Supramolecular Polymers

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Topochemical Polymerization in Supramolecular Polymers of Oligopeptide-Functionalized Diacetylenes**

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New generations of synthetic polymers targeting applications at the interface of optoelectronics and the biosciences must "speak the language" of biomaterials and mimic their functioning. They must provide the chemical functionality to interact with biological systems on the molecular level and exhibit a similar ability to form hierarchical structures.[1] Supramolecular self-assembly has proven to be a powerful tool for the preparation of materials with structural features on the nanometer scale.[2] Recently, the self-assembly of oligopeptides through aggregation and formation of β sheets has received increasing attention. This approach has been prompted by research activities in the field of neurodegenerative diseases.[3] Notable examples include the self-assembly of oligopeptides based on amyloids,[4] the formation of organogels from synthetic oligopeptides and their deposition on surfaces,[5] the aggregation of peptidomimetic molecules[6] and PEG conjugates,[7] multiblock copolymers inspired by spider silk,[8] as well as the use of self-assembled oligopeptides in the manufacture of gold nanowires.[9]

Poly(diacetylene)s are optoelectronically active materials. Topochemical polymerizations of diacetylenes are possible whenever the required crystalline order of the monomers is established.[10] They have, for example, been performed in self-assembled mono- or multilayers of diynoic acids and their salts[11] as well as along 1D lamellar structures in self-assembled monolayers on surfaces.[12] Diacetylene-containing

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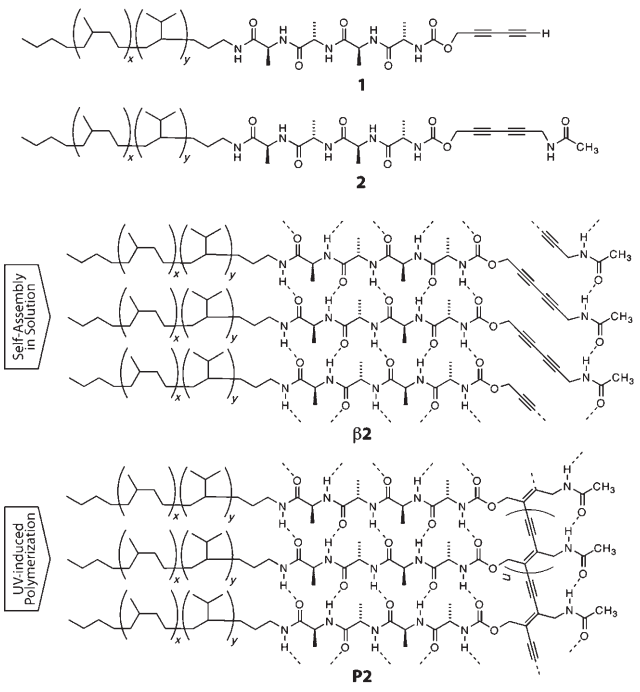
lipid amphiphiles with chiral polar head groups, such as phosphatidyl cholines, amino acids, or aldonamides were found to form tubular or helical superstructures in the submicrometer range.[13] Related materials have been used in sensing applications.[14] Finally, diacetylene polymerizations have been carried out in hydrogen-bonded organogels and supramolecular polymers.[15]

Here we describe the use of self-assembled supramolecular polymers consisting of β-sheet-forming oligopeptides as scaffolds for the topochemical polymerization of diacetylenes in solution. Thus, we designed and prepared the macromonomers **1** and **2** which include 1) a hydrogenated poly(isoprene) segment (hPI) as a polydisperse aliphatic coil to provide solubility in organic solvents and prevent global ordering; 2) a tetra(L-alanine) segment to induce anisotropic self-assembly through formation of a β sheet; 3) a diacetylene moiety integrated directly into the hydrogen bonding array without a spacer; and 4) in the case of **2**, an NHAc end group capable of forming hydrogen bonds to promote a parallel arrangement of the molecules. The macromonomer **2** self-assembled into a supramolecular polymer with a double-helical topology which was, then, converted into the corresponding poly(diacetylene) **P2** by UV irradiation (Scheme 1).



