Light-driven control of the composition of a supramolecular network

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Abstract: The composition of a supramolecular network, constituted by several cucurbituril receptors and guests, can be controlled by the reversible and all-photonic switching of a dithienylethene guest.

The creation of chemical complexity and diversity in dynamic networks,[1-3] built on reversible chemical reactions or supramolecular interactions, is in the focus of systems chemistry.[4, 5] The use of such networks for the storage and processing of information,[6] the identification of innovative and tailored receptors,[7] and dynamic materials showcases these efforts.[3] They are frequently addressed by the addition of external chemical stimuli[8] that drive the coupled equilibria into a programmed outcome. However, light as stimulus is likewise very attractive for controlling combinatorial dynamic libraries[9-12] and supramolecular assemblies,[13-15] because it constitutes a very clean means to induce chemical changes in a spatiotemporally and remotely controlled fashion. Further, the interaction of light with specific components of a network can be very selective, based on the implicated chromophoric fingerprints, allowing for orthogonally triggered processes.

There has been a good deal of work related to the use of light-induced switching for the release of functional guests from their supramolecular complexes with artificial receptors.[16-23] However, comparably little effort has been made to achieve light-control of the complex supramolecular equilibria and composition of multi-component mixtures, consisting of several receptors and guests. This task is not trivial, as the prediction of such systems depends on coupled equilibria between all possible guest/receptor

combinations, which has to be integrated with differential binding situations created by photoswitching of at least one of the guests. In this context the all-photonic (i.e., the exclusive use of light as signal), reversible, and fatigue-resistant switching of supramolecular networks would be a valuable functional asset. This is especially true for applications that are related to (supra)molecular information processing,[22, 24, 25] enabling all-photonic write-read-erase cycles of specific fingerprints, characterized by the network composition.

Herein we report an approach to light-induced control in a network of four supramolecular host-guest complexes that are constituted by two cucurbit[*n*]uril macrocycles[26, 27] (*n* = 7, 8 - abbreviated as CB7 and CB8, respectively; see structures in Figure 1) as hosts and two guests, one of them being a dithienylethene (DTE) photoswitch. The latter is a textbook example of robust and all-photonic bistable switching in functional applications.[28-30] Noteworthy, in the context of cucurbituril chemistry DTE photoswitches have been used for the demonstration of guest release[31] and the control of supramolecular polymers.[32]

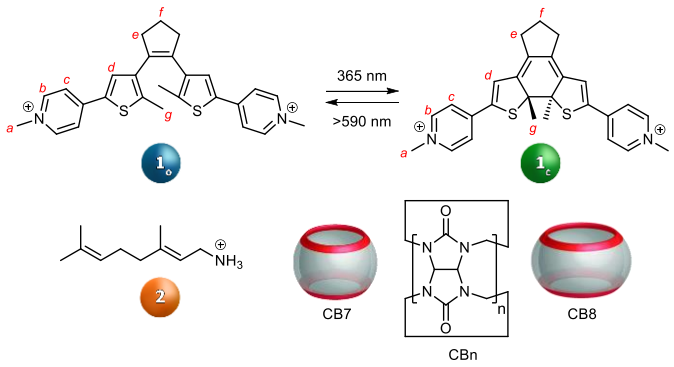

Figure 1. Structures of the DTE photoswitch (**1**; iodide is the counterion), geranylamine (**2**), and the hosts CB7 and CB8. The all-photonic interconversion between the two isomeric forms of **1** (subscripts: o - open, c - closed) is shown at the top. The red letters assign the chemically different protons of **1** (see main text).

