Self-Assembly

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A Morphological Transition of Inverse Mesophases of a Branched-Linear Block Copolymer Guided by Using Cosolvents**

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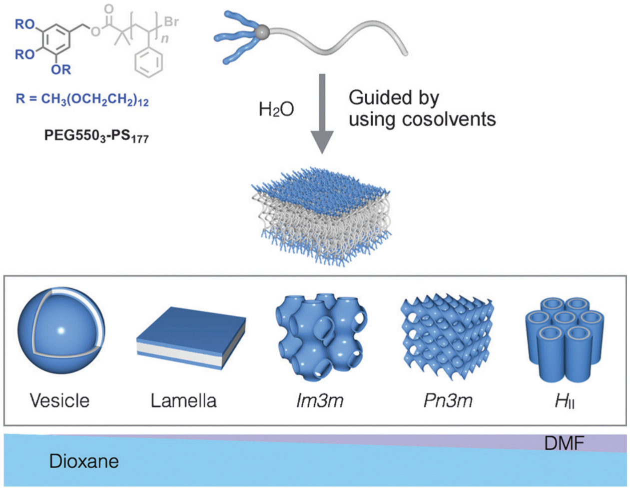
Abstract: *We report here a strategy for influencing the phase and lattice of the inverse mesophases of a single branched-linear block copolymer (BCP) in solution which does not require changing the structure of the BCP. The phase of the self-assembled structures of the block copolymer can be controlled ranging from bilayer structures of positive curvature (polymersomes) to inverse mesophases (triply periodic minimal surfaces and inverse hexagonal structures) by adjusting the solvent used for self-assembly. By using solvent mixtures to dissolve the block copolymer we were able to systematically change the affinity of the solvent toward the polystyrene block, which resulted in the formation of inverse mesophases with the desired lattice by self-assembly of a single branched-linear block copolymer. Our method was also applied to a new solution self-assembly method for a branched-linear block copolymer on a stationary substrate under humidity, which resulted in the formation of large mesoporous films. Our results constitute the first controlled transition of the inverse mesophases of block copolymers by adjusting the solvent composition.*

The direct self-assembly of amphiphilic block copolymers (BCPs) into inverse bicontinuous structures in solution is an emerging strategy for creating highly ordered porous polymers with three-dimensionally interconnected networks of large pores.[1–9] In a manner similar to the self-assembly of lipids such as monoolein into colloidal particles of inverse bicontinuous cubic mesophases (cubosomes) in water,[10–15] BCPs in solution could be directly self-assembled into colloidal particles of inverse bicontinuous cubic phases of the BCP bilayer (polymer cubosomes).[1–7,16–19] We recently reported that diblock copolymers, composed of a dendritic or branched hydrophilic block and a hydrophobic linear polymer block, preferentially self-assemble into triply periodic minimal surfaces (TPMSs) of the BCP bilayers in solution, resulting in the creation of polymer cubosomes having highly defined internal large-pore networks.[16–18] The TPMSs of the BCP bilayers exhibited distinct crystalline structures such as primitive cubic (*Im*3*m*, P surface), double diamond (*Pn*3*m*, D surface), and gyroid (*Ia*3*d*, G surface) lattices, depending on the architecture of the dendritic hydrophilic block as well as the block ratio between two distinct polymer domains. The polymer cubosomes of these BCPs exhibited a large surface area, which could be functionalized by implementing the desired functional groups through co-assembly with linear BCPs with α-functionalized hydrophilic blocks. Moreover, the TPMSs of the BCP bilayer could be expanded to large-scale films by the diffusion of water under saturated humidity into a concentrated solution of BCP cast on a stationary substrate.[18]

Our previous studies suggested that the branched architecture of the hydrophilic block played a crucial role in the preferential self-assembly of branched-linear BCPs (Scheme 1) into inverse mesophases by affecting the chain dimension of the hydrophobic block with respect to the bilayer plane.[17] This altered chain dimension caused the critical packing factor (P, defined as $P = V/a_0l_c$, in which V is the volume of the hydrophobic part, a_0 is the molecular area per amphiphile, and l_c is the critical length of the hydrophobic part) of the BCP to be greater than unity, which was presumed



Scheme 1. A branched-linear block copolymer and its self-assembly into inverse mesophases with desired lattices guided by using cosolvents.

