Self-Assembly

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Photocontrol over Cooperative Porphyrin Self-Assembly with Phenylazopyridine Ligands**

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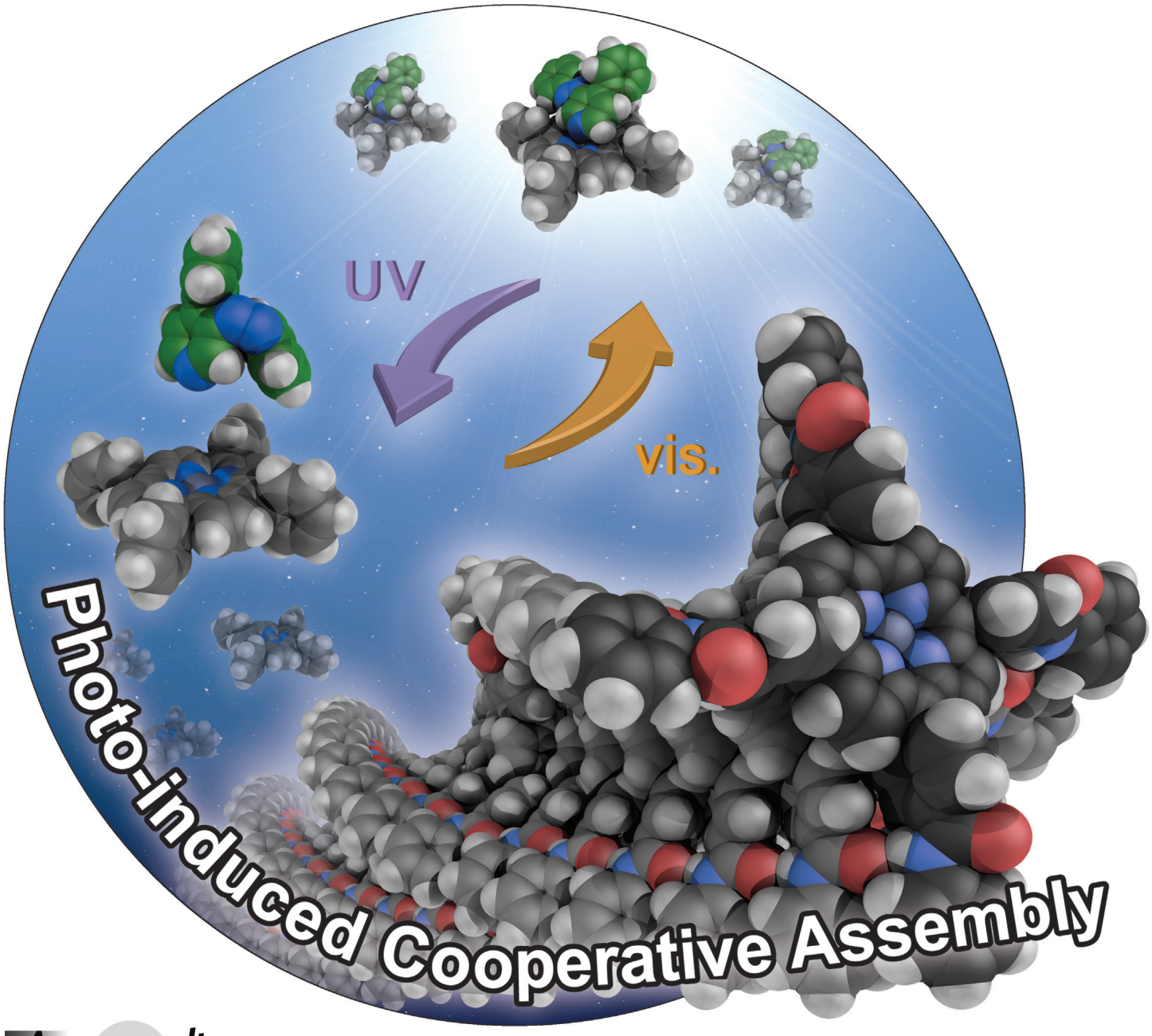

