Photo/chemo dual-controlled reversible morphological conversion and chiral modulation of supramolecular nanohelixes with nanosquares and nanofibers†

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A photo/chemo dually interconvertible system was constructed through the supramolecular assembly of azobenzene-diphenylalanine (Azo-FF) with β-cyclodextrin. The resultant chiral nanohelix was able to interconvert into a nanosquare upon irradiation at different wavelengths, but into a nanofiber upon changing solvent polarity, which provides a feasible way to achieve highly ordered nanostructures with various morphologies, dimensions and chiralities.

Supramolecular assemblies with stimuli-responsivity have attracted considerable research interest because of their applications in various fields such as drug carriers, catalysts, sensors, protein probes, and optoelectronic materials. Various external triggers, such as pH, temperature, solvent, photoirradiation, enzyme, and (electro)chemical redox, have been used in these systems. Among them, light is widely regarded as a very important approach to achieve the smart control of supramolecular assembly because of its noninvasive, clean and remote-controlling properties. In the last decade, many photocontrolled supramolecular assemblies based on azobenzene–cyclodextrin have been constructed taking advantage of the reversible photosomerization of azobenzene and the different binding behaviors of trans- and cis-azobenzenes with cyclodextrin. However, most of these studies were focused on the photocontrolled assembly/disassembly process, while the morphological conversion of supramolecular assembly switched by light irradiation was rarely reported. Kim et al. reported a chemocontrolled one-cycle nanotube–nanoparticle morphological conversion of pyrene-modified dendritic self-assembly induced by the sequential addition of cyclodextrin and poly(propylene glycol). Stupp et al. reported a chemocontrolled reversible nanohelical-nanocylinder conversion of a simultaneous covalent and noncovalent hybrid polymer though the addition/extraction of supramolecular compartments.

Recently, we reported a photocontrolled reversible nanotube–nanoparticle conversion mediated by β-cyclodextrin dimers. More recently, when we were preparing this manuscript, Chi, Tian and Zhu reported a photocontrolled reversible nanohelix–amorphous particle conversion accompanied by the dynamic amplification of chirality with photoreversibility.

On the other hand, the diphenylalanine (L-Phe–L-Phe, FF) peptide, a core recognition motif of Alzheimer’s β-amyloid polypeptide, was found to be able to self-assemble into stable nanotubes in 2003. From then on, lots of effort was contributed to organize FF-based building blocks into various well-defined supramolecular nanostructures such as nanotubes, spherical vesicles, nanofibers, nanowires, macroporous honeycomb scaffolds and peony-flower-like hierarchical nanostructures through the self-assembly of diphenylalanine and its derivatives such as Ac-FF, Boc-FF, Z-FF, Cbz-FF, Nap-FF, Fc-FF and Cys-FF. He et al. introduced a ferrocene group to diphenylalanine and made it capable of being reversibly controlled by altering its redox state. They also created a range of rigid chiral nanostructures through the modulation of counterions, temperature, and solvent.

Li and co-workers used the photoswitchable sulfoniacobenzene to co-assemble with diphenylalanine to achieve the photo-induced structural transition. Therefore, one can believe that the association of azobenzene–cyclodextrin with FF may become a significant approach to the construction of nano-scaled supramolecular assemblies with a smart stimuli-responsivity and structural diversity. In this work, we wish to report a photo/chemo dual-controlled nanotube based on azobenzene–diphenylalanine (Azo-FF) and β-cyclodextrin (Scheme 1), which can be reversibly converted into a nanosquare using a photocontrol but into a nanofiber using a chemocontrol.

Azo-FF was prepared via a four-stepped synthesis as described in Scheme S1 (ESI†). Firstly, diphenylalanine was esterified through a reaction with AcCl and CH3OH, and the residue was cast to the next step directly. After the reaction with bromoacetyl bromide at a low temperature (~10 °C), N-terminus-modified bromide was obtained and then undertook a substitution

† Electronic supplementary information (ESI) available: Detailed synthesis, characterization data, Job’s plot, 2D NMR spectra, DLS date, CD, and scanning electron micrograph. See DOI: 10.1039/c6cc07089b

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reaction with hydroxyazobenzene to give compound 3. Through
a subsequent hydrolysis under basic conditions, Azo-FF was
obtained as an orange solid in 44% yield.

