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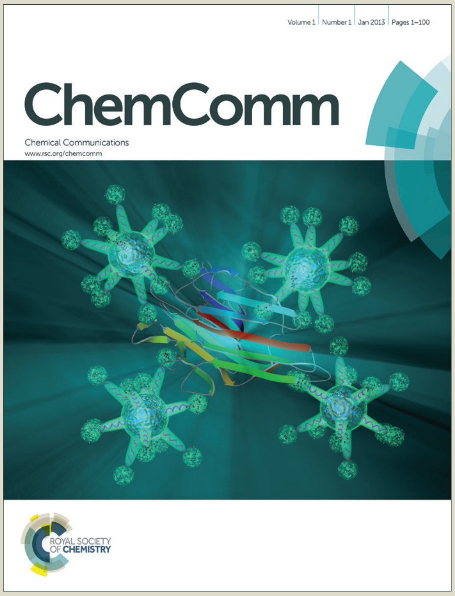

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COMMUNICATION

Nanoparticle-to-vesicle and nanoparticle-to-toroid transitions of pH-sensitive ABC triblock copolymer by in-to-out switch

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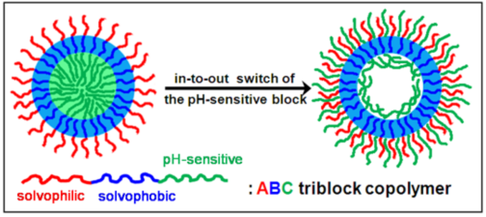
An efficient way to nanoparticle-to-vesicle transition of ABC triblock copolymer by in-to-out switch of the pH-sensitive core-forming C block is enclosed.

Vesicles of block copolymers have aroused great interest.[1-8] Diblock copolymer vesicles formed either by micellization in the block-selective solvent or by polymerization-induced self-assembly are widely reported.[9-16] However, generating ABC triblock copolymer vesicles is rather limited.[17-24] Compared with the AB diblock copolymer vesicles, ABC triblock copolymer vesicles are identified by their unsymmetrical structure, in which the short block chains with weak steric repulsion are generally located at the inner surface of the bilayer structure and the long block chains are tethered at the outer surface.[23,24] For triblock copolymers, the morphology of their nano-assemblies is determined either by the block order (ABC, ACB, and BAC),[25-29] the block length and the solvophilic/solvophobic ratio[30-33] or by the experimental conditions including the solvent temperature and pH.[34-38] By changing one of the above-mentioned parameters, the morphology of the triblock copolymer nano-assemblies may be tuned. Recently, Grubbs et al. have reported an elegant strategy to achieve micelle-to-vesicle transition of ABC triblock copolymers containing a central thermo-responsive B block.[39,40] When temperature increased, the temperature-sensitive soluble-to-insoluble phase transition of the central thermo-responsive B block occurred at temperature above the lower critical solution temperature (LCST), the packing parameter p[41] or the solvophilic/solvophobic ratio of the triblock copolymer was changed, and therefore the micelle-to-vesicle transition took place. Despite the success,[39,40] very limited morphology transition of ABC triblock copolymers has been reported possibly due to the complex structure and the slow motion of the triblock copolymer chains at temperature below the glass transition temperature (T_g).



Scheme 1. The proposed strategy of the nanoparticle-to-vesicle transition of ABC triblock copolymer through the in-to-out switch of the pH-sensitive core-forming C block.

In this contribution, well-defined corona-shell-core nanoparticles of poly(*N*,*N*-dimethylacrylamide)-*block*-polystyrene-*block*-poly[*N*-(4-vinylbenzyl)-*N*,*N*-dibutylamine] (PDMA-*b*-PS-*b*-PVBA) are prepared by a new heterogeneous RAFT polymerization named seeded dispersion RAFT polymerization,[42] and then the nanoparticle-to-vesicle transition of the pH-sensitive ABC triblock copolymer to form unsymmetrical ABC triblock copolymer vesicles through the in-to-out switch of the pH-sensitive core-forming C block as shown in Scheme 1 is proposed.

