Light-induced unfolding and refolding of supramolecular polymer nanofibres

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Unlike classical covalent polymers, one-dimensionally (1D) elongated supramolecular polymers (SPs) can be encoded with high degrees of internal order by the cooperative aggregation of molecular subunits, which endows these SPs with extraordinary properties and functions. However, this internal order has not yet been exploited to generate and dynamically control well-defined higher-order (secondary) conformations of the SP backbone, which may induce functionality that is comparable to protein folding/unfolding. Herein, we report light-induced conformational changes of SPs based on the 1D exotic stacking of hydrogen-bonded azobenzene hexamers. The stacking causes a unique internal order that leads to spontaneous curvature, which allows accessing conformations that range from randomly folded to helically folded coils. The reversible photoisomerization of the azobenzene moiety destroys or recovers the curvature of the main chain, which demonstrates external control over the SP conformation that may ultimately lead to biological functions.

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ne-dimensionally (1D) elongated molecular assemblies with high degrees of internal order, categorized as supramolecular polymers (SPs) (ref. 2), represent emerging stimuli-responsive materials with interesting functions and properties \(^{3-9}\). A variety of functional SPs have been developed, while precise supramolecular polymerization has been devised recently, which is inspired by the biological system as well as synthetic polymers \(^{10,19}\). An important issue that has not yet been addressed in the context of SPs is dynamic control over their higher-order structures at the nanoscale (for example, helical coils), despite the fact that typical helical columnar structures at the primary level \(^{1-15}\) have been well studied in terms of internal order. Changes in the higher-order conformation of biopolymers play an important role in biological systems, which is arguably best reflected in protein folding \(^{16}\). For instance, folded proteins are functional, whereas unfolded/misfolded proteins generally lose their functionality. Inspired by these naturally occurring polymers, the control over folding has been explored in synthetic covalent polymers \(^{17-22}\) and oligomers \(^{23-26}\) which are referred to as foldamers \(^{27-29}\). In order to mimic the functions of biopolymers and/or compete with oligomeric as well as polymeric foldamers, remote control over the conformation of the SP backbone is required.

To address this issue, herein, we have used a previously reported barbiturated naphthalene derivative, which polymerizes non-covalently into uniform toroidal nanostructures via stacking of hydrogen-bonded hexamers \(^{30,31}\). The introduction of a photosensitive azobenzene into the parent-barbiturated naphthalene results in increased attractive forces between the stacking molecules, and causes light-induced changes of the molecular shape \(^{32-36}\). Depending on the polymerization conditions, the new molecule non-covalently polymerizes into various quasi 1D structures with spontaneous curvature, ranging from randomly coiled to helically folded fibres. Photosomeration of the azobenzene unit by exposure to ultraviolet (UV) or visible (Vis) light provides a means to reversibly destroy or recover the curvature of the main chain, respectively. Thus, an external dynamic control over helical secondary structures of SPs is demonstrated. Although the terminologies conformation and folding/unfolding are commonly reserved for covalent polymer chains, we are using them here in the context of non-covalent polymer chains to illustrate the conceptual similarity.

**Results**

**Molecular design.** For the construction of well-defined helically coiled conformations, the design of foldamers is usually based on covalent local constraints, which manifest in covalently curved units that typically arise from meta-isomers of aromatics (Fig. 1a) \(^{21,23-26}\). As these helically coiled structures are generally stabilized by non-covalent interactions between non-adjacent monomer units (interloop interactions), external stimuli afford dynamic control over helically coiled and extended/randomly coiled conformations \(^{21,23-25}\). As an alternative strategy, Hecht and co-workers introduced azobenzene moieties into the backbone of foldamers to realize direct folding and unfolding by light \(^{21,22,26}\). Exploiting a similar strategy in order to gain dynamic conformational control over SPs with a high degree of internal order thus initially requires non-covalently curved stacks with shape persistence (Fig. 1b). Moreover, the main chain of the SPs should be amendable to dynamic tuning of the internal order, that is, the ability to switch on/off the non-covalent curvature (Fig. 1b), as—unlike typical foldamers—the main chains of SPs are generally not strong enough to allow for a selective dissociation of the non-covalent interactions between non-adjacent monomer units by external stimuli.

