*Helical Nanofibers*

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# Reversible Photochemical Conversion of Helicity in Self-Assembled Nanofibers from a 1,ω-Thymidylic Acid Appended Bolaamphiphile

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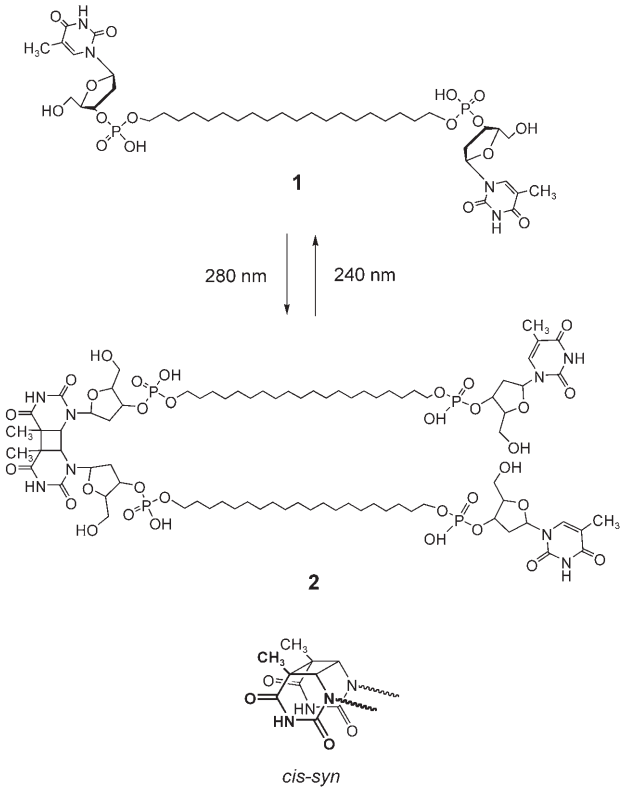
Activation of photoreactive compounds, such as azobenzene-containing derivatives,[1–3] stilbene-containing compounds,[4] dithienylcyclopentene,[5] maleic acid amide derivatives,[6] and 2*H*-chromene-containing compounds,[7] is known to induce changes in the self-assembly behavior of the molecules. For example, UV light can act as a switching trigger not only to drive a change in the self-assembled morphology from spheres to rods[1] but also to induce gel-to-sol phase transitions.[2,4,6,7] Sometimes, linearly polarized light allows a single film of a liquid crystal network containing an azobenzene chromophore to bend in any direction.[8] In all cases, configurational or conformational changes in the molecular structures lead to a substantial change in the self-assembled morphologies based on each molecule. The most widely used photoswitching molecules are azobenzene derivatives because of the large photoinduced changes in their molecular geometry.

UV light is also known to cause diverse chemical reactions, such as photodimerization in the nucleobase moieties of DNA.[9,10] The major photoproduct is a *cis–syn* cyclobutane pyrimidine dimer. Except for our previous study,[11] there have been no reports of direct visualization focusing on the effect of thymine photodimerization on the morphologies of self-assembled nanofibers. Moreover, no one has ever addressed reversible induction of helical and non-helical morphologies, driven by light or photoreaction, in molecular self-assemblies consisting of bilayer or monolayer membranes. Here we describe for the first time the reversible conversion of helicity, driven by a photochemical process of the thymine moiety with UV light, in self-assembled nanofibers from a 1,ω-thymidylic acid appended bolaamphiphile, **1** (Scheme 1).




***Scheme 1.*** Conversion of the monomer **1** into the photodimer **2** and the structure of the *cys–syn* isomer.

Scanning electron microscopy (SEM) and atomic force microscopy (AFM) provided evidence that the bolaamphiphile **1** self-assembles in aqueous solutions into fiber structures with 10-nm thickness and 80-nm width as typical dimensions.[12] A field emission (FE) SEM[13] image of the self-assembled nanofibers from **1** revealed the presence of nonhelical nanorod or nanofiber structures with diameters ranging from 100–300 nm (Figure 1a). A high-magnification image allowed us to observe a bundle formation of four fibers, each 50 nm in diameter (Figure 1b). UV irradiation at $\lambda =$ 280 nm ($UV_{280}$) for 2–3 h gave helical features to parts of the

