Synthesis and Self-Assembly of a Heteroarm Star Amphiphile with 12 Alternating Arms and a Well-Defined Core

Jing Teng and Eugene R. Zubarev*

Department of Materials Science and Engineering, Iowa State University, Ames, Iowa 50011

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Although star-shaped molecules have been know since the late 1940s, only recently did they become synthetically available. The progress was primarily due to recent advances in living anionic[1] and radical polymerization.[2] However, a number of challenges remain, including control over the structure of a core and the number of arms in such molecules.[3] In addition, living polymerization conditions are very demanding, and that necessitates development of alternative synthetic approaches.[4] Here, we demonstrate that a stepwise synthesis starting from commercially available linear precursors can produce well-defined starlike molecules with a precisely controlled number and position of arms. The amphiphile described here self-assembles into spherical and wormlike supermicelles[5] in aqueous and methanol solutions, and forms reverse micelles in chloroform. This morphological diversity has not been previously observed in star-shaped amphiphiles and is believed to be a direct consequence of the well-defined molecular architecture.

The synthesis of amphiphile **1** consists of two parts: the preparation of a Y-shaped copolymer **3** and the synthesis of a hexafunctional core **4** (Scheme 1). Carboxyl-terminated polystyrene ($M_w = 2400$, PDI = 1.1, Polymer Source, Inc.) was coupled with an excess of silyl-protected 3,5-dihydroxybenzoic acid under mild esterification conditions. Analogous coupling of **2** with poly(*tert*-butyl acrylate) followed by cleavage of the silyl group with DMAP afforded functional polymer **3** ($M_n = 7300$, PDI = 1.07). All products were obtained in high yields and were purified by flash chromatography. The second part of the synthesis involved preparation of an aromatic core which could offer a reduced steric hindrance and higher accessibility of the functional hydroxyl groups. The esterification reaction between silyl-protected 4′-hydroxy-biphenyl-4-carboxylic acid and hexahydroxybenzene, followed by deblocking of DTS under acidic conditions, produced hexafunctional core **4** in high yield and purity, as confirmed by MALDI mass spectrometry, ^{1}H NMR, and ^{13}C NMR.[6] The key step of the overall synthesis was the coupling reaction between the core **4** and the Y-shaped copolymer **3**. Remarkably, the esterification was found to proceed in nearly quantitative yield within just 1 h, and the product was easy to purify by conventional flash chromatography. The reaction was monitored by GPC, which demonstrated formation of a high molar mass product with a molecular weight of 35 100 and a very low polydispersity ($M_w/M_n = 1.07$). The final step involved deprotection of polyacrylate arms under acidic conditions (TFA). Interestingly, the reaction can be monitored most effectively by ^{13}C NMR because the resonance generated by the tertiary carbon of *tert*-butyl groups (80.9 ppm) does not overlap with other signals in the spectrum. The average length of polystyrene and poly(acrylic acid) arms in the resulting heteroarm amphiphile **1** was calculated from NMR spectra using biphenyl protons as the internal reference. The average molecular weight of **1** was determined by GPC in a 0.1 M solution of LiBr in DMF and was found to be 31 300 ($M_w/M_n = 1.14$).[6]

Compound **1** (Figure 1a) contains a well-defined hexabiphenyl core, six hydrophobic arms of polystyrene, and six hydrophilic arms
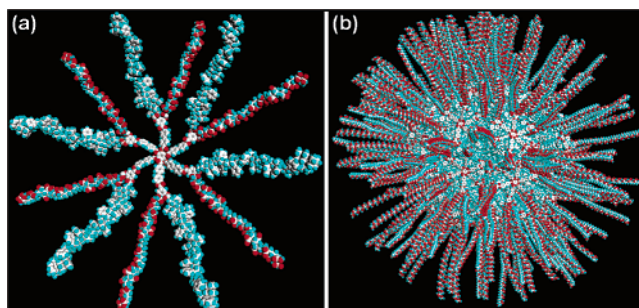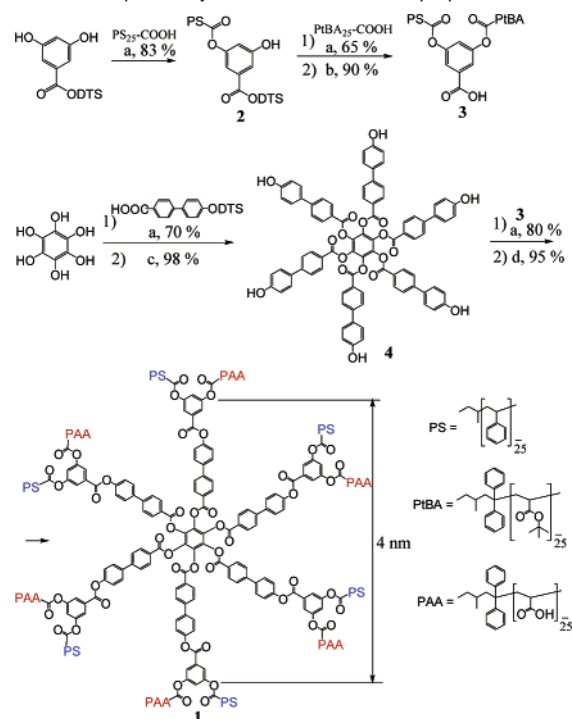

Figure 1. Molecular graphics representation of starlike amphiphile **1** (a) and a spherical supermicelle (b) formed via a closed association of 30 molecules of **1**.

