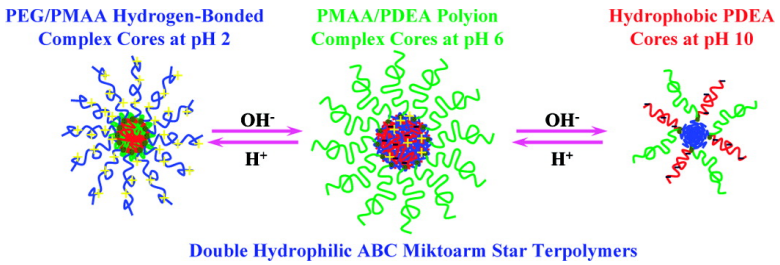
Article

pH-Responsive Supramolecular Self-Assembly of Well-Defined Zwitterionic ABC Miktoarm Star Terpolymers

Hao Liu, Changhua Li, Hewen Liu, and Shiyong Liu

Langmuir, **2009**, 25 (8), 4724-4734• DOI: 10.1021/la803813r • Publication Date (Web): 24 February 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Langmuir is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Langmuir
Article
pubs.acs.org/langmuir

pH-Responsive Supramolecular Self-Assembly of Well-Defined Zwitterionic ABC Miktoarm Star Terpolymers

Hao Liu, Changhua Li, Hewen Liu, and Shiyong Liu*

CAS Key Laboratory of Soft Matter Chemistry, Department of Polymer Science and Engineering, Hefei National Laboratory for Physical Sciences at the Microscale, University of Science and Technology of China, Hefei, Anhui 230026, China

Received November 17, 2008. Revised Manuscript Received January 12, 2009

We report the first example of the synthesis and pH-responsive supramolecular self-assembly of double hydrophilic ABC miktoarm star terpolymers. Well-defined ABC miktoarm star terpolymers consisting of poly(ethylene glycol), poly(*tert*-butyl methacrylate), and poly(2-(diethylamino)ethyl methacrylate) arms [PEG(-*b*-P*t*BMA)-*b*-PDEA] were synthesized via the combination of consecutive click reactions and atom transfer radical polymerization (ATRP), starting from a trifunctional core molecule, 1-azido-3-chloro-2-propanol (ACP). The click reaction of monoalkynyl-terminated PEG with an excess of ACP afforded difunctional PEG bearing a chlorine and a secondary hydroxyl moiety at the chain end, PEG_{113}(-*Cl*)-*OH* (**1**). After azidation with NaN_3, PEG-based macroinitiator PEG_{113}(-N_3)-*Br* (**3**) was prepared by the esterification of PEG_{113}(-N_3)-*OH* (**2**) with 2-bromoisobutyryl bromide and then employed in the ATRP of *tert*-butyl methacrylate (*t*BMA). The obtained PEG(-N_3)-*b*-P*t*BMA copolymers (**4**) possessed an azido moiety at the diblock junction point. The preparation of PEG(-*b*-P*t*BMA)-*b*-PDEA miktoarm star terpolymers was then achieved via the click reaction of **4** with an excess of monoalkynyl-terminated PDEA. The obtained miktoarm star terpolymers were successfully converted into PEG(-*b*-PMAA)-*b*-PDEA, where PMAA is poly(methacrylic acid). In aqueous solution, PEG(-*b*-PMAA)-*b*-PDEA zwitterionic ABC miktoarm star terpolymers can self-assemble into three types of micellar aggregates by simply adjusting solution pH at room temperature. Above pH 8, PDEA-core micelles stabilized by PEG/ionized PMAA hybrid coronas were formed due to the insolubility of PDEA block. In the range of pH 5−7, micelles possessing polyion complex cores formed as a result of charge compensation between partially ionized PMAA and partially protonated PDEA sequences. At pH $<$ 4, hydrogen bonding interactions between fully protonated PMAA and PEG led to the formation of another type of micellar aggregates possessing hydrogen-bonded complex cores stabilized by protonated PDEA coronas. The fully reversible pH-responsive formation of three types of aggregates were characterized by ^{1}H NMR, dynamic and static laser light scattering (LLS), and transmission electron microscopy (TEM).

Introduction

In the past few years, there has been increasing interest in stimuli-responsive double hydrophilic block copolymers (DHBCs), which can self-assemble into one or more types of micellar aggregates in water upon selectively rendering one of the blocks water-insoluble under proper external stimuli.[1−24] Previous studies concerning DHBCs mainly focused on the synthesis and supramolecular self-assembly of linear DHBCs.[6,10,11,13,15,18] The effects of block composition, molecular weights (MWs), and solution conditions on the properties of self-assembled aggregates of DHBCs, such as shape, size, critical micellization concentration (CMC), and aggregation number (N_{agg}), have been well-established.[1,2,7,9,12,14,19]

*To whom correspondence should be addressed. E-mail: sliu@ustc.edu.cn.

(1) Colfen, H. *Macromol. Rapid Commun.* **2001**, *22*, 219–252.
(2) Gohy, J. F. *Adv. Polym. Sci.* **2005**, *190*, 65–136.
(3) Alarcon, C. D. H.; Pennadam, S.; Alexander, C. *Chem. Soc. Rev.* **2005**, *34*, 276–285.
(4) Butun, V.; Liu, S.; Weaver, J. V. M.; Bories-Azeau, X.; Cai, Y.; Armes, S. P. *React. Funct. Polym.* **2006**, *66*, 157–165.
(5) Thomas, D. B.; Vasilieva, Y. A.; Armentrout, R. S.; McCormick, C. L. *Macromolecules* **2003**, *36*, 9710–9715.
(6) Dai, S.; Ravi, P.; Tam, K. C.; Mao, B. W.; Gang, L. H. *Langmuir* **2003**, *19*, 5175–5177.
(7) Zhu, Z. Y.; Armes, S. P.; Liu, S. Y. *Macromolecules* **2005**, *38*, 9803–9812.
(8) Xu, J.; Ge, Z. S.; Zhu, Z. Y.; Luo, S. Z.; Liu, H. W.; Liu, S. Y. *Macromolecules* **2006**, *39*, 8178–8185.
(9) Wang, D.; Yin, J.; Zhu, Z. Y.; Ge, Z. S.; Liu, H. W.; Armes, S. P.; Liu, S. Y. *Macromolecules* **2006**, *39*, 7378–7385.
(10) Mountrichas, G.; Pispas, S. *Macromolecules* **2006**, *39*, 4767–4774.
(11) Pispas, S. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 606–613.
(12) Zhu, Z. Y.; Xu, J.; Zhou, Y. M.; Jiang, X. Z.; Armes, S. P.; Liu, S. Y. *Macromolecules* **2007**, *40*, 6393–6400.
(13) Zhou, Y. M.; Jiang, K. Q.; Song, Q. L.; Liu, S. Y. *Langmuir* **2007**, *23*, 13076–13084.
(14) Zhang, Y. F.; Wu, T.; Liu, S. Y. *Macromol. Chem. Phys.* **2007**, *208*, 2492–2501.
(15) Liu, H.; Jiang, X. Z.; Fan, J.; Wang, G. H.; Liu, S. Y. *Macromolecules* **2007**, *40*, 9074–9083.
(16) Rao, J. Y.; Luo, Z. F.; Ge, Z. S.; Liu, H.; Liu, S. Y. *Biomacromolecules* **2007**, *8*, 3871–3878.
(17) Ge, Z. S.; Cai, Y. L.; Yin, J.; Zhu, Z. Y.; Rao, J. Y.; Liu, S. Y. *Langmuir* **2007**, *23*, 1114–1122.
(18) Mountrichas, G.; Pispas, S. *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 5790–5799.
(19) Zhang, J. Y.; Xu, J.; Liu, S. Y. *J. Phys. Chem. B* **2008**, *112*, 11284–11291.
(20) Nuopponen, M.; Kalliomaki, K.; Laukkanen, A.; Hietala, S.; Tenhu, H. *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 38–46.
(21) Feng, C.; Shen, Z.; Gu, L. N.; Zhang, S.; Li, L. T.; Lu, G. L.; Huang, X. Y. *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 5638–5651.
(22) Gu, L. N.; Shen, Z.; Feng, C.; Li, Y. G.; Lu, G. L.; Huang, X. Y. *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 4056–4069.
(23) Luo, S. Z.; Xu, J.; Zhang, Y. F.; Liu, S. Y.; Wu, C. *J. Phys. Chem. B* **2005**, *109*, 22159–22166.
(24) Jiang, X. Z.; Luo, S. Z.; Armes, S. P.; Shi, W. F.; Liu, S. Y. *Macromolecules* **2006**, *39*, 5987–5994.

The chain architectures (topology) of block copolymers can also play an important role in determining their self-assembling behavior in both organic solvents and aqueous solution.[13,17,21,22,25−52] Hadjichristidis, Pispas, and their coworkers[28−41,43−45,50] have systematically investigated the aggregation properties of AB_2 Y-shaped,[33,38] AB_3 miktoarm star copolymers,[31] A_3BA_3 super-H shaped,[29] and $(AB)_8$ star copolymers[45] consisting of polystyrene (PS) and polyisoprene (PI) sequences in selective solvents. It was found that nonlinear block copolymers exhibit fundamentally different aggregation behavior (CMC, N_{agg}, sizes) compared to that of linear PS-*b*-PI block copolymers with comparable block lengths.[29,31−38,45] Lodge et al.[27,53] synthesized ABC miktoarm star terpolymers consisting of water-soluble poly(ethylene oxide), hydrophobic perfluorinated polyether, and hydrogenated polybutadiene arms. In dilute aqueous solution, they self-assemble into discrete multicompartment micelles and extended wormlike structures with segmented cores depending on the relative block lengths, which has been ascribed to the miktoarm star topology and intrinsic incompatibility within micellar cores.