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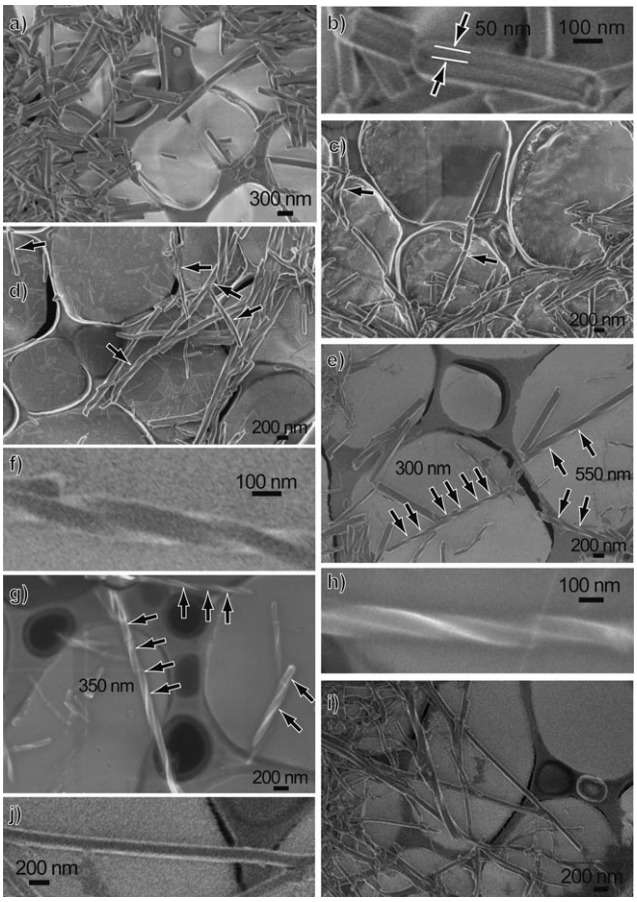


***Figure 1.*** FE-SEM images of the self-assembled nanofibers from **1** in aqueous solution. a,b) Images before UV irradiation. c–h) Images after UV irradiation at $\lambda = 280$ nm for c) 2 h, d) 3 h, e) and f) 4 h, and g) and h) 3 days. i,j) Images after the successive UV irradiation at $\lambda = 280$ nm for 5 h and then at $\lambda = 240$ nm for 3 h.

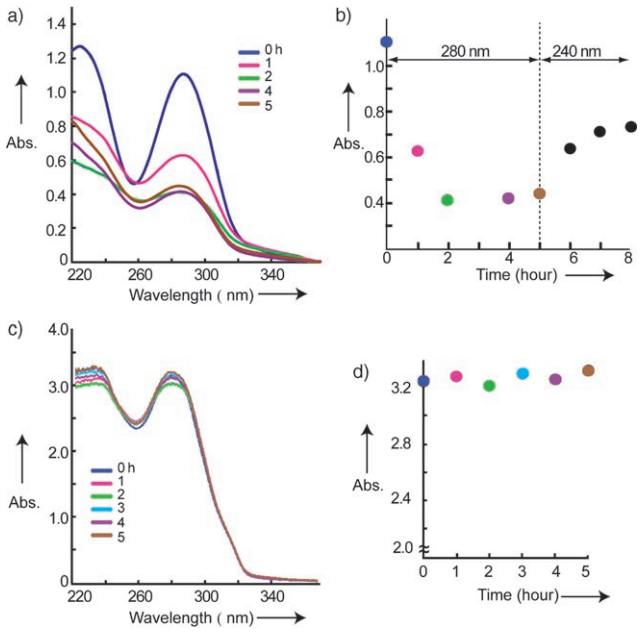


***Figure 2.*** a) Time dependence of UV-spectral changes for the self-assemblies of **1** in aqueous solution ($2.2\times10^{-3}$ M) on UV irradiation at $\lambda = 280$ nm. b) Time dependence of UV absorbance at $\lambda = 270$ nm on UV irradiation at $\lambda = 280$ nm (0–5 h) and then at $\lambda = 240$ nm (5–8 h). c) Time dependence of the UV-spectral changes for the binary mixture of **1** and $dA_6$ in aqueous solution ($2.2\times10^{-3}/7\times10^{-5}$ M) upon UV irradiation at $\lambda = 280$ nm. d) Time dependence of the UV absorbance at $\lambda = 270$ nm for the binary mixture of **1** and $dA_6$ upon UV irradiation at $\lambda = 280$ nm.