The use of external stimuli to control the self-assembly of multicomponent systems has great potential to interconvert the system's morphology and functions.[1] In this area, an interesting field is the dynamic photoregulation of artificial self-assembling systems[2] that comprises archetypical elements for biological mechanical activities, such as cell migration and mass transfer. In biological systems, the interconversion of small molecules as secondary components, such as GTP and GDP, brings about the dynamic character of supramolecular structures, for instance the dynamic instability of microtubules.[3] A major challenge in chemistry is to regulate artificial supramolecular structures in a similar way, in which multiple components interact with each other and dynamically alter the structures and functions of the system. Similar to biological systems, the dynamic response will be significantly enhanced in cooperative mechanisms in which self-assembly features distinctive nucleation and elongation events. In contrast, most artificial systems show non-cooperative or isodesmic aggregation behavior.[4] So far, many intriguing photostimulated self-assembly approaches have been published; in these approaches photochemical switching is performed on the supramolecular building block itself.[2] We now describe a successful example of the photoregulation of the cooperative self-assembly of zinc porphyrins by photochromic auxillaries, which are based on phenylazopyridine axial ligands.

Previously, we reported the hydrogen-bond-assisted and highly cooperative self-assembly of chiral zinc porphyrin **S**-Zn in the presence of pyridine (Figure 1a).[5] In methylcyclohexane (MCH), **S**-Zn forms helical, cofacial stacks upon the formation of four intermolecular hydrogen bonds. Axial coordination of pyridine sterically blocks one porphyrin face for hydrogen bonding, thus resulting in the formation of hydrogen-bonded, pyridine-capped dimers. Thermodynamic modeling revealed that the cooperativity of the system played a prime role in the mechanism that led to a pronounced dilution-induced self-assembly effect. Herein, we employ a phenylazopyridine-based axial ligand (**1**, Figure 1a) to establish a photoresponsive supramolecular (de)polymerization process. The concept of photoresponsive ligands was developed by the groups of Inoue and Otsuki and recently this binding–switching event has been applied to regulate the magnetic bistability of nickel metals inside porphyrin monomers.[6] In our case, however, photoisomerization of *trans*-**1** to *cis*-**1** destabilizes the coordinated state of the zinc center inside the porphyrin owing to steric hindrance of the bulky mesityl groups. Therefore, disassociation of the complex

