Polymer Bulletin 55, 225–233 (2005)
DOI 10.1007/s00289-005-0428-8

Polymer Bulletin

Synthesis of star-shaped PCL-*b*-PMMA/PSt from cyclotriphosphazene initiator by ring-opening polymerization and atom transfer radical polymerization

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Received: 23 April 2005 / Revised version: 21 June 2005 / Accepted: 21 July 2005

Summary

Star-shaped block copolymers PCL-*b*-PMMA and PCL-*b*-PSt were successfully synthesized by ring-opening polymerization (ROP) and atom transfer radical polymerization (ATRP) on the basis of hydroxyl-terminated cyclotriphosphazene. The star-shaped PCL was synthesized by bulk polymerization of ε-caprolactone with hydroxyl-terminated cyclotriphosphazene initiator. Star-shaped PCL was converted into a macroinitiator via esterification with 2-bromopropionyl bromide. Star-shaped block copolymers could be obtained by ATRP of methacrylate (MMA) and styrene (St). The molecular weight of these star-shaped block copolymers could be adjusted by the variation of monomer conversion.

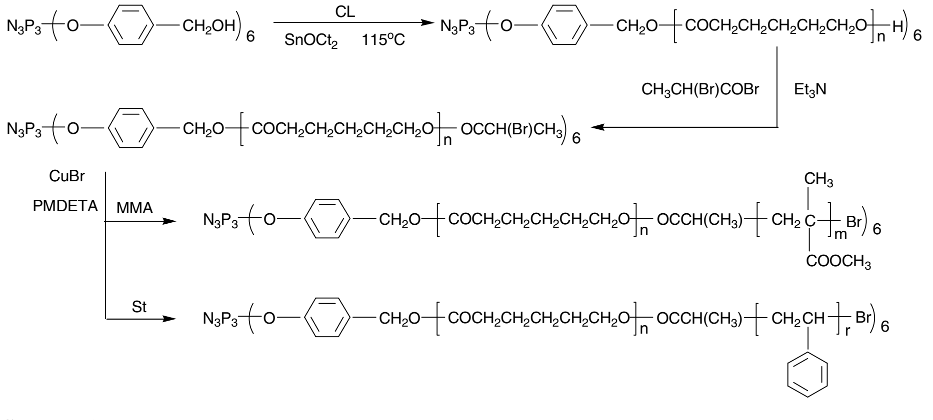
Introduction

Considerable attention has been attracted to star-shaped polymers due to their unique physicochemical properties [1-3]. In general, there are two different methods to synthesize star-shaped polymers: the arm-first strategy [4] and the core-first approach in which a multifunctional initiator is used to the polymerization of monomer to form star-shaped polymers [5-7]. Nowadays the latter has been widely utilized to synthesize well-defined star-shaped polymers with predetermined number of arms. The synthesis of star-shaped polymers from vinyl monomers using living radical polymerizations, especially atom transfer radical polymerization (ATRP), has been extensively studied [8-12]. More recently, the combination of various living polymerization techniques such as ATRP and ROP to synthesize novel star-shaped polymers and star-shaped block copolymers has attracted much interest since these combinatorial methods not only enrich the types of polymerizable monomers but also enable variable compositions, architectures, and properties into one polymeric structure [13-15].

Poly(ε-caprolactone) (PCL) and its copolymers possess excellent biocompatibility and permeability [16-18]. Therefore, they have potential application as biomaterials. However, it is necessary to modify its physical properties because it has suffered from the lack of controlled degradation based on its high crystallinity. Star-shaped and star-shaped block structures have been introduced to improve the physicochemical properties of PCL. Star-shaped PCLs were obtained by ROP of ε-caprolactone (CL) using a multifunctional initiator [19-21]. Qiu et al. reported the synthesis of star-shaped block copolymer PCL-*b*-DL-PLAGA50 with pentaerythritol or trimethylolpropane initiator [22].

