Available online at www.sciencedirect.com
ScienceDirect
Polymer 49 (2008) 1777–1782
polymer
www.elsevier.com/locate/polymer

Precise preparation of four-arm-poly(ethylene glycol)-*block*-poly(trimethylene carbonate) star block copolymers via activated monomer mechanism and examination of their solution properties

Jae Song Cho [a,b,1], Byung Soo Kim [a,1], Hoon Hyun [a], Ju Yong Youn [a,b], Moon Suk Kim [a,*], Jae Hoon Ko [c], Young Hwan Park [c], Gilson Khang [b], Hai Bang Lee [a]

[a] *Fusion Biotechnology Research Center, Korea Research Institute of Chemical Technology, P.O. Box 107, Yuseong, Daejeon 305-600, South Korea*
[b] *BK-21 Polymer BIN Fusion Research Team, Chonbuk National University, 664-14, Duckjin, Jeonju 561-756, South Korea*
[c] *Digital Dyeing & Finishing Technology Team, Korea Institute of Industrial Technology, KITECH B-#110, 1271-18, Sa-1 dong, Sangrok-gu, Ansan-si, Kyeonggi-do 426-791, South Korea*

Received 18 November 2007; received in revised form 17 January 2008; accepted 19 February 2008
Available online 21 February 2008

Abstract

The polymerization of trimethylene carbonate (TMC) in the presence of $HCl \cdot Et_2O$ via activated monomer mechanism was performed to synthesize 4a-PEG-*b*-PTMC star block copolymers composed of poly(ethylene glycol) (PEG) and poly(trimethylene carbonate) (PTMC) using four-arm (4a) PEG as an initiator. The TMC conversion and molecular weight of PTMC increased linearly with the polymerization time or the feed ratios of the TMC to 4a-PEG in the presence of $HCl \cdot Et_2O$ in CH_2Cl_2 at 25 °C. The obtained PTMC had molecular weights close to the theoretical value calculated from TMC to PEG molar ratio and exhibited monomodal GPC curve. We prepared successfully 4a-PEG-*b*-PTMC star block copolymers without metal catalyst at room temperature via living ring-opening polymerization (ROP) of TMC from 4a-PEG as an initiator in the presence of $HCl \cdot Et_2O$ as a monomer activator. The CMCs of the 4a-PEG-*b*-PTMC star block copolymers determined from fluorescence measurements. The CMCs of the 4a-PEG-*b*-PTMC star block copolymers decreased in the order of the increase in the PTMC segment. The partition equilibrium constant, K_v, which is an indicator of the hydrophobicity of the micelles of the 4a-PEG-*b*-PTMC star block copolymers in aqueous media, increased with the increase in the PTMC segment. In conclusion, we confirmed that the 4a-PEG-*b*-PTMC star block copolymers form micelles and hence may be potential hydrophobic-drug delivery vehicles.

Keywords: Poly(ethylene glycol); Poly(trimethylene carbonate); Star block copolymer

1. Introduction

Amphiphilic block copolymers are of particular interest because their microstructure can be modified to possess both hydrophobic and hydrophilic properties and can form a micellar structure in selective solvents, which are thermodynamically favorable for one block but unfavorable for the other [1,2]. Polymeric micelles as colloidal drug carriers are being widely investigated due to their potential [3]. To this goal, different types of drug carriers have been designed. Recently, effort is given on the synthesis of more complex macromolecular architectures in order to prepare specific drug carriers. Thus, star amphiphilic block copolymers with hydrophilic and hydrophobic segments have attracted much interest because of their microdomain separation feature, and are expected to display diverse morphologies in comparison with linear amphiphilic block copolymers [4,5].

Polyethylene glycol (PEG) is a nontoxic and has been found to possess biocompatibility demanded when introducing

* Corresponding author. Tel.: +82 42 860 7095; fax: +82 42 860 7228.
E-mail address: mskim@krict.re.kr (M.S. Kim).
[1] Both authors contributed equally.

0032-3861/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2008.02.030

synthetic materials into biological systems [6]. Aliphatic polycarbonate with carbonate group in the backbone, such as poly(trimethylene carbonate) (PTMC), have attracted much research interest due to their biodegradability, and biocompatibility [7,8]. These unique properties render PTMC homo- and copolymers potential candidates for biomedical application such as drug delivery, tissue engineering, surgical sutures, etc. [9].