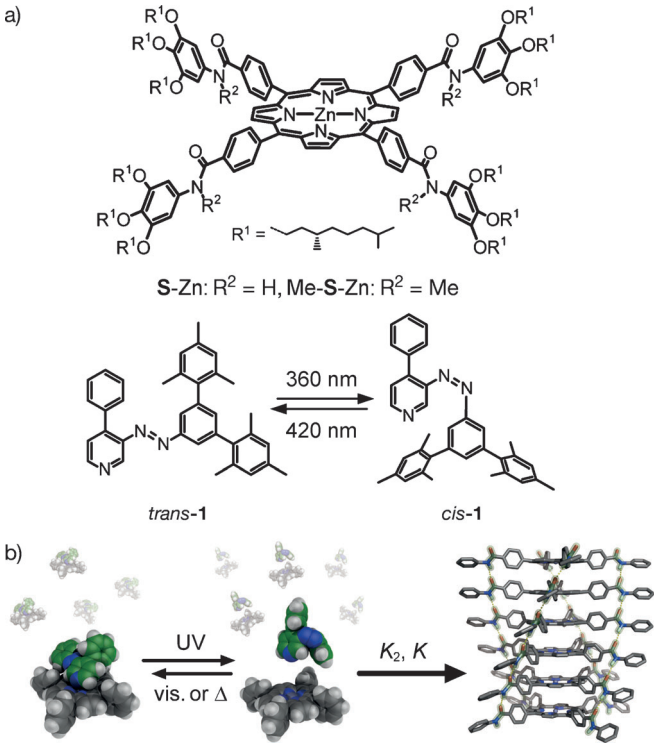

Figure 1. a) Molecular structures of chiral amide-functionalized zinc porphyrin derivative **S**-Zn, *N*-methylated model compound Me-**S**-Zn, and *cis*/*trans* isomers of phenylazopyridine **1**. b) Schematic representation of photoinduced cooperative porphyrin self-assembly upon the formation of a fourfold hydrogen-bond network.

results in the release of free **S**-Zn monomers that subsequently self-assemble (Figure 1b). As a result of the cooperativity of the system, the change in the conformation of the ligand provides an appropriate stimulus to achieve a significant change of the self-assembled state. This highly sensitive process therefore requires a delicate approach, which we present herein. After ligand optimization,[7] we first analyzed the optical properties and the isomerization of **1** in the absence of zinc porphyrins, after which we evaluated its complexation with a zinc porphyrin monomer model compound. We then introduced these parameters in a multiple-equilibrium thermodynamic model to deduce the photoregulation of the **S**-Zn self-assembly. Lastly, we verified the simulations by photoinduced switching experiments on mixtures of **S**-Zn and **1**.

The photoisomerization properties of **1** in MCH were investigated. Pure *trans*-**1** shows a characteristic strong π–π* absorption band at 330 nm and a weak n–π* band at 470 nm. Upon irradiation with 360 nm light, the π–π* band strongly decreases, while another prominent n–π* band appears at 442 nm (Figure 2a). An almost identical spectrum was obtained upon irradiation at 420 nm; this result is indicative of a high photostationary state of the *trans* isomer (PSS_{trans}). The thermal stability of *cis*-**1** was investigated by monitoring the spectral changes at different temperatures. Based on the Eyring plot of the thermal fading rates, the activation free energy of the thermal reversion process from *cis*-**1** to *trans*-**1** was calculated at $\Delta G^{\ddagger} = 105.3\ kJ\,mol^{-1}$ at 25 °C ($\Delta H^{\ddagger} =$

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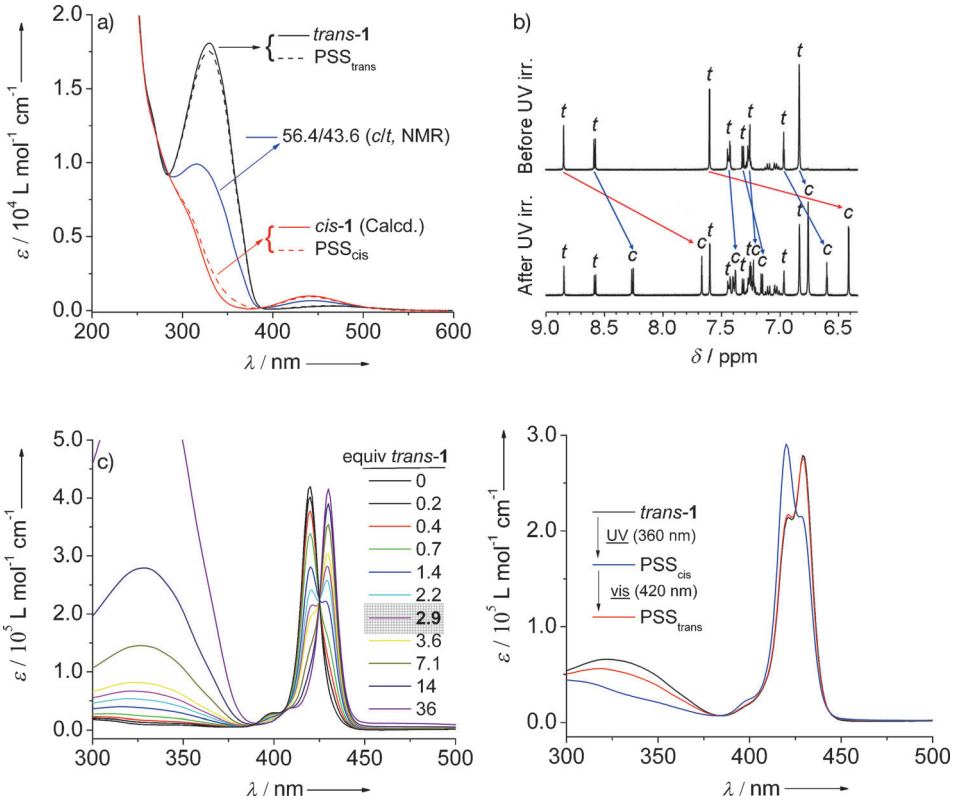