Phopsphazenes possess special properties and play an important role in the chemistry of heteroatom compounds [23-25]. Among them, cyclotriphosphazenes exhibit useful thermal properties and excellent biocompatibility [26, 27]. Moreover, cyclotriphosphazenes could be used as multifunctional initiators [28]. Star-shaped polymers possessing unique structures and properties could be achieved with cyclotriphosphazene cores. Inoue et al. reported the synthesis of hexaarmed star poly(β-benzyl-L-aspartates) and poly(γ-benzyl-L-glutamate) initiated by hexakis(4-aminophenoxy)cyclotriphosphazene [29, 30].

In this paper, a star-shaped hydroxyl-terminated PCL was synthesized by ROP with hexakis[p-(hydroxymethyl)phenoxy]cyclotriphosphazene as initiator, and then star-shaped block copolymers PCL-*b*-PMMA and PCL-*b*-PSt were prepared via ATRP with star-shaped PCLBr as macroinitiator (scheme 1).



Scheme 1. Synthesis of star-shaped block copolymer.

Experimental

Materials

Hexakis[p-(hydroxymethyl)phenoxy]cyclotriphosphazene was prepared by the reaction of hexachlorocyclotriphosphazene with the sodium salt of 4-hydroxybenzaldehyde and subsequent reduction of aldehyde groups to alcohol groups by using sodium borohydride [31]. The melting point of the purified products was 217-218 °C. ε-Caprolactone (Aldrich, USA) was distilled from CaH_2 in vacuo under dry nitrogen. Stannous octoate ($SnOCt_2$) (Aldrich, USA) was distilled under reduced pressure before use. Methyacrylate (MMA), styrene (St), and pentamethyldiethylenetriamine (PMDETA) were stirred overnight over CaH_2 and distilled under reduced pressure prior to use. CuBr was purified by stirring in acetic acid and washing with ethanol and then dried in vacuo. Triethylamine and methylene chloride were dried over CaH_2 and distilled before use.

Instruments

${}^1H$ NMR spectra were obtained from a Varian Mercury Plus-400 NMR spectrometer (Varian, USA) with $CDCl_3$ as solvent. Chemical shifts were relative to tetramethylsilane at $\delta=0$ ppm for protons. Fourier transform infrared spectroscopic (FTIR) analyses were performed on a Paragon 1000 FT-IR spectrometer (Perkin Elmer, USA) with potassium bromide discs. The molecular weight and molecular weight distribution were measured on a Waters gel permeation chromatography equipped with three Waters Styragel columns (HR3+HR4+HR5) at 30 °C. Tetrahydrofuran (THF) was used as eluent and narrow-distributed polystyrene standards were used as calibrations.

Synthesis of star-shaped hydroxyl-terminated PCL [32]

ε-Caprolactone (8.071g, 56mmol), hexakis[p-(hydroxymethyl)phenoxy]cyclotriphosphazene (0.4077g, 0.4667mmol) and tannous octoate (22.7mg, 0.056mmol) were added into a dried glass tube. Then the tube was purged three times with dry nitrogen and sealed under vacuum. The bulk polymerization was carried out at 115 °C in an oil bath with stirring for 24 h. After reaction, the crude product was dissolved in chloroform, microfiltered through a 0.45-μm-pore membrane filter and then precipitated in hexane for three times. The purified polymer was dried in a vacuum until constant weight. $M_{n,NMR}$=14100, $M_{n,GPC}$=11000, M_w/M_n=1.083. IR (KBr): 3300-3600 ($\nu_{O\text{-}H}$), 2944 ($\nu_{C\text{-}H}$), 2864 ($\nu_{C\text{-}H}$), 1731 ($\nu_{C=O}$), 1462 ($\nu_{C\text{-}H}$), 1246 ($\nu_{C(=O)\text{-}O}$), 1173 ($\nu_{P=N}$), 1058 ($\nu_{C\text{-}O\text{-}C}$), 732 ($\nu_{P\text{-}N}$) cm^{-1}. ${}^1H$ NMR ($CDCl_3$,δ): 7.15 (d, C_6H_4), 6.88 (d, C_6H_4), 5.04 (s, CH_2O), 4.04 (m, CH_2O in PCL), 3.63 (t, terminal CH_2O in PCL), 2.30 (m, $COCH_2$ in PCL), 1.63 (m, CH_2 in PCL), 1.39 (m, CH_2 in PCL).

