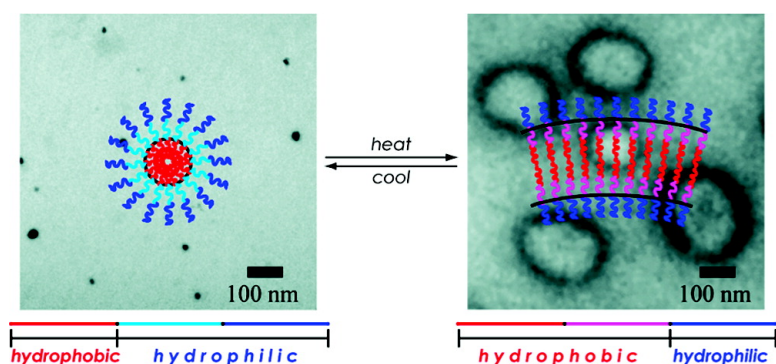


Reversible Restructuring of Aqueous Block Copolymer Assemblies through Stimulus-Induced Changes in Amphiphilicity

Anand Sundararaman, Tim Stephan, and Robert B. Grubbs

J. Am. Chem. Soc., **2008**, 130 (37), 12264-12265 • DOI: 10.1021/ja8052688 • Publication Date (Web): 23 August 2008

Downloaded from <http://pubs.acs.org> on February 8, 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](#)

Reversible Restructuring of Aqueous Block Copolymer Assemblies through Stimulus-Induced Changes in Amphiphilicity

Anand Sundararaman, Tim Stephan, and Robert B. Grubbs*

Department of Chemistry and Center for Nanomaterials Research, Dartmouth College,
Hanover, New Hampshire 03755

Received July 15, 2008; E-mail: robert.b.grubbs@dartmouth.edu

Controlling the self-assembly of amphiphiles into nanometer- and micron-scale aggregates is of interest in applications that involve biphasic systems, including drug delivery and catalysis.¹ As the relative volumes occupied by the hydrophobic and hydrophilic components of amphiphiles strongly influence the structural characteristics of the assemblies they form in water,² amphiphiles for which the hydrophilic/hydrophobic volume ratio can be reversibly switched between two values should be capable of undergoing drastic changes in the sizes and shapes of the assemblies that they form. As an example of this behavior, we herein describe the solution behavior of amphiphilic ABC triblock copolymers that form small spherical micelles at low temperatures and reassemble into large vesicles at higher temperatures.

Controlled polymerization methods have enabled the synthesis of amphiphilic copolymers that self-assemble into a variety of structures.³ Incorporation of a polymer that has stimulus-dependent miscibility with a given solvent into an amphiphile provides a powerful method for reversibly changing the size and structure of the resulting assemblies.⁴ Thermomorphic polymers such as poly(*N*-isopropylacrylamide) (PNIPA), which exhibit a lower critical solution temperature (LCST) in an appropriate solvent (water for PNIPA) below which they are miscible and above which they are immiscible, have been extensively investigated in such systems. The temperature-induced assembly of block and graft copolymers with water-soluble and thermomorphic components has been shown, among other factors, to be strongly influenced by the hydrophilic/thermomorphic balance.⁵

Prior studies have largely focused upon binary amphiphiles where transitions from individual chains to aggregates occur upon application of an appropriate stimulus. Polymer amphiphiles that form differently structured assemblies at different pH values have been reported,⁶ but those that form assemblies at temperatures both above and below the LCST have been less well studied.⁷ Here we describe the solution behavior of a three-component ABC triblock copolymer with a thermally responsive block located between a hydrophilic and a hydrophobic block (Figure 1). Such copolymers should be more hydrophilic below the LCST of the central block, thus forming smaller assemblies with highly curved interfaces, and more hydrophobic above the LCST, thus assembling into larger aggregates with less interfacial curvature. If the glass-transition temperature (T_g) of the hydrophobic block is lower than the LCST of the thermoresponsive block, adjusting the solution temperature through the LCST should result in transitions between larger and smaller aggregates with structures that depend upon the molecular weight and composition of the copolymers.

