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Functional mikto-arm star terpolymers by an association-and-reaction strategy

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ABSTRACT

Two functional mikto-arm star terpolymers μ-(PB)(PSm)(PC) were prepared, where PB, PC, and PSm denote poly(*tert*-butyl acrylate), poly[2-(cinnamoyloxy)ethyl methacrylate], and poly(solketal methacrylate), respectively. To prepare the samples, two PB-*b*-PCOOH-*b*-PSm triblock copolymers containing a carboxyl-bearing PCOOH block of 5 units and a PNH_2-*b*-PC diblock copolymer incorporating an amino-bearing PNH_2 block of 5 units were first prepared. The PCOOH and PNH_2 blocks were then associated in solution, bringing together a triblock copolymer chain and a diblock copolymer chain. Functional μ-(PB)(PSm)(PC) copolymers were obtained from amidation of the associated PCOOH and PNH_2 blocks. The effect of varying the reactant concentration on the yield and selectivity of μ-(PB)(PSm)(PC) synthesis was examined. Further, we developed fractional precipitation protocols for purifying the crude reacted mixtures to yield essentially pure μ-(PB)(PSm)(PC) samples.

1. Introduction

Covalently bonding three different polymer chains P1-P3 by one end yields a μ-(P1)(P2)(P3) mikto-arm star terpolymer. μ-(P1)(P2)(P3) may self-assemble into various nanostructures with exotic morphologies, in a selective solvent or in bulk, depending on the copolymer composition and/or solvent selectivity [1–6]. While some of these morphologies have been observed by the groups of Hadjichristidis [12–15], Hirao [16], Matsushita [17–21], as well as Hillmyer and Lodge [7–11], other theoretically predicted morphologies [22–27] remain undiscovered. To gain an improved understanding of μ-(P1)(P2)(P3) micellization or solid-state block segregation, polymers with chemical constitutions and compositions that differ from those that have been previously studied are needed. In addition, micellar chemical processing involving the selective crosslinking [28,29] and/or degradation [30–33] of particular domains (blocks) of copolymer micelles is an effective post-self-assembly strategy to create novel nanostructures, and this strategy has rarely been used on μ-(P1)(P2)(P3) micelles [34]. Thus, the synthesis of μ-(P1)(P2)(P3) bearing readily crosslinkable or degradable blocks is required to facilitate the chemical processing of μ-(P1)(P2)(P3) micelles. This report describes the synthesis of a novel family of two μ-(P1)(P2)(P3) copolymers via a modular approach.

The μ-(P1)(P2)(P3) samples that we have synthesized are μ-(PB)(PSm)(PC) (Scheme 1), where PB, PSm, and PC denote poly(*tert*-butyl acrylate), poly(solketal methacrylate), and poly[2-(cinnamoyloxy)ethyl methacrylate], respectively. In this modular approach, two PB-*b*-PCOOH-*b*-PSm triblock copolymers containing a carboxyl-bearing PCOOH block of 5 units and a PNH_2-*b*-PC diblock copolymer containing an amino-bearing PNH_2 block of 5 units were first prepared. The PCOOH and PNH_2 blocks were then associated together in solution, thus merging a triblock terpolymer chain and a diblock copolymer chain together. Functional μ-(PB)(PSm)(PC) copolymers were eventually obtained after some groups of the associated PCOOH and PNH_2 blocks amidized (Scheme 2).

We have used this new strategy to prepare the μ-(PB)(PSm)(PC) samples because the synthesis of μ-(P1)(P2)(P3) copolymers is generally challenging. The preparation of μ-(P1)(P2)(P3) with arms possessing low polydispersity and functionality is especially challenging [35]. Traditionally, miktoarm copolymers have been prepared through three general strategies. The first method is known as the "arms-first" approach [36,37]. The different arms are prepared via living or controlled polymerizations first and then linked together to yield the star polymers. For instance, different polymer chains bearing a terminal anion can be linked by molecules containing multi-terminating sites [e.g. (chloromethylphenylethyl)methyl dichlorosilane] [38]. These linkage reactions can take days to finish and one can imagine the challenge of ensuring that the anions (and especially the anions

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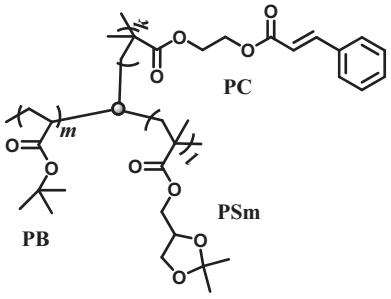


Scheme 1. Chemical structure of μ-(PB)(PSm)(PC).

of polymethacrylates) remain alive for so long. The second strategy is called the "grafting-from" approach, which involves using a trifunctional initiator and different monomers that are polymerized by different mechanisms in sequence [39–41]. Meanwhile, the third strategy is known as the "hybrid" approach, which combines features of the first two approaches [35,42–45]. For example, a core molecule containing a mixture of terminating and initiating sites can be used to prepare μ-(P1)(P2)(P3) [35]. Our approach differs from the previous approaches and our chain coupling chemistry can be performed under very mild conditions.

2. Experimental

2.1. Materials

Cinnamoyl chloride (98%), Z-glycine (99%), succinic anhydride (99%), hexamethylenediamine (98%), trifluoroacetic acid (TFA, 99%), 2-chloro-1-methylpyridinium iodide (CMPI, 97%), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 99%), tetrabutylammonium bromide (99%), 2-hydroxyethyl methacrylate (HEMA, 97%), hexamethyldisilazane (98%), chlorotrimethylsilane (99%), *tert*-butyldimethylsilyl chloride (97%), *D*,*L*-1,2-isopropylideneglycerol (98%), methacryloyl chloride (97%), *n*-butylamine (99.5%), triethyl aluminum (1 M solution in hexanes), and *N*,*N*-dimethylformamide (anhydrous, DMF) were purchased from Aldrich and used as received. Pyridine (Fisher Scientific) was refluxed and distilled over CaH_2 under argon. Tetrahydrofuran (Fisher Scientific) was refluxed and distilled over sodium under nitrogen with benzophenone as indicator. *p*-Toluenesulfonic acid monohydrate (TSA, 98%) was dehydrated at 110 °C under vacuum for 4 h and was then recrystallized in chloroform before use. Triethylamine (TEA, Aldrich, 99.5%) was refluxed with *p*-toluensulfonyl chloride for 8 h and then distilled. 1,1-Diphenylethylene was sequentially distilled over calcium hydride and *n*-butyl lithium. *t*-Butyl acrylate (Aldrich) was initially distilled over CaH_2, and was then freshly titrated and redistilled over triethyl aluminum before polymerization. The monomers 2-(trimethylsilyloxy)ethyl methacrylate (HEMA-TMS) [46], 2-(*tert*-butyldimethylsilyloxy)ethyl methacrylate (HEMA-tBDMS) [47] and solketal methacrylate (SMA) [47] were prepared and purified according to literature methods.

