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Light-Triggered Crystallization of a Molecular Host−Guest Complex

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Abstract: The control of structural changes in supramolecular assemblies is a key point in the development of molecular machines. The reversible photoisomerization of organic compounds such as azobenzene using light as an external input is especially suited because no waste products are generated. Based on our previous studies on the quantitative encapsulation of suitably sized bis-sulfonate guests by a self-assembled, metal−organic cage consisting of four rigid, bent bis-monodentate pyridyl ligands and two Pd(II) ions, we show here how the light-switchable guest *cis*-4,4′-azobenzene bis-sulfonate can be expelled from its 1:1 host−guest complex triggered by its photoisomerization to the *trans*-isomer. Using a highly soluble, PEGylated cage derivative, the full reversibility of this light-driven encapsulation/release process is demonstrated. In contrast, a sample of the less soluble, unsubstituted cages including 1 equiv of the *cis*-guest was shown to result in immediate crystallization upon photoisomerization of the guest. X-ray structure analysis confirmed the guest molecules having left the cavity of the host and on the contrary joining the cages into a polymeric material by binding to their Pd(II) centers from outside.

The self-assembly of polymeric supramolecular nanostructures is the key feature of a number of processes forming biological materials such as the cellular cytoskeleton[1] and virus capsids.[2] On the way to mimic nature's sophisticated self-assembled architectures by artificial compounds, a great number of elaborate examples of discrete structures (e.g., molecular cages)[3] and infinite constructs such as hydrogen-bonded coordination polymers[4] have been reported.

Beyond the static artificial systems of molecular self-assembly, the possibility to control the formation process and functions of a supramolecular architecture by external stimuli can be seen as the next step in the development of new intelligent materials.[5]

Light as a reagent offers the advantages of being easy to apply for a chosen time and intensity and does not result in the accumulation of waste products even during a reversible switching sequence using light of various wavelengths.[6]

In the context of host−guest chemistry, the control of encapsulation of light-switchable compounds such as stilbene or azobenzene derivates by molecular cages has been reported before by Fujita,[7] Rebek,[8] and Jiang[9] et al.

Recently we reported the ability of a new type of molecular cage **1** formed from four rigid, bent bis-monodentate pyridyl ligands and two Pd(II) or Pt(II) ions favoring a square-planar geometry to encapsulate suitably sized bis-sulfonate guests by a specific anion recognition process.[10,11]

Based on our observation that, depending on its size, a bis-anionic compound can act either as a guest being quantitatively encapsulated or as a cross-linking agent connecting the cages to form a crystalline material,[10] we examined bis-sulfonate guest **2** whose size (S−S distance) can be switched reversibly by photoisomerization.

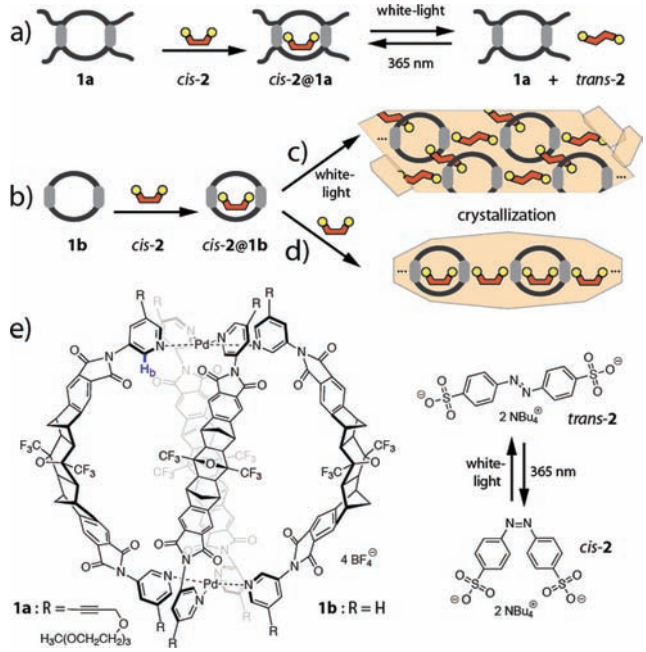

Figure 1. (a) Quantitative encapsulation of *cis*-**2** by PEGylated cage **1a** and reversible switching between host−guest complex *cis*-**2**@**1a** and the mixture of *trans*-**2** + **1a** by photoisomerization of the guest; (b) Quantitative encapsulation of *cis*-**2** by cage **1b**; (c) crystallization of [(**1b**)(*trans*-**2**)$_2$] by photoisomerization; (d) crystallization of [(**1b**)(*cis*-**2**)$_2$] by addition of a second equivalent of *cis*-**2**; (e) structures of cage **1** and guest **2**.