To verify this hypothesis in this study, we have used our previously reported barbiturated naphthalene molecule 1 (Fig. 2a), which self-assembles into uniform toroidal nanostructures \(^{30,31}\) that can serve as non-covalently curved stacks to realize target helically folded SP systems with dynamically controllable conformations. In methylcyclohexane (MCH), the parent molecule 1 assembles into hydrogen-bonded cyclic hexamers that stack quasi 1D via \(\pi-\pi\) interactions to form uniform toroidal nanostructures (SPtoroid, Fig. 2b,c). The shape persistency of SPtoroid and their uniformity of the diameter (14 \(\pm\) 0.1 nm) implies that the spontaneous curvature comprising non-covalently curved stacks occurs by highly idiosyncratic internal order \(^{2}\) within the continuous hexamer stacking. The cohesive forces between these hexamers should thus be strengthened by introducing additional aromatic moieties into 1, which could prevent the growing polymer from closing into discrete shorter assemblies, instead yielding extended and robust SPs (ref. 4) with well-defined conformations due to non-covalently curved stack. This curvature-inducing internal order is likely due to the complex pinwheel architecture of the hexamers (Fig. 2b,c) \(^{30}\) any deformation should enable a modulation of the polymer conformation by changing the internal order of the non-covalently curved stacks. This strategy may allow access to a unique class of SPs with controllable conformations.

Accordingly, we designed and synthesized molecule 2 (Supplementary Methods) wherein a photoresponsive azobenzene is introduced into the parent molecule in order to increase attractive forces between the stacking molecules, as well as cause light-induced changes of the molecular shape (Fig. 2d) \(^{32-36}\). The trans-isomer of 2 (trans-2), containing an additional planar \(\pi\)-surface, should strengthen the cohesive forces between the hexamers (Fig. 2e,f). This assumption is justified by the results of temperature-dependent UV–Vis spectroscopy measurements (Fig. 2g), which reveal a higher elongation temperature \(T_E\) and a larger enthalpy change in the elongation regime \(\Delta H_E\) of the cooperative nucleation-elongation process for trans-2 \((T_E = 83.6^\circ C, \Delta H_E = -108 kJ mol^{-1})\) relative to 1 \((T_E = 42.5^\circ C\) and \(\Delta H_E = -83.4 kJ mol^{-1}\)) (Fig. 2h) \(^{37,38}\). The enhanced cohesive forces should reduce the photosomeration of azobenzene moieties, resulting in the partial formation of cis-2 in the stacked hexamers (Fig. 2e). This would cause the formation of defected hexamers and affect internal order, thus antagonizing the spontaneous curvature (Fig. 2f).

**Thermally obtainable SPs.** Atomic force microscopy (AFM) measurements showed that cooling a MCH solution of trans-2 \((1.0 \times 10^{-4} M)\) from 90 to 20 \(^\circ C\) without temperature control resulted in the formation of randomly folded coils (SPrandom) with a defined spontaneous curvature (Fig. 3a,c; Supplementary Fig. 1a–c). To quantify these structures, the radius of curvature, \(r\), evaluated by manually fitting a circle with radius \(r\) along each curve, and the turning angle, \(\theta\), of the polymer segment before the clockwise or counter-clockwise change of direction, were used (Fig. 3e). The similarity in the appearance of the spontaneous curvature of SPrandom \((r_{ave} = 10.4 \pm 0.2 nm, \theta_{ave} = 370 \pm 5^\circ\) (Fig. 3f,g) with that of the toroids of 1 indicates that the introduction of a trans-azobenzene unit in 2 does not considerably affect the internal order responsible for the curvature. The formation of a very minor amount of SPtoroid of 2 (Fig. 3c), which exhibit the same \(r_{ave}\) as SPrandom, suggests that the latter is formed by an extension of the polymerization beyond the toroid due to enhanced cohesive forces between hexamers.

A cooling rate of 0.1 \(^\circ C\) min\(^{-1}\) the conditions that favour a thermodynamic polymerization \(^{39,40}\) resulted in the formation of spirally folded fibres (SPspiral) \((r_{ave} = 11.4 \pm 0.2 nm, \theta_{ave} = 510 \pm 5^\circ\) with more organized conformations and higher degrees of
internal order (Fig. 3d,f,g; Supplementary Figs 1g–l; 3, 22; Supplementary Discussion). Conversely, the spontaneous curvature was not observed upon fast quenching of the solution from 90 to 20 °C (>100 °C min⁻¹, ice bath). Instead, linear fibres (SPlinear; Fig. 3b; Supplementary Fig. 1d–f) were formed. These SPs including SPrandom share the same cross-sectional width (~9.7 ± 0.3 nm) and thickness (2.7 ± 0.2 nm) of their backbones, suggesting that they organize via an identical self-assembly process, that is, a translationally offset stacking of hexamers (Supplementary Fig. 2)³⁰,³¹. In order to generate a spontaneous curvature for SPrandom and SPspiral, an additional rotational offset is required (Fig. 2f). Thus, a unique internal order, that is, the specific stacking of hexamers, that produces the spontaneous curvature should arise from a more thermodynamic supramolecular polymerization process⁹,³⁹, and the lack of spontaneous curvature in SPlinear likely suggests a decrease of the internal order. This notion is supported by the decreased absorbance at λ = 410–430 nm for SPlinear that likely measures the level of internal order (Supplementary Fig. 3). Hence, storing a quenched sample of SPlinear for 24 h at 20 °C led to the almost complete conversion into SPrandom (Supplementary Fig. 4), which demonstrates the spontaneous recovery of a higher degree of the internal stacking order of hexamers (Fig. 3a).