Figure 2. a) UV/Vis spectral change of **1** at RT in MCH upon photoisomerization measured for PSS_{cis}, PSS_{trans}, pure *trans*-**1**, and the diluted NMR sample at *cis*/*trans* = 56.4:43.6. The spectrum of *cis*-**1** is calculated from the last two spectra. b) ^{1}H NMR spectra acquired at 25 °C of **1** in [D_{14}]-MCH before (top) and after (bottom) UV irradiation. c) UV/Vis spectra of Me-**S**-Zn in MCH (1.75×10^{-5} M) at RT with different molar equivalents of *trans*-**1** (from 0 to 36 equiv). d) UV/Vis spectra at RT before/after UV (360 nm) and subsequent Vis (420 nm) photoirradiation of the sample containing 2.9 equivalents of **1**. Conversion ratio at the PSS_{cis} was estimated at 76.9 ± 0.005 %.

88.4 ± 1.9 kJ mol^{-1}, $\Delta S^{\neq} = -56.8 \pm 5.7$ J mol^{-1}).[8] Based on these parameters, the halflife of the *cis*-**1** is $\tau_{1/2} = 3.5$ days at room temperature; this halflife is highly appropriate for switching a self-assembling system that features slow supramolecular dynamics.[9] In addition, it allows for a reliable determination of the conversion ratios by UV/Vis after dilution of an irradiated NMR sample.[6c] Upon irradiation at 360 nm of a sample of *trans*-**1** in [D_{14}]-MCH, *cis*-**1** was generated, as determined from the NMR spectra, in which upfield shifts were seen for all protons, most prominently for those at the *ortho*-positions with respect to the diazenyl group (Figure 2b). After determination of the conversion ratio of the NMR sample, the sample was diluted in MCH and its acquired UV/Vis spectrum was combined with the spectrum of the initial *trans*-**1** to construct the spectrum of pure *cis*-**1**. By using a spectral fitting procedure, the conversion ratio of **1** was determined to be 95 % (*cis*/*trans* = 95:5) at PSS_{cis} and 97 % (*cis*/*trans* = 3:97) at PSS_{trans} upon irradiation at 360 and 420 nm, respectively. The high conversion ratios are most likely related to the lack of spectral overlap of both isomers, thereby allowing selective excitation at 360 and 420 nm.