self-assembled nanofibers (Figures 1 c,d, indicated by arrows). The helical structures stood out clearly after 4 h of $UV_{280}$ irradiation. The helical pitches of the self-assemblies were estimated to be 300–550 nm (Figures 1 e,f). Finally, 3 days of $UV_{280}$ irradiation caused all of the nanofibers to form helical structures with pitches of 350–400 nm (Figures 1 g,h). The number of helical nanofibers increases with time after $UV_{280}$ irradiation. We thus found that exposure to UV light strongly affects the self-assembled morphologies of **1** and eventually induces helical twisting in the nanofiber structures. The helicity observed by FE-SEM was found to be right-handed for all of the nanofibers. Interestingly, irradiation of this sample with UV light at $\lambda = 240$ nm ($UV_{240}$) for 3 h converted the helical fibers to intrinsically nonhelical ones (Figures 1 i,j).

To examine the photodimerization behavior of the thymine moiety in **1**, we carried out UV spectroscopy and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurements for the self-assembled nanofibers. The $UV_{280}$ irradiation gradually caused a decrease in the absorption intensity at 270 nm[9] to 30 % of the original value for the self-assembled nanofibers of **1** over a period of 5 h (Figures 2 a,b). This finding gives strong evidence for the formation of thymine photodimers in the self-assembly of **1**. MALDI-TOF MS measurements also support this fact. The spectrum for the nanofibers after $UV_{280}$ irradiation for 3 days gave the peak ascribable to the dimerized component **2** (Scheme 1) at $m/z$ 1844, in addition to the peak assignable to the monomer **1** at $m/z$ 922. We were unable to observe any peaks corresponding to other high-mass components such as trimers or oligomers. Therefore, we concluded that the dimerization of the thymine moiety takes place between one end of two molecules in the self-assembly of **1**.

On the other hand, $UV_{240}$ irradiation of previously $UV_{280}$-irradiated nanofibers for 3 h induced the recovery of up to 60 % of the absorption intensity of the thymine moiety (Figure 2 b). This finding clearly indicates that photodissociation of the thymine dimer occurs in the self-assembly system.

Next, we performed $UV_{280}$ irradiation on the self-assembled nanofibers of **1** in the presence of complementary 6-mer oligoadenylic acid, $dA_6$. The UV absorption maximum of the nucleic acids, that is, thymine and adenine, scarcely changed upon $UV_{280}$ irradiation (Figures 2 c,d), which means that no thymine photodimers form in the presence of the complementary component $dA_6$.

Figure 3 shows partial $^1$H NMR spectra for the self-assembled nanofibers before and after UV irradiation. Two additional peaks appeared at $\delta = 1.22$ and 1.23 ppm in the methyl-proton region after UV irradiation (Figure 3 b); these peaks were ascribable to the C5 position of the thymine photodimer. The appearance of these two signals after the

  

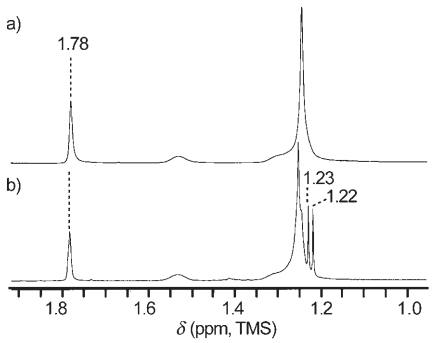


***Figure 3.*** Partial $^1$H NMR spectra (600 MHz, at 80 °C in [D$_6$]DMSO) of a) the self-assembled nanofibers from **1** before UV irradiation and b) those after UV irradiation at $\lambda = 280$ nm for 3 days.