This folding variation of SPs was investigated in solution by small-angle X-ray scattering (SAXS)⁳¹. In MCH, the SAXS plots of SPrandom and SPspiral exhibited increased scattering at Q < 0.15 nm⁻¹, which probably originates from the elongated polymer chains and their fractal structure (Supplementary Fig. 5a–c). Additionally, both data sets exhibit features at Q = 0.3–1.2 nm⁻¹, which should arise from the comparable spontaneous curvature of the SPs (cf. AFM results). Similar SAXS plots were observed for the toroidal nanostructures of 1 within that Q-range, which corresponds to a length scale of ~5–20 nm (ref. 31). This is hardly surprising, considering that the difference between overlapping loops (spirals/random coils) and closed toroids is relatively small at this length scale. Data fits using toroid or hollow cylinder models (Supplementary Fig. 5a–c; Supplementary Discussion) were consistent with the SAXS data and afforded curvature radii for SPrandom (rave = 9.8 ± 0.2 nm) and SPspiral (rave = 9.9 ± 0.2 nm) that agree well with the AFM values. Conversely, the SAXS data from SPlinear retained the fractal-like scattering, but maxima/minima were not observed (Supplementary Fig. 5d). This result is indicative for the presence of an elongated polymer without spontaneous curvature (Fig. 3b), in reasonable agreement with the AFM results.

**Photochemically transmuted SPs.** Subsequently, we examined the morphological effect of the photoisomerization of the azobenzene moiety. UV–Vis and NMR spectroscopical analyses showed that irradiation of an SPspiral solution with UV light (λ = 365 nm) induced partial photoisomerization (23% cis-2) (Supplementary Figs 6a and 7). Despite this relatively low isomerization yield, a dynamic light scattering (DLS) analysis showed a substantial increase in average hydrodynamic diameter (Dh) from ~320 to ~670 nm (Fig. 4a, Supplementary Fig. 8). An increase in aggregate size upon trans-to-cis isomerization in azobenzene-based supramolecular systems is, however, counterintuitive⁴¹, considering that the bent cis-isomer is generally less favourable for extended aggregation than the planar trans-isomer⁴²,⁴³.

SAXS analysis of the UV-irradiated SPspiral solution revealed a complete disappearance of the scattering features of the spiral structures (Fig. 4b, Supplementary Fig. 9). This implies a considerable conformational change of the SP and a loss of the spontaneous curvature, caused by the trans-to-cis isomerization of the azobenzene moieties. Subsequent irradiation with Vis light (λ = 470 nm) resulted in a partial cis-to-trans isomerization (~11% cis-2). Although the SAXS pattern did not recover fully (vide infra), the DLS analysis suggested reversible size changes upon irradiation with Vis light, which could be repeated multiple times upon alternating exposure to UV and Vis irradiation (Fig. 4a).

As expected from the SAXS and DLS results, dramatic conformational changes for SPspiral could also be observed by AFM and TEM after consecutive exposure to UV and Vis light. Exposure to UV irradiation transformed SPspiral (Fig. 4c,d) into stretched SP fibres with linear segments (SPlinear)UV (Fig. 4e,f), most likely by reducing the internal order as evident from the increased absorbance at λ = 410–430 nm (Supplementary Fig. 6b). Subsequent exposure of (SPlinear)UV to weak Vis light recovered most of the spontaneous curvature and internal order, affording randomly coiled SP fibres (SPrandom)Vis (Fig. 4g–i; Supplementary Fig. 6b). An AFM analysis confirmed that (SPlinear)UV and (SPrandom)Vis could be interconverted several times (Supplementary Fig. 10). Although the value of (SPrandom)Vis (rave = 12 ± 0.2 nm; θave = 267 ± 5°) and SPrandom (10.4 ± 0.2 nm; 370 ± 5°) are comparable, the value of (SPrandom)Vis resembles that of the elongated state. The recovery
and Vis light, respectively. (open-ended extended SPs with photo-switchable spontaneous curvature, wherein the reversible loss and recovery of the curvature are controlled by UV electron cloud models) of hydrogen-bonded hexamers of six change in its molecular shape as shown by the electron cloud model of hydrogen-bonded hexamers of six aggreg) as a function of temperature for cooling processes of 1 (c = 2.5 × 10⁻⁵ M, MCH) upon cooling at a cooling rate of 1 °C/min⁻¹. Upon cooling, the π-π transitions of both azobenzene (360–375 nm) and naphthalene moieties (380–430 nm to 430–500 nm) are bathochromically shifted, suggesting slipped π-π stacking arrangement (so called J-type stacking) of both chromophores. (h) Plots of molar fractions of aggregated molecules (κ_agg) as a function of temperature for cooling processes of 1 (c = 2.5 × 10⁻⁵ M, monitored at λ = 470 nm) and trans-2 (c = 2.5 × 10⁻⁵ M, monitored at λ = 455 nm) in MCH.