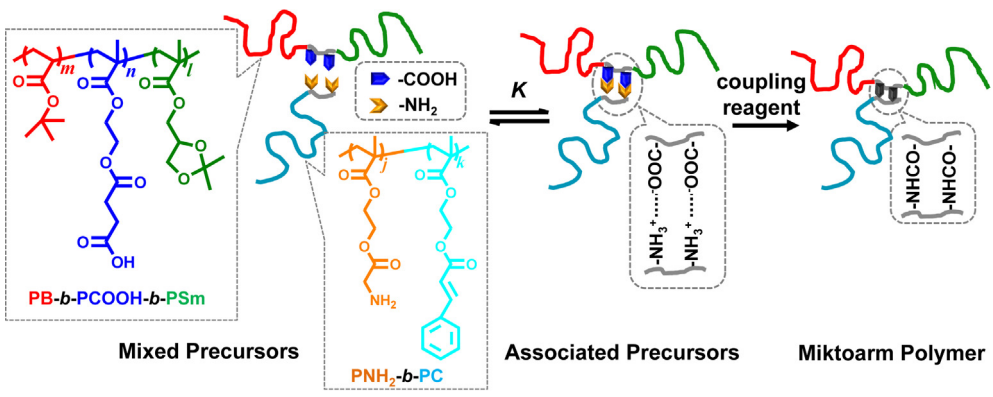
2.2. P(HEMA-tBDMS)-b-PHEMA

P(HEMA-tBDMS)-*b*-P(HEMA-TMS) was a precursor to PNH_2-*b*-PC and was synthesized via sequential anionic polymerization in THF at −78 °C [48]. To a three-neck 1-L round-bottom flask connected to a vacuum line was added 0.5624 g of LiCl. The flask containing this salt was then vacuum-pumped and flamed with a propane torch. Approximately 600 mL of THF was then distilled into this flask. After the addition of 0.20 mL of 1,1-diphenylethylene (1.14 mmol, excess), *sec*-butyl lithium (1.4 M in cyclohexane) was added dropwise to titrate the impurities. After a persistent faint pink color developed, 0.56 mL (0.78 mmol) of the *sec*-butyl lithium solution was added. Subsequently, HEMA-tBDMS (0.99 mL, 3.9 mmol) was added dropwise and 2 h was allowed for the monomer to fully polymerize. This was followed by the slow addition of HEMA-TMS (20.6 mL, 94.5 mmol) and another 2 h polymerization period. The polymerization was terminated by adding 5.0 mL of degassed methanol/H_2O at v/v = 1/1.

To remove the trimethylsilyl group from the P(HEMA-TMS) block to yield poly(2-hydroxyethyl methacrylate) or PHEMA, another 100 mL of methanol/H_2O at v/v = 5/2 was added into the polymerization flask. The resultant mixture was stirred overnight at room temperature. Subsequently, the solution was rotary-evaporated to ~100 mL, and the condensate was sprayed onto crushed ice crystals that were added between different layers of the added condensate. After the ice melted, the polymer was collected via filtration and dried under vacuum overnight to yield 12.67 g of product in a 96% yield.

2.3. P(HEMA-tBDMS)-b-PC

To prepare P(HEMA-*t*BDMS)-*b*-PC, P(HEMA-*t*BDMS)-*b*-PHEMA (5.10 g containing 36.5 mmol of hydroxyl groups) and cinnamoyl chloride (12.2 g, 73.2 mmol) were dissolved into freshly distilled pyridine (50 mL). The mixture was stirred overnight before the pyridinium chloride salt that had formed was settled by centrifugation and separated. The supernatant was added to 300 mL of methanol/H_2O (v/v = 9/1) to precipitate P(HEMA-*t*BDMS)-*b*-PC [49]. The polymer was re-dissolved into 40 mL of THF and added into 300 mL of methanol/H_2O (v/v = 9/1) to precipitate the polymer. After the precipitate had been dried under vacuum at room temperature overnight, 9.45 g of the product was obtained in a 96% yield.



Scheme 2. Illustration of the steps involved in the preparation of μ-(PB)(PSm)(PC).

2.4. PHEMA-b-PC

To remove the *t*-butyldimethylsiloxy groups from the P(HEMA-tBDMS) block and thus yield a PHEMA block, 9.00 g of P(HEMA-tBDMS)-*b*-PC was dissolved into 50 mL of THF. To this solution was then added 12.5 mL of a 1.0 M aqueous HCl solution. The mixture was stirred for 2 h before it was added into 300 mL of water to precipitate the polymer. After the precipitate was dried under vacuum at room temperature overnight, 8.61 g of PHEMA-*b*-PC was obtained in a 97% yield.

2.5. PNH_2-b-PC

To prepare P(NH_2-Cbz)-*b*-PC, where P(NH_2-Cbz) denotes poly[2-(carbobenzyloxy-glycyl)ethyl methacrylate], 2.000 g of PHEMA-*b*-PC (containing 0.31 mmol of hydroxyl groups) was dissolved into 12 mL of dry pyridine. To this solution under vigorous stirring were then added 0.130 g (0.62 mmol) of carbobenzyloxyglycine, 0.014 g (0.08 mmol) of TSA, and 0.150 g (0.74 mmol) of DCC (dispersed in 2 mL of dry pyridine). After the reaction mixture had been stirred for 12 h at room temperature, it was centrifuged. The supernatant was separated by decantation and was diluted to 25 mL with THF before it was added into excess methanol to precipitate the polymer. The precipitate was re-dissolved into 25 mL of THF and the polymer solution was added into excess methanol to precipitate the polymer again. This procedure was repeated another time. The final precipitate was dried under vacuum to give 1.938 g of P(GNH_2-Cbz)-*b*-PC in a 94% yield.

To remove the carbobenzyloxy protecting group, 1.800 g of P(GNH_2-Cbz)-*b*-PC was dissolved into 10 mL of trifluoroacetic acid (TFA), and the solution was refluxed at 70 °C for 4 h. The TFA was then evaporated under vacuum. The resulting solid was subsequently dissolved in 25 mL of pyridine, and this solution was added into excess methanol to precipitate the polymer. The polymer was re-dissolved in 25 mL of THF, and the solution was added into methanol to precipitate the polymer again. This procedure was repeated twice. After the precipitate was dried under vacuum, 1.622 g of PNH_2-*b*-PC was obtained in a 92% yield.

2.6. PB-b-PHEMA-b-PSm

Two PB-*b*-PCOOH-*b*-PSm samples were used to prepare μ-(PB)(PSm)(PC). While the respective targeted repeat units were 100 and 5 for the PB and PCOOH blocks, the targeted PSm repeat unit numbers were 66 and 200 for the PB-*b*-PCOOH-*b*-PSm_{66} and PB-*b*-PCOOH-*b*-PSm_{200} samples, respectively. The PB-*b*-PCOOH-*b*-PSm samples were derived from PB-*b*-P(HEMA-TMS)-*b*-PSm copolymers that were prepared via anionic polymerization.

The PB-*b*-P(HEMA-TMS)-*b*-PSm samples were prepared at −78 °C analogously as P(HEMA-tBDMS)-*b*-P(HEMA-TMS) using THF as the solvent. The polymerization time for each block was 2 h. To prepare PB-*b*-P(HEMA-TMS)-*b*-PSm_{200}, the following reagents were used: LiCl (0.0788 g), THF (6×10^2 mL), 1,1-diphenylethylene (0.20 mL or 1.14 mmol), *sec*-butyl lithium (0.265 mL at 1.4 M, or 0.37 mmol), B (5.39 mL, 37.2 mmol), HEMA-TMS (0.40 mL, 1.86 mmol), and Sm (14.4 mL, 74.3 mmol). Meanwhile, the recipe used to prepare PB-*b*-P(HEMA-TMS)-*b*-PSm_{66} consisted of LiCl (0.147 g), THF (6×10^2 mL), 1,1-diphenylethylene (0.30 mL or 1.71 mmol), *sec*-butyl lithium (0.496 mL at 1.4 M or 0.69 mmol), B (10.1 mL, 69.4 mmol), HEMA-TMS (0.76 mL, 3.47 mmol), and Sm (10.1 mL, 46.2 mmol).

