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Zheng, Jie; Goto, Atsushi

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Systematic Study on Evolution of Self-Assembly Morphologies of CABC Tetrablock Terpolymers with Varied Segment Lengths

Jie Zheng and Atsushi Goto*

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The self-assembly structures of PEEA-PMMA-PGLMMA-PEEA CABC-type tetrablock terpolymers with a fixed length of the PGLMMA segment and varied lengths of the PMMA and PEEA segments were systematically studied, where PMMA is poly(methyl methacrylate), PGLMMA is poly(glycerol monomethacrylate), and PEEA is poly(2-(2-ethoxyethoxy)ethyl acrylate). The morphological evolution from spherical flower-like micelles to discs, toroids, and porous structures was demonstrated by tuning the lengths of the PEEA and PMMA segments. Two smart toroids were also synthesized. One is the temperature-directed morphology-changeable toroid. The temperature-responsiveness of the PEEA segment enabled a reversible morphological transformation from toroids to spherical star-like micelles. The other is the crosslinked toroid. The toroid was successfully crosslinked, and the crosslinked toroid enabled the change in the hole size of the toroid in response to temperature. The obtained toroids (uncrosslinked and crosslinked) may serve as red blood cell-like containers in delivery applications, act as ring-shaped molecular templates in material design, and also be used in stimuli-responsive systems.

Introduction

Self-assembled nanoparticles have attracted great attention due to their various applications.¹ Block copolymers have extensively been used for preparing self-assembled nanostructures in selective solvents.^{1–5} Depending on the length and composition of each segment, polymer concentration, solvent, temperature, and ionic strength, various morphologies such as spherical micelles, cylinders, vesicles, discs, toroids, and other complex structures can be prepared.^{6–10} Among them, the toroidal (ring-shaped) nanostructures are of growing interest for their unique geometry and potential applications in biological materials and nanotechnology.^{11–13} For example, toroids are found in DNA packing structures in bacteria and used for artificial gene delivery.¹⁴ Because of the hollow structure, toroids are also used as scaffolds for fabricating organic and inorganic nanostructures with pores.^{15,16}

Polymer toroids have successfully been obtained using di-block and tri-block copolymers via sophisticated design in several factors such as the kind, length, and composition of each block segment, the preparation procedure, and the solvent property.^{17–19} For example, a poly(acrylic acid)-*b*-poly(methyl acrylate)-*b*-polystyrene ABC-type tri-block copolymer¹¹ and a polystyrene-*b*-poly(4-vinylpyridine)-*b*-polystyrene ABA-type tri-block copolymer²⁰ generated toroids. A polyisoprene-*b*-poly(2-vinylpyridine) di-block copolymer was also self-assembled to yield a toroid with highly uniform shape

and size.²¹ However, to date, toroids formed with more complex block copolymers such as CABC tetrablock terpolymers have not been reported.

Living radical polymerization, also termed reversible deactivation radical polymerization, is an effective tool for preparing well-defined block copolymers.^{22–31} Our research group developed an organocatalyzed living radical polymerization using an alkyl iodide (R-I) as an initiator and an organic molecule [such as tetrabutylammonium iodide (Bu₄N⁺I[−])] as a catalyst. Mechanistically (Scheme 1), the dormant species (Polymer-I) and the catalyst are supposed to form a halogen bonding complex (Polymer-I...catalyst). The complex subsequently reversibly generates the propagating radical (Polymer•). This polymerization is termed reversible complexation mediated polymerization (RCMP).^{32–36} Previously, we synthesized CABC tetrablock terpolymers using a temperature-selective alkyl diiodide initiator [I-R²-R¹-I, methyl 2-iodo-2-(4'-(2"-iodopropionyloxy)phenyl)acetate (I-MEPE-I)]³⁷ and studied a reversible change in the self-assembly structure from a star-like micelle to a flower-like micelle using the obtained PEEA-PMMA-PGLMMA-PEEA (CABC) tetrablock terpolymers (Figure 1a),³⁸ where PMMA is poly(methyl methacrylate), PGLMMA is poly(glycerol monomethacrylate), and PEEA is poly(2-(2-ethoxyethoxy)ethyl acrylate). Block A (PMMA) is a hydrophobic segment (coloured in blue in Figure 1a), block B (PGLMMA) is a hydrophilic segment (red), and block C (PEEA) is a thermosensitive segment (green) having a lower critical solution temperature (LCST) (cloud point) in water.³⁹ Below LCST, block C is soluble in water. Hence, only block A is insoluble to form a core, giving a star micelle with blocks BC and C in the shell.³⁸ Above LCST, block C is insoluble in water. Blocks A and C are insoluble to form a core, giving a flower micelle with block B in the shell (petal) (Scheme 2a).