Generally, upon irradiation with UV light, the trans-isomer
of an azobenzene compound can transform to the cis-isomer,
which can reverse back to the trans-isomer through either visible
light irradiation or heating. Herein, $^1$H NMR experiments were
performed in D$_2$O: DMSO (v:v)/9:1 to investigate the binding
behavior of the trans- (trans-Azo-FF) or cis-isomer (cis-Azo-FF) of
Azo-FF with $\alpha$-cycloextrin. With the addition of $\alpha$-cycloextrin to
a solution of trans-Azo-FF, the $^1$H NMR signals of azobenzene
protons (marked by orange dots) of trans-Azo-FF shifted to the
low field, while the $^1$H NMR signals of aromatic protons of the
diphenylalanine moiety (marked by green dots) showed no
significant shifts (Fig. 1a and b). Moreover, the NOESY spectrum of
an equimolar trans-Azo-FF + $\alpha$-cycloextrin mixture showed the
clear NOE correlations between the inner protons of $\alpha$-cycloextrin
and the azobenzene protons of Azo-FF (Fig. S4, ESI†). These jointly
indicate that the azobenzene moiety of trans-Azo-FF was included
in the $\alpha$-cycloextrin cavity to form the trans-Azo-FF/$\alpha$-cycloextrin
complex. On the other hand, after irradiating the trans-Azo-FF/
$\alpha$-cycloextrin complex using UV light (365 nm) for 10 min, all of
the aromatic protons in the Azo-FF/$\alpha$-cycloextrin complex gave
$^1$H NMR signals very similar to those of free cis-Azo-FF (Fig. 1c
and d). Moreover, no NOE correlations between the inner protons
of $\alpha$-cycloextrin and the protons of Azo-FF could be observed
after expositing the trans-Azo-FF/$\alpha$-cycloextrin complex to UV
light (Fig. S6, ESI†). A possible reason for these observations
may be that the photo-induced conversion from trans-Azo-FF to
cis-Azo-FF led to the dissociation of the Azo-FF/$\alpha$-cycloextrin
complex (Scheme 2), because $\alpha$-cycloextrin was reported as
unfavorable to bind the cis-isomer of azobenzene. In addition,
the mass spectrum also gave evidence for the photo-responsive
host–guest association/dissociation (Fig. S5 and S7, ESI†). Through
a comparison of the integral area in the $^1$H NMR spectra,
the conversion ratio of cis-trans isomerization was calculated
to be 90%.

The interconversion between the trans-Azo-FF/$\alpha$-cycloextrin
and cis-Azo-FF/$\alpha$-cycloextrin systems can also be tracked using
UV-vis spectroscopy. As seen in Fig. 2a, the absorption band of
the trans-Azo-FF/$\alpha$-cycloextrin complex around 344 nm
dramatically decreased under the irradiation at 365 nm, accom-
panied by the obvious hypsochromic shift of the absorption
maximum. In addition, the appearance of a new absorption
band around 431 nm and a clear isosbestic point at 410 nm
jointly indicated the one-step transformation of the trans-Azo-FF/
$\alpha$-cycloextrin complex to the simple mixture of $\alpha$-cycloextrin
with cis-Azo-FF, because the free cis-Azo-FF has a $\pi$–$\pi^*$ transition
that is less intense and blue-shifted relative to its trans isomer as
well as a weak n–$\pi^*$ transition that is more intense in the cis
form than in the trans one in the visible region. However, the
decreased intensity at 344 nm was recovered to its original level
upon the subsequent irradiation at 450 nm. A possible reason
may be that, owing to the reverse photoisomerization from cis
to trans form of Azo-FF, the simple mixture of cis-Azo-FF with
$\alpha$-cycloextrin could revert to the trans-Azo-FF/$\alpha$-cycloextrin

**Scheme 2** Self-assembly/disassembly based on the photo-responsive
interconversion of Azo-FF and $\alpha$-cycloextrin.

**Fig. 1** Partial $^1$H NMR spectra (400 MHz, D$_2$O: DMSO-d$_4$ (v/v) 9:1, 25 °C
of (a) trans-Azo-FF, (b) trans-Azo-FF + $\alpha$-cycloextrin (1:1), and (c) after
365 nm irradiation of (a) and (d) after 365 nm irradiation of (b), Azo-FF =
[$\alpha$-cycloextrin] = 1 mM.

