

# Self-Assembling Molecular Dumbbells: From Nanohelices to Nanocapsules Triggered by Guest Intercalation\*\*

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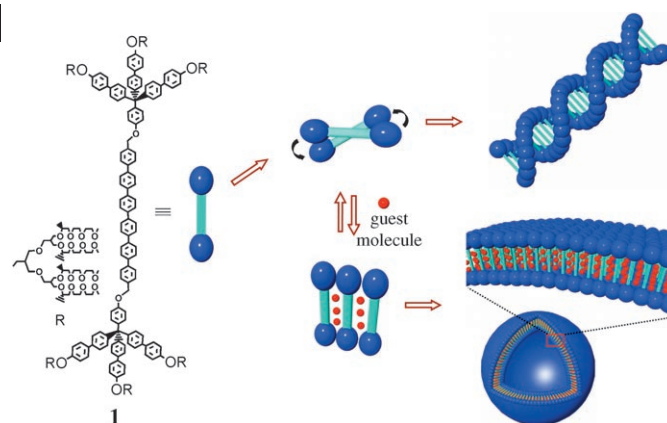
Controlled self-assembly of incompatible molecular components is a challenging topic of interdisciplinary research in chemistry, biology, and materials science.<sup>[1]</sup> For example, self-assembling molecules consisting of rodlike aromatic and flexible aliphatic segments have proved to be promising scaffolds for well-defined supramolecular structures, such as vesicles, tubules, and twisted ribbons.<sup>[2]</sup> Precise control of molecular arrangements at the supramolecular level is essential to obtain well-defined nanoscopic architectures with specific shape. Recently, we showed that incorporation of a conjugated rod into an amphiphilic dumbbell-shaped molecular architecture results in the formation of a helical nanostructure consisting of hydrophobic aromatic cores surrounded by hydrophilic flexible segments that are exposed to the aqueous environment.<sup>[3]</sup> We also showed that rod building blocks in rigid-flexible macrocycles self-assemble into a discrete barrel-like structure with hydrophilic channels.<sup>[4]</sup>

We present herein the formation of helical strands from the self-assembly of a dumbbell-shaped molecule based on a conjugated rod segment in aqueous solution and reversible transformation between helical strands and nanocages triggered by the addition of aromatic guest molecules (Scheme 1). The dumbbell-shaped molecule **1** consists of a hexa-*para*-phenylene rod and aliphatic polyether dendrons based on a tetrahedral core, which are covalently linked at both ends of the rod segment. To synthesize **1**, aromatic tetrahedral cores containing three oligoether dendrons were prepared according to procedures described previously (Scheme 2).<sup>[5]</sup> The final dumbbell-shaped molecules were synthesized by using a palladium-catalyzed homocoupling reaction. The resulting compound was characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopies, elemental analysis, and MALDI-TOF mass spectrometry, the data of which were in full agreement with the structures presented.

