### Dendronized Triangular Oligo(phenylene ethynylene) Amphiphiles: Nanofibrillar Self-Assembly and Dye Encapsulation

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Abstract: Triangular-shaped oligo(phenylene ethynylene) amphiphiles 1a and 1b decorated in their periphery with two- and four-branched hydrophilic triethyleneglycol dendron wedges, have been synthesized and their self-assembling properties in solution and onto surfaces investigated. The steric demand produced by the dendritic substituents induces a face-to-face rotated  $\pi$  stacking of the aromatic moieties. Studies on the concentration and temperature dependence confirm this mechanism and provide binding constants of  $1.2 \times 10^5$  and  $1.7 \times 10^5 \text{ M}^{-1}$  in acetonitrile for 1a and 1b, respectively.

#### Introduction

Knowledge of a set of rules governing the self-assembly of organic molecules and, in consequence, the properties and function stemming from the self-assembly process, is crucial in the quest for new organic materials that are useful for semiconductor-based technologies.<sup>[1]</sup>  $\pi$ -Conjugated systems are especially relevant for this purpose because the noncovalent forces, and more specifically  $\pi$ - $\pi$  stacking aromatic interactions<sup>[2]</sup> between their  $\pi$ -conjugated frameworks, allows modulation of the optical and electronic properties of the final materials.<sup>[3]</sup> The decoration of  $\pi$ -conjugated systems with polar groups gives rise to monodisperse amphiphilic molecules capable of precise self-organization into supra-

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Dynamic and static light scattering measurements complement the study of the self-assembly in solution and demonstrate the formation of rod-like supramolecular structures in aqueous solution. The nanofibers formed in solution can be efficiently transferred onto surfaces. Thus, TEM images reveal the presence of strands of various thickness, with the most common being several micrometers long and

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with diameters of around 70 nm. Some of these nanofibers present folded edges that are indicative of their ribbon-like nature. Interestingly, compound 1b can also form thick filaments with a rope-like appearance, which points to a chiral arrangement of the fibers. AFM images under highly diluted conditions also reveal long fibers with height profiles that fit well with the molecular dimensions calculated for both amphiphiles. Finally, we have demonstrated the intercalation of the hydrophobic dye Disperse Orange 3 within the filaments and its subsequent release upon increasing the temperature.

molecular architectures with different morphologies and dimensionalities.<sup>[4]</sup> The relative ratio of the hydrophilic/ -phobic groups in the  $\pi$ -conjugated amphiphilic systems, together with the influence of external factors (concentration, temperature, and/or solvent polarity), finely tunes the delicate balance between the noncovalent forces that finally determines the "soft-matter polymorphism"<sup>[5]</sup> and, consequently, the change in the shape, size, physico-chemical properties, and applications of the resulting supramolecular structures.<sup>[3,4]</sup>

Calixarenes,<sup>[6]</sup> pyridine-based derivatives,<sup>[7]</sup> squaraines,<sup>[8]</sup> perylenebisimides,<sup>[9]</sup> hexabenzocoronenes,<sup>[10]</sup> oligo-*p*-phenylenes,<sup>[11]</sup> oligo(phenylene vinylenes),<sup>[12]</sup> and oligo(phenylene ethynylenes) (OPE)<sup>[13]</sup> exemplify the variety of  $\pi$ -conjugated moieties that have been used as hydrophobic cores in amphiphilic systems. Amphiphiles based on the organic compounds mentioned above are able to self-organize into a variety of well-ordered noncovalent architectures such as micelles,<sup>[6,11d]</sup> fibers,<sup>[8b,9,11a,b]</sup> rolled lamellae,<sup>[10a,b,11a]</sup> and vesicles,<sup>[8b,9b,12c,13a,b]</sup> Among these morphologies, 1D nanostructures<sup>[14]</sup> are being fully investigated due to their potential application as nanowires and biomimetic macromolecules.<sup>[15]</sup> In addition, amphiphiles that are able to form 1D fibers are



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also relevant due to that fact that: 1) their hierarchical assembly can induce a gelation process to form gels with applicability in food, cosmetics, or advanced materials,[16-18] and 2) the incorporation of bioinspired moieties results in chiral assemblies that are structurally comparable to those of natural peptide systems.<sup>[19]</sup>

In our research group, we have recently reported the preparation of radial amphiphilic OPEs as building blocks

for the construction of supramolecular structures such as vesicles,<sup>[20]</sup> toroids,<sup>[21]</sup> and microcrystalline lamellae.[22] The different molecular geometries of these radial OPEs (triangular or rectangular), together with the variable number of polar or paraffinic chains, makes them useful benchmarks for the study and quantification of the noncovalent forces participating in the self-assembly of small organic amphiphiles and also enables an evaluation of their capacity to transfer onto surfaces as ordered supramolecular structures.

Herein, we report the synthesis of dendronized, triangular OPEs (1a and 1b) and a study of their self-assembling features in solution and onto surfaces. We compare the synthesized

OPEs with those of our previously reported triangular amphiphilic equivalent, which was endowed with only three triethyleneglycol (TEG) chains (2).<sup>[20a]</sup> The attachment of TEG polar dendritic wedges in the periphery of the radial OPE skeleton induces a rotated stacking of the amphiphiles that alleviates the steric repulsion of the bulky substituents. The twisted packing of the aromatic moieties provokes a 1D growth that finally generates nanofibers with lengths of several micrometers. We have also investigated the capability of these supramolecular fibers to intercalate and release hydrophobic dye molecules.