The binding constant of *trans*-**1** was determined by a titration experiment with *N*-methylated porphyrin model compound Me-**S**-Zn.[5] At a concentration of 1.75×10^{-5} M of Me-**S**-Zn, the titration of *trans*-**1** led to a two-state equilibrium between free monomer ($\lambda_{max} = 420$ nm) and a 1:1 complex ($\lambda_{max} = 430$ nm); this result was corroborated by an isosbestic point at 425 nm (Figure 2c). The binding constant of *trans*-**1** was estimated at $K_{trans} = 36.000 \pm 730\ M^{-1}$, after simultaneous curve-fitting of the binding isotherms deduced from the Soret band of both species.[8] The binding constant of *cis*-**1** was determined by a successive photoirradiation experiment. Upon UV irradiation of a solution containing 2.9 molar equivalents of *trans*-**1**, the absorbance at 330 nm decreased, which is indicative of the *trans*→*cis* isomerization. Concomitantly, the Soret absorbance of the 1:1 complex at 430 nm decreases, while the Soret absorbance for free Me-**S**-Zn at 420 nm increases (Figure 2d). Indeed, weaker binding for *cis*-**1** was evidenced by the instantaneous generation of free monomers and according to a full-spectrum fitting procedure,[8] the conversion ratio was determined together with the molar ratio of free/complexed Me-**S**-Zn. After spectral fitting, the binding constant of *cis*-**1** was estimated at $K_{cis} = 8.100 \pm 150\ M^{-1}$, which is a 4.4 fold reduction in binding strength upon photoisomerization. Notably, PSS_{cis} decreased by ± 20 % in the presence of Me-**S**-Zn, possibly owing to spectral overlap between the two.

After determination of the binding constants K_{trans} and K_{cis}, the previously reported multiple-equilibrium model was modified to assess the switchability of the cooperative self-assembly upon photoirradiation of the ligand (Figure 3a).[5] The model considers the cooperative assembly of the porphyrins, which is described by a moderate dimerization constant K_2 and a more-preferable elongation constant K. Free monomers (**S**-Zn) are removed from the stacking process by complexation described by K_{trans} and K_{cis}, and the resulting Me-**S**-Zn:*trans*/*cis*-**1** (1:1) complexes dimerize; this dimerization is described by K_d.[10] Model simulations demonstrate that the binding constant ratio $\gamma = K_{trans}/K_{cis}$ assisted by high conversion ratios is an important factor to enhance the photoswitchability of the entire system. On the other hand, the magnitude of binding constants and porphyrin concentration have less influence on self-assembly since they merely affect the critical amount of ligand necessary to fully depolymerize the stacks.[8]

The simulation of the pyridine-induced stack-dimer transition provides insights into the switchability of the