Our initial efforts to prepare such hydrophilic–thermomorphic–hydrophobic block copolymers have used the sequential nitroxide-mediated polymerization of *N*-isopropylacrylamide and isoprene from alkoxyamine-functionalized poly(ethylene oxide) (PEO) macroinitiators⁸ to afford the ABC triblock copolymers PEO-*block*-

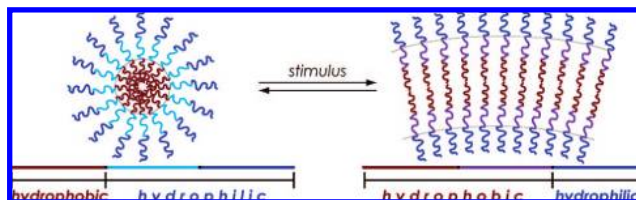
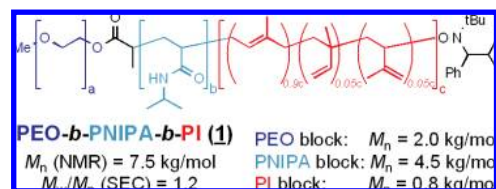


Figure 1. Schematic illustration of the expected change in amphiphilic balance for ABC triblock copolymer chains with a stimulus-responsive B block (bottom) and interfacial curvature for assemblies of these triblock copolymers (top) in water upon passage through the lower critical solution temperature of the B block.

Chart 1



PNIPA-*block*-poly(isoprene) (PEO-*b*-PNIPA-*b*-PI, **1**, Chart 1). Our initial structural studies of these polymers have focused upon a low molecular weight copolymer (7.5 kg/mol) with a relatively large central PNIPA block (LCST ≈ 32 °C) and a small PI block ($T_g < -58$ °C) to maximize the shift in amphiphilic balance upon heating through the LCST.

Assembly of copolymer **1** in water was clearly demonstrated by the absence of the characteristic poly(isoprene) (PI) peaks in ¹H NMR spectra taken in D₂O (Figure S3).⁹ Fluorescence studies with pyrene showed the strong increase of excitation intensity expected to result from sequestration of pyrene within the hydrophobic PI core and gave a critical micelle concentration of 6 mg/L (0.9 μ m) (Figures S4, S5).¹⁰ Further solution characterization of assemblies of copolymer **1** in water was performed at concentrations above the CMC.

¹H NMR studies¹¹ of the thermoresponsive behavior of copolymer **1** in D₂O showed the dehydration of the PNIPA block to occur at a slightly higher temperature (39 °C) than that observed for the parent diblock copolymer PEO-*b*-PNIPA (34 °C) (Figures S6, S7). The hydration/dehydration cycle was repeated four times without appreciable change in the appearance of the solution. After five cycles, a small amount of precipitate, which could be redissolved with agitation, was observed. Turbidimetry showed no significant change in transmittance below 60 °C over 2.5 h. As turbidity arises from large light-scattering aggregates and the reassembly of copolymer **1** into larger aggregates takes several weeks (see below), the lack of an observed cloud point does not seem unusual.

Dynamic light scattering (DLS) at 20 °C of an aqueous solution (6 mg/mL) of copolymer **1** showed an average hydrodynamic radius

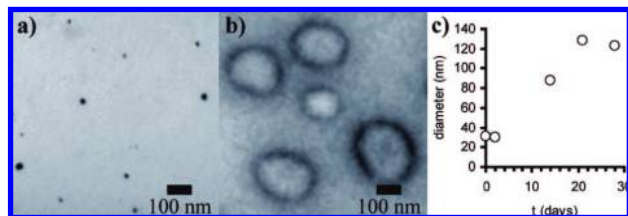


Figure 2. TEM images of copolymer **1** (a) as drop-cast from aqueous solution at room temperature (OsO₄ stain) and (b) as drop-cast from aqueous solution heated at 65 °C for 4 weeks (OsO₄ stain). (c) DLS diameter with time of aqueous aggregates of **1** at 65 °C.

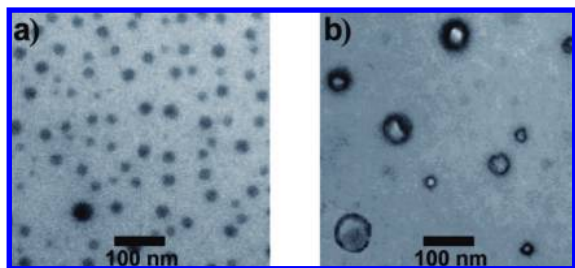


Figure 3. TEM images of (a) room temperature and (b) 65 °C cross-linked samples of copolymer **1** stained with OsO₄.