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to be a qualitative prerequisite for inverse mesophase formation by self-assembly of BCPs and lipids in solution.[15,17]

In spite of this architectural effect on self-assembly, the block ratio (f_{PEG}, defined by the ratio of the molecular weight of the hydrophilic poly(ethylene glycol) (PEG) domain to that of the hydrophobic polystyrene (PS) chain) remained as a dominant factor governing the phase behavior of the BCP.[16,17] Therefore, the block ratio of the BCP should be carefully adjusted by using controlled radical polymerization of the hydrophobic PS block to restrict the molecular weight of the PS block to the narrow range required for the preferential self-assembly of the BCPs into inverse bicontinuous cubic mesophases. This stringent requirement of the architecture of branched-linear BCPs might hinder the availability of the resulting self-assembled structures for further studies and applications. Here we demonstrate that the phase of the self-assembled structures of a branched-linear BCP consisting of branched PEG and linear PS blocks can be controlled to favor the formation of inverse mesophases over conventional polymer vesicles by adjusting the composition of the solvent mixture.

In this study, we synthesized branched-linear BCPs (bPEG–PS$_n$; n = number of repeat units in the polystyrene chain) through atom-transfer radical polymerization (ATRP) of styrene in the presence of a macroinitiator, which has three PEG550 chains ($M_n = 550\,\mathrm{g\,mol^{-1}}$) tethered to a 3,4,5-trihydroxybenzyl ester core (Scheme 1). This method allowed to control the block ratio (f_{PEG}) by adjusting the molecular weight of the PS chain (Table S1 in the Supporting Information, SI). The resulting bPEG–PS$_n$ was allowed to self-assemble in solution by the cosolvent method involving the addition of a PEG-block-selective solvent (water) to a solution of BCPs dissolved in an organic solvent (0.5 wt% in dioxane) at a controlled rate. Under this condition, the f_{PEG} value of the BCP should be maintained at 6.5–8.5% for the preferential formation of inverse bicontinuous cubic mesophases (Figure 1 a). As observed by small-angle X-ray scattering (SAXS) and electron microscopy, PEG550$_3$-PS$_{211}$ ($f_{\mathrm{PEG}} = 7.5\%$) self-assembled into polymer cubosomes with an internal P minimal surface consisting of BCP bilayers ($Im3m$ space group, lattice constant $a = 82.5$ nm; Figures 1 b,c and S1). On the other hand, bPEG–PS$_n$ with a higher-molecular-weight PS chain (PEG550$_3$-PS$_{231}$, $f_{\mathrm{PEG}} = 6.9\%$) self-assembled into large cubosomes (diameter > 20 μm), exhibiting the D minimal surface structure ($Pn3m$ space group, $a = 47.9$ nm; Figures 1 d,e and S1). As shown in a simple phase diagram (Figure 1 a), bPEG–PS$_n$ only formed polymer vesicles (Figure 1 f) when the value of f_{PEG} was greater than 8.9%, and bPEG–PS$_n$ preferentially self-assembled into large hexasomes with an internal H_{II} phase if the f_{PEG} value was less than 5.6% ($P6mm$, $a = 28.8$ nm; Figures 1 g and S1). Even though controlled radical polymerization methods such as ATRP could provide accurate control over the molecular weight of the PS block and, thus, the f_{PEG} value of the bPEG–PS$_n$, the stringent block ratio requirement for the preferential self-assembly of BCP into inverse bicontinuous cubic phases imposed difficulty in synthesizing BCPs for the preparation of the polymer cubosomes and mesoporous films having well-defined internal bicontinuous structures.

