

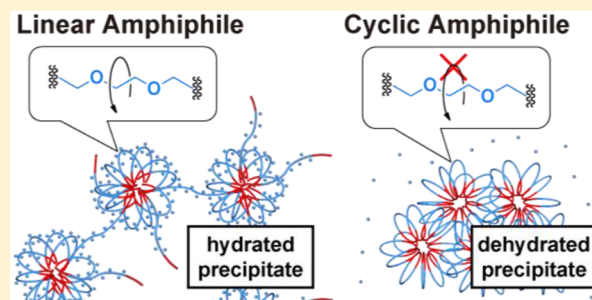
NMR Relaxometry for the Thermal Stability and Phase Transition Mechanism of Flower-like Micelles from Linear and Cyclic Amphiphilic Block Copolymers

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S Supporting Information

ABSTRACT: Linear and cyclic amphiphilic block copolymers consisting of poly(ethylene oxide) (PEO) as the hydrophilic segment and poly(methyl acrylate) or poly(ethyl acrylate) as the hydrophobic segments were synthesized and self-assembled to form flower-like micelles. The micelles from linear (methyl acrylate)₁₂(ethylene oxide)₇₃(methyl acrylate)₁₂ ($M_n = 1000\text{--}3200\text{--}1000$, *l*-MOM) showed a cloud point (T_c) at 46 °C by the transmittance of the micellar solution, whereas that of cyclic (methyl acrylate)₃₀(ethylene oxide)₇₉ ($M_n = 2600\text{--}3500$, *c*-MO) increased to 72 °C, as previously reported. DLS showed comparable diameters (*l*-MOM, 14 nm; *c*-MO, 12 nm) and T_c values (*l*-MOM, 48 °C; *c*-MO, 75 °C). For the investigation of the difference in T_c and the phase transition mechanism based on the polymer topology, NMR relaxometry was performed to determine the spin–lattice (T_1) and spin–spin (T_2) relaxation times. A decrease in T_2 of the PEO segment in both *l*-MOM and *c*-MO was observed above T_c , suggesting that slow large-scale motions, such as the detachment of a chain end from the core, bridging, and interpenetration of the micelles, were inhibited. T_1 of the PEO segment in *l*-MOM continuously increased in the experimental temperature range, indicating that the segment is hydrated even above its T_c . On the other hand, that of *c*-MO reached a ceiling above its T_c , likely due to the prevention of the rotation of the PEO main chain bonds caused by dehydration. Similar results were obtained for linear (ethyl acrylate)₈(ethylene oxide)₇₉(ethyl acrylate)₈ ($M_n = 800\text{--}3500\text{--}800$, *l*-EOE) and its cyclic (ethyl acrylate)₁₅(ethylene oxide)₇₈ ($M_n = 1500\text{--}3400$, *c*-EO).



Due to the absence of chain ends, cyclic polymers are unique, from a topological viewpoint, compared to their traditional linear and branched counterparts.^{1,2} By the use of cyclic polymers with prescribed chemical structures, remarkable topology effects have been revealed.³ In particular, the unusual behaviors of cyclic amphiphilic block copolymers were recently extensively investigated.^{4–6} Moreover, the properties arising from cyclic topology have attracted attention in theoretical studies.^{7,8}

We previously reported a significant increase in the stability of flower micelles formed from cyclic amphiphilic block copolymers compared to those from their linear counterparts.^{9,10} The thermal stability was increased by more than 40 °C, and the salt stability was enhanced nearly 30-fold under selected conditions. However, the mechanism of the stability enhancement remains unknown. Although intermicellar bridging for the linear block copolymers was suggested,^{9–14} the actual mechanism has not been proven.