The trimethylsilyl groups were removed from the P(HEMA-TMS) blocks via overnight stirring in methanol/water mixtures. The resultant polymers were concentrated and sprayed onto ice crystal layers to yield solid polymers. After they had been dried under vacuum, 19.210 g of PB-*b*-PHEMA-*b*-PSm_{200} and 18.230 g of PB-*b*-PHEMA-*b*-PSm_{66} were obtained at yields of 97% and 93%, respectively.

2.7. PB-b-PCOOH-b-PSm

Excess succinic anhydride was reacted with PB-*b*-PHEMA-*b*-PSm_{200} and PB-*b*-PHEMA-*b*-PSm_{66} to produce PB-*b*-PCOOH-*b*-PSm_{200} (triblock copolymer 1, or TBC1) and PB-*b*-PCOOH-*b*-PSm_{66} (TBC2). To produce TBC1, PB-*b*-PHEMA-*b*-PSm_{200} (4.000 g containing 0.35 mmol of hydroxyl groups) and 0.50 g (5.0 mmol) of succinic anhydride were dissolved into 30 mL of dry pyridine. After the mixture had been stirred for 12 h at room temperature, it was added into 300 mL of methanol/water (v/v = 8/2) to precipitate the polymer. The polymer was subsequently re-dissolved into 40 mL of THF and acetic acid was added until the pH reached 5 as measured by pH paper. The acidified solution was subsequently added into methanol/water (v/v = 8/2) to precipitate the polymer. The polymer was subsequently re-dissolved into 40 mL of THF and precipitated from methanol/water (v/v = 8/2). This procedure was repeated once. After the precipitate had been dried under vacuum, 3.645 g of PB-*b*-PCOOH-*b*-PSm_{200} was obtained in a 91% yield. PB-*b*-PHEMA-*b*-PSm_{66} was succinated and purified analogously.

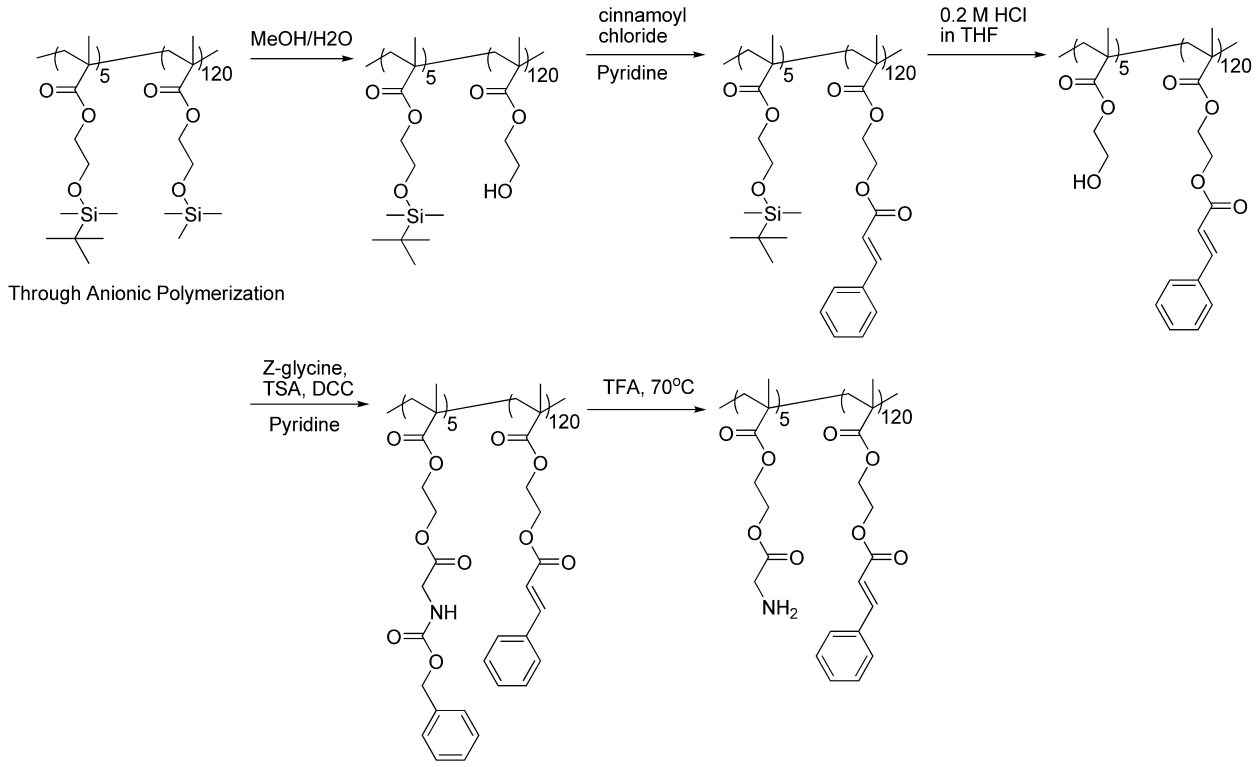
2.8. μ-(PB)(PSm)(PC)

In a typical run, PNH_2-*b*-PC (0.3747 g or 1.17×10^{-2} mmol of chains) and TBC1 (0.6289 g or 1.17×10^{-2} mmol of polymer chains) were mixed and stirred in 200 mL of THF. After 2 h had passed, 5.0 mL of THF containing 17.9 mg of CMPI (7.02×10^{-2} mmol) and 19.5 μL of TEA (14.1×10^{-1} mmol) were added. The mixture was stirred for 6 h at room temperature before 4.6 μL of *n*-butylamine was added and the mixture was stirred for another 2 h to deactivate un-reacted carboxyl groups. A crude product was obtained by removing the THF via rotary-evaporation.

2.9. μ-(PB)(PSm)(PC) purification

The μ-(PB)(PSm)(PC) copolymers that were derived from TBC1 and TBC2 are denoted as μ-1 and μ-2, respectively. To purify μ-2, water was added to 20 mL of THF containing 500 mg of crude μ-2 until cloudiness developed. This cloudy solution was left standing in a fridge at 4 °C overnight before it was centrifuged at 450 × *g* for 5 min to settle the dense layer. Our size-exclusion chromatography (SEC) analysis indicated that the dense layer consisted mostly of μ-(PB)(PSm)$(PC)_2$. The supernatant was subsequently rotary-evaporated and the solid was re-dissolved into ~20 mL of THF. The fractionation–precipitation protocol was repeated for this sample. SEC analysis of the new dense layer indicated that it consisted mostly of μ-2 as well as PNH_2-*b*-PC. Thus, the dense layer was re-dissolved into ~20 mL of THF and the fractionation was repeated another time. SEC analysis revealed that the dense layer was essentially pure μ-2. The dense layer was subsequently diluted to ~2 mL with THF and added into 100 mL of water to precipitate the polymer. The polymer was subsequently dried under vacuum to yield 120 mg of μ-2.

To purify μ-1, a THF solution containing the crude product was fractionated using the protocol mentioned above by adding water to mainly remove μ-(PB)(PSm)$(PC)_2$. The sample was then fractionated again to obtain μ-1 and PNH_2-*b*-PC as the dense layer. To separate the two copolymers, the mixture was re-dissolved into ~10 mL of a pre-made 0.2 M HCl solution (in THF) to hydrolyze PSm into poly(monoglyceryl methacrylate) or PGMA. The solvent was subsequently removed via rotary-evaporation. The solid residue (without being fully dried) was dissolved in pyridine and added into excess nitromethane in order to precipitate μ-1.