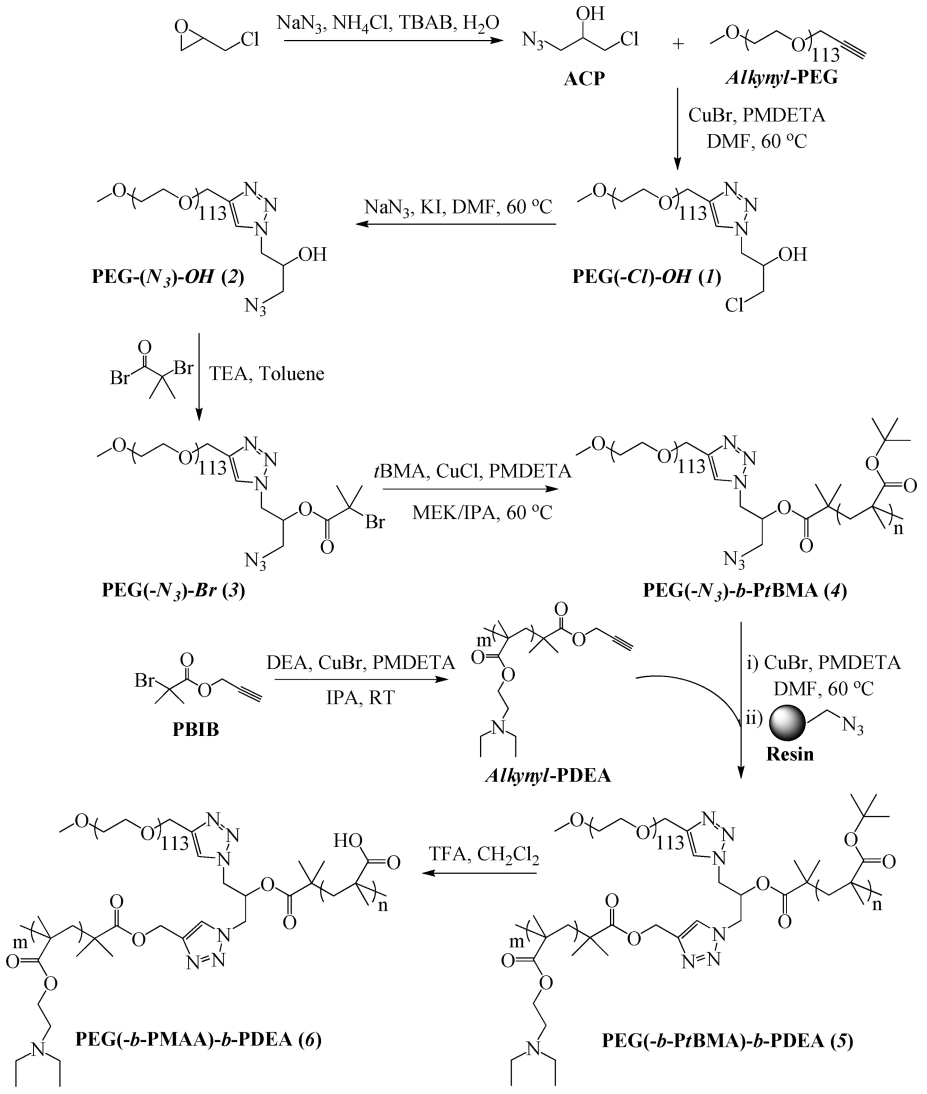
In the context of nonlinear-shaped DHBCs, Armes et al.[42,46] reported the first two examples of stimuli-responsive Y-shaped (AB_2) miktoarm star copolymers, which can self-assemble into micelles with different dimensions compared to those of linear diblock copolymers. Previously, we synthesized double hydrophilic H-shaped A_2BA_2 and A_4BA_4 miktoarm star copolymers consisting of poly(propylene oxide) (PPO) and poly(2-(diethylamino)ethyl methacrylate) (PDEA) sequences.[8] At pH 8.5 and 5 °C, they form much larger PDEA-core micelles compared to AB diblock copolymers with comparable PPO contents and MWs. On the other hand, both types of nonlinear block copolymers form unimolecular micelles with the core consisting of a single PPO block upon heating the aqueous solution at pH 6.4. In another example, double hydrophilic AB_4 miktoarm star copolymers consisting of poly(*N*-isopropylacrylamide) (PNIPAM) and PDEA arms were synthesized, and the chain architectural effects on the micelle structure and assembling kinetics were investigated.[17]

It can be expected that if more than two types of polymer sequences are arranged in a nonlinear fashion in DHBCs, their stimuli-responsive assembly behavior will be more intriguing.[8,17] A simplest representative of the above system would be double hydrophilic ABC miktoarm star terpolymers, in which three different polymer segments are covalently connected to a common junction point.[27,49,54,55] To the best of our knowledge, the synthesis and stimuli-responsive self-assembly behavior of double hydrophilic ABC miktoarm star terpolymers have not been reported yet. In terms of their synthesis, the past five years have evidenced a surge in the synthesis of miktoarm star terpolymers via a combination of click chemistry,[56−58] ring-opening polymerization (ROP),[57−61] Diels−Alder (DA) reaction,[62] and controlled radical polymerization techniques including nitroxide-mediated radical polymerization (NMP),[56,57,60−62] atom transfer radical polymerization (ATRP),[56,58,60−62] and reversible addition−fragmentation chain transfer (RAFT) polymerization.[59]

Herein, we report the first example of the synthesis and pH-responsive micellization behavior of well-defined double hydrophilic ABC miktoarm star terpolymers. Miktoarm star terpolymers consisting of poly(ethylene glycol) (PEG), poly(*tert*-butyl methacrylate (P*t*BMA), and PDEA arms were synthesized via a combination of consecutive click reactions and ATRP. The hydrolysis of PEG(-*b*-P*t*BMA)-*b*-PDEA afforded zwitterionic miktoarm star terpolymers consisting of PEG, poly(methacrylic acid) (PMAA), and PDEA arms, PEG(-*b*-PMAA)-*b*-PDEA (Scheme 1). Their pH-responsive aggregation behavior in aqueous solution was then investigated by a combination of ^{1}H NMR, dynamic and static laser

(25) Pitsikalis, M.; Pispas, S.; Mays, J. W.; Hadjichristidis, N. *Adv. Polym. Sci.* **1998**, *135*, 1–137.
(26) Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Pispas, S.; Avgeropoulos, A. *Prog. Polym. Sci.* **2005**, *30*, 725–782.
(27) Li, Z. B.; Kesselman, E.; Talmon, Y.; Hillmyer, M. A.; Lodge, T. P. *Science* **2004**, *306*, 98–101.
(28) Floudas, G.; Hadjichristidis, N.; Iatrou, H.; Pakula, T.; Fischer, E. W. *Macromolecules* **1994**, *27*, 7735–7746.
(29) Iatrou, H.; Willner, L.; Hadjichristidis, N.; Halperin, A.; Richter, D. *Macromolecules* **1996**, *29*, 581–591.
(30) Floudas, G.; Hadjichristidis, N.; Iatrou, H.; Pakula, T. *Macromolecules* **1996**, *29*, 3139–3146.
(31) Hadjichristidis, N.; Tselikas, Y.; Iatrou, H.; Efstratiadis, V.; Avgeropoylos, A. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1996**, *A33*, 1447–1457.
(32) Beyer, F. L.; Gido, S. P.; Poulos, Y.; Avgeropoulos, A.; Hadjichristidis, N. *Macromolecules* **1997**, *30*, 2373–2376.
(33) Anastasiadis, S. H.; Chrissopoulou, K.; Fytas, G.; Fleischer, G.; Pispas, S.; Pitsikalis, M.; Mays, J. W.; Hadjichristidis, N. *Macromolecules* **1997**, *30*, 2445–2453.
(34) Lee, C.; Gido, S. P.; Poulos, Y.; Hadjichristidis, N.; Tan, N. B.; Trevino, S. F.; Mays, J. W. *J. Chem. Phys.* **1997**, *107*, 6460–6469.
(35) Lee, C.; Gido, S. P.; Poulos, Y.; Hadjichristidis, N.; Tan, N. B.; Trevino, S. F.; Mays, J. W. *Polymer* **1998**, *39*, 4631–4638.
(36) Beyer, F. L.; Gido, S. P.; Velis, G.; Hadjichristidis, N.; Tan, N. B. *Macromolecules* **1999**, *32*, 6604–6607.
(37) Beyer, F. L.; Gido, S. P.; Uhrig, D.; Mays, J. W.; Tan, N. B.; Trevino, S. F. *J. Polym. Sci. Part B: Polym. Phys.* **1999**, *37*, 3392–3400.
(38) Pispas, S.; Hadjichristidis, N.; Potemkin, I.; Khokhlov, A. *Macromolecules* **2000**, *33*, 1741–1746.
(39) Sotiriou, K.; Nannou, A.; Velis, G.; Pispas, S. *Macromolecules* **2002**, *35*, 4106–4112.
(40) Mavroudis, A.; Avgeropoulos, A.; Hadjichristidis, N.; Thomas, E. L.; Lohse, D. J. *Chem. Mater.* **2003**, *15*, 1976–1983.
(41) Pispas, S.; Floudas, G.; Pakula, T.; Lieser, G.; Sakellariou, S.; Hadjichristidis, N. *Macromolecules* **2003**, *36*, 759–763.
(42) Cai, Y. L.; Tang, Y. Q.; Armes, S. P. *Macromolecules* **2004**, *37*, 9728–9737.
(43) Hu, X. C.; Gido, S. P.; Russell, T. P.; Iatrou, H.; Hadjichristidis, N.; Abuzaina, F. M.; Garetz, B. A. *Macromolecules* **2005**, *38*, 4719–4728.
(44) Hu, X. C.; Zhu, Y. Q.; Gido, S. P.; Russell, T. P.; Iatrou, H.; Hadjichristidis, N.; Abuzaina, F. M.; Garetz, B. A. *Faraday Discuss.* **2005**, *128*, 103–112.
(45) Mountrichas, G.; Mpiri, M.; Pispas, S. *Macromolecules* **2005**, *38*, 940–947.
(46) Cai, Y. L.; Armes, S. P. *Macromolecules* **2005**, *38*, 271–279.
(47) Liu, H.; Xu, J.; Jiang, J. L.; Yin, J.; Narain, R.; Cai, Y. L.; Liu, S. Y. *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 1446–1462.
(48) Van Durme, K.; Van Assche, G.; Aseyev, V.; Raula, J.; Tenhu, H.; Van Mele, B. *Macromolecules* **2007**, *40*, 3765–3772.
(49) Zhulina, E. B.; Borisov, O. V. *Macromolecules* **2008**, *41*, 5934–5944.
(50) Christodoulou, S.; Driva, P.; Iatrou, H.; Hadjichristidis, N. *Macromolecules* **2008**, *41*, 2607–2615.
(51) Pan, Q. M.; Liu, S. Y.; Xie, J. W.; Jiang, M. *J. Polym. Sci. Part A: Polym. Chem.* **1999**, *37*, 2699–2702.
(52) Xu, J.; Liu, S. Y. *Soft Matter* **2008**, *4*, 1745–1749.
(53) Liu, C.; Hillmyer, M. A.; Lodge, T. P. *Langmuir* **2008**, *24*, 12001–12009.
(54) He, X. H.; Huang, L.; Liang, H. J.; Pan, C. Y. *J. Chem. Phys.* **2003**, *118*, 9861–9863.
(55) Zhu, Y. T.; Li, R. K. Y.; Jiang, W. *Chem. Phys.* **2006**, *327*, 137–143.
(56) Altintas, O.; Hizal, G.; Tunca, U. *J. Polym. Sci. Part A: Polym. Chem.* **2006**, *44*, 5699–5707.
(57) Altintas, O.; Yankul, B.; Hizal, G.; Tunca, U. *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 3588–3598.
(58) Deng, G. H.; Ma, D. Y.; Xu, Z. Z. *Eur. Polym. J.* **2007**, *43*, 1179–1187.
(59) Li, Y. G.; Wang, Y. M.; Pan, C. Y. *J. Polym. Sci. Part A: Polym. Chem.* **2003**, *41*, 1243–1250.
(60) Tunca, U.; Ozyurek, Z.; Erdogan, T.; Hizal, G. *J. Polym. Sci. Part A: Polym. Chem.* **2004**, *42*, 4228–4236.
(61) He, T.; Li, D. J.; Sheng, X.; Zhao, B. *Macromolecules* **2004**, *37*, 3128–3135.
(62) Durmaz, H.; Karatas, F.; Tunca, U.; Hizal, G. *J. Polym. Sci. Part A: Polym. Chem.* **2006**, *44*, 499–509.