During the last decade, a significant effort in polymer synthesis has been devoted to the synthesis of PEG–PTMC block copolymers using a variety of catalyst systems. PTMC can be synthesized by ring-opening polymerization (ROP) techniques by the hydroxyl end group of PEG using various metal catalyst systems, based mainly on metal alkoxides of lithium, stannous, potassium, etc. [10–14]. Among them, stannous octanoate $Sn(Oct)_2$ was one of the most successful catalyst system to prepare PEG–PTMC block copolymers. However, its cytotoxicity has recently caused deep concern about biosafety of the materials synthesized using it particularly when the materials are used for biomedical applications [15].

Recently Endo and our groups have investigated the ROP of ester or carbonate cyclic monomer with $HCl \cdot Et_2O$ to replace the tin catalyst and suggested it as one of the most powerful methods to control ROP via an activated monomer mechanism [16–19].

In our previous study, we have reported the synthesis of PEG–PTMC block copolymers using $HCl \cdot Et_2O$. As a continuation of these studies the effectiveness of this $HCl \cdot Et_2O$ system toward star amphiphilic block copolymers has been undertaken. In the present work, we examine the preparation of 4a-PEG-*b*-PTMC star block copolymers using four-arm-PEG as initiator and $HCl \cdot Et_2O$ as monomer activator. The effects of trimethylene carbonate (TMC) to PEG and HCl molar ratio on the polymerization are discussed. In addition, we examine the micelle formation behavior of the 4a-PEG-*b*-PTMC star block copolymers in order to understand how the changes in the PTMC segment of four-arm-PEG-*b*-PTMC star block copolymers influence the critical micelle concentration (CMC) and partitioning of the hydrophobic molecule pyrene.

2. Experimental

2.1. Materials

Four-arm-PEG (4a-PEG, M_n 2000 g/mol, NOF, Japan) and HCl (Aldrich; 1.0 M solution in diethyl ether, Aldrich, USA) were used as received. Pure-grade TMC was obtained from Boehringer Ingelheim and used without further purification. CH_2Cl_2 was distilled sequentially from $CaCl_2$ and CaH_2 under nitrogen before use.

2.2. Measurements

^1H NMR spectra were measured using Bruker 500 MHz instrument with $CDCl_3$ in the presence of tetramethylsilane (TMS) as an internal standard or with D_2O. Molecular weights and polydispersity index (PDI) of 4a-PEG and 4a-PEG-*b*-PTMC were measured by Futecs At-3000 GPC system (Shodex RI-71 detector) using two columns (Shodex K-802 polystyrene gel column and Shodex Asahipak GF-510 HQ polyvinyl alcohol gel column) at 45 °C. $CHCl_3$ was used as the eluent at a flow rate of 0.8 mL/min.

2.3. Synthesis of four-arm-PEG-b-PTMC star block copolymers (4a-PEG-b-PTMC)

All glasses were dried by heating in vacuum and handled under a dry nitrogen stream. The typical process for the polymerization to give 4a-PEG-*b*-PTMC with PTMC molecular weight (4000 g/mol) is as follows. 4a-PEG (1 g, 0.5 mmol) and toluene (60 mL) were introduced into a flask. The toluene was distillated by azeotropic distillation to remove water in 4a-PEG. Toluene was then distilled off completely. The CH_2Cl_2 (8 mL) was added to 4a-PEG, followed by the addition of TMC (2 g, 19.6 mmol). The polymerization was initiated by the addition of 1.0 M solution of HCl in diethyl ether (1 mL, 1 mmol) at 25 °C. After 24 h, the reaction mixture was poured into methanol to precipitate a polymer, which was separated from the supernatant by decantation. The obtained polymer was redissolved in CH_2Cl_2 and then filtered. The polymer solution was concentrated by a rotary evaporator and dried *in vacuo* to give a colorless polymer of a quantitative yield. The TMC monomer conversion was determined by ^1H NMR spectroscopy before precipitation with methanol. The molecular weight of PTMC segment in the star block copolymers was determined by the intensity of methylene proton signal of 4a-PEG at $\delta = 3.64$ ppm and methylene proton signal of PTMC at $\delta = 4.24$ ppm in ^1H NMR spectroscopy.