Scheme 3. Synthetic pathways toward PNH_2-*b*-PC.

2.10. ^1H NMR analyses

^1H NMR spectra were recorded using a Bruker 300 MHz spectrometer. Depending on the solubility of the sample, either deuterated chloroform ($CDCl_3$) or deuterated pyridine (pyridine-d_5) were used as the solvents.

2.11. Size exclusion chromatography

The number-average molecular weight (M_n) and polydispersity index (M_w/M_n) of each polymer were determined using a Waters size exclusion chromatograph (SEC) that was equipped with a Waters 2410 refractive index (RI) detector. A DMF solution containing tetrabutylammonium bromide (5 mg/mL) was heated at 70 °C and used as the eluent at a flow rate of 0.90 mL/min. The columns used were packed with ultra-styragel with the pore sizes of 1000, 10 000 and 100 000 Å. The system was calibrated with narrowly-dispersed PS standards.

3. Results and discussion

As mentioned in the Introduction, two μ-(PB)(PSm)(PC) samples (μ-1 and μ-2) were synthesized by a modular approach involving first the preparation of a PNH_2-*b*-PC copolymer and two PB-*b*-PCOOH-*b*-PSm copolymers (TBC1 and TBC2). While the targeted repeat unit numbers for PNH_2 and PCOOH blocks were 5, the targeted lengths for the PC and PB blocks were 120 and 100 units, respectively. The PSm blocks of TBC1 and TBC2 were targeted at 200 and 66 repeat units, respectively. TBC1 or TBC 2 was reacted with PNH_2-*b*-PC to yield μ-1 or μ-2.

Short PCOOH and PNH_2 blocks of five units were used, because we failed to produce a miktoarm copolymer when we reacted TBC1 with a 120-unit-long poly(methyl methacrylate) (PMMA) polymer bearing only one terminal amino group. This was presumably due to the weak attraction between only one amino group and a PCOOH block as well as the strong repulsion between the PMMA chain and both the PB and PSm blocks of TBC1.

3.1. PNH_2-*b*-PC

PNH_2-*b*-PC was prepared in six steps (Scheme 3). First, P(HEMA-tBDMS)-*b*-P(HEMA-TMS) was prepared via anionic polymerization [46,47]. Since P(HEMA-tBDMS) was more stable than P(HEMA-TMS), the TMS protecting groups were selectively removed in step 2 to yield P(HEMA-tBDMS)-*b*-PHEMA [3]. The PHEMA block was then reacted with cinnamoyl chloride in step 3 to yield a PC block. This was followed by the cleavage of the tBDMS protecting groups in step 4 to yield PHEMA-*b*-PC. In step 5, the PHEMA block was reacted with *N*-carbobenzyloxyglycine (Z-glycine) to yield P(HEMA-GlyCbz)-*b*-PC. Finally, the removal of carbobenzyl protecting group by trifluoroacetic acid produced PNH_2-*b*-PC.

PNH_2-*b*-PC and its precursors were characterized by ^1H NMR using pyridine-d_5 as the solvent. Fig. 1 compares the ^1H NMR spectra of P(HEMA-tBDMS)-*b*-PHEMA, PHEMA-*b*-PCEMA, P(NH_2-Cbz)-*b*-PC, and PNH_2-*b*-PC together with their peak assignments. The data suggest our success in each derivatization. In addition, the ratios between the repeat unit numbers of the first and second blocks were determined from their characteristic peak integrals. For example, we determined at the P(HEMA-tBDMS)-*b*-PHEMA stage an integral ratio of 45/490 between the *f* peak and the (*c* + *g*) peaks. This value allowed us to calculate a repeat unit ratio of 22 for the PHEMA and P(HEMA-tBDMS) blocks. The value was consistent within experimental error with the value of 24 expected for the targeted polymer consisting of 120 HEMA and 5 HEMA-tBDMS units, respectively.

PNH_2-*b*-PC and some of its precursors P(HEMA-tBDMS)-*b*-PC, PHEMA-*b*-PC, and P(NH_2-Cbz)-*b*-PC were also characterized by size-exclusion chromatography (SEC). Fig. 2 shows the SEC traces of these samples. The key observation was that all of the peaks had a similar shape and were narrow, possessing polydispersity indices of

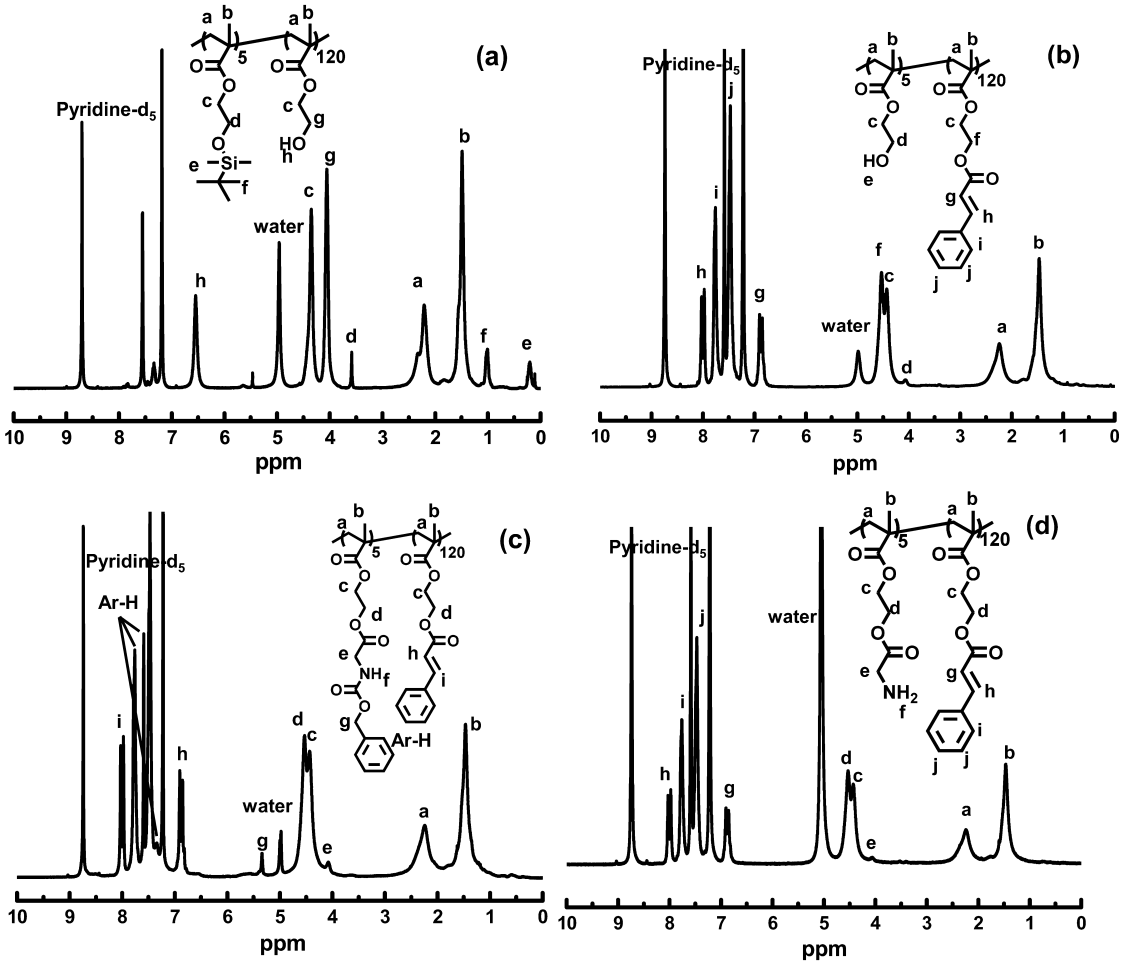


Fig. 1. ^{1}H NMR spectra of (a) P(HEMA-tBDMS)-*b*-PHEMA, (b) PHEMA-*b*-PC, (c) P(NH_2-Cbz)-*b*-PC, and (d) PNH_2-*b*-PC. Pyridine-d_5 was used as the solvent in each case.

less than 1.05 in terms of PS standards. The similar shapes suggested that the derivatization did not change the backbone structure of the polymer, but only the targeted pendant groups. The low polydispersity confirmed that the anionic polymerization had proceeded smoothly.