Scheme 1. Synthetic Routes Employed for the Preparation of PEG(-*b*-PMAA)-*b*-PDEA Zwitterionic ABC Miktoarm Star Terpolymers



light scattering (LLS), and transmission electron microscopy (TEM). Depending on solution pH, PEG(-*b*-PMAA)-*b*-PDEA miktoarm star terpolymers self-assembled into three types of micellar aggregates in aqueous solution at room temperature. Above pH 8, PDEA-core micelles stabilized by PEG/ionized PMAA hybrid coronas formed as a result of insolubility of the PDEA block. In the range of pH 5−7, micelles possessing polyion complex cores formed as a result of charge compensation between partially ionized PMAA and partially protonated PDEA sequences. At pH < 4, hydrogen bonding interactions between fully protonated PMAA and PEG arms led to formation of the third type of micellar aggregates possessing hydrogen-bonded complex cores.

Experimental Section

Materials. PEG monomethyl ether (PEG_{113}-OH, M_n = 5.0 kDa, M_w/M_n = 1.06, mean degree of polymerization, DP, is 113) was purchased from Aldrich and used as received. *tert*-Butyl methacrylate (*t*BMA, Aldrich, 98%) and 2-(diethylamino)ethyl methacrylate (DEA, 99%, Aldrich) were dried over calcium hydride, vacuum-distilled, purged with nitrogen, and stored at −20 °C prior to use. Triethylamine (TEA), isopropyl alcohol (IPA), and toluene were dried over CaH_2 and distilled prior to use. *N,N,N′,N″,N″*- Pentamethyldiethylenetriamine (PMDETA, 99%, Aldrich), 2-bromoisobutyryl bromide (98%, Aldrich), copper(I) bromide (CuBr, 98%, Aldrich), copper(I) chloride (CuCl, 99.995%, Aldrich), sodium azide (NaN_3, 99%, Alfa Aesar), sodium hydride (NaH, 57−63% in oil, Alfa Aesar), and propargyl bromide (80% in toluene stabilized with MgO, Alfa Aesar) were used as received. Epichlorohydrin, tetrabutylammonium bromide (TBAB), trifluoroacetic acid (TFA), *N*,*N*-dimethylformamide (DMF), methyl ethyl ketone (MEK), *n*-hexane, and all other chemicals were purchased from Sinopharm Chemical Reagent Co. and used as received. Propargyl 2-bromoisobutyrate (PBIB) was prepared by the esterification reaction of propargyl alcohol with 2-bromoisobutyryl bromide according to literature procedures.[63,64] Azido-functionalized Merrifield resin was available from previous studies.[65,66]

(63) Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3558–3561.
(64) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238–4239.
(65) Opsteen, J. A.; van Hest, J. C. M. *Chem. Commun.* **2005**, 57–59.
(66) Gheorghe, A.; Matsuno, A.; Reiser, O. *Adv. Synth. Catal.* **2006**, *348*, 1016–1020.

Synthesis of 1-Azido-3-chloro-2-propanol (ACP). The trifunctional core molecule ACP was prepared by the azidation of epichlorohydrin according to literature procedures.[67−69] To a 100 mL round-bottomed flask, sodium azide (16.25 g, 0.25 mol), 0.196 g of TBAB, and water (40 mL) were added. After the addition of epichlorohydrin (19.6 mL, 0.25 mol), the reaction mixture, protected from light, was stirred overnight at room temperature. After extraction with CH_2Cl_2, the combined organic phase was dried over anhydrous $MgSO_4$, followed by filtration and evaporation to dryness using a rotary evaporator. The residues were purified by silica gel column chromatography using ethyl acetate and *n*-hexane (9:1 by volume) to yield a colorless liquid (27.1 g, yield: 80%). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 3.97−4.04 (m, 1H, −C*H*OH), 3.60−3.64 (m, 2H, −CH_2Cl), 3.47−3.49 (m, 2H, −CH_2N$_3$), and 2.6 (br s, 1H, −CHO*H*). ^{13}C NMR ($CDCl_3$, δ, ppm, TMS): 70.22 (C-2), 53.39 (C-3), and 46.16 (C-1). FT-IR ($CHCl_3$, cm^{-1}): 3417, 2930, 2103, 1442, 1285, 1068, 930, and 753. GC: 6.42 min; MS *m*/*z* (%): 137.1 (1.0), 135.1 (3.1), 86.1 (4.9), 81.1 (35.6), 79.0 (100), 56.1 (2.2), 51.1 (7.0), 49.1 (17.3).

Synthesis of Monoalkynyl-Terminated PEG (*Alkynyl*-PEG). Typical procedures employed for the preparation of *alkynyl*-PEG was as follows. PEG$_{113}$-OH (15.0 g, 3.0 mmol) was dissolved in toluene (180 mL) at 60 °C. After azeotropic distillation of 30−40 mL of toluene at reduced pressure to remove traces of water, sodium hydride (0.216 g, 9.0 mmol, 3 times molar excess to hydroxyl groups) was added to the solution under stirring. After H_2 evolution for about 15 min, propargyl bromide (1.33 mL, 15 mmol, 5 times molar excess to hydroxyl groups) in 20 mL of dry toluene was added dropwise. The reaction was then stirred at 60 °C for 18 h. After filtration of insoluble salts, the filtrates were evaporated to dryness. The obtained solid was dissolved in 100 mL CH_2Cl_2. After extraction with an aqueous solution of saturated $NaHCO_3$ (3 × 30 mL), the organic phase was dried over anhydrous Na_2SO_4 and treated with activated charcoal. After filtration, the solution was precipitated into *n*-hexane. The above dissolution−precipitation cycle was repeated three times. After drying in a vacuum oven overnight at room temperature, *alkynyl*-PEG was obtained as a white solid (12.24 g, yield: 81%; $M_{n,GPC}$ = 5.1 kDa, M_w/M_n = 1.10). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 4.2 (2H, −OCH_2C≡CH), 3.7 (450H, −OCH_2CH_2O−), 3.4 (3H, CH_3O−), and 2.4 (1H, −OCH$_2$C≡C*H*).

Click Reaction of Alkynyl-PEG with ACP. To a Schlenk tube equipped with a magnetic stirring bar, *alkynyl*-PEG (5.0 g, 1.0 mmol), PMDETA (210 μL, 1.0 mmol), ACP (0.407 g, 3.0 mmol), and DMF (15 mL) were added. After one brief freeze−thaw cycle, CuBr (0.143 g, 1.0 mmol) was introduced under protection of N_2 flow. The reaction tube was carefully degassed by three freeze−pump−thaw cycles, sealed under vacuum, and placed in an oil bath thermostatted at 60 °C. After stirring for 12 h, the reaction mixture was exposed to air, diluted with tetrahydrofuran (THF), and passed through a basic alumina column to remove copper catalysts. After removing the solvents, the residues were dissolved in THF and precipitated into an excess of cold diethyl ether. The above dissolution−precipitation cycle was repeated three times. After drying in a vacuum oven overnight at room temperature, PEG$_{113}$(-*Cl*)-*OH* (**1**) was obtained as a white solid (4.9 g, yield: 95%; $M_{n,GPC}$ = 5.2 kDa, M_w/M_n = 1.10). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 7.85 (1H, 1,2,3-triazole ring), 4.7 (2H, −OCH_2-1,2,3-triazole ring), 4.4 −4.6 (2H, −CH_2CHOHCH$_2$Cl), 4.2 (1H, −CH$_2$C*H*OHCH$_2$Cl), 3.7 (452H, −OCH_2CH_2O−), and 3.4 (3H, CH_3O−).

Azidation of PEG$_{113}$(-Cl)-OH. A typical procedure was as follows. The reaction mixture of PEG$_{113}$(-*Cl*)-*OH* (3.1 g, 0.6 mmol), NaN_3 (0.39 g, 6.0 mmol), KI (10 mg, 0.06 mmol), and DMF (10 mL) was stirred for 24 h at 60 °C. The reaction mixture was diluted with THF and passed through a silica gel column to remonve insoluble salts. The eluents were evaporated to dryness on a rotary evaporator. The residues were dissolved in THF and precipitated into an excess of cold diethyl ether. The above dissolution−precipitation cycle was repeated three times. After drying in a vacuum oven overnight at room temperature, PEG$_{113}$(-N_3)-*OH* (**2**) was obtained as a white solid (2.9 g, yield: 93%; $M_{n,GPC}$ = 5.2 kDa, M_w/M_n = 1.10). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 7.81 (1H, 1,2,3-triazole ring), 4.7 (2H, −OCH_2-1,2,3-triazole ring), 4.4−4.6 (2H, −CH_2CHOHCH$_2$N$_3$), 4.2 (1H, −CH$_2$C*H*OHCH$_2$N$_3$), 3.7 (452H, −OCH_2CH_2O−), 3.4 (3H, CH_3O−), and 3.3 (2H, −CH$_2$CHOHCH_2N$_3$).

Synthesis of PEG-Based Macroinitiator PEG$_{113}$-(N_3)-*Br* (3). PEG$_{113}$(-N_3)-*Br* was prepared by the esterification reaction of PEG$_{113}$(-N_3)-*OH* with 2-bromoisobutyryl bromide, typical procedures employed was as follow. PEG$_{113}$(-N_3)-*OH* (2.08 g, 0.4 mmol) was dissolved in 50 mL of anhydrous toluene in a dry round-bottomed flask, followed by azeotropic distillation of ∼10 mL toluene out of the solution. After addition of TEA (0.28 mL, 2.0 mmol) and cooling to 0 °C, 2-bromoisobutyryl bromide (0.46 g, 2 mmol) was added dropwise. The mixture was then stirred at room temperature for 24 h. After filtration, the filtrate was further diluted with THF and passed through a silica gel column, and the eluents were evaporated to dryness on a rotary evaporator. The residues were then dissolved in THF and precipitated into an excess of cold diethyl ether. The above dissolution−precipitation cycle was repeated for three times. After drying in a vacuum oven overnight at room temperature, PEG$_{113}$(-N_3)-*Br* (**3**) was obtained as a white solid (2.0 g, yield: 94%; $M_{n,GPC}$ = 5.2 kDa, M_w/M_n = 1.10). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 7.75 (1H, 1,2,3-triazole ring), 5.3 (1H, −CH$_2$C*H*OOCCBr(CH$_3$)$_2$CH$_2$N$_3$), 4.7 (2H, −OCH_2-1,2,3-triazole ring), 4.6−4.7 (2H, −CH_2CHOOCCBr(CH$_3$)$_2$CH$_2$N$_3$), 3.7 (452H, −OCH_2CH_2O−), 3.4 (3H, CH_3O−), and 2.0 (6H, −CH$_2$CHOOCCBr(CH_3)$_2$CH$_2$N$_3$).

