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Synthesis and Supramolecular Nanostructure of Amphiphilic Rigid Aromatic-Flexible Dendritic Block Molecules

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We synthesized ABC triblock rigid aromatic-flexible dendritic block molecules consisting of a docosyl chain, rigid aromatic segment, and poly(ethylene oxide) dendrimer. These block molecules were observed to exhibit an ordered structure in the solid state. Small-angle X-ray scattering experiments showed that the rigid-dendritic block molecule based on a more rodlike aromatic unit self-assembles into a 2-D hexagonal columnar structure, whereas the block molecule based on a more wedgelike aromatic unit self-assembles into a 3-D micellar cubic structure. Dynamic light scatterings, scanning electron microscopic (SEM) observations, and UV/vis spectroscopic measurements were carried out to investigate the encapsulation behavior of hydrophobic guests with the block molecules in an aqueous environment. The rigid-dendritic block molecules self-assemble into stable capsulelike micellar aggregates in aqueous solutions in the presence of $CHCl_3$. In addition, the resulting micellar aggregates encapsulate hydrophobic dye molecules within their micellar core. The critical micellar concentration (cmc) values appeared to be very low, as compared to those of conventional surfactants. These results demonstrate that the introduction of a hydrophilic dendritic segment into an extended rigid aromatic segment can lead to a unique self-assembling system that shows aggregation behavior in both solid and dilute solution phases.

Introduction

The construction of supramolecular architectures with well-defined shapes and dimensions by the self-assembly of designed molecules is a subject of great current interest.[1] Dendritic units are attractive building blocks to form such materials because they are well-defined in molecular architecture.[2] Furthermore, self-assemblies of dendrimers have great potentials in the fields of drug delivery, nanoreactors, and photoresponsive materials as a result of their binding,[3] catalytic,[4] and optical properties.[5] Incorporation of such a dendritic building block into the end of an incompatible linear chain gives rise to novel self-assembling systems because the molecule shares certain general characteristics of both block copolymers and small amphiphiles.[6] For example, polystyrene-dendrimer block copolymers have been reported to self-assemble into a wide variety of supramolecular structures in aqueous solution, from spherical micelles, micellar rods, to vesicular aggregates as a function of generation.[7] Similar to this example, a number of linear-dendritic block copolymers were reported to show interesting aggregation behavior.[8]

Amphiphilic dendrimers containing an extended rigid block represent another class of self-assembling systems that are increasingly used for the construction of su-

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Scheme 1. Synthesis of Amphiphilic Rigid-Dendritic Block Molecules

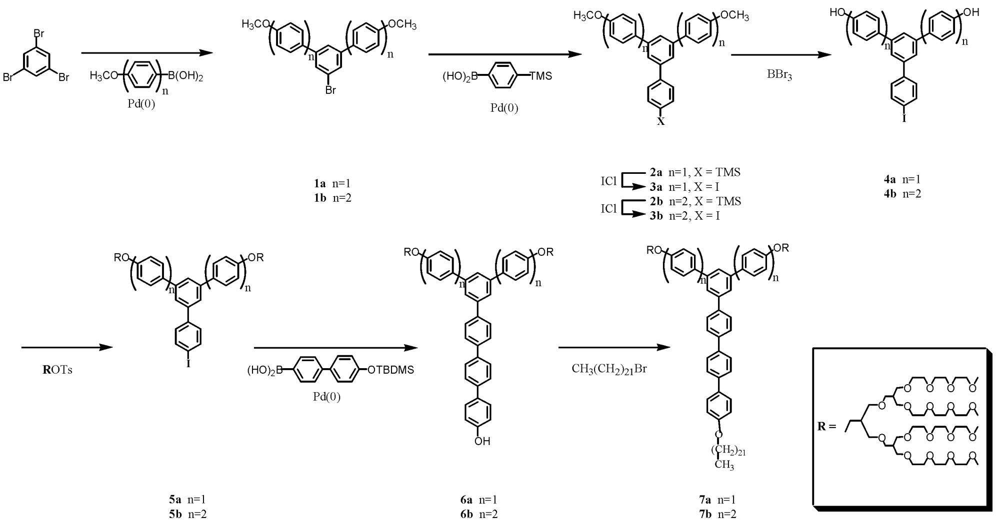

Table 1. Characterization of 7a and 7b

compound	molecular weight (g/mol) theo.	molecular weight (g/mol) exp.[a]	M_w/M_n (GPC)	melting transition (°C) and corresponding enthalpy change (kJ/mol) heating	melting transition (°C) and corresponding enthalpy change (kJ/mol) cooling	lattice constant *a* (nm)
7a	2511.60	2511.61	1.04	col 36.4(14.6) i	i 33.1(13.2) col	8.1
7b	2686.67	2686.67	1.04	cub 46.1(6.7) i	i 41.1(6.1) cub	11.6