(R_h) of 12 nm. When the temperature was gradually increased (20 °C/h) from 20 to 60 °C, R_h initially decreased between 20 and 40 °C to 10.5 nm as the PNIPA block dehydrated and increased only slightly to 13.0 nm between 40 and 65 °C (Figure S8).

Longer-term heating allowed reassembly of the polymer aggregates. No change in R_h was observed after 48 h at 65 °C. After 2 weeks at 65 °C, R_h had increased to 44 nm, and after 3 weeks a substantial increase of R_h to 64 nm was observed (Figures 2c, S9). Longer heating did not result in further change in assembly size. Cooling these solutions to 20 °C resulted in the reformation of smaller assemblies over ~48 h (Figure S10).

TEM micrographs of samples prepared from aqueous solutions at room temperature and stained with OsO₄ show spherical micelles with a mean radius of ~9 nm (Figure 2a). The aggregates formed at higher temperatures were visualized by heating a copolymer solution at 65 °C for 4 weeks, adding a drop of this solution to a TEM grid set on a hotplate at 65 °C, and allowing it to dry for a few minutes before staining with OsO₄ vapors. TEM micrographs of the resulting samples confirm the formation of large vesicular assemblies (Figure 2b) with a mean radius greater than 100 nm. The TEM sample preparation techniques lead to the observation of aggregate sizes that differ from those observed by solution techniques, but these results qualitatively confirm a large change in aggregate size after heating above the LCST of the PNIPA block.

In efforts to stabilize the favored high-temperature structures at lower temperatures, the assemblies were cross-linked by treatment of aqueous solutions of copolymer **1** with a radical source that has previously been used to cross-link PEO-*b*-poly(diene) micelles.^{8,12} Room-temperature cross-linked structures have slightly larger sizes (TEM radius \approx 15 nm; LS R_h = 13 nm) than do the noncross-linked samples (Figures 3a, S11). Cross-linking was also carried out above the LCST (65 °C) on samples that had been heated at 65 °C for 14 days. After cross-linking, these samples were stirred at room temperature for 48 h before being cast onto TEM grids

and stained with OsO₄. The resulting TEM images show larger assemblies, most of which appear to be vesicles with apparent diameters ranging from 45 to 120 nm (Figure 3b). The cross-linking process and conditions clearly influence the assembly size, but the observation of large vesicular aggregates above the LCST clearly reflects the shift in amphiphilic balance in these systems.

These results demonstrate that incorporation of a thermoresponsive block into an amphiphilic block copolymer results in discrete hydrophobic/hydrophilic volume ratios above and below the LCST of the thermoresponsive block, thus allowing the polymer assembly to be switched between large and small aggregates as a function of temperature. Copolymers with different compositions and comprising other hydrophilic, hydrophobic, and thermoresponsive blocks should be capable of similar transformations and are currently under investigation.

Acknowledgment. This work was supported by the National Science Foundation (DMR-0239697) and the Donors of the Petroleum Research Fund, administered by the American Chemical Society. Ryan Lau carried out preliminary experiments related to this work.