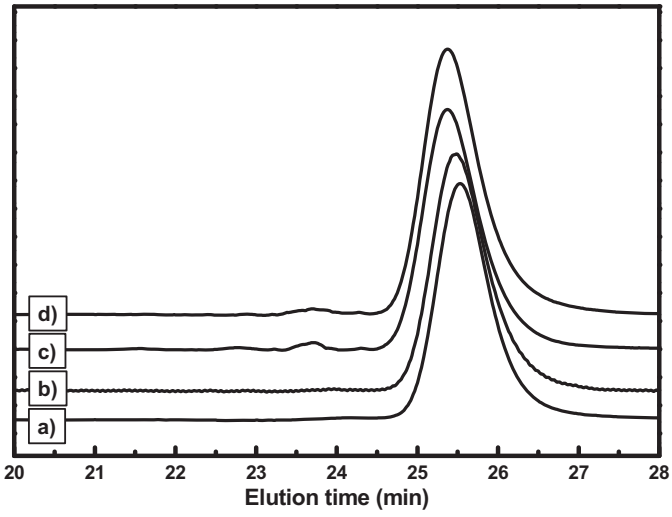


Fig. 2. SEC traces of (a) P(HEMA-tBDMS)-*b*-PC, (b) PHEMA-*b*-PC, (c) P(NH_2-Cbz)-*b*-PC, and (d) PNH_2-*b*-PC.

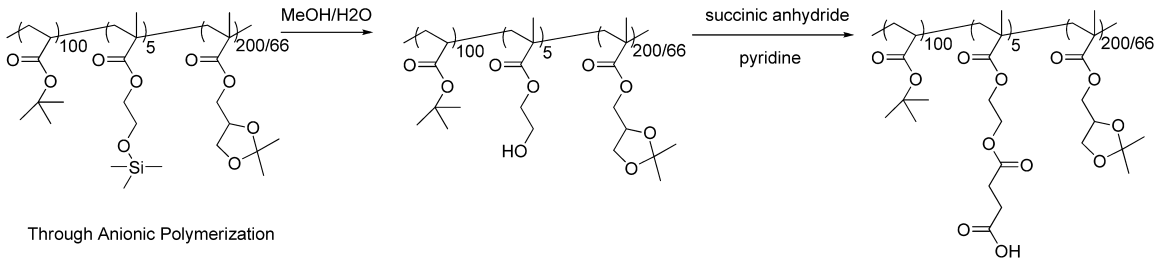
We did not determine the absolute molecular weight of PNH_2-*b*-PC because the main object of this work was to prepare the new functional μ-(PB)(PSm)(PC) copolymer. Furthermore, the molecular weight of PNH_2-*b*-PC should be close to the targeted value of 32 kg/mol for PNH_2-*b*-PC consisting of 5 amino-bearing units and 120 C units because the precursor P(HEMA-tBDMS)-*b*-P(HEMA-TMS) was prepared via anionic polymerization. Incidentally, 32 kg/mol agreed reasonably well with the value of 40 kg/mol determined by SEC calibrated using PS standards (Table 1).

3.2. PB-b-PCOOH-b-PSm

While the respective targeted repeat units were 100 and 5 for the PB and PCOOH blocks for both TBC1 and TBC2, the Sm repeat unit numbers were 66 and 200 for these respective copolymers. TBC1 and TBC2 were prepared via the synthetic pathways depicted in Scheme 4. First, the PB-*b*-P(HEMA-TMS)-*b*-PSm copolymers were

Table 1
SEC and NMR characteristics of the precursors.

Sample	SEC M_n (kg/mol)	SEC M_w/M_n	NMR *j*/*k* or *m*/*n*/*l*
PHEMA-*b*-PC	38	1.02	5/122
P(NH_2-Cbz)-*b*-PC	40	1.02	5/121
PNH_2-*b*-PC	40	1.02	
PB-*b*-PHEMA-*b*-PSm_{200}	60	1.05	
PB-*b*-PCOOH-*b*-PSm_{200}	61	1.05	102/5/201
PB-*b*-PHEMA-*b*-PSm_{66}	37	1.03	
PB-*b*-PCOOH-*b*-PSm_{66}	38	1.03	101/5/66



Scheme 4. Synthetic pathways toward PB-*b*-PCOOH-*b*-PSm.

prepared via anionic polymerization. The TMS protecting groups were then selectively removed in step 2 [3]. The resultant hydroxyl groups of the PHEMA block were then reacted with excess succinic anhydride to yield PB-*b*-PSCOOH-*b*-PSm.

The PHEMA block was reacted with succinic anhydride in pyridine. To ensure that the pendant carboxyl groups were mostly in their acidic form, the precipitated crude PB-*b*-PCOOH-*b*-PSm was re-dissolved into a THF solution containing acetic acid before it was re-precipitated out from a water/methanol mixture. The weak acetic acid was used because PSm readily hydrolyses when it is treated with a strong acid such as hydrochloric acid.

The PB-*b*-PCOOH-*b*-PSm samples and their precursory PB-*b*-PHEMA-*b*-PSm samples were characterized by ^{1}H NMR in pyridine-d_5. Fig. 3 shows the spectra for these samples along with their peak assignments. The peaks g in Fig. 3b and d clearly show our success at the targeted reactions. Our quantitative analysis yielded the integration ratios of 910/20/1060 and 900/20/350 among the *c*, *g*, and (*e* + *f* + *i*) peaks for TBC1 and TBC2, respectively. Using the targeted repeated units ratios of 100/5/200 for B, COOH, and C for TBC1, the integration ratios should be 900/20/1020. Meanwhile, these ratios should be 900/20/350 for TBC2. The experimental values were consistent with the targeted values.

The samples were also analyzed by SEC and the results are shown in Fig. 4. TBC1 had a shorter retention time than TBC2, as expected. Based on PS standards, the M_n values of TBC1 and TBC2 were 61 and 38 kg/mol, respectively (see Table 1), which were reasonably consistent with the targeted molecular weights of 54 and 27 kg/mol. The two sets of data did not exactly agree because the PS standards used for SEC calibration bear no structural resemblance to the triblock copolymers. The low polydispersity indices of the polymers (Table 1) suggested again our successful execution of the polymerization and polymer derivatization reactions.