**Fig. 2** (a) UV-vis spectra of Azo-FF/$\alpha$-cycloextrin (1:1) (0.03 mM in H$_2$O)
to determine the photoisomerization rate constant ($k_i$) in water. The duration
of UV light was set at 0 → 121 s at 365 nm. Inset: Determination of the
$k_i$ value of Azo-FF/$\alpha$-cycloextrin (1:1) upon exposure to UV light at 365 nm.
(b) Cyclic responses of the absorbance values at 344 nm of trans-Azo-FF/
$\alpha$-cycloextrin solution (0.03 mM) on alternating irradiation between UV
and visible light.
system (Scheme 2). Significantly, this assembly/disassembly cycle could be repeated several times (Fig. 2b). In addition to the light irradiation, the continuous heating of a cis-Azo-FF/α-cyclodextrin mixture at 80 °C for 2 h could also result in the conversion of the cis-Azo-FF + α-cyclodextrin mixture to the trans-Azo-FF/α-cyclodextrin system (Fig. S8, ESI†). By utilizing first-order kinetics, the trans → cis photoisomerization rate constant (k) of trans-Azo-FF in solution was measured to be 0.03628 s⁻¹ (Fig. S9, ESI†), but increased to 0.04906 s⁻¹ in the presence of 1.0 equiv. of α-cyclodextrin (Fig. 2a, inset). This result suggested that the association of Azo-FF with α-cyclodextrin could accelerate the isomerization of Azo-FF.20

Moreover, the circular dichroism spectrum of trans-Azo-FF showed a positive Cotton effect peak (Δε = 2.63 dm³ mol⁻¹ cm⁻¹) at 325 nm and a negative Cotton effect peak (Δε = −3.17 dm³ mol⁻¹ cm⁻¹) at 367 nm, but these peaks changed to Δε = 4.06 dm³ mol⁻¹ cm⁻¹ at 329 nm and Δε = −1.39 dm³ mol⁻¹ cm⁻¹ at 382 nm, respectively, in the circular dichroism spectrum of the trans-Azo-FF/α-cyclodextrin system, probably due to the chirality transfer of FF and α-cyclodextrin to the azobenzene moiety. With the gradual irradiation of UV light, the circular dichroism signal intensity of either the trans-Azo-FF/α-cyclodextrin system or free trans-Azo-FF gradually decreased and nearly vanished after 100–100 s (Fig. S10, ESI†). The circular dichroism experiment showed that the trans-Azo-FF/α-cyclodextrin or trans-Azo-FF system would lose most of its chirality when irradiated by UV light.

The photo-controlled morphological interconversion of the Azo-FF/α-cyclodextrin assembly was characterized using a scanning electron microscope (SEM). As shown in Fig. 3a, the free trans-Azo-FF exists as one-dimensional ambiguous spiral nanofibers with a uniform width of ca. 25 nm and a length of over 10 μm, although a very slight helix could not be rigorously ruled out. However, the SEM image of the trans-Azo-FF/α-cyclodextrin system showed a number of right-handed nanohelices (Fig. 3b) with a length of over 10 μm, a width of ca. 40 nm and a helical pitch of ca. 100 nm, which were conformationally uniform in size and shape. Significantly, after the irradiation of the trans-Azo-FF/α-cyclodextrin solution at 365 nm for 3 min, the original nanohelices turned to a number of nonhelical nanosquares with a side length of 100–500 nm (Fig. 3c). In the control experiment, similar nanosquares could also be obtained by irradiating the nanofibers of free trans-Azo-FF at 365 nm (Fig. S11, ESI†). Besides the SEM images, the morphological conversion of the assembly could also be distinguished by the naked eye through the turbidity experiments. As shown in Fig. 3d, the subtransparent trans-Azo-FF/α-cyclodextrin solution became completely transparent after the irradiation of UV light for 10 min due to the conversion of the nanohelix to the nanosquare, and the resultant transparent solution of the nanosquare would revert to being subtransparent after the irradiation of visible light owing to the photoreversible nanohelix–nanosquare transformation. DLS data (Fig. S12, ESI†) showed that the assembly of the trans-Azo-FF/α-cyclodextrin complex and the trans-Azo-FF monomer possess a hydrodynamic diameter of up to thousands of nanometers, which is dramatically larger than the diameter observed for their cis-Azo-FF system. Consequently, UV-vis, circular dichroism, turbidity, DLS and SEM experiments jointly confirmed the good reversibility and repetitiveness of the photo-controlled nanohelix–nanosquare morphological conversion as well as the chiroptical property change. A similar photo-switchable nanofiber–nanosquare morphological conversion was also observed in the case of free Azo-FF (Fig. S11, ESI†).

