

Intramolecular Cross-Linking of Helical Folds: An Approach to Organic Nanotubes**

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The design and synthesis of hollow tubular, functional nanostructures of controlled dimensions and defined surface chemistry remains a challenging and attractive target in both bio- and nanosciences.^[1,2] Integration of these molecular building blocks into larger, more complex structures by self-assembly or manipulation promises potential applications in several areas, including chemical and charge transport as well as sensing and catalysis.

Here, we report on an approach to organic nanotubes^[1] that is based on intramolecular cross-linking^[3–5] of helically folded polymer backbones.^[6] Our concept (Figure 1) is inspired by the hierarchical structural evolution in nature and involves polymerization of an appropriately functionalized monomer containing folding-promoting features as well as cross-linking units. The formed polymer strand (primary structure) is able to adopt a helical conformation (secondary structure), in which reactive groups are oriented within

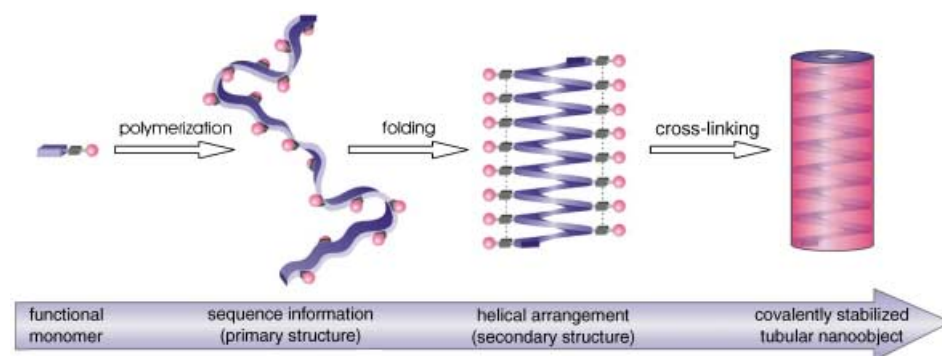


Figure 1. Formation of organic nanotubes by the intramolecular cross-linking of folded helical polymer backbones: Polymerization of a functional monomer carrying both solvophilic (magenta) and cross-linking groups (gray) generates a polymer strand that folds (solvophobicity driven) into a helical conformation that is subsequently stabilized by covalent cross-linking using adjacent reactive groups.

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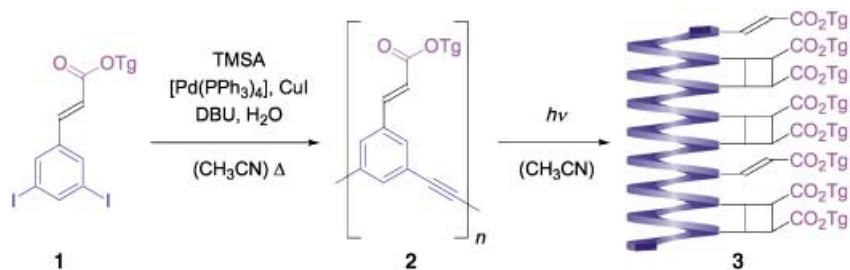
proximity to allow for subsequent covalent stabilization of the tubular nanoobject.

Amphiphilic poly(*m*-phenyleneethynylene)s^[7] were chosen as the backbone for several reasons: 1) the corresponding (oligomeric) foldamer family pioneered by Moore and co-workers^[8] displays well-characterized conformational behavior that can easily be monitored by using a variety of spectroscopic techniques, including UV/Vis absorption and fluorescence spectroscopy; 2) π - π stacking of neighboring units in adjacent turns positions the reactive groups in proximity (ca. 3.4 Å) to ensure efficient cross-linking reactions; 3) the 6-helix^[9] enables several cross-links to be introduced per turn, thus potentially increasing the stability of the structure, and contains a large internal void (diameter ca. 0.8 nm). The reactive groups were incorporated as cinnamates to utilize [2+2] photodimerization reactions for intramolecular cross-linking,^[10,11] thereby minimizing the structural changes during the cross-linking process.^[12]

A newly developed $A_2 + BB'$ polycondensation route^[13] starting from the diiodocinnamate monomer **1** affords poly(*m*-phenyleneethynylene) **2** (Scheme 1), which has a respectable number-average degree of polymerization (DP ca. 60)^[14] and a typical polydispersity index (PDI = 1.3). Most importantly, the polymer does not contain diyne defects as evidenced by ¹³C NMR spectroscopy.^[15] Such defects would perturb the folding process and disrupt the tubular helical structure.

