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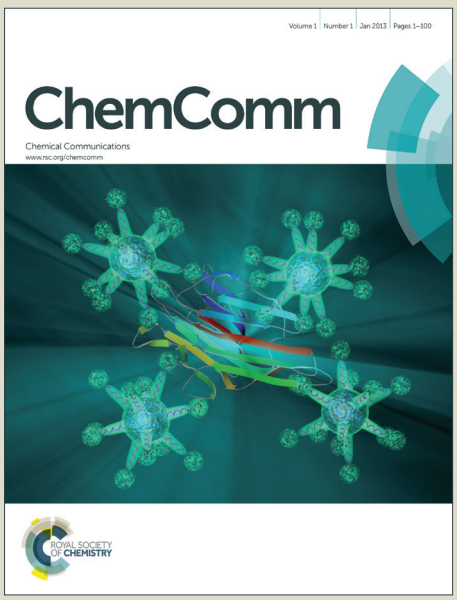

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Photoinduced Guest Transformation Promotes Translocation of Guest from Hydroxypropyl-β-Cyclodextrin to Cucurbit[7]uril

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We report that three-component systems comprising styryl dyes (1 or 2) and two hosts (hydroxypropyl-β-cyclodextrin (HP-β-CD) and cucurbit[7]uril (CB[7])) undergo photoinduced transformation and translocation of the styryl guest from the cavity of HP-β-CD to CB[7]. We find that the protonation of guest *trans*-1 or the addition of Ba^{2+} as competitor for CB[7] triggers dissociation of the container•guest complexes.

The development of supramolecular chemistry over the past few decades has lead to a deep understanding of the fundamental non-covalent interactions (e.g. H-bonds, metal•ligand, electrostatic interactions, π–π, hydrophobic effect) that hold host•guest complexes together.[1] Central to the field has been the preparation of versatile classes of macrocyclic containers (e.g. cyclodextrins, crown ethers, calixarenes, cyclophanes, cucurbit[n]urils (CB[n]), pillararenes), studies of their host-guest recognition properties, and their use in advanced applications.[2] In recent years, the development of stimuli responsive systems have become a focus of the field with application toward molecular machines and drug delivery systems.[3] We, and others, have been very interested in the synthesis and supramolecular chemistry of the cucurbit[n]uril family of molecular containers (Figure 1).[2f,4] The distinguishing feature of CB[n] containers are the superior binding affinities (K_a up to 10^{17} M^{-1}) and high selectivities they display toward hydrophobic cations (e.g. alkylammonium ions) in water.[5] Accordingly, CB[n]•guest complexes are highly stimuli responsive (e.g. pH, chemical, electrochemistry, photochemical)[6] and have been used to construct a variety of contemporary functional systems including molecular machines, supramolecular materials, and chemical sensors.[6b,7] Amongst the various stimuli, the use of light offers many advantages including fast response, remote sensitivity, addressability, and lack of chemical waste. In this paper, we report a three component system whose molecular and intermolecular constitution can be controlled by photochemistry and also by pH change or metal-ion addition.

For the design of a system that would display light induced changes in molecular and intermolecular constitution (e.g. translocation between hosts) we selected HP-β-CD and CB[7] as the two hosts (Figure 1).[8] Both HP-β-CD and CB[7] exhibit good water solubility which allowed us to work in the less competitive neutral H_2O solution and are appropriately sized (cavity diameter 7.8 Å for HP-β-CD and 5.4 Å for CB[7]).[4a] HP-β-CD is known as a rather promiscuous host that displays modest affinity and selectivity toward neutral and anionic guests in water whereas CB[7] is quite selective and binds preferentially with hydrophobic cations.[2d,2f] Accordingly, we envisioned that a light induced chemical change of guest from neutral to cationic could trigger translocation of the guest from HP-β-CD to CB[7]. As photochemically active guests, we selected styryl dyes *trans*-**1** and *trans*-**2** (Scheme 2) which feature a common 15-crown-5 ring that greatly enhances their water solubility. Previously, we have reported the oxidative photodehydrocyclization of benzothiazolylphenylethenes and styrylquinoline derivatives to yield polycyclic heteroaromatic cations.[9] The photochemical transformations of *trans*-**1** and *trans*-**2** and related structures includes two steps: 1) a photochemical *trans-cis* isomerization to yield *cis*-**1** and *cis*-**2**, and 2) 6π-electron electrocyclic ring closure (6π ERC) and oxidative aromatization to yield heteroaromatic cations **3** and **4** (Scheme 1). These photochemical transformations of **1** and **2** alone occur efficiently in aqueous solution.[10]