$UV_{280}$-irradiated self-assembly of **1** is compatible with the previous results on related *cys–syn* photodimers.[14,15] Thus, the MS and $^1$H NMR measurements strongly support the conclusion that the major photodimer product from **1** is the *cis–syn* isomer **2**, in which one end of the bolaamphiphile is associated with the end of another molecule.

CD spectra for the self-assembly of **1** before and after exposure to UV light gave two relatively strong CD bands (positive and negative ones at 290 and 235 nm, respectively), in addition to zero crossing at 246 nm (Figure 4). Similar split

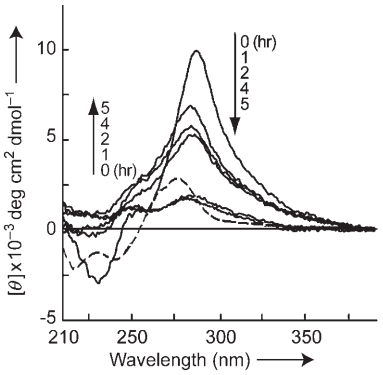


***Figure 4.*** CD spectral changes for the diluted self-assemblies from **1** in aqueous solution ($2.2\times10^{-3}$ M) upon UV irradiation at $\lambda = 280$ nm (black lines). For reference, the CD spectrum of 3′-thymidine monophosphate in aqueous solution is shown as a dashed line ($4.3\times10^{-3}$ M).

patterns were also observed for the CD spectrum of right-handed oligo- and polynucleotides.[16,17] $UV_{280}$ irradiation induced the blue shift of the positive band from 290 to 285 nm and a reduction in the intensities of both bands. The large alterations in the CD spectra indicate the different molecular orientation of the thymidylic acid moieties associated with the photodimerization.[17] Interestingly, the CD intensities at 285 nm gradually decreased over a period of 4 h of $UV_{280}$ irradiation, whereas the reduction in the UV absorption intensities at around 270 nm was complete even after 2 h (Figures 2 a,b). CD spectroscopy is more sensitive to the observed helical-nanofiber formation than the UV measurements and probes the later changes in molecular packing owing to the photodimerization (Figures 1 e,f).

The self-assembled nanofibers from **1** consist of monolayer sheets with a long period of 3.59 nm (Figure 5 a).[12]

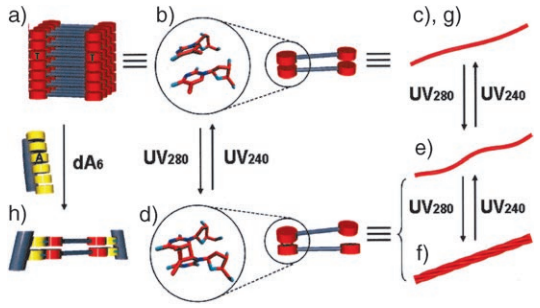


***Figure 5.*** A proposed mechanism for the reversible photochemical conversion by UV irradiation in the self-assembled nanofibers from **1**. a) Monolayer sheets of the self-assembly of **1** with a long period of 3.59 nm. b) Molecular model of two thymidine moieties and schematic illustration of the two **1** molecules in the monolayer sheets before UV irradiation. c) Self-assembled nonhelical nanofiber from **1** before UV irradiation. d) Molecular model of a thymidine photodimer and schematic illustration of the dimer molecule **2** in the monolayer sheets after UV irradiation. e) Twisted monolayer. f) The resultant helical nanofiber. g) Recovery of the nonhelical nanofiber after $UV_{240}$ irradiation of the *cis–syn* thymine dimer in the self-assembly from **1**. h) Inhibition of the photodimerization of thymine moieties in **1** in the presence of complementary $dA_6$ by the formation of A–T base pairs. The molecular structures of the models in (b) and (d) were drawn by using the VMD software[22] on the basis of information in ref. [10] and the Protein Databank (http://www.pdb.org/; PDB file code: 1T4L).