A theoretical study of the association of flower-like micelles formed by a linear hydrophobic–hydrophilic–hydrophilic amphiphile was performed by Joanny and co-workers.¹² The authors found that the flower-like micelles strongly attract each other, even in a dilute solution, and that the micelles reversibly transform into a gel above a certain concentration by

interconnecting through multiple bridges of the amphiphile. Furthermore, the dynamics of individual micelles in the gel was governed by the exchange rate between the bridge and loop forms of the amphiphile. Russel and co-workers reported on the entropy-driven phase transition of poly(ethylene oxide) (PEO) end-capped with hexadecyl and octadecyl groups.¹³ The entropic attraction of the flower-like micelles was caused by the bridging through the end-capped PEO. Thus, when the polymer concentration was increased beyond a certain limit, a constant fraction of the polymer formed bridges, resulting in the formation of a network.

NMR relaxometric studies have been performed on the micellization of linear amphiphilic block copolymers, especially on commercially available poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide), PEO–PPO–PEO (pluronic), around the critical micelle temperature (CMT).^{15–18} In these studies, the motions of the polymers were investigated by the ¹H spin–lattice (T_1) and spin–spin (T_2) relaxation times. T_1 mainly depends on the local segmental motions.¹⁹ On the other hand, T_2 is determined

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Table 1. Properties of Amphiphilic Block Copolymers and Flower-like Micelles for NMR Relaxometry

abbreviation	formula	M_n (NMR)	PDI	D_h (nm)	T_c (°C) by DLS	T_c (°C) by %T
<i>l</i> -MOM	linear (methyl acrylate) ₁₂ - <i>b</i> -(ethylene oxide) ₇₃ - <i>b</i> -(methyl acrylate) ₁₂	1000–3200–1000	1.28	14	48	46
<i>c</i> -MO	cyclic (methyl acrylate) ₃₀ - <i>b</i> -(ethylene oxide) ₇₉	2600–3500	1.24	12	75	72
<i>l</i> -EOE	linear (ethyl acrylate) ₈ - <i>b</i> -(ethylene oxide) ₇₉ - <i>b</i> -(ethyl acrylate) ₈	800–3500–800	1.09	10	30	29
<i>c</i> -EO	cyclic (ethyl acrylate) ₁₅ - <i>b</i> -(ethylene oxide) ₇₈	1500–3400	1.07	10	90	89

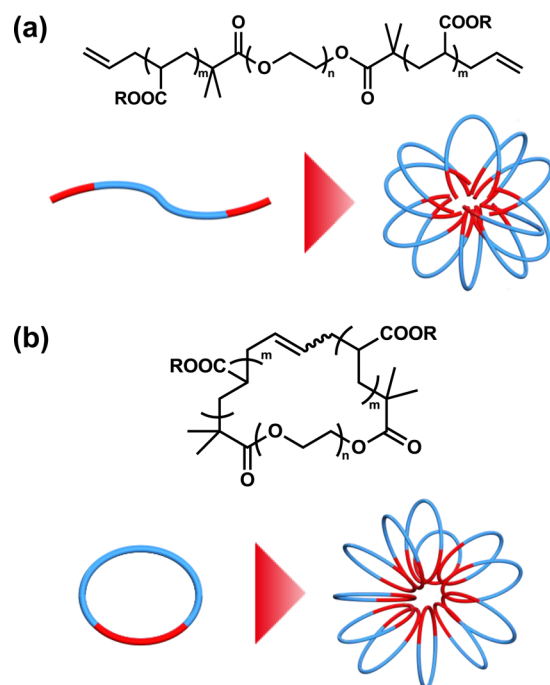


Figure 1. Chemical structures of (a) linear (*l*-MOM and *l*-EOE) and (b) cyclic (*c*-MO and *c*-EO) amphiphilic block copolymers (R = Me, Et) and schematic representation for the formation of respective micelles.

by large-scale motions including bridging and interpenetration of the micelles,^{19,20} along with the fast motions.