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, 21 Nanyang Link, 637371 Singapore. E-mail: agoto@ntu.edu.sg
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Scheme 1. Reversible activation in organocatalyzed living radical polymerization.

Scheme 2. (a) Assembly structures formed by CABC tetrablock terpolymers. (b) Star-to-toroid transformation. (c) Swelling and de-swelling of crosslinked toroid, where block A (blue segment) is crosslinked.

In the present paper, we report a systematic study on the evolution of the self-assembly morphology of PEEA-PMMA-PGLMMA-PEEA (CABC-type) tetrablock terpolymers with different lengths of the PMMA (block A) and PEEA (block C) segments. Above LCST, by varying the lengths of blocks A and C (varying the hydrophobicity), the assembled morphology may evolve from flower micelles to discs, toroids, and porous nanostructures (Scheme 2a). The sphere-disc-toroid-porous nanostructure type morphological transition of the CABC tetrablock terpolymers is new. We also demonstrate two features. One is that the toroid can undergo temperature-directed morphological transformation. Because of the temperature-responsiveness of PEEA segment (block C), the toroid (above LCST) is reversibly transformable to the spherical star micelle (below LCST) in a temperature-directed manner (Scheme 2b). The other is the synthesis of a crosslinked toroid. The toroidal micelle can be crosslinked by exploiting a post-crosslinkable monomer in block A. The obtained crosslinked toroid can exhibit a swelling-shrinking behaviour in response to a temperature change (Scheme 2c). The obtained toroids (both uncrosslinked and crosslinked) may serve as red blood cell-like containers in delivery applications, act as ring-shaped molecular templates in material design, and also be used in stimuli-responsive systems.

Results and discussion

Synthesis of PEEA-PMMA-PGLMMA-PEEA Tetrablock Terpolymers

We synthesized PEEA-PMMA-PGLMMA-PEEA (CABC) tetrablock terpolymers with different lengths of the PMMA (block A) and PEEA (block C) segments, according to the synthetic procedure reported in our previous publication.³⁸ Figure 1a shows the synthesis of a PEEA-PMMA-PGLMMA-PEEA tetrablock terpolymer. In a typical run, a mixture of MMA (50 equiv), I-MEPE-I (1 equiv) (alkyl di-iodide initiator), and tetraoctylammonium iodide (ONI) (0.5 equiv) (catalyst) was heated at 60 °C, yielding an I-ME-PMMA-I polymer with $M_n = 3000$ (25 monomer units of MMA) and dispersity $\mathcal{D}$ ($= M_w/M_n$) = 1.10 after purification by reprecipitation, where M_n and M_w are the number- and weight-average molecular weights, respectively [Table S1 (entry 1) in the ESI]. 100% of the PE-I moiety initiated and 97% of the I-ME moiety remained unreacted, demonstrating the high selectivity of the initiation from the two sites (Figure S1b in the ESI). After that, the purified I-ME-PMMA-I was employed as a macroinitiator to polymerize solketal methacrylate (SMA) at 60 °C to prepare a diblock copolymer I-ME-PMMA-PSMA-I with $M_n = 5100$ (10 monomer units of SMA) and $\mathcal{D} = 1.16$ after purification. 91% of I-ME remained unreacted after the two polymerizations (Figure S1c in the ESI). The purified I-ME-PMMA-PSMA-I macroinitiator was subsequently used to polymerize 2-(2-ethoxyethoxy)ethyl acrylate (EEA) at an elevated temperature 110 °C, producing an I-PEEA-PMMA-PSMA-PEEA-I tetrablock terpolymer with $M_n = 27000$ (66 monomer units in each EEA segment) and $\mathcal{D} = 1.35$ after purification. The GPC traces (Figure 1b) show that a large fraction of the I-ME-PMMA-PSMA-I macroinitiator was extended to the I-PEEA-PMMA-PSMA-PEEA-I tetrablock terpolymer, confirming the high block-efficiency of the macroinitiator. Thereafter, the obtained precursor CAB'C copolymer was deprotected to remove the acetal group in the PSMA segment to produce the desired CABC tetrablock terpolymer (PEEA-PMMA-PGLMMA-PEEA) with $M_n = 25000$ and $\mathcal{D} = 1.24$ after purification [Table 1 (entry 1)]. Table 1 (entries 1-13) lists the obtained PEEA_x-PMMA_n-PGLMMA_m-PEEA_x tetrablock terpolymers with different degrees of polymerization (DPs), where n , m , and x denote the DPs of the PMMA, PGLMMA, and PEEA segments, respectively. In the previous study, we studied only PEEA₈₂-PMMA₂₅-PGLMMA₂₇-PEEA₈₂.³⁸ In the present study, we fixed the DP of PGLMMA to 10 and studied a series of DPs in the PMMA (block A) and PEEA (block C) segments. The synthetic details for the polymers in Table 1 (entries 2-13) are given in the ESI (Tables S1 and S2).