Synthesis of star-shaped PCLBr macroinitiator

The star-shaped PCL sample was converted into ATRP initiator via esterification with 2-bromopropionyl bromide. Star-shaped PCL (6.62g, 0.46mmol) was dissolved in dry methylene chloride (80mL) under stirring. To this solution was added triethylamine (0.62mL, 4.43mmol) under dry nitrogen at room temperature. The mixture was stirred and cooled to 0 °C, and then 2-bromopropionyl bromide (0.956g, 4.43mmol) in methylene chloride (20mL) was added dropwise to the mixture within 40 min. The reaction mixture was stirred for 30 h at room temperature before it was washed with solution of $NaHCO_3$ and deionized water, and then the combined organic layer was dried overnight with $MgSO_4$. After evaporation of solvent, the resulting product was purified by precipitating from methanol. $M_{n,NMR}$=14900, $M_{n,GPC}$=11700, M_w/M_n=1.083. IR (KBr): 2946 ($\nu_{C\text{-}H}$), 2863 ($\nu_{C\text{-}H}$), 1730 ($\nu_{C=O}$), 1468 ($\nu_{C\text{-}H}$), 1245 ($\nu_{C(=O)\text{-}O}$), 1172 ($\nu_{P=N}$), 1059 ($\nu_{C\text{-}O\text{-}C}$), 732 ($\nu_{P\text{-}N}$) cm^{-1}. ${}^1H$ NMR ($CDCl_3$,δ): 7.15 (d, C_6H_4), 6.88 (d, C_6H_4), 5.03 (s, CH_2O), 4.34 (q, CHBr), 4.14 (t, terminal CH_2O in PCL), 4.04 (m, CH_2O in PCL), 2.31 (m, $COCH_2$ in PCL), 1.68 (d, CH_3Br), 1.64 (m, CH_2 in PCL), 1.38 (m, CH_2 in PCL).

Synthesis of star-shaped block copolymer

Star-shaped PCLBr was used as macroinitiator to prepare star-shaped block copolymers PCL-*b*-PMMA and PCL-*b*-PSt via ATRP in solution. CuBr and PMDETA were used as catalytic system. A dry Schlenk flask with magnetic stirrer was charged with CuBr (91.8mg, 0.64mmol), star-shaped PCLBr macroinitiator (1.588g, 0.1066mmol, $M_{n,NMR}$=14900, Mw/Mn=1.083, containing 0.6365mmol of C-Br group), MMA (6.402g, 63.95mmol), and anisole (16mL). The flask was degassed with three freeze-evacuate-thaw cycles. PMDETA (134μL, 0.64mmol) was deoxygenated by bubbling dry nitrogen for 0.5 h before injection into the reaction system by syringe. Then the flask was immersed into an oil bath thermostated at 80 °C. At time intervals (1, 2, 4 and 6 h), about 2.0 mL of solution was withdrawn from the flask. The crude product was dissolved in chloroform, passed through a column of basic alumina, and precipitated from methanol. The synthesis of star-shaped PCL-*b*-PSt was similar to that of star-shaped PCL-*b*-PMMA. Star-shaped PCL-*b*-PMMA: IR (KBr): 2951 ($\nu_{C\text{-}H}$), 2864 ($\nu_{C\text{-}H}$), 1731 ($\nu_{C=O}$), 1454 ($\nu_{C\text{-}H}$), 1246 ($\nu_{C\ (=O)\text{-}O}$), 1172 ($\nu_{P=N}$), 1057 ($\nu_{C\text{-}O\text{-}C}$), 740 ($\nu_{P\text{-}N}$) cm^{-1}. ^1H NMR ($CDCl_3$,δ): 7.16 (d, C_6H_4), 6.93 (d, C_6H_4), 5.04 (s, CH_2O), 4.04 (m, CH_2O in PCL), 3.59 (s, $COOCH_3$ in PMMA), 2.32 (m, $COCH_2$ in PCL), 1.85-2.25 (m, CH_2 in PMMA), 1.62 (m, CH_2 in PCL), 1.38 (m, CH_2 in PCL), 0.82-1.28 (m, CH_3 in PMMA). Star-shaped PCL-*b*-PSt: IR (KBr): 2945 ($\nu_{C\text{-}H}$), 2858 ($\nu_{C\text{-}H}$), 1730 ($\nu_{C=O}$), 1455 ($\nu_{C\text{-}H}$), 1246 ($\nu_{C\ (=O)\text{-}O}$), 1170 ($\nu_{P=N}$), 1057 ($\nu_{C\text{-}O\text{-}C}$), 742 ($\nu_{P\text{-}N}$) cm^{-1}. ^1H NMR ($CDCl_3$,δ): 6.63-7.40 (m, PhH in PSt and ArH in phosphazene core), 5.05 (s, CH_2O), 4.05 (m, CH_2O in PCL), 2.33 (m, $COCH_2$ in PCL), 0.90-2.18 (m, CH and CH_2 in PSt), 1.63 (m, CH_2 in PCL), 1.37 (m, CH_2 in PCL).