Scheme 1. Self-assembly and topochemical polymerization of diacetylenes functionalized with a β-sheet-forming oligopeptide.

1 and **2** were prepared by anionic polymerization of isoprene, high-pressure hydrogenation, stepwise solution-phase peptide synthesis, and acetylene heterocoupling reactions.[16] Solutions of **1** and **2** in CH_2Cl_2 or $CHCl_3$ showed no tendency toward gelation, but ^1H NMR spectra as well as solution-phase IR spectra gave a clear indication of aggregation.[16] In the IR spectrum of **2** (Figure 1), the main amide A (ν_{NH}) band at 3283 cm^{-1}, the predominating amide I (ν_{CO}) band at 1632 cm^{-1}, as well as the amide II and amide III bands were in excellent agreement with a β-sheet structure. A detailed analysis[16] suggested that **2** may form bent or twisted β-sheet structures **β2** with a parallel arrangement of the chains. It is worth noting that, by contrast, the IR spectra of **1** were consistent with a predominantly antiparallel packing of the chains in the β-sheet structure, and a higher proportion of other (unordered) structures.[16] This difference is remarkable given the close structural relationship between **1** and **2**. The NHAc end group in **2** appears to enforce a parallel arrangement of the molecules within the aggregates because, only in this way, can the maximum number of hydrogen bonds be achieved.

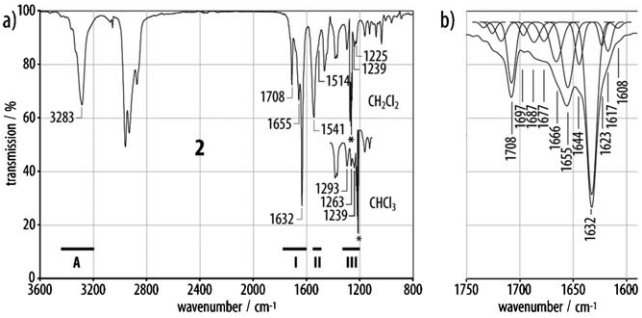


Figure 1. IR spectrum of **2** and assignment of the amide I bands.

Transmission electron microscopy (TEM) images of unstained samples of **2** as well as images obtained after carbon shadowing (Figure 2 a–d) showed remarkably straight fibrillar features which were several micrometers long and, upon qualitative inspection, appeared to have a uniform diameter and height (as concluded from the widths of the carbon shadows). Histographic analyses revealed a bimodal width distribution with two narrow distributions centered around maxima of 6.5(±1.4) nm and 8.7(±2.5) nm. An upper limit for the height of the fibrils was determined to be approximately 1.7(±1.3) nm. This height is about twice the value that is typically expected for an individual β sheet. Nevertheless, the observed fibrils are flat objects—flat ribbons or collapsed tubes—that are preferentially adsorbed flat on the carbon surface. Scanning force microscopy (SFM) images of samples of **2** spin-coated onto highly oriented pyrolytic graphite (HOPG) substrates (Figure 2 e–j) showed similar fibrillar features.[17] The apparent height of the fibrils was 4.7(±0.5) nm according to a histographic analysis, and their widths were estimated to be on the order of 5 nm.[18] Remarkably, the fibrils were consistently found to be right-handed double helices with a pitch of about 17.8(±1.7) nm which were constituted from two flat ribbon-type substructures.[19]

X-ray diffraction studies[16] on solid samples of **2** showed a main meridional reflection at a spacing of 4.59 Å. Electron diffraction studies[16] on multilayer films of **2** revealed a doublet of reflections at 4.76 and 4.59 Å as well as additional reflections at spacings of 8.04 and 4.25 Å. The results were in agreement with the expected β-sheet-type aggregation. Furthermore, they were similar to X-ray data reported for related

