



## Supramolecular Self-Assembly

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## **Tunable Supramolecular Assembly and Photoswitchable Conversion of Cyclodextrin/Diphenylalanine-Based 1D and 2D Nanostructures**

He-Lue Sun, Yong Chen, Xu Han, and Yu Liu\*

**Abstract:** A photocontrolled, interconvertible supramolecular 2D-nanosheet/1D-nanotube system was constructed through the supramolecular assembly of adamantanyl-modified diphenylalanine with azobenzene-bridged bis( $\beta$ -cyclodextrin). The nanosheet exhibited a greater fluorescence enhancement effect than the nanotube. Significantly, these nanosheets and nanotubes could interconvert via the photocontrolled trans/cis isomerization of azobenzene linkers in bis( $\beta$ -cyclodextrin), and this photo-switchable one-dimensional/two-dimensional morphological interconversion was reversible and recyclable. This enables convenient routes to highly ordered nanostructures with various morphologies and dimensions that can be controlled by external stimuli.

Controlling the assembly of low-molecular-weight molecules into well-defined and nanoscaled architectures with various dimensions has become a fascinating topic in materials science and supramolecular chemistry.<sup>[1]</sup> These nanomaterials always display various fascinating functions due to their special dimensional advantages.<sup>[2]</sup> Among them, onedimensional nanomaterials have been widely studied owing to their anisotropy, high axial ratios, and highly rigid mechanical properties,<sup>[3]</sup> while two-dimensional nanomaterials also become popular in various fields because of their low densities, structural controllability, and flexibility.<sup>[4]</sup> Recently, numerous controllable one-dimensional and two-dimensional supramolecular assemblies, including polyrotaxanes,<sup>[5]</sup> supramolecular nanotubes,<sup>[6]</sup> supramolecular nanowires,<sup>[7]</sup> and supramolecular nanosheets,<sup>[8]</sup> have been successfully constructed. However, these studies have focused mainly on the controlled assembly/disassembly process, while the switchable morphological conversion of supramolecular assembly has rarely been reported. Kim et al. reported a one-cycle zero-dimensional/one-dimensional conversion of pyrenemodified dendritic self-assembly between vesicles and nanotubes induced by the sequential addition of cyclodextrin (CD) and poly(propylene glycol).<sup>[9]</sup> We also reported a photocon-

[*]	HL. Sun, Dr. Y. Chen, X. Han, Prof. Y. Liu
	College of Chemistry,
	State Key Laboratory of Elemento-Organic Chemistry
	Nankai University
	Tianjin 300071 (P.R. China)
	E-mail: yuliu@nankai.edu.cn
	Prof. Y. Liu
	Collaborative Innovation Center of Chemical Science and Engineer-
	ing
	Nankai University
	Tianjin 300071 (P.R. China)

Supporting information for this article can be found under: https://doi.org/10.1002/anie.201612629. trolled, reversible zero-dimensional/one-dimensional conversion between nanoparticles and nanotubes mediated by permethylated β-CD dimers.<sup>[10]</sup> More recently, Takeuchi and Sugiyasu et al. achieved one- and two-dimensional supramolecular assemblies (nanofibers/nanosheets) via control of the kinetic self-assembly process of a metastable porphyrin.<sup>[11]</sup> Herein, we report a photocontrolled, reversible, and repeatable nanotube-nanosheet, that is, one-dimensional/twodimensional, morphological conversion of the supramolecular assembly of adamantanyl-modified diphenylalanine with azobenzene-bridged  $bis(\beta-CD)$ (Ada-FF) (**H**: Scheme 1). With respect to the luminescent molecule, 2D nanosheets gave better fluorescence enhancement effects than 1D nanotubes.