Results and discussion

The copolymerization of CL was carried out with hydroxyl-terminated cyclotriphosphzaene and $SnOCt_2$ catalyst by ROP in bulk at 115 °C. The resulting polymer was characterized by IR spectroscopy, ^1H NMR spectroscopy (Figure 1 a), and GPC analysis. Especially, the methylene proton (δ=3.64ppm, h in Figure 1 a) signal in the spectrum of the obtained PCL showed that PCL was terminated by hydroxy end groups. All these could demonstrate that the pure star-shaped PCL was synthesized successfully. The number-average molecular weight of star-shaped PCL determined by ^1H NMR spectroscopy could be calculated from the integration ratio between the methylene protons in the repeat units (4.04ppm, g) and the methylene protons in the terminal unit (3.63ppm, h). According to our previous work, the hydroxyl-terminated cyclotriphosphzaene could be used as effective propagation centers [32].

When star-shaped hydroxyl-terminated PCL reacted with 2-bromopropionyl bromide, star-shaped PCLBr with slightly increased molecular weight and similar molecular weight distribution could be obtained. In FTIR spectra, the absorption peak at 3300-3600 cm^{-1} corresponding to hydroxyl groups was absent. According to ^1H NMR spectra (Figure 1 b), the signal at 3.64ppm disappeared (the signal of methylene protons was appeared at 4.14ppm, h), while novel signals corresponding to methyl protons (j) and methine proton (i) of 2-bromopropionrates appeared at 1.80ppm and 4.34ppm, indicating that all the terminal hydroxyl groups have been quantitatively functionalized.

Star-shaped block copolymers PCL-*b*-PMMA and PCL-*b*-PSt were synthesized from macroinitiator star-shaped PCLBr and MMA and St via ATRP at 80 °C and 100 °C respectively. These block copolymers were characterized by FTIR spectra, ^1H NMR spectra (Figure 2), and GPC analysis. ^1H NMR spectrum (Figure 2 c) showed peaks at