Cucurbiturils have been identified as prime hosts for self-sorting,[33] because they interact with a structurally and chemically diverse range of guests, very often characterized by pronounced differential binding.[34] Noteworthily, these water-soluble macrocycles have found wide attention for their application in bio-relevant contexts, such as drug delivery or binding to biomolecular structures.[17, 35-41]

Table 1. Binding constants of the guests 1 (in both isomeric forms) and 2 with CB7 and CB8.[a]

	K/ M^{-1}
1$_o$-CB7	2.6×10^4 [b]
1$_o$-CB8	5.4×10^7
1$_c$-CB7	8.4×10^3 [b]
1$_c$-CB8	6.2×10^9
2-CB7	3.2×10^6 [c]
2-CB8	1.4×10^{10} [d]

[a] The binding constants of **2** were measured at pH 5, assuring complete protonation of the primary amine. The binding constants of **1** correspond to pH 7. **1** contains no protonable groups and the binding is therefore expected to be pH-independent. [b] The apparent 1:1 binding constants of both forms of **1** with CB7 are calculated as square root of the global 2:1 constants; see values in ref. 31. [c] The binding constant of **2** with CB7 is taken from ref. 42. [d] The binding constant of **2** with CB8 was re-measured in this work by competitive displacement titration of **1**$_c$. Note that this constant is somewhat higher than the previously reported value; ref. 43.

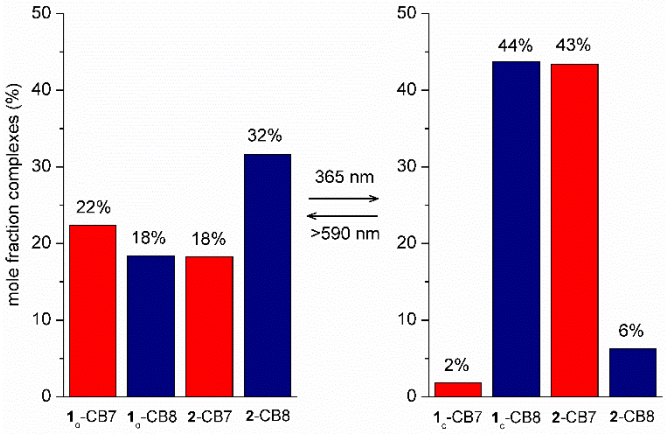

Figure 2. Simulated distribution of the host-guest complexes (all guests and hosts were 500 μM) for the different switching states of the photoswitch **1**. The fraction of the unbound hosts is not shown in this graphic. Red bars – CB7 complexes, blue bars – CB8 complexes.

Based on the above discussed premise we selected two guests (DTE derivative - **1** and geranylamine - **2**; see structures in Figure 1) that would provide a network of four possible host-guest complexes (**1**-CB7, **1**-CB8, **2**-CB7, and **2**-CB8) with two cucurbituril homologues and with the detailed network composition being dependent on the actual form of the photoswitch [open (o) or closed (c)]. DTE **1** was previously shown to maintain efficient photoreactivity for the ring-closing reaction when encapsulated by CB8 (quantum yield $\Phi_{o\text{-}c}$ = 0.32), while the reverse process occurs with a typically lower quantum yield ($\Phi_{c\text{-}o} = 3 \times 10^{-4}$).[31] The photoreactions yield

virtually quantitative and reversible conversion of the open to the closed form of the DTE and vice versa. The binding constants of the two DTE photoisomers $\mathbf{1}_o$ and $\mathbf{1}_c$ as well as of guest **2** are listed in Table 1.44 The pronounced differential binding properties of the guests form the fundament for the herein devised system. These data were used to simulate the distribution of the complexes for both switching situations ($\mathbf{1}_o$ and $\mathbf{1}_c$) at equimolar concentration of all host and guest components (500 μM); see Figure 2. All four possible complexes are predicted to be present when the DTE is in its open form ($\mathbf{1}_o$). However, upon converting the DTE with UV-light (365 nm) into the more strongly CB8-binding ring-closed form ($\mathbf{1}_c$), a clear-cut change of the network composition towards the two complexes $\mathbf{1}_c$-CB8 and **2**-CB7 is expected (see below for experimental results).