**Scheme 1.** Chemical structure of Ada-FF and H, and schematic illustration of their assembly.

The azobenzene-bridged bis( $\beta$ -CD) (**H**) was designed and synthesized via a "click" reaction in THF/H<sub>2</sub>O solution. There are two inherent advantages for designing **H** as a host molecule: 1) **H** can undergo a reversible photoisomerization between its *trans*-isomer (**H**-*trans*) and *cis*-isomer (**H**-*cis*) with the external stimuli of light, which is noninvasive, clean, and remote-controllable;<sup>[12]</sup> 2) the significant conformational difference between **H**-*trans* and **H**-*cis* may lead to different binding behaviors or assembly morphologies. Firstly, the conformation of **H** was investigated. Combining the results of NMR (Figures S8, S10, and S11, Supporting Information) and CD spectra (Figure S9), we can reasonably deduce that **H** adopted a symmetric conformation in DMSO, in which the

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azobenzene linker was located out of both  $\beta$ -CD moieties; while **H** adopted an asymmetric conformation in aqueous solution, where the azobenzene linker was partly included in one  $\beta$ -CD cavity via an external 360° rotation (tumbling) of the triazole-substituted glucopyranose unit<sup>[13]</sup> (Figure S12). Meanwhile, the photo-isomerization behaviors of **H** were investigated by UV/Vis and NMR experiments (Figures S8, S11, S13, and S14). The results jointly indicated that **H** displayed high photoisomerization efficiency and good reversibility. Furthermore, TEM experiments (Figure S15) indicated that neither **H**-*trans* nor **H**-*cis* could form large nanostructures in aqueous solution, probably due to the high hydrophilicities of the two  $\beta$ -CD groups.

As the host molecule **H** comprises a free  $\beta$ -CD cavity, it could associate with the guest molecule in aqueous solution, and the resultant supramolecular assembly was expected to have an alternative topology owing to the photo-switchable conformation of H. The adamantanyl-modified diphenylalanine (Ada-FF) was selected as a model substrate because the diphenylalanine (L-Phe-L-Phe, FF) peptide, a core recognition motif of Alzheimer's β-amyloid polypeptide, was found to self-assemble into various nanostructures.<sup>[14]</sup> The Job's analysis (Figure S16) demonstrated the 1:1 complexation stoichiometry between H-trans (or H-cis) and Ada-FF, and the apparent binding constant was calculated as  $5.32 \times 10^4 \,\mathrm{M}^{-1}$  (or  $5.18 \times 10^4 \text{ m}^{-1}$ ) for the association of **Ada-FF** with **H**-*trans* (or H-cis). This indicates that the adamantanyl moiety could strongly bind with the free  $\beta$ -CD cavity in **H**. In addition, the <sup>1</sup>H NMR spectra (Figure S17) and the 2D ROESY spectra (Figures S18 and S19) of Ada-FF⊂H-trans and Ada-FF⊂Hcis further demonstrated that either H-trans or H-cis retained the self-included conformation in aqueous solution, even after the association with Ada-FF.

The assembly behaviors of H with Ada-FF were investigated by transmission electron microscopy (TEM), atomic force microscopy (AFM), scanning electron microscopy (SEM), Fourier transform infrared spectrometry (FT-IR) and X-ray diffraction (XRD). Ada-FF itself was also analyzed as a control. In Figure 1a, TEM images showed that the selfassembly of Ada-FF formed as one-dimensional nanofibers with lengths of several micrometers. Meanwhile, AFM and SEM images (Figure S20) also showed similar fiber-like nanostructures. The height of these nanofibers was determined to be approximately 3.5 nm by AFM analysis, which was almost equal to two times the calculated length (1.74 nm) of Ada-FF molecule. Moreover, FT-IR analyses of Ada-FF gave the absorption bands at  $1636 \text{ cm}^{-1}$  and  $1604 \text{ cm}^{-1}$ (Figure S22), indicating that Ada-FF formed a  $\beta$ -sheet secondary structure.<sup>[15]</sup> Meanwhile, the circular dichroism spectrum of self-assembled Ada-FF showed a positive Cotton peak at 198 nm (Figure S23), which also confirmed the twisted β-sheet structures.<sup>[16]</sup> On the basis of these observations, a possible self-assembly mode of Ada-FF was proposed in Figure 1b.