Table 1. Self-assemblies of CABC tetrablock terpolymers.^[a]

Entry	$x-n-m-x$ units for PEEA _x -PMMA _n - PGLMMA _m -PEEA _x tetrablock terpolymers ^[a]	M_n (GPC) ^[b] (g mol ⁻¹)	$\bar{D}$ (GPC) ^[b]	f_{PMMA}	f_{PGLMMA}	f_{PEEA}	Hydrodynamic diameter (nm) ^[c]	DLS size Distribution index	Assembly structure	Code in Figures 1 and 2
1	66-25-10-66	25000	1.24	0.09	0.06	0.85	50	0.263	Sphere	A
2	81-25-10-81	33000	1.37	0.07	0.05	0.88	79	0.153	Sphere	B
3	92-25-10-92	38000	1.63	0.06	0.04	0.90	91	0.160	Sphere	
4	103-25-10-103	38000	1.60	0.06	0.04	0.90	106	0.182	Disc	C
5	112-25-10-112	46000	1.76	0.05	0.03	0.92	122	0.265	Disc	
6	128-25-10-128	47000	1.60	0.05	0.03	0.92	122	0.275	Disc	D
7	140-25-10-140	47000	1.69	0.04	0.03	0.93	122	0.106	Toroid	E
8	150-25-10-150	51000	2.04	0.04	0.03	0.93	154	0.164	Toroid	
9	170-25-10-170	57000	1.88	0.04	0.02	0.94	164	0.346	Toroid	F
10	150-33-10-150	55000	2.17	0.05	0.03	0.92	164	0.254	Toroid	
11	150-50-10-150	58000	2.00	0.08	0.03	0.89	130	0.188	Oval	G
12	161-60-10-161	55000	2.02	0.09	0.02	0.89	164	0.178	Oval	
13	156-98-10-156	51000	2.00	0.14	0.02	0.84	149	0.049	Porous	H

[a] The polymer was dissolved in DMF at 60 °C, to which hot water (60 °C) was added to generate the assembly at 60 °C [0.5 wt% polymer in water/DMF = 10/1 (v/v)]. [b] The M_n and M_w values were obtained with PMMA-calibrated DMF-GPC. [c] The DLS peak top value at 60 °C.

Morphology Diagram

The obtained amphiphilic PEEA-PMMA-PGLMMA-PEEA CABC tetrablock terpolymers formed self-assemblies in an aqueous solution. In the present work, *N,N*-dimethyl formamide (DMF) was used to dissolve all of the three (PMMA, PGLMMA, and PEEA) segments, and water was used to aggregate the hydrophobic segments to form the assemblies. We first dissolved the polymer in DMF and obtained a homogeneous solution, to which water was added to generate the assembly at 60 °C [0.5 wt% polymer in water/DMF = 10/1(v/v)]. PEEA (block C) was hydrophobic at 60 °C, because the LCST (cloud point) of PEEA is 11 °C.³⁸ [We used 60 °C instead of room temperature (20-25 °C) in order to obtain assemblies with

relatively narrow size distribution and clear contrast. At a higher temperature, the PEEA segment is more hydrophobic and can aggregate more firmly, which would lead to more uniform structures. A comparison at room temperature and 60 °C is given in Figures S15 and S17 in the ESI]. At 60 °C, the PMMA (block A) and PEEA (block C) segments were hydrophobic and formed the core, and the PGLMMA (block B) segment was hydrophilic and formed the loop-structured shell. Therefore, the flower micelle (Scheme 2a) was obtained using PEEA₆₆-PMMA₂₅-PGLMMA₁₀-PEEA₆₆ [Figure 1c (sample A)]. The dynamic light scattering (DLS) analysis shows that the hydrodynamic size (diameter) of the assembly was 50 nm (peak top) [Table 1 (entry 1)]. The contour length of this polymer (167 units) is 42 nm (= 0.25 nm × 167 units). The

particle size (50 nm) was reasonably smaller than the twice of contour length (84 nm), indicating that the assembly was a micelle (sphere) (not vesicle or other structures). Transmission electron microscope (TEM) image also shows spheres [Figure 2 (sample A)].