# 1b' B RC



Synthesis: Dendronized amphiphiles 1a and 1b were obtained in 36 and 32% yield, respectively, by utilizing the Sonogashira cross-coupling reaction<sup>[23]</sup> between 1,3,5-triethynylbenzene  $(3)^{[24]}$  and the corresponding iodoaryl derivatives endowed with two (5a) or four (5b) dendritic TEG wedges (Scheme 1). Unlike for compound 2, which is endowed with

**Results and Discussion** 



Scheme 1. Synthesis of the dendronized amphiphilic OPEs 1a and 1b.

only three TEG chains,<sup>[20a]</sup> we used tris(dibenzylideneacetone)dipalladium(0) [Pd<sub>2</sub>(dba)<sub>3</sub>] as a catalyst in the Sonogashira reaction to overcome the steric demand exerted by the dendritic TEG substituents, which could significantly decrease the yield of the reaction, and avoid the Glaser-type homocoupling reaction.<sup>[25]</sup> It is well established that the presence of the dibenzylideneacetone ligand controls the concentration and the reactivity of the active Pd<sup>0</sup> species within the catalytic cycle and results in higher yields.<sup>[25]</sup> The peripheral polyether dendrons 4a and 4b, and compounds 5a and 5b, which allow the modulation of the ratio of hydrophilic to hydrophobic groups, were prepared by following previously reported procedures.<sup>[26]</sup> All of the compounds reported herein were fully characterized through a wide variety of spectroscopic techniques (see the Supporting Information).

Unambiguous confirmation of the proposed structure for both amphiphiles 1a and 1b was obtained from the <sup>1</sup>H NMR spectra. Thus, whereas **1a** shows only one isochronous quintuplet at  $\delta \approx 2.5$  ppm, which is ascribable to the -CH- group supporting the two-branched dendron wedge (filled circle in Scheme 1), compound 1b shows two quintuplets at  $\delta \approx 2.2$  and 2.1 ppm (filled and empty circles in Scheme 1) corresponding to three and six protons, respectively. At the same time, the presence of six aromatic reso-

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nances and two signals diagnostic of the triple bonds in the  ${}^{13}C$  NMR spectra, confirm the  $C_3$  symmetry of the investigated amphiphiles.

The MALDI-TOF mass spectrum of amphiphile **1a** shows a weak set of peaks corresponding to the isotopic distribution at m/z 1566, together with a highly intense set of peaks at m/z 1589 and a further weaker set at m/z 1605, which have been assigned to the  $[M+Na]^+$  and  $[M+K]^+$  molecular ions (Figure 1). The mass spectra for compound **1b** exhibits only one set of peaks at m/z 2994 and a second at m/z 3010, which correspond to the  $[\mathbf{1b}+Na]^+$  and  $[\mathbf{1b}+K]^+$  molecular ions (Figure S1 in the Supporting Information). This behavior has also been observed for other, related amphiphilic dendritic block molecules.<sup>[26b]</sup> Nevertheless, the MALDI-TOF spectra of compounds **1a** and **1b** also provides a first indication of their ability to self-assemble, and peaks corresponding to the dimer and trimer are noticeable for both amphiphiles (Figure S2 in the Supporting Information).



Figure 1. MALDI-TOF (ditranol) mass spectrum of amphiphile 1a showing the molecular ion peaks corresponding to  $[M]^+$ ,  $[M+Na]^+$ , and  $[M+K]^+$  species.

Self-assembly in solution: The self-assembly of amphiphiles **1a** and **1b** was initially investigated by UV/Vis spectroscopy experiments that looked at the concentration dependence in two solvents of distinct polarity (acetonitrile and benzene) and by considering the isodesmic model<sup>[27]</sup> as the mechanism by which these compounds aggregate (Figures S3 and S4 in the Supporting Information). Both amphiphiles **1a** and **1b** show identical spectroscopic features in which the depletion of the high energy band at approximately 260 nm is accompanied by an increase of two lower energy bands at approximately 300 and 314 nm; this observation is similar to those reported for triangular OPE **2** and is diagnostic of  $\pi$  stacking.<sup>[20]</sup> The calculated values for the binding constant ( $K_a$ ) in acetonitrile are  $1.2 \times 10^5$  and  $1.7 \times 10^5 \text{ M}^{-1}$  for **1a** and **1b**, respectively. These values are approximately half the  $K_a$  value

of amphiphile 2, which is endowed with only three peripheral TEG chains.<sup>[20a]</sup> This difference was the first indication of the face-to-face rotated  $\pi$  stacking of the aromatic framework of amphiphiles **1a** and **1b**, which results in a lower  $K_a$ value. In addition, the  $K_a$  value determined for **1b** was higher than that calculated for 1a, despite the higher volume of the four-branched peripheral dendrons. The direct correlation between a higher hydrophobicity-and consequently a higher tendency to form supramolecular structures in polar solvents-and the generation of dendrimers explain this phenomenon,<sup>[28]</sup> which was also previously observed for related amphiphilic structures endowed with dendritic substituents.<sup>[29]</sup> The relevance of the solvophobic component in the self-assembly of these amphiphiles has been quantified by using apolar benzene as a solvent in concentration-dependent UV/Vis spectroscopy experiments. In this solvent, the coiling effect experienced by the dendritic TEG chains, together with a better solvation of the aromatic fragments, results in weaker  $\pi$ - $\pi$  interactions and, ultimately, in lower values for  $K_a$  (4.7×10<sup>4</sup> and 6.5×10<sup>4</sup> m<sup>-1</sup> for **1a** and 1b, respectively; see Figures S3 and S4 in the Supporting Information).

Attempts to determine the  $K_a$  values with water as the solvent demonstrated the extremely high value for this thermodynamic parameter under these conditions; spectroscopic features corresponding to the monomeric species were not observed until concentrations were as low as around  $10^{-7}$  M. To further investigate the self-assembly mechanism, temperature-dependent UV/Vis spectroscopy experiments in aqueous solutions were conducted (Figure 2 and Figure S5 of the Supporting Information). In aqueous solution, less energetic wavelength absorption appears as a shoulder, which is in contrast to the profile observed in less polar acetonitrile and benzene where this band is the most intense (Figure 2 and



Figure 2. Temperature-dependent UV/Vis absorption spectra of **1b** (H<sub>2</sub>O,  $1 \times 10^{-4}$  M, 278–348 K). Arrows indicate the spectroscopic changes with increasing temperature. The isosbestic point occurs at 296 nm (a). Inset b) depicts the nonlinear variation of the absorbance as a function of temperature at 305 ( $\bullet$ ) and 259 nm ( $\bullet$ ).