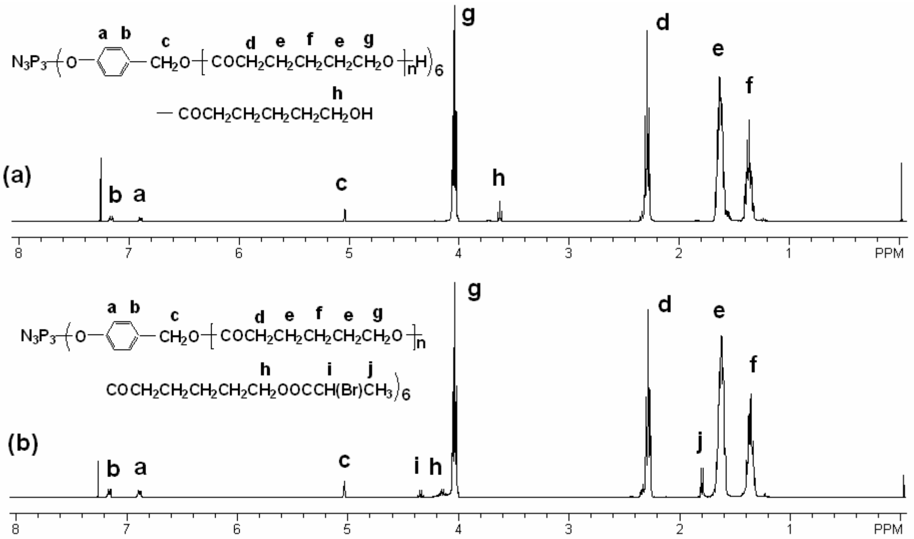


Figure 1. ^{1}H NMR spectra of star-shaped PCL (a) and star-shaped PCLBr (b).

3.59ppm ($COOCH_3$ in PMMA), 1.85-2.25ppm (CH_2 in PMMA), and 0.82-1.28ppm (CH_3 in PMMA). The average chain length of PMMA was estimated by comparison of signal intensity ratios of methylene protons of PCL (4.04ppm) to methyl protons of PMMA (3.59ppm). The peaks (Figure 2 d) at 6.63-7.40ppm were attributed to the protons of the benzyl group (PhH in PSt and ArH in phosphazene core). The average chain length of PSt was estimated by comparison of signal intensity ratios of methylene protons of PCL (4.04ppm) to phH protons of PSt (6.63-7.40ppm).

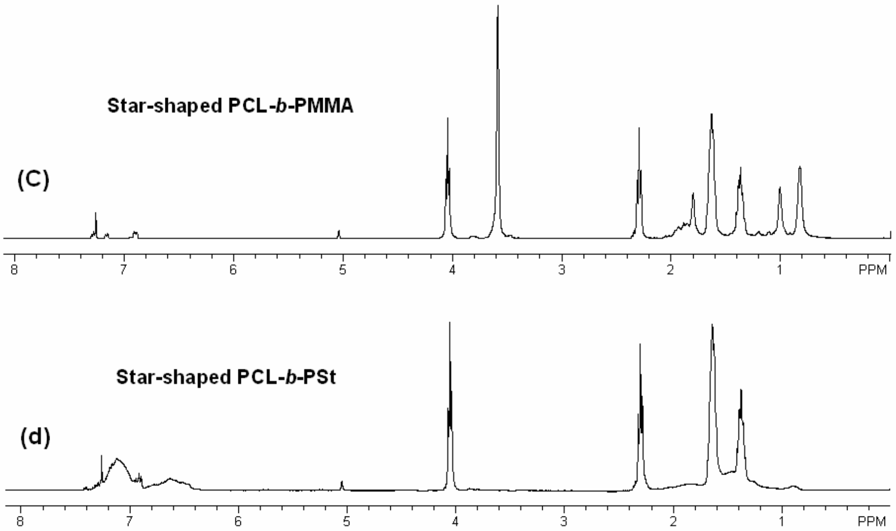


Figure 2. ^{1}H NMR spectra of star-shaped PCL-*b*-PMMA (c) and star-shaped PCL-*b*-PSt (d).

The GPC traces were shown in Figure 3. It could be seen that these traces were symmetrical and monomodal, suggesting that pure star-shaped copolymers were obtained successfully. For star-shaped polymer, the GPC analysis underestimates the molecular weight because it has smaller hydrodynamic volume than that of linear polystyrene having the same molecular weight [33]. However, the GPC analysis could monitor the purity of polymers and polydispersion of molecular weight. Table 1 presents the molecular weights and molecular weight distributions of star-shaped PCL-*b*-PMMAs or PCL-*b*-PSts synthesized by ATRP initiated with star-shaped PCLBr. These copolymers showed relatively narrow molecular weight distributions. Moreover, conversions of MMA or St were also listed in Table 1.