Preparation of PEG(-N_3)-*b*-P*t*BMA Copolymer (4). PEG(-N_3)-*b*-P*t*BMA diblock copolymer bearing an azido moiety at the diblock junction was synthesized by ATRP of *t*BMA monomer in an MEK/IPA mixture using PEG$_{113}$(-N_3)-*Br* as the macroinitiator. A typical procedure was as follows. A reaction flask equipped with a magnetic stirring bar and a rubber septum was charged with PMDETA (42 μL, 0.2 mmol), PEG$_{113}$(-N_3)-*Br* (1.07 g, 0.2 mmol), *t*BMA (3.3 mL, 20.0 mmol), and 7 mL of MEK/IPA mixture (7:3 v/v). The flask was degassed by three freeze−pump−thaw cycles, back-filled with N_2, and then placed in an oil bath thermostatted at 60 °C. After ∼5 min, CuCl (20 mg, 0.2 mmol) was added to start the polymerization under N_2 atmosphere. After 8 h, the monomer conversion was determined to be 81% as judged by ^{1}H NMR. The reaction flask was quenched into liquid nitrogen, exposed to air, and diluted with THF. After passing though a column of neutral alumina to remove the copper catalysts and removing all the solvent by a rotary evaporator, the residues were dissolved in THF and precipitated into *n*-hexane to remove residual monomers. The above dissolution−precipitation cycle was repeated three times. After drying in a vacuum oven overnight at room temperature, PEG(-N_3)-*b*-P*t*BMA (**4**) was obtained as a white solid (3.3 g, yield: 84%; $M_{n,GPC}$ = 12.5 kDa, M_w/M_n = 1.21). The actual DP of the P*t*BMA block was calculated to be 83 by ^{1}H NMR analysis in $CDCl_3$. Thus, the obtained product was denoted as PEG$_{113}$(-N_3)-*b*-P*t*BMA$_{83}$.

Synthesis of Monoalkynyl-Terminated PDEA (*Alkynyl*-PDEA). Monoalkynyl-terminated PDEA (*alkynyl*-PDEA) was synthesized by ATRP of DEA monomer using PBIB as the initiator. In a typical example, PBIB (0.123 g, 0.6 mmol),

(67) Jameela, S. R.; Lakshmi, S.; James, N. R.; Jayakrishnan, A. *J. Appl. Polym. Sci.* **2002**, *86*, 1873–1877.
(68) Bhaumik, K.; Mali, U. W.; Akamanchi, K. G. *Synth. Commun.* **2003**, *33*, 1603–1610.
(69) Spelberg, J. H. L.; Tang, L. X.; Kellogg, R. M.; Janssen, D. B. *Tetrahedron: Asymmetry* **2004**, *15*, 1095–1102.

PMDETA (125 μL, 0.6 mmol), DEA monomer (5.55 g, 30.0 mmol), and IPA (6 mL) were charged into a reaction flask. The flask was degassed via three freeze−thaw−pump cycles and back-filled with N_2. CuBr (86 mg, 0.6 mmol) was introduced into the reaction mixture under protection of N_2 flow to start the polymerization at room temperature under N_2 atmosphere. After 6 h, the polymerization was terminated by exposing to air and diluting with THF. After passing though a column of neutral alumina to remove the copper catalysts and removing all the solvent by a rotary evaporator, the residues were dissolved in THF and precipitated into cold *n*-hexane (−50 °C) to remove residual monomers. After drying in a vacuum oven overnight at room temperature, *alkynyl*-PDEA was obtained as a white viscous solid (4.8 g, yield: 85%; $M_{n,GPC}$ = 8.1 kDa, M_w/M_n = 1.17). The actual DP of *alkynyl*-PDEA was calculated to be 48 by ^{1}H NMR analysis in $CDCl_3$. Thus, the obtained product was denoted as *alkynyl*-$PDEA_{48}$. According to similar procedures, *alkynyl*-$PDEA_{85}$ was also prepared ($M_{n,GPC}$ = 14.6 kDa, M_w/M_n = 1.15).

Preparation of PEG(-*b*-P*t*BMA)-*b*-PDEA Miktoarm Star Terpolymers via Click Chemistry. The synthesis of PEG(-*b*-P*t*BMA)-*b*-PDEA miktoarm star terpolymers was accomplished by the click coupling between PEG(-N_3)-*b*-P*t*BMA diblock copolymer and *alkynyl*-PDEA using CuBr as the catalyst (Scheme 1), and a typical procedure was as follows. *Alkynyl*-$PDEA_{48}$ (1.36 g, 0.15 mmol) and PEG_{113}(-N_3)-*b*-P*t*BMA_{83} (1.71 g, 0.1 mmol) were dissolved in 20 mL of DMF. After one brief freeze−thaw cycle, CuBr (9 mg, 0.06 mmol) was introduced under the protection of N_2 flow. The reaction tube was then carefully degassed by three freeze−pump−thaw cycles, and placed in an oil bath thermostatted at 60 °C. After stirring for 24 h, azide-functionalized Merrifield resin (0.188 g, 0.15 mmol azido moieties) was then added. The suspension was kept stirring for another 8 h at 80 °C. After suction filtration, the filtrate was diluted with THF, and passed through a basic alumina column to remove the copper catalyst. After removing all the solvents at reduced pressure, the residues were dissolved in THF and precipitated into an excess of *n*-hexane. The final product was dried in a vacuum oven overnight at room temperature, yielding a white solid (2.4 g, yield: 92%; $M_{n,GPC}$ = 13.7 kDa, M_w/M_n = 1.20). According to similar procedures, click reaction between *alkynyl*-$PDEA_{85}$ and PEG_{113}(-N_3)-*b*-P*t*BMA_{83} was also conducted ($M_{n,GPC}$ = 17.3 kDa, M_w/M_n = 1.19).

Hydrolysis of PEG(-*b*-P*t*BMA)-*b*-PDEA Miktoarm Star Terpolymers. The *tert*-butyl groups of the above obtained PEG(-*b*-P*t*BMA)-*b*-PDEA (0.32 g) were hydrolyzed using TFA (0.8 mL) in CH_2Cl_2 (6 mL) at room temperature for 24 h. After evaporating all the solvents, the residues were dissolved in THF and precipitated into an excess of *n*-hexane. The final product, PEG(-*b*-PMAA)-*b*-PDEA, was dried in a vacuum oven overnight at room temperature, and the yield was quantitative.

Preparation of Micellar Solutions. Under vigorous stirring, 20 mg of PEG(-*b*-PMAA)-*b*-PDEA was directly dissolved in 20 mL of deionized water at room temperature. Stock solution with a characteristic bluish tinge was obtained. The micellar solution exhibited no macroscopic phase separation upon standing at room temperature for more than 3 weeks, suggesting the formation of stable aggregates. The solution pH of the stock solution was adjusted by the addition of NaOH or HCl.

Characterization. Nuclear Magnetic Resonance (NMR) Spectroscopy. All ^{1}H NMR spectra were recorded on a Bruker AV300 NMR spectrometer (resonance frequency of 300 MHz for ^{1}H and 75 MHz for ^{13}C) operated in the Fourier transform mode. $CDCl_3$ or D_2O was used as the solvent.

Fourier Transform Infrared Spectroscopy (FT-IR). FT-IR spectra were recorded on a Bruker VECTOR-22 IR spectrometer. The spectra were collected at 64 scans with a spectral resolution of 4 cm^{-1}.

Gel Permeation Chromatography (GPC). MW distributions were determined by GPC using a series of three linear Styragel columns HT2, HT4, HT5 and an oven temperature of 40 °C. Waters 1515 pump and Waters 2414 differential refractive index detector (set at 30 °C) was used. The eluent was THF at a flow rate of 1.0 mL/min. A series of six PS standards with MWs ranging from 800 to 400 000 g/mol were used for calibration.

Gas Chromatography/Mass Spectrometry (GC/MS). The GC/MS system consists of a Trace GC2000 (Thermo Finnigan, USA) and a Trace MS detector (Thermo Finnigan, USA). A CP-Sil 8CB column (30 m × 0.25 mm i.d., 0.25 μm film thickness, VARIAN) was used. The carrier gas was helium at a flow of 1 mL/min. The oven temperature was held at 70 °C for 2 min, programmed to 250 °C at a rate of 10 °C/min, then held isothermal at 250 °C for 10 min; transfer line temperature, 250 °C; injector temperature, 250 °C; sample volume, 2 μL; split ratio, 30:1. The electron impact energy was set at 70 eV.

Laser Light Scattering. A commercial spectrometer (ALV/DLS/SLS-5022F) equipped with a multitau digital time correlator (ALV5000) and a cylindrical 22 mW UNIPHASE He−Ne laser (λ_0 = 632 nm) as the light source was employed for dynamic and static LLS measurements. Scattered light was collected at a fixed angle of 90° for duration of ~10 min. Distribution averages and particle size distributions were computed using cumulants analysis and CONTIN routines. All data were averaged over three measurements.

Transmission Electron Microscopy. TEM observations were conducted on a Hitachi H-800 electron microscope at an acceleration voltage of 100 kV. The sample for TEM observations was prepared by placing 10 μL of solutions on copper grids coated with thin films of Formvar and carbon successively. No staining was required.

Results and Discussion

Synthesis of Difunctional PEG-Based Macroinitiator (3). As described in the Experimental Section, the azidation of epichlorohydrin afforded ACP. It was found that the azidation of epichlorhydrin proceeded presumably with the attack of azide ion on the terminal position of epoxide. This result is in accordance with literature reports[68,69] in which the FT-IR spectrum of ACP clearly shows a sharp peak at 2103 cm^{-1} and 3417 cm^{-1}, which are characteristic of azido and hydroxyl groups, respectively.