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Figures S3 and S4 of the Supporting Information). In these experiments, the decrease of the absorption maxima at 305 nm and also the shoulder at 319 nm mentioned above occurs in concert with an increasing absorbance at 259 nm, which can be ascribed to the formation of the monomeric form. The isosbestic points observed at 281 and 296 nm thus stem from amphiphiles **1a** and **1b**, respectively (Figure 2 and Figure S5 of the Supporting Information).

The nonlinear behavior of the spectroscopic changes with temperature (insets in Figure 2 and Figure S5 of the Supporting Information) cannot be used to calculate the mole fraction of aggregates at each temperature  $[\alpha_{agg}(T)]$ , because most of the sample is aggregated under these conditions;<sup>[9a]</sup> determination of  $\alpha_{agg}(T)$  would require recording UV/Vis spectra at higher temperatures. However, the dendritic peripheral wedges do play a relevant role in these temperature-dependence experiments. Thus, increasing temperatures resulted in turbid dispersions due to the lower critical solution temperature (LCST) transition in aqueous media. Above this LCST, the TEG chains are dehydrated to yield new supramolecular ensembles that are less soluble in the aqueous solution.<sup>[30]</sup> The LCST for amphiphiles 1a and 1b have been determined to be 318 and 338 K, respectively, by plotting the absorbance at 600 nm versus temperature (Figure S6 of the Supporting Information).

The aggregation behavior in solution has also been studied by temperature-dependent <sup>1</sup>H NMR spectroscopy experiments in different deuterated solvents. In deuterated acetonitrile, there is a fast exchange between the monomeric and aggregated species and relatively sharp resonances appear that slightly shield upon increasing temperature (Figures S7 and S8 of the Supporting Information).<sup>[31,32]</sup> Plotting the variation of the chemical shift against temperature shows a linear relationship for both *para* aromatic protons ( $\bullet$  and  $\bullet$ ) and the aliphatic ( $\bigcirc$ ) resonances (insets in Fig-

ure S7 and S8 of the Supporting Information). The <sup>1</sup>H NMR spectra for **1a** and **1b** in  $D_2O$  are significantly broader and the upfield shift of most resonances are more pronounced than those observed in CD<sub>3</sub>CN due to the strong propensity of OPEs **1a** and **1b** to stack in aqueous solution and also due to the LCST effect (Figure 3 and Figure S9 of the Supporting Information).

As stated before, the high  $K_a$  values for **1a** and **1b** in aqueous solution impede an accurate determination of the thermodynamic parameters associated with the self-assembly process by a van't Hoff analysis under these conditions. However, when the isodesmic aggrega-

tion was approximated to a simpler dimerization mechanism, the data obtained by the temperature-dependent <sup>1</sup>H NMR spectroscopy experiments allowed the  $\Delta H$  and  $\Delta S$  parameters that control the thermodynamics of the assembly to be determined. To calculate these thermodynamic values, we have utilized Equation (1), which was reported by Lee et al.:<sup>[33]</sup>

$$\delta obs = (\delta \mathbf{A} - \delta \mathbf{B}) \left[ exp \left\{ -\frac{\Delta H}{R} \left( \frac{1}{T} \right) + \frac{\Delta S}{R} \right\} + 1 \right]^{-1} + \delta \mathbf{B} \quad (1)$$

in which  $\delta_A$  and  $\delta_B$  are the chemical shift values at lower and higher temperatures, respectively. The nonlinear fit of the observed chemical shift changes versus temperature for amphiphile **1b**, results in  $\Delta H = (-30.3 \pm 1.5) \text{ kJ mol}^{-1}$  and  $\Delta S = (-91.9 \pm 4.8) \text{ J mol}^{-1}$  (inset in Figure 3). The calculated  $\Delta H$  and  $\Delta S$  values indicate that the self-assembly process is enthalpically driven and entropically disfavored and, hence, lowering temperatures enhances the self-association process.<sup>[20b,34]</sup>

The aggregation of **1a** and **1b** in aqueous solution  $(\approx 10^{-4} \text{ M})$  has also been investigated by dynamic (DLS) and static (SLS) light-scattering measurements. CONTIN analysis of the correlation functions obtained in the former shows a major contribution centered at hydrodynamic radii ( $R_{\rm H}$ ) of approximately 130 and 90 nm for amphiphiles **1a** and **1b**, respectively (Figure 4a), which is in good agreement with previously reported examples of organic amphiphiles that self-assemble into cylindrical micelles.<sup>[29]</sup> By plotting the inverse of time versus the square of the scattering vector (Figure S10 in the Supporting Information), it is possible to accurately determine the diffusion coefficient (D) for the supramolecular structures formed under these experimental conditions. Such measurements gave D values of  $1.870 \times 10^{-8}$ 



Figure 3. Partial <sup>1</sup>H NMR spectra (D<sub>2</sub>O, 300 MHz, 1 mM) of **1b** at different temperatures. The inset shows plots of  $\delta_{obs}$  versus *T* and the fit of the data to Equation (1).

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Figure 4. a) Distribution of hydrodynamic radii of aggregates of **1a** ( $\bullet$ ) and **1b** ( $\bullet$ ). The inset shows the angular dependence of the apparent diffusion coefficient vs. the angle q; b) Static light scattering intensity data for **1b** superimposed on the theoretically derived curves for a random coil (gray) and a rod (black). All measurements were carried out with  $\approx 10^{-4}$  M aqueous solutions.

and  $2.801 \times 10^{-8} \text{ cm}^2 \text{s}^{-1}$  for **1a** and **1b**, respectively. In addition, the slope obtained by plotting the angular dependence of *D* is lower than 0.03 (0.01 for **1a** and 0.02 for **1b**), suggesting the presence of elongated aggregates (inset in Figure 4a).<sup>[35]</sup>