The tetrabutylammonium salt of *trans*-4,4′-azobenzene bis-sulfonate *trans*-**2** was prepared according to reported procedures and converted into its isomer *cis*-**2** by irradiation of its solution in acetonitrile with UV light of 365 nm wavelength.[12] First, we examined molecular cage **1a** comprising eight polyethylene glycol (PEG) chains rendering the cage highly soluble in organic solvents regardless of the presence of a cross-linker in the solution. *cis*-4,4′-Azobenzene bis-sulfonate (*cis*-**2**) has an ideal size for being quantitatively incorporated into molecular cage **1** in the previously reported fashion.[10] The complete uptake of 1 equiv of *cis*-**2** inside the cage **1a** could be unambiguously shown by ^{1}H NMR spectroscopy (Figure 2). In good accordance with our previous observation for the structurally related guest compound 1,1′-ferrocene bis-sulfonate, the cage's NMR spectrum shows characteristic changes upon addition of the guest.[10] Most notably, the ^{1}H NMR signal of the cage's inward pointing hydrogen atom H_b (blue in Figures 1 and 2) undergoes a downfield shift by ∼0.5 ppm upon encapsulation of the guest *cis*-**2**. Additionally, the NMR signals of guest *cis*-**2** show a characteristic upfield shift of approximately 1.1 and 0.7 ppm, respectively, upon encapsulation by the cage. A comparison of molecular sizes of the free anion *cis*-**2** and the encapsulated guest

cis-**2** in the host−guest complex *cis*-**2**@**1a** by a DOSY-NMR experiment confirmed the full uptake of the relatively small guest inside the much bigger host compound. Finally, we observed the occurrence of a peak at $m/z = 2586.7$ for the molecular ion of the host−guest complex $[cis\text{-}\mathbf{2}@\mathbf{1a}]^{2+}$ in the ESI-TOF mass spectrum (Supporting Information).

When the solution containing the host−guest compound *cis*-**2**@**1a** was irradiated for ∼3 h using a conventional white-light compact fluorescent lamp, guest compound *cis*-**2** was quantitatively converted back to its isomer *trans*-**2** accompanied by a characteristic change in the ^{1}H NMR spectrum of the sample. First, the characteristic downfield shift of H_b is lost with the formation of a new, broad signal at 8.5 ppm, and second, the signals of the encapsulated guest at approximately 5.7 and 6.9 ppm vanish, which indicates the formation of a loosely associated system composed of cage **1a** and compound *trans*-**2** undergoing a fast exchange process on the NMR time scale. A DOSY experiment indicates a slight increase in the hydrodynamic radius of the cage upon release of the guest which is explainable by electrostatic binding of *trans*-**2** to the outside of the cage rather than to the inside.

Most interesting, however, is the observation that this process is fully reversible. Again irradiating the sample with UV light of 365 nm wavelength results in a full regeneration of the spectrum assignable to the host−guest complex *cis*-**2**@**1a** (Figures 1a and 2). Subsequent exposure to white-light again leads to release of the guest from the cage, and we were able to repeat this process four times without notable major changes in the NMR spectra (Supporting Information).

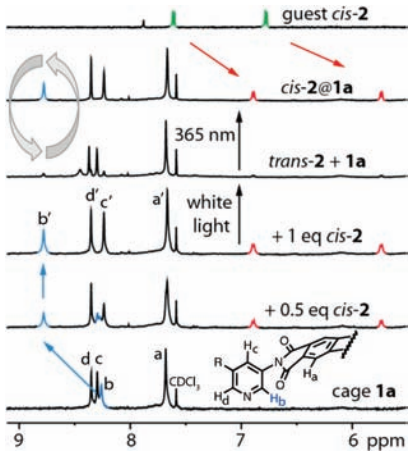

Figure 2. ^{1}H NMR titration (500 MHz, CD_3CN, 293 K) of cage **1a** with *cis*-**2** to form the host−guest complex *cis*-**2**@**1a** followed by reversible photoswitching between *cis*-**2**@**1a** and *trans*-**2** + **1a**. Signals of encapsulated *cis*-**2** shown in red, free *cis*-**2** in green, inward pointing hydrogen atom of cage in blue.