We fixed the DPs of PMMA (block A) (DP = 25) and PGLMMA (block B) (DP = 10) and varied the DP of PEEA (block C) from 132 (66 for each block) to 340 (170) [Figure 1c (samples A-F), Figure 2 (samples A-F), and Table 1 (entries 1-9)]. The sphere size increased from 50 nm to 91 nm with an increase in the DP of PEEA from 132 (66 for each block) to 184 (92) [Figure 1c (samples A and B), Figure 2 (samples A and B), and Table 1 (entries 1-3)].

A further increase in the DP of PEEA to 206 (103 for each block), 224 (112), and 256 (128) led to a different morphology [Table 1 (entries 4-6), Figure 1c (samples C and D), Figure 2 (samples C and D), and Figure S16 in the ESI]. DLS showed that the sizes of the assemblies were 106, 122 and 122 nm, respectively [Table 1 (entries 4-6)]. These sizes were approximately the twice of the contour lengths (120 nm, 130 nm, and 145 nm, respectively), suggesting that the assemblies were not spherical micelles. The atomic force microscopy (AFM) measurement [Figure 3 (sample D)] demonstrated the formation of a disc-like nanostructure with an average diameter of approximately 50 nm in the dry state.

Figure 1. (a) The synthesis of PEEA-PMMA-PGLMMA-PEEA. (b) GPC (DMF eluent) curves for the synthesis of PEEA-PMMA-PGLMMA-PEEA [Table 1 (entry 1) and Table S1 (entries 1, 2, and 3-1) in the ESI]. For I-PMMA-I, the chromatogram of polymer overlapped with those of small molecules or LiBr-cluster in the DMF eluent in the low molecular-weight region. To avoid the overlap, I-PMMA-I was also analysed with THF eluent-GPC, giving accurate M_n (= 3000) and $\bar{D}$ (= 1.10) values, and these values are given in Figure 1b and Table S1 (entry 1). In Figure 1b, for the GPC curve comparison purpose, the DMF eluent-GPC curves are given for IPMMA-I and the three other polymers. (c) Morphology diagram of the self-assemblies of PEEA-PMMA-PGLMMA-PEEA tetrablock terpolymers with a fixed DP of PGLMMA (block B) (DP = 10) and varied DPs of PMMA (block A) and PEEA (block C).

Interestingly, a further increase in the DP of PEEA to 280 (140 for each block), 300 (150), and 340 (170) provided toroids [Table 1 (entries 7-9), Figure 1c (samples E and F), Figure 2 (samples E and F), and Figure S17 (sample E) in the ESI]. The sizes of the assemblies determined with DLS were 122-164 nm. The TEM image clearly showed the ring-shaped structures with a hole in the center [Figure 2 (samples E and F) and Figure S17 (sample E in a wider TEM view area) in the ESI]. The AFM height profile [Figure 3 (sample F)] for PEEA₁₇₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₇₀ (sample F) demonstrates that the center of the assembly was lower than the edges, confirming the presence of the hole in the center.

TEM

Figure 2. TEM images of the self-assemblies, where A = PEEA₆₆-PMMA₂₅-PGLMMA₁₀-PEEA₆₆, B = PEEA₈₁-PMMA₂₅-PGLMMA₁₀-PEEA₈₁, C = PEEA₁₀₃-PMMA₂₅-PGLMMA₁₀-PEEA₁₀₃, D = PEEA₁₂₈-PMMA₂₅-PGLMMA₁₀-PEEA₁₂₈, E = PEEA₁₄₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₄₀, F = PEEA₁₇₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₇₀, G = PEEA₁₅₀-PMMA₅₀-PGLMMA₁₀-PEEA₁₅₀, and H = PEEA₁₅₆-PMMA₉₈-PGLMMA₁₀-PEEA₁₅₆.