Additional information on the shape of the supramolecular structures present in aqueous solution has been obtained by studying the corresponding particle scattering factor, also known as the form factor  $[P(\theta)]$ , determined by SLS techniques. Figure 4b (and Figure S11 of the Supporting Information) shows a plot of the dependence of the form factor  $P(\theta)$  on the scattering data. Considering the angular dependence of D, we have fitted the  $P(\theta)$  values by applying the equations corresponding to random coils [Eq. (2)] and rods [Eq. (3)]:<sup>[36]</sup>

$$P(\theta) = 2[e^{-x} - 1 + x]/x^2, x = (qR_{\rm G})^2$$
<sup>(2)</sup>

$$P(\theta) = P_0 / [1 - x^2 / 9 + 2x^4 / 225], \ x = ql/2 \tag{3}$$

in which  $R_G$  is the radius of gyration and l is the length of the rod. The random coil model [Eq. (2)] failed in fitting the scattering data. However, fitting these scattering data to the form factor for a rod model [Eq. (3)] provided correlation factors ( $R^2$ ) of 0.999 and 0.992 for **1a** and **1b**, respectively, which is diagnostic of the presence of supramolecular structures with a rod shape. In addition, the application of Equation (2) allows the calculation of length values of 907 and 718 nm for the rods formed from **1a** and **1b**, respectively. The combination of the concentration-dependent UV/Vis and light-scattering experiments unambiguously demonstrate the isodesmic mechanism followed by these amphiphiles to self-assemble.<sup>[27d]</sup>

Self-assembly onto surfaces: The studies performed in solution demonstrate the presence of elongated aggregates that could be effectively transferred onto a substrate. The rotated stacking of the aromatic moieties of amphiphiles **1a** and **1b** frustrates the three-dimensional growth of the supramolecular structures into vesicles observed for  $2^{[20a]}$  and, in consequence, induces the formation of 1D aggregates. This is indeed what we have observed upon depositing aqueous solutions ( $\approx 10^{-4}$  M) of amphiphilic OPEs **1a** or **1b** onto carbon-coated copper grids and registering the corresponding transmission electron micrographs. Micrographs of both amphiphilic OPEs **1a** and **1b** recorded by using this technique, show their organization into long fibrillar structures (Figures 5 and 6 and Figure S12 of the Supporting Information).

Compound 1a forms fibers with average widths of around 70 nm (Figure 5) that can be entangled into thicker filaments (Figure 5a). Considering the molecular dimensions of OPE 1a (around 4.5 nm in height), the fibers observed in the TEM images would be formed by the interconnection of unimolecular wires through the hydrophilic dendritic peripheral substituents (see Scheme 2 below and Scheme S1 of the Supporting Information). A closer examination of some of the TEM micrographs reveals a ribbon-like shape for some of the fibers that, in addition, exhibit folded edges with a thickness of around 10 nm (inset in Figure 5b). This dimension is in good agreement with a bimolecular packing of molecules of 1a.

Similar images were recorded when amphiphile **1b** was used for TEM imaging. Drop-casting a  $\approx 10^{-4}$  M aqueous solution of this four-branched dendronized amphiphile onto carbon-coated copper grids allowed the observation of fibers several micrometers long (Figure 6 a and Figure S12b of the Supporting Information). As for the previous amphiphile, a closer examination of the TEM micrographs also reveals the presence of ribbon-like strands that can be folded (Figure 6 b). Interestingly, the TEM images also demonstrate that large ribbon-like fibers around 300 nm wide can become entangled into coiled rope-like supramolecular structures (Figure 6 c) that resemble those observed for other, related  $\pi$ -conjugated oligomers decorated with chiral

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Figure 5. TEM images, stained with uranyl acetate, of the fibers formed from the self-assembly of **1a** in aqueous solution ( $\approx 10^{-4}$  M). a) Fibers approximately 70 nm wide entangled into thicker filaments. b) Ribbon-like shape of some regions (the insets shows a twisted ribbon).



Figure 6. TEM images of the fibers obtained from  $\approx 10^{-4}$  M aqueous solution of **1b**, stained with uranyl acetate, onto carbon-coated copper grids. a) Long fibers; b) expanded view of the black rectangle in a) showing a folded edge. c) Left-handed rope-like strand obtained by the hierarchical assembly of **1b**. The inset in c) shows the density profile along 600 nm, indicated by the black line.

substituents.<sup>[12b]</sup> This supramolecular organization would imply a helical arrangement of amphiphile **1b**, despite the lack of any chiral center in the molecule. The formation of chiral objects is diagnostic of a hierarchical packing of **1b** in which van der Waals contacts between the dendritic wedges, and also  $\pi$ -stacking interactions between the aromatic moiety, play a pivotal role in the final self-assembly process. Although both amphiphiles **1a** and **1b** are able to form thick strands, the induced chirality observed only for **1b** could be attributed to the steric constraints imposed by the four-branched TEG dendrons.

To gain a deeper insight into the self-assembly mechanism followed by amphiphiles **1a** and **1b**, we have carried out AFM imaging in highly diluted ( $\approx 10^{-6}$  M) aqueous solutions utilizing highly ordered pyrolytic graphite (HOPG) as the substrate. AFM images of both radial OPEs **1a** and **1b** under these conditions showed long fibrous structures (Figure 7 and Figure S13 of the Supporting Information).



Figure 7. Height-tapping-mode AFM images (air, 298 K) of drop-cast **1b** on HOPG from  $\approx 10^{-6}$  M aqueous solution. a) z scale = 19 nm; b) z scale = 10 nm. The inset in b) shows the height profile along the white line.

The observed fibers are around 4.5 and 4.8 nm in height for **1a** and **1b**, respectively, as demonstrated by their corresponding profiles. These dimensions are in good agreement with those calculated for these dendronized amphiphiles (see Scheme 2) and are diagnostic of unimolecular packing to form the fibers. The AFM images also allowed the effective fiber width to be calculated by subtracting the tip broadening factor.<sup>[37]</sup> Thus, amphiphile **1a** forms fibers of  $(30\pm2)$  nm in width and, analogously, the fibers formed from **1b** present a diameter of  $(25\pm2)$  nm. These width values imply the interaction of several single wires through their peripheral dendritic substituents to form thicker fibers.