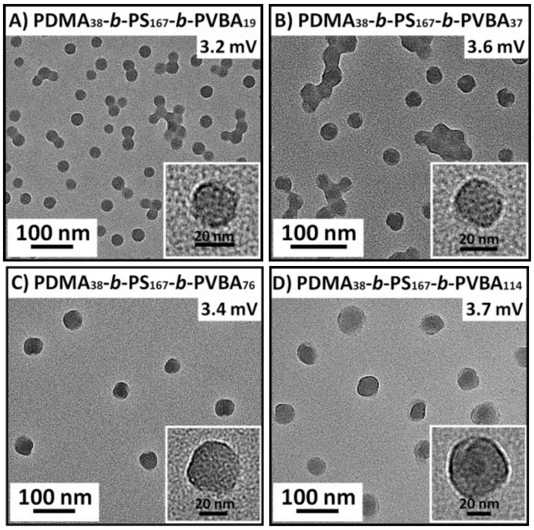


Figure 1. The TEM images of the PDMA-*b*-PS-*b*-PVBA nanoparticles prepared by seeded dispersion RAFT polymerization. Insets: the zeta potential of the triblock copolymer nanoparticles.

The PDMA-*b*-PS-*b*-PVBA corona-shell-core nanoparticles were prepared by seeded dispersion RAFT polymerization as shown in Scheme S2. This seeded dispersion RAFT polymerization includes three steps: (1) synthesis of the $PDMA_{38}$-TTC macro-RAFT agent [Note: the subscript herein and in the subsequent discussion represents the polymerization degree (DP) of the monomer and TTC represents the RAFT terminal of trithiocarbonate], (2) the preparation of the diblock copolymer seed-nanoparticles of $PDMA_{38}$-*b*-PS_{167}-TTC by dispersion RAFT polymerization (Figure S1), and (3) the preparation of the PDMA-*b*-PS-*b*-PVBA triblock copolymer corona-shell-core nanoparticles. Four triblock copolymer corona-shell-core nanoparticles with different DP of the core-forming PVBA block as listed in Table 1 are prepared. The synthesized polymers are characterized by GPC analysis (Figure S2), ^{1}H NMR analysis (Figure S3), and differential scanning calorimeter (DSC) analysis

(Figure S4), and the results are summarized in Table 1. Figure 1 shows the TEM images of the four triblock copolymer corona-shell-core nanoparticles, from which the increasing size of the nanoparticles with the increasing DP of the core-forming PVBA block is indicated. The ABC triblock copolymer nanoparticles should have corona-shell-core structure as shown in Scheme 1, in which the pH-sensitive C block of PVBA forms the core, the solvophobic B block of PS forms the shell, and the solvophilic A block of PDMA forms the corona, since the PVBA and PS blocks are immiscible as indicated by the two separate T_g peaks corresponding to the PS and PVBA blocks (Figure S4).

Table 1. Summary of the synthesized polymers.

Polymer[a]	$M_{n,th}$[b] (kg/mol)	$M_{n,NMR}$[c] (kg/mol)	$M_{n,GPC}$[d] (kg/mol)	PDI	Size (nm)
A_{38}-TTC	4.0	4.0	2.3	1.03	-
$A_{38}B_{167}$-TTC	21.3	21.5	18.6	1.12	25
$A_{38}B_{167}C_{19}$	26.2	26.2	20.6	1.11	26
$A_{38}B_{167}C_{37}$	30.6	30.6	27.3	1.13	29
$A_{38}B_{167}C_{76}$	40.2	40.1	35.9	1.17	34
$A_{38}B_{167}C_{114}$	49.1	49.4	46.2	1.11	36

[a] A represents the PDMA block, B represents the PS block and C represents the PVBA block. [b] Theoretical molecular weight by eq S1. [c] Molecular weight by ^{1}H NMR analysis. [d] Molecular weight by GPC analysis.

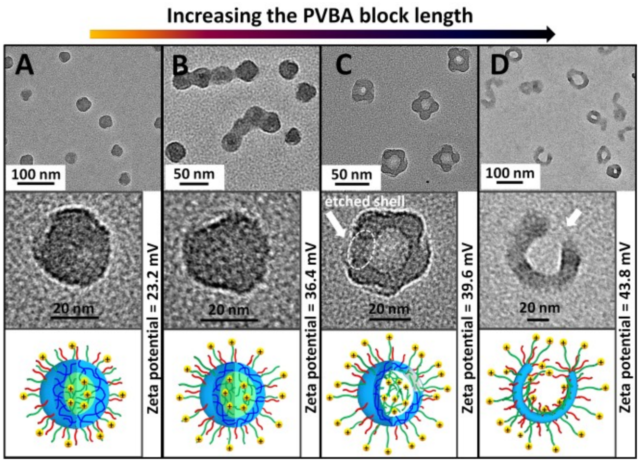


Figure 2. The TEM images of the triblock copolymer nano-objects of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{19}$ (A), PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{37}$ (B), PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ (C), and PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{114}$ (D) after acidification in the 8/2 ethanol/water mixture. Insets: the schematic structure and zeta potential of the triblock copolymer nanoparticles.