2.4. Determination of critical micelle concentration

The CMC was determined using pyrene as a fluorescence probe. One milliliter of pyrene solution in THF (1.2 mM) was added to 1000 mL of distilled water. THF was removed by a rotary evaporator at 30 °C for 2 h to give pyrene solution in water (1.2×10^{-6} M). Stock solutions of 4a-PEG-*b*-PTMC star block copolymers were prepared by dissolving the star block copolymer samples in distilled water under stirring. From the stock solution a series of concentration was prepared by dilution. The pyrene solution added to the star block copolymer solution. The solutions after filtration using 0.45 μm membrane filter were allowed to stand overnight at room temperature to equilibrate. The micelle concentration in these experiments varied from 0.5×10^{-7} to 1.0 mg/mL. The pyrene concentration in star block copolymer solution was 6×10^{-7} M. For the measurements of pyrene excitation spectra scan speed was set at 240 nm/min and, emission and excitation slit widths were set at 2.5 nm. For the excitation spectra, the emission wavelength was 373 nm. Fluorescence intensities of the pyrene entrapped in the micelle core were determined by an F-4500 fluorescence spectrophotometer (Hitachi Co. LTD, Japan) at room temperature.

3. Results and discussion

3.1. Preparation of 4a-PEG-b-PTMC star block copolymers

Four-arm-PEG-*b*-PTMC star block copolymers were synthesized via the ROP of TMC as the monomer using the four hydroxyl end group of four-arm-PEG (M_n, 2000 g/mol) as an initiator in the presence of $HCl \cdot Et_2O$ at room temperature.

First, to examine the time dependence for TMC conversion and molecular weight of PTMC, the polymerization of TMC (39.2 equiv) was carried out with 4a-PEG in the presence of $HCl \cdot Et_2O$ in CH_2Cl_2 at 25 °C for 0–24 h (Table 1). It was found that both the TMC conversion and molecular weight of PTMC increased linearly with the polymerization time. At 24 h, TMC reached at almost quantitative conversion. This polymerization gave colorless 4a-PEG-*b*-PTMC star block copolymers with almost quantitative yield after isolation by precipitation in methanol. The molecular weights (M_ns) determined by NMR were close to theoretical values calculated from conversion of TMC. Polydispersity indexes (PDI) of 4a-PEG-*b*-PTMC star block copolymer increased slightly with polymerization time and the PDI at complete monomer conversion reached about 1.14, but have maintained still narrow PDI compared to 4a-PEG (1.09) as an initiator. This result implies that the ROP in this system is based on the equal attack of the hydroxyl end group to the TMC monomer activated by $HCl \cdot Et_2O$.

Fig. 1a shows the ^{1}H NMR spectrum of 4a-PEG-*b*-PTMC star block copolymer obtained by the polymerization. The star block copolymer exhibited characteristic peaks of PTMC and 4a-PEG. The peaks at 3.64 and 2.04 ppm are due to the methylene protons of homosequences of PEG oxyethylene units and methylene protons of the PTMC main chain, respectively. The signals assignable to terminal ω-methylene protons of PTMC were observed around 1.92–3.74 ppm. The molecular weight can be calculated by integration of the ^{1}H NMR spectrum that is by calculating the ratio of the ethylene oxide protons of the PEG main chain to the characteristic methylene protons of the PTMC main chain (ethylene oxide units/PTMC units).

The variation in molecular weight upon changing the feed ratio of TMC to 4a-PEG as an initiator was examined. The molecular weight of PTMC was calculated by ^{1}H NMR and

Table 1
Dependence of ROP of TMC on time

Time (h)	Conversion (%)[a]	$M_{n,\ calcd}$	$M_{n,\ NMR}$[a]	M_w/M_n[b]
0	–	–	2000 (4a-PEG)	1.090
1	11.5	2460	2450	1.094
2	18.3	2730	2710	1.119
3	25.2	3010	2950	1.122
4	33.4	3330	3300	1.135
8	61	4440	4400	1.139
12	72.4	4900	4800	1.143
24	99.9	6000	5990	1.143

Condition: [HCl]/[Initiator] = 2 and [TMC]/[CH_2Cl_2] = 0.5 M.
[a] Determined by ^{1}H NMR.
[b] Measured by gel permeation chromatography (based on standard polystyrene).