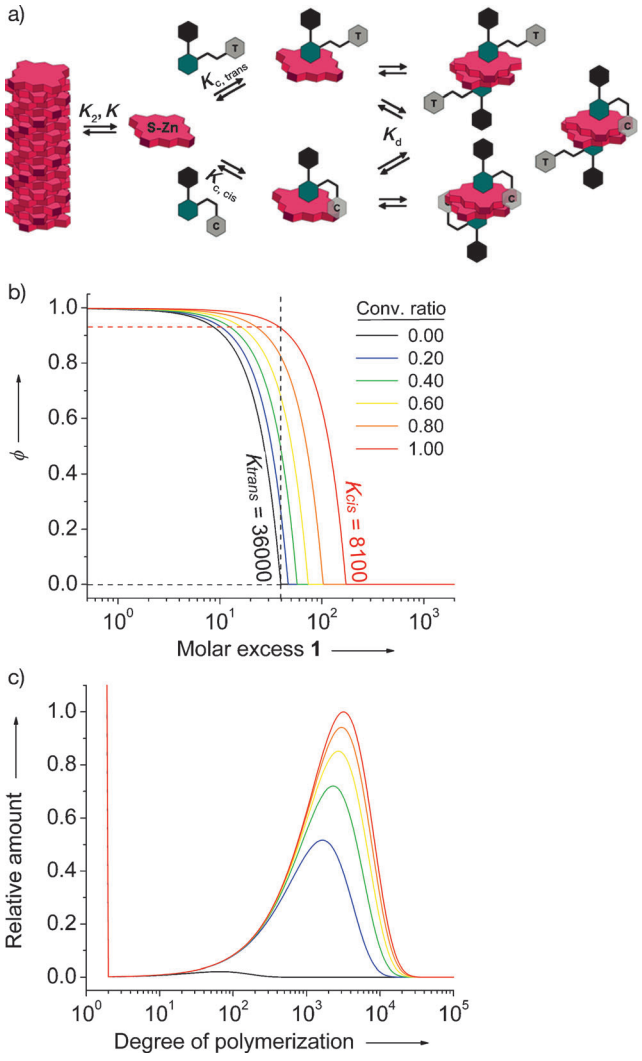

Figure 3. a) Multiple-equilibrium model of the thermodynamic system comprising the cooperative aggregation of **S**-Zn stacks, free monomers, **S**-Zn:*trans*/*cis*-**1** (1:1) complexes, and their hydrogen-bonded homo/hetero dimers. b) Fraction of porphyrin stacks (ϕ) at 4.0×10^{-5} M against the molar excess of ligand at different conversion ratios (stack–dimer transition). c) Size distribution of the porphyrin stacks at 4.0×10^{-5} M with a fixed excess of 40 equivalents of **1** at different conversion ratios. Thermodynamic parameters applied in the simulations: $K_2 = 685\ M^{-1}$, $K = 1.37\times10^7\ M^{-1}$, $K_d = 1.1\times10^6\ M^{-1}$, $K_{trans} = 3.6\times10^4\ M^{-1}$ and $K_{cis} = 8.1\times10^3\ M^{-1}$ ($\gamma = 4.4$).

fraction of aggregated porphyrins (ϕ; Figure 3b). At a porphyrin concentration of 4.0×10^{-5} M, a critical ligand excess of 40 equivalents of *trans*-**1** will lead to the full depolymerization of the porphyrin stacks ($\phi = 0$). At $\gamma = 4.4$, the simulation shows a considerable change in the fraction of aggregated monomers; $\phi = 0.02$ at PSS_{trans} (97%), whereas this value increases to $\phi = 0.90$ at PSS_{cis} (95%). Obviously, this change is accompanied by a difference in aggregate size. At 40 equivalents of **1**, only 2% of short stacks are predicted at PSS_{trans}, whereas an average stack length of 3100 monomers is calculated at PSS_{cis} (Figure 3c). In contrast, when analyzed with the isodesmic model ($K_2 = K$), photoinduced isomerization only leads to a stack size of 22, thereby showing the marked effect that cooperative self-assembly has on aggregate size.[8] Furthermore, the characteristically sharp transition for the latter mechanism fulfils a prominent role in switching. Strengthened by high conversion ratios, the relatively weak stimulus characterized by γ provides, nevertheless, high-contrast switching properties.

The simulated behaviour exhibited by the system was experimentally verified by a titration experiment of *trans*-**1** to **S**-Zn at 4.0×10^{-5} M and subsequent irradiation experiments of a sample with the critical amount of ligand excess. In the UV/Vis spectra acquired at room temperature (Figure 4a, upper panel), titration of *trans*-**1** led to an isosbestic point in the transition of the Soret band from stacks ($\lambda_{max} = 390$ nm) to dimer complexes ($\lambda_{max} = 428$ nm). Depolymerization was also evidenced by the disappearance of the Cotton effect at $\lambda_{max} = 392$ nm, while a weak CD effect ($\Delta\varepsilon_{max} = 30\ L\,mol^{-1}\,cm^{-1}$) appears in the dimer absorbance region (Figure 4a, lower panel). As observed in the titration curve (Figure 4b) the dimer spectrum has fully developed after the addition of ± 50 equivalents *trans*-**1**, while a critical amount of ligand excess of only 40 equivalents was estimated by the simulation (see above). Considering the high stimuli responsiveness of the system owing to its cooperativity, this difference could be related to minor experimental deviations, slow supramolecular dynamics, and temperature fluctuations. For the latter, we remarkably observe that a lower critical amount of ligand is required when the temperature is slightly raised from room temperature to 30 °C (Figure 4b).[11] Since the CD intensity of **S**-Zn stacks is hardly affected at this concentration, we expect a stronger response in CD activity when photoirradiation is performed at 30 °C. Considering the inability to reach high conversion ratios in the presence of porphyrins (see above), we investigated a sample containing 54 equivalents of **1**.

