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Topology-Directed Control on Thermal Stability: Micelles Formed from Linear and Cyclized Amphiphilic Block Copolymers

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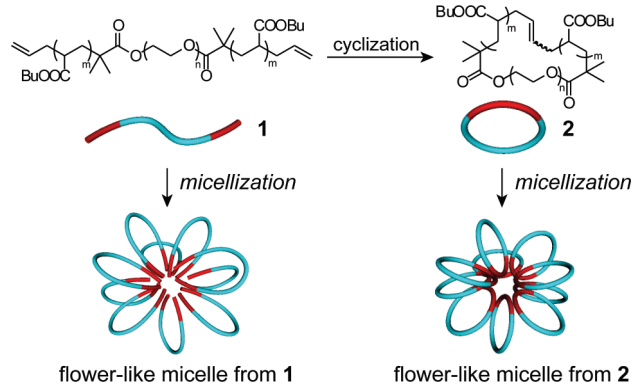
Abstract: The thermal stability of a self-assembled micelle was remarkably enhanced by a topology effect. Linear poly(butyl acrylate)-*block*-poly(ethylene oxide)-*block*-poly(butyl acrylate) (**1**) and the cyclized product, poly(butyl acrylate)-*block*-poly(ethylene oxide) (**2**), were self-assembled to form flower-like micelles. By means of viscometry, the critical micelle concentrations were determined to be 0.13 and 0.14 mg/mL for **1** and **2**, respectively. Dynamic light scattering, atomic force microscopy, and transmission electron microscopy studies revealed that both micelles are spherical and approximately 20 nm in diameter. Despite no distinctive change in the chemical composition or structure of the micelle, we found that the cloud point (T_c) was elevated by more than 40 °C through the linear-to-cyclic topological conversion of the polymer amphiphile. Furthermore, the T_c was tuned by coassembly of **1** and **2**.

Scheme 1. Chemical Structures of Linear (**1**) and Cyclic (**2**) Amphiphilic Block Copolymers and Schematic Representation for the Formation of Flower-like Micelles



Self-assembly is a powerful means to construct functional nanostructures with molecular-level precision.[1] However, due to their noncovalent nature, the ensembles are inherently susceptible to their surroundings. Although the structural robustness has been improved by, for example, the introduction of secondary interactions[2] and post cross-linking,[3] appending additional functional groups to component molecules or polymers often disturbs the formation of desired suprastructures.[4] The development of an alternative methodology for stabilization that does not affect the structural integrity of ensembles is a challenging issue in supramolecular chemistry. In nature, certain types of living organisms have evolved to adapt to hostile environments by exploiting a topology effect to preserve their self-assembled biological systems. Some thermophilic archaea, single-cell microorganisms living in high-temperature circumstances such as hot springs and submarine volcanoes, have cyclic lipids in their cell membranes.[5] The cyclic structure is believed to endow the self-assembled membrane with a significant thermal resistance. Inspired by this, we expected that self-assembled synthetic nanostructures can be stabilized by the topology-directed strategy. Here we report the first example of a remarkable topology effect by a cyclized[6] block copolymer against its linear counterpart, demonstrating a drastic elevation ($\geq$40 °C) of the cloud point (T_c)[7] of the flower-like micelle[8] commonly formed therefrom (Scheme 1).[9−11] Importantly, other chemical and physical properties such as composition, critical micelle concentration (CMC), morphology, and dimensions remained essentially unaffected. Furthermore, the T_c was tuned by coassembly of the linear and cyclized polymers.

Based on the recently developed protocol,[12] amphiphilic linear poly(butyl acrylate)-*block*-poly(ethylene oxide)-*block*-poly(butyl acrylate) (**1**) and cyclized poly(butyl acrylate)-*block*-poly(ethylene oxide) (**2**) were prepared, where the M_n values were prescribed suitable for the formation of micelles.[13] Aqueous micellar solutions of **1** and **2** were prepared by a common method.[14,15] To determine the CMCs by viscometry, the micellar solutions were diluted to sequential concentrations. Plots of η versus concentration show the slopes of the linearly fitted lines change at 0.13 and 0.14 mg/mL for **1** and **2**, respectively (Figure S3, Supporting Information),[16] indicating the CMC is not influenced significantly by the topology of the polymer component. By means of dynamic light scattering (DLS), the number-average hydrodynamic diameters (D_h) were determined to be 20 nm, with a narrow distribution for both micelles from **1** and **2** (Figure S4, Supporting Information).[16] Furthermore, the size and morphology of the micelles were directly observed by atomic force microscopy (AFM) (Figure S5, Supporting Information)[16,17] and transmission electron microscopy (TEM) (Figure S6a,b, Supporting Information),[16] revealing spherical structures having consistent diameters with DLS. Noteworthy, diffractions in fast Fourier-transformed TEM images are visible presumably due to crystalline poly(ethylene oxide) segments (Figure S6c,d, Supporting Information).[16]

Despite no apparent differences in the structures of the micelles, we found that the thermal stability was dramatically improved by the cyclization. The turbidity of the micellar solutions was measured by increasing the temperature from 20 °C in stepwise fashion (Figure 1a,b). The micellar solutions of **1** became cloudy at 24 °C (1.0 and 0.5 mg/mL) and 27 °C (0.25 mg/mL),[7,17] indicating the formation of a larger agglomerate. In sharp contrast, 1.0, 0.5, and 0.25 mg/mL micellar solutions of **2** were stable up until 74, 73, and 71 °C, respectively,[7,17] demonstrating that the T_c was increased by more than 40 °C through the topological conversion of the polymer component.