General approaches employed for the preparation of difunctional PEG-based macroinitiator containing one Br and one azido moieties, PEG_{113}(-N_3)-*Br* (**3**),are shown in Scheme 1. Well-defined monoalkynyl-terminated PEG (*alkynyl*-PEG) was prepared by reacting PEG_{113}-OH with propargyl bromide in the presence of NaH. Figure 1a shows the ^{1}H NMR spectrum of *alkynyl*-PEG together with the peak assignments. The integral ratio of peak *c* (δ = 4.2 ppm, $-OCH_2C{\equiv}CH$) to that of peak *b* (δ = 3.7 ppm, methylene protons of PEO main chain) was calculated to be 1:225, indicating that the degree of end-group functionalization is nearly quantitative.

Next, the click reaction of *alkynyl*-PEG with an excess of ACP afforded difunctional PEG bearing one chlorine and one secondary hydroxyl moiety at the chain end, PEG_{113}(-*Cl*)-*OH* (**1**). ^{1}H NMR studies indicated that the 1,3-dipolar cycloaddition reaction was essentially complete (Figure 1b). The characteristic signals of alkynyl groups at δ = 2.4 ppm ($-OCH_2C{\equiv}CH$) completely disappeared after click reaction, which was accompanied with the appearance of a new peak at ~7.9 ppm corresponding to the proton of 1,2,3-triazole ring. Moreover, NMR signals associated with terminal ACP residues in **1** are also clearly discernible in the range

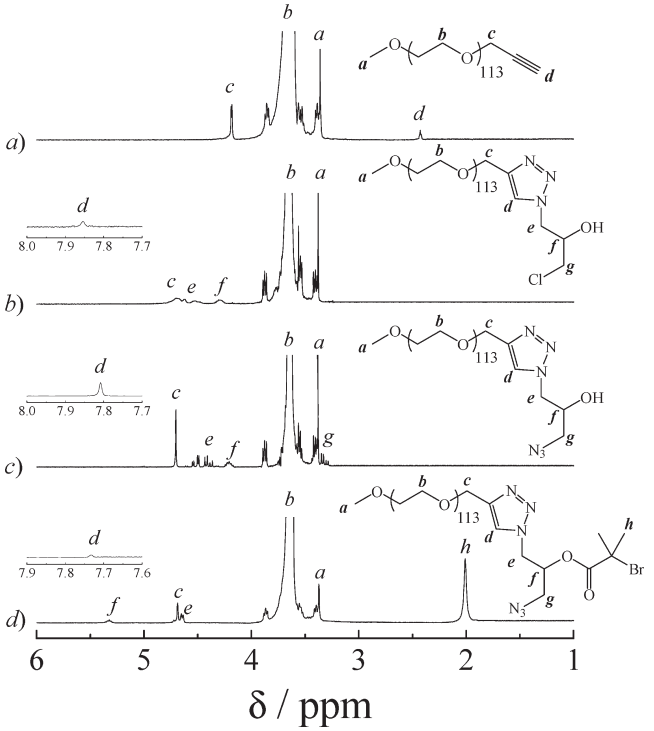


Figure 1. ^{1}H NMR spectra recorded for (a) *alkynyl*-PEG, (b) PEG_{113}(-*Cl*)-*OH*, (c) PEG_{113}(-N_3)-*OH*, and (d) difunctional PEG macroinitiator PEG_{113}(-N_3)-*Br* in $CDCl_3$.

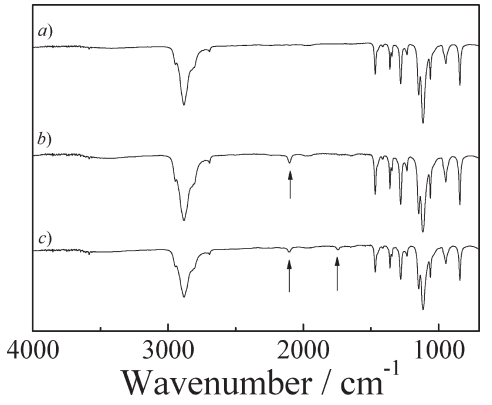


Figure 2. FT-IR spectra of (a) PEG_{113}(-*Cl*)-*OH*, (b) PEG_{113}(-N_3)-*OH*, and (c) difunctional PEG macroinitiator PEG_{113}(-N_3)-*Br*.

of 4.2−4.8 ppm (see peak assignments in Figure 2b). Peak integrals were consistent with the chemical structure of PEG_{113}(-*Cl*)-*OH*. On the other hand, the signal of methylene protons adjacent to chlorine (−$CH_2CHOHCH_2$Cl) was overlapped by those of methylene protons in PEG main chain.

The subsequent azidation of **1** with NaN_3 led to the formation of PEG_{113}(-N_3)-*OH* (**2**). The ^{1}H NMR spectrum for **2** and the corresponding peak assignments are shown in Figure 1c. The new resonance peak at 3.3 ppm can be ascribed to methylene protons neighboring to the terminal azide group (−$CH_2CHOHCH_2N_3$), which shifted to high field after azidation. Moreover, compared to that of **1**, the FT-IR spectrum of PEG_{113}(-N_3)-*OH* (Figure 2) clearly reveals the new appearance of an absorbance peak at 2102 cm^{-1}, which is characteristic of a terminal azido group. Difunctional PEG-based macroinitiator, PEG_{113}(-N_3)-*Br* (**3**), was prepared by the esterification reaction of **2** with 2-bromoisobutyryl bromide. From Figure 1, we can clearly see that multiplet peak *f* (−$CH_2CHOHCH_2N_3$) at 4.2 ppm in ***2*** completely shifted to 5.3 ppm in **3**. Moreover, the presence of a single peak *h* at δ = 1.99 ppm indicated that excess 2-bromoisobutyryl bromide was completely removed. Moreover, the integral ratio of peak *h* to that of peak *f* was close to 6:1. All of these results confirmed that the esterification reaction was complete. The FT-IR spectrum of **3** (Figure 2c) clearly reveals the presence of two absorbance peaks at 2104 and 1746 cm^{-1}, which can be ascribed to those of terminal azide and carbonyl groups, respectively.

Synthesis of PEG(-*b*-P*t*BMA)-*b*-PDEA and PEG(-*b*-PMAA)-*b*-PDEA Miktoarm Star Terpolymers. The above prepared difunctional PEG-based macroinitiator, PEG_{113}(-N_3)-*Br* (**3**), was employed for the subsequent ATRP of *t*BMA monomer and click reaction with *alkynyl*-PDEA, affording PEG(-*b*-P*t*BMA)-*b*-PDEA (**5**). Zwitterionic ABC miktoarm star terpolymer, PEG(-*b*-PMAA)-*b*-PDEA, was then obtained by the hydrolysis of ***5*** (Scheme 1).

Well-defined PEG(-N_3)-*b*-P*t*BMA diblock copolymer (**4**) was synthesized using PEG_{113}(-N_3)-*Br* macroinitiator and CuCl/PMDETA catalysts in an MEK/IPA mixture at 60 °C. GPC traces in Figure 3 clearly show that the elution peak of **4** shifted to the higher MW side after the polymerization of *t*BMA. The elution peak is relatively symmetric and shows no tailing at the lower MW side, suggesting a high initiating efficiency. GPC analysis revealed an M_n of 12.5 kDa and an M_w/M_n of 1.21 (Table 1). The ^{1}H NMR spectrum of **4** is shown in Figure 4a, and all signals characteristic of PEG and P*t*BMA segments can be clearly observed. The actual DP of P*t*BMA block was determined to be 83 by ^{1}H NMR from the integral ratio of peak *d* (1.4 ppm, −$C(CH_3)_3$) to that of peak *a* (3.7 ppm, methylene protons of PEG main chain). Thus, the obtained polymer was denoted as PEG_{113}(-N_3)-*b*-P*t*BMA_{83}. The FT-IR spectrum of **4** (Figure 5b) clearly reveals the presence of absorption peaks of the P*t*BMA block (1724 cm^{-1}, 1394 and 1369 cm^{-1}). Most importantly, the signal characteristic of azido group at 2102 cm^{-1} is still clearly evident, indicating the presence of an azido group at the diblock junction.

The subsequent click reactions of PEG_{113}(-N_3)-*b*-P*t*BMA_{83} with monoalkynyl-terminated PDEA (*alkynyl*-$PDEA_{48}$ or *alkynyl*-$PDEA_{85}$) led to the facile preparation of well-defined ABC miktoarm star terpolymers, PEG(-*b*-P*t*BMA)-*b*-PDEA (**5**). An excess of *alkynyl*-PDEA was used to ensure the complete consumption of azido moieties in

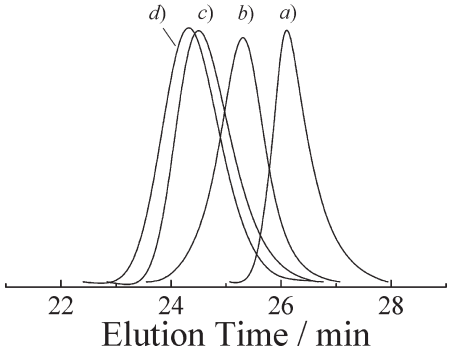


Figure 3. GPC traces of (a) PEG macroinitiator PEG_{113}(-N_3)-*Br*, (b) *alkynyl*-$PDEA_{48}$, (c) PEG_{113}(-N_3)-*b*-P*t*BMA_{83} copolymer, and (d) PEG_{113}(-*b*-P*t*BMA)$_{83}$-*b*-$PDEA_{48}$ miktoarm star terpolymer.

Table 1. Summary of Structural Parameters of Polymers Synthesized in This Work

samples	initiator	$M_{n,NMR}$ (kDa)	DP_{NMR}	$M_{n,GPC}$ (kDa) [a]	M_w/M_n [a]
alkynyl-$PDEA_{48}$	PBIB	9.1	48	8.1	1.17
alkynyl-$PDEA_{85}$	PBIB	16.0	85	14.6	1.15
PEG_{113}(-N_3)-*Br*		5.3	113	5.2	1.10
PEG_{113}(-N_3)-*b*-P*t*BMA_{83}	PEG_{113}(-N_3)-*Br*	17.1	83	12.5	1.21
PEG_{113}(-*b*-P*t*$BMA)_{83}$-*b*-$PDEA_{48}$		26.2	48	13.7	1.20
PEG_{113}(-*b*-P*t*$BMA)_{83}$-*b*-$PDEA_{85}$		33.1	85	17.3	1.19

[a]Molecular weight (M_n) and molecular distributions (M_w/M_n) were determined by GPC using THF as the eluent.