Micelle–liquid crystal and micelle–gel transitions have also been studied by NMR relaxometry.^{19–21} La Mesa and co-workers reported the temperature- and concentration-dependent phase transition of pluronic F68.²² T_1 of the PPO segments, which formed the micelle core, significantly changed at the molecule–micelle equilibrium. On the other hand, the micelle–liquid crystal transition was governed by the dehydration of the PEO segments determined by T_1 of the segment. In these ways, NMR relaxometry has been shown to effectively investigate the mechanism of the temperature-dependent phase transition of amphiphilic block copolymers.

Here we investigated the mechanism of the phase transition using NMR relaxometry to evaluate the mobility of the hydrophilic and hydrophobic segments in the linear and cyclic amphiphiles forming flower-like micelles, which had significantly different cloud points (T_c). The changes in T_1 and T_2 at the phase transition were exploited to determine the difference in the mechanisms. T_1 of the PEO segment in *l*-MOM continuously increased in the experimental temperature range, indicating that the segment is hydrated even above its T_c . On the other hand, that of *c*-MO reached a ceiling above its T_c , likely due to the prevention of the rotation of the PEO main chain bonds caused by dehydration. Thus, the substantial difference in the phase transition mechanism of the flower-like

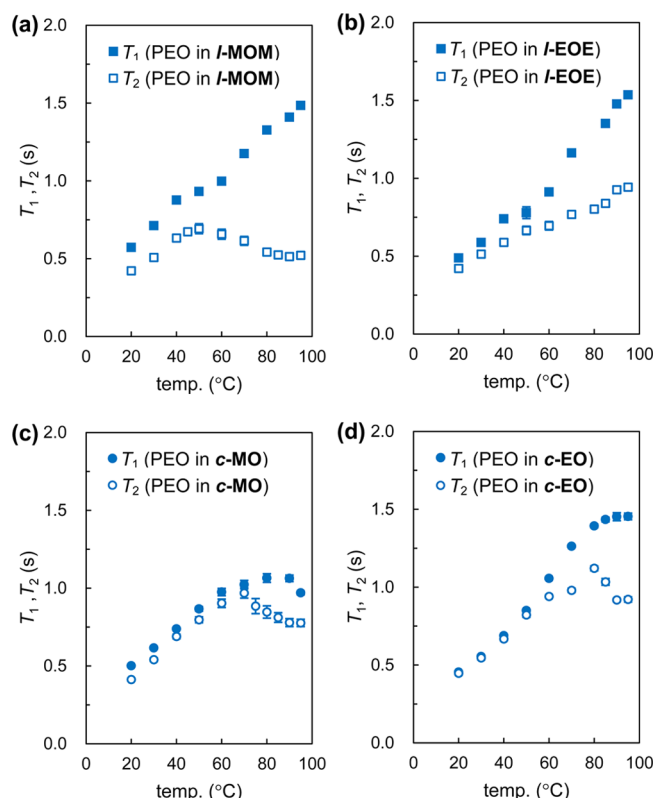


Figure 2. Temperature dependence of T_1 (filled squares and circles) and T_2 (open squares and circles) of the PEO segments in the amphiphiles in D_2O at a concentration of 10 mg/mL. (a) *l*-MOM, (b) *l*-EOE, (c) *c*-MO, and (d) *c*-EO.²⁸

micelles formed from linear and cyclic amphiphiles was revealed.

In the present study, linear (methyl acrylate)₁₂(ethylene oxide)₇₃(methyl acrylate)₁₂ (*l*-MOM, M_n (NMR) = 1000–3200–1000) and the corresponding cyclic (methyl acrylate)₃₀(ethylene oxide)₇₉ (*c*-MO, M_n (NMR) = 2600–3500) were synthesized and characterized according to previously reported protocols (Table 1, Figures S1 and S2).²³ Similarly, linear (ethyl acrylate)₈(ethylene oxide)₇₉(ethyl acrylate)₈ (*l*-EOE, M_n (NMR) = 800–3500–800) and cyclic (ethyl acrylate)₁₅(ethylene oxide)₇₈ (*c*-EO, M_n (NMR) = 1500–3400) were prepared to study the effects of the hydrophobic segments (Table 1, Figures S1 and S2). The obtained amphiphilic block copolymers were self-assembled in D_2O to form micellar solutions with a concentration of 10 mg/mL (Figure 1). The average values of the D_h distribution by number for the micelles formed from *l*-MOM, *c*-MO, *l*-EOE, and *c*-EO were 14, 12, 10, and 10 nm, respectively, with a narrow distribution determined by dynamic light scattering (DLS) (Table 1, Figure S3). The phase transition temperatures or T_c of the micellar solutions was determined by DLS and the transmittance, which were in good agreement (Table 1, Figure S4). As reported previously,^{9,10} the T_c values of *c*-MO (75 and 72 °C) and *c*-