The thermal stability of the micelle likely derives from the entropic advantage of the cyclic topology of the polymer compo-

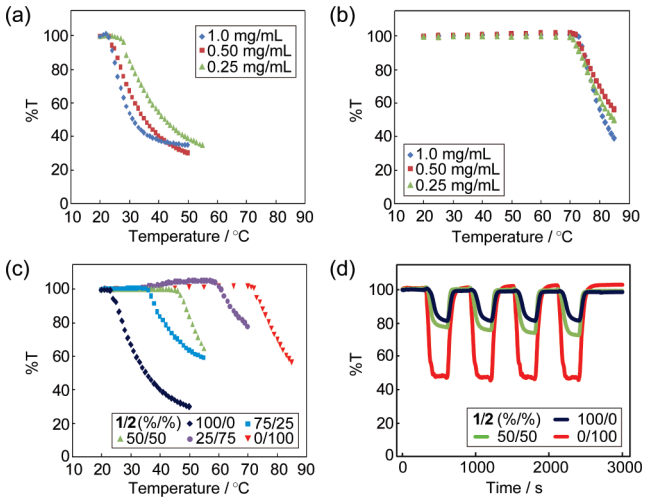


Figure 1. Turbidity measurements. Temperature dependence of (a) **1** and (b) **2** (1.0, 0.50, 0.25 mg/mL). (c) Temperature dependence of homoassemblies and coassemblies (25%/75%, 50%/50%, and 75%/25%). The total concentration of **1** and **2** in a solution was 0.50 mg/mL. (d) Response to heating and cooling (0.50 mg/mL). The temperature was equilibrated at T_c − 5 °C prior to the measurements, set to T_c + 5 °C at 300, 900, 1500, and 2100 s, and reset to T_c − 5 °C at 600, 1200 1800, and 2400 s.

nent. When linear polymer **1** in water aggregates to form a flower-like micelle, the polymer chain should fold at a suitable position to put together the poly(butyl acrylate) segments. On the other hand, no such conformational control is necessary for cyclic **2**. In other words, **1** suffers from decreases in entropy by folding and aggregating, while the latter is the only entropic disadvantage for the self-assembly of **2**. Upon heating the micellar solution of **1**, one of the chain ends gets loose from the core of the micelle (Scheme S1, Supporting Information). The polymer having a free chain end presumably bridges between micelles. Assisted by the loss of hydration water, the micelle from **1** consequently transforms into an agglomerate. In contrast, the bridging is suppressed by the cyclic topology of **2**, resulting in the high thermal stability of the micelle.

By taking advantage of the considerably different T_c's, we attempted to tune the T_c in the wide temperature range via the coassembly of **1** and **2**. The micelles formed from three mixtures of **1** and **2** (75%/25%, 50%/50%, and 25%/75%) were subjected to turbidity measurements (Figure 1c).[17] The T_c of the resulting micelles increased along with the proportion of **2** (37 °C for 25%, 47 °C for 50%, and 62 °C for 75%). This suggests that coassembly takes place to form comparable micelles.

Furthermore, the response of the micelle−agglomerate transformation was measured by repetitive heating and cooling of 0.5 mg/mL solutions around the cloud points (T_c + 5 and T_c − 5 °C). Thus, the temperature was set at 29 and 19 °C for **1**, 78 and 68 °C for **2**, and 52 and 42 °C for a 50%/50% coassembly with a 300 s interval (Figure 1d).[17] All showed a reversible phase transition, suggesting that the micelle−agglomerate transformation is under a thermodynamic control. Interestingly, transmittance for **2** dropped sharply to less than 50% in 100 s by heating to T_c + 5 °C, while that for **1** slowly decreased only to approximately 80% even after 300 s. The response of the coassembly is between the homoassemblies. The transmittance of all the samples was fully restored in 150 s by cooling to T_c − 5 °C.

In conclusion, we have succeeded in significantly improving the thermal stability of a flower-like micelle through the topological conversion of the polymer component. The coassembly of the linear and cyclic polymers likely allows for tuning the T_c to any temperature between those of homoassemblies. The topology-based control of the stabilization may provide potential new developments for the field of supramolecular chemistry. Practically, the present methodology is ideal for human body-related applications such as drug delivery system, food, and cosmetics, which require meticulous care in the modification of the chemical and self-assembled structures, concerning toxicity and biocompatibility.[6i,18]

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Supporting Information Available: Experimental section, ^{1}H NMR spectra, size exclusion chromatography traces, viscosity plots, DLS plots, AFM images, TEM images, and a supporting scheme. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) See Supporting Information.

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