Due to the appending dibutylamine groups, the PVBA block is pH-sensitive. That is, the PVBA block can be ionized by hydrochloride (HCl) to form poly[*N*-(4-vinylbenzyl)-*N*,*N*-dibutylamine hydrochloride] (PVBAH) and becomes soluble in acidic aqueous solution with pH < 4.5 as discussed elsewhere.[43] To check the pH-sensitive morphology transition of the corona-shell-core nanoparticles of PDMA-*b*-PS-*b*-PVBA, these nanoparticles are initially acidified by HCl (pH ≈ 2) in the ethanol/water mixture (8/2 by weight) at room temperature (~25 ^{0}C) for three days, then separated by centrifugation (12500 rpm, 15 min), and lastly re-dispersed in water or deuterated water (D_2O) for the next characterization. It is found that the chain length or DP of the core-forming C block of PVBA greatly affects the morphology transition of the ABC triblock copolymer nanoparticles. As shown in Figure 2, for the triblock copolymers of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{19}$ and PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{37}$ containing a short core-forming PVBA block, 29 nm nanoparticles (Figure 2A) and 33 nm nanoparticles (Figure 2B) with size slightly larger than those before acidification are observed, suggesting no morphology transition of the two triblock copolymers. Whereas, when the DP of the core-forming C block of PVBA increases to 76, the nanoparticle-to-vesicle transition occurs, and 39 nm petal-like vesicles of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ with etched shell are formed (Figure 2C). When the DP of the core-forming PVBA block increases to 114, the nanoparticle-to-toroid transition occurs, and the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{114}$ toroids with size ranging from 60 to 80 nm are formed (Figure 2D). Interestingly, some of the ABC triblock copolymer toroids are disjointed into wormlike rods. The formation of triblock copolymer toroids of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{114}$ is also confirmed by SEM and AFM (Figure S5).

The nanoparticle-to-vesicle and nanoparticle-to-toroid transitions of the triblock copolymer containing a long PVBA block are ascribed to the in-to-out switch of the ionized core-forming PVBA block (PVBAH), which is confirmed by the zeta potential analysis and the H NMR analysis of the triblock copolymer nano-objects before and after acidification in the 8/2 ethanol/water mixture. It is found that the zeta potential of the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ nano-objects greatly increases after the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ being acidified (Figure S6). Besides, based on the ^{1}H NMR spectra of the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ nano-objects before and after acidification, it is found that the normalized intensity of the typical signal at δ = 0.76 ppm $[N(CH_2CH_2CH_2C\boldsymbol{H}_3)_2]$ corresponding to the PVBA$_{76}$ block is greatly enhanced (Figure 3). Whereas, in the control experiment at the case of the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{37}$ nanoparticles without nanoparticle-to-vesicle transition, the intensity corresponding to the short PVBA$_{37}$ block just slightly increases compared with those before acidification (Figure S7). These results confirm the in-to-out switch of the long core-forming PVBA$_{76}$ block during the nanoparticle-to-vesicle transition. Furthermore, the amount of the out-migrated PVBAH chains from the core-layer to the corona can be approximately calculated based on the normalized intensity (see eq S2 for the calculation in Supporting Information). For example, for the petal-like vesicles of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$, about 87% of the PVBAH$_{76}$ chains are tethered at the outer surface and about 13% of the PVBAH$_{76}$ chains are at the inner surface of the petal-like vesicles. In comparison, about 93% of the PVBAH$_{37}$ chains are in the core-layer of the corona-shell-core nanoparticles of PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{37}$ after acidification in the 8/2 ethanol/water mixture. Based on the above-mentioned discussion, the structure of the ABC triblock copolymer nano-objects before and after acidification is schemed out by the insets in Figure 2.

The in-to-out switch just occurring at case of the long PVBA block but not at case of the short PVBA block is due to the unsymmetrical ABC triblock copolymer vesicles with the long polymer chains at the outer side being thermodynamic stable as discussed elsewhere.[23,24] Besides, it is found that the morphology transition of the triblock copolymer is greatly affected by the solvent character, and the nanoparticle-to-vesicle transition occurs just in the ethanol/water mixture with ethanol content above 60 wt% (Figures S8 and S9). The possible reason is due to the PS shell of the ABC triblock copolymer nanoparticles being tightly frozen in the water-rich solvent, and therefore both the in-diffusion of the HCl molecules and the in-to-out switch of the pH-sensitive core-forming C block of PVBA are restricted.