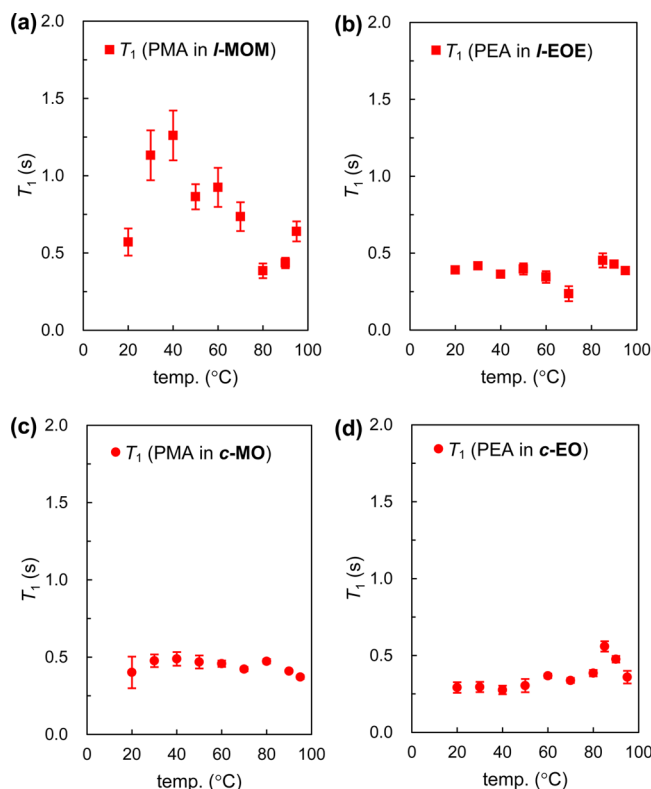


Figure 3. Temperature dependence of T_1 of the hydrophobic PMA and PEA segments of the amphiphiles in D_2O at a polymer concentration of 10 mg/mL. (a) *l*-MOM, (b) *l*-EOE, (c) *c*-MO, and (d) *c*-EO.²⁸

EO (90 and 89 °C) were notably higher than those of the prepolymers, *l*-MOM (48 and 46 °C) and *l*-EOE (30 and 29 °C), respectively, via cyclization. The difference in the thermal property was more distinct for the PEA copolymers, suggesting that the stronger hydrophobicity of the segments leads to a more significant enhancement of the thermal stability of the resulting micelles. A slight change in the molecular weights caused by purification may have also affected the thermal stability.

These micelles were subjected to NMR relaxometry measurements by increasing the temperature from 20 to 95 °C. A typical 1H NMR spectrum of a D_2O micellar solution is shown in Figure S5. T_1 and T_2 of the hydrophilic PEO and hydrophobic PMA/PEA segments were determined by the peaks at approximately 3.8 ($-OC^*H_2C^*H_2O-$) and 2.2 ppm ($-C^*H(CO_2R)-$), respectively. The protons directly attached to the main chain, not to the side chains, were selected to properly evaluate the mobility of the main chains of each segment. T_1 was measured by the inversion recovery method. T_2 of the PEO and PMA/PEA segments was measured by the Carr–Purcell–Meiboom–Gill pulse sequence and spin echo sequence, respectively. T_1 and T_2 depend on spectral density functions $J(n\omega_0)$ ($n = 0, 1, 2$) according to the following equations:²⁴

$$1/T_1 = Q[J(\omega_0) + 4J(2\omega_0)] \quad (1)$$

$$1/T_2 = (Q/2)[3J(0) + 5J(\omega_0) + 2J(2\omega_0)] \quad (2)$$

$J(\omega_0)$ and $J(2\omega_0)$ depend on fast motions, whereas slow motions are responsible for $J(0)$. Therefore, T_1 is primarily governed by the local segmental motions of the polymers.¹⁹

