

ORGANIC NANOTUBES BASED ON INTRAMOLECULAR CROSSLINKING OF HELICALLY FOLDING POLYMERS

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Introduction

The design and synthesis of hollow tubular, functional nanostructures with controlled dimensions and defined surface chemistry remains a challenging and attractive target in both bio- and nanosciences. Integration of these molecular building blocks into larger, more complex structures using 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 a novel approach to organic nanotubes¹ based on intramolecular crosslinking²⁻⁴ of helically folded polymer backbones.⁵ Inspired by the hierarchical structural evolution in Nature, our concept (Figure 1) involves polymerization of an appropriately functionalized monomer containing folding promoting features as well as crosslinking units. The formed polymer strand (primary structure) is able to adopt a helical conformation (secondary structure), in which reactive groups are oriented within close proximity to allow for subsequent covalent stabilization of the tubular nanoobject.

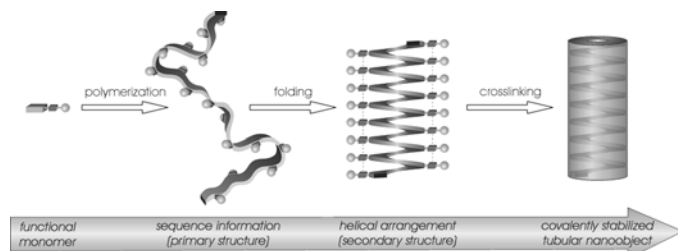


Figure 1. Organic nanotubes via intramolecular crosslinking of helical folds.

To demonstrate this concept, amphiphilic poly(*m*-phenyleneethynylene)s⁶ were chosen as the backbone for several reasons: i) the corresponding (oligomeric) foldamer family pioneered by Moore and coworkers⁷ displays well-characterized conformational behavior that can easily be monitored using a variety of spectroscopic techniques including UV/vis absorption and fluorescence spectroscopy; ii) π,π -stacking of neighboring units in adjacent turns positions the reactive groups in close proximity (distance ~ 3.4 Å) to assure for efficient crosslinking reactions; iii) the 6-helix⁸ enables several crosslinks to be introduced per turn potentially increasing the stability of the structure and furthermore contains a large internal void (diameter ~ 0.8 nm). The reactive groups were incorporated as cinnamates to utilize [2+2]photodimerization reactions for intramolecular crosslinking⁹ thereby minimizing structural changes during the crosslinking process.¹⁰ In this preprint, synthesis and characterization of the helical polymer and its crosslinked photoproduct are presented (Figure 2).¹¹

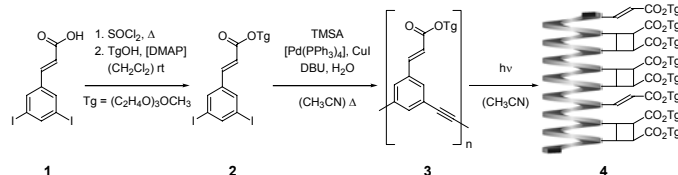


Figure 2. Synthesis of monomer 2, polymer 3, and crosslinked polymer 4.

Experimental

3,5-Diiodocinnamic acid 1. 3,5-Diiodobenzaldehyde (1.07 g, 3 mmol), malonic acid (0.31 g, 3 mmol), piperidine (1 mL), DMF (8 mL), glacial acetic acid (1 mL), and acetic anhydride (1 mL) were suspended in toluene (10 mL) and heated overnight at 120 °C. Then, water (30 mL) was added and it was refluxed for 1 h. The formed white solid was isolated by filtration and washed

with water to afford the crude acid that can be further purified by recrystallization from ethanol furnishing 0.70 g of a white solid (56% yield). ¹H NMR (250 MHz, DMSO-*d*₆, 23±2 °C): δ 8.08 (broad s, 3 H, Ar-H), 7.42 (d, ³*J*(H,H) = 16.4 Hz, 1 H, C=CH-), 6.61 (d, ³*J*(H,H) = 16.4 Hz, 1 H, C=CH-); ¹³C NMR (125 MHz, DMSO-*d*₆, 23±2 °C): δ 172.17, 150.47, 145.86, 143.58, 140.95, 127.20, 101.57; EI-MS (80 eV, 100 °C): *m/z* = 400.0 (calcd 399.9 for C₉H₆I₂O₂⁺); Anal. C: 26.87, H: 1.19 (calcd C: 27.03, H: 1.51).