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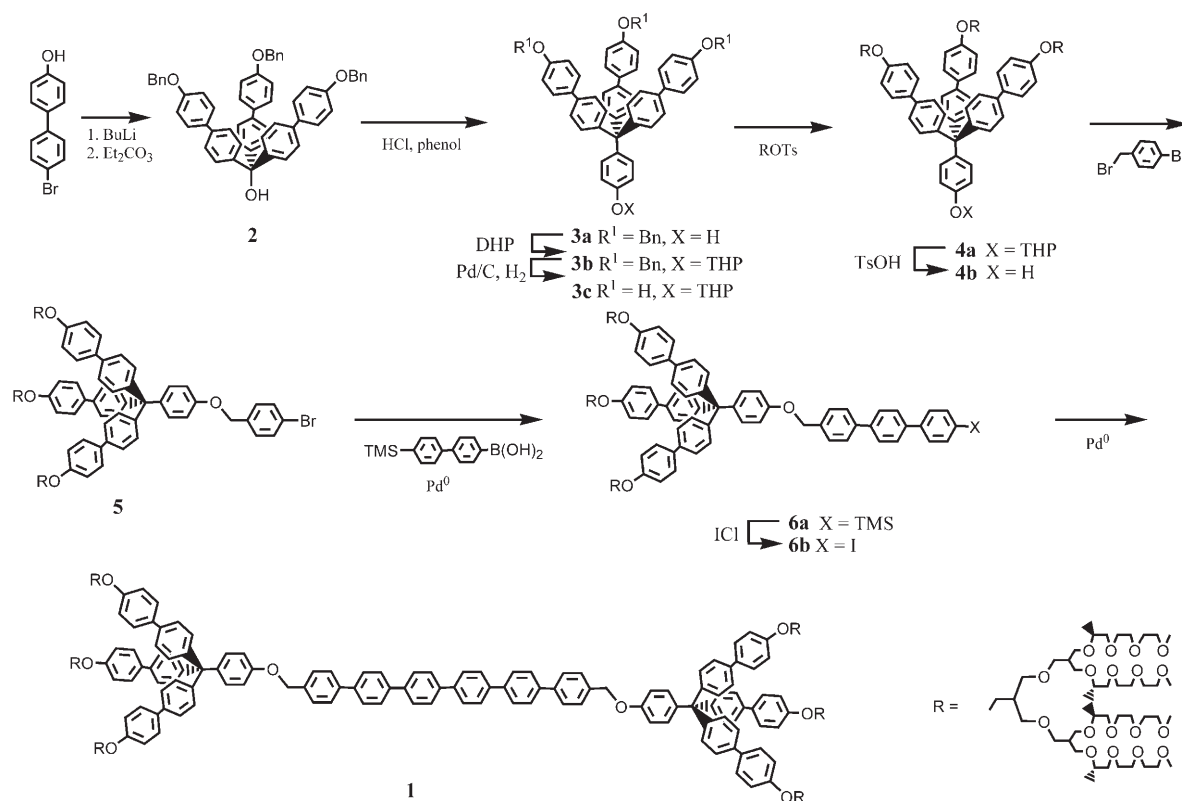
Supporting information for this article is available on the WWW under <http://www.angewandte.org> or from the author.



**Scheme 1.** Representation of the reversible transformation of helical fibers into a spherical capsule.

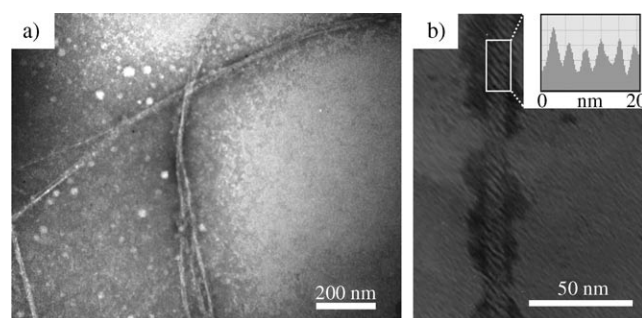
When dissolved in a solvent suitable for the oligoether block such as water, **1** self-assembles into an aggregate structure because of its amphiphilic characteristics. The aggregation behavior of the compound was subsequently studied in aqueous solution by using UV/Vis, fluorescence, and circular dichroism (CD) spectroscopies (see the Supporting Information). The absorption spectrum of **1** in aqueous solution (0.01 wt %) exhibits a broad transition with a maximum at 278 nm and a shoulder at 332 nm arising from the tripodal biphenyl segments and the conjugated rod block, respectively. The fluorescence spectrum of **1** in chloroform (0.01 wt %) excited at 332 nm exhibits two strong emission maxima at 381 and 400 nm. However, the emission maximum in aqueous solution is red-shifted with respect to that observed in chloroform, which is indicative of aggregation of the conjugated rod segments.<sup>[6]</sup> CD spectra of aqueous solutions of **1** show a positive Cotton effect followed by a negative Cotton effect at higher wavelengths with the CD signal passing through zero near the absorption maximum of the oligo(phenylene) chromophore, thus indicating the formation of a helical superstructure with a preferred handedness.<sup>[7]</sup>

Dynamic light-scattering (DLS) experiments were performed with **1** in aqueous solution to further investigate its aggregation behavior.<sup>[8]</sup> Analysis of the autocorrelation function with the CONTIN program shows a broad peak corresponding to an average hydrodynamic radius ( $R_H$ ) of approximately 60 nm. The angular dependence of the apparent diffusion coefficient ( $D_{app}$ ) was measured, and the gradient of the slope was 0.03, which is consistent with the value predicted for anisotropic objects (see the Supporting Information).<sup>[9]</sup> The formation of cylindrical micelles was further confirmed by using the Kratky plot, which shows a linear angular dependence on the intensity of the light scattered by the aggregates (see the Supporting Information). In addition to DLS experiments, static light-scattering (SLS) experiments were performed in aqueous solution under the same conditions. The radius of gyration of the aggregates,  $R_g = 78$  nm, was obtained from the gradient of the angular dependence of the SLS signal. The ratio  $R_g/R_H$  is 1.25, which is evidence of the formation of cylindrical aggregates.<sup>[10]</sup>



**Scheme 2.** Synthesis of the dumbbell molecule **1**. DHP: dihydropyran, THP: tetrahydropyran, Ts: *para*-toluenesulfonyl, TMS: trimethylsilyl.