**Dye intercalation experiments**: One of the most important potential applications of self-assembled structures is their capability to transport and release different species. The encapsulation of substances by supramolecular structures could be utilized as drug-delivery containers capable of controlling the concentration of the released drug and also of enabling site-specific delivery of a drug to the desired point of action.<sup>[11b,29,38]</sup> We have evaluated the molecular encapsulation and release of the hydrophobic dye 4-(4-nitrophenyl-

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**1a**, which implies a tight binding between this amphiphile and the dye and that, therefore, a higher temperature is required to completely liberate the dye. In addition, the higher temperatures reached in these experiments, in comparison to those performed with pristine **1a** and **1b**, could be considered to be indirect proof of the formation of different supramolecular structures.

#### Conclusion

Scheme 2. Molecular dimensions and schematic representation of the self-assembly of compounds 1a and 1b into nanofibrillar structures.

azo)aniline (Disperse Orange 3) by the fibers formed by amphiphiles **1a** and **1b** in aqueous solution by means of temperature-dependent UV/Vis experiments (Figure 8).

To carry out the temperature-dependent UV/Vis encapsulation studies we have utilized a  $\approx 10^{-5}$  M solution of both amphiphiles in water to evaluate the spectroscopic changes brought about by the release of dye molecules. To efficiently intercalate the hydrophobic dye molecules, we added ten equivalents of Disperse Orange 3, sonicated the resulting mixtures for three hours and filtered them off with 0.45 µm filters. Upon heating the mixtures, the diagnostic band for Disperse Orange 3 at around 400 nm increased gradually, while the maxima at around 284 and 303 nm decreased. However, the lack of defined isosbestic points in the UV/Vis spectra obtained during these experiments is indicative of the coexistence of aggregates with different stoichiometries.<sup>[39]</sup> These findings suggest the dye molecules are intercalated in the aggregated structure previously formed by the amphiphiles and can be considered to be indirect proof of the encapsulation of hydrophobic guests within the supramolecular structure formed by the artificial organic amphiphiles.<sup>[29]</sup> Plotting the absorbance at 400 nm, which corresponds to the dye, versus temperature showed a nonlinear dependence that is diagnostic of dye release (insets in Figure 8). The increased absorbance as a function of temperature can be fitted to the Boltzmann function with correlation factors of 0.99. For both amphiphiles, release of the dye molecules started at around 310 K; below this temperature, the change in the absorbance at 400 nm was negligible. At higher temperatures, the changes in the absorbance were slightly different for compounds 1a and 1b. In the latter case, at high temperature (>350 K) the absorbance at 400 nm remained practically unaltered, suggesting that most of the dye was already released. However, the absorbance at 400 nm continues to increase above 350 K for compound

We have synthesized two triangular-shaped, amphiphilic OPEs decorated in their periphery with hydrophilic TEGbased dendron wedges (com-

pounds 1a and 1b) that allows their dissolution in aqueous media. All of the studies carried out, both in solution and on surfaces, support the idea of a face-to-face rotated  $\pi$ stacking of the aromatic units, which avoids the steric demand caused by the hydrophilic dendron wedges and brings about the generation of the fibers through the plausible mechanism detailed above. This stacking mode decreases the value of the binding constant in comparison to our previously synthesized, triangular OPE-based amphiphile **2**.<sup>[20a]</sup> At low concentrations in water, the initial  $\pi$ - $\pi$  interactions between amphiphilic molecules grow only in one dimension to create unimolecularly stacked aggregates that can ultimately interact by means of the van der Waals contacts, solvophobic interactions, and/or hydrogen bonding exerted by the hydrophilic chains to form bundles of fibers. By using more concentrated aqueous solutions, it was possible to generate thicker and longer fibers, with thicknesses of around 70 nm, through efficient interaction between thinner aggregates (Scheme 2). Some of these fibers also present folded edges that suggest a ribbon-like nature. Compound 1b was also able to self-associate into thick strands with rope-like features, despite the lack of any chiral element in its chemical makeup. This helical arrangement implies a hierarchical self-assembly to form the helical supramolecular structures.

Finally, temperature-dependent UV/Vis experiments have demonstrated the ability of the aggregates formed by the new amphiphilic OPEs reported to intercalate and release dye molecules in aqueous solution. These features suggest that these materials can be exploited for drug-delivery purposes. In addition, work is in progress to synthesize new chiral dendronized congeners that should be useful to prepare helical supramolecular structures.

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Figure 8. Temperature-dependent UV/Vis spectra of aqueous solutions ( $\approx 10^{-5}$  M) of: a) **1a** and b) **1b** containing ten equivalents of Disperse Orange 3. Arrows indicate the spectroscopic changes upon increasing temperature. The insets in a) and b) depict the changes in the absorbance at 400 nm as a function of temperature.

#### **Experimental Section**

Amphiphile 1a: Compound 5a (0.65 g, 1.08 mmol), 3 (0.04 g, 0.30 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.04 g, 0.04 mmol), and triphenylarsine (0.005 g, 0.01 mmol) were dissolved in triethylamine (20 mL) and dry THF (5 mL). The mixture was subjected to several vacuum/ argon cycles and heated at reflux for 48 h. After cooling to RT, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; ethyl acetate/EtOH, 5:1) affording **1a** as a brown oil (0.17 g, 36%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta = 7.58$  (s, 3H; H<sub>a</sub>), 7.45 (d, J=8.8 Hz, 6H; H<sub>b</sub>), 6.90 (d, J=8.8 Hz, 6H; H<sub>c</sub>), 4.07 (d, J = 5.8 Hz, 6H; H<sub>d</sub>), 3.78–3.59 (br, 84H; H<sub>f-l</sub>), 3.39 (s, 18H; H<sub>m</sub>), 2.52 ppm (q, J = 5.8 Hz, 3H; H<sub>e</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta = 159.8$ , 133.7, 133.5, 124.6, 115.1, 115.0, 90.8, 87.1, 72.3, 71.0, 71.0, 70.9, 70.8, 69.6, 66.5, 59.4, 40.2 ppm; FTIR (neat):  $\tilde{\nu}$  = 684, 756, 837, 876, 948, 1028, 1107, 1248, 1290, 1355, 1464, 1509, 1576, 1606, 1676, 1731, 1954, 2209, 2867, 2921 cm<sup>-1</sup>; MALDI-TOF: m/z: 1566 [M]<sup>+</sup>; HRMS: m/z calcd for [C<sub>84</sub>H<sub>128</sub>O<sub>27</sub>]<sup>2+</sup>: 784.4322; found: 784.4316.