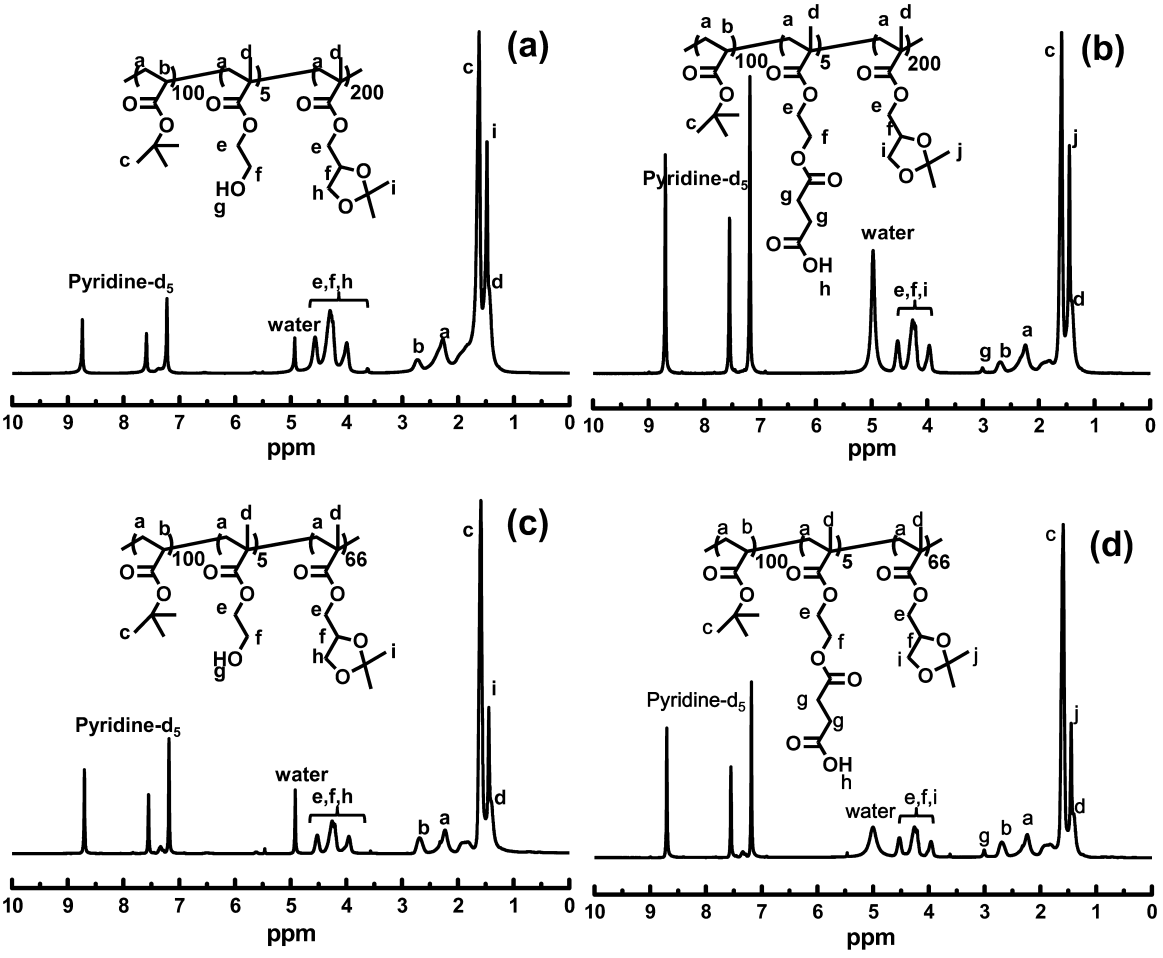


Fig. 3. Comparison of ^{1}H NMR spectra of (a) PB-*b*-PHEMA-*b*-PSm$_{200}$, (b) TBC1, (c) PB-*b*-PHEMA-*b*-PSm$_{66}$, and (d) TBC2.

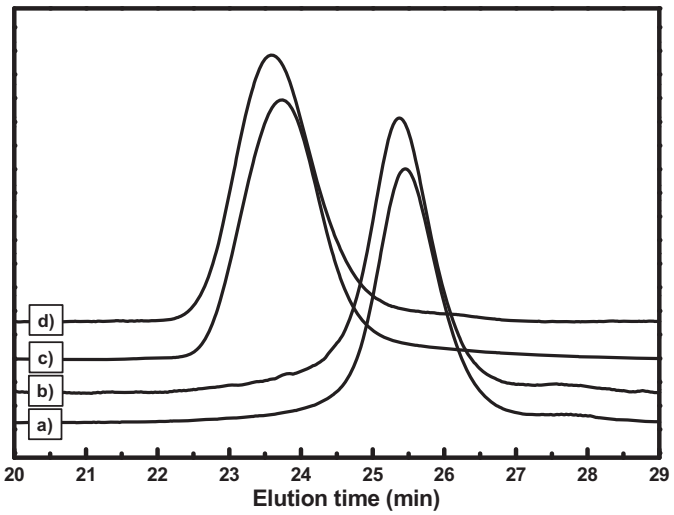


Fig. 4. SEC traces of (a) PB-*b*-PHEMA-*b*-PSm_{66}, (b) TBC2, (c) PB-*b*-PHEMA-*b*-PSm_{200}, and (d) TBC1.

3.3. *μ-(PB)(PSm)(PC)*

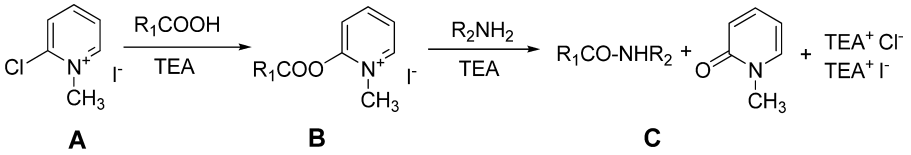
The *μ*-(PB)(PSm)(PC) miktoarm star copolymers were prepared in two steps. In step 1, PNH_2-*b*-PCEMA and either TBC1 or TBC2 were stirred in THF to establish an association equilibrium between these precursors. In step 2, a coupling agent 2-chloro-1-methylpyridinium iodide (CMPI) was added with triethylamine to stitch the associated chains together. Triethylamine was added to neutralize the HCl and HI that was generated from the stitching reaction (Scheme 5).

We note that this method has previously been used to prepare a μ-$(P1)_1(P2)_2$ miktoarm copolymer [50]. However, the work here differs from the previous one in the following aspects. First, the PNH_2 and PCOOH blocks used in that case were longer than 22 repeat units. On the other hand, these blocks were only 5 repeat units long in the current study. Thus, the *μ*-(PB)(PSm)(PC) samples resembled miktoarm copolymers better than the previous μ-$(P1)_1(P2)_2$ samples. Second, the prior paper was aimed at proof of concept and this paper is focused on the application of the methodology developed there. Because of this, P2 in the previous study consisted of poly(methyl methacrylate) that was not readily derivatized. On the contrary, PSm and PB here can be readily derivatized. For example, PSm can be selectively hydrolyzed by dilute hydrochloric acid to yield water-soluble poly(monoglyceryl methacrylate). Further, PB can be selectively hydrolyzed over PC to yield poly(acrylic acid). Third, both the solid-state and the micellar morphologies of μ-$(P1)_1(P2)(P3)$ should be far more diversified and interesting than those of μ-$(P1)_1(P2)_2$.