2-[2-(2-methoxy-ethoxy)-ethoxy]-ethyl 3,5-diiodocinnamate 2. Crude acid **1** (4.60 g, ~ 11.5 mmol) was mixed with thionyl chloride (15 mL), 3 drops of DMF added, and it was heated at 60 °C for 2 h. Excess thionyl chloride was evaporated and the remaining compound dried on a vacuum pump for 3 h to afford the crude acid chloride as a light brown solid. Triethylene glycol monomethyl ether (2.7 mL, 17.25 mmol), triethylamine (3.2 mL, 23.0 mmol), and 4-dimethylaminopyridine (DMAP; 0.14 g, 1.15 mmol) were dissolved in CH₂Cl₂ (10 mL), the solution cooled to 0 °C (ice bath), a solution of the acid chloride in CH₂Cl₂ (30 mL) slowly added over a period of 30 min, the resulting reaction mixture allowed to warm to rt and stirred overnight. Filtration followed by washing of the filtrate with sat. aqueous NH₄Cl and brine, drying over MgSO₄, evaporation of the solvent, and column chromatography (40 % ethyl acetate in hexane, R_f = 0.2) gave 4.136 g of the product as slightly yellow oil ($\sim 66\%$ yield). ¹H NMR (500 MHz, CDCl₃, 23±2 °C): δ 8.01 (t, ⁴*J*(H,H) = 1.5 Hz, 1 H, Ar-H), 7.77 (d, ⁴*J*(H,H) = 1.5 Hz, 2 H, Ar-H), 7.44 (d, ³*J*(H,H) = 16.0 Hz, 1 H, C=CH-), 6.40 (d, ³*J*(H,H) = 16.0 Hz, 1 H, C=CH-), 4.33 (t, ³*J*(H,H) = 4.8 Hz, 2 H, CO₂-CH₂), 3.74 (t, ³*J*(H,H) = 4.8 Hz, 2 H, O-CH₂), 3.68-3.62 (m, 6 H, O-CH₂), 3.53 (t, ³*J*(H,H) = 4.8 Hz, 2 H, O-CH₂), 3.35 (s, 3 H, O-CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 165.95, 146.30, 141.47, 138.08, 135.97, 120.53, 71.92, 70.62, 70.58, 69.09, 63.94, 59.04; EI-MS (80 eV, 150 °C): 546.1 (M⁺, 21%), 501 (M-C₂H₅O⁺, 6%), 427 (M-C₅H₁₁O₃⁺, 100%), 383 (M-C₇H₁₅O₄⁺, 80%), 256 (M-C₅H₁₁O₃I⁺, 61%), EI-HRMS: *m/z* = 545.94333 (calcd 545.94000 for C₁₆H₂₀O₅I₂⁺), 426.86577 (calcd 426.86920 for C₁₁H₉O₂I₂⁺), 382.84455 (calcd 382.84299 for C₆H₅O₂I₂⁺); Anal. C: 35.29, H: 3.39 (calcd C: 35.19, H: 3.69); HPLC (90% MeOH in H₂O, 1 mL/min): 99.0% peak area.