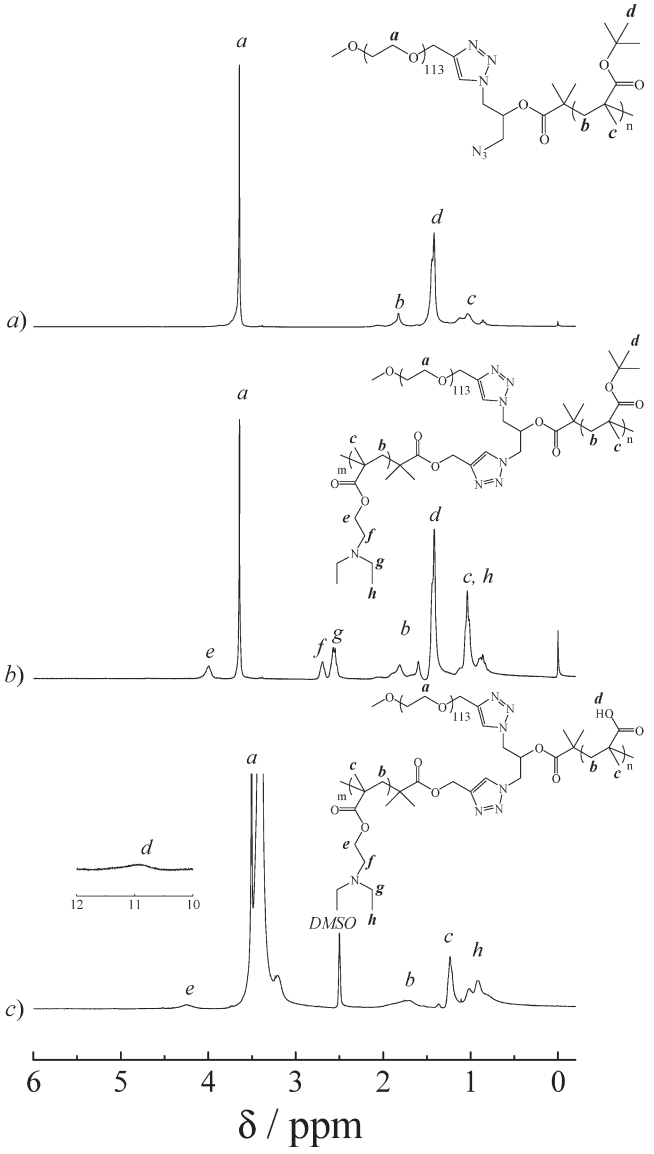


Figure 4. ^{1}H NMR spectra of (a) PEG_{113}(-N_3)-*b*-P*t*BMA_{83} copolymer in $CDCl_3$, (b) ABC miktoarm star terpolymer PEG_{113}(-*b*-P*t*$BMA)_{83}$-*b*-$PDEA_{48}$ in $CDCl_3$, and (c) PEG_{113}(-*b*-$PMAA)_{83}$-*b*-$PDEA_{48}$ miktoarm star terpolymer in DMSO-d_6.

PEG_{113}(-N_3)-*b*-P*t*BMA_{83}, and the reaction was conducted at 60 °C for 24 h. The removal of excess *alkynyl*-PDEA was facilely achieved by "clicking" onto azido-functionalized Merrifield resin and the subsequent precipitation step.[65,70]

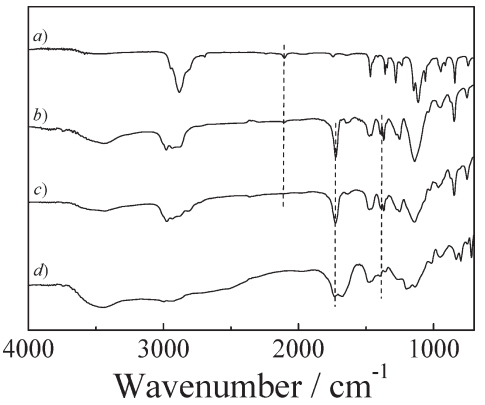


Figure 5. FT-IR spectra of (a) PEG macroinitiator PEG_{113}(-N_3)-*Br*, (b) PEG_{113}(-N_3)-*b*- P*t*BMA_{83} copolymer, (c) PEG_{113}(-*b*-P*t*$BMA)_{83}$-*b*-$PDEA_{48}$ miktoarm star terpolymer (**5**), and (d) PEG_{113}(-*b*-$PMAA)_{83}$-*b*-$PDEA_{48}$ miktoarm star terpolymer (**6**).

Figure 5 also shows the FT-IR spectrum of PEG_{113}(-*b*-P*t*$BMA)_{83}$-*b*- $PDEA_{48}$. Compared to that of **4**, we can clearly observe the complete disappearance of the absorbance peak characteristic of the azido group at 2102 cm^{-1}. This suggested the successful covalent attachment of PDEA arm to the diblock junction in **4**.

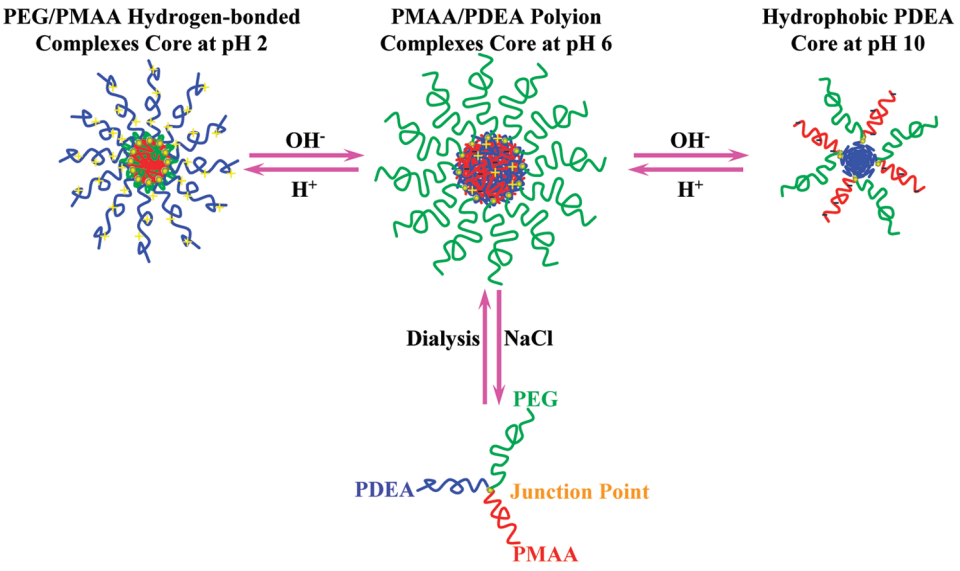
GPC analysis further supported the successful preparation of ABC miktoarm star terpolymer. When *alkynyl*-$PDEA_{48}$ was employed, GPC trace of PEG_{113}(-*b*-P*t*BMA_{83})-*b*-$PDEA_{48}$ was monomodal and symmetric (Figure 3d). Compared to those of the diblock precursor (**4**) and *alkynyl*-$PDEA_{42}$, the elution peak of PEG_{113}(-*b*-P*t*BMA_{83})-*b*-$PDEA_{48}$ shifted to higher MW side. GPC analysis revealed an M_n of 13.7 kDa and an M_w/M_n of 1.20 (Table 1). The relatively small elution peak shift of **5** relative to that of the diblock precursor (**4**) can be ascribed to the miktoarm star topology of the former.[8,56,61] From the ^{1}H NMR spectrum of **5** (Figure 4b), we can discern all characteristic signals of PEG, PDEA, and P*t*BMA segments, and the integral ratios between these peaks agreed quite well with designed block lengths. On the basis of the above results, we concluded that well-defined miktoarm star terpolymers, PEG(-*b*-P*t*BMA)-*b*-PDEA, have been reliably obtained via a combination of consecutive click reactions and ATRP.

PEG(-*b*-P*t*BMA)-*b*-PDEA were converted into zwitterionic ABC miktoarm star terpolymers, PEG(-*b*-PMAA)-*b*-PDEA (***6***), via hydrolysis under acidic conditions (TFA/CH_2Cl_2).[71] From Figure 4c, we can see the complete disappearance of characteristic resonance signal of *tert*-butyl groups at 1.4 ppm, indicating the complete hydrolysis of the P*t*BMA block. From the FT-IR spectrum of **6**

(70) Chen, G. J.; Tao, L.; Mantovani, G.; Ladmiral, V.; Burt, D. P.; Macpherson, J. V.; Haddleton, D. M. *Soft Matter* **2007**, *3*, 732–739.

(71) Mori, H.; Muller, A. H. E. *Prog. Polym. Sci.* **2003**, *28*, 1403–1439.

Scheme 2. Schematic Illustration of the pH-Responsive Formation of Three Types of Micellar Aggregates from PEG(-*b*-PMAA)-*b*-PDEA Zwitterionic ABC Miktoarm Star Terpolymers



(Figure 5d), we can also observe that the characteristic absorbance peak of the *tert*-butyl group at 1394 and 1369 cm^{-1} totally disappeared, as compared to that of **5**. Under the above hydrolysis conditions, PDEA block is expected to be unaffected.[6] Thus, the relatively narrow MW distribution of PEG(-*b*-P*t*BMA)-*b*-PDEA should be retained in the zwitterionic ABC miktoarm star terpolymer, PEG(-*b*-PMAA)-*b*-PDEA. The structural parameters of all the intermediate and final products obtained in this work are summarized in Table 1.

pH-Responsive Supramolecular Self-Assembly of Zwitterionic ABC Miktoarm Star Terpolymers. PEG is a well-known to be highly hydrophilic and water-soluble. PDEA homopolymer is a weak polybase, and its conjugated acid possesses a pK_a of 7.3; it exhibits pH-dependent solubility in aqueous solution.[72,73] It is water-insoluble at neutral or alkaline pH, whereas, below pH 6−7, it is soluble as a weak cationic polyelectrolyte due to protonation of tertiary amine residues. In contrast, PMAA, with a pK_a of 5.5, is an ionizable hydrophilic polymer.[6,74,75] It is molecularly soluble as a weak anionic polyelectrolyte in basic media and becomes less soluble in acidic solution.

Recently, Armes and co-workers[76] reported the pH-dependent micellization of a binary mixture of PEG-*b*-PDEA diblock copolymer and a PMAA homopolymer. This system forms three types of micellar aggregates in aqueous solution at ambient temperature, depending on the solution pH. A "trinity" of micelles form at varying pH conditions, with the cores comprising hydrophobic PDEA at high pH, interpolyelectrolyte complexes between cationic diblock copolymer and anionic homopolymer at intermediate pH, and interchain hydrogen-bonded complexes between PMAA and PEO block at low pH. Similarly, intriguing micellization behavior was also observed by Gohy et al.[77] from a binary mixture of poly(2-vinylpyridine)-*b*-PEG (P2VP-*b*-PEG) and PMAA-*b*-PEG diblock copolymers. More recently, Armes et al.[78] reported a novel linear zwitterionic ABC triblock copolymer comprising of a hydrophilic PEG block, a weak PDEA polybase block, and a weak polyacid block of poly(2-succinyloxyethyl methacrylate) (PSEMA). It can also form a "trinity" of micelles in aqueous solution at ambient temperature by simply adjusting solution pH.