The *μ*-1 or *μ*-2 miktoarm copolymers were prepared by reacting PNH_2-*b*-PC and either TBC1 or TBC2 at a molar ratio of 1.00/1.00. In order to calculate the molar concentrations, the number-average molecular weights M_n of the polymers were evaluated based on their targeted repeat unit numbers for the individual blocks. The crude products were then analyzed via SEC. Fig. 5 shows the SEC traces for crude products obtained from trials that used a total polymer concentration of 10.0 mg/mL. Also shown are traces that were measured using a refractive index detector for their precursors. In the case of *μ*-2, the SEC trace of a physical mixture consisting of PNH_2-*b*-PC and TBC2 at the molar ration of 1/1 is also provided.

In both cases, a peak with a shorter retention time or a higher molecular weight was seen for the crude reaction mixture, suggesting the formation of *μ*-1 and *μ*-2. Based on PS standards, the peak molecular weights of *μ*-1 and *μ*-2 were 95 and 59 kg/mol, respectively. However, unreacted precursors were also seen in the crude products, although they were in lower amounts. In addition, a shoulder peak with a PS-equivalent peak molecular weight of 120 or 90 kg/mol was observed for the *μ*-1 or *μ*-2 crude product, respectively.

These shoulders are likely due to formation of μ-$(PB)(PSm)(PC)_2$ through the linkage of two PNH_2-*b*-PC chains by one TBC chain. This was possible because of the distributions in the number of amino and carboxyl groups in the PNH_2 and PCOOH blocks. The shoulders arose most likely due to μ-$(PB)(PSm)(PC)_2$ rather than from the formation of μ-$(PB)_2(PSm)_2(PC)$ by the linkage of 2 TBC chains with 1 PNH_2-*b*-PC chain. The latter formation would be less likely because the steric hindrance associated with clustering of



Scheme 5. Amidization reaction facilitated by the coupling agent CMPI.

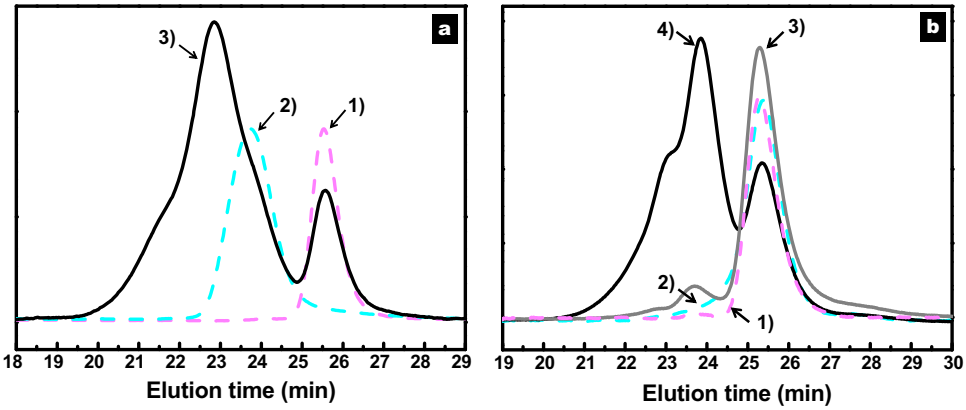


Fig. 5. (a) SEC traces of (1) PNH_2-*b*-PC, (2) TBC1, and (3) a crude reaction mixture of PNH_2-*b*-PC and TBC1 at a molar ratio of 1.00/1.00. (b) SEC traces of (1) PNH_2-*b*-PC, (2) TBC2, (3) a physical mixture of PNH_2-*b*-PC and TBC2 at a molar ratio of 1.00/1.00, and (4) crude reaction mixture of PNH_2-*b*-PCEMA and TBC2 at a molar ratio of 1.00/1.00.

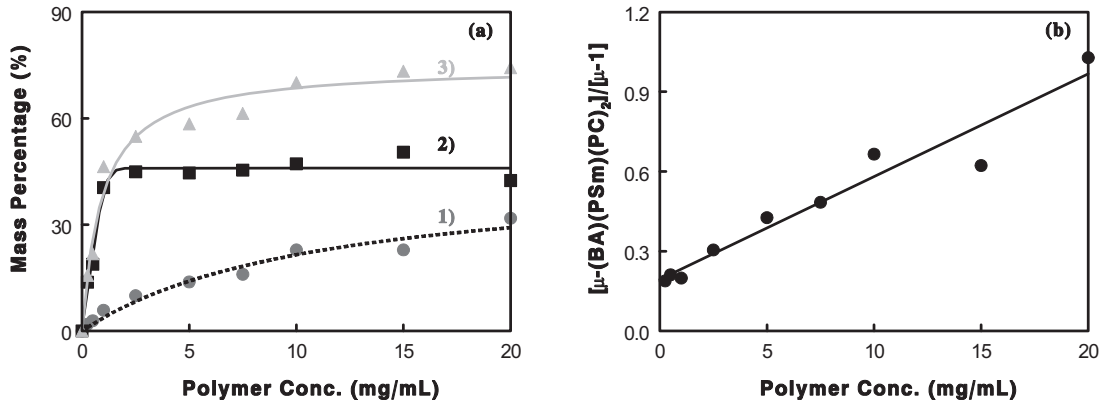


Fig. 6. (a) Variations in the yields of (1) μ-(PB)(PSm)$(PC)_2$, (2) μ-1, and (3) μ-(PB)(PSm)$(PC)_2$ plus μ-1 as a function of the total concentration c_P for TCP1 and PNH_2-*b*-PCEMA used during μ-1 preparation. (b) Variation in [μ-(PB)(PSm)$(PC)_2$]/[μ-1] as a function of c_P.

two TBC chains around the same PNH_2 block of a PNH_2-*b*-PC chain would be much higher than that encountered to bring two PNH_2-*b*-PC chains closer to a TBC chain. Furthermore, a shoulder peak was also observed in our previously reported μ-$(P1)(P2)_2$ synthesis [50]. In that case, we fractionated the polymer that corresponded to the shoulder and our ^{1}H NMR analysis of the shoulder component confirmed that it consisted of a product derived from the reaction between two diblock copolymer chains and one triblock copolymer chain.

Another notable observation was that a weak peak at the μ-2 peak position was detected for the physical mixture of PNH_2-*b*-PC and TBC2 before the coupling agent CMPI was added. This provided direct evidence for the association of the PNH_2-*b*-PC and TBC2 precursors even when the sample was highly diluted by the SEC eluent that consisted of a DMF solution containing tetrabutylammonium bromide.

3.4. *Effect of varying the reactant concentration*

The SEC traces of the crude μ-1 and μ-2 products could de-convoluted using a commercial software into component peaks (SI). For crude μ-1 products, their SEC traces were de-convoluted into four peaks belonging to μ-(PB)(PSm)$(PC)_2$, μ-1, TBC1, and PNH_2-*b*-PC. The area of each peak was then integrated. Dividing each area by the d*n*/d*c* value yielded the mass amount for a particular component of a crude product. The total mass amount present in a sample was calculated from sum of the d*n*/d*c*-corrected areas of all peaks. The yield of a product was then obtained from the ratio of its d*n*/d*c*-corrected area to the total d*n*/d*c*-corrected area. Dividing the d*n*/d*c*-corrected area of a particular product by its molar mass yielded its molar amount present and the molar quantities of μ-(PB)(PSm)$(PC)_2$ and μ-1 produced were thus used to calculate the molar ratio for these two components in a given sample. In these calculations, we used the d*n*/d*c* values determined experimentally for TBC1 and PNH_2-*b*-PC. The d*n*/d*c* values for μ-(PB)(PSm)$(PC)_2$ and μ-1 were calculated from those of TBC1 and PNH_2-*b*-PC and their known polymer compositions (SI).

