Self-assembly of polystyrene-*b*-poly(4-vinylpyridine) in deoxycholic acid melt

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ABSTRACT

It is well known that amphiphilic block copolymers in selective solvents self-assemble into micellar structures, where solvophilic blocks tend to contact with solvents while solvophobic blocks are shielded from the solvents. Different from the conventional micellization in liquid systems, we report that the block copolymer, polystyrene-*b*-(4-vinylpyridine) (PS-*b*-P4VP), can self-assemble in melted deoxycholic acid (DCA) at high temperatures and the structures are retained in "solid state" after being cooled down to room temperature. Probing by transmission electron microscopy (TEM), we found that a series of self-assembled structures, including spherical micelles, wormlike micelles and vesicles can be obtained by varying the length of the block copolymers and the morphologies are dependent on the annealing temperature and time. We also demonstrate how to extract the structures that are trapped in solid state by removing DCA using appropriate solvents. The extracted vesicles, which are loaded with solid molecules, are potential for applications in nanocapsules and controlled release.

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1. Introduction

Amphiphilic molecules, such as surfactants or lipids, which are molecules with distinct hydrophilic and hydrophobic portions can spontaneously organize into structures in aqueous or organic solutions [1]. Much similar to amphiphilic molecules, block copolymers comprised of two or more homopolymers linked by covalent bonds, when dispersed in selective solvents, self-assemble into a variety of structures due to the interplay of solvents with the solvophilic and solvophobic blocks [2–9]. One major difference between surfactants and block copolymers is their molecular weight: common surfactants have ∼ 10-carbon alkyl tails while block copolymers typically have tens or more repeat units. Upon micellization, surfactants are able to rapidly exchange between the micellar state and the unimer state in solvents due to their low molecular weight and furthermore, the alkyl tails are liquid-like in the aggregates so that the structures can adopt shapes with minimum free energy [10]. The exchange process, however, is very slow for block copolymers since the thermal energy in mild conditions is insufficient to transfer bulky chains from micelles into solvents [11]. In other words, the entropic gain of mixing solvophobic chains with solvents is quite small compared to the free energy loss of breaking structures. Thus, once

self-assembled structures are formed, they are more or less locked, which implies that more structures other than those commonly seen in surfactant systems can be kinetically frozen during micellization [6]. Moreover, the long chains could lead to entanglements, which in turn reduces the chain mobility and enhances the mechanical properties of the structures [12]. The designable molecular architectures, the kinetic stability and the robustness of the self-assembled structures provide block copolymers the potency for applications in nanomaterial synthesis [13–16] and control release [5,17].

While most micellization of block copolymers were studied in liquid aqueous or organic media near room temperature, a couple of systems have been reported in special conditions. He et al. reported the amphiphilic block copolymer, polybutadiene-*b*-poly(ethylene oxide), form micelles and vesicles in ionic liquids and their shapes are dependent on the length of PEO block [18]. Several groups have created block copolymer micelles and vesicles in supercritical fluids at high pressure, such as CO_2 [19–21]. Supercritical fluids were then vented and the structures formed at high pressure retained after being re-dispersed in analogous selective solvents under ambient conditions. In addition to the above fluidic systems, the micellization of block copolymers was found in polymeric media [22,23]. When blending block copolymers with a large amount of homopolymers which are compatible with one of the blocks, the homopolymers mix with the compatible block while repel the others above the glass transitions of the polymers, leading to the micellization of block copolymers. Kinning et al. has reported

a variety of structures, including spherical micelles, wormlike micelles and vesicles, in polystyrene-*b*-polybutadiene/polystyrene blends [24]. Note that polystyrene is in glassy state at room temperature, which means that the structures formed in melted state can be trapped in solids after cooling down. Moreover, the introduction of polystyrene block covalently bonded with polybutadiene promotes the dispersion of polybutadiene in originally immiscible polystyrene. This strategy is useful to produce well-dispersed composites and can efficiently improve the properties of homopolymers [25].

In this study, we produced self-assembled structures by a new route, that is, instead of liquid and polymeric media, a low-mass molecule which is a crystalline solid at room temperature was used as a "solvent." The molecule we used is a bile acid, deoxycholic acid (DCA), whose structure is schemed in Fig. 1. The melting temperature of DCA is 175 °C. Since the hydroxyl and carboxyl groups lie on the same side of the four-ring structure (steroid ring), DCA is an unusual amphiphiles: unlike typical surfactants, which present a polar head and a non-polar tail, DCA is a facial amphiphile, with a polar and a non-polar face [26]. We mixed polystyrene-*b*-poly(4-vinylpyridine) (PS-*b*-P4VP) in a large amount of DCA and heated it above the melting temperature of DCA. Interestingly, PS-*b*-P4VP self-assemble in DCA melt and the structures formed at high temperature could be retained in crystalline solids after being cooled down to room temperature.