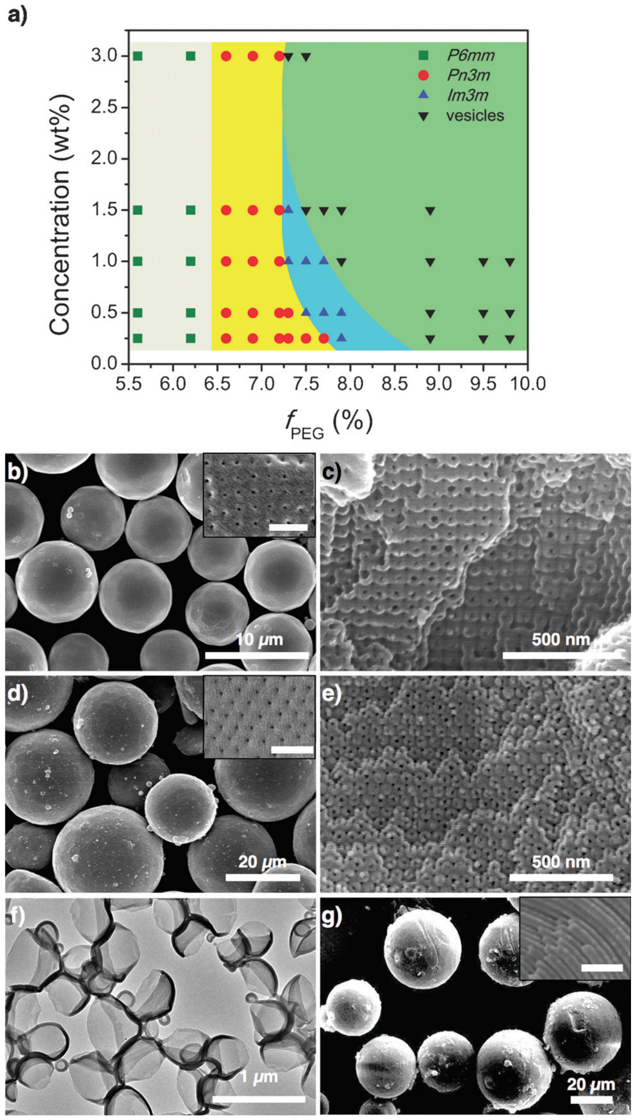

Figure 1. a) A simple phase diagram of self-assembly of PEG550$_3$-PS$_n$ from dioxane solutions. b–e) SEM images of the polymer cubosomes of b) PEG550$_3$-PS$_{211}$ ($f_{\mathrm{PEG}} = 7.5\%$) and d) PEG550$_3$-PS$_{231}$ ($f_{\mathrm{PEG}} = 6.9\%$). The insets show the perforated surface layer of the polymer cubosomes (scale bars: 200 nm). SEM images of the internal structures of the polymer cubosomes of c) PEG550$_3$-PS$_{211}$ showing [100] projection of $Im3m$ and e) PEG550$_3$-PS$_{231}$ showing [111] projection of $Pn3m$. f) TEM image of the polymersomes of PEG550$_3$-PS$_{177}$ ($f_{\mathrm{PEG}} = 8.9\%$). g) SEM image of the hexasomes of PEG550$_3$-PS$_{283}$ ($f_{\mathrm{PEG}} = 5.6\%$). The inset shows the internal H_{II} structure (scale bar: 200 nm).

Control over the thermodynamic parameters and kinetic pathways of the self-assembly of BCPs has been pursued as a means for influencing the self-assembly process to create nanostructures with desired morphologies without synthesizing new BCPs.[21–27] Controlling the solvent composition—and thereby the affinity of the solvent toward the polymer chain—is a facile method for controlling the conformation and properties of polymer chains in solution.[28,29] The solvent composition was simply adjusted by mixing solvents with different interaction parameters toward the target polymers. The solvent composition has already been shown to play an important role in determining the morphology of self-assembled block copolymer structures in solution. Cheng and co-workers demonstrated the morphological transition of the self-assembled structure of a single diblock copolymer in a binary mixture of solvents, ranging from spherical micelles to cylindrical micelles and vesicles, depending on the composition of the solvent.[23] The Eisenberg group also showed that the size of polymersomes could be reversibly adjusted using a binary solvent mixture of varying ratio.[25,26] Recently, Truong et al. reported that a single BCP, consisting of a cationic hydrophilic block and a glassy PS block, could reproducibly exhibit different morphologies, depending on the nature of the solvent and the kinetic conditions of the self-assembly process.[27]