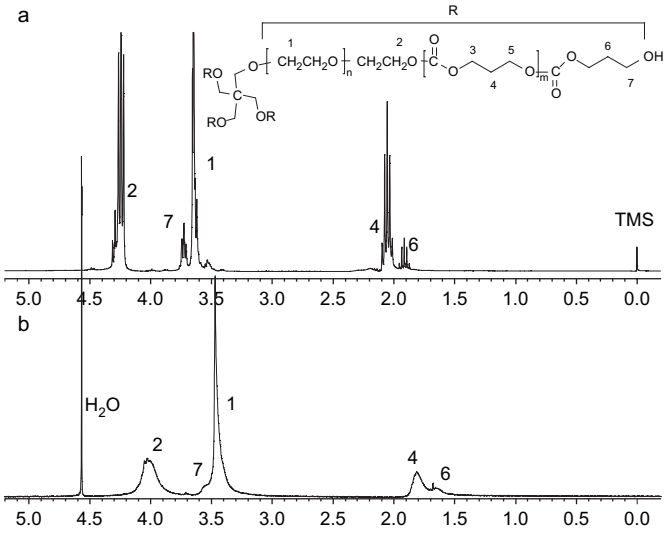

Fig. 1. ^{1}H NMR spectra of 4a-PEG-*b*-PTMC star block copolymer ($E_{45}T_{20}$) in (a) $CDCl_3$ and (b) D_2O.

measured by GPC. Fig. 2 illustrates the relationships between [TMC]/[4a-PEG], M_n of PTMC, and M_w/M_n of 4a-PEG-*b*-PTMC obtained in the polymerization at 25 °C in CH_2Cl_2. M_n of PTMC increased almost linearly with an increasing feed ratio of TMC to 4a-PEG, and the obtained PTMC showed good agreement with the theoretical value in every case. Increasing the feed ratios of TMC to 4a-PEG led to PDI decreasing, probably because the apparent PDI of 4a-PEG-*b*-PTMC star block copolymer can remain relatively low. The GPC peaks of the 4a-PEG-*b*-PTMC star block copolymers shifted to the higher M_n region with narrow PDI (1.21–1.10) in comparison with 4a-PEG [20]. Table 2 summarizes the polymerization results obtained by changing the feed ratios of TMC to 4a-PEG. The yields of 4a-PEG-*b*-PTMC star block copolymers were almost quantitative. These findings indicate that in the polymerization using $HCl \cdot Et_2O$ as

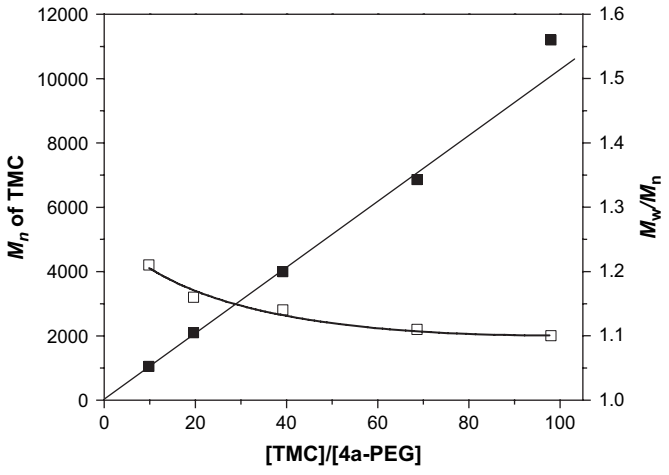

Fig. 2. Relationships between [TMC]/[4a-PEG] and $M_{n,\ NMR}$ (determined by ^{1}H NMR; ■) and $M_{n,\ theor}$ (theoretical value calculated from the feed ratio of the monomer and initiator; a straight line) of PTMC obtained by the polymerization of TMC, and M_w/M_n of 4a-PEG-*b*-PTMC measured by GPC (□).

Table 2
Synthesis of 4a-PEG-*b*-PTMC star block copolymers

Initiator (I)[a]	No.[b]	[TMC]/[I]	Yield[c] (%)	$M_{n,\ calcd}$	$M_{n,\ NMR}$[d]	M_w/M_n[e]
4a-PEG-OH ($M_w = 2000$)	$E_{45}T_{10}$	9.8	96	2000–1000	2000–1050	1.21
	$E_{45}T_{20}$	19.6	98	2000–2000	2000–2100	1.16
	$E_{45}T_{40}$	39.2	98	2000–4000	2000–3990	1.14
	$E_{45}T_{70}$	68.6	99	2000–7000	2000–6860	1.11
	$E_{45}T_{100}$	98	99	2000–10,000	2000–11,200	1.10