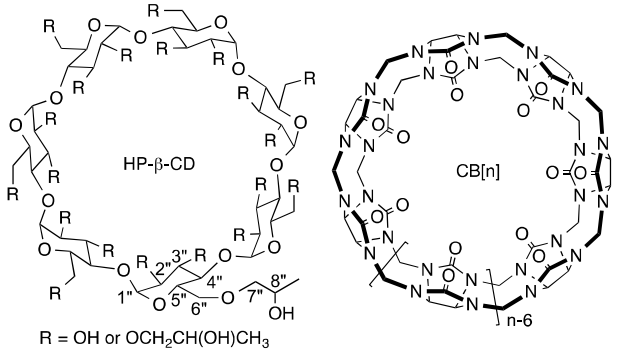
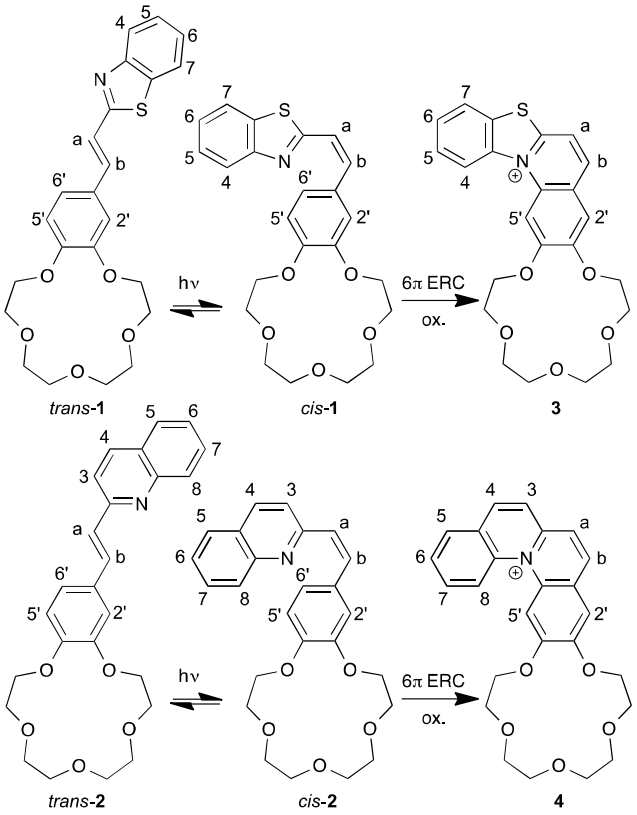


Figure 1. Chemical structures of the HP-β-CD and CB[n] containers used in this work.