Figure 3. AFM images and cross-sectional height profiles along the red line for sample D (PEEA₁₂₈-PMMA₂₅-PGLMMA₁₀-PEEA₁₂₈) and sample F (PEEA₁₇₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₇₀).

For the formation of a toroid, two mechanisms have been proposed.^{17,40} Most of the toroids reported in the literature are supposed to be generated via end-to-end coalescence of cylindrical micelles. Long flexible thread-like micelles are connected at the chain ends, giving a flexible toroid, for example. The other lesser-reported mechanism is a sphere-disc-toroid transition proposed by He and Schmid.⁴⁰ A spherical micelle grows to a disc-like micelle, which further develops a hole in the center to form a toroid. The present toroids seemed to be generated via the sphere-disc-toroid transition pathway, because no cylindrical precursors were observed. Also, the inner diameters of the toroids [Figure 2 (samples E and F)] were smaller than the cross sectional diameters of the circular rings. It would be unlikely that such toroids were generated by end-to-end coalescence of very short cylinders bending with very high curvature. Therefore, the present toroids would most likely be generated by the sphere-disc-toroid transition.

Mechanistically, with an increase in the hydrophobicity, a sphere starts to be deformed to a cylinder or a disc. The disc has a smaller surface area and is favourable with respect to solvation but has a large curvature. When the hydrophobic segment is rigid with a low mobility, it is difficult to form such a large curvature. In contrast, when the whole or a part of the hydrophobic segment is flexible, the flexibility can facilitate the large curvature, possibly generating the disc. A further increase in the hydrophobic volume can eventually produce a hole as a result of the expansion of the disc rim. The importance of the flexible boundary layer to form the disc and toroid was thoroughly discussed by Pochan and Wooley.¹⁷ In the present system, PMMA is rigid and would constitute the rigid hydrophobic core, PEEA would serve as a flexible segment to facilitate the curvature, and PGLMMA would serve

as a solvating segment in water. In the same context, it was also empirically suggested that the sphere-disc-toroid mechanism is operational when the hydrophobic segment has a low glass transition temperature (T_g).^{12,21} In the present system, PEEA (block C) has a low T_g (-70 °C to -60 °C),⁴¹ which would be consistent with the empirical implication. The high mobility in the hydrophobic segment is critical to facilitate the formation of the disc and toroid.¹⁷

The mass (weight) fractions of PMMA (block A), PGLMMA (block B) and PEEA (block C) segments in the polymer are defined as f_{PMMA} , f_{PGLMMA} , and f_{PEEA} , respectively. As a rough estimate, the polymer formed spheres with $f_{\text{PGLMMA}} \geq 4\%$, discs with $f_{\text{PGLMMA}} = 3\text{--}4\%$, and toroids with $f_{\text{PGLMMA}} \leq 3\%$ in this studied system (Table 1).

As mentioned, a toroid was generated with PEEA₁₅₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₅₀ (Figure 1c). Based on this polymer, we kept the DPs of PGLMMA (block B) (DP = approximately 10) and PEEA (block C) (DP = approximately 150 for each block), varied the DP of the PMMA (block A) segment from 25 to 98, and studied their morphologies [Table 1 (entries 8 and 10–13), Figure 1c, Figure 2 (samples G and H), Figures S18 and S19 in the ESI]. While circular ring toroids were obtained with 25 and 33 DPs of PMMA, an increase in the DP of PMMA to 50 and 60 gave an oval-shaped nanostructure [Figure 1c (sample G), Figure 2 (sample G), and Figure S18 (sample G in a wider TEM view area) in the ESI]. A further increase in the DP of PMMA to 98 led to a porous nanostructure [Figure 1c (sample H), Figure 2 (sample H), and Figure S19 (sample H in a wider TEM view area with more pores) in the ESI]. With an increase in the hydrophobicity, the segregation energy at the hydrophobic-hydrophobic interface becomes larger, which can be balanced with an increase in the surface area (larger surface energy). Namely, with an increase in the segregation energy, the morphology can change to those with higher surface areas. Via the sphere-disc-toroid transition mechanism, the disc is favoured to develop one or more holes, when the hydrophilic segment is more segregated from the hydrophobic segment to allow a larger surface area. We suppose that with an increase in the DP of PMMA (block A), the shell-forming hydrophilic segment [PGLMMA (block B)] is more segregated from the core-forming hydrophobic segments [PMMA (block A) and PEEA (block C)], forcing the circular ring toroid to generate more holes to obtain the porous nanostructures. Therefore, circular ring toroids and porous nanostructures were obtained by varying the DP of PMMA (block A). It should be noted that sample H is likely a porous nanostructure [Figure 2 (sample H) and Figure S19 (sample H) in the ESI], the possibility of other structures such as a multi-component micelle with a core with patches^{42–43} may not be excluded at this moment.