Condition: [HCl]/[Initiator] = 2; [TMC]/[CH_2Cl_2] = 0.5 M; room temperature; and 24 h.
[a] 4a-PEG molecular weight = 2000 ($M_w/M_n = 1.09$).
[b] Subscript numbers represent the unit of each segment, and E and T represent 4a-PEG and PTMC, respectively.
[c] Methanol insoluble part.
[d] Determined by ^{1}H NMR.
[e] Measured by gel permeation chromatography (based on standard polystyrene).

a monomer activator, the molecular weight of the PTMC segment can be controlled well by varying the [PEG core]/[ester monomer] ratio.

A second-feed experiment was examined to confirm the living nature of the polymerization. When the 4a-PEG-*b*-PTMC star block copolymer was kept under the polymerization system for an additional 24 h polymerization after complete monomer conversion, the GPC profile of the polymer showed the same M_n and PDI, indicating that there was no side reaction in the presence of HCl·Et_2O and in the absence of TMC. After confirming the quantitative monomer conversion at 24 h, a similar amount of monomer (30 equiv) was added into the reaction mixture to restart the polymerization. The GPC curve completely shifted to a higher M_n field and exhibited a monomodal without any trace of dead polymer (Fig. 3). The M_n of the final polymer was 8800 g/mol, close to theoretical $M_{n,\ total}$, and kept a narrow PDI (1.11). This result clearly showed that this system was still living even after the monomer was entirely converted into the polymer, indicating no termination. In addition, this indicated that the four hydroxyl end group of 4a-PEG equally served as an initiator in this polymerization system.

To investigate the effect of HCl·Et_2O as monomer activator, the kinetics of TMC polymerization by 4a-PEG as an initiator were studied with different concentrations of HCl·Et_2O (12, 8, 4, 2, and 1 equiv to initiator) in CH_2Cl_2 at 25 °C. The $\ln[M]/[M]_o$ versus reaction time plots exhibited linear variations (Fig. 4). The linear relationship suggests that the polymerization is first order for monomer concentration. From the slopes of the plots, the values of the apparent rate constant (k_{app}) for the polymerization of TMC activated by HCl·Et_2O were estimated as follows; $k_{app} = 23.2 \times 10^{-5}\ s^{-1}$, $8.98 \times 10^{-5}\ s^{-1}$, $3.68 \times 10^{-5}\ s^{-1}$, $2.73 \times 10^{-5}\ s^{-1}$, and $1.75 \times 10^{-5}\ s^{-1}$ for HCl·Et_2O 12, 8, 4, 2, and 1 equiv to initiator, respectively. The k_{app} increased as the ratio of $[H^+]_o/[I]_o$ increased, indicating that k_{app} was greatly affected by the ratio of $[H^+]_o/[I]_o$. This strongly indicated that HCl served as an activator in the ROP of TMC.

Since we prepared successfully amphiphilic star block copolymers without metal catalyst, we, next, examined their micelle formation behavior. In general, when amphiphilic star block copolymers add to an aqueous phase, they may form micelles with a core–shell structure.

Fig. 1b shows the ^{1}H NMR spectra for 4a-PEG-*b*-PTMC star block copolymer at 1 wt% concentration in D_2O at

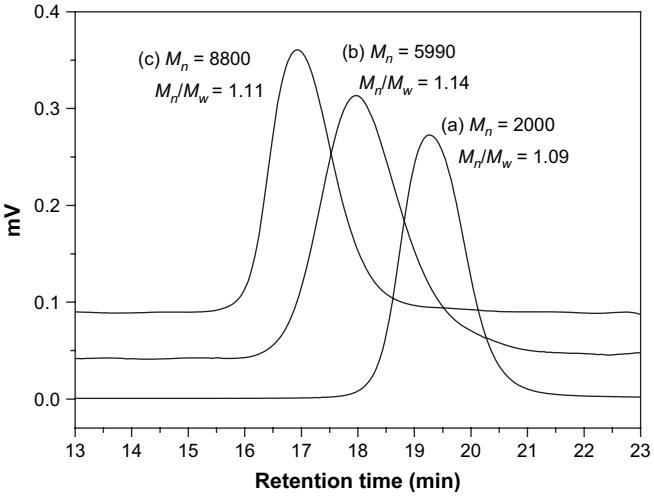

Fig. 3. GPC traces of polymer obtained by the polymerization in the presence of HCl·Et_2O in CH_2Cl_2 at 25 °C: (a) 4a-PEG; (b) 4a-PEG-*b*-PTMC star block copolymer obtained using 39.2 equiv of TMC for 24 h; and (c) 4a-PEG-*b*-PTMC star block copolymer obtained after an additional 24 h polymerization after the further addition of 30 equiv of TMC.

