Communication

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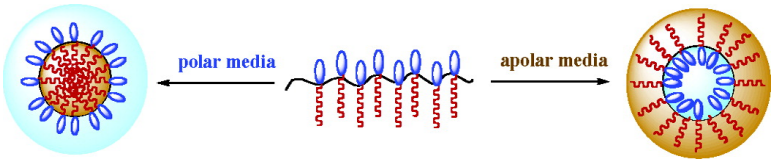

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Invertible Amphiphilic Homopolymers

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Self-organization of amphiphilic polymers has resulted in assemblies such as micelles, vesicles, fibers, helical superstructures, and macroscopic tubes.[1] These nanoscale to macroscale morphologies are of interest in areas ranging from material science to biology.[2] Stimuli-responsive versions of these assemblies are likely to further enhance their scope as "smart" materials. Thermo- or pH-sensitive polymer micelles[3a,b] and vesicles[3c] have been reported in which the nature of the functionality at the corona changes in response to the stimulus. To date, little attention has been paid to realize an environment-dependent switch from a micelle-type assembly with a hydrophilic corona to an inverted micelle-type assembly with a lipophilic corona.[4] Here, we report on a new class of polymer superstructures that exhibit such properties. We demonstrate that the change in the surface of the assembly is an amplified consequence of change in molecular-level conformation within each monomer unit. Polymers with such properties could find use in applications such as carriers for trafficking drugs through the lipid bilayers and as components of smart adhesives.

Block copolymers are often the choice for a wide variety of supramolecular assemblies, in which the fundamental driving force involves the mutual immiscibility of the blocks and/or the immiscibility of one of the blocks in the bulk solvent. For example, poly(styrene-*co*-acrylic acid) block copolymers exhibit several interesting amphiphilic assemblies.[5] These self-assembled structures are the result of the incompatibility between the hydrophobic polystyrene block and the hydrophilic poly(acrylic acid) block. The consequences of incorporating carboxylic acid and benzyl moieties, the key hydrophilic and hydrophobic functionalities in poly(acrylic acid) and polystyrene respectively, within the same monomer of a homopolymer should be interesting from an intramolecular phase separation perspective.[6] Accordingly, we conceived a styrene-based monomer shown by the structure **1a** (Figure 1). The hydrophilic carboxylic acid functionality, the hydrophobic benzyl moiety, and the polymerizable olefinic bond are all placed at meta-positions with respect to each other on a benzene ring. The design strategy is that the relative placement of these three functionalities should facilitate the phase segregation of the amphiphilic moieties within the polymer assembly. Monomers **1a** and **1b**, which have the carboxylic acid functionality in its masked form for synthetic reasons, were derived from 3,5-dihydroxybenzoic acid in six steps.[7] Free radical polymerization of the monomer **1a** using AIBN (1 mol %) as the initiator afforded polymer **2a**, with M_n = 57 000, PDI = 2.3, and an average DP = 167, as determined by size exclusion chromatography (SEC) against polystyrene standards.[7] Hydrolysis of polymer **2** afforded the carboxylic acid-based polymer **3a**. Addition of 1 to 2 equiv of bases such as NaOH or KOH per carboxylic acid functionality renders the polymer soluble in water. Interestingly, polymer **3a** was found not to be soluble in apolar solvents such as dichloromethane and toluene. However, addition of 1 equiv of base along with 2 to 3 equiv of water rendered the resultant carboxylate polymer **3c** soluble in these apolar solvents.

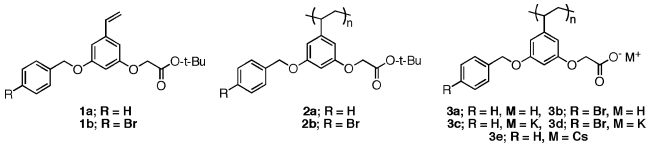
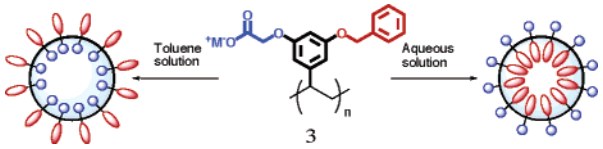


Figure 1. Structures of monomers and polymers.

Scheme 1. Schematic Representation of Micelle-Type and Inverse Micelle-Type Assemblies



All these solutions were optically clear. We hypothesized that the observed solubility characteristics could be the result of formation of a micelle-like structure in water, in which the hydrophilic carboxylate groups are exposed to the bulk solvent and the hydrophobic benzyl substituents are tucked in the interior of an assembly (Scheme 1). Similarly, an inverted micelle-like structure would be expected in apolar solvents, in which the functional group placements are reversed.

To investigate the structure of the assemblies, we utilized the darker contrast provided by heavy atoms in TEM images as the probe. To identify the placement of the hydrophilic carboxylic acid moiety, we treated the polymer **3a** (M = H) with CsOH to convert the acid to the corresponding carboxylate species (**3e**). The resulting Cs^+ counterion is a high atomic weight species that should provide the necessary contrast to identify the placement of the hydrophilic functionality within the polymer assemblies. In this case, the aqueous solution of the polymer (micelle-like assembly) would place the heavier Cs^+ counterion at the corona to afford a dark ring. The experimental observations correspond to this structure as shown by comparing parts A and B of Figure 2, which are obtained from aqueous solutions containing KOH and CsOH, respectively. Note the presence of a dark ring around the particles in the corona in Figure 2B relative to the core; no such contrast could be seen in Figure 2A. Similarly, the inverse micelle-type structure should place the carboxylate moiety and thus the Cs^+ counterions at the core. This placement should afford a dark spotted core in the TEM image. As expected, the toluene solution of polymer **3e** (Figure 2D) exhibits the image containing a darker core spot compared to that derived from KOH (**3c**) (Figure 2C).