Inspired by these previous studies, we postulated that the composition of the solvent could affect the chain dimension of the hydrophobic PS block, which might result in a morphological change of the self-assembled inverse structures of bPEG–PS$_n$. Using dioxane (with the Hildebrand solubility parameter $\delta = 20.5\ \mathrm{MPa}^{-1/2}$)[30] as a common solvent for both PEG and PS domains, PEG550$_3$-PS$_{211}$ preferentially formed polymer cubosomes under our standard conditions for self-assembly. When tetrahydrofuran (THF; $\delta = 18.6\ \mathrm{MPa}^{-1/2}$) was used as a solvent, the transmission electron microscopy (TEM) images of the self-assembled structures of PEG550$_3$-PS$_{211}$ showed the appearance of polymer vesicles and sponge-phase particles as minor structures along with a majority of fully developed polymer cubosomes (Figure S2). Dimethylformamide (DMF) is a pseudo-theta solvent for PS, in which PS adopts a reduced chain dimension such as R_g compared to the value of the same PS chain dissolved in dioxane.[31,32] When DMF ($\delta = 24.7\ \mathrm{MPa}^{-1/2}$) was used as a common solvent, PEG550$_3$-PS$_{211}$ only forms irregular aggregates without any internal order at a low water content (> 3 %). From these observations, we suspected that the affinity of the solvent toward the PS block ($\delta = 16.6$–$20.2\ \mathrm{MPa}^{-1/2}$) might have an influence on the compatibility of the PS chain in solution, which could, in turn, affect the chain stretching of the PS block when the BCP forms aggregates.

To support this assumption, we changed the solvent composition of the initial BCP solution by mixing dioxane with DMF. We tested PEG550$_3$-PS$_{177}$ ($f_{\mathrm{PEG}} = 8.9\,\%$), which, under our standard conditions for self-assembly, only formed polymersomes when THF or dioxane was used as the only solvent (Figure 2 a). However, when the solvent was changed to a dioxane/DMF mixture (98:2 v/v), PEG550$_3$-PS$_{177}$ self-assembled into the inverse mesophase structure, forming small polymer cubosomes coexisting with polymer vesicles (Figure 2 b). When we increased the DMF content in dioxane to 5 vol %, we observed the formation of polymer cubosomes (average diameter of 8 μm) without the coexistence of polymer vesicles (Figure 2 c). Further increasing the amount of DMF in dioxane (dioxane/DMF = 92:8 v/v) only increased the average diameter (26 μm) of the polymer cubosomes of PEG550$_3$-PS$_{177}$ (Figure 2 d). Essentially, the self-assembled structure of PEG550$_3$-PS$_{177}$ was transformed into large hexasomes with an internal inverse hexagonal phase (H_{II}) when the solvent mixture had a high DMF content (dioxane/DMF = 85:15 v/v). This morphological transition exhibited by self-assembly of PEG550$_3$-PS$_{177}$ in a series of solvent mixtures coincided with the transition of the self-assembled structures of PEG550$_3$-PS$_n$ with an increasing degree of polymerization of the PS block (Figure 1). We also note that the self-assembly of a linear BCP, PEG2000-PS$_{180}$, did not show any phase transition under the identical conditions used for the self-assembly of PEG550$_3$-PS$_{177}$ (Figure S3), suggesting that the architecture of bPEG–PS$_n$ is responsible for the self-assembly into inverse mesophases.

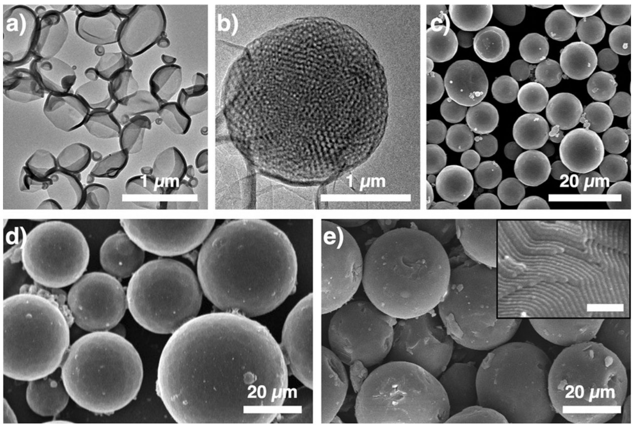

Figure 2. a–e) TEM and SEM images of the self-assembled structures of PEG550$_3$-PS$_{177}$ prepared from the dioxane/DMF mixtures at varying ratios: a) 0 vol % DMF (vesicle), b) 2 vol % DMF (vesicle + polymer cubosome), c) 5 vol % DMF ($Im3m + Pn3m$), d) 8 vol % DMF ($Pn3m$), and e) 15 vol % DMF (H_{II}). The inset in (e) shows the internal hexagonal structures (scale bar: 200 nm).