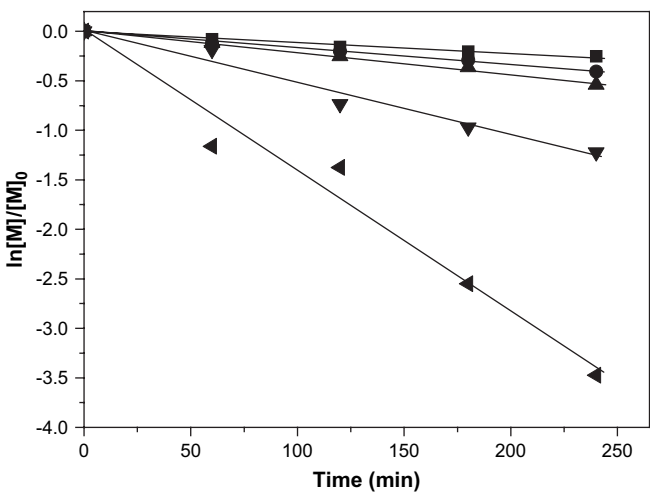

Fig. 4. Kinetics for the ROP of TMC initiated by 4a-PEG ($M_n = 2000$ g/mol) in CH_2Cl_2 at 25 °C, [TMC]/[CH_2Cl_2] = 0.5 M: (■) $[H^+]_o/[I]_o = 1$ and $k_{app} = 1.75 \times 10^{-5}\ s^{-1}$; (●) $[H^+]_o/[I]_o = 2$ and $k_{app} = 2.73 \times 10^{-5}\ s^{-1}$; (▲) $[H^+]_o/[I]_o = 4$ and $k_{app} = 3.68 \times 10^{-5}\ s^{-1}$; (▼) $[H^+]_o/[I]_o = 8$ and $k_{app} = 8.98 \times 10^{-5}\ s^{-1}$; and (◀) $[H^+]_o/[I]_o = 12$ and $k_{app} = 23.2 \times 10^{-5}\ s^{-1}$.

room temperature. While the resonance peaks from both the PEG and PTMC blocks showed clear resonance peaks, the peaks arising from the PTMC blocks are broader in the D_2O spectrum. This indicates that in D_2O the molecular motion of the PTMC blocks is limited, whereas that of the PEG blocks is not. Thus, the 4a-PEG-*b*-PTMC star block copolymers prepared herein form micelles in which the hydrophobic outer PTMC arms are encapsulated by the hydrophilic core PEG.

The CMC for the resulting micelles was measured to determine whether the 4a-PEG-*b*-PTMC star block copolymers can be considered as potential hydrophobic-drug carriers. Fluorescence measurements using pyrene as a probe were carried out to determine the CMCs of the 4a-PEG-*b*-PTMC star block copolymers in aqueous solution. Pyrene, a hydrophobic molecule, is preferentially distributed inside or close to the hydrophobic PTMC domain of micelles. Consequently photophysical characteristics of pyrene in micelles are different from those of free pyrene molecules in water. The pyrene excitation spectrum shifted from 335 nm for free pyrene to 338 nm for the micellar system, indicating partitioning of pyrene into the hydrophobic micellar core PTMC. This shift was utilized to determine the CMC values of the 4a-PEG-*b*-PTMC star block copolymers in aqueous solution. The fluorescence intensity ratio (I_{338}/I_{335}) of pyrene excitation spectra was plotted against the logarithm of the concentration of the 4a-PEG-*b*-PTMC star block copolymers. A substantial increase of the intensity ratio begins at a certain concentration, indicating the onset of micelle formation. The intercept of straight line fits of the intensity ratio data above and below this onset point is taken as the CMC. The CMCs are listed in Table 3. CMC values are in the range of 4.98×10^{-2}–5.70×10^{-3} mg/mL. The CMCs of 4a-PEG-*b*-PTMC star block copolymers decrease with the increase in the PTMC segment. This is attributed to increased hydrophobic PTMC segment [21,22].