[a] exp, determined by MALDI-TOF mass spectrometry; col, 2-D hexagonal columnar structure; cub, 3-D body-centered cubic structure; i, isotropic.

pramolecular architectures with well-defined shape. Stupp et al. reported on the rod-dendron block molecules based on a rigid rod block and benzyl ether dendritic segments.[9] They demonstrated that, depending on the size of the rod segment and generation number of the dendritic segment, lamellar, columnar, and cubic supramolecular structures can be obtained. In addition, they also demonstrated that dendron rod-coil molecules based on a linear polyisoprene chain self-assemble into a unique 1-D ribbonlike supramolecular structure.[10] A previous publication from our laboratory reported on the dumbbell-shaped molecules consisting of a conjugated rod and aliphatic poly(ethylene oxide) dendritic segments.[11] These molecules were demonstrated to self-assemble into discrete bundles with tunable size that organize into a 3-D superlattice.

The introduction of a hydrophobic docosyl chain and hydrophilic dendrimer into each end of an extended rigid segment would give rise to a unique amphiphilic ABC triblock system consisting of a hydrophilic dendritic block, rigid aromatic, and hydrophobic docosyl chain. In this system, an extremely stiff, hydrophobic block is expected to contribute not only to self-assemble into an ordered structure in the bulk, but also to form a stable aggregation in an aqueous solution. In this Article, we describe the synthesis of docosyl-rigid aromatic-ethylene oxide dendritic ABC triblock molecules and their self-assembling behavior in the bulk and aqueous solution. In addition, we report the encapsulation of hydrophobic guests within the aggregation interior in aqueous media and the subsequent characterization of this supramolecular assembly.

Results and Discussion

Synthesis. The synthesis of ABC triblock rigid aromatic-flexible dendritic block molecules consisting of a docosyl chain, Y-shaped rigid aromatic segment, and flexible poly(ethylene oxide) dendrimer is outlined in Scheme 1 and starts with the preparation of an aromatic scaffold and polyether dendrons according to the procedures described previously.[11−13]

The design of a dendritic flexible chain was focused on the construction of an aliphatic poly(ethylene oxide) dendritic segment that is soluble in water and a number of organic solvents. The basic synthetic methodology to generate such a flexible dendrimer employed a facile convergent route reported previously,[12] to control the dendritic architecture precisely. The first step was performed by a Suzuki coupling reaction of 1,3,5 tirbromobenzene with boronic acid derivatives in the presence of Pd(0) catalyst.[13] Trimethylsilyl-substituted aromatic derivatives **2** were prepared from a Suzuki coupling reaction of **1**. For the next Suzuki coupling reaction, the trimethylsilyl group of **2** was substituted to aryl iodide, which is the most active in Suzuki-type aromatic couplings, and then a subsequent aromatic coupling reaction produced **3**. After iodination with ICl,

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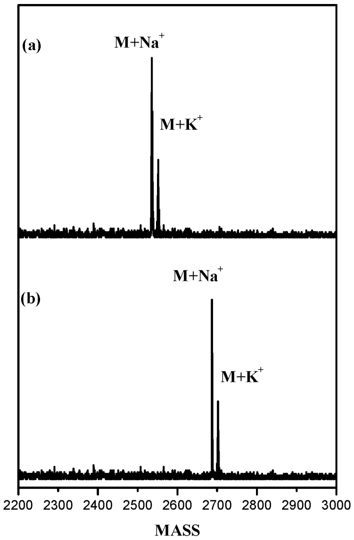

Figure 1. MALDI-TOF mass spectra of (a) **7a** and (b) **7b**.