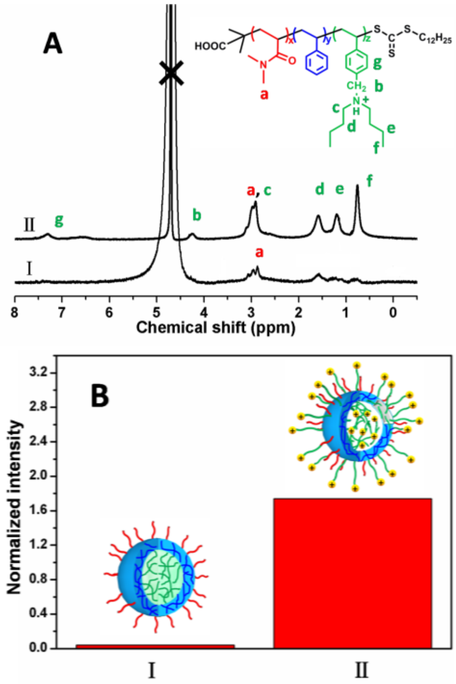


Figure 3. (A) ^{1}H NMR spectra of the PDMA$_{38}$-*b*-PS$_{167}$-*b*-PVBA$_{76}$ nano-objects in D_2O, and (B) the normalized intensity of the signal corresponding to the PVBA block under conditions (I) before acidification and (II) after acidification in the 8/2 ethanol/water mixture.

In conclusion, we have demonstrated the nanoparticle-to-vesicle and nanoparticle-to-toroid transitions of pH-sensitive ABC triblock copolymer by the in-to-out switch strategy of the core-forming C block. It is found that the chain-length of the core-forming C block of PVBA and the solvent character are crucial in the morphology transition of the triblock copolymer. Our results are anticipated to broad a new way to achieve nanoparticle-to-vesicle and nanoparticle-to-toroid transitions of block copolymers.