Scheme 1. Stepwise Synthesis of Starlike Amphiphile **1**[a]

[a] Reagents: (a) DPTS/DIPC, CH$_2$Cl$_2$, room temperature, 1 h; (b) DMAP, room temperature, 12 h; (c) HF, THF, room temperature, 24 h; (d) TFA (70% vol.), CH$_2$Cl$_2$, room temperature, 24 h.

of poly(acrylic acid). The arms are fairly short, and each type contains on average 25 monomer units. Thus, the starlike structure **1** has a rigid core and a flexible oligomeric shell. However, the shell is not compositionally uniform, and it is the shell itself which is amphiphilic (Figure 1a). Most importantly, all molecules have an identical hexafunctional core, and its size (4 nm) is comparable to the length of the arms (6 nm). This is in great contrast to the heteroarm high polymers,[7] where the average size of the central
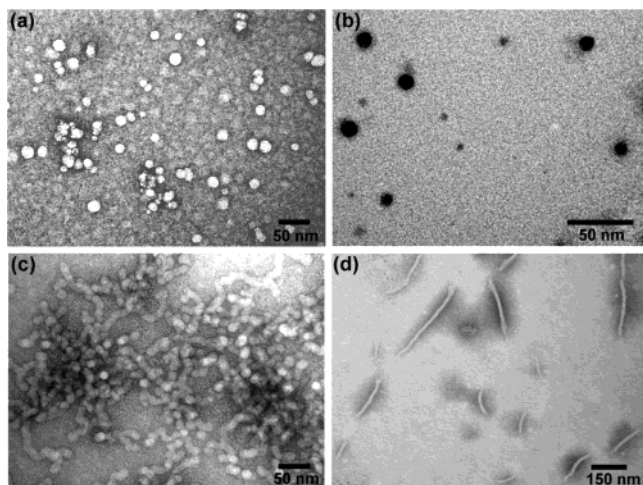
Figure 2. TEM micrographs of structures formed by amphiphile **1**. (a) Negatively stained sample cast from 3.3×10^{-6} M aqueous solution. (b) Positively stained (RuO$_4$) sample cast from 3.3×10^{-6} M aqueous solution. (c) Sample cast from 3.3×10^{-5} M aqueous solution. (d) Sample cast from 3.3×10^{-6} M chloroform solution.

core is negligible in comparison with the arms. Therefore, interactions of molecules **1** with selective solvents will be defined by the interplay of three structural elements, that is, a rigid hydrophobic core and two flexible subshells: hydrophilic (6 PAA arms) and hydrophobic (6 PS arms), respectively.

We conceived structure **1** on the basis of several simple assumptions. Interactions of molecule **1** (Figure 1a) with water should cause solvation of PAA arms, whereas PS chains would try to minimize their exposure to such a polar environment. However, the presence of a relatively large and rigid core would keep PS arms spatially separated, and their mere collapse on the scale of one molecule may not be sufficient to avoid unfavorable contacts with water. Instead, the free energy of the system could be minimized in a much more efficient way if PS arms of many molecules **1** were brought together to form a large hydrophobic core of a supermicelle as illustrated in Figure 1b.

Transmission electron microscopy (TEM) studies of samples cast from very dilute (3.3×10^{-6} M) aqueous solutions of **1** revealed the presence of round-shaped objects that are fairly uniform and measure 17 ± 4 nm in diameter (Figure 2a). To confirm that these objects are spheres and not flat disks, we obtained height profiles that showed that the size of these structures in vertical dimension is also about 17 nm. A more important question, however, is whether these spheres are vesicles or micelles formed via a closed-association mechanism.[8]

Ruthenium tetroxide is a selective staining agent because it reacts only with polystyrene arms. For that reason, we used positive staining with RuO$_4$ to reveal the internal structure of the spheres. As shown in Figure 2b, round-shaped objects with a dark core are present in samples cast from aqueous solution. The average size of the black dots is about 13 nm, and there is a gray area (corona) around each dot. Such contrast suggests the presence of PS arms in the center and PAA arms on the periphery of these spheres. These data are consistent with molecular dynamic simulations (Materials Studio Program), which predict that aggregation of approximately 30 amphiphiles of **1** via a closed-association mechanism would form supermicelles with a diameter ranging from 15 to 22 nm depending on the conformation of PAA arms. That model also assumes that self-assembly is preceded by a spatial separation of hydrophilic (6 PAA arms) and hydrophobic (6 PS arms) subshells, placing them above and below the plane of the aromatic core (Figure 1b).