The entanglement can be evaluated in terms of sinuosity (S), defined as L/d, wherein d is the shortest distance between the two ends of a given fibre with the length L. The value of S for a perfectly straight fibre (S = 1.0) increases upon increasing the degree of entanglement. Histograms of L, d and S values for randomly chosen fibres of SP_spiral, (SP_linear)_Vis and (SP_random)_Vis are shown in Supplementary Fig. 12. The L of the above three SPs are widely distributed in the range of 100–1,500 nm, and the distribution showed no arguable difference before and after light irradiation. In contrast, the distribution of d displayed a great change before and after light irradiation. While the d of most SP_spiral and (SP_random)_Vis fibres are in the range of 100–500 nm, those of (SP_linear)_Vis fibres are distributed in a wider range up to 1,200 nm due to extension. As a result, most of the (SP_linear)_Vis fibres have S values in the range of 1.0–3.0, which illustrates their extended form, whereas those of SP_spiral and (SP_random)_Vis are more widely distributed in the range of 2–20, which illustrate the substantial difference in entanglement well.
Figure 3 | Morphological analysis of thermally obtainable SPs. (a) Schematic representation for the preparation of three SPs (SPlinear, SPrandom and SPspiral) with variable foldability and internal order. These SPs are prepared by cooling hot solutions of trans-2 (c = 1 × 10^{-4} M) from 90 to 20 °C using three different cooling protocols. (b–d) AFM images (scale bar, 100 nm) of SPs of trans-2 spin-coated from MCH solutions onto highly oriented pyrolytic graphite. (b) Linearly elongated SP (SPlinear) fibres were obtained from a cooling rate of ~100 °C min^{-1} (ice bath). (c) Randomly folded coils (SPrandom) were obtained using a cooling rate of ~15 °C min^{-1}; these coils change direction of the curves almost at every cycle. A few nanotoroids were also observed (red dotted circles). (d) Spirally folded SPs (SPspiral) fibres were obtained from a cooling rate of 0.1 °C min^{-1}; SPspiral consists predominantly of several spiral-millipede segments that are connected in a single continuous SP chain. (e–g) Morphological insight into SPrandom and SPspiral. (e) Illustration of radius (r) and turning angle (θ) of the spontaneous curvature in representative curved domains. (f) Histogram for the distribution of r obtained by analyzing >100 curved segments. (g) Histogram for the distribution of θ obtained by analyzing >100 curved domains.
**Mechanistic Insight.** The light-induced conformational changes of SPs could occur via two different pathways, that is, direct or indirect pathways (Fig. 5a). In the direct pathway, the azobenzene moieties, that are embedded in the SP chains, isomerize and change the stacking arrangement of hexamers, thus antagonizing the spontaneous curvature. In the indirect pathway, on the other hand, the conformational changes are induced by the photoisomerization of the azobenzene moieties. This results in a change of the overall shape of the SPs, which can be visualized using various imaging techniques (Figures 4 and 5).