After irradiation of the sample with 360 nm light, the generation of *cis*-**1** was evidenced by a decreased absorbance at 330 nm (Figure 4c). After a delay of ± 30 minutes after reaching PSS_{cis} (estimated at $\pm 90\%$), the absorbance at 428 nm decreases, while the aggregate Soret band at 390 nm increases. Concomitantly with the latter, the CD signal at 392 nm increases up to an intensity of 81% relative to the reference solution of pure **S**-Zn in the absence of **1** (Figure 4d). Successive irradiation with 420 nm light shows the reversal of the process with a similar time delay owing to the supramolecular dynamics. At PSS_{trans}, only 1% magnitude of the CD signal remains, hence this photoisomerization process controls the fraction of stacked porphyrin monomers between 1 and 81%.

As well as differences in optical activity, we also analyzed changes in rheological properties. Supported by the simulation results, the reversible photo-(de)polymerization of fibrous aggregates of up to 3100 monomers should affect the solution viscosity; we indeed observed a change in the viscosity upon photoswitching a sample containing 47 equivalents of **1** (Figure 4e). The reference solution of pure **S**-Zn at 4.0×10^{-5} M in MCH has a viscosity of 0.685 cP at 30 °C, 10% higher than the solvent. After the addition of 1.88 mM *trans*-**1** the viscosity was lowered to 0.637 cP, which is nearly identical to that of pure MCH. After UV irradiation and