A sphere-disc-toroid-porous structure morphological transition by CABC tetrablock terpolymers facilitates the construction of novel morphologies, which can be used as smart nanoparticles. In this present work, we studied a temperature-directed morphology-transformable toroid (Scheme 2b) and a crosslinked toroid (Scheme 2c), as shown below.

Temperature-Directed Morphology-Transformable Toroid

As mentioned, PEEA (block C) has an LCST (cloud point) at 11 °C. Above the LCST (Scheme 2a), PEEA is insoluble in water and hence both PMMA (block A) and PEEA (block C) form the core, generating the flower micelles, toroids, and porous structure with PGLMMA (block B) in the corona (shell). Below the LCST (Scheme 2b), PEEA (block C) turns to be soluble in water and only PMMA (block A) can form the core for generating a star micelle with blocks BC and C in the corona. We tested the reversible morphological transformation using PEEA₁₄₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₄₀ at 60 °C (above LCST) and 4 °C (below LCST) (Figure 4a). As mentioned, at 60 °C, the size of the assembly determined with DLS was 122 nm [Figure 4a (red line) and Table 1 (entry 7)] and the morphology determined with TEM was a circular ring toroid [Figure 4b (sample E)]. At 4 °C, the size significantly decreased to 21 nm [Figure 4a (blue line)] and the morphology turned to be a sphere [Figure 4b (sample E')], demonstrating the morphology was transformed by the LCST transition of PEEA. Upon heating the solution to 60 °C again, the toroid was regenerated, as confirmed with the DLS [Figure 4a (black line) and TEM (Figure 4b (sample E'')) analyses. Thus, we successfully achieved the reversible toroid-to-star transformation directed by temperature.

The morphology-transformable toroid can be a charming nano-carrier in the delivery area. The toroid with a large core size can act as a red blood cell-like container to encapsulate a large number of external molecules in the core (ring) and release them when the toroid is transformed to the star micelle which only has a small core size (small spherical core).

Crosslinked Toroid

The polymers studied above contained a non-crosslinkable monomer, i.e., methyl methacrylate (MMA) in block A, enabling the reversible morphological transformation. Here, to fix the assembly structure (Scheme 2c), we used a post-crosslinkable monomer, i.e., allyl methacrylate (AMA) in block A and obtained a cross-linkable PEEA₁₅₄-PAMA₃₀-PGLMMA₉-PEEA₁₅₄ tetrablock terpolymer, where PAMA is poly(allyl methacrylate) (Table S2, ESI). The obtained polymer formed a toroid with the size of 187 nm (DLS value) at 60 °C. To this solution, we added a radical source, i.e., 4,4'-azobis(4-cyanovaleric acid) (V501) and crosslinked the AMA (block A) segment at 60 °C. The size of the crosslinked assembly was 182 nm (DLS value) [Figure 5a (red line)], which is slightly smaller than that before crosslinking (187 nm) because of the reduced core volume via the crosslinking. The crosslinking did not change the morphology, as a toroid was observed with TEM [Figure 5b (sample I)]. By cooling the solution to 4 °C (below LCST), the size significantly increased to 240 nm [Figure 5a (blue line)]. We froze and dried the 4 °C sample and analysed the sample with TEM. We observed the expanded toroid containing a smaller (unclear) hole [Figure 5b (sample I')]. This is because the ring-shaped structure was fixed by the

crosslinking and was not able to undergo the rearrangement to form the star. Below LCST, the PEEA segment turned to be soluble in water and hence swelled the ring. This temperature-directed toroidal size change was reversible. By heating the solution to 60 °C again, the size decreased to 182 nm again [Figure 5a (black line)], and the toroid with a clear hole was regenerated, as the TEM image shows [Figure 5b (sample I'')]. This was ascribed to the crosslinking of PAMA segment and

the de-swelling of the PEEA segment above LCST. Thus, the circular ring toroid was successfully fixed by the crosslinking, which exhibited a ring swelling-shrinking behaviour upon the change in temperature. (Although it is difficult to quantitatively determine the crosslinking density, this result in turn suggests that the crosslinking density is high enough to retain the structure.) Unlike the non-crosslinked toroid, the crosslinked toroid is stable and keeps the ring-shape at different temperatures, which may be attractive for a nano-reactor use for producing inorganic nanoparticles at various temperatures, for example.