In the next step we proceeded to seek experimental confirmation for these predictions. For this purpose, ^{1}H NMR spectroscopic measurements were undertaken. The individual complexes show typical fingerprints of the chemical shift changes in agreement with deep immersion of the guests in the case of **1** (in both isomeric forms) with CB8 and **2** with CB7 and CB8. The situation that was observed for DTE **1** is rather clear-cut. On the one hand, the thiophene proton signal (*d*, see Figure 1 for the assignment of this and the other protons that are used in the following discussion) shows rather small changes (slight downfield shifts of ca. +0.10 ppm and +0.11 ppm for $\mathbf{1}_c$ and $\mathbf{1}_o$, respectively) for complexation with CB7. However, the aromatic protons closest to the pyridinium nitrogen (*b*) experience significant upfield shifts for the interaction with CB7 (–0.40 ppm for 1o and –0.39 ppm for $\mathbf{1}_c$). The same is true for the N-methyl protons (*a*, –0.16 ppm for $\mathbf{1}_o$ and –0.18 ppm for $\mathbf{1}_c$). The combined observations point to the formation of a 2:1 *exo* complex with the pyridinium units.

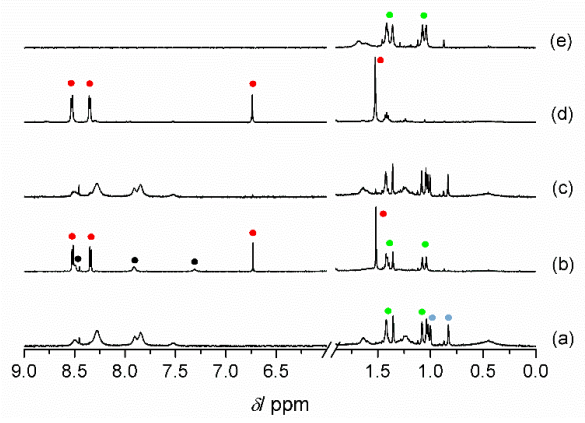

Figure 3. Partial ^{1}H NMR spectra (all at pD 5.0) of (a) the four-component mixture (all at 500 μM) with **1** in its open form ($\mathbf{1}_o$), (b) the same mixture as for (a) after irradiation at 365 nm for 30 minutes, (c) the same mixture as for (b) after irradiation at >590 nm for 2 hours, (d) the closed form of **1** in presence of an equimolar amount of CB8 (both at 500 μM), (e) geranylamine (**2**)

with CB7 (both at 500 μM). All spectra are referenced for the HOD solvent signal. The spectra (d) and (e) are included for the sake of comparison. The key signals in the spectra (a) and (b) are marked with colored points (green: **2**-CB7, blue: **2**-CB8, black: $\mathbf{1}_c$-CB7, red: $\mathbf{1}_c$-CB8; see additional NMR spectra in ESI)

On the other hand, for complexation with CB8 pronounced upfield shifts were seen for the thiophene proton (*d*, –0.32 ppm for $\mathbf{1}_o$ and –0.56 ppm for $\mathbf{1}_c$) and the methyl protons (*g*, –0.82 ppm for $\mathbf{1}_o$ and –0.56 ppm for $\mathbf{1}_c$), while one of the pyridinium ring protons is downfield shifted (*c*, ?0.31 ppm for $\mathbf{1}_o$ and ?0.41 ppm for $\mathbf{1}_c$). Hence, the CB8 macrocycle can be safely assumed to be positioned over the central photochromic unit in **1** for both isomeric forms. The other guest (**2**) in the network can be straightforward identified as free or bound to either CB7 or CB8 by monitoring the chemical shifts of the methyl protons as indicator signals.[43] These are typically upfield shifted on complexation and easily differentiable for the CB7 and CB8 complexes.