Supporting Information Available: Synthesis, characterization details, and DLS/¹H NMR/TEM data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) (a) Rapoport, N. *Prog. Polym. Sci.* **2007**, *32*, 962–990. (b) Tan, Y.-C.; Hettiarachchi, K.; Siu, M.; Pan, Y.-R.; Lee, A. P. *J. Am. Chem. Soc.* **2006**, *128*, 5656–5658. (c) Cui, H.; Chen, Z.; Zhong, S.; Wooley, K. L.; Pochan, D. J. *Science* **2007**, *317*, 647–650. (d) Harada, A.; Kataoka, K. *Prog. Polym. Sci.* **2006**, *31*, 949–982. (e) Savariar, E. N.; Aathimaniandan, S. V.; Thayumanavan, S. *J. Am. Chem. Soc.* **2006**, *128*, 16224–16230.
- (2) Israelachvili, J. N. *Intermolecular and Surface Forces*, 2nd ed.; Academic Press: San Diego, 1991.
- (3) (a) Lazzari, M.; Liu, G.; Lecommandoux, S. Eds. *Block Copolymers in Nanoscience*; Wiley-VCH: Hoboken, NJ, 2006. (b) Discher, B. M.; Won, Y.-Y.; Ege, D. S.; Lee, J. C. M.; Bates, F. S.; Discher, D. E.; Hammer, D. A. *Science* **1999**, *284*, 1143–1146. (c) Discher, D. E.; Ortiz, V.; Srinivas, G.; Klein, M. L.; Kim, Y.; Christian, D.; Cai, S.; Photos, P.; Ahmed, F. *Prog. Polym. Sci.* **2007**, *32*, 838–857. (d) O'Reilly, R. K.; Hawker, C. J.; Wooley, K. L. *Chem. Soc. Rev.* **2006**, *35*, 1068–1083. (e) Read, E. S.; Armes, S. P. *Chem. Commun.* **2007**, 3021–3035.
- (4) (a) Aoshima, S.; Kanaoka, S. *Adv. Polym. Sci.* **2008**, *210*, 169–208. (b) Aseyev, V.; Tenhu, H.; Winnik, F. *Adv. Polym. Sci.* **2006**, *196*, 1–85. (c) Gohy, J.-F. In *Block Copolymers in Nanoscience*; Lazzari, M., Liu, G., Lecommandoux, S. Eds.; Wiley-VCH: Weinheim, 2006; pp 91–116.
- (5) (a) Van Durme, K.; Van Assche, G.; Aseyev, V.; Raula, J.; Tenhu, H.; Van Mele, B. *Macromolecules* **2007**, *40*, 3765–3772. (b) Qin, S.; Geng, Y.; Discher, D. E.; Yang, S. *Adv. Mater.* **2006**, *18*, 2905–2909. (c) Zhang, W.; Shi, L.; Wu, K.; An, Y. *Macromolecules* **2005**, *38*, 5743–5747. (d) Li, Y.; Lokitz, B. S.; McCormick, C. L. *Macromolecules* **2006**, *39*, 81–89.
- (6) (a) Liu, S.; Armes, S. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 1413–1416. (b) Büttin, V.; Liu, S.; Weaver, J. V. M.; Bories-Azeau, X.; Cai, Y.; Armes, S. P. *React. Funct. Polym.* **2006**, *66*, 157–165. (c) Liu, F.; Eisenberg, A. *J. Am. Chem. Soc.* **2003**, *125*, 15059–15064. (d) Xu, C.; Wayland, B. B.; Fryd, M.; Winey, K. I.; Composto, R. J. *Macromolecules* **2006**, *39*, 6063–6070.
- (7) (a) Aubrecht, K. B.; Grubbs, R. B. *J. Polym. Sci. Part A: Polym. Chem.* **2005**, *43*, 5156–5167. (b) Hay, D. N. T.; Rickert, P. G.; Seifert, S.; Firestone, M. A. *J. Am. Chem. Soc.* **2004**, *126*, 2290–2291.
- (8) Wegrzyn, J. K.; Stephan, T.; Lau, R. N.; Grubbs, R. B. *J. Polym. Sci. Part A: Polym. Chem.* **2005**, *43*, 2977–2984.
- (9) Kim, B. J.; Chang, J. Y. *Macromolecules* **2006**, *39*, 90–94.
- (10) Kalyanasundaram, K.; Thomas, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 2039–2044.
- (11) (a) Vamvakaki, M.; Palioura, D.; Spyros, A.; Armes, S. P.; Anastasiadis, S. H. *Macromolecules* **2006**, *39*, 5106–5112. (b) Nolan, C. M.; Reyes, C. D.; Debord, J. D.; Garcia, A. J.; Lyon, L. A. *Biomacromolecules* **2005**, *6*, 2032–2039. (c) Gan, D.; Lyon, L. A. *Macromolecules* **2002**, *35*, 9634–9639.
- (12) Discher, B. M.; Bermudez, H.; Hammer, D. A.; Discher, D. E.; Won, Y.-Y.; Bates, F. S. *J. Phys. Chem. B* **2002**, *106*, 2848–2854.

JA8052688