Most importantly, a TEM investigation demonstrated that an increase in concentration results in a morphological transition from spherical to cylindrical wormlike micelles (Figure 2c). When the concentration of the aqueous solution of **1** is increased 10 times, a small amount of spheres is still present, but the majority of the sample is in the form of one-dimensional winding objects with a fairly uniform diameter ($\sim$18 nm) and the length ranging from 40 to 200 nm. Given the overall contrast and the diameter of these structures, it is reasonable to believe that PS chains are confined in the center of cylinders and PAA arms are localized on the periphery. In addition, very similar structures were found in methanol solutions.[6]

Our recent investigation revealed that amphiphile **1** also forms reverse micelles in chloroform. Figure 2d shows a TEM image of one-dimensional structures which measure 17 ± 2 nm in width and up to 1 μm in length.[6] NMR analysis of chloroform solutions demonstrated that the signals of PAA are significantly suppressed, unlike those from PS arms, which is indicative of reverse micellar aggregates. Static light-scattering experiments also confirmed the presence of micelles in chloroform solutions, and their radius of gyration ($\sim$120 nm), apparent molecular weight (1.1×10^8 g/mol), and the second virial coefficient (4.6×10^{-4} mol mL/g^2) were determined from the Zimm plot.[6] In contrast, micelles were not observed in chloroform solutions of the star-shaped precursor PS$_6$-PtBA$_6$-core. Therefore, the self-assembly requires not only a well-defined molecular architecture but also the amphiphilicity of the shell.

It is worth noting that, regardless of solvent and the type of micelles, that is, spherical or cylindrical, regular or reverse, the hexabiphenyl cores of molecules **1** will always be confined at the interface between the solvophilic corona and the solvophobic core (Figure 1b). This brings to mind one potential application of such systems. If the cores, connecting the arms, were carriers of some function, that is, nanoparticles or catalytic centers, this micellization process would provide an effective way to organize them into well-defined zero- and one-dimensional arrays.

Supporting Information Available: Experimental details, ^{1}H and ^{13}C NMR spectra, GPC, SLS data, and TEM images (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. *Chem. Rev.* **2001**, *101*, 3747−3792. (b) Hong, K.; Uhrig, D.; Mays, J. W. *Curr. Opin. Solid State Mater. Sci.* **1999**, *4*, 531−538 and references therein.

(2) (a) Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26*, 337−377. (b) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661−3688 and references therein.

(3) Recent examples of star-shaped molecules with a well-defined core: (a) Jacob, S.; Majoros, I.; Kennedy, J. P. *Macromolecules* **1996**, *29*, 8631−8641. (b) Heise, A.; Hedrick, J. L.; Frank, C. W.; Miller, R. D. *J. Am. Chem. Soc.* **1999**, *121*, 8647−8648. (c) Heise, A.; Trollsas, M.; Magbitang, T.; Hedrick, J. L.; Frank, C. W.; Miller, R. D. *Macromolecules* **2001**, *34*, 2798−2804. (d) Ohno, K.; Wong, B.; Haddleton, D. M. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 2206−2214. (e) Angot, S.; Murthy, K. S.; Taton, D.; Gnanou, Y. *Macromolecules* **1998**, *31*, 7218−7225. (f) Ueda, J.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1998**, *31*, 6762−6768. (g) Klok, H. A.; Hernandez, J. R.; Becker, S.; Mullen, K. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 1572−1583. (h) Hirao, A.; Hayashi, M.; Tokuda, Y.; Haraguchi, T.; Higashihara, T.; Ryu, S. W. *Polym. J.* **2002**, *34*, 633−658. (i) Jin, R. H. *Macromol. Chem. Phys.* **2003**, *204*, 403−409.

(4) (a) Chen, Y.; Smid, J. *Langmuir* **1996**, *12*, 2207−2213.

(5) Strictly speaking, these aggregates cannot be called micelles because the PS core is below T_g. Such nonequilibrium structures are normally referred to as micelle-like aggregates. However, by convention currently adopted in the literature and for the sake of simplicity, we use the term micelle.

(6) See Supporting Information.

(7) (a) Voulgaris, D.; Tsitsilianis, C. *Macromol. Chem. Phys.* **2001**, *202*, 3284−3292. (b) Kanaoka, S.; Nakata, S.; Yamaoka, H. *Macromolecules* **2002**, *35*, 4564−4566.

(8) Alexandridis, P.; Holzwarth, J. F.; Hatton, T. A. *Macromolecules* **1994**, *27*, 2414−2425.

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