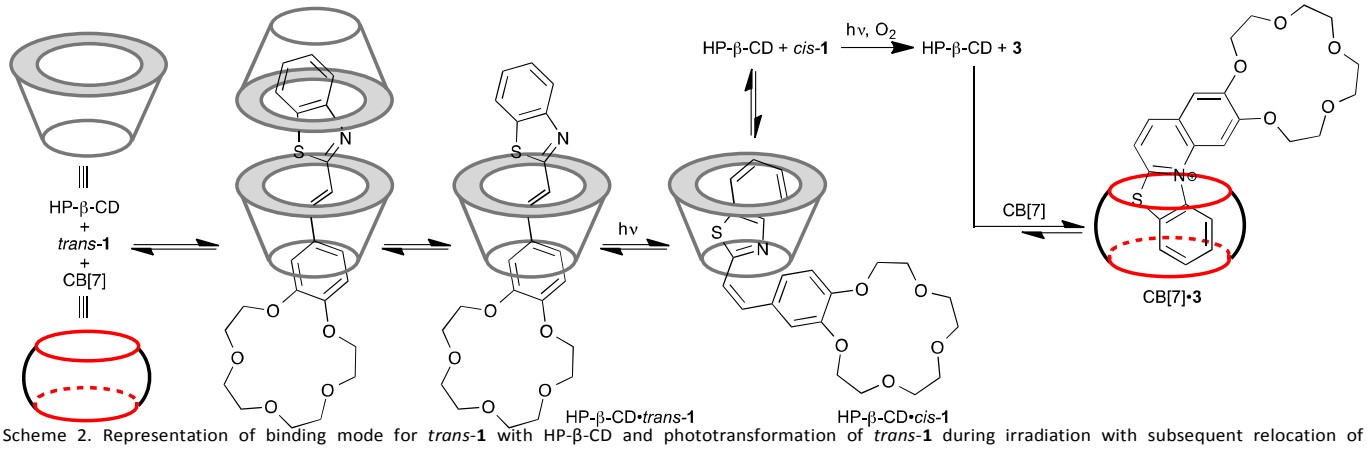


Scheme 1. Chemical structures of styryl dyes **1** and **2** and their photochemical transformation into **3** and **4**.

In previous work, we found that *trans*-**1** forms both 1:1 and 1:2 host:guest complexes with HP-β-CD (Scheme 2).[11] Experimentally, the addition of HP-β-CD to a solution of *trans*-**1** results in negligible changes in the absorption maximum of *trans*-**1** (Table S1, Fig. S1 and S2 in ESI). However, in the fluorescence spectrum of *trans*-**1** there is a pronounced increase in fluorescence and a 17-nm blue shift in the wavelength of maximum fluorescence upon titration with HP-β-CD. Fitting a plot of the change in fluorescence versus [HP-β-CD] allowed us to calculate the association constants of the HP-β-CD•**1** (log K_{11}=3.58±0.01 M^{-1}) and (HP-β-CD)$_2$•**1** (logK_{21}=4.70±0.15 M^{-1}) complexes (Scheme 2, Table S1). Similarly, titration of *trans*-**2** with HP-β-CD does not result in significant changes in the UV/Vis spectrum of the dye, but does result in significant enhancement in the fluorescence intensity and a 27 nm blue shift in the wavelength of maximum fluorescence intensity (Fig. S3 and S4 in ESI). Fitting of a plot of change in fluorescence intensity versus [HP-β-CD] fits well to a 1:1 binding model with log K_{11}= 3.04±0.06 M^{-1} (Table S1).

To further investigate the nature of the complexes between HP-β-CD and dyes *trans*-**1** and *trans*-**2** we performed ^{1}H NMR and 2D NMR measurements. Unfortunately, the chemical shift of the protons of guests *trans*-**1** and *trans*-**2** did not undergo significant shifts upon formation of HP-β-CD•guest complexes because the cavity of HP-β-CD – unlike many molecular containers – does not constitute an NMR shielding region. However, we were able to observe cross peaks in the ROESY spectrum between protons of *trans*-**1** and HP-β-CD (e.g. H4, H5, H6, H7, H2′, H6’, Ha, Hb of *trans*-**1** with protons H3″, H5″, H6″, H8″ of HP-β-CD) as shown in Figure 2. The observed cross peaks indicate that the HP-β-CD units reside on the aromatic fragments of *trans*-**1** within the HP-β-CD•**1** and (HP-β-CD)$_2$•**1** complexes as depicted in Scheme 2. Similarly, the ROESY spectrum of complex *trans*-**2**•HP-β-CD (Fig. S5 in ESI) confirms the localization of HP-β-CD molecule on the quinoline and ethylene units of *trans*-**2** within the HP-β-CD•*trans*-**2** complex.