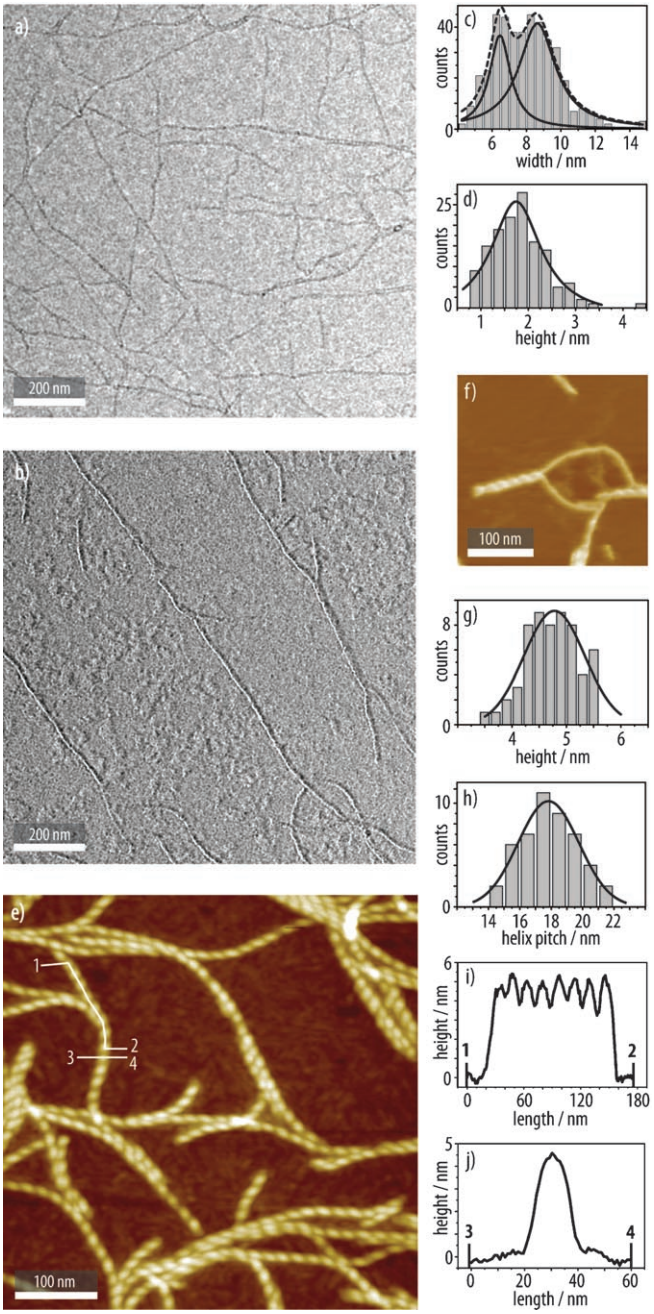


Figure 2. TEM images of samples of **2**: a) unstained and b) after carbon shadowing; histograms showing the c) width and d) height of the fibrils (derived from the TEM images); e,f) SFM images of **2**; g,h) height profiles along and across the fibrils; histograms of the i) height and j) helical pitch (derived from the SFM images).

systems,[8] and closely matched X-ray investigations on helical amyloid fibrils.[4]

On the basis of the above results, we propose as a working hypothesis the following model for the self-assembly of **2** (Figure 3). The observed helix dimensions translate into a ribbon width on the order of 13–14 nm. As the extended length of **2** is about 6.7 nm, we assume that the ribbons are constituted of two parallel β-sheet-type aggregates **β2**. Thus, the oligopeptide would form crystalline cores that would be