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Notes and references

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1 J. Du, R. K. O'Reilly, *Soft Matter*, 2009, **5**, 3544-3561.
2 R. C. Hayward, D. J. Pochan, *Macromolecules*, 2010, *43*, 3577-3584.
3 F. Meng, Z. Zhong, *J. Phys. Chem. Lett.*, 2011, **2**, 1533-1539.
4 M. J. Greenall, P. Schuetz, S. Furzeland, D. Atkins, D. M. A. Buzza, M. F. Butler, T. C. B. McLeish, *Macromolecules*, 2011, **44**, 5510-5519.
5 H. Huang, B. Chung, J. Jung, H.-W. Park, T. Chang, *Angew. Chem. Int. Ed.,* 2009, **48**, 4594-4597.
6 J. Fu, D. H. Kim, W. Knoll, *Chem. Phys. Chem.*, 2009, **10**, 1190-1194.
7 Y. Shi, E. T. A. van den Dungen, B. Klumperman, C. F. van Nostrum, W. E. Hennink, *ACS Macro Lett.*, 2013, **2**, 403-408.
8 A. Blanazs, R. Verber, O. O. Mykhaylyk, A. J. Ryan, J. Z. Heath, C. W. I. Douglas, S. P. Armes, *J. Am. Chem. Soc.*, 2012, **134**, 9741-9748.
9 R. T. Pearson, N. J. Warren, A. L. Lewis, S. P. Armes, G. Battaglia, *Macromolecules*, 2013, **46**, 1400-1407.
10 A. O. Moughton, J. P. Patterson, R. K. O'Reilly, *Chem. Commun.*, 2011, **47**, 355-357.
11 G. Battaglia, A. J. Ryan, *J. Am. Chem. Soc*., 2005, *127*, 8757-8764.
12 J. Braun, N. Bruns, T. Pfohl, W. Meier, *Macromol. Chem. Phys.*, 2011*,* **212**, 1245-1254.
13 S. Sugihara, A. Blanazs, S. P. Armes, A. J. Ryan, A. L. Lewis, *J. Am. Chem. Soc*., 2011, **133**, 15707-15713.
14 E. Groison, S. Brusseau, F. D'Agosto, S. Magnet, R. Inoubli, L. Couvreur, B. Charleux, *ACS Macro Lett*., 2012, **1**, 47-51.
15 S. Kessel, C. N. Urbani, M. J. Monteiro, *Angew. Chem. Int. Ed*., 2011, **50**, 8082-8085.
16 W.-D. He, X.-L. Sun, W.-M. Wan, C.-Y. Pan, *Macromolecules*, 2011, **44**, 3358-3365.
17 S. Yu, T. Azzam, I. Rouiller, A. Eisenberg, J. Am. Chem. Soc., 2009, **131**, 10557-10566.
18 K. Kempe, R. Hoogenboom, S. Hoeppener, C.-A. Fustin, J.-F. Gohy, U. S. Schubert, *Chem. Commun.*, 2010, **46**, 6455-6457.
19 A. Blanazs, M. Massignani, G. Battaglia, S. P. Armes, A. J. Ryan, *Adv. Funct. Mater*., 2009, **19**, 2906-2914.
20 P. Chambon, A. Blanazs, G. Battaglia, S. P. Armes, *Macromolecules*, 2012, **45**, 5081-5090.
21 Q. Yan, Y. Zhao, *Angew. Chem. Int. Ed.*, 2013*,* **52**, 9948-9951.
22 J. Du, L. Fan, Q. Liu, *Macromolecules*, **2012***,* **45**, 8275-8283.
23 I. W. Wyman, G. Liu, *Polymer*, 2013, **54**, 1950-1978.
24 L. Luo, A. Eisenberg, *J. Am. Chem. Soc*., 2001, **123**, 1012-1013.
25 J.-N. Marsat, M. Heydenreich, E. Kleinpeter, H. v. Berlepsch, C. Bottcher, A. Laschewsky, *Macromolecules*, 2011, **44**, 2092-2105.
26 Y. Zhang, W. Lin, R. Jing, J. Huang, *J. Phys. Chem. B*, 2008, **112**, 16455-16460.
27 A. O. Moughton, M. A. Hillmyer, T. P. Lodge, *Macromolecules*, 2012, **45**, 2-19.
28 Z. Chen, H. Cui, K. Hales, Z. Li, K. Qi, D. J. Pochan, K. L. Wooley, *J. Am. Chem. Soc*., 2005, **127**, 8592-8593.
29 J. Weiss, A. Laschewsky, *Langmuir*, 2011, **27**, 4465-4473.
30 C. Pietsch, U. Mansfeld, C. Guerrero-Sanchez, S. Hoeppener, A. Vollrath, M. Wagner, R. Hoogenboom, S. Saubern, S. H. Thang, C. R. Becer, J. Chiefari, U. S. Schubert, *Macromolecules*, 2012, **45**, 9292-9302.
31 T. Jiang, L. Wang, S. Lin, J. Lin, Y. Li, *Langmuir*, 2011, **27**, 6440-6448.
32 Z. Li, J. Ma, N. S. Lee, K. L. Wooley, *J. Am. Chem. Soc.*, 2011, **133**, 1228-1231.
33 X. Xu, J. D. Flores, C. L. McCormick, *Macromolecules*, 2011, **44**, 1327-1334.
34 M. Rabnawaz, G. Liu, *Macromolecules*, 2012, **45**, 5586-5595.
35 M. T. Savoji, S. Strandman, X. X. Zhu, *Langmuir*, 2013, **29**, 3898-3903.
36 J.-Z. Du, H.-Y. Long, Y.-Y. Yuan, M.-M. Song, L. Chen, H. Bi, J. Wang, *Chem. Commun*., 2012, **48**, 1257-1259.
37 I. Koonar, C. Zhou, M. A. Hillmyer, T. P. Lodge, R A. Siegel, *Langmuir*, 2012, **28**, 17785-17794.
38 C. Zhou, M. A. Hillmyer, T. P. Lodge, Macromolecules, 2011, **44**, 1635-1641.
39 Y. Cai, K. B. Aubrecht, R. B. Grubbs, *J. Am. Chem. Soc.*, 2011, **133**, 1058-1065.
40 A. Sundararaman, T. Stephan, R. B. Grubbs, *J. Am. Chem. Soc*., 2008, **130**, 12264-12265.
41 J. N. Israelachvili, D. J. Mitchell, B. W. Ninham, *J. Chem. Soc.*, *Faraday Trans.*, 1976, **72**, 1525-1568.
42 F. Huo, C. Gao, M. Dan, X. Xiao, Y. Su, W. Zhang, *Polym. Chem.*, 2014, DOI: 10.1039/C3PY01569F.
43 J. Xu, X. Wang, Y. Zhang, W. Zhang, P. Sun, *J. Polym. Sci. Part A: Polym. Chem.*, 2012, **50**, 2484-2498.