Conclusions

The self-assembled morphologies of PEEA-PMMA-PGLMMA-PEEA (CABC) tetrablock terpolymers depended on the DPs of the PEEA (block C) and PMMA (block A) segments, where PMMA is a hydrophobic segment, PGLMMA is a hydrophilic segment, and PEEA is a thermosensitive flexible segment. Above LCST, with an increase in the DP of PEEA, the morphology changed from spherical flower micelles to discs and then circular toroids. With an increase in the DP of PMMA, the morphology further changed from toroids to a porous nanostructure. Two smart toroids were also prepared. One is the temperature-directed morphology-transformable toroid, which underwent a reversible toroid-to-star transformation upon the temperature change. The other is the crosslinked toroid. The crosslinked toroid retained the ring-shape structure and underwent the swelling-deswelling of the ring driven by the temperature change. The obtained toroids (uncrosslinked and crosslinked) may find applications as useful nano-containers and nano-reactors, for example.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- 1 U. Tritschler, S. Pearce, J. Gwyther, G. R. Whittell and I. Manners, *Macromolecules*, 2017, **50**, 3439-3463.
- 2 L. P. D. Ratcliffe, M. J. Derry, A. Ianaro, R. Tuinier and S. P. Armes, *Angew. Chem. Int. Ed.*, 2019, **58**, 18964-18970.
- 3 A. Blanz, S. P. Armes and A. J. Ryan, *Macromol. Rapid Commun.*, 2009, **30**, 267-277.
- 4 B. Nandan and A. Horechyy, *ACS Appl. Mater. Interfaces*, 2015, **7**, 12539-12558.
- 5 S. C. Larnaudie, J. C. Brendel, K. A. Jolliffe and S. Perrier, *ACS Macro Lett.*, 2017, **6**, 1347-1351.

Figure 4. (a) DLS curves and (b) TEM images of the self-assemblies of PEEA₁₄₀-PMMA₂₅-PGLMMA₁₀-PEEA₁₄₀ by changing the temperature from 60 °C (sample E) to 4 °C (sample E') and then to 60 °C (sample E'').

Figure 5. (a) DLS curves and (b) TEM images of the crosslinked self-assemblies of PEEA₁₅₄-PAMA₃₀-PGLMMA₉-PEEA₁₅₄ by changing the temperature from 60 °C (sample I) to 4 °C (sample I') and then to 60 °C (sample I'').