On the basis of chemical intuition, at alkaline pH conditions, zwitterionic ABC miktoarm star terpolymer, PEG(-*b*-PMAA)-*b*-PDEA, will also self-assemble into micelles consisting of neutral and insoluble PDEA cores and hybrid coronas of PEG and ionized PMAA. In the pH range of 5−7, micelles possessing polyion complexes cores should be formed as a result of charge-compensation between partially ionized PMAA and partially protonated PDEA sequences. On the other hand, PEG and PMAA are well-known to form hydrogen-bonded complexes with 1:1 repeating molar units in aqueous solution.[79] Thus, upon further decreasing solution pH to <4, micelles consisting of hydrogen-bonded complex cores formed between fully protonated PMAA and PEG arms and protonated PDEA coronas will form (Scheme 2).

Figure 6 shows typical plots of the hydrodynamic radius distribution, $f(R_h)$, of micellar solutions prepared from PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ zwitterionic ABC miktoarm star terpolymer at varying pH and 25 °C, revealing the presence of only one type of diffusing species for all three cases. The polydispersity of the micelles, as evaluated by the ratio μ_2/Γ^2 from cumulants analysis, were relatively narrow (<0.1). At pH 10, tertiary amine residues of PDEA blocks

(72) Lee, A. S.; Gast, A. P.; Butun, V.; Armes, S. P. *Macromolecules* **1999**, *32*, 4302–4310.
(73) Butun, V.; Armes, S. P.; Billingham, N. C. *Polymer* **2001**, *42*, 5993–6008.
(74) Patrickios, C. S.; Sharma, L. R.; Armes, S. P.; Billingham, N. C. *Langmuir* **1999**, *15*, 1613–1620.
(75) Zhang, J.; Peppas, N. A. *Macromolecules* **2000**, *33*, 102–107.
(76) Weaver, J. V. M.; Armes, S. P.; Liu, S. Y. *Macromolecules* **2003**, *36*, 9994–9998.
(77) Gohy, J. F.; Varshney, S. K.; Jerome, R. *Macromolecules* **2001**, *34*, 3361–3366.
(78) Cai, Y. L.; Armes, S. P. *Macromolecules* **2004**, *37*, 7116–7122.
(79) Jiang, M.; Li, M.; Xiang, M. L.; Zhou, H. *Adv. Polym. Sci.* **1999**, *146*, 121–196.

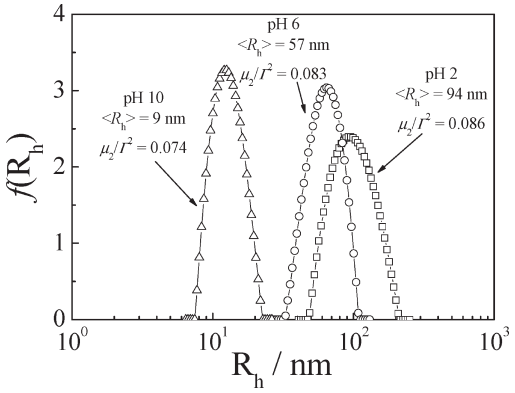


Figure 6. Typical hydrodynamic radius distributions, $f(R_h)$, obtained at various pH obtained for the aqueous solutions of zwitterionic PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ miktoarm star terpolymer at 25 °C. The polymer concentration was 1.0 g/L.

were completely deprotonated and they became hydrophobic. Moreover, PMAA blocks were completely ionized at pH 10. Dynamic LLS results revealed the formation of micelles with PDEA cores, with an intensity-average hydrodynamic radius, $\langle R_h \rangle$, of approximately 9 nm. Compared to those reported by Armes for linear ABC block copolymers,[78] the small size of PDEA-core micelles should be ascribed to the star topology of PEG(-*b*-PMAA)-*b*-PDEA, i.e., the costabilization of PEG and ionized PMAA chain sequences within micellar coronas.[38,47]

As chain segments in a micelle core possess decreased mobility compared to those of free chains in aqueous solution, ^{1}H NMR spectroscopy can be conveniently utilized to investigate the micellization of stimuli-responsive block copolymers, providing the structural information of which block sequence in the copolymer is forming the micellar core. Figure 7 shows ^{1}H NMR spectra of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ zwitterionic ABC miktoarm star terpolymer in D_2O at varying pH. At pH 10 and 25 °C, signal characteristic of PDEA block at δ = 1.4 ppm completely disappeared (it is worth note that methacrylate backbone signals observed at 0.8−1.8 ppm are due to PMAA block, rather than the PDEA block), while the signals from PEG and PMAA blocks are clearly visible. In agreement with dynamic LLS results, ^{1}H NMR studies further confirmed the formation of PDEA-core micelles at high pH, with the micelle coronas comprising a mixture of deprotonated PMAA chains and neutral PEG chains. A schematic illustration for the formation of PDEA-core micelles from PEG(-*b*-PMAA)-*b*-PDEA is shown in Scheme 2.

Figure 8 shows the variation of $\langle R_h \rangle$ with solution pH for micelles self-assembled from PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ and PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ in aqueous solution at 25 °C. $\langle R_h \rangle$ remains constant above pH 8 for both terpolymers. A comparison tells us that PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ forms considerably larger PDEA-core micelles with a $\langle R_h \rangle$ of ∼14 nm, as compared to that of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$. This is due to the higher PDEA content in PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$. Below approximately pH 8, $\langle R_h \rangle$ shows a considerable increase for both terpolymers, and the inflection point agrees reasonably well with the pK_a of PDEA. Below pH 8, carboxylic acid residues of PMAA block become progressively ionized, while the PDEA block starts to lose some of their cationic character due to partial deprotonation. Thus, charge-compensated micelles form with mixed PMAA/PDEA cores and

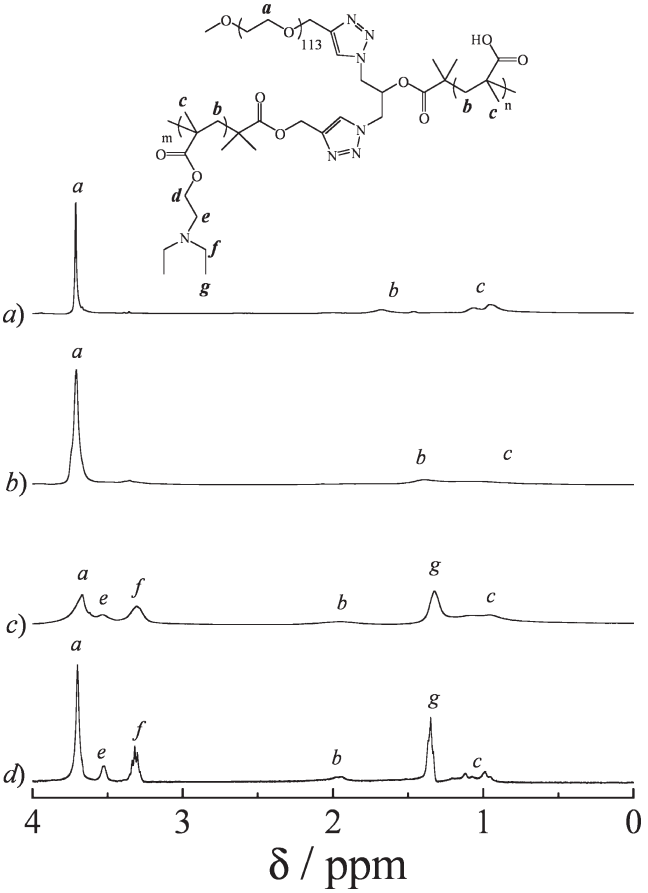


Figure 7. ^{1}H NMR spectra of the zwitterionic ABC miktoarm star terpolymer, PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$, in D_2O at different conditions: (a) pH 10 and 25 °C, (b) pH 6 and 25 °C, (c) pH 2 and 25 °C, and (d) pH 2 and 60 °C.

PEG coronas. Inspection of the ^{1}H NMR spectrum of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ recorded pH 6 and 25 °C confirmed that almost no PDEA and PMAA signals can be detected (Figure 7b), suggesting the formation of micelles possessing polyion complexes cores (Scheme 2).

In the case of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$, dynamic LLS revealed a $\langle R_h \rangle$ of 57 nm at pH 6 and 25 °C (Figure 6). On the other hand, static LLS revealed a $\langle R_h \rangle$ of 49 nm at the same condition, resulting in a $\langle R_h \rangle / \langle R_h \rangle$ ratio of 0.86. The ratio is in reasonable agreement with that predicted for nondraining hard spheres.[80] From Figure 8a, we can see that $\langle R_h \rangle$ increased and reached a local plateau (∼58 nm) in the pH range of 4.7−6.5. The theoretical isoelectric point (IEP) of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ was calculated to be 5.62, according to the equation proposed by Patrickios and co-workers.[74,81] Thus, the midpoint of the plateau region in the $\langle R_h \rangle$−pH curve generally agreed with the calculated IEP for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$. With longer PDEA arms, PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ possessed a theoretical IEP of 6.45. It was found that the aggregation behavior of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ is quite different compared to that of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$. In this case, $\langle R_h \rangle$ increased dramatically below pH 8 and reached a maximum

(80) Brown, W. *Light Scattering: Principles and Development*; Clarendon Press: Oxford, England, **1996**.
(81) Patrickios, C. S.; Hertler, W. R.; Abbott, N. L.; Hatton, T. A. *Macromolecules* **1994**, *27*, 930–937.

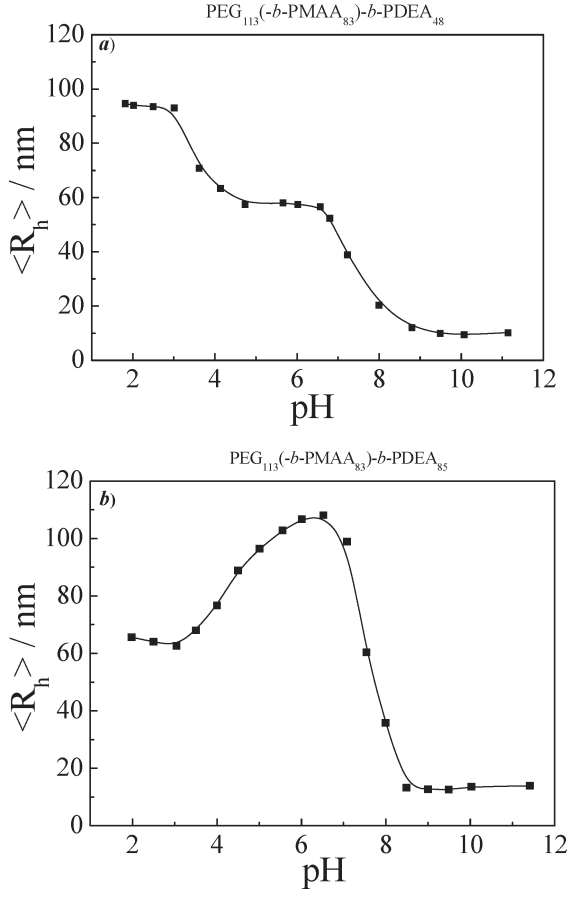


Figure 8. Variation of intensity-average hydrodynamic radius, $\langle R_h \rangle$, as a function of solution pH obtained for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ and PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ in aqueous solution at 25 °C. The polymer concentration was fixed at 1.0 g/L.