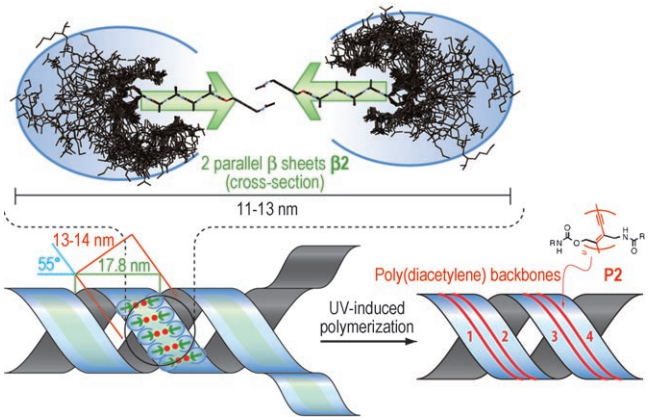


Figure 3. Proposed model for the self-assembly and polymerization of macromonomer **2**; ribbons are formed from two parallel β sheets **β2** (shown in cross-section) and wound into a tubular double-helical aggregate.

embedded into a "cushion" of the coil segments and shielded from the hydrophobic environment. In conclusion, the observed aggregates are to be regarded as well-defined supramolecular polymers with dimensions directly correlated to their molecular constituents rather than as helical micellar or tubular vesicular structures, as have been observed in the case of diacetylene-containing lipid amphiphiles.[13] They are, at the same time, a synthetic example of a "jelly-roll" morphology which has been described in the context of protein superstructures.[20]

Finally, we investigated the polymerizability of the macromonomers **1** and **2** in organic solution. Solutions of the macromonomers in CH_2Cl_2 were degassed in a thermostated quartz Schlenk tube, cooled to 0 °C, and exposed to UV irradiation from a 250 W Ga-doped Hg light source. Solutions of **1** turned only slightly yellow, and the UV spectra[16] showed that the diacetylene functions were consumed probably in the sense of an unspecific cross-linking reaction. By contrast, solutions of **2** attained an intense purple color within less than one minute. The UV spectra of the reaction mixtures showed two strong bands at about 520 nm and 580 nm, which are consistent with the formation of a poly(diacetylene) backbone (Figure 4). Raman spectra as well as solid state CP-MAS ^{13}C NMR spectra provided further evidence for the successful

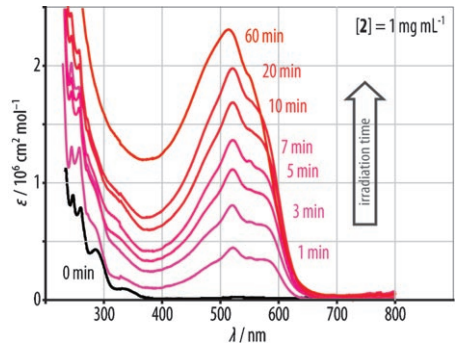


Figure 4. UV spectra of the UV-induced polymerization of **2** in CH_2Cl_2; [**2**] = 1 mg mL^{-1}.

conversion into the poly(diacetylene) **P2**.[16] We attribute the remarkable difference in polymerizability between **1** and **2** to the role of the NHAc end group, which is necessary for the formation of the required parallel β-sheet structures.

In conclusion, we have successfully self-assembled the diacetylene derivative **2** into aggregates with dimensions of a few nanometers. We have, thus, used β-sheet-type hydrogen-bonding networks to obtain a well-defined supramolecular polymer with a double-helical topology. A "1D topochemical polymerization" was then performed and these supramolecular polymers were converted into the poly(diacetylene) **P2**. The obtained poly(diacetylene) features a conjugated backbone, a high degree of functionalization with biochemically relevant substituents, as well as, most importantly, a defined hierarchical structure. It is these properties which may make this system attractive as a platform for optoelectronic applications at the interface with the biosciences.

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[16] See the Supporting Information.
[17] In addition to the fibrils, one could observe an ultrathin layer of **2** which was adsorbed onto the HOPG surface.
[18] The apparent height of the fibrils was measured at the maxima of the helical fine structure. The width was estimated from the apparent width of 18 nm after correction for the radius of the SFM tip.
[19] Figure 4c shows the SFM picture recorded after UV irradiation. This irradiation, however, had no influence on the appearance of the fibrils in the SFM images.
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