Our structural hypothesis also suggests that the hydrophilic carboxylic acid unit and the hydrophobic benzyl moiety will be placed on the opposite sides of the polymer backbone in solvents of different polarity. While the above experiments show the position of the hydrophilic carboxylic acid moieties, it does not provide information on whether the benzyl moieties are placed on the opposite face. For this purpose, we synthesized polymer **3b** (M_n = 41 410, PDI = 2.5, average DP = 114), which is similar to the

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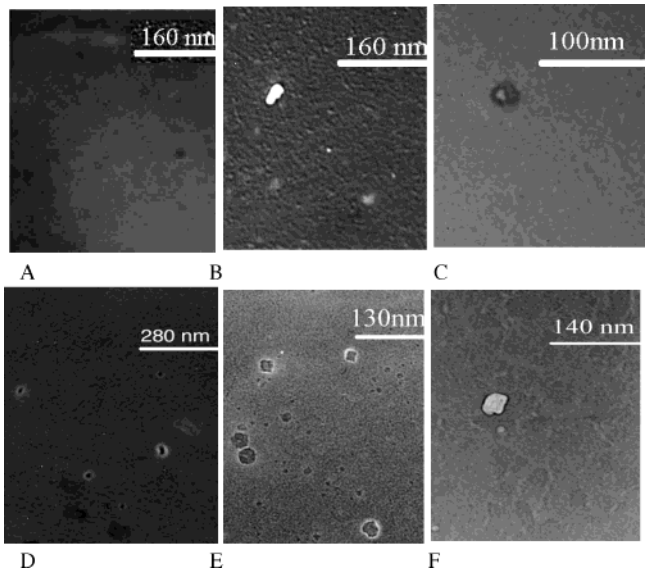

Figure 2. TEM images of the micelle-like and inverted micelle-like structures formed by polymers **3c**, **3d**, and **3e**. (A) Image of normal micelle-like particle from aqueous solution of the polymer **3c**. (B) Image from an aqueous polymer **3e**. (C) Image of an inverted micelle-like particle formed by a toluene solution of the polymer **3c**. (D) Image from a toluene solution of polymer **3e**. (E) Image from an aqueous solution of the polymer **3d**. (F) Image from a toluene solution of the polymer **3d**.

polymer **3a** (Figure 1), but with an additional bromine functionality in the 4-position of the hydrophobic benzyl substituent. Assemblies obtained from both aqueous and toluene solutions of **3c** and **3d** were then compared using TEM. The locale where the bromine atoms are concentrated should exhibit a higher contrast in TEM images. If the hydrophobic benzyl moieties are directed toward the interior in an aqueous solution, the image for polymer **3d** should have a darker spotted core relative to **3c** (Scheme 1). This was indeed the observed result, as could be seen by comparing the images in Figure 2A and E obtained from aqueous solutions of polymers **3c** and **3d**, respectively. Note that the images obtained from polymer **3c** exhibit uniform darkness, whereas the images from polymer **3d** show a darker core compared to the corona. Similarly, if the hydrophobic benzyl moieties are directed toward the exterior in the inverse micelles, the heavier bromine functionalities in **3d** are now placed at the corona. The resulting image for the polymer **3d** should exhibit a dark ring in the corona relative to **3c** (Scheme 1). The images in Figure 2C and F obtained from toluene solutions of polymers **3c** and **3d**, respectively, are consistent with the expected features.

The spatial distribution of the dark corona, which is indicative of the spatial distribution of the heavy atom species, is about 5 nm for an average particle size of 55 nm. However, the darker core from Figure 2D and E seems to be distributed throughout the interior. Note that the hydrophobic and the hydrophilic functionalities are stitched together within the same monomer in polymers **3c**, **3d**, and **3e**. Therefore, it would be expected that the spatial distribution of the interior groups of the assembly closely follow the distribution of functionalities in the corona. Close examination of the normal micelle-like structure in Figure 2E using a density profiling software ImageJ indicated that the dark spot within Figure 2E is not uniformly distributed.[8] In fact, there is a darker ring followed by a lighter gray core in these assemblies. Thus, the distribution of the bromophenyl functionality within a micelle-like assembly is consistent with the spatial distribution of the carboxylate groups indicated in Figure 2B. However, similar density profiling of the spots in Figure 2D indicated a uniform distribution of darkness at the core. This is not surprising, since the contrast providing Cs^+ ions are not covalently attached to the polymer backbone and the solvated ion is likely to be distributed throughout the water-filled core. We also noted that the integrity of both micelle-like and inverted micelle-like assemblies was intact even at 10^{-9} M concentration of the polymers.[7]

In summary, a new class of amphiphilic homopolymers containing both hydrophilic and lipophilic functionalities in each repeat unit has been synthesized. These polymers are soluble in both aqueous and organic solvents, where they assemble into micelle-like or inverse micelle-like structures. Amphiphilic functions reported here are likely to form the basis for new nanoscale assemblies in solution and in solid state, which could have implications in a broad range of applications.

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Supporting Information Available: Synthetic, TEM, and other experimental details are outlined. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) See Supporting Information for details.

(8) ImageJ is free software that can be downloaded from the National Institute of Health web site (http://www.nih.gov).

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