Combining the results described above, we propose a possible mechanism for the assembly and transformation process. As illustrated in Fig. 4, mainly through the π–π stacking among aromatic units, the free trans-Azo-FF, which adopted a linear conformation, tended to self-assemble along the one-dimensional direction to form nanofibers. In contrast, the cis-Azo-FF, which adopted an L-type conformation, firstly formed a quadruple dimer through hydrogen bonding between the carboxyl groups of FF fragments, and then the resultant dimers further self-assembled along the two-dimensional direction mainly though π–π stacking among aromatic units to form nanosquares. With the addition of α-cyclodextrin, the azobenzene moiety of trans-Azo-FF would be included into the cavity of α-cyclodextrin. Therefore, the large steric hindrance between the adjacent α-cyclodextrin cavities would lead to twisting of the trans-Azo-FF units in the nanofiber and consequently the conversion of the nanofiber into a nanohelix. Therein, the π-configuration of glucose moieties in α-cyclodextrin was deduced to play an important role in the formation of a right-hand twist, although there was no direct evidence. On the other hand, once the trans-Azo-FF/α-cyclodextrin nanohelix was exposed to UV light, trans-Azo-FF photo-isomerized

![Fig. 3](image-url)  
**Fig. 3** SEM images of (a) nanofibers formed by trans-Azo-FF and (b) nanohelices formed by trans-Azo-FF/α-cyclodextrin. (c) trans-Azo-FF/α-cyclodextrin after being irradiated by UV light (365 nm) for 3 min. (d) Photograph of Azo-FF/α-cyclodextrin solution under UV and visible light.

![Fig. 4](image-url)  
**Fig. 4** Possible assembly mode of Azo-FF and trans-Azo-FF/α-cyclodextrin.
into cis-Azo-FF. Because the α-cyclodextrin cavity was unfavorable to include cis-Azo-FF, + the trans-Azo-FF/α-cyclodextrin nanohelix was disrupted. As a result, the dissociated cis-Azo-FF self-assembled into a nanosquare like in the case of free cis-Azo-FF (Fig. S11, ESI†).

In addition to the light irradiation, the change in polarity could also adjust the morphology of assembly owing to the non-covalent nature of the supramolecular interactions working between α-cyclodextrin and trans-Azo-FF. For example, the addition of ethanol to the aqueous solution of trans-Azo-FF/α-cyclodextrin would lead to the conversion of a nanohelix into a nanofiber (Fig. S13a and b, ESI†). A possible reason for this may be that the addition of ethanol weakened the hydrophobic interactions between α-cyclodextrin and trans-Azo-FF, which consequently resulted in the dissociation of the trans-Azo-FF/α-cyclodextrin complex. Then, the dissociated trans-Azo-FF self-assembled into a nanofiber (Fig. S13b, ESI†), like in the case of free trans-Azo-FF. However, when further adding water to the above described H2O/ETOH solution, the nanofiber reversibly converted into a nanohelix (Fig. S13b and c, ESI†).

In conclusion, taking advantage of the photositisomerization properties of azobenzene derivatives, the distinct binding affinity of α-cyclodextrin with trans- and cis-conformers of azobenzene, as well as the non-covalent nature of supramolecular interactions, a photo/chemo dual-controlled supramolecular assembly was successfully constructed. Crucially, the morphology of the assembly could be switched between the nanohelix and nanosquare under light irradiation, and could be switched between the nanohelix and nanofiber by changing the polarity of the solvent; both of these morphological conversions were reversible and repeatable, accompanied by a controlled chiral amplification or attenuation. The photoswitchable and/or chemoswitchable morphological conversion and chiral modulation properties, along with the facile preparation and good water solubility, may make this supramolecular assembly approach well-suited for the design and smart control of new functional materials.

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Notes and references