Poly(*m*-aryleneethynylene) 3. Monomer **2** (546 mg, 1 mmol), CuI (15 mg, 0.08 mmol), and Pd(PPh₃)₄ (69 mg, 0.06 mmol) were loaded in a flame dried 10 mL Schlenk tube, which was evacuated and refilled with argon. Dry and degassed acetonitrile (4 mL) was submitted to the tube via syringe, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.9 mL, 6 mmol) and trimethylsilylacetylene (TMSA; 142 μ L, 1 mmol) were added immediately followed by addition of distilled H₂O (18 μ L, 1 mmol). The tube was covered with aluminum foil and the reaction mixture was allowed to stir at rt for 3 d after which it was precipitated in ether (500 mL). The resulting polymer was redissolved in CH₂Cl₂ and passed through a short column of silica gel to give ~ 250 mg of **3** as a greyish powder ($\sim 79\%$ yield). ¹H NMR (500 MHz, CDCl₃, 23±2 °C): δ 7.68-7.62 (broad m, 4 H, Ar-H, C=CH), 6.53 (broad d, ³*J*(H,H) = 15.7 Hz, 1 H, C=CH), 4.35 (broad t, 2 H, CO₂-CH₂), 3.75 (broad t, 2 H, O-CH₂), 3.67-3.62 (broad m, 6 H, O-CH₂), 3.52 (broad t, 2 H, O-CH₂), 3.34 (broad s, 3 H, O-CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 166.40, 142.90, 135.82, 135.35, 131.13, 124.07, 120.16, 89.21, 77.04, 70.73, 69.24, 63.99, 59.10; IR (KBr): 3434, 2923, 2853, 1716, 1641, 1593, 1288, 1177, 1106 cm⁻¹; Anal. C: 69.91/69.52, H: 7.75/8.22 (calcd for (C₁₈H₂₀O₅)_n C: 68.34, H: 6.37); GPC (THF, 40 °C): M_w = 24700, M_n = 18400, PDI (M_w/M_n) = 1.34.

Crosslinked poly(*m*-aryleneethynylene) 4. Preparative irradiations were performed using a Philips HPK 125 W high-pressure mercury lamp equipped with a water cooled photoreactor of Duran® (pyrex) glass ($\lambda_{5\%T} = 316$ nm). The solutions (10 mg polymer **3** / 100 mL CH₃CN, $\sim 7 \cdot 10^{-6}$ M) were degassed with nitrogen for 10 min, continuously irradiated, and samples for GPC and UV/vis taken at given time intervals. For ¹H NMR spectra, the solvent was evaporated at a given time, the sample thoroughly dried on a vacuum pump, and redissolved in CDCl₃.

Results and Discussion

Starting from diiodocinnamate monomer **2**, a newly developed A₂+BB' polycondensation protocol¹² affords poly(*m*-phenyleneethynylene) **3** (Figure 2) having a respectable number average degree of polymerization (DP ~ 60)¹³ and a typical polydispersity index (PDI = 1.3). Most importantly, the polymer does not contain diyne defects as evidenced by ¹³C NMR spectroscopy. Such

defects would perturb the folding process and disrupt the tubular helical structure.

Solvent denaturation experiments using UV/vis spectroscopy to monitor the population of random-coiled and helical conformations using differences in transoid and cisoid absorptions,^{7a} respectively, reveal a typical sigmoidal, i.e. cooperative, folding behavior (Figure 3). Fluorescence spectroscopy, monitoring emission of isolated vs. packed "pseudoexcimer"-like repeat units, independently yields a similar solvent titration curve with a slightly shifted transition point.^{7b} With respect to shorter oligomers of similar structure,⁷ denaturation of **3** occurs at higher chloroform contents indicating a more stable helix as predicted by the helix-coil model.^{5,14} Both UV/vis as well as fluorescence spectroscopy in THF at 40 °C, simulating GPC conditions, suggest major population of the helical conformation and therefore the molecular weight determined by GPC most likely represents a lower limit.