The internal crystalline structure of the polymer cubosomes of PEG550$_3$-PS$_{177}$ prepared from the binary mixture of dioxane and DMF as a solvent for self-assembly was studied by SAXS and SEM (Figure 3). From the SAXS results, we observed that the internal crystalline structure of the polymer cubosomes of PEG550$_3$-PS$_{177}$ self-assembled from the mixed solvent with 5 vol % DMF in dioxane was a mixed phase of Schwartz P and Schwartz D surfaces ($Im3m + Pn3m$) (Figure 3 a,d). Upon increasing the amount of DMF in the solvent mixture (dioxane/DMF = 92:8 v/v), the internal structure was completely changed to the Schwartz D surface ($Pn3m$ symmetry, $a = 46.0$ nm; Figure 3 b,e). The inverse hexagonal phase (H_{II}) appeared within the large particles when PEG550$_3$-PS$_{177}$ was self-assembled from a solvent mixture with a higher DMF content (dioxane/DMF = 85:15 v/v; Figure 3 c,f). This result corresponds with the phase behavior of PEG550$_3$-PS$_n$ upon increasing the degree of polymerization (DP$_n$) of the PS block, leading to the phase change of the self-assembled structures from polymersomes to polymer cubosomes and hexasomes.[17] Given the fixed molecular weight of both polymer blocks in PEG550$_3$-PS$_{177}$, the addition of DMF might affect the chain dimension of the PS block in a binary mixture of common solvents. If a constant PS block volume is assumed, the chain stretching of the PS block would decrease in the presence of DMF, which could reduce the critical chain length of the hydrophobic domain (l_c) and, thus, would increase the critical packing factor (P) of the BCP upon self-assembly.

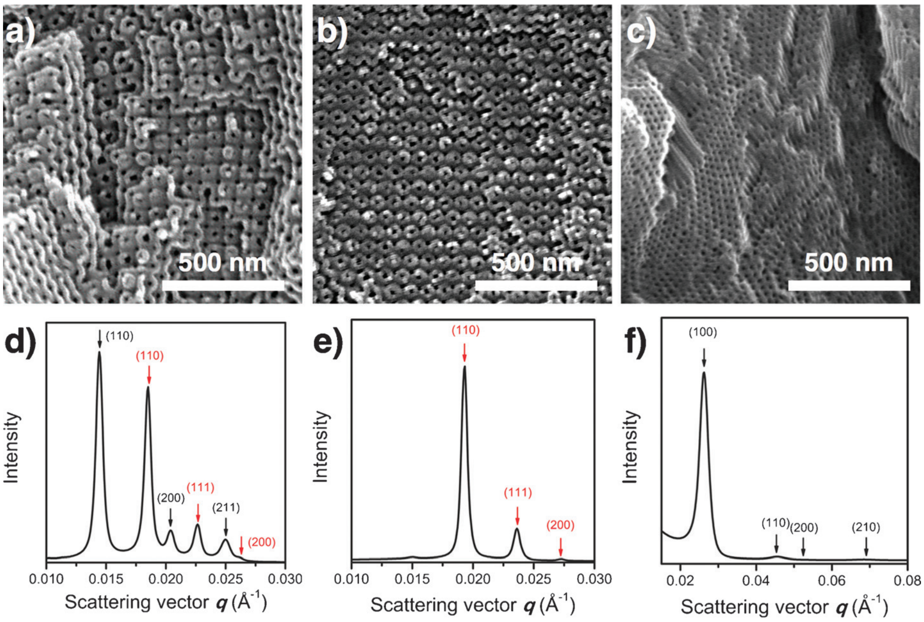

Figure 3. a–c) SEM images of the internal structures of the polymer cubosomes of PEG550$_3$-PS$_{177}$ prepared from a) 5 vol% DMF in dioxane showing the [100] projection of *Im3m*, b) 8 vol% DMF in dioxane showing the [111] projection of *Pn3m*, and c) 15 vol% DMF in dioxane showing the cross-section view of the inverse hexagonal phase. d–f) SAXS results corresponding to the polymer cubosomes in Figure 3 a–c: d) Mixed phase of *Im3m* and *Pn3m* symmetries ($a = 61.5$ nm (*Im3m*) and 48.0 nm (*Pn3m*)); d) *Pn3m* symmetry ($a = 46.0$ nm); f) *P6mm* symmetry ($a = 27.7$ nm).