The above data analysis method allowed us to examine the SEC traces of samples prepared at different total polymer concentrations c_p. Shown in Fig. 6 are results that we obtained from a series of coupling experiments performed in THF at room temperature for 6 h after CMPI addition. In these experiments, the total precursor concentration c_p was changed but the molar concentration ratio for PNH_2-*b*-PC and TBC1 was fixed at 1.00/1.00. The yields of μ-(PB)(PSm)$(PC)_2$ and μ-1 as well as the total yield of μ-(PA)(PB)$(PC)_2$ and μ-1 increased initially as c_p increased. The yields plateaued at high c_p's.

Fig. 6a further suggests that the yield of μ-1 increased more sharply with c_P, before it plateaued, than that of μ-(PB)(PSm)$(PC)_2$. Thus, the targeted product μ-1 was preferentially formed at low at c_P's. This trend was more apparent in Fig. 6b where the molar concentration ratios of μ-(PB)(PSm)$(PC)_2$ and μ-1 formed at different c_P's were plotted as a function of c_P. [μ-(PB)(PSm)$(PC)_2$]/[μ-1] increased almost linearly with c_p.

Thus, data of Fig. 6 suggest that μ-1 should be prepared at c_P ~2.5 mg/mL, where the overall product yield and the selectivity for μ-1 were reasonably high. For large scale preparations, we normally used c_P = 5 mg/mL to reduce solvent consumption.

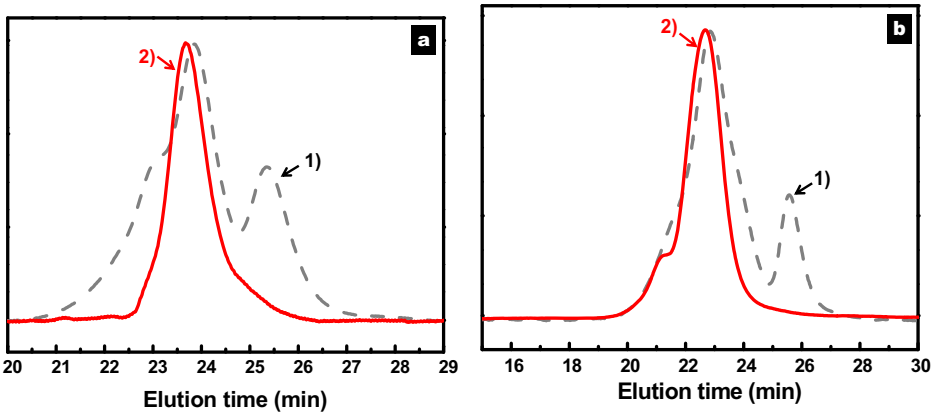


Fig. 7. (a) SEC traces of μ-2 (1) before and (2) after purification. (b) SEC traces of (1) crude μ-1 and (2) purified μ-PB($PGMA_{200}$)PC.

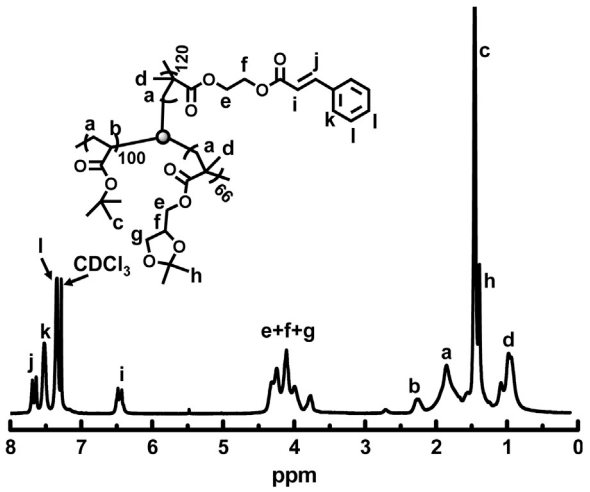


Fig. 8. ^{1}H NMR spectrum of μ-2 recorded in $CDCl_3$.

3.5. Miktoarm copolymer purification

Crude products of μ-1 and μ-2 were purified via fractional precipitation. The polymers were each dissolved in THF and enough water was added to induce first the separation of μ-(PB)(PSm)$(PC)_2$ as a bottom dense layer. The fractionation was continued until μ-1 or μ-2 was separated as the dense phase. While μ-2 could be purified by this method alone, the μ-1 fraction always contained a significant amount of PNH_2-*b*-PC. Thus, the PSm block in μ-1 was hydrolyzed to yield a PGMA block. The resultant polymer μ-(PB)$(PGMA)_{200}$(PC) precipitated in nitromethane and was readily separated from PNH_2-*b*-PC, which dissolved in nitromethane.

The purified μ-2 and μ-(PB)$(PGMA_{200})$(PC) were analyzed by SEC and their traces are shown in Fig. 7. While the μ-2 peak showed some tailing on the low-molecular-weight side (suggesting the presence of unreacted precursors), a shoulder alluding to μ-(PB)$(PGMA_{200})(PC)_2$ was seen for the μ-(PB)$(PGMA_{200})$(PC) trace. Despite the impurities, the purified μ-2 and μ-(PB)$(PGMA_{200})$(PC) samples had low polydispersity indices of 1.04 and 1.08, respectively. Their PS-equivalent M_n were 59 and 95 kg/mol, respectively.

A ^{1}H NMR spectrum of μ-2 was recorded in $CDCl_3$ and is shown in Fig. 8. Our quantitative analysis yielded an integration ratio of 600/1268 between the $(k+l)$ peaks (phenyl ring protons of PC) and the $(c+h)$ peaks for PB and PSm. This ratio is consistent with the expected ratio of 600/1296 for μ-2. We did not obtain a ^{1}H NMR spectrum of μ-(PB)$(PGMA_{200})$(PC) because this polymer did not re-dissolve fully after it was fully dried, presumably due to the condensation of the PGMA chains.

4. Conclusions

Anionic polymerization was used to prepare two PB-*b*-P(HEMA-TMS)-*b*-PSm triblock copolymers. The selective removal of the TMS groups and the reaction of the resultant PHEMA blocks with succinic anhydride yielded PB-*b*-PCOOH-*b*-PSm, where the PCOOH block was only 5 units long. Anionic polymerization was also used to prepare P(HEMA-tBDMS)-*b*-P(HEMA-TMS). After the selective removal of the TMS groups to yield P(HEMA-tBDMS)-*b*-PHEMA, the sample was cinnamated to yield P(HEMA-tBDMS)-*b*-PC. Further derivatization eventually yielded PNH_2-*b*-PC, where the PNH_2 block was 5 units long.

Coupling PB-*b*-PCOOH-*b*-PSm and PNH_2-*b*-PC together using an association-and-reaction strategy yielded a functional miktoarm copolymer μ-(PB)(PSm)(PC). μ-(PB)(PSm)(PC) was produced in the highest yield and selectivity at a total polymer concentration of ~2.5 mg/mL in THF. We also discovered methods for the purification of the miktoarm copolymers of different compositions. These copolymers are likely to exhibit fascinating micellization behavior in selective solvents and the subsequent chemical processing of the resultant micelles should yield a fascinating array of novel functional nanostructures.

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Appendix A. Supplementary data

d*n*/d*c* results. De-convolution of the SEC peaks using the Peakfit program is provided. Additional discussion of factors affecting the μ-(PB)(PSm)(PC) formation is also provided. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.mtcomm.2014.09.001.

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