From the partitioning of pyrene to the micellar core, Wilhelm et al. made an equation to calculate the partition equilibrium constant, K_v, characteristic of the hydrophobicity of the micellar core [23]. The K_v of pyrene was calculated by considering the incorporation of pyrene into the micelles as a simple equilibrium between the micellar phase ($[Py]_m$) and the aqueous phase ($[Py]_w$). Thus, the ratio of pyrene concentration in the micellar to the aqueous phase ($[Py]_m/[Py]_w$) can be correlated to the volume ratio of each phase according to:

$$[Py]_m/[Py]_w = K_v V_m/V_w \quad (1)$$

Table 3
Critical micelle concentration (CMC) and K_v of 4a-PEG-*b*-PTMC star block copolymers

No.	CMC $\times 10^3$ (mg/mL)	$K_v \times 10^{-4}$
$E_{45}T_{10}$	49.8	1.11
$E_{45}T_{20}$	18.8	1.50
$E_{45}T_{40}$	15.9	2.05
$E_{45}T_{70}$	12.8	4.38
$E_{45}T_{100}$	5.7	5.68

which can be rewritten as

$$[Py]_m/[Py]_w = K_v x(c - CMC)/1000\rho \quad (2)$$

where x is the weight fraction of hydrophobic PTMC block, c is the concentration of the 4a-PEG-*b*-PTMC star block copolymer, and ρ is the density of the PTMC micellar core, which is assumed to be equal to the value for bulk PTMC (1.01) [24]. $[Py]_m/[Py]_w$ can be written as

$$[Py]_m/[Py]_w = (F - F_{min})/(F_{max} - F) \quad (3)$$

where F_{min} and F_{max} correspond to the average magnitude of I_{338}/I_{335} in the flat region of low and high concentration ranges and F is the I_{338}/I_{335} intensity ratio in the intermediate concentration range of the block copolymer. By combining Eqs. 2 and 3, K_v was determined from the slope of a plot of $(F - F_{min})/(F_{max} - F)$ versus star block copolymer concentration at concentrations above the CMC (Fig. 5).

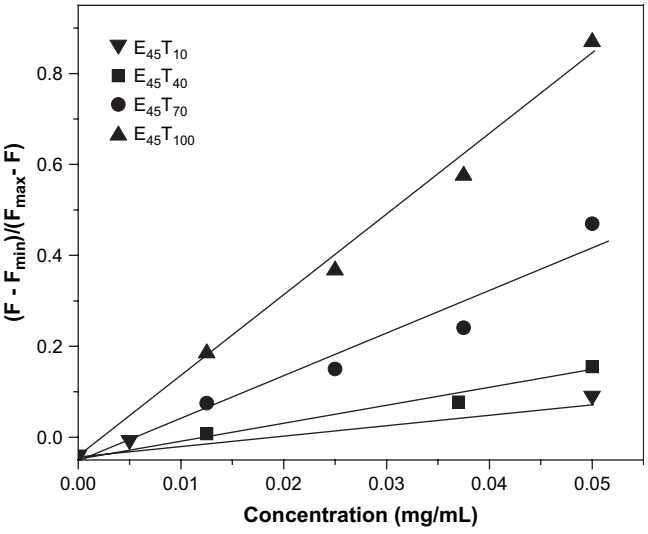

Fig. 5. Plots of $(F - F_{min})/(F_{max} - F)$ versus concentration of 4a-PEG-*b*-PTMC star block copolymers at 25 °C.

The K_v values for the 4a-PEG-*b*-PTMC star block copolymers are summarized in Table 3. The K_v values ranged from 1.1×10^4 to 5.7×10^4, in the opposite order to the CMCs. As the hydrophobic PTMC segment of the 4a-PEG-*b*-PTMC star block copolymers increases, the K_v value increases. These findings indicate that the partition coefficient for pyrene is higher in a-PEG-*b*-PTMC star block copolymers with the increase in the PTMC segment, suggesting that pyrene is more easily trapped with the increase in the PTMC segment. Thus, K_v may be an indicator of the hydrophobicity of the 4a-PEG-*b*-PTMC star block copolymers.