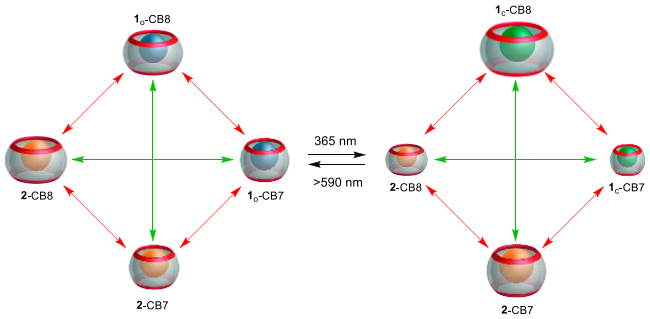

Figure 4. Model of the supramolecular dynamic network. The sizes of the complexes are meant to illustrate the trends of their relative concentrations in an approximate manner. The green arrows connect agonistic members of the network, while the red arrows link antagonistic members. Color coding of guest species: blue - $\mathbf{1}_o$, green - $\mathbf{1}_c$, orange – **2.**

Based on the signatures of the individual complexes we set out for competition experiments (see Figure 3 and ESI). In agreement with the binding constants (Table 1), both isomeric forms of **1** favour CB8 over CB7. As for CB7, neither of $\mathbf{1}_o$ and $\mathbf{1}_c$ can compete for the host in the presence of **2**. However, in the case of CB8 as host, the closed form $\mathbf{1}_c$ displaces **2** to some extent (*ca*. 40% of $\mathbf{1}_c$ is bound under equimolar concentration conditions; [$\mathbf{1}_c$] = [**2**] = [CB8] = 500 ?M), while the open form $\mathbf{1}_o$ does not. This is in full concordance with the expectations based on the measured binding constants. The key experiment was performed with an equimolar mixture (500 ?M) of all four components (**1**, **2**, CB7, CB8). The ^{1}H NMR spectrum (Figure 3), that was recorded for the DTE in its open form ($\mathbf{1}_o$), resembles the situation of all four

possible complexes being present, as predicted by the simulations (see above). On the one hand, the typical fingerprint of the geranylamine methyl protons in both complexes, i.e., with CB7 and CB8, was clearly identified. On the other hand, the aromatic region of the DTE showed significant broadening and some signal displacement with respect to the individual complexes, hinting on a slow/intermediate exchange on the NMR timescale for a multicomponent mixture. This situation resolved into a simpler composition on irradiation at 365 nm, which produced the closed DTE form $\mathbf{1}_c$. Now practically only two complexes were detected (Figure 3): $\mathbf{1}_c$-CB8 and **2**-CB7, again in good agreement with the predictions of the modelling (see Figure 2). Upon photoswitching from $\mathbf{1}_o$ to $\mathbf{1}_c$ the concentrations of the agonistic complexes $\mathbf{1}_c$-CB8 and **2**-CB7 are increased at the expense of their antagonistic counterparts, as illustrated in Figure 4. Curiously, although the closed DTE $\mathbf{1}_c$ is a moderate competitor with **2** for binding by CB8 (see binding constant in Table 1 and ESI), the presence of CB7 resolves this situation in favour of an efficient displacement of **2** from CB8. Such cooperative effect is interpreted as the result of the stronger CB7-binding of **2** than observed for $\mathbf{1}_c$, i.e., three orders of magnitude difference. This observation underlines the inherent complexity of the photoswitchable network, as opposed to simpler and rather predictable competitive displacement situations.[31] As a functional surplus, the situation can be reversed by back-isomerization of $\mathbf{1}_c$ to $\mathbf{1}_o$ upon irradiation with light at >590 nm, as seen in the ^{1}H NMR spectra (Figure 3). After that a new switching cycle can be initiated without notable fatigue.

In conclusion, the light-induced control of the composition of a supramolecular network, based on host-guest complexes with two homologous cucurbituril receptors, was achieved by drawing on the reversible all-photonic photoswitching of a DTE guest. These features are of elevated interest in the context of information processing and storage with light-responsive supramolecular systems.

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Conflicts of interest

There are no conflicts to declare.

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44. The difference in the CB8 affinity of the two forms of **1** is likely caused by the entropic penalty that is associated to the reorganization of the open form into the anti-parallel conformation upon binding. This is also the required conformation for the light-induced cyclization reaction, explaining therefore the previously observed enhanced quantum yield of this reaction inside the CB8 cavity, see ref. 31. Such conformational reorganization is not implicated in the binding of the far more rigid ring-closed isomer.