**Figure 4 | Morphological analysis of photochemically transmuted SPs.** (a) DLS analysis of SP_{spiral} showing photoinduced changes in the distribution of the hydrodynamic diameters ($D_h$). SP_{spiral} solutions ($c = 1.0 \times 10^{-4} \text{ M}$) were successively exposed to UV and Vis light; after each irradiation step, sample solutions were diluted to $c = 2.5 \times 10^{-5} \text{ M}$ to reduce agglomeration. (b) Photoinduced change of the SAXS profiles of SP_{spiral} ($c = 1.0 \times 10^{-4} \text{ M}$) upon successive exposure to UV and Vis light. (c-h) AFM (c,e,g; scale bar, 200 nm) and TEM images (d,f,h; scale bar, 100 nm) of SP_{spiral} (c,d), (SP_{linear})_{UV} (e,f) and (SP_{random})_{Vis} (g,h). Samples were prepared by exposing SP_{spiral} ($c = 1.0 \times 10^{-4} \text{ M}$) to UV irradiation for 20 min, followed by exposure to weak Vis light for 20 min. (i) Schematic representation of photochemically transmuted SPs. Irradiation with UV light transmutes spirally folded SP_{spiral} into linear (SP_{linear})_{UV}, which is further transmuted into randomly folded (SP_{random})_{Vis} by exposure to Vis light. (SP_{linear})_{UV} and (SP_{random})_{Vis} are interconvertible by light.
monomer exchange does not occur or occurs very slowly, two individual SP morphologies will be retained after 24 h. (aggregate–monomer exchange occurs, a single morphology with mixed characters of the individual SPs will be observed. In the case where aggregate–monomer exchange does not occur or occurs very slowly, two individual SP morphologies will be retained after 24 h. (aggregate–monomer exchange directly through in situ the loss and recovery of spontaneous curvature should occur appreciable morphology change in the given time scale. Hence, reshuffling in our SP system, if it occurs, is too slow to show (Fig. 5c). This finding illustrates that the chain exchange/reshuffling on subpicosecond to picosecond timescales occur in the hand, the isomerization of azobenzene that typically occur for a given fibre, although each linear alignment may possess high levels of internal order. In case of the homogeneous mechanism, we should observe homogeneous changes in curvature for every loops simultaneously with the progress of isomerization (Fig. 6b). Conversely, the continuous mechanism should generate high levels of internal order throughout, which should result in the formation of very straight fibres (Fig. 6c). To address this issue unequivocally, we wanted to monitor the photoinduced issue unequivocally, we wanted to monitor the photoinduced morphology change for a SP with a more organized and homogeneous conformation, for example, a helical SP. The formation of increasingly organized structures as a function of decreasing cooling rates has already been discussed. Consequently, a very slow cooling rate (for example, 0.01 °C min⁻¹) may be able to afford more folded SPs, although this approach is experimentally impractical. Therefore, we changed the solvent system to a chloroform (CHCl₃)–MCH mixture, wherein the polar CHCl₃ should weaken the intermolecular interactions and guide the supramolecular polymerization towards more thermodynamic control. Eventually, we identified conditions (cooling rate: 0.1 °C min⁻¹; c = 1.0 × 10⁻⁴ M; CHCl₃:MCH = 15:85, v/v; Supplementary Discussion) that were able to afford helically folded SPhelical (Fig. 6d; Supplementary Figs 13 and 14). While most SPhelical are partially unfolded, their helical handedness is retained throughout the entire fibre to afford left- (M) and right-handed (P)-SPhelical (Supplementary Fig. 14d,e), suggesting that a highly cooperative supramolecular polymerization occurred at a higher-order level. A SAXS analysis of an SPhelical solution exhibited maxima/minima at Q = 0.3–1.2 nm⁻¹, arising from the spontaneous curvature (rave = 10.0 ± 0.2 nm) of the helical loops (Supplementary Fig. 15). The investigation of the unfolding process of SPhelical confirmed the occurrence of a random isomerization of the azobenzene moieties, which reduces the overall internal order in the fibres. The AFM images (Fig. 6d–h; Supplementary Fig. 16).
Figure 6 | Light-induced unfolding of helical SP fibres and refolding of the resulting straight fibres into randomly coiled fibres. (a-c) Schematic representation of three possible mechanisms for unfolding of SP<sub>helical</sub> with intermediate and final states. (a) Random mechanism, where photoinduced loss of curvature starts randomly at several points within a fibre. (b) Homogeneous mechanism, where loss of curvature occurs homogeneously at every loop simultaneously. (c) Continuous mechanism, where loss of curvature starts at one terminus and proceeds continuously towards the other terminus, leading to very straight fibre with high degree of internal order. (d-h) AFM images showing an unfolding process of SP<sub>helical</sub> into (SP<sub>linear</sub>)<sub>UV</sub> upon gradually increasing the cis-2 content by irradiation with UV light. (i) AFM image of (SP<sub>random</sub>)<sub>Vis</sub> obtained from irradiation of (SP<sub>linear</sub>)<sub>UV</sub> with weak Vis light for 20 min. Exposure to Vis light is able to steadily recover the spontaneous curvature. (j) AFM image of (SP<sub>linear</sub>)<sub>Vis</sub> obtained from irradiation of (SP<sub>linear</sub>)<sub>UV</sub> with intense Vis light for 30 s. Even though irradiation with Vis light causes a drop of cis-2 content from 30 to 11%, the spontaneous curvature does not recover immediately to produce straight fibres (kinetic product). (k) AFM image of (SP<sub>random</sub>)<sub>Vis</sub>, which develops spontaneously and slowly from (SP<sub>linear</sub>)<sub>Vis</sub> over 20 h. Scale bar, 100 nm (d-f) or 200 nm (g-k). (l) Schematic illustration of the loss and recovery of spontaneous curvature upon exposure to UV and Vis light, respectively. The curved stacks transform directly into linear stacks via trans-to-cis isomerization of the azobenzene moieties, as the non-planar hexamers involving cis-2 cannot stack with rotational offset due to the steric repulsion arising from the cis-azobenzene moieties. For hexamers involving cis-2, only linear stacking (translational displacement) is possible. The recovery of the spontaneous curvature by Vis light depends on the intensity of the light source.
show the morphology changes of SP_{helical} as a function of the content of cis-2, which is controlled by irradiation with UV light. The unfolding occurs in a highly controlled and linear fashion upon increasing the content of cis-2. At 12\% cis-2, unfolded domains occur locally (Fig. 6e), and further increase up to 16\% cis-2 produces (SP_{random})_{UV} (Fig. 6f). At 20\% cis-2, most helical domains disappear to generate waving fibres ($\theta_{ave} < 180^\circ$) (Fig. 6g). In the presence of CHCl$_3$, the content of cis-2 can be further increased, and a drastic change in curvature occurs up to 30\% cis-2, where most of the curvature is lost to afford more extended (SP_{linear})_{UV} fibres (Fig. 6h). However, (SP_{linear})_{UV} fibres are not very straight (Fig. 6h), again supporting the random isomerization occurs in this case. As a proof of principle, cis-2 monomers (in fact a mixture of trans-2-cis-2 = 60:40) were subjected to thermal polymerization conditions, which afforded very straight fibres with long-range domains (~500 nm) as a result of cooperatively scattered of well-distributed cis containing rosettes by aligning all cis-arms linearly (Supplementary Figs 17 and 18).