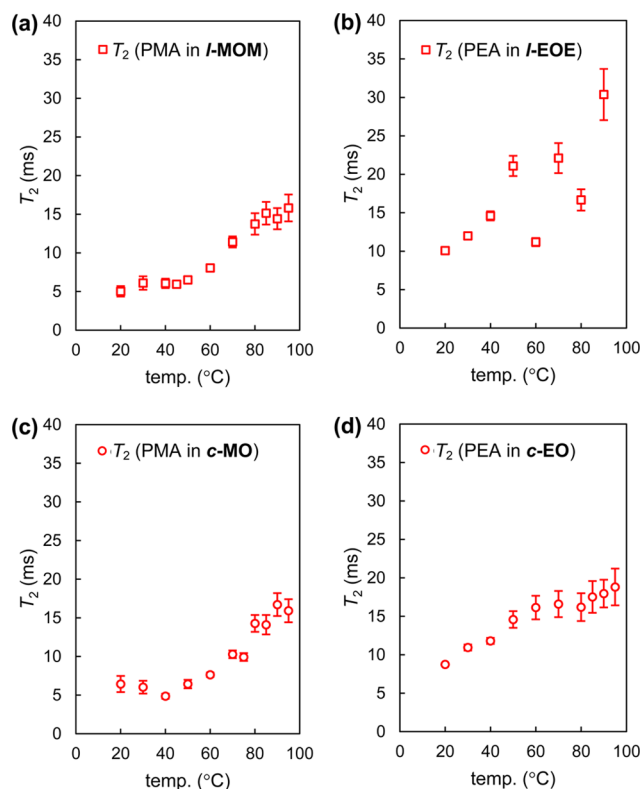
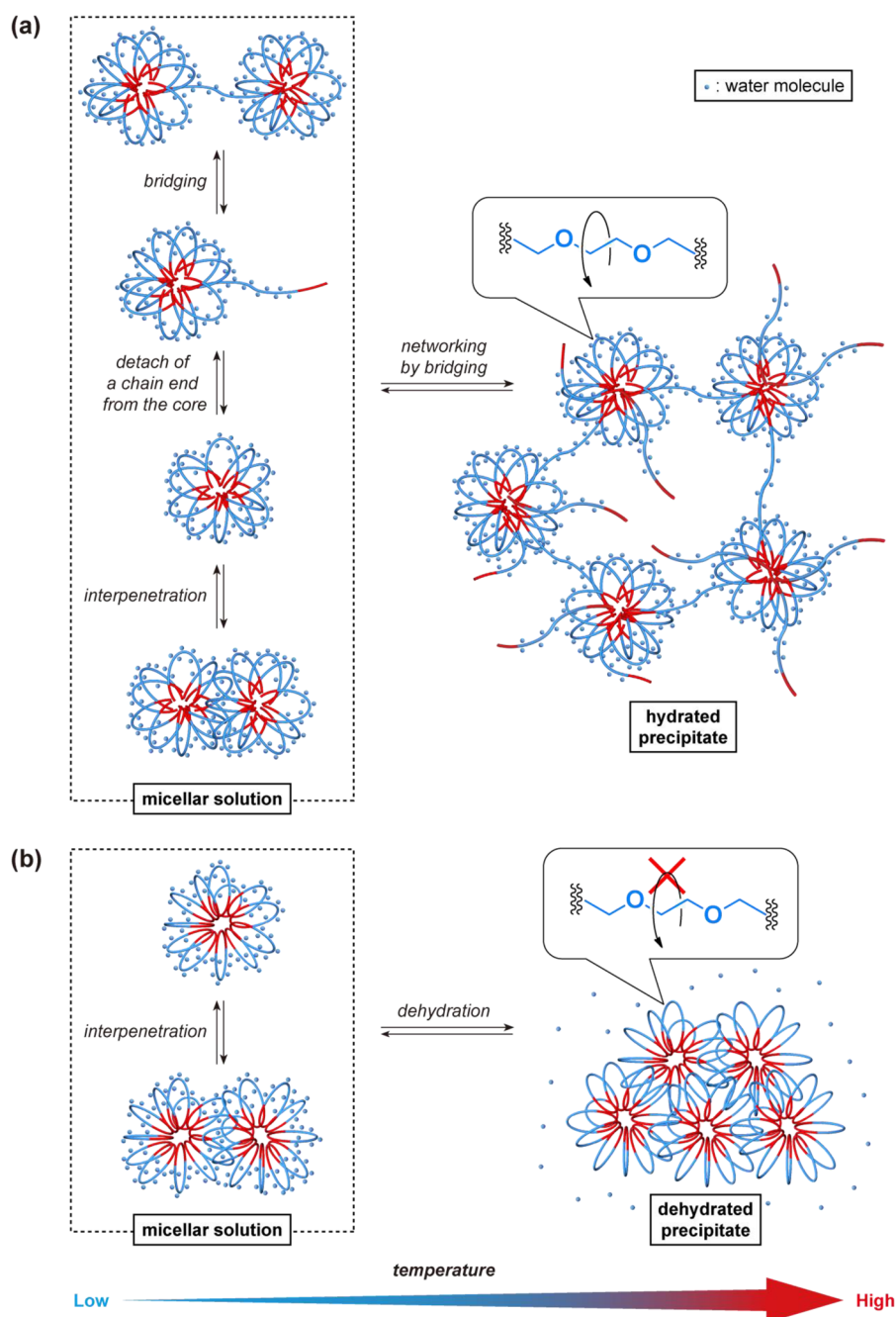