4. Conclusions

We prepared 4a-PEG-*b*-PTMC star block copolymers via ROP of TMC initiated at the hydroxyl end groups of 4a

PEG in the presence of $HCl \cdot Et_2O$ as a monomer activator. These polymerization reactions afforded large quantities of the 4a-PEG-*b*-PTMC star block copolymers without residual products. The ROP in this system is based on the equal attack of the terminal hydroxyl group to the monomer activated with $HCl \cdot Et_2O$. This polymerization procedure yielded 4a-PEG-*b*-PTMC star block copolymers with well-defined structures without a metal catalyst. The 4a-PEG-*b*-PTMC star block copolymers studied herein form micelles with the PTMC blocks inside the micellar core and the PEG blocks at the outer shell of the micelles adjoining the aqueous phase. The CMC and partition equilibrium constant depended on the PTMC segment of the 4a-PEG-*b*-PTMC star block copolymers. We believe that 4a-PEG-*b*-PTMC star block copolymers may extend as potential hydrophobic-drug carriers in practical biomedical applications. In ongoing studies, we are investigating the biomedical application of hydrophobic-drug-loaded micelles prepared using 4a-PEG-*b*-PTMC star block copolymers.

Acknowledgments

This study was supported by a grant from KMOCIE (10030022) and KMOHW (A050082).

References

[1] Discher DE, Ortiz V, Srinivas G, Klein ML, Kim Y, Christian D, et al. Prog Polym Sci 2007;32:838–57.
[2] Hadjiantoniou NA, Patrickios CS. Polymer 2007;48:7041–8.
[3] Rapoport N. Prog Polym Sci 2007;32:962–90.
[4] Strandman S, Zarembo A, Darinskii AA, Loflund B, Butcher SJ, Tenhu H. Polymer 2007;48:7008–16.
[5] Tang X, Hu Y, Pan C. Polymer 2007;48:6354–65.
[6] Vonarbourg A, Passirani C, Saulnier P, Benoit JP. Biomaterials 2006;27:4356–73.
[7] Mindemark J, Hilborn J, Bowden T. Macromolecules 2007;40:3515–7.
[8] Pego AP, Grijpma DW, Feijen J. Polymer 2003;44:6495–504.
[9] Nederberg F, Lohmeijer BGG, Leibfarth F, Pratt RC, Choi J, Dove AP, et al. Biomacromolecules 2007;8:153–60.
[10] Zeng F, Liu J, Allen C. Biomacromolecules 2004;5:1810–7.
[11] Dobrzynski P. Polymer 2007;48:2263–79.
[12] Morinaga H, Ochiai B, Endo T. J Polym Sci Part A Polym Chem 2006;44:6633–9.
[13] Morinaga H, Ochiai B, Mori H, Endo T. J Polym Sci Part A Polym Chem 2006;44:1985–96.
[14] Lee JW, Hyun H, Cho JS, Kim MS, Khang G, Lee HB. Tissue Eng Regen Med 2007;4:399–405.
[15] Tanzi MC, Verderio P, Lampugnani MG, Resnati M, Dejana E, Sturani E. J Mater Sci Mater Med 1994;5:393–6.
[16] Shibasaki Y, Sanda F, Endo T. Macromol Rapid Commun 1999;20:532–5.
[17] Shibasaki Y, Sanada H, Yokoi M, Sanda F, Endo T. Macromolecules 2000;33:4316–20.
[18] Kim MS, Hyun H, Khang G, Lee HB. Macromolecules 2006;39:3099–102.
[19] Kim MS, Seo KS, Khang G, Lee HB. Macromol Rapid Commun 2005;26:643–8.
[20] One referee pointed out the preparation of 4a-PEG-*b*-PTMC star block copolymer with higher chain length of PTMC. Although we obtain 4a-PEG-*b*-PTMC star block copolymers with DP 200 in different polymerization condition ($[HCl]/[Initiator] = 4$, $[TMC]/[CH_2Cl_2] = 1$ M) with the condition used in this work, we suppose that this polymerization procedure can yield 4a-PEG-*b*-PTMC star block copolymers with well-defined structures without a metal catalyst.
[21] Li P, Li Z, Huang J. Polymer 2007;48:1557–66.
[22] Cao N, Wang X, Song L, Zhang ZC. J Polym Sci Part A Polym Chem 2007;45:5800–10.
[23] Wilhelm M, Zhao C, Wang Y, Xu R, Winnik MA, Mura J, et al. Macromolecules 1991;24:1033–40.
[24] Doneva TA, Yin HB, Stephens P, Bowen WR, Thomas DW. Spectroscopy 2004;18:587–96.