With these highly extended (SP_{linear})_{UV} fibres in hand, we examined if the recovery of spontaneous curvature occurs linearly with gradual decrease in the content of cis-2. When (SP_{linear})_{UV} was exposed to weak Vis light, while progressively diminishing the cis-2 content (Supplementary Fig. 19), the spontaneous curvature gradually recovered to produce (SP_{random})_{Vis} fibres (Fig. 6i; Supplementary Fig. 20). Then, we wanted to find out if an abrupt reduction of the cis-2 content in the planar trans-2 hexamers would lead to an immediate formation of their thermodynamically preferred stacking mode (spontaneous curvature) or if the kinetically preferred stacking mode (linear stacks) would be maintained for some time (Fig. 6i). Interestingly, an exposure of (SP_{linear})_{UV} to intense Vis light did not induce any apparent morphology change (Fig. 6i). This result illustrates that the photochemical formation of kinetic (SP_{linear})_{Vis} fibres lacks the high degree of internal order that is required to generate spontaneous curvature, observed for thermally obtained SP_{linear}. (SP_{linear})_{Vis} slowly converts into (SP_{random})_{Vis} over the course of 20 h (Fig. 6k; Supplementary Fig. 21), which is similar to the kinetic product SP_{linear}.

Discussion

In conclusion, this study demonstrates that a SP approach may confer 1D fibres that exhibit levels of higher-order conformations similar to those of polypeptides. The strong advantage of this strategy is that these higher-order conformations can be controlled by modulating the internal staking order by non-invasive external stimuli such as light. The observed nonlinear morphological change of photochemically regulated fibres upon exposure to intense Vis light could be useful for the synthesis of supramolecular nanomaterials that may be able to store photon energy in kinetically favoured structures. The remote control over the internal order of non-equilibrated/robust SP fibres to execute conformational changes may advance the frontiers of SP towards applications by mimicking the functionality of biopolymer. Although the photoinduced disassembly–reassembly of 1D aggregates has already been realized, the light-induced unfolding–refolding approach presented herein guides supramolecular as well as polymer chemistry towards unchartered territory. However, in the present study, the unfolding–refolding of helical coils is not fully reversible with respect to the first refolding. Achieving complete light-controlled reversibility between helical coils and unfolded structures represents the next goal of our research. This may be accomplished by inducing complete and continuous back-isomerization of azobenzene from one termini to the other of the non-equilibrated SP fibres.

Methods

Materials. Compound 2 was synthesized according to Supplementary Fig. 23. For characterization, $^1$H NMR, $^{13}$C NMR and HRMS of compound 2 were included in Supplementary Methods. Commercially available reagents and solvents were of reagent grade and used without further purification. MCH and CHCl$_3$ were the solvents used as media for supramolecular polymerization, were all spectral grade and used without further purification.

Small-angle X-ray scattering measurements. SAXS measurements were carried out at BL-6A at the Photon Factory of the High Energy Accelerator Research Organization (KEK) in Tsukuba, Japan.$^{25}$ The sample solutions were placed in the stainless-steel sample cell with the light path length of 1 mm and 20-μm-thick quartz glass windows. The cell was maintained at around 293 K. PILATUS3 1 M (DECTRIS) was used as a detector. The X-ray wavelength was adjusted to 1.5 Å, and the sample-detector distance was 481 and 1966 mm, calibrated using a silver behenate as a standard sample. These settings provided a detectable Q-range of order 0.2–15 and 0.05–2.5 nm$^{-1}$, respectively. Sixty frames were collected with the exposure time of 10 s. Since any radiation damages were not seen in all data, all the data in each sample were averaged to improve signal-to-noise ratio. The total integration time was 600 s. The two-dimensional scattering data were circularly averaged to convert into the 1D scattering intensity data, normalizing the scattering intensity to the absolute intensity scale (cm$^{-1}$) by using water as a reference. The background subtraction was also performed to get the final scattering intensities. The magnitude of the scattering vector is given by $Q = (4\pi/\lambda) \sin \theta/2$, where $\lambda$ is the X-ray wavelength and $\theta$ is the scattering angle. The software XAngler was used for these data processing.$^{26}$