Figure 4. Temperature dependence of T_2 of the hydrophobic PMA and PEA segments of the amphiphiles in D_2O at a polymer concentration of 10 mg/mL. (a) *l*-MOM, (b) *l*-EOE, (c) *c*-MO, and (d) *c*-EO.²⁸

Especially for PEO, the rotation of the main-chain bonds is known to be the principal factor in the T_1 relaxation.²⁵ T_2 depends on large-scale motions, such as the detachment of a chain end from the core, bridging, and interpenetration of the micelles,^{19,20} in addition to the fast motions. As the contribution of the large-scale motions becomes dominant, T_2 is shortened. T_1 and T_2 of the hydrophilic PEO segment were on the order of seconds (Figure 2). According to the Bloembergen–Purcell–Pound theory,^{26,27} comparable T_1 and T_2 suggest that the PEO segment was reasonably mobile because the micelle shell formed by the PEO segment was solvated. In the meantime, T_1 of the hydrophobic PMA/PEA segments was on the order of seconds (Figure 3), while T_2 was on the order of milliseconds (Figure 4). The large deviation between T_1 and T_2 indicates that the PMA/PEA segments, which formed the micelle core, were restricted in their mobility.^{16,19,20} Certain plots (T_1 of *l*-MOM in Figure 3a and T_2 of *l*-EOE in Figure 4b) were scattered, most likely due to the short T_1 and T_2 values. Nevertheless, no significant difference was observed for T_1 and T_2 of the hydrophobic PMA/PEA segments.