the methoxy group in the molecules was deprotected, and then the subsequent etherification with tosylated polyether dendron yielded **5**, showing sufficient solubility for further couplings of rigid conjugated building blocks in the reaction medium. The final rigid-dendritic triblock molecules were synthesized by an etherification reaction of phenolic precursors with docosyl bromide. The resulting block molecules were purified by silica gel column chromatography using a mixture eluent of ethyl acetate and methanol (4:1 v/v) as described in the Supporting Information. The resulting molecules were characterized by NMR spectroscopy, elemental analysis and gel permeation chromatography (GPC), and MALDI-TOF mass spectroscopy. The rigid-dendritic block molecules show narrow polydispersities of less than 1.04 in GPC, and elemental analysis data of **7a** and **7b** are also in good agreement with the theoretical values. As shown in Figure 1 and Table 1, the MALDI-TOF mass spectra of the rigid-dendritic block molecules exhibit two signals, which can be assigned as the Na$^+$- and K$^+$-labeled molecular ions. The experimental mass based on the peak positions in the spectrum is well matched with the theoretical molecular weight of each of the rigid-dendritic block molecules.

Solid-State Structure. The self-assembling behavior of the rigid-dendritic block molecules in the bulk was investigated by means of differential scanning calorimetry (DSC), thermal optical polarized microscopy, and X-ray scatterings. The molecules show an ordered structure, as shown in DSC traces (Figure 2) and small-angle X-ray diffraction patterns (Figure 3), and the transition temperatures and the corresponding enthalpy changes determined from DSC scans are summarized in Table 1. The molecules appear to melt into an isotropic liquid at 36 and 46 °C for **7a** and **7b**, respectively. In contrast to **7a**, that shows strong birefringence between the cross polarizer, the solid film of **7b** displays only an optical isotropic phase, indicative of the presence of a 3-D cubic structure.

To corroborate the solid-state structure of the rigid-dendritic block molecules, X-ray scattering experiments were performed, as shown in Figure 3. The small-angle X-ray diffraction pattern of **7a** displays sharp reflections that correspond to a 2-D hexagonal columnar structure with a lattice constant of 8.1 nm.

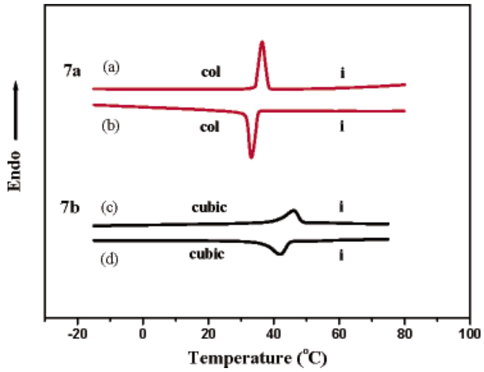

Figure 2. DSC traces recorded during the heating scan (a) and the cooling scan (b) of **7a**, and the heating scan (c) and the cooling scan (d) of **7b**.

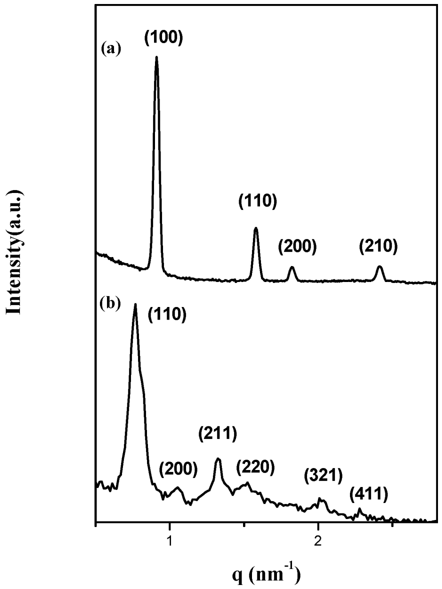

Figure 3. Small-angle X-ray diffraction patterns of (a) **7a** and (b) **7b** at 25 °C.