Photo-irradiation experiments of SPSs. For the trans-to-cis isomerization of trans-2 in SP_{spiral} a UV LED lamp ($\lambda = 365 \text{ nm}$) with the intensity of 17 mW cm$^{-2}$ at a distance of 5 cm and using its maximum intensity was used as a light source. The lamp was placed at a distance of 1 cm from a quartz cuvette (path length: 1 mm) containing SP solution and the UV light was irradiated. Under this condition, an apparent photostationary state (PSS) is typically achieved within 20 min of UV exposure. The photoinduced unfolding of SP_{linear} into (SP_{random})_{UV} was performed under the careful control of increasing content of cis-2 by the LED lamp with increasing irradiation time and regulating the light intensity upon changing the distance between the cuvette and the light source. When solutions of SPS consisting of trans-2 were exposed to the UV light, a decrease in absorbance around 370 nm was observed in UV–Vis spectra, indicating the extent of photoisomerization of azobenzene unit. The content of cis-2 in UV-irradiated SPSs in MCH was determined by comparing the decrease in absorbance intensity of the photoisomerization of azobenzene unit. The content of cis-2 was calculated within the article and its Supplementary Information files, and from the corresponding author upon reasonable request.

Data availability. All data supporting the findings of this study are available within the article and its Supplementary Information files, and from the corresponding author upon reasonable request.