Solvent denaturation experiments carried out using UV/Vis spectroscopy (Figure 2a) to monitor the population of random-coiled and helical conformations through differences in transoid and cisoid absorptions,^[8a,c] respectively, reveal a typical sigmoidal, that is, cooperative, folding behavior (Figure 3). A similar solvent titration curve with a slightly shifted transition point^[8b,c] is obtained independently by monitoring the emission of isolated versus packed “pseudoexcimer”-like repeat units by fluorescence spectroscopy.^[15] Denaturation occurs at higher chloroform content than that of shorter oligomers of similar structure,^[8] which indicates that a more-stable helix is formed, as predicted by the helix-coil model.^[6a,16] Both UV/Vis and fluorescence spectroscopic studies performed in THF at 40 °C (to simulate conditions used in gel-permeation chromatography (GPC)) suggest a major population of the helical conformation and, therefore, the molecular weight determined by GPC most likely represents a lower limit.

Polymer **2** was irradiated under high-dilution conditions in the folding-promoting solvent acetonitrile.^[17] Clean photo-conversion of the cinnamate moieties was observed, as evidenced by a smoothly decreasing UV/Vis absorbance and the corresponding extinction difference analysis.^[15] After



Scheme 1. Synthesis and irradiation of amphiphilic poly(*m*-phenyleneethynylene) **2** (Tg = CH₂CH₂OCH₂CH₂OCH₂CH₂OCH₃). TMSA = trimethylsilylacetylene, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

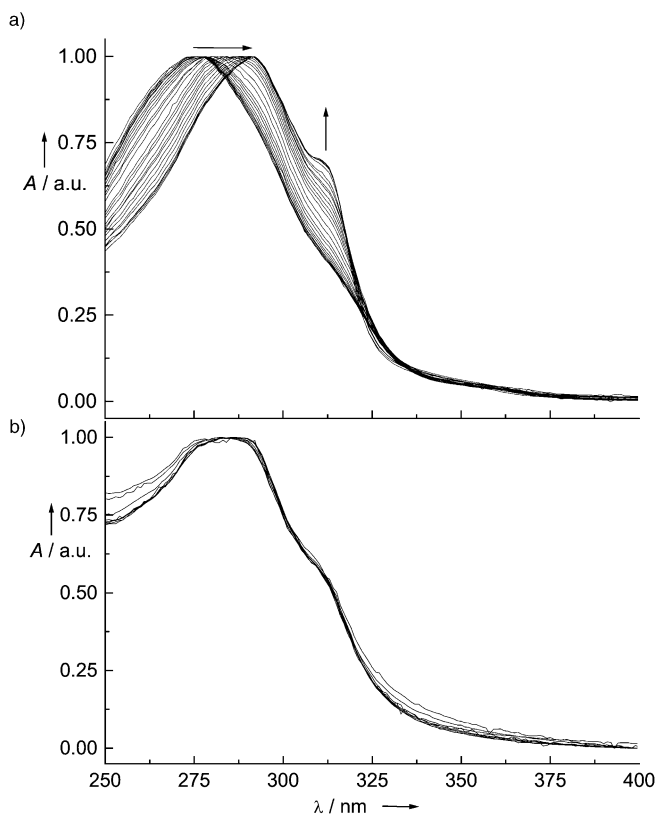


Figure 2. UV/Vis absorption spectra of: a) polymer **2** and b) cross-linked polymer **3** recorded in acetonitrile with increasing chloroform content (100% CH₃CN → 100% CHCl₃). The spectra, measured at approximately the same concentration, have been normalized with respect to their maximum intensity.

20 minutes of irradiation, the resulting cross-linked polymer **3** was again subjected to a UV/Vis titration experiment (Figure 2b and 3). No significant spectral changes were observed with increasing amounts of the chloroform denaturant,^[17] thus clearly demonstrating the presence of the locked helical conformation. The slightly higher absorbance ratio ($A_{312\text{nm}}/A_{292\text{nm}}$) relative to that of folded polymer **2** is presumably a result of the structural changes occurring during the photodimerization leading to a slightly twisted cisoid conformation. Further support for the cross-linked helical structure arises from the fluorescence spectrum of **3**

recorded in chloroform (Figure 4). The almost negligible emission band (Figure 4, inset) is reminiscent of “pseudoexcimer” **4**. However, the much lower emission intensity can be explained by the diminished π - π overlap in **5** resulting from a considerable tilt angle (ca. 30°) introduced during cross-linking, as evident from molecular mechanics calculations (Figure 5).