Having achieved a solid understanding of the complexation behaviour between HP-β-CD and *trans*-**1** or *trans*-**2** we turned our attention to their photochemical transformations. Irradiation with high pressure mercury light (≥ 320 nm) of the complex HP-β-CD•*trans*-**1** or HP-β-CD•*trans*-**2** in water in the presence of oxygen produces new compounds. The first step of the photochemical reaction is the formation of a mixture of *trans* and *cis* isomers as shown in Scheme 2 and Fig. 3 for HP-β-CD•*trans*-**1** and Scheme S1, Fig. S6 in ESI for dye *trans*-**2**). Fig. 3 shows the decrease of absorbance for the complex HP-β-CD•*trans*-**1** upon irradiation (1 minute) which corresponds to the *trans-cis* isomerization; the observation of cross peaks in the ROESY spectrum of HP-β-CD•*cis*-**1** indicate the preservation of the complex (Figure S8). The subsequent slow increase in absorbance at 410 nm results from electrocyclization followed by oxidative aromatization to give **3**. The ^{1}H NMR spectrum of the reaction mixture showed the disappearance of the olefinic protons (H_a, H_b) and a substantial



Scheme 2. Representation of binding mode for *trans*-**1** with HP-β-CD and phototransformation of *trans*-**1** during irradiation with subsequent relocation of photoproduct from HP-β-CD into the CB[7] cavity.

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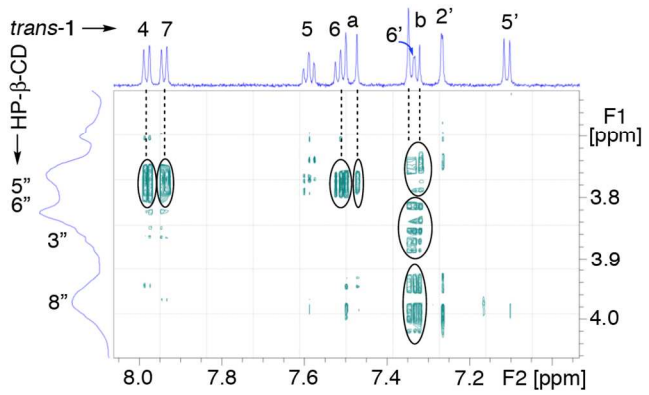


Figure 2. Partial ROESY spectra recorded (600 MHz, D_2O) for *trans*-**1** and HP-β-CD ([**1**] = 300 μM, [HP-β-CD] = 0.01 M).

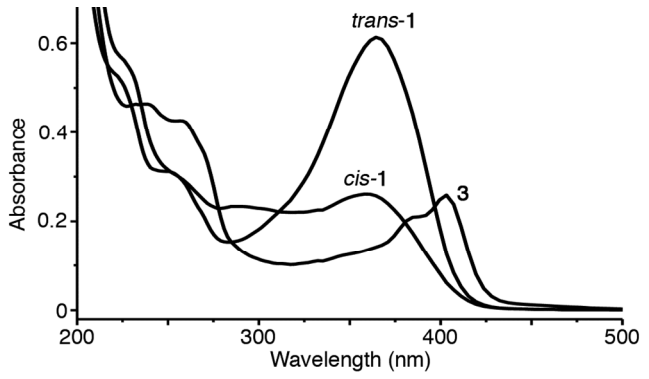


Figure 3. Absorption spectra of HP-β-CD•*trans*-**1**, HP-β-CD•*cis*-**1**, and **3** in H_2O. [**1**] = [**3**] = 20 μM.

downfield shift of the aromatic protons relative to *trans*-**1** which is consistent with the formation of heteroaromatic cation **3** (Scheme 2, Fig. S7).