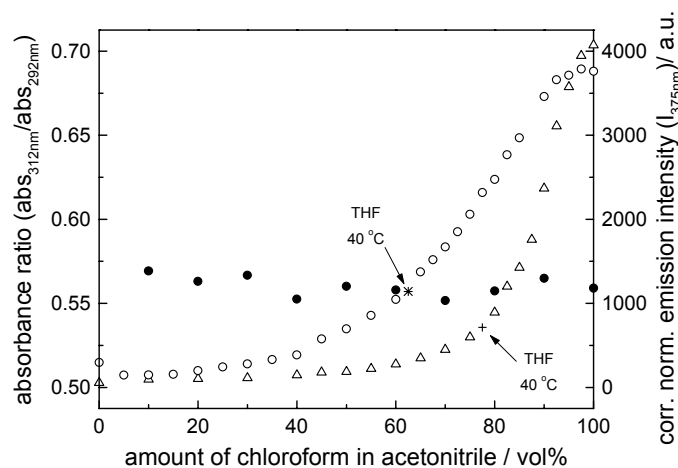


Figure 3. Solvent denaturation curves for amphiphilic poly(*m*-phenyleneethynylene) before (**3**) and after (**4**) irradiation: plot of UV/vis absorbance ratio (A_{312nm}/A_{292nm}) and corrected normalized fluorescence intensity (I_{375nm}), respectively, as a function of the volume percent chloroform in acetonitrile (25 °C). UV/vis of **3** (○), fluorescence of **3** (△), UV/vis of **4** (●). In addition, the UV/vis of **3** in THF at 40 °C (*) and fluorescence of **3** in THF at 40 °C (+) are shown.

Irradiation of polymer **3** was carried out under high dilution conditions in the folding promoting solvent acetonitrile. Clean photoconversion of the cinnamate moieties was observed as evidenced by a smoothly decreasing UV/vis absorbance and the corresponding extinction difference analysis. After 20 minutes of irradiation, the resulting crosslinked polymer **4** was again subjected to an UV/vis titration experiment (Figure 3). With increasing amount of the denaturant chloroform, no significant spectral changes were observed clearly demonstrating the locked helical conformation. The slightly higher absorbance ratio (abs_{312nm}/abs_{292nm}) values as compared to folded polymer **3** are presumably due to the structural changes during the photodimerization leading to a slightly twisted cisoid conformation.

Further support for the crosslinked helical structure arises from the fluorescence spectrum of **4** in chloroform. The almost negligible emission band is reminiscent of the folded "pseudoexcimer". However, the much lower emission intensity can be explained by the diminished π,π -overlap due to a considerable tilt angle ($\sim 30^\circ$) introduced during crosslinking according to molecular mechanics calculations. Following the topochemical principle,¹⁰ the helical structure should exclusively lead to the formation of β -truxinate, i.e. syn head-head photodimers, since this process involves the least structural changes during crosslinking. The characteristic signature of this predicted product stereochemistry was indeed detected by H-NMR spectroscopy. In addition, NMR gives further support for locked helical structure and indicates an approximate degree of crosslinking of ca. 20-30 %, which is in reasonable agreement with the UV/vis absorption decrease during the course of irradiation.

Short irradiation times favor formation of mainly intramolecularly crosslinked polymers as indicated by GPC. However, extensive irradiation leads to additional intermolecular crosslinking of unreacted cinnamate

moieties in aggregating adjacent tubes as suggested by the strongly bimodal distribution in the GPC chromatogram after 2 h of irradiation. In a control experiment, irradiation in chloroform yielded a polymer with high degree of intermolecular crosslinks and transoid conformations.

Conclusions

In summary, all experimental methods employed thus far are consistent with a covalent stabilization of the helical conformation and therefore demonstrate the feasibility of our novel approach to organic nanotubes disclosed herein (Figure 1).¹¹ Current work in our laboratories involves in depth characterization of the generated tubes, increasing their aspect ratio, and improving crosslinking chemistry to further minimize structural reorganization and include polymeric instead of dimeric crosslinks. Utilizing our concept, organic nanotubes of controlled dimensions¹⁵ and specific local surface functionality¹⁶ should ultimately be realized.

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