Considering the possible geometrical isomers in the cinnamate photodimerization process, the hel-

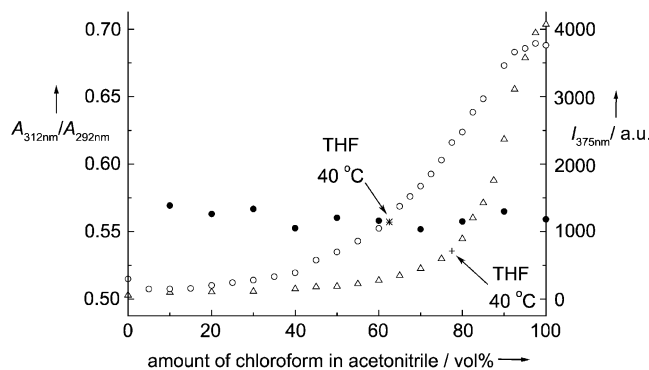


Figure 3. Solvent denaturation curves for amphiphilic poly(*m*-phenyleneethynylene) before (**2**) and after (**3**) irradiation: plot of the UV/Vis absorbance ratio ($A_{312\text{nm}}/A_{292\text{nm}}$) and corrected normalized fluorescence intensity ($I_{375\text{nm}}$), respectively, as a function of the volume percent of chloroform in acetonitrile (25 °C). ○: UV/Vis data of **2**, △: fluorescence data of **2**, ●: UV/Vis data of **3**. The UV/Vis data (*) and fluorescence data (+) of **2** recorded in THF at 40 °C are also shown.

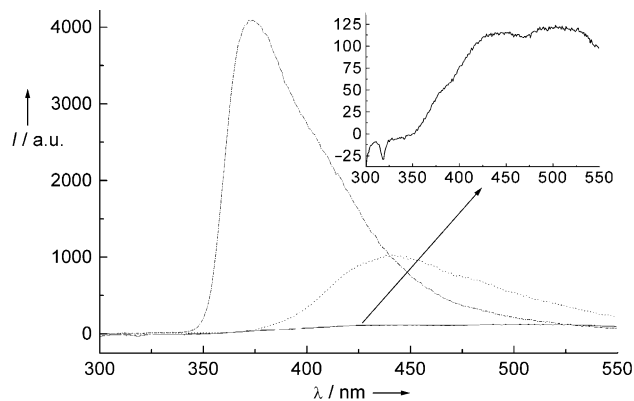


Figure 4. Corrected normalized fluorescence spectra of amphiphilic poly(*m*-phenyleneethynylene) before (**2**) and after (**3**) irradiation (25 °C): - - -: **2** in CHCl₃, ·····: **2** in CH₃CN, —: **3** in CHCl₃. The inset shows a magnification of the spectrum of **3** in CHCl₃.

ical structure should exclusively lead to the formation of truxinates, that is, head-head dimers.^[18] Following the topochemical principle,^[12] the least conformational changes occur during the formation of β -truxinate **5** (*syn* head-head photodimer). Structural evidence for the proposed stereochemistry of **5** arises from NMR spectroscopic analysis (Figure 6), since the doublet at $\delta = 4.0$ ppm is diagnostic for β -truxinates.^[19] Furthermore, the signal corresponding to the

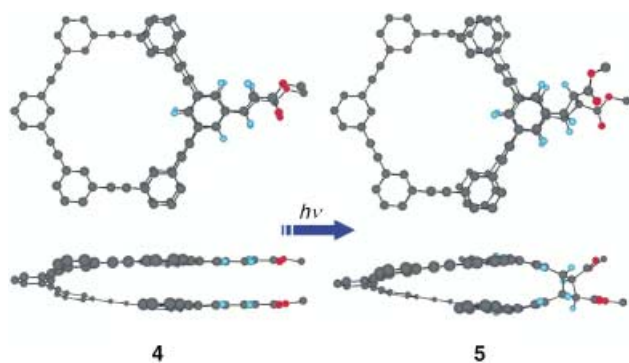


Figure 5. Molecular models of two π - π -stacking cross-linking units in the folded helical conformation of amphiphilic poly(*m*-phenyleneethynylene) **2**. Left: parallel-stacked cinnamate pair **4** (3.4 Å apart) before irradiation. Right: β -truxinate **5** (*syn* head-head) dimer after irradiation, with a 3.4 Å distance between the centers of the phenyl rings that are tilted by 30.5°. The models were optimized by using molecular mechanics calculations (MM2). For clarity, only the carbon atoms (gray) of the helical backbone as well as the oxygen (red), hydrogen (cyan), and carbon atoms of the cinnamate units are shown.