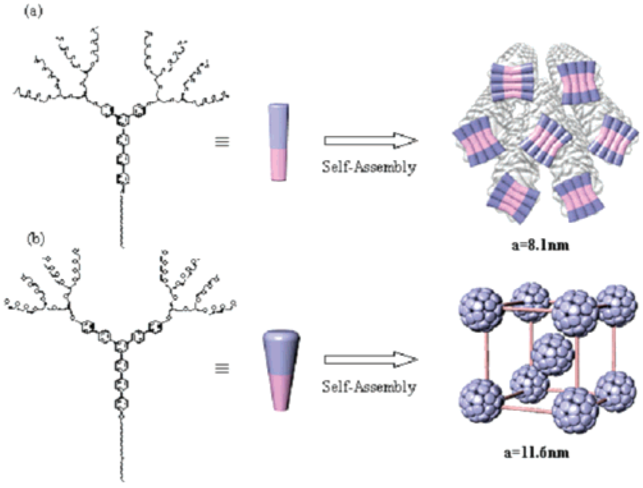

Figure 4. Schematic representation for (a) the hexagonal columnar structure of **7a** and (b) the body-centered cubic structure of **7b**.

This dimension implies that the more rodlike rigid segments arrange axially with their preferred direction within a cross-sectional slice of the column, in which docosyl chains pack in an interdigitated fashion and distort conformationally (Figure 4a). In contrast, the

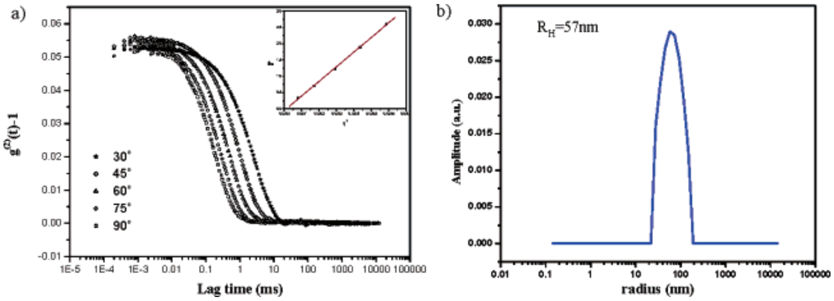

Figure 5. Dynamic laser light scattering of **7a** (5×10^{-3} g/mL) in H_2O in the presence of $CHCl_3$ (1×10^{-2} mL/mL). (a) Autocorrelation function (scattering angular range of 30−90°), a monoexponential decay function (inset), and (b) size distribution graph of the aggregates at a scattering angle of 90° (from CONTIN analysis of the autocorrelation function).

small-angle X-ray diffraction pattern of **7b** shows a strong reflection together with a number of low intensity reflections at higher angles (Figure 3b), indicative of the existence of a highly ordered nanoscopic structure. These reflections indeed can be indexed as a 3-D body-centered cubic phase with a lattice parameter of 11.6 nm.[14] Considering the space filling requirement and cone-shaped building block, the radial arrangement of the rigid segments is expected to be the best way to close pack the hydrophobic core, leading to a discrete nanostructure.[14−16] Accordingly, **7b** based on a more wedgelike aromatic segment can be described to self-organize into an optically isotropic cubic phase consisting of a 3-D body-centered arrangement of discrete aggregates, as shown in Figure 4b.

Aggregation Behavior in Aqueous Solution. Dendritic molecules containing rigid aromatic segments can be considered as a new class of amphiphiles because they consist of a hydrophobic rigid segment and a hydrophilic flexible dendrimer. As a result of their amphiphilic characteristics, the rigid-dendritic block molecules can encapsulate hydrophobic guest molecules in an aqueous environment. The encapsulation behavior of the rod-dendritic molecules was subsequently studied by adding $CHCl_3$ (1×10^{-2} mL/mL) into an aqueous solution. Dynamic light scattering experiments were performed with the $CHCl_3$/water solutions of **7a** with a concentration of 5×10^{-3} g/mL over a scattering angular range of 30−90° at 25 °C. The aggregate size in the presence of a hydrophobic solvent was estimated using the CONTIN analysis for evaluation of the autocorrelation function.[17−19] An example for the results of the CONTIN analysis used for the determination of the hydrodynamic radius is shown in Figure 5.

The curve shows a monomodal size distribution, thus confirming the formation of only one family of aggregate sizes with a narrow size distribution, indicating well-equilibrated structures. The average hydrodynamic radius (R_H) of the aggregate containing $CHCl_3$ (1×10^{-2} mL/mL) was observed to be approximately 54 nm.