References

1. Aida, T., Meijer, E. W. & Stupp, S. I. Functional supramolecular polymers. Science 335, 813–817 (2012).
2. Brunsved, L., Folmer, J. B. B., Meijer, E. W. & Sijbesma, R. P. Supramolecular polymers. Chem. Rev. 101, 4071–4097 (2001).
3. Hoeben, F. J., Jonkheijm, P., Meijer, E. W. & Schenning, A. P. H. J. About supramolecular assemblies of $\pi$-conjugated systems. Chem. Rev. 105, 1491–1546 (2005).
4. De Greef, T. F. A. & Meijer, E. W. Supramolecular polymers. Nature 453, 173 (2008).
5. Chen, Z., Lohr, A., Saha-Möller, C. R. & Würthner, F. Self-assembled $\pi$-stacks of functional dyes in solution: structural and thermodynamic features. Chem. Soc. Rev. 38, 564–584 (2009).
6. Rosen, B. M. et al. Dendron-mediated self-assembly, disassembly, and self-organization of complex systems. Chem. Rev. 109, 6275–6540 (2009).
7. Babu, S. S., Praveen, V. K. & Ajayaghosh, A. Functional $\pi$-gellers and their applications. Chem. Rev. 114, 1971–2019 (2014).
8. Krieg, E., Bastings, M. M. C., Besenius, P. & Rybtchinski, B. Supramolecular polymers in aqueous media. Chem. Rev. 116, 2414–2477 (2016).
9. Ogì, S., Sugiyasu, K., Manna, S., Samitsu, S. & Takeuchi, M. Living supramolecular polymerization realized through a biomimetic approach. Nat. Chem. 6, 188–195 (2014).
10. Kang, J. et al. A rational strategy for the realization of chain-growth supramolecular polymerization. Science 347, 646–651 (2015).
11. Engelkamp, H., Middelbeek, S. & Nolte, R. J. M. Self-assembly of disk-shaped molecules to coiled-coil aggregates with tunable helicity. Science 284, 785–788 (1999).
12. Hinselberg, J. H. et al. Helical self-assembled polymers from cooperative stacking of hydrogen-bonded pairs. Nature 407, 167–170 (2000).
13. Yao, S., Beginn, U., Gress, T., Lysetska, M. & Würthner, F. Supramolecular polymerization and gel formation of bis(merocyanine) dyes driven by dipolar aggregation. J. Am. Chem. Soc. 126, 8336–8348 (2004).
14. Borzsonyi, G. et al. Water-soluble J-type rosette nanotubes with giant molar ellipticity. J. Am. Chem. Soc. 132, 15136–15139 (2010).
15. Yamauchi, M., Ohba, T., Karatsu, T. & Yagai, S. Photoreactive helical nanoaggregates exhibiting morphology transition on thermal reconstruction. Nat. Commun. 6, 8936 (2015).
16. Engslander, S. W. & Mayne, L. The nature of protein folding pathways. Proc. Natl Acad. Sci. USA 111, 15873–15880 (2014).
17. Percec, V. et al. Controlling polymer shape through the self-assembly of dendritic side-groups. Nature 391, 161–164 (1998).
18. Yashima, E., Maeda, K. & Okamoto, Y. Memory of macromolecular helicity assisted by interaction with achiral small molecules. Nature 399, 449–451 (1999).
19. Nakano, T. & Okamoto, Y. Synthetic helical polymers: conformation and mechanism to tune pitch in supramolecular helices. Acc. Chem. Res. 34, 9–17 (2001).
20. Pieroni, O., Fissi, A., Angelini, N. & Lenci, F. Photoreversible polypeptides. Angew. Chem. Int. Ed. 50, 12559–12563 (2011).
21. Nelson, J. C., Saven, J. G., Moore, J. S. & Wolynes, P. G. Solvophobically driven folding of nonbiological oligomers. Science 279, 1793–1796 (1997).
22. Bendl, V., Huc, L., Khoury, R. G., Krische, M. J. & Lehn, J.-M. Interconversion of single and double helices formed from synthetic molecular strands. Nature 407, 720–722 (2000).
23. Dolain, C., Maurizot, V. & Huc, I. Protonation-induced transition between two distinct helical conformations of a synthetic oligomer via a linear intermediate. Angew. Chem. Int. Ed. 42, 2378–2374 (2003).
24. Khan, A., Kaiser, C. & Hecht, S. Prototype of a photoswitchable foldamer. Angew. Chem. Int. Ed. 45, 1878–1881 (2006).
25. Hill, D. J., Mio, M. J., Prince, R. B., Hughes, T. S. & Moore, J. S. A field guide to foldamers. Chem. Rev. 101, 3893–4011 (2001).
26. Gelfman, S. H. Foldamers: a manifesto. Acc. Chem. Res. 31, 173–180 (1998).
27. Guichard, G. & Huc, I. Synthetic foldamers. Chem. Commun. 49, 5933–5941 (2013).
28. Yamada, S. et al. Self-organization of hydrogen-bonding naphthalene chromophores into J-type nanorings and H-type nanorods: impact of regioisomerism. Angew. Chem. Int. Ed. 51, 6643–6647 (2012).
29. Hollamby, M. J. et al. Simultaneous SAXS and SANS analysis for the detection of toroidal supramolecular polymers composed of noncovalent supermacromolecules in solution. Angew. Chem. Int. Ed. 55, 9890–9893 (2016).
30. Yagai, S. & Kitamura, A. Recent advances in photoresponsive supramolecular self-assemblies. Chem. Soc. Rev. 37, 1520–1529 (2008).
31. Li, L.-s., Jiang, H., Messmore, B. W., Bull, S. R. & Stupp, S. I. A torsional strain mechanism to tune pitch in supramolecular helices. Angew. Chem. Int. Ed. 46, 5873–5876 (2007).
32. Kameta, N., Masuda, M. & Shimizu, T. Photoinduced morphological transformations of soft nanotubes. Chem. Eur. J. 21, 8832–8839 (2015).
33. Yagai, S. et al. Control over hierarchy levels in the self-assembly of stackable nanorotoids. J. Am. Chem. Soc. 134, 18205–18208 (2012).
34. Kundu, P. K. & Klein, R. Watching single molecules move in response to light. ACS Nano 8, 11913–11916 (2014).
35. Jonkheijm, P., Van der Schoot, P., Schenning, A. P. H. J. & Meijer, E. W. Probing the solvent-assisted nucleation pathway in chemical self-assembly. Science 313, 80–83 (2006).
36. De Greef, T. F. et al. Supramolecular polymerization. Chem. Rev. 109, 6586–6574 (2009).
37. Korevaar, P. A. et al. Pathway complexity in supramolecular polymerization. Nature 481, 492–496 (2012).
38. Ogì, S., Sugiyasu, K., Manna, S., Samitsu, S. & Takeuchi, M. Living supramolecular polymerization realized through a biomimetic approach. Nat. Chem. 6, 188–195 (2014).
39. Murata, K. et al. Thermal and light control of the sol-gel phase transition in cholesterol-based organic gels. Novel helical aggregation modes as detected by circular dichroism and electron microscopic observation. J. Am. Chem. Soc. 116, 6664–6696 (1994).
40. Kawasaki, T., Tokuhiko, M., Kimizuka, N. & Kunitake, T. Hierarchical self-assembly of chiral complementary hydrogen-bond networks in water: reconstitution of supramolecular membranes. J. Am. Chem. Soc. 123, 6792–6800 (2001).
41. Tamai, N. & Miyasaka, H. Ultrafast dynamics of photoswitchable helices. Chem. Rev. 100, 1875–1890 (2000).
42. Albertazzi, L. et al. Probing exchange pathways in one-dimensional aggregates with super-resolution microscopy. Science 344, 491–495 (2014).
43. Yagi, S., Ogi, S., Stepanenko, V., Thein, J. & Würthner, F. Impact of alkyl spacer length on aggregation pathways in kinetically controlled supramolecular polymerization. J. Am. Chem. Soc. 138, 670–678 (2016).
44. Mahesh, S., Gopal, A., Thirumalai, R. & Jayagough, A. Light-induced oscillatory ripening of organic nanodots to rods. J. Am. Chem. Soc. 134, 7227–7230 (2012).