrachain and interchain interactions in polyelectrolytes. Copolymers with various compositions of caprolactone and L-lysine were analyzed to investigate the relation between particle size distribution and composition of the copolymer. Copolymers with a poly(Z-Lys) to PCL ratio 1:1 and 1:4 were analyzed. First, it is noteworthy that both copolymers spontaneously form micelle-like objects in solution. Second, it can be observed that the copolymer with a poly(Z-Lys) to PCL ratio 1:1 has a larger particle size distribution. Comparing the micelle-like objects dissolved in water with a concentration of 5 mg/mL, it can be noticed that the copolymer with a poly(Z-Lys) to PCL ratio 1:1 is 10 times larger than the copolymer with a poly(Z-Lys) to PCL ratio 1:4. Third it can be noticed that a decreasing concentration causes the decrease of particle size. When the concentration decreases from 5 to 0.1 mg/mL, the particle size varies from 122 to 68 nm (Figure 5). As the polymer chains adopt a more extended structure, they form larger aggregates having a size around 120 nm. In PBS, a salty medium, a drastic contraction of the polymer chains is observed, which leads to a contraction of the whole structure and to the formation of small sized objects. At a concentration of 5 mg/mL the particle size decreases from 122 to approximately 3 nm from distilled water to PBS (Figure 5, dotted lines). This phenomenon shows the shielding of charges in PBS. These effects have also been observed with graft copolymers, poly(CL-*g*-L-Lys).[3]

In Figure 6 the particle size distribution of the copolymer poly(Z-Lys) to PCL ratio 1:4 is shown. The particle size decreases in the same time from 12 to 9 nm, when the concentration of the solution decreases from 5 mg/mL to 0.1 mg/mL in water. But in this case there is hardly a difference in particle size between the micelle-like objects in PBS and in water. They only have a difference of 4 nm. A reason for this

behavior is the higher ratio of PCL that causes longer PCL sequences.

The micelle-like objects with a size around 10 nm would suggest the formation of core−shell micelles while the larger particles around 70 nm would be more in line with a vesicle morphology.

4. Conclusions

We have reported on the synthesis of well-defined amphiphilic block poly(ester−peptide) copolymers using an amino-terminated poly(Z-L-lysine) as macroinitiator to polymerize ε-CL, which is an original approach with regards to previous work. This synthetic method presents a number of advantages in that a reduced number of steps are involved in accessing the desired copolymers and we make use of the biocompatible tin(II) octanoate in our polymerization reactions. We have also shown that the copolymers spontaneously self-organize into nanometer size objects whose morphology varied from core−shell micelles to vesicle-type depending upon the ratio of hydrophilic to hydrophobic sequences. We thus have a range of well-defined polymers, which should be interesting candidates for drug delivery applications.

Acknowledgment. The Tertiary Education Commission (Mauritius) is gratefully acknowledged for providing a Post Doctoral Fellowship to S.M.T.

References and Notes

(1) (a) Griffith, L. G. *Acta Mater.* **2000**, *48*, 263–277. (b) Cottin-Bizonne, S.; Chakfé, N.; Beaufigeau, M.; Le Magnen, J. F.; Dieval, F.; Doillon, C.; Kretz, J. G.; Durand, B. *Rev. Eur. Biotechnol. Med.* **1999**, *2*, 62–75.
(2) Okada, M. *Prog. Polym. Sci.* **2002**, *27*, 87–133, and references therein.
(3) Nottelet, B.; El Ghzaoui, A.; Coudane, J.; Vert, M. *Biomacromolecules* **2007**, *8*, 2594–601.
(4) Jeong, J. H.; Park, T. G. *J. Controlled Release* **2002**, *82*, 159–66.
(5) Degée, P.; Dubois, P.; Jérôme, R.; Teyssié, P. *J. Polym. Sci., Polym. Chem. Ed.* **1993**, *31*, 275–278.
(6) Gotsche, M.; Keul, H.; Höcker, H. *Macromol. Chem. Phys.* **1995**, *196*, 3891–3903.
(7) Kricheldorf, H. R.; Hauser, K. *Biomacromolecules* **2001**, *2*, 1110–1115.
(8) Rong, G.; Deng, M.; Deng, C.; Tang, Z.; Piao, L.; Chen, X.; Jing, X. *Biomacromolecules* **2003**, *4*, 1800–1804.
(9) Fan, Y.; Chen, G.; Tanaka, J.; Tateishi, T. *Biomacromolecules* **2005**, *6*, 3051–3056.
(10) Li, Y.; Li, Q.; Li, F.; Zhang, H.; Jia, L.; Yu, J.; Fang, Q.; Cao, A. *Biomacromolecules* **2006**, *7*, 224–231.
(11) Schappacher, M.; Soum, A.; Guillaume, S. M. *Biomacromolecules* **2006**, *7*, 1373–1379.
(12) Bhaw-Luximon, A.; Jhurry, D.; Motala-Timol, S.; Lochee, Y. *Macromol. Symp.* **2006**, *231*, 60–67.
(13) Motala-Timol, S.; Jhurry, D. *Polym. Int.* **2007**, *56*, 1053–1062.
(14) Motala-Timol, S.; Jhurry, D. *Eur. Polym. J.* **2007**, *43*, 3042–3049.

MA800917C