The self-assembly behaviors of **Ada-FF** $\subset$ **H** were further investigated. The  $\beta$ -sheet signals in FT-IR spectra of **Ada-FF** weakened upon the addition of **H**, indicating that the  $\beta$ -sheet structure was destroyed.<sup>[15b]</sup> As shown in Figure 1c and Figure S24, TEM and SEM images of the **Ada-FF** $\subset$ **H**-*trans* 



*Figure 1.* TEM images of a) **Ada-FF** self-assembly (scale bar = 0.2 µm); c) **Ada-FF**⊂**H-***trans* (scale bar = 0.5 µm); d) **Ada-FF**⊂**H-***cis* (scale bar = 0.2 µm), and b) the proposed assembly mode of **Ada-FF** in aqueous solution.

assembly showed many two-dimensional planar nanosheets, whose lengths and widths reached several micrometers. Moreover, the heights of these thin planar nanostructures were measured as approximately 7 nm by AFM experiments (Figure S24), concordant with two times the length of Ada-FFCH-trans (calculated as 6.51 nm by a computational simulation). The XRD spectrum of Ada-FFCH-trans (Figure S25) presented two diffraction peaks at  $2\theta = 2.10$  and 4.24, indicating the formation of lamellar nanostructures,<sup>[8,17]</sup> and the d value (4.2 nm) was close to the length of Ada-**FF**⊂**H**-*trans*. Interestingly, the **Ada-FF**⊂**H**-*cis* assembly presented an entirely different morphology from those of Ada-FF and Ada-FFCH-trans. TEM (Figure 1 d) and SEM images (Figure S26) showed a number of open-ended, curved tubular structures. It is noteworthy that the wall thickness of the Ada-FFCH-cis assembly was nearly equal to two times the length of the Ada-FF/H-cis complex, which was also confirmed by the XRD experiment. In the wide-angle X-ray scattering (WAXS) spectrum of Ada-FFCH-trans or Ada-FFCH-cis, the peak at 0.35 nm was assigned to the  $\pi$ - $\pi$  stacking of Ada-FF, and the peaks at 0.47 and 0.69 nm were assigned to the distance of neighboring Ada-FF/H-trans or Ada-FF/H-cis complexes.

Owing to the good photoisomerization properties of the azobenzene moiety in H, the 1D-nanotubes (formed by Ada-FFCH-cis) and 2D-nanosheets (formed by Ada-FFCH-trans) could mutually interconvert via light irradiation at different wavelengths. Typically, after irradiation of the solution of Ada-FFCH-trans with UV light (365 nm) for 10 min, nearly all of the 2D nanosheets converted into 1D-nanotubes. Meanwhile, the formed 1D nanotubes could revert to the original 2D nanosheets upon their subsequent irradiation with visible light (450 nm) for 30 min. Interestingly, the timedependent TEM and SEM images (Figure S27) revealed that, when irradiating the solution of Ada-FFCH-trans for a short time, a number of open nanotubes were observed (Figure S27). After lengthening the irradiation time, these nanotubes converted into closed ones. Combining these observations with the results of XRD and FT-IR, we can reasonably



deduce the possible assembly modes of **Ada-FF** $\subset$ **H**-*trans* and **Ada-FF** $\subset$ **H**-*cis* as illustrated in Figure 2. In this process two **Ada-FF** $\subset$ **H** complexes firstly form end-to-end dimers via  $\pi$ - $\pi$  and/or hydrogen bonding interactions between the **FF** 



*Figure 2.* Schematic representation of the assembly mode of nanosheets, nanotubes, and the proposed interconversion process.

moieties. Next, these dimers further self-assemble to bilayer nanosheets (for Ada-FF⊂H-*trans*) or nanotubes (for Ada-FF⊂H-*cis*) through a secondary assembly process. Under UV light irradiation, the planar nanosheets with a bilayer structure bend into nanotubes, while the as-formed nanotubes could revert to nanosheets under visible light irradiation (Figure 2). These phenomena may result from the conformational difference between H-*trans* and H-*cis*. That is, the inclusion complex of Ada-FF with H-*trans* could be considered as a cylindrically symmetric structure, which is predisposed toward forming the planar bilayer nanosheet.<sup>[18]</sup> However, isomerization of the azobenzene moiety from the *trans* form to *cis* form led to the bending of the cylindrically symmetrical structure and resulted in the formation of nanotubes.<sup>[19]</sup>