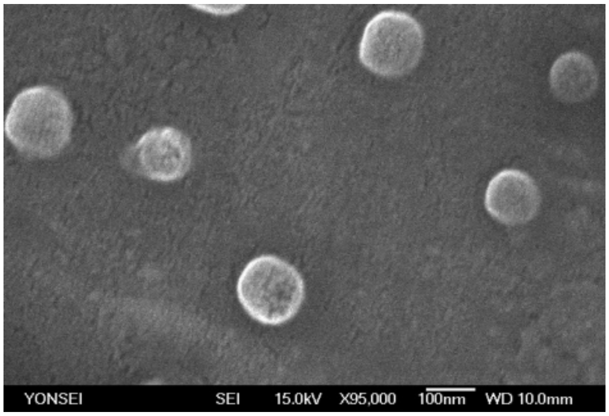

Figure 6. SEM image of the capsules formed by **7a** (5×10^{-3} g/mL) in H_2O in the presence of $CHCl_3$ (1×10^{-2} mL/mL).

The formation of aggregate of **7a** in the presence of $CHCl_3$ was also confirmed by FE-SEM experiments, which show spherical entities. As shown in Figure 6, the micrograph shows spherical aggregates that are approximately 100 nm in diameter and are thus consistent with the results obtained from dynamic light scattering experiments. The measured diameters exceed the extended molecular length (approximately 5 nm) by a factor of about 20, suggesting that these aggregates encapsulate $CHCl_3$ molecules within their hydrophobic interior. It should be noted that the objects preserve their spherical morphology even after their isolation from the solution under high vacuum as confirmed by SEM observations, indicating that the capsulelike aggregates formed in $CHCl_3$/water are stable. This stability in shape could be attributed to the self-assembly of rigid building blocks with low conformational entropy.[20,21]

To further investigate the encapsulation of a hydrophobic solvent within the micellar aggregate, dynamic light scattering experiments were performed with variation of $CHCl_3$ concentration in aqueous solution at the fixed concentration of **7a** (5×10^{-3} g/mL). As shown in Figure 7, the average hydrodynamic radii (R_H) of the

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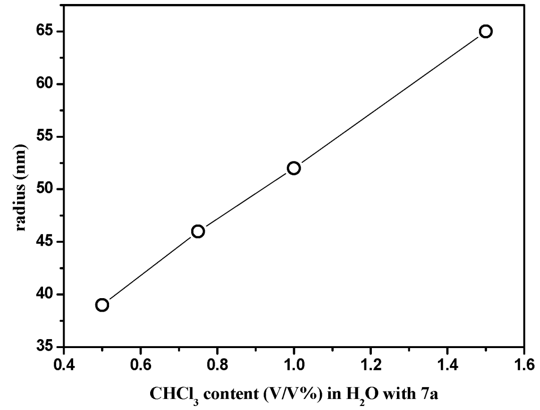

Figure 7. Hydrodynamic radii of the aggregates of **7a** (5×10^{-3} g/mL) as a function of $CHCl_3$ content.

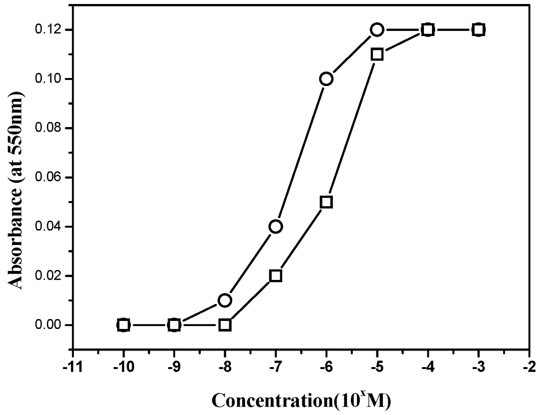

Figure 8. Absorbance intensity of Nile Red at 550 nm as a function of the concentration of **7a** solution in water (□) and **7b** solution in water (○).

corresponding aggregates were observed to increase with an increase in the $CHCl_3$ content, suggesting that hydrophobic guest molecules are encapsulated within the hydrophobic micellar core.