Before $UV_{280}$ irradiation, the molecules hold together, stabilized by noncovalent interactions, such as base stacking between the thymine moieties and hydrophobic interactions between the oligomethylene chains (Figures 5 b,c).[12] The stacking features of the thymine moieties in the self-assembly of **1**[12] should be favorable for effective photodimerization, even in the absence of a triplet photosensitizer such as acetone.[9] Actually, $UV_{280}$ irradiation of the self-assembly of **1** causes the photodimerization of the thymine moieties with the formation of covalent bonds partially in the monolayer sheets. The generation of a *cis–syn* derivative after the UV irradiation is compatible with the fact that the *cis–syn* isomer is a major product when the stacked thymine bases in DNA or dinucleotide are exposed to UV light.[9] The UV absorption change (Figure 2 a) indicated the amount of photodimerized thymine to be 63 %. The estimated quantity is enough to convert all of the molecular packing of the self-assembly of **1** into helical-nanofiber structures. The formation of the *cis–syn* isomer generates no chiral centers, which are commonly seen in the molecular building blocks of helical assemblies.[18] Therefore, we think that the role of the *cis–syn* isomer is to enhance and to stabilize the chirality of the D-sugar moiety in **1**.

After $UV_{280}$ irradiation, each thymine base tilts to form a nonparallel orientation with the central cyclobutane ring puckering by 20°, as seen in the DNA crystal structure[10]

  

(Figure 5d, molecular models). Therefore, the photodimerization of the thymine moieties should greatly affect the molecular packing in the self-assembly of **1**. The covalent formation of a *cis–syn* cyclobutane pyrimidine dimer allows a half molecule of the dimer to pack at a nonzero angle with respect to their nearest neighbors. This feature leads us to suppose that the chiral molecular packing induces twisting in the monolayer sheets, which results in twisting of the resultant nanofibers (Figures 5d–f).[19] The nanofiber structures with no helical features were recovered after the $UV_{240}$ irradiation on the *cis–syn* thymine dimer in the self-assembly system of **1** (Figure 5g). FE-SEM and UV measurements clearly evidenced the photolysis of the thymine dimer into the thymine monomer. On the other hand, the presence of the complementary $dA_6$ molecule acts to effectively suppress the photodimerization of the thymine moiety in **1**. The nucleotide bolaamphiphile **1** and the complementary oligoadenylic acids form binary complexes through the complementary A–T base pair. We have indeed found the formation of intertwined, nonhelical nanofibers based on binary self-assembly of **1** and $dA_6$.[20] The complementary base pairing will provide the self-assembled structures of **1** with molecular packing that is resistant to the photodimerization of the thymine moiety.[21]

In conclusion, we have demonstrated that UV light directs the reversible photochemical conversion between self-assembled helical nanofibers and nonhelical ones from the 1,ω-nucleotide bolaamphiphile **1**. The photodimerization of a part of the thymine moiety of **1** produces a *cis–syn* photodimer, **2**, in the self-assemblies and this results in right-handed helical nanofibers. Photodissociation of the dimer **2** converts the helical fibers into nonhelical ones again. These findings are of great importance in terms of the photochemical switching of nanofiber morphologies.

## Experimental Section

**1** was synthesized by coupling 1,20-icosanediol with thymidylic acid by use of phosphoramidite methods, as reported elsewhere.[12] The self-assembly of **1** ($2.2 \times 10^{-3}$ M) was irradiated with monochromated light (Bunkoh-keiki, SM-5) at $\lambda = 280$ or 240 nm for photodimerization and photodissociation, respectively. For the UV irradiation at $\lambda =$ 280 nm, a UV 28 colored optical glass (Hoya) was used to cut off the light below $\lambda = 280$ nm. To prepare the binary self-assembly solutions for UV irradiation, we added $dA_6$ to the aqueous solution of **1** and adjusted the concentrations of **1** and $dA_6$ to $2.2 \times 10^{-2}$ and $0.7 \times 10^{-3}$ M, respectively. This aqueous solution was treated in the same manner as the self-assembly of **1** mentioned above. FE-SEM observation was conducted on a JEOL S-4800 instrument (accelerate voltage 0.5–1.8 kV, working distance 4 mm). UV, $^1$H NMR, and CD spectroscopy and MALDI-TOF mass spectrometry were carried out by using UV-3300 (Hitachi), LA600 (600 MHz, JEOL), J-820 (Jasco), and Kratos Kompact-MALDI III (Shimadzu) instruments, respectively. See the Supporting Information for further details of the experiments.

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