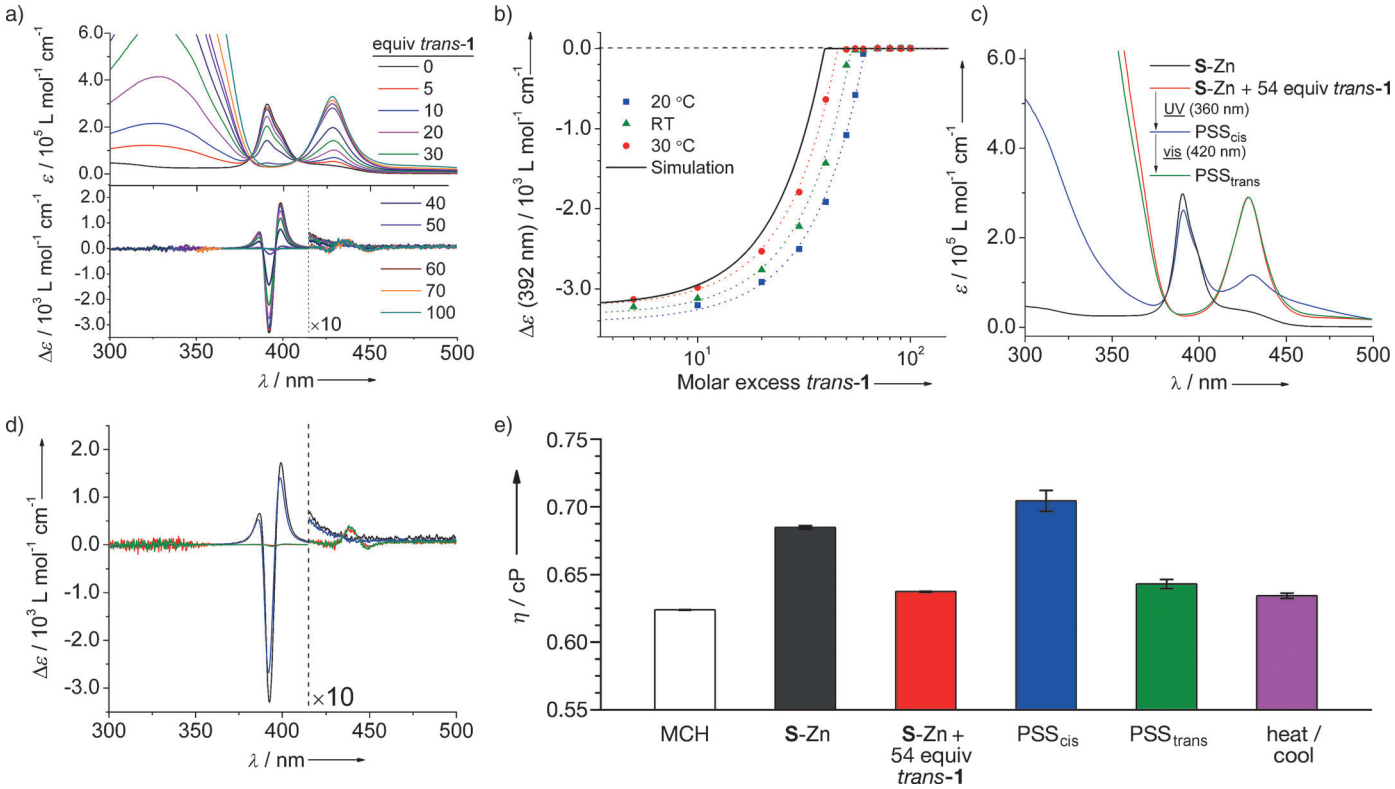

Figure 4. a) UV/Vis (top) and CD (bottom) spectra of **S**-Zn in MCH (4.0×10^{-5} M) at RT with different molar equivalents of *trans*-**1** (from 0 to 100 equiv). b) Titration curve probed by CD spectroscopy at 392 nm at RT, 20 °C, and 30 °C overlaid with the simulation shown in Figure 3 b. The dotted lines are shown to guide the eye. UV/Vis (c) and CD (d) spectra of **S**-Zn at 4.0×10^{-5} M and 30 °C in the absence of ligand and in the presence of 54 equivalents of *trans*-**1** before irradiation, at PSS_{cis} and PSS_{trans}. e) Change in viscosity of the corresponding solutions.

subsequent annealing at 30 °C, the viscosity increased to 0.704 cP at PSS_{cis}, whereas successive irradiation with visible light caused a decrease to 0.643 cP. Switching from PSS_{trans} to pure *trans* by heating and cooling the solution resulted in a slight decrease in the viscosity towards an identical value corresponding to the initial state of depolymerized **S**-Zn in the presence of pure *trans*-**1**.

In conclusion, we have introduced control over the cooperative porphyrin self-assembly with a photoresponsive ligand that provides sufficient stimulus to regulate the formation of fibrous aggregates in the range of 1 to 81 %, resulting in a viscosity change. The steady-state properties of the system were assessed by the introduction of photochromic parameters in a multiple-equilibrium model, which gave valuable insights into the system in terms of feasibility, experimental design, and sensitivity. This approach gives a new direction to the well-established field of photoswitching of organic molecules and will open new avenues to functions related to out-of-equilibrium situations. Investigations along these lines are underway.

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[7] The design constraints in the development of **1** will be discussed in a manuscript in preparation.
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[10] As the dimerization process is driven by hydrogen bonds only, K_d is assumed to be independent on the ligand type, hence the value for pyridine is used in the current model. Furthermore, no distinction is made between homodimerization ((**S**-Zn:*trans*-**1**)$_2$ or (**S**-Zn:*cis*-**1**)$_2$), and heterodimerization (*cis*-**1**:**S**-Zn$_2$:*trans*-**1**).
[11] The critical amount of ligand excess drops to ± 47 equivalents at 30 °C, indicating that the cooperative self-assembly of porphyrin stacks, characterized by K_2 and K is more sensitive to temperature than the metal–ligand interaction characterized by K_{trans}. This observation might be related to a counterintuitive temperature-effect of a system that reveals a pronounced dilution-induced self-assembly.