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Amphiphile 1b: Compound 5b (1.17 g, 1.02 mmol), 3 (0.045 g, 0.30 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.02 g, 0.03 mmol) and triphenylarsine (0.004 g, 0.01 mmol) were dissolved in triethylamine (10 mL). The mixture was subjected to several vacuum/argon cycles and heated at reflux for 24 h. After cooling to RT, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; CHCl<sub>3</sub>/methanol, 10:1) affording 1b as a brown oil (0.28 g, 32 %). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta = 7.51$  (s, 3 H; H<sub>a</sub>), 7.38 (d, J = 8.8 Hz, 6H; H<sub>b</sub>), 6.82 (d, J = 8.8 Hz, 6H; H<sub>c</sub>), 3.96 (d, J = 5.4 Hz, 6H;  $H_d$ ), 3.58–3.39 (br, 192 H;  $H_{f=0}$ ), 3.30 (s, 36 H;  $H_p$ ), 2.28 (q, J = 5.4 Hz, 3 H; H<sub>e</sub>), 2.10 ppm (q, J = 5.8 Hz, 6H; H<sub>h</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta =$ 159.4, 133.3, 133.1, 124.2, 114.7, 114.6, 90.4, 87.7, 76.7, 71.9, 70.9, 70.6, 70.57, 70.52, 70.4, 69.6, 66.4, 69.1, 66.1, 59.0, 40.1, 39.9 ppm; FTIR (neat):  $\tilde{\nu}\!=\!687,\ 772,\ 840,\ 1030,\ 1104,\ 1248,\ 1291,\ 1356,\ 1462,\ 1508,\ 1577,\ 2860,$ 2921 cm<sup>-1</sup>; MALDI-TOF: *m/z*: 2994 [*M*+Na]<sup>+</sup>; HRMS: *m/z* calcd for [C150H258NaO57]+: 2994.7199; found: 2994.7222.

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- a) C. Kim, A. Facchetti, T. J. Marks, *Science* 2007, *318*, 76–80; b) V. Burtman, G. Hukic, A. S. Ndobe, T. Drori, Z. V. Vardeny, *J. Appl. Phys.* 2007, *101*, 54502–54507.
- [2] a) C. A. Hunter, J. K. M. Sanders, J. Am. Chem. Soc. 1990, 112, 5525–5534; b) C. A. Hunter, K. R. Lawson, J. Perkins, C. J. Urch, J. Chem. Soc. Perkin Trans. 2 2001, 651–669; c) C. H. Hunter, Angew. Chem. 2004, 116, 5424–5439; Angew. Chem. Int. Ed. 2004, 43, 5310– 5324.
- [3] a) J. Wu, W. Pisula, K. Müllen, Chem. Rev. 2007, 107, 718-747;
  b) A. Ajayaghosh, V. K. Praveen, Acc. Chem. Res. 2007, 40, 644-656;
  c) F. J. M. Hoeben; P. Jonkheijm, E. W. Meijer, A. P. H. J. Schenning, Chem. Rev. 2005, 105, 1491-1546;
  P. Jonkheijm, E. W. Meijer, A. P. H. J. Schenning, Chem. Rev. 2005, 105, 1491-1546;
  P. Jonkheijm, E. W. Meijer, A. P. H. J. Schenning, Chem. Rev. 2005, 105, 1491-1546.
- [4] a) J.-H. Ryu, D.-J. Hong, M. Lee, *Chem. Commun.* 2008, 1043– 1054; b) E. Lee, Y.-H. Jeong, J.-K. Kim, M. Lee, *Macromolecules* 2007, 40, 8355–8360.
- [5] N. Arai, K. Yasuoka, X. C. Zeng, J. Am. Chem. Soc. 2008, 130, 7916–7920.
- [6] a) M. Kellermann, W. Bauer, A. Hirsch, B. Schade, K. Ludwig, C. Böttcher, Angew. Chem. 2004, 116, 3019–3022; Angew. Chem. Int. Ed. 2004, 43, 2959–2962; b) A. Hirsch, Pure Appl. Chem. 2008, 80, 571–587; c) M. S. Becherer, B. Schade, C. Böttcher, A. Hirsch, Chem. Eur. J. 2009, 15, 1637–1648.
- [7] a) R. M. Meudtner, M. Ostermeier, R. Goddard, C. Limberg, S. Hecht, *Chem. Eur. J.* 2007, *13*, 9834–9840; b) L. Piot, R. M. Meudtner, T. El Malah, S. Hecht, P. Samorì, *Chem. Eur. J.* 2009, *15*, 4788–4792.
- [8] a) S. Sreejith, K. P. Divya, A. Ajayaghosh, Angew. Chem. 2008, 120, 8001–8005; Angew. Chem. Int. Ed. 2008, 47, 7883–7887; b) A. Ajayaghosh, P. Chithra, R. Varghese, Angew. Chem. 2007, 119, 234–237; Angew. Chem. Int. Ed. 2007, 46, 230–233.
- [9] a) X. Zhang, S. Rehm, M. M. Safont-Sempere, F. Würthner, *Nat. Chem. Biol.* 2009, *1*, 623–629; b) S. Ghosh, X.-Q. Li, V. Stepanenko, F. Würthner, *Chem. Eur. J.* 2008, *14*, 11343–11357; c) X. Zhang, Z. Chen, F. Würthner, *J. Am. Chem. Soc.* 2007, *129*, 4886–4887.