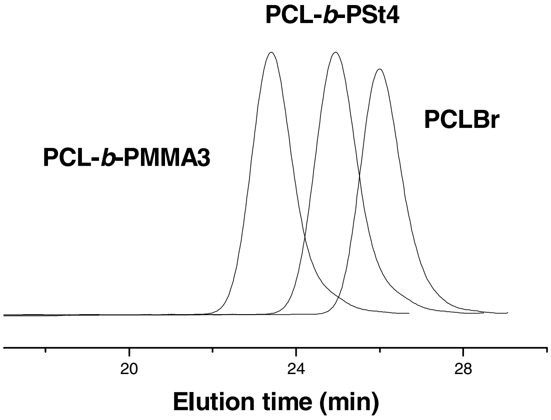


Figure 3. GPC traces of star-shaped PCLBr initiator, star-shaped PCL-*b*-PMMA3, and PCL-*b*-PSt4.

Table 1. Results for ATRP of MMA and St with star-shaped PCLBr initiator.

Sample	Time (h)	$M_{n,th}$ [a]	$M_{n,NMR}$ [b]	$M_{n,GPC}$ [c]	M_w/M_n [c]	Conversion [d] (%)
PCL-*b*-PMMA1	1	20800	19500	16400	1.116	9.4
PCL-*b*-PMMA2	2	27800	25500	22300	1.112	21.1
PCL-*b*-PMMA3	4	37600	35000	29900	1.146	37.4
PCL-*b*-PMMA4	6	45100	41900	35900	1.221	49.9
PCL-*b*-PSt1	1	16800	16200	13400	1.105	2.7
PCL-*b*-PSt2	2	18600	17800	14800	1.123	5.5
PCL-*b*-PSt3	4	21900	20400	17100	1.117	10.8
PCL-*b*-PSt4	6	24600	22600	19500	1.128	15.1

[a] $M_{n,th}=M_{monomer}\times([monomer]/[C\text{-}Br])\times 6\times conversion\ \%+M_{initiator}$, $[monomer]/[C\text{-}Br]=100$.

[b] $M_{n,NMR}$ was determined by ^1H NMR spectroscopy of star-shaped block copolymer.

[c] $M_{n,GPC}$ and Mw/Mn were determined by GPC analysis with polystyrene standards. THF was used as eluent.

[d] Calculated from: $[W_p/(W_i+W_m)]\times 100\%$, where W_p, W_i, and W_m were the weight of the block copolymer produced, and the initial weights of the related macroinitiator and monomer, respectively.

The kinetic plot of star-shaped PCL-*b*-PMMA copolymer formation was shown in Figure 4. The plot of ln([M$_0$]/[M]) against polymerization time seemed linear, and it crossed the zero point. This result could demonstrate that the first-order kinetics could be maintained until high conversion, which suggested that the concentration of active species remained constant throughout the course of polymerization for MMA. As shown in Figure 5, $M_{n,NMR}$ values were close to $M_{n,th}$, increased linearly with conversion, indicating the molecular weight of the resulting copolymer could be manipulated by the control of monomer conversion. Moreover, the molecular weight distribution was narrow and the GPC trace was monomodal and symmetric, suggesting the high initiation efficiency and negligible radical-radical coupling in polymerization. It was obvious that star-shaped PCLBr could be used as an efficient initiator for living polymerization of MMA.

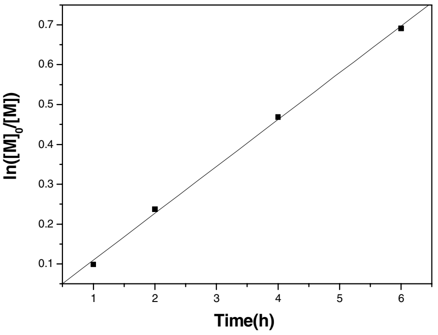


Figure 4. Semilogarithmic kinetic plot for ATRP of MMA with star-shaped PCLBr initiator. [MMA]: [C-Br]: [CuBr]: [PMDETA] =100:1:1:1, reaction temperature: 80 °C.

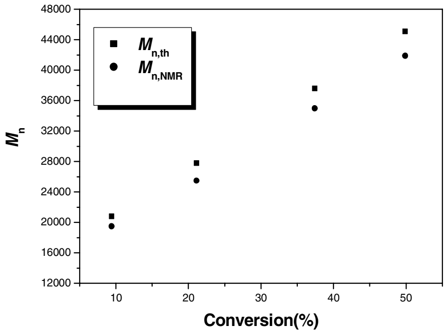


Figure 5. Evolution of M_n of star-shaped PCL-*b*-PMMA with conversion for ATRP of MMA.