To determine whether the *cis*-**1** or electrocyclic product **3** formed in HP-β-CD cavity, we carried out a detailed analysis of the structure of the photoproducts by ROESY spectroscopy. As can be seen from Fig. S8a,b in ESI, the protons of *cis*-**1** show correlations with protons of HP-β-CD, whereas, no cross peaks between the proton signals of **3** and HP-β-CD have been found (see Fig. S8b). Thus, we surmise that *cis*-**1** forms within HP-β-CD which is an agreement with literature reports on photoisomerization of olefinic molecules in CD cavity.[12] HP-β-CD does not form strong host-guest complexes with positively charged molecules, thus, the formation of heteroaromatic cation **3** leads to the destruction of complex with HP-β-CD (Scheme 2). Similar behavior has been observed for HP-β-CD•*trans*-**2** upon irradiation (Scheme S1, Fig. S9-S11 in ESI).

Having established that photochemistry transforms guests *trans*-**1** and *trans*-**2** and results in destruction of their HP-β-CD complexes we turned to studying their translocation to the CB[7] container. Photoproducts **3** and **4** contain cationic heteroaromatic rings which constitute binding sites for CB[7]. Indeed, addition of CB[7] to solutions of **3** or **4** causes a bathochromic shift in the UV/Vis spectrum (Table S1, Fig. S12-S15) and small changes in fluorescence which reflect the inclusion of the dye in a less polar environment. The stability constants of CB[7]•**3** (log K=3.14±0.01 M^{-1}) and CB[7]•**4** (log K=2.47±0.15 M^{-1}) were calculated using the observed optical changes within SpecFit/32. The ^{1}H NMR spectra recorded for **3** alone and in the presence of CB[7] in D_2O are shown in Fig. 3a,b. The well known shielding region inside the CB[7] cavity and the deshielding region nearby the C=O portals allows us to use the observed direction and magnitude of the changes in chemical shift to formulate the depicted geometry of CB[7]•**3** (Scheme 2).[2f,5d]

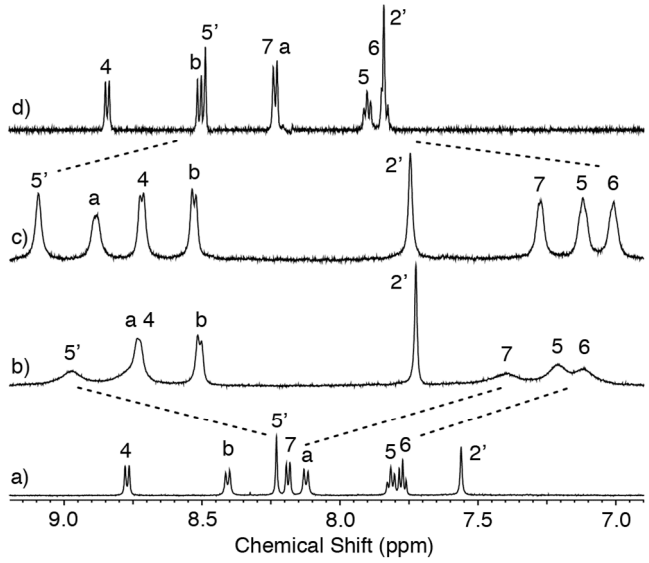
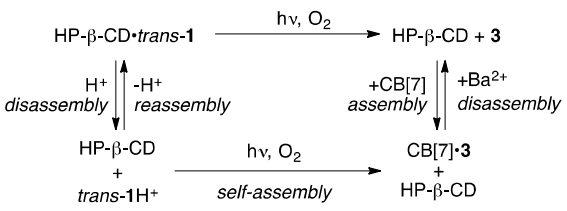


Figure 4. ^{1}H NMR spectra recorded (600 MHz, D_2O) for **3**: a) free ($2\cdot10^{-3}$ M); b) in presence of CB[7] ($2\cdot10^{-3}$ M); c) in presence of CB[7] ($2\cdot10^{-3}$ M) and HP-β-CD ($4\cdot10^{-3}$ M); d) in the presence of CB[7] ($1\cdot10^{-2}$ M) and $Ba(ClO_4)_2$ ($2\cdot10^{-1}$ M).