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#### CHEMISTRY

- [10] a) J. P. Hill, W. S. Jin, A. Kosaka, T. Fukushima, H. Ichihara, T. Shimomura, K. Ito, T. Hashizume, N. Ishii, T. Aida, *Science* 2004, 304, 1481–1483; b) Y. Yamamoto, T. Fukushima, Y. Suna, N. Ishii, A. Saeki, S. Seki, S. Tagawa, M. Taniguchi, T. Kawai, T. Aida, *Science* 2006, 314, 1761–1764; c) M. Yin, J. Shen, W. Pisula, M. Liang, L. Zhi, K. Müllen, J. Am. Chem. Soc. 2009, 131, 14618–14619.
- [11] a) E. Lee, J.-K. Kim, M. Lee, Angew. Chem. 2009, 121, 3711–3714; Angew. Chem. Int. Ed. 2009, 48, 3657–3660; b) J.-K. Kim, E. Lee, Y. Lim, M. Lee, Angew. Chem. 2008, 120, 4740–4744; Angew. Chem. Int. Ed. 2008, 47, 4662–4666; c) D.-J. Hong, E. Lee, J.-K. Lee, W.-C. Zin, M. Han, E. Sim, M. Lee, J. Am. Chem. Soc. 2008, 130, 14448– 14449; d) J.-K. Kim, E. Lee, Z. Huang, M. Lee, J. Am. Chem. Soc. 2006, 128, 14022–14023.
- [12] a) J. van Herrikhuyzen, S. J. George, M. R. J. Vos, N. A. J. M. Sommerdijk, A. Ajayaghosh, S. C. J. Meskers, A. P. H. J. Schenning, Angew. Chem. 2007, 119, 1857–1860; Angew. Chem. Int. Ed. 2007, 46, 1825–1828; b) A. Ajayaghosh, R. Varghese, S. J. George, C. Vijayakumar, Angew. Chem. 2006, 118, 1159–1162; Angew. Chem. Int. Ed. 2006, 45, 1141–1144; c) S. J. George, A. Ajayaghosh, P. Jonkheijm, A. P. H. J. Schenning, E. W. Meijer, Angew. Chem. 2004, 116, 3504–3507; Angew. Chem. Int. Ed. 2004, 43, 3422–3425; d) F. J. M. Hoeben, L. M. Herz, C. Daniel, P. Jonkheijm, A. P. H. J. Schenning, C. Silva, S. C. J. Meskers, D. Beljonne, R. T. Phillips, R. H. Friend, E. W. Meijer, Angew. Chem. 2004, 116, 2010–2013; Angew. Chem. Int. Ed. 2004, 43, 1976–1979.
- [13] a) A. Ajayaghosh, R. Varghese, S. Mahesh, V. K. Praveen, Angew. Chem. 2006, 118, 7893-7896; Angew. Chem. Int. Ed. 2006, 45, 7729-7732; b) A. Ajayaghosh, R. Varghese, V. K. Praveen, S. Mahesh, Angew. Chem. 2006, 118, 3339-3342; Angew. Chem. Int. Ed. 2006, 45, 3261-3264.
- [14] L. C. Palmer, S. I. Stupp, Acc. Chem. Res. 2008, 41, 1674-1684.
- [15] a) J. H. K. Ky Hirschberg, L. Brunsveld, A. Ramzi, J. A. J. M. Vekemans, R. P. Sijbesma, E. W. Meijer, *Nature* 2000, 407, 167–170;
  b) M. Enomoto, A. Kishimura, T. Aida, *J. Am. Chem. Soc.* 2001, 123, 5608–5609; c) S. Kawano, N. Fujita, S. Shinkai, *J. Am. Chem. Soc.* 2004, 126, 8592–8593.
- [16] a) J. H. van Esch, B. L. Feringa, Angew. Chem. 2000, 112, 2351–2354; Angew. Chem. Int. Ed. 2000, 39, 2263–2266; b) N. M. Sangee-tha, U. Maitra, Chem. Soc. Rev. 2005, 34, 821–836; c) A. Ajaya-ghosh, V. K. Praveen, C. Vijayakumar, Chem. Soc. Rev. 2008, 37, 109–122.
- [17] a) J. C. Tiller, Angew. Chem. 2003, 115, 3180-3183; Angew. Chem. Int. Ed. 2003, 42, 3072-3075; b) L. A. Estroff, A. D. Hamilton, Chem. Rev. 2004, 104, 1201-1217; c) K. J. C. van Bommel, A. Friggeri, S. Shinkai, Angew. Chem. 2003, 115, 1010-1030; Angew. Chem. Int. Ed. 2003, 42, 980-999.
- [18] a) S. Srinivasan, P. A. Babu, S. Mahesh, A. Ajayagosh, J. Am. Chem. Soc. 2009, 131, 15122–15123; b) C. Vijayakumar, V. K. Praveen, A. Ajayaghosh, Adv. Mater. 2009, 21, 2059–2063; c) S. S. Babu, S. Mahesh, K. K. Kartha, A. Ajayaghosh, Chem. Asian J. 2009, 4, 824– 829; d) S. S. Babu, V. K. Praveen, S. Prasanthkumar, A. Ajayaghosh, Chem. Eur. J. 2008, 14, 9577–9584; e) A. Ajayaghosh, V. K. Praveen, S. Srinivasan, R. Varghese, Adv. Mater. 2007, 19, 411–415; f) S. J. George, A. Ajayaghosh, Chem. Eur. J. 2005, 11, 3217–3227.
- [19] a) T. Muraoka, C.-Y. Koh, H. Cui, S. I. Stupp, Angew. Chem. 2009, 121, 6060–6063; Angew. Chem. Int. Ed. 2009, 48, 5946–5949; b) T. Muraoka, H. Cui, S. I. Stupp, J. Am. Chem. Soc. 2008, 130, 2946–2947; c) H. A. Behanna, K. Rajangam, S. I. Stupp, J. Am. Chem. Soc. 2007, 129, 321–327.
- [20] a) G. Fernández, F. García, L. Sánchez, *Chem. Commun.* 2008, 6567–6569; b) F. García, F. Aparicio, G. Fernández, L. Sánchez, *Org. Lett.* 2009, 11, 2748–2751.
- [21] F. García, G. Fernández, L. Sánchez, Chem. Eur. J. 2009, 15, 6740– 6747.