Next, we examined the interaction of guest *cis*-**2** with cage **1b** which differs from cage **1a** in the way that it has no solubility-enhancing PEG chains. Likewise to cage **1a**, the addition of up to 1 equiv of guest *cis*-**2** results in the quantitative formation of a soluble host−guest complex *cis*-**2**@**1b**. A DOSY-NMR experiment and ESI-TOF mass spectrum again support the formation of the anticipated host−guest complex (Supporting Information).

Surprisingly, when the clear, yellow solution of *cis*-**2**@**1b** was exposed to white-light, yellow crystals of [(**1b**)(*trans*-**2**)$_2$] formed immediately (Figure 3a−e). An X-ray structure, albeit of low quality due to extensive solvent disordering, showed the presence of 2 equiv of *trans*-**2** inside the crystal: one linking individual cages by binding to the outer faces of the coordinated Pd(II) centers to form infinite chains [(**1b**)(*trans*-**2**)]$_n$ and the other "dipping" into the interior space of two cages of neighboring chains, each with both its sulfonate groups in the fashion of a cross-link (Supporting Information). The composition [(**1b**)(*trans*-**2**)$_2$] was additionally confirmed by ^{1}H NMR spectroscopy after dissolution of the crystalline material in hot DMSO-d_6.

In contrast, when a solution of cage **1b** was treated with 2 equiv of guest *cis*-**2**, immediate crystallization was observed even under the exclusion of white-light (Figure 3f−j; separating the sample from the white-light source by a yellow filter did prevent the formation of the *trans*-isomer but allowed monitoring the sample chamber by light microscopy). In this case, however, the crystals were of a totally different morphology from that of the crystals formed in the previous experiments, being rather oval than square-shaped (compare Figure 3e and j). Since 2 equiv of guest *cis*-**2** were needed to afford the formation of crystals and no white-light was administered to the sample, the composition most likely can be explained by the formula [(**1b**)(*cis*-**2**)$_2$]. After this crystalline sample was exposed to white-light, the oval crystals dissolved and gave place to concomitantly forming square-shaped crystals (Figure 3j to k). Although the new crystals formed at the same spots where the oval crystals were located before, this process most probably is not a topotactic "crystal-to-crystal" phase transition[13] but rather the remains of the dissolving oval crystals functioning as seeds for the growth of the new square-shaped crystals.

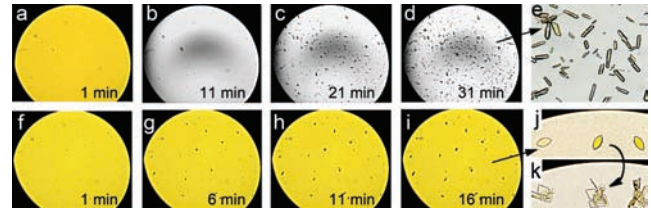

Figure 3. (a) **1b** + 1 equiv of *cis*-**2** under yellow-light; (b−e) crystallization of [(**1b**)(*trans*-**2**)$_2$] after changing to white-light at $t = 11$ min; (f−j) **1b** + 2 equiv of *cis*-**2** leads to crystallization of [(**1b**)(*cis*-**2**)$_2$] even under yellow-light; (k) transformation of the crystals upon changing to white-light at $t =$ 16 min.

The soluble host−guest system that we present here may be seen as a supramolecular building block, which contains a kind of noncovalent glue as a guest hidden in its cavity. Irradiation with light of an appropriate wavelength triggers the release of this glue and leads to aggregation of the cage units into a higher structure. This principle of a light-induced phase change from soluble host−guest complexes into insoluble materials may be useful for the development of new strategies for nanoconstruction and the spatially controlled lithographic deposition of supramolecular networks on surfaces.

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Supporting Information Available: Synthetic procedures, NMR, mass spectra, X-ray structure, and movies of the light-initiated crystallization. This material is available free of charge via the Internet at http://pubs.acs.org.

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