vinyl protons illustrates that not all the cinnamate moieties have reacted, which is in agreement with the UV/Vis

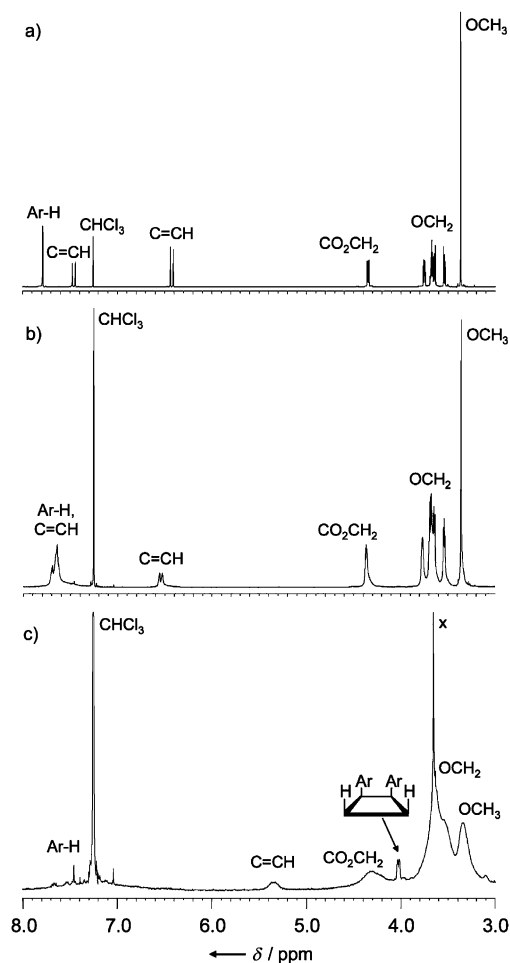


Figure 6. ^1H NMR spectral comparison (CDCl_3 , $23 \pm 2^\circ\text{C}$): a) monomer **1**, b) polymer **2**, and c) polymer **3** (after 20 min irradiation period).

spectra.^[15] The pronounced upfield shift of the vinyl protons and the diminished signal of the aryl protons provide additional support for the locked helical structure.^[20] As a consequence of the overlapping signals in the ^1H NMR spectrum, the degree of cross-linking can only roughly be estimated to be about 20–30%. This value is in reasonable agreement with the decrease in the UV/Vis absorption during the course of irradiation.^[15]

Short irradiation times favor the formation of mainly intramolecularly cross-linked polymers, as indicated by GPC.^[15] However, extensive irradiation leads to additional intermolecular cross-linking of cinnamate moieties in aggregating adjacent tubes, as suggested by the strongly bimodal distribution in the GPC trace after two hours of irradiation. In a control experiment, irradiation in chloroform yielded a polymer with a high degree of intermolecular cross-links and transoid conformations.

In summary, all the experimental methods employed thus far^[21] are consistent with a covalent stabilization of the helical conformation and therefore demonstrate the feasibility of our approach to the formation of organic nanotubes (Figure 1). Current work in our laboratories involves in-depth characterization of the generated tubes, increasing their aspect ratio, and improving the cross-linking chemistry to further minimize structural reorganization and include polymeric instead of dimeric cross-links. By utilizing our concept, organic nanotubes of controlled dimensions^[22] and specific local surface functionality^[23] should ultimately be realized.

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- [22] The outer and inner diameters are encoded in the foldamer motif used. Length control—currently not possible by means of self-assembly—could be achieved using a folding polymer of low polydispersity prepared by advanced living polymerization techniques.
- [23] In principle the use of heterosequences (alternating as well as block copolymers) enables nonstatistical, location-specific outer/inner functionalization. Currently, such control over surface chemistry cannot be realized in carbon or inorganic nanotubes.