- [22] G. Fernández, F. García, F. Aparicio, E. Matesanz, L. Sánchez, *Chem. Commun.* 2009, 7155–7157.
- [23] Metal-Catalyzed Cross-Coupling Reactions (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, 1998.
- [24] W. Uhl, H. R. Bock, F. Breher, M. Claesener, S. Haddadpour, B. Jasper, A. Hepp, Organometallics 2007, 26, 2363–2369.
- [25] a) C. Amatore, A. Jutand, *Coord. Chem. Rev.* 1998, *178–180*, 511–528; b) R. W. Wagner, T. E. Johnson, F. Li, J. S. Lindsey, *J. Org. Chem.* 1995, *60*, 5266–5273; c) C. Amatore, A. Jutand, F. Khalil, M. A. M'Barki, L. Mottier, *Organometallics* 1993, *12*, 3168–3178.
- [26] a) M. Jayaraman, J. M. J. Fréchet, J. Am. Chem. Soc. 1998, 120, 12996–12997; b) C.-J. Jang, J.-H. Ryu, J.-D. Lee, D. Sohn, M. Lee, Chem. Mater. 2004, 16, 4226–4231; c) K.-S. Moon, E. Lee, M Lee, Chem. Commun. 2008, 3061–3063.
- [27] a) R. B. Martin, Chem. Rev. 1996, 96, 3043-3064; b) D. Zhao, J. S. Moore, Org. Biomol. Chem. 2003, 1, 3471-3491; c) Z. Chen, A. Lohr, C. R. Saha-Möller, F. Würthner, Chem. Soc. Rev. 2009, 38, 564-584; d) T. F. A. De Greef, M. M. J. Smulders, M. Wolffs, A. P. H. J. Schenning, R. P. Sijbesma, E. W. Meijer, Chem. Rev. 2009, 109, 5687-5754.
- [28] a) Y. Haba, C. Kojima, A. Harada, K. Kono, Angew. Chem. 2007, 119, 238–241; Angew. Chem. Int. Ed. 2007, 46, 234–237; b) S. V. Aathimanikandan, E. N. Savariar, S. Thayumanavan, J. Am. Chem. Soc. 2005, 127, 14922–14929.
- [29] K.-S. Moon, H.-J. Kim, E. Lee, M. Lee, Angew. Chem. 2007, 119, 6931–6934; Angew. Chem. Int. Ed. 2007, 46, 6807–6810.
- [30] a) G. D. Smith, D. Bedrov, J. Phys. Chem. B 2003, 107, 3095-3097;
  b) S. V. Aathimanikandan, E. N. Savariar, S. Thayumanavan, J. Am. Chem. Soc. 2005, 127, 14922-14929;
  c) Z. Jia, H. Chen, X. Zhu, D. Yan, J. Am. Chem. Soc. 2006, 128, 8144-8145;
  d) T. Hirose, K. Matsuda, Chem. Commun. 2009, 5832-5834.
- [31] W. Wang, J. J. Han, L.-Q. Wang, L.-S. Li, W. J. Shaw, A. D. Q. Li, Nano Lett. 2003, 3, 455–458.
- [32] a) Y. Zhou, D. Yan, W. Dong, Y. Tian, J. Phys. Chem. B 2007, 111, 1262–1270; b) F. Hua, X. Jiang, B. Zhao, Macromolecules 2006, 39, 3476–3479.
- [33] X. Jiang, Y.-K. Lim, B. J. Zhang, E. A. Opsitnick, M.-H. Baik, D. Lee, J. Am. Chem. Soc. 2008, 130, 16812–16822.
- [34] a) M. M. J. Smulders, A. P. H. J.; Schenning, E. W. Meijer, J. Am. Chem. Soc. 2008, 130, 606–611; Schenning, E. W. Meijer, J. Am. Chem. Soc. 2008, 130, 606–611; Schenning, E. W. Meijer, J. Am. Chem. Soc. 2008, 130, 606–611; b) E. M. García-Frutos, B. Gómez-Lor, J. Am. Chem. Soc. 2008, 130, 9173–9177.
- [35] M. Schmidt, W. H. Stockmayer, Macromolecules 1984, 17, 509-514.
- [36] a) Dynamic Light Scattering, (Eds.: J. Berne, R. Pecora) Wiley, New York, **1976**; b) for a recent example, see: M. Yuasa, K. Oyaizu, A. Yamaguchi, M. Kuwakado, J. Am. Chem. Soc. **2004**, 126, 11128– 11129.
- [37] a) H.-J. Butt, R. Guckenberger, J. P. Rabe, *Ultramicroscopy* 1992, 46, 375–393; b) P. Samorí, V. Francke, T. Mangel, K. Müllen, J. P. Rabe, *Opt. Mater.* 1998, 9, 390–393. The radius of the tip (Veeco probes, MPP-11100-10) has been considered to be 12.5 nm. The calculated tip broadening factors are of (19.2±2) and (19.5±1) nm for 1a and 1b, respectively.
- [38] a) E. Soussan, S. Cassel, M. Blanzat, I. Rico-Lattes, Angew. Chem.
  2009, 121, 280–295; Angew. Chem. Int. Ed. 2009, 48, 274–288; b) M. Kellermann, W. Bauer, A. Hirsch, B. Schade, K. Ludwig, C. Böttcher, Angew. Chem. 2004, 116, 3019–3022; Angew. Chem. Int. Ed.
  2004, 43, 2959–2962; c) J.-H. Ryu, E. Lee, Y. Lim, M. Lee, J. Am. Chem. Soc. 2007, 129, 4808–4814.
- [39] G. Fernández, L. Sánchez, E. M. Pérez, N. Martín, J. Am. Chem. Soc. 2008, 130, 10674–10683.

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