Further evidence of the formation of cylindrical aggregates was provided by transmission electron microscopy (TEM; Figure 1). The micrographs, which were negatively



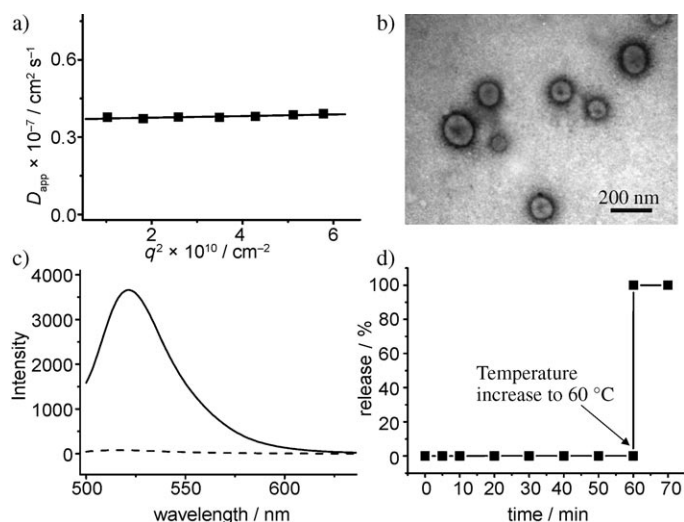
**Figure 1.** a) TEM image of **1** with negative staining. b) Magnified image; the inset shows the density profile.

stained with a 2 wt % aqueous solution of uranyl acetate, show helical objects with a uniform diameter of about 10 nm and a pitch length of 3.6 nm. When the extended molecular length (9.8 nm in a CPK model) is taken into consideration, the image indicates that the diameter of the elementary cylindrical objects corresponds to one molecular length.

On the basis of these results, we consider that **1** self-assembles into cylindrical micelles in which the rods are aligned perpendicular to the cylinder axis. However, the rod segments stack on top of each other with mutual rotation in

the same direction to avoid steric hindrance between the bulky dendritic wedges. Consequently, this stacking of the aromatic rod segments leads to helical objects comprising hydrophobic aromatic cores surrounded by hydrophilic dendritic segments that are exposed to the aqueous environment. This formation process is similar to that of other helical structures of self-assembling molecules that are based on a conjugated rod block.<sup>[3,7,11]</sup>

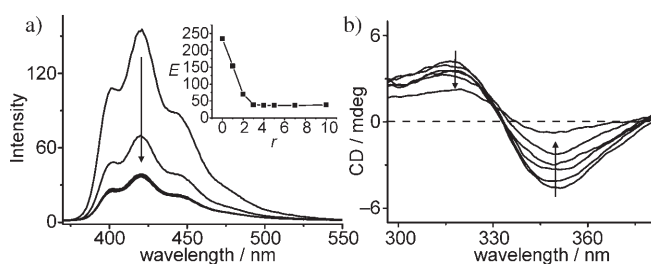
Remarkably, these cylindrical objects transformed into spherical objects on adding three equivalents of 4-bromonitrobenzene (Scheme 1) to an aqueous solution of **1**. CONTIN analysis of the correlation functions in DLS experiments of the resulting solution showed  $R_H$  to be 70 nm and the SLS results showed  $R_g$  to be 73 nm. Thus, the radius of gyration of the mixture solution is nearly identical to the hydrodynamic radius. The measured diameter exceeds the extended molecular length (approximately 10 nm) by a factor of about 14, which also strongly suggests that these aggregates are capsulelike entities rather than simple micelles.<sup>[12]</sup> In contrast to the results derived for **1**, the gradient of the slope of the angular dependence of the apparent diffusion coefficient ( $D_{app}$ ) was approximately zero (Figure 2a), which suggests that the self-assembled architecture is spherical.<sup>[13]</sup> The formation of spherical objects was further confirmed by TEM (Figure 2b), which revealed the presence of spherical objects with an average diameter of about 140 nm. This is in good agreement with the results obtained by DLS and SLS experiments. Atomic force microscopy (AFM) measurements showed that the spherical objects consist of a unilamellar membrane.<sup>[14]</sup>