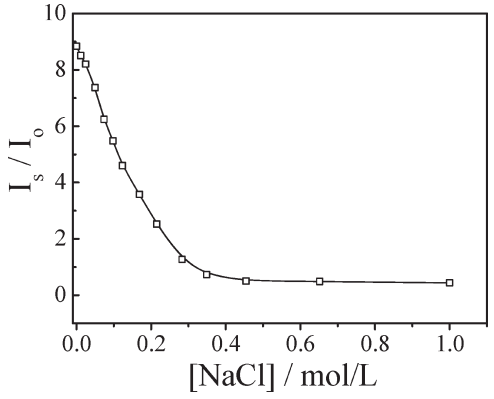


Figure 9. Variation of scattered intensity I_s/I_o as a function of NaCl concentrations obtained for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ in aqueous solution at 25 °C and pH 6.0.

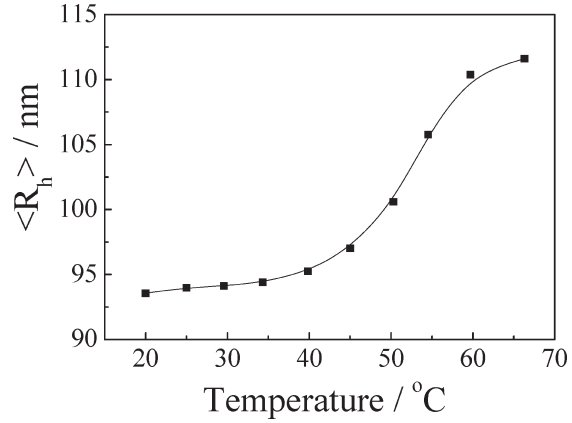


Figure 10. Variation of intensity-average hydrodynamic radius, $\langle R_h \rangle$, as a function of temperatures obtained for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ in aqueous solution at pH 2 and a concentration of 1.0 g/L.

at approximately pH 6.5 (Figure 8b). It is well-known that zwitterionic diblock copolymers usually precipitate from aqueous solution at their IEPs. In the present study, nonionic PEG block can act as a steric stabilizer for polyion complexes, allowing the formation of stable micellar aggregates at intermediate pH.

It is well-known that the colloidal stability of polyion complexes was very sensitive to the ionic strengths of the aqueous solution and polyion complexes micelles cannot form at high salt concentrations, due to that electrostatic interaction can be substantially attenuated under those conditions. To test the hypothesis that micelles formed from the PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ zwitterionic miktoarm star terpolymer in the range of pH 4.7−6.5 were due to polyion complexation, additional dynamic LLS studies were carried out in the presence of increasing amounts of small molecule electrolyte. The scattering intensity of the aqueous PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ solution at pH 6.0 sharply decreased upon increasing NaCl concentration (Figure 9), indicating that micelle dissociation occurred as a result of electrostatic screening. No micelle persisted when NaCl concentration exceeded 0.4 mol/L, and this confirmed that electrostatic interactions are the driving force for micellization in the pH range of 4.7−6.5.

Upon further decreasing solution pH, PMAA segments will be protonated, and this will break up electrostatic interactions between partially ionized PMAA and partially protonated PDEA blocks at intermediate pH. However, hydrogen bonding interactions between protonated PMAA and PEG will occur below pH 4.[77,82−84] So it is quite reasonable to speculate that colloid aggregates with PMAA/PEG hydrogen-bonded complexes cores will form at low pH range, with the fully protonated PDEA blocks forming micellar coronas. Dynamic LLS measurement indicated the formation of colloid aggregates with $\langle R_h \rangle$ of 94 nm for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ (Figure 8a). Moreover, static LLS revealed a $\langle R_h \rangle$ of 85 nm, and the $\langle R_h \rangle/\langle R_h \rangle$ ratio was calculated to be 0.89, again suggesting the formation of spherical aggregates. From the ^{1}H NMR spectrum recorded for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ at pH 2 and 25 °C (see Figure 7c), we can clearly observe the suppression of the PEG signals at $\delta = 3.7$ ppm, suggesting the formation of hydrogen-bonded PEG/PMAA complexes cores. The residual PEG signals can be ascribed to PEG repeating units that have not participated in hydrogen bonding interactions with protonated PMAA. This is rea-

(82) Mathur, A. M.; Drescher, B.; Scranton, A. B.; Klier, J. *Nature* **1998**, *392*, 367–370.
(83) Holappa, S.; Karesoja, M.; Shan, J.; Tenhu, H. *Macromolecules* **2002**, *35*, 4733–4738.
(84) Holappa, S.; Kantonen, L.; Winnik, F. M.; Tenhu, H. *Macromolecules* **2004**, *37*, 7008–7018.

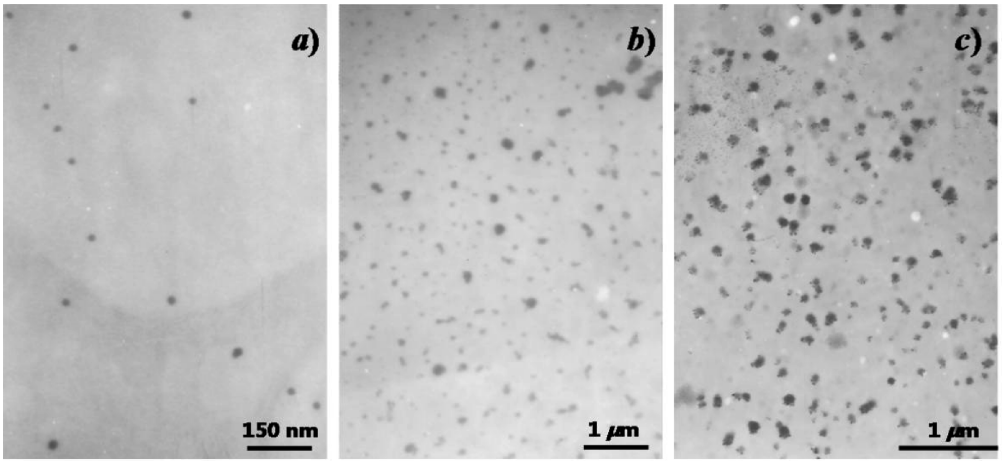


Figure 11. Typical TEM images obtained by drying aqueous solutions of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ zwitterionic ABC miktoarm star terpolymer at 25 °C and different pH: (a) 10, (b) 6, and (c) 2.

sonable considering that PMAA and PEG tend to form complexes at a 1:1 repeating molar ratio, as long as the MW of PEG exceeds a threshold value of ~2000.[71] It should be noted that at pH 2, PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ formed smaller micellar aggregates with a $\langle R_h \rangle$ of ~65 nm, compared to that that of PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$. This can be explained by the fact that fully protonated PDEA with larger chain lengths can exhibit stronger stabilization capability for the hydrogen-bonded complexes cores.

Hydrogen-bonding interactions are known to be temperature-sensitive, and micellar aggregates possessing hydrogen-bonded complexes cores tend to be disrupted at elevated temperatures.[85,86] Figure 10 shows the variation of $\langle R_h \rangle$ as a function of temperatures for aggregates formed from PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ at pH 2.0. It can be clearly seen that $\langle R_h \rangle$ abruptly increases above ~40 °C. The observed $\langle R_h \rangle$ increase with temperatures can be ascribed to the structural rearrangement from micelles possessing hydrogen-bonded complex cores at room temperature to micelles possessing hydrophobic PMAA cores. This has been further confirmed by ^{1}H NMR analysis, which reveals a relatively intense PEG signal at δ = 3.7 ppm (see Figure 7d) for PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{48}$ at 60 °C and pH 2, compared to that at 25 °C and pH 2 (Figure 7c). This suggests the disruption of hydrogen-bonding interactions between protonated PMAA and PEG sequences at elevated temperatures. Similar temperature-dependent structural rearrangement has also been reported by Gohy et al.[77] and Armes et al.[78]

The actual morphology of different types of micellar aggregates formed from PEG_{113}(-*b*-$PMAA_{83}$)-*b*-$PDEA_{85}$ in aqueous solution at various pH were observed by TEM at 25 °C (Figure 11). All the images clearly revealed the presence of spherical nanoparticles around 20, 120, and 70 nm in diameter for micelles at pH 10, pH 6, and pH 2, respectively. As TEM determines micelle dimensions in the dry state, while dynamic LLS reports the intensity-average dimensions of micelles in solution which contains considerable contribution from the swollen corona, it is reasonable that the micelle sizes determined by TEM were smaller than those determined by LLS.

(85) Liu, S. Y.; Jiang, M.; Liang, H. J.; Wu, C. *Polymer* **2000**, *41*, 8697–8702.
(86) Liu, S. Y.; Pan, Q. M.; Xie, J. W.; Jiang, M. *Polymer* **2000**, *41*, 6919–6929.

Conclusion

Well-defined ABC miktoarm star terpolymers, PEG(-*b*-P*t*BMA)-*b*-PDEA, were synthesized via a combination of consecutive click reactions and ATRP. The obtained miktoarm star terpolymers were successfully converted into corresponding PEG(-*b*-PMAA)-*b*-PDEA zwitterionic ABC miktoarm star terpolymers by hydrolysis in acidic conditions. Three types of micellar aggregates can be formed by these zwitterionic ABC miktoarm star terpolymers in aqueous solution at ambient temperature by simply adjusting solution pH at room temperature. The driving forces for forming these three types of micelles were hydrophobic interactions, interpolyelectrolyte complexation, and hydrogen-bonding, respectively. At high pH, conventional micelles with hydrophobic PDEA cores and PEG/ionized PMAA hybrid coronas are formed. At around the IEP, micelles possessing polyion complex cores, which are very sensitive to the ionic strength of solutions, are formed. Another type of micellar aggregates possessing hydrogen-bonded complex cores stabilized by protonated PDEA coronas are formed at low pH. This is believed to be the first report of the synthesis and remarkable reversible pH-responsive supramolecular self-assembly of double hydrophilic ABC miktoarm star terpolymers.

Acknowledgment. The financial support of the National Natural Scientific Foundation of China (NNSFC) Projects (20534020, 20674079, 20874092, and 50425310), the Specialized Research Fund for the Doctoral Program of Higher Education (SRFDP), and the Program for Changjiang Scholars and Innovative Research Team in University (PCSIRT) are gratefully acknowledged.