T_2 of the hydrophilic PEO segment in *l*-MOM, *c*-MO, and *c*-EO turned downward around the respective T_c (Figure 2). This result was likely caused by precipitation, which immobilized the slow large-scale motions, such as the detachment of a chain end from the core, bridging, and interpenetration of the micelles,^{19,20} possibly in addition to inhibiting the fast local motions of the main-chain bond rotation,^{19,25} according to eq 2. T_2 of *l*-EOE was also expected to decrease around its T_c . However, the degree of the reduction was not obvious, most likely because the local and large-scale motions were moderate

Scheme 1. Schematic Representation of the Proposed Mechanisms of the Phase Transition of Micellar Solutions Formed from (a) *l*-MOM and *l*-EOE and (b) *c*-MO and *c*-EO^a



^aThe size and interspace of the precipitates were not determined in the present study, and those depicted in this scheme may not reflect the actual dimensions.

in the micelles at relatively low temperature ($T \lesssim 30\text{ }^{\circ}\text{C}$). Thus, the phase transition at T_c did not significantly cause a decrease in T_2 . The PEO macroinitiator that was used as the prepolymer for *l*-MOM and *l*-EOE was also subjected to temperature-dependent phase transition and NMR relaxometry studies. T_c of the PEO macroinitiator was initially measured in water. However, no precipitate formed, even at the boiling temperature. Thus, NaCl (151 mg/mL) was added to lower T_c by salting out (Figure S6a).¹⁰ T_c was determined as $60\text{ }^{\circ}\text{C}$, and a significant decrease in T_2 at that temperature was observed (Figure S6b). Therefore, these experiments confirmed that the tuning downward of T_2 corresponds to T_c of the PEO

homopolymer and the PEO segments in the amphiphilic block copolymers.

In contrast to T_2 , T_1 of the PEO segment in *l*-MOM and *l*-EOE monotonically increased over the experimental temperature range, regardless of the T_c value (Figure 2a,b). This result suggests that the fast local segmental motions (rotation of the main chain bonds) of the PEO segment are not suppressed even above T_c .²⁵ Thus, a sufficient number of water molecules were expected to be included in the precipitate, which was likely formed via networking by bridging of the micelles, to retain water in the network (Scheme 1a).^{9–14} On the other hand, the increasing rate in T_1 of the PEO segment in *c*-MO

and *c*-EO was suppressed around the respective T_c values (*c*-MO, 75 and 72 °C; *c*-EO, 90 and 89 °C). This result indicates that the main-chain bond rotation of the PEO segment was inhibited by dehydration.²⁵ Therefore, the precipitates formed from *c*-MO and *c*-EO did not include a substantial amount of water compared to those of *l*-MOM and *l*-EOE (Scheme 1b). Linear diblock²⁰ and linear triblock amphiphiles with two hydrophilic units at the ends^{19–21} also formed hydrogels with similar T_1 and T_2 behaviors to present *l*-MOM and *l*-EOE. In this regard, the present cyclic amphiphiles were found to have a unique phase transition mechanism.

In conclusion, linear amphiphilic *l*-MOM and *l*-EOE and cyclic *c*-MO and *c*-EO were synthesized and subjected to temperature-dependent NMR relaxometry studies. The determination of T_1 and T_2 explained the difference in the hydration state and phase transition mechanism arising from the topology of the amphiphiles. The phase transition behavior of the cyclic amphiphiles was fundamentally different from the well-known gelation mechanism of linear triblock and diblock amphiphiles. The present results provide insight into the drastically enhanced thermal properties of micelles formed from cyclic amphiphilic block copolymers^{9,10} and would maximize their applications.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.langmuir.5b01902.

Experimental section, ¹H NMR spectra, SEC profiles, D_h distributions, plots for the temperature dependence of %T, and z-average average diameter. (PDF)

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Notes

The authors declare no competing financial interest.

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(28) Throughout the main text and [Supporting Information](#), the following symbols and colors are applied for the NMR relaxometry plots: square, *l*-**MOM** and *l*-**EOE**; circle, *c*-**MO** and *c*-**EO**; blue, hydrophilic PEO segment; red, hydrophobic PMA/PEA segments; filled square/circle, T_1 ; open square/circle, T_2 .