- 6 C. J. Kim, X. Hu and S. J. Park, *J. Am. Chem. Soc.*, 2016, **138**, 14941-14947.
- 7 J. Zhang, B. A. Grzybowski and S. Granick, *Langmuir*, 2017, **33**, 6964-6977.
- 8 R. C. Hayward and D. J. Pochan, *Macromolecules*, 2010, **43**, 3577-3584.
- 9 S. J. Holder and N. A. J. M. Sommerdijk, *Polym. Chem.*, 2011, **2**, 1018-1028.
- 10 Z. Li, Z. Chen, H. Cui, K. Hales, K. L. Wooley and D. J. Pochan, *Langmuir*, 2007, **23**, 4689-4694.
- 11 D. J. Pochan, Z. Chen, H. Cui, K. Hales, K. Qi and K. L. Wooley, *Science*, 2004, **306**, 94-97.
- 12 H. Qiu, A. M. Oliver, J. Gwyther, J. Cai, R. L. Harniman, D. W. Hayward and I. Manners, *Macromolecules*, 2019, **52**, 113-120.
- 13 C. Yang, L. Gao, J. Lin, L. Wang, C. Cai, Y. Wei and Z. Li, *Angew. Chem. Int. Ed.*, 2017, **56**, 5546-5550.
- 14 C. C. Conwell, I. D. Vilfan and N. V. Hud, *Proc. Natl. Acad. Sci.*, 2003, **100**, 9296-9301.
- 15 J. Cai, K. P. Mineart, X. Li, R. J. Spontak, I. Manners and H. Qiu, *ACS Macro Lett.*, 2018, **7**, 1040-1045.
- 16 S. Al-Rehili, K. Fhayli, M. A. Hammami, B. Moosa, S. Patil, D. Zhang, O. Alharbi, M. N. Hedhili, H. Möhwald and N. M. Khashab, *J. Am. Chem. Soc.*, 2017, **139**, 10232-10238.
- 17 H. Cui, Z. Chen, K. L. Wooley and D. J. Pochan, *Soft Matter*, 2009, **5**, 1269-1278.
- 18 Z. Chen, H. Cui, K. Hales, Z. Li, K. Qi, D. J. Pochan and K. L. Wooley, *J. Am. Chem. Soc.*, 2005, **127**, 8592-8593.
- 19 H. Yu and W. Jiang, *Macromolecules*, 2009, **42**, 3399-3404.
- 20 J. Zhu, Y. Liao and W. Jiang, *Langmuir*, 2004, **20**, 3809-3812.
- 21 H. Huang, B. Chung, J. Jung, H. W. Park and T. Chang, *Angew. Chem. Int. Ed.*, 2009, **48**, 4594-4597.
- 22 K. Matyjaszewski, *Adv. Mater.*, 2018, **30**, 1706441.
- 23 P. B. Zetterlund, S. C. Thickett, S. Perrier, E. Bourgeat-Lami and M. Lansalot, *Chem. Rev.*, 2015, **115**, 9745-9800.
- 24 J. Nicolas, Y. Guilleaneuf, C. Lefay, D. Bertin, D. Gigmes and B. Charleux, *Prog. Polym. Sci.*, 2013, **38**, 63-235.
- 25 K. Matyjaszewski and N. V. Tsarevsky, *J. Am. Chem. Soc.*, 2014, **136**, 6513-6533.
- 26 M. Ouchi and M. Sawamoto, *Macromolecules*, 2017, **50**, 2603-2614.
- 27 D. J. Keddie, G. Moad, E. Rizzardo and S. H. Thang, *Macromolecules*, 2012, **45**, 5321-5342.
- 28 G. David, C. Boyer, J. Tonnar, B. Ameduri, P. Lacroix-Desmazes and B. Boutevin, *Chem. Rev.*, 2006, **106**, 3936-3962.
- 29 S. Yamago, *Chem. Rev.*, 2009, **109**, 5051-5068.
- 30 M. J. Monteiro and M. F. Cunningham, *Macromolecules*, 2012, **45**, 4939-4957.
- 31 A. Goto and T. Fukuda, *Prog. Polym. Sci.*, 2004, **29**, 329-385.
- 32 A. Goto, T. Suzuki, H. Ohfuji, M. Tanishima, T. Fukuda, Y. Tsujii and H. Kaji, *Macromolecules*, 2011, **44**, 8709-8715.
- 33 A. Goto, A. Ohtsuki, H. Ohfuji, M. Tanishima and H. Kaji, *J. Am. Chem. Soc.*, 2013, **135**, 11131-11139.
- 34 A. Ohtsuki, L. Lei, M. Tanishima, A. Goto and H. Kaji, *J. Am. Chem. Soc.*, 2015, **137**, 5610-5617.
- 35 C. G. Wang and A. Goto, *J. Am. Chem. Soc.*, 2017, **139**, 10551-10560.
- 36 H. Xu, C. G. Wang, Y. Lu and A. Goto, *Macromolecules*, 2019, **52**, 2156-2163.
- 37 J. Zheng, C. G. Wang, Y. Yamaguchi, M. Miyamoto and A. Goto, *Angew. Chem. Int. Ed.*, 2018, **57**, 1552-1556.
- 38 J. Zheng, C. Chen and A. Goto, *Angew. Chem. Int. Ed.*, 2020, **59**, 1941-1949.
- 39 K. Skrabania, J. Kristen, A. Laschewsky, O. Akdemir, A. Hoth and J. F. Lutz, *Langmuir*, 2007, **23**, 84-93.
- 40 X. He and F. Schmid, *Phys. Rev. Lett.*, 2008, **100**, 137802.
- 41 Y. S. Ramírez-Fuentes, J. Illescas, A. Gelover-Santiago and E. Rivera, *Mater. Chem. Phys.*, 2012, **135**, 772-779.
- 42 J. Huang, Y. Guo, S. Gu, G. Han, W. Duan, C. Gao and W. Zhang, *Polym. Chem.*, 2019, **10**, 3426-3435.
- 43 P. Shi, Y. Qu, C. Liu, H. Khan, P. Sun and W. Zhang, *ACS Macro Lett.*, 2016, **5**, 88-93.

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