**Figure 2.** a) Angular dependence of  $D_{app}$  ( $q$  is the scattering vector); b) TEM image for the spherical capsules with negative staining; c) emission spectra of calcein measured at 25 °C (weak emission) and calcein measured at 60 °C (strong emission) of an aqueous solution of **1** (0.01 wt%) containing three equivalents of 4-bromonitrobenzene; d) release of calcein from the capsule as a function of time.

Further evidence for the formation of hollow capsules was provided by the encapsulation of the fluorescence dye calcein.<sup>[15]</sup> Calcein, a hydrophilic fluorescent guest, was encapsulated at a sufficiently high, self-quenching concentration, and free calcein was removed by filtration over a Sephadex column. Release of calcein into solution from the inside of the capsules was accompanied by an increase in fluorescence emission (Figure 2c).<sup>[16]</sup> As shown in Figure 2d, no leakage of entrapped calcein was observed over periods of 60 min. Heating the calcein-loaded vesicular solution to 60 °C resulted in the rapid and complete release of encapsulated calcein, thus demonstrating that the dye molecules are effectively enveloped within the interior of a capsule.<sup>[17]</sup> These results show that addition of guest molecules to a solution of **1** leads to the transformation of the helical nanofibers into hollow capsulelike structures.

This unique structural variation on the addition of guest molecules can be rationalized by considering the packing arrangement of the rod segments. With amphiphilic molecular dumbbells in aqueous media, aromatic guest molecules are intercalated between the rod segments through intermolecular interactions, including hydrophobic and  $\pi$ – $\pi$  interactions. As a result, this intercalation of the guest molecules drives the twisted packing arrangement of the rod segments into a parallel arrangement, which allows more space for guest molecules while maintaining uniform density of the dendron dumbbell ends. This parallel arrangement of the rod segments is responsible for the formation of a cage-like structure. Intercalation of the aromatic substrates within the rod segments was confirmed with 4-bromonitrobenzene as a guest molecule in an aqueous solution of **1** by fluorescence spectroscopy (Figure 3). Upon addition of the guest molecules, the fluorescence intensity of the aqueous rod-coil solution of **1** was suppressed, thus demonstrating that the



**Figure 3.** a) Emission spectra of **1** (0.01 wt% aqueous solution, excited at 332 nm) with the addition of 4-bromonitrobenzene. The inset shows the emission intensity at 420 nm ( $E$ ) as a function of the molar ratio bromonitrobenzene:**1** ( $r$ ). b) CD spectra of **1** with the addition of bromonitrobenzene (increase in molar ratio from 0 to 1).

guest molecules are effectively intercalated between the rod segments.<sup>[18]</sup>

Consistent with the intensity changes in the emission spectra, the CD intensity decreases rapidly upon addition of up to one equivalent of the guest molecule to give a very small CD signal, which infers the depletion of the twisted arrangement of the rod segments (Figure 3b). Upon removal of the guest molecule by extraction with *n*-hexane, the CD spectrum fully recovered, thus indicating that this structural transformation is reversible.<sup>[19]</sup> These results demonstrate that the addition of guest molecules into the solution of **1** forces the twisted arrangement of the rod segments into a parallel arrangement that leads to the formation of a capsulelike structure.

In summary, the results described herein demonstrate that the dumbbell-shaped molecules based on a hexa-*p*-phenylene rod and bulky dendritic segments self-assemble into well-defined left-handed helical cylinders with a diameter of approximately the length of one molecule and a pitch of 3.6 nm. Interestingly, the helical structure transforms into a capsulelike structure on addition of guest molecules. This reversible transformation between helical strands and nanocages in response to the addition of guest molecules is attributed to the intercalation of aromatic substrates within the rod segments and subsequent packing change of the rod segments from a twisted to a parallel arrangement to allow more space for guest molecules. This dynamic structural variation triggered by external stimuli may find useful applications in many areas including the development of responsive supramolecular materials.

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