Encapsulation characteristics of the rigid-dendritic block molecules were also investigated with a hydrophobic dye, Nile Red, in aqueous solutions by using UV/vis spectroscopy. When a clear aqueous solution of the rod-dendritic molecules was layered on Nile Red−hexane solution, the color of the aqueous phase gradually changed to red, indicating the solubilization of the nonpolar Nile Red with the rigid-dendritic molecules. The critical micellar concentrations (cmc) of the molecules were determined by plotting the absorption intensity of Nile Red in an aqueous phase against dye concentration, as shown in Figure 8. In the low concentration range, a negligible absorption peak was detected. However, above a certain concentration, the absorption intensity exhibited a substantial increase, indicating that dye molecules are encapsulated into the hydrophobic core region upon micellar aggregation. Therefore, the critical micellar concentrations were determined from the cross-over point at the low concentration range. As shown in Figure 8, the cmc values of **7a** and **7b** appeared to be 2×10^{-7} and 3×10^{-8} M, respectively. It is remarkable that these values are very low, as compared to conventional surfactants such as sodium dodecyl sulfonate (cmc = 7×10^{-3} M). The low cmc values suggest the effectiveness of rigid rod and dendritic blocks for stabilizing micellar aggregates.

To get further quantitative information of dye encapsulation, the absorbance at absorption maximum of Nile Red was plotted against the mole ratio of dye and **7a**. As shown in Figure 9, the absorbance increases with an increase in the ratio up to a certain point at which the absorbance does not change with further increment of the ratio. Therefore, the maximum number of dye loading per molecule of **7a** in the aqueous phase can be estimated to be approximately 50 Nile Red molecules per amphiphilic molecule. These results demonstrate that hydrophobic compounds can be effectively encapsulated within micelles composed of rigid aromatic-flexible dendritic building blocks. The entrapment of a hydrophobic guest within the micelles can be rationalized by the strong association between the guest and the amphiphilic molecule, and the poor solubility of the guest molecule. The aggregation behavior coupled with the good water solubility and biocompatibility of polyether unit might make these supramolecular capsules promising candidates for many applications including drug delivery and controlled drug release.[22]

Conclusions

Rigid-dendritic block molecules consisting of a hydrophobic docosyl, an extended rigid segment, and a hydrophilic dendritic segment were successfully synthesized, and their self-assembling behavior in the solid and solution phases was investigated. X-ray scatterings demonstrated that the molecule based on a more rodlike aromatic unit self-organizes into a 2-D hexagonal columnar structure, while the molecule based on a more wedgelike aromatic unit self-organizes into a 3-D mi-

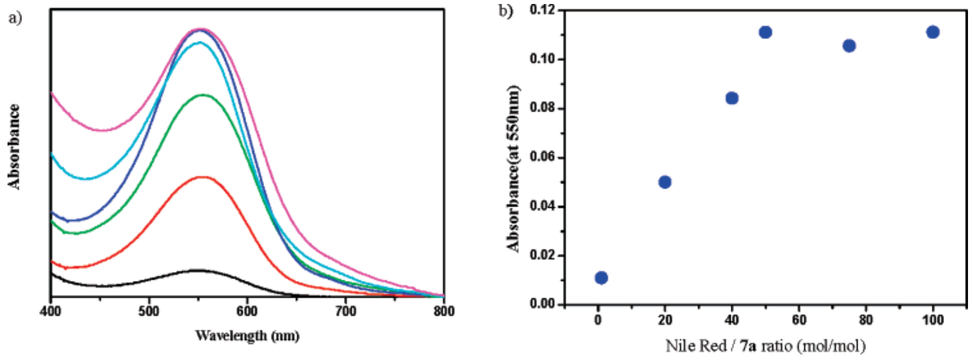

Figure 9. (a) UV−vis spectrum for Nile Red dye encapsulated within **7a** solution in water at various ratios of Nile Red/**7a** (mol/mol) (a range of ratio from 1 to 100 mol/mol). (b) Absorbance intensity of Nile Red at 550 nm as a function of the ratio of Nile Red/**7a** (mol/mol).

cellar cubic structure. Dynamic light scattering and SEM studies of aqueous solution with the addition of $CHCl_3$ showed that the rigid-dendritic block molecules self-assemble into stable capsulelike micellar aggregates in the presence of a hydrophobic solvent. In addition, the resulting micellar aggregates were demonstrated to encapsulate hydrophobic dye molecules within the micellar core via UV/vis spectroscopic measurements. The cmc values appeared to be very low, as compared to those of conventional surfactants. Supramolecular capsulelike aggregates and their ability to encapsulate hydrophobic guest molecules offer an attractive potential for use in a wide variety of applications ranging from controlled drug release, solubilization of hydrophobic molecules in aqueous media, to the design of nanoreactors.

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Supporting Information Available: Detailed synthetic procedures, characterization (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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