In general, well-defined multiarmed star-shaped PSt with core-first approach via controlled radical polymerization could be achieved at low conversion. The polymerization process would be uncontrolled at high conversion due to the existence of coupling reaction. For instance, Angot et al. reported that ATRP of St using an octafunctional initiator and found that the controlled polymerization could be maintained at low conversion, typically below 15-20% [34, 35]. In this study, the ATRP of St using star-shaped PCLBr macroinitiator was conducted at 100 °C in anisole. From Table 1, it was found that the living polymerization of St could be performed under low conversion, which was consistent with the results reported by Angot et al. [34, 35]. The semilogarithmic kinetic plot was shown in Figure 6. The kinetic study demonstrated that the semilogarithmic plot of St conversion vs time seemed to display first-order kinetics with respect to St at low conversion. From Figure 7, $M_{n,NMR}$ could increase linearly with conversion when the conversion was low. As the conversion was less than certain value, the polymerization took place smoothly, and the first-order polymerization kinetics was maintained. Beyond certain conversion, the molecular weight control was lost owing to the irreversible star-star coupling and intrastar termination [34, 35]. In this study, when hexa-armed star-shaped PCLBr was used as macroinitiator for ATRP of styrene ([monomer]:[C-Br]:[CuBr]:[PMDETA]=100:1:1:1), the first-order polymerization kinetic could be maintained as the conversion was less than 19%. In this process, the polymerization was of living nature, and the GPC trace was symmetrical and unimodal. Moreover, the plots of $M_{n,NMR}$ to monomer conversion keep a good linear relationship. When the conversion was more than 19% (not shown in Figure 6 and Figure 7), the plots of $M_{n,NMR}$ to monomer conversion departed from the original linear relationship, which indicated that the synthesis process was out of control in this period. These results indicated that well-defined star-shaped PCL-*b*-PSt could be achieved via ATRP by stopping the polymerization at a low conversion.

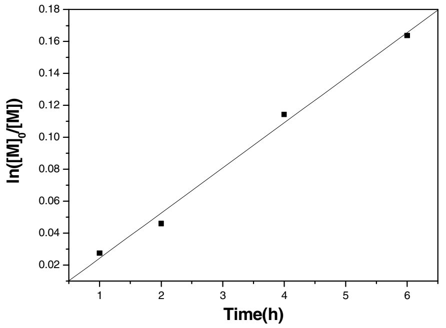


Figure 6. Semilogarithmic kinetic plot for ATRP of St with star-shaped PCLBr initiator. [St] :[C-Br]: [CuBr] :[PMDETA]=100:1:1:1, reaction temperature: 100 °C.

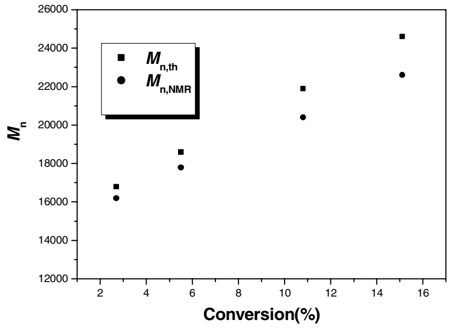


Figure 7. Evolution of Mn of star-shaped PCL-*b*-PSt with conversion for ATRP of St.

Conclusions

The star-shaped PCL was synthesized by living ROP of ε-caprolactone in the presence of cyclotriphosphazene initiator and stannous octoate catalyst in bulk at 115 °C. Then, well-defined star-shaped block copolymers PCL-*b*-PMMA and PCL-*b*-PSt were synthesized by ATRP of MMA, St and star-shaped PCLBr as macroinitiator under suitable conditions. The star-shaped PCLBr could be used as an efficient initiator for ATRP of MMA. But the well-defined star-shaped PCL-*b*-PSt could be obtained only at low conversion. The thermal properties, hydrolysis stability, and physical properties of these copolymers are currently in progress.

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