Finally, we sought to create three component systems comprising HP-β-CD, CB[7], and *trans*-**1** or *trans*-**2** that undergo phototriggered transformation and translocation. Accordingly, solutions of *trans*-**1** or *trans*-**2** (2 mM), CB[7] (4 mM) and HP-β-CD (4 mM) in H_2O were prepared. The UV/Vis and fluorescence maxima of the dyes in this mixture were the same as those of their HP-β-CD complexes measured separately. Photolysis of the mixtures (≥ 320 nm) results in the formation of the CB[7]•**3** or CB[7]•**4** complexes, respectively, as evidenced by their characteristic UV/Vis and fluorescence maxima (Table S1). The ^{1}H NMR spectrum of the product mixture is very similar to that of CB[7]•**3** (or CB[7]•**4**) prepared separately (Figure 4b,c) which provides additional evidence for the translocation of guest to CB[7] triggered photochemically (Scheme 2).

We have also found that the present system can be manipulated by chemical stimuli in the form of changes in pH

or Ba^{2+} ion concentration (Scheme 3).[4b,13] For example, addition of $HClO_4$ to a pH 7 solution of HP-β-CD•**1** and CB[7] triggers dissociation of the HP-β-CD•**1** complex by formation of the weak binder **1**H$^+$ perchlorate. This process was monitored by UV/Vis disappearance of the 363 nm band for HP-β-CD•*trans*-**1** and the appearance of a band at 415 nm for **1**H$^+$ (Fig S17-18). Similarly, addition of $HClO_4$ also induces dissociation of HP-β-CD•*trans*-**2** by formation of **2**H$^+$ (Fig. S19 and S20 in ESI). We found that addition of $Ba(ClO_4)_2$ to a solution of CB[7]•**3** results in the dissociation of the complex to yield free **3** and the CB[7]•Ba^{2+} complex by coordination to the ureidyl C=O portals of CB[7]. Fig. 4d shows the ^{1}H NMR spectrum recorded after addition of $Ba(ClO_4)_2$; the resonances are much sharper and shift back toward those for free **3**. The differences observed between Figure 4a and 4d are probably due to the interaction between the crown ether ring and the Ba^{2+} cations. The observed fluorescence bands also shift back toward those of free **3** upon addition of $Ba(ClO_4)_2$ (Fig. S22 and S23). Similar observations were made with CB[7]•**4** (Fig. S21 in ESI).



Scheme 3. H^+ and Ba^{2+} responsive behavior of the system.

In summary, we have reported three component systems comprising HP-β-CD, CB[7], and styryl dyes *trans*-**1** or *trans*-**2** that undergo photochemically triggered transformation of guest (yielding **3** and **4**) and translocation of the guest from HP-β-CD to CB[7]. The critical structural feature that enables this process is the irreversible transformation of neutral styryl dyes *trans*-**1** and *trans*-**2** into cationic dyes **3** and **4**. The contrasting preferences of HP-β-CD for neutral guests and CB[7] for cationic guests drives the translocation process. Furthermore, this system is responsive to changes in pH and Ba^{2+} ion concentration which cause dissociation of the complexes by guest protonation and formation of CB[7]•Ba^{2+}. Overall, the work further establishes the CB[n] family of containers as particularly well suited for the creation of multi-stimuli responsive systems. Ongoing work is directed toward the implementation of fully reversible photochemical transformations that would enable the development of more complex multichromophoric, multi-stimuli responsive systems required for complex logic devices.

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Notes and references

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