The supramolecules formed by block copolymers and low-mass molecules via secondary bonding, such as hydrogen bonding and electrostatic interactions, have been widely studied, especially the PS-*b*-P4VP-based systems [27–29]. The microphase separation behaviors of block copolymers were tailored by the addition of low-mass molecules due to the association of the molecules with one of the blocks and more interestingly, many hierarchical structure-*within*-structure morphologies were observed. In such systems, the amounts of added low-mass molecules are normally in stoichiometric ratio to the repeat units of the associated block. The present system, in a sense, can be regarded as an extension of the supramolecular assembly, where various structures different from those in conventional block copolymer-based supramolecules are formed in the presence of a much greater amount of low-mass molecules which similarly interact with one of the blocks. Since the self-assembly process in this system is very slow, it provides a platform to study the evolution of the structures.

In addition to the scientific curiosity about the mechanism of the self-assembly, this technique provides some advantages over others in applications. For example, low-mass molecules here serve as "solvent" that can fill the entire enclosed portions of vesicles, which may give high encapsulation efficiency of the low-mass molecules in vesicles. Furthermore, since low-mass molecules inside the vesicles are protected by bilayers while the exterior ones can be washed away by proper solvents, the vesicles filled with low-mass molecules can be extracted in an intact form. We will show that the PS-*b*-P4VP structures in solid DCA can be successfully extracted by alcohol or sodium hydroxide (NaOH) aqueous solutions.
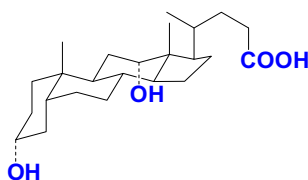
2. Experimental section

2.1. Materials

PS(40000)-*b*-P4VP(5600) (PDI = 1.09), PS(41500)-*b*-P4VP-(17500) (PDI = 1.07) and PS(20000)-*b*-P4VP(17000) (PDI = 1.08) were purchased from Polymer Source Inc. Deoxycholic acid (DCA) was purchased from Sigma Aldrich. Tetrahydrofuran (THF) was purchased from Mallinckrodt Chemicals. All chemicals were used as received.

2.2. Sample preparation

The diblock copolymer PS-*b*-P4VP and DCA were first dried in vacuum oven for 1 day and then dissolved in THF with desired amounts, followed by stirring for 2 days at room temperature. After well-mixed, the polymer/DCA solutions were placed in Teflon beakers covered by an inverted dish and THF was allowed to evaporate slowly at room temperature for several days. Samples were further dried and annealed in an oven purged with nitrogen at 175 °C or 185 °C for 1–4 days. After being annealed, the samples were either quenched in liquid nitrogen or slowly cooled down to room temperature. The morphologies are basically the same using these two cooling processes, as described later in the paper. The samples of PS-*b*-P4VP without DCA were also dissolved in THF first and after the removal of THF, the samples were annealed at 175 °C for 2 days. The characteristics of all samples used in this paper were listed in Table 1.

2.3. Fourier transform infrared spectra (FT-IR)

FT-IR samples were prepared by mixing ground powders of PS-*b*-P4VP/DCA mixtures in KBr with a ratio of 1:30. The spectra were recorded in the transmission mode at room temperature by a PerkinElmer Spectrum 100 Model FT-IR spectrometer.

2.4. Transmission electron microscopy (TEM)

Pieces of non-annealed or annealed solid samples were embedded in resin and cured at 60 °C overnight and then were sectioned to a thickness ∼ 80 nm. The thin sections were exposed to iodine vapor for 2 h that selectively stains the P4VP block to enhance the contrast. To image the extracted structures, a small piece of self-assembled PS-*b*-P4VP/DCA mixtures was placed in methanol, ethanol or NaOH aqueous solutions where DCA was dissolved while the structures were suspended. The solutions were further diluted and then dropped onto a carbon-coated copper grid, followed by air-drying before imaging was conducted. TEM images were collected on a Joel JEM-1230 transmission electron microscope at an accelerating voltage of 100 kV.

Fig. 1. Molecular structure of deoxycholic acid (DCA). The hydrophilic groups are all on the same side, i.e. a facial amphiphile.

Table 1
Characteristics of Samples.

Sample	$M_{n,PS}$ (g/mole)	$M_{n,P4VP}$ (g/mole)	Morphology[a]	
			Without DCA	In DCA
PS(40000)-*b*-P4VP(5600)	40,000	5600	Sphere	Vesicle
PS(41500)-*b*-P4VP(17500)	41,500	17,500	Gyroid	Wormlike micelle
PS(20000)-*b*-P4VP(17000)	20,000	17,000	Lamella	Spherical micelle

[a] Samples were annealed at 175 °C in nitrogen atmosphere for 2 days.