Similar effects of the presence of DMF in the solvent mixture were also observed in the self-assembly of PEG550$_3$-PS$_{177}$ mediated by the diffusion of water vapor into the BCP solution cast on a stationary substrate.[18] This method, the solvent-diffusion/evaporation-mediated self-assembly (SDEMS) of BCPs, allowed the solution self-assembly of bPEG–PS$_n$ on a stationary substrate under static conditions (see SI for a detailed procedure). The dioxane solution of PEG550$_3$-PS$_{177}$ (15 wt%) cast on a glass substrate (1 cm^2 area) only turned into a translucent film (thickness of 50 μm) consisting of stacked lamellae of BCP upon the diffusion of water in the humidity chamber (saturated with water/dioxane 1:1 v/v) for 1 h at 23 °C (Figure 4 a,b). When a dioxane/DMF mixture (90:10 v/v) was used as solvent for PEG550$_3$-PS$_{177}$, the same procedure yielded a mesoporous film with an internal D minimal surface structure (*Pn3m*, $a = 50.6$ nm) throughout the film (Figures 4 c,d and S5). The internal structure of the film changed to the inverse hexagonal phase (H_{II}) when the DMF content was increased (dioxane/DMF 85:15 v/v) (Figure 4 e,f).

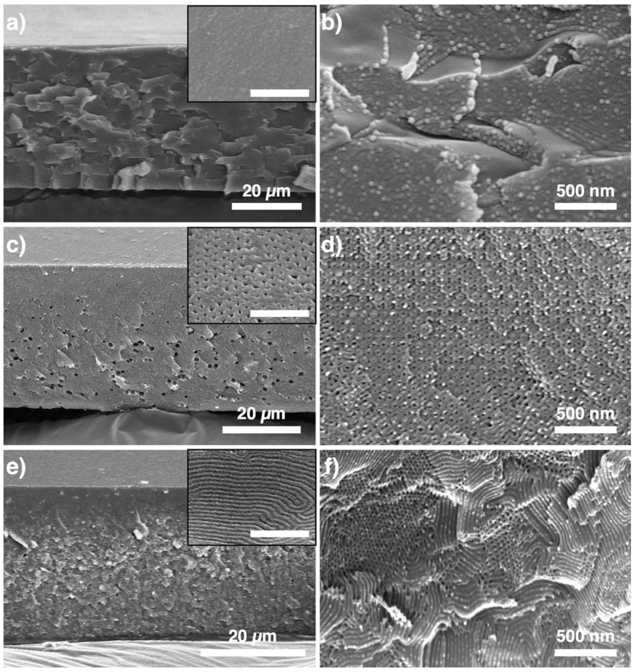

Figure 4. a,c,e) Low-resolution SEM images of the cross-section of the mesoporous films of PEG550$_3$-PS$_{177}$ prepared by the SDEMS method using DMF/dioxane mixtures as a common solvent. a) 0 vol% DMF, c) 10 vol% DMF, and e) 15 vol% DMF. (The insets show the top layer of the films; scale bars: 500 nm). b,d,f) High-resolution SEM images of the films of (a), (c), and (e). b) Stacked lamellae, d) *Pn3m* symmetry ($a = 50.6$ nm), and f) *P6mm* symmetry ($a = 29.3$ nm).

In summary, we demonstrated that the solution self-assembly of a branched-linear BCP, namely PEG550$_3$-PS$_{177}$, could be controlled to favor the formation of inverse mesophases over conventional polymer vesicles by adjusting the solvent composition. By gradually deteriorating the solvent affinity toward the PS block by mixing two solvents with different interaction parameters, the resulting self-assembled structures of a single branched-linear BCP exhibit a morphological transition from vesicles and flat bilayers to triply periodic minimal surfaces of the block copolymer bilayer as well as inverse hexagonal structures. The crystalline lattice of the TPMSs of the BCPs could also be changed from the primitive cubic structure to double diamond structures depending on the composition of the common solvent mixture. This nonsynthetic pathway for accessing the desired inverse mesophases of a single BCP could expand the availability of well-defined mesoporous structures of BCPs for applications such as separation and nanotemplating by providing block ratio tolerance for BCP synthesis.

Keywords: block copolymers · inverse mesophases · mesoporous structures · minimal surfaces · self-assembly

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