It is also important to test the reversibility of the photodriven morphology conversion. As shown in Figure 3, the absorbance of Ada-FFCH-trans at 356 nm, assigned to the characteristic absorption of the  $\pi$ - $\pi^*$  transition of *trans*azobenzene, dramatically decreased when Ada-FFCH-trans was irradiated with UV (365 nm). This was accompanied by a distinct hypsochromic shift, indicating the photoisomerization of the azobenzene moiety from the trans form to the cis form. The reverse isomerization (from the cis form to the trans form) was realized with either irradiation at 450 nm or heating the aqueous solution to 70 °C. Significantly, this cycle could be repeated tens of times without obvious change. In addition, TEM experiments also confirmed that nanosheets and nanotubes could mutually interconvert by photoirradiation under different wavelengths over several cycles (Figure S28). These results jointly indicate the good reversibility and repeatability of the photocontrolled 2D nanosheet and 1D nanotube morphological conversions.

We have established that the 2D nanosheets and 1D nanotubes constructed from Ada-FF and H could intercon-



Figure 3. UV/Vis spectra and absorption changes ( $\lambda = 356$  nm) of Ada-FF $\subset$ H in aqueous solution. a, b) Under light irradiation at 365 nm or 450 nm; c, d) under irradiation at 365 nm or heating at 70 °C.

vert with perfect reversibility. We decided to investigate the absorption and fluorescence enhancement behaviors of these 1D- and 2D-nano-assemblies using Nile Red, a well-established polarity-sensing dye.<sup>[20]</sup> As shown in Figure 4a, Nile Red barely fluoresced in aqueous solution, while it greatly increased upon combination with nano-assemblies. Interestingly, the fluorescence intensity of Nile Red loaded with 2Dnanosheets was much stronger than with nanotubes. The fluorescence lifetimes and quantum yields of Nile Red-loaded nanosheets were quite similar to those of Nile Red-loaded nanotubes (Figure S29), indicating that the hydrophilicity of the environment of the absorbed Nile Red was similar in the 1D and 2D structures. Therefore, a possible explanation regarding the stronger fluorescence of the 2D-nanosheet/Nile Red system is that, since **H-cis** was more polar owing to the



*Figure 4.* a) Fluorescence emission spectra of Nile Red, Nile Red@Ada-FF $\subset$ H-*trans* and Nile Red@Ada-FF $\subset$ H-*cis* ( $\lambda_{ex}$  = 580 nm); b) plot of fluorescence intensity at 649 nm versus light irradiation time, blue areas = UV (365 nm) and orange area = Vis (450 nm) irradiation; fluorescence microscopy images of c) Nile Red@Ada-FF $\subset$ H*trans* and d) Nile Red@Ada-FF $\subset$ H-*cis*.

dipole formed upon switching, lower amounts of H and Ada-FF were involved in the assembly formation when H was in its cis state. This would lead to less absorption and/or more selfquenching of the dye as a result of denser packing.<sup>[20a]</sup> Moreover, the larger BET surface area of the nanosheets  $(14.25 \text{ m}^2 \text{g}^{-1})$  compared to that of the nanotubes  $(9.03 \text{ m}^2 \text{g}^{-1})$ may have also contributed to the higher absorption ability of nanosheets toward Nile Red (Figure S30). In a recycling experiment, the fluorescence intensity of Nile Red decreased upon the morphological transformation from nanosheets to nanotubes, but increased to the original level when the morphology reverted to nanosheets (Figure 4b). The fluorescence microscopy images also demonstrated the much stronger fluorescence emission of Nile Red-loaded 2D nanosheets than that of Nile Red-loaded 1D nanotubes. These indicated that the 2D-nanosheet gave better absorption and fluorescence enhancement abilities than the 1D nanotube.

In summary, the azobenzene-bridged bis( $\beta$ -CD) and adamantanyl-modified diphenylalanine were rationally designed and applied in the construction of 1D and 2D nanostructures. Crucially, these 1D and 2D nanostructures could reversibly and repeatedly interconvert under light irradiation at different wavelengths. These findings provide a convenient avenue for controlling the assembly morphologies by using different wavelengths of light.

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## **Conflict of interest**

The authors declare no conflict of interest.

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