Molecular Devices

A Lockable Light-Driven Molecular Shuttle with a Fluorescent Signal**

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Rotaxanes have received considerable interest in recent years because of their potential applications in nanostructured functional materials and molecular devices.[1–5] Deeper insight into biological molecular motors have stimulated a surge of activity towards the construction of artificial molecular machines, especially molecular shuttles, which offer possibility of long-range translational motion of a threaded macrocyclic "shuttle" along a "rail track". Such a supramolecular system could be also used to store information if the shuttling motion (output) is controlled by proper external stimulus (input).[6] The use of photons as input (light-driven shuttling) is now under prominent consideration because excitation with lasers can lead to a fast response and can function in a small space without producing any by-products.[7] Temperature change (entropy-driven shuttling) is another clean input because no chemical reaction and no covalent structural changes are involved.[8] However, recording of the changes by ^{1}H NMR, absorption, and circular dichroism spectroscopies are the usual methods used to monitor the coconformational

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[**] H.T. acknowledges the support by NSFC/China (20273020) and Education Committee of Shanghai. We thank Professor Yu Liu (NanKai University/China) for his relevant advice on the synthesis and Dr. H. L. Anderson (Oxford University/UK) for his helpful discussion.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200453708

change of rotaxanes, and this might not be convenient in future applications because the difficulty in transforming these spectral signal changes into the easily detected output signals. In contrast, the use of changes in fluorescence as an output signal is preferable because the signal enables easy remote reading and is inexpensive. However, reports based on rotaxanes that can be induced to switch between different fluorescent states (output) in response to clean inputs are rare.

Herein, we report an example of [2]rotaxane α-CD-NPSI (Figure 1; CD is cyclodextrin), in which the hydrogen bonding between the α-CD macrocycle and the isophthalic acid unit stops the shuttling motion of the α-CD macrocycle between two binding sites. The disruption of the hydrogen bonding by adding a base enables shuttling, which is exclusively controlled by light energy without the formation of by-products, fully reversible, and accompanied by an obvious change in the intensity of fluorescence. This molecular machine can be a switch, and features the convenient use of optical input and easy reading of the optical output.

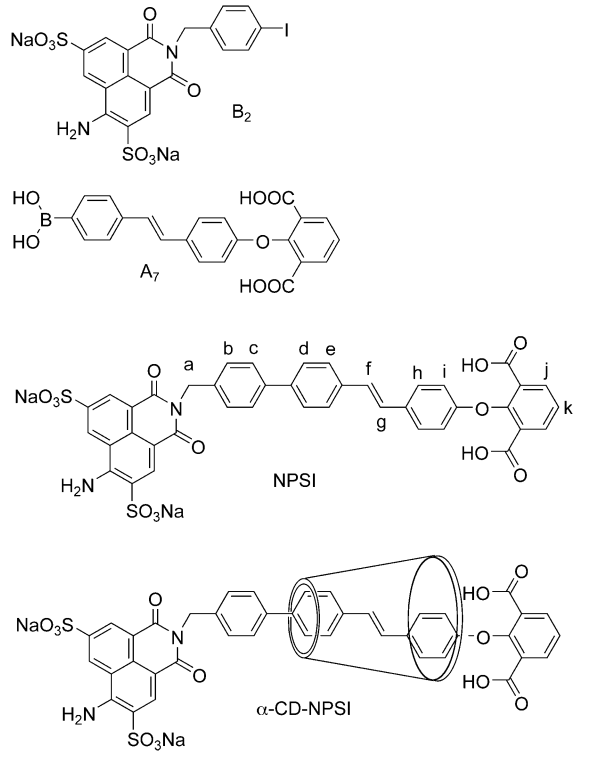

Figure 1. The chemical structures of B$_2$, A$_7$, NPSI and [2]rotaxane α-CD-NPSI.

α-CD-NPSI consists of an α-CD macrocycle locked into a thread, which has two binding sites—a biphenyl (P) site and a stilbene (S) site—linked covalently, and trapped mechanically by two stoppers: 4-amino-3,6-disulfonic-1,8-naphthalimide disodium salt (N) unit and a isophthalic acid (I) unit as shown in Figure 1. It was reported that [2]rotaxanes can be prepared by the Pd-catalyzed Suzuki coupling in the presence of CD.[4a,b] We treated A$_7$ with B$_2$ in an alkaline aqueous α-CD solution, with a Pd(OAc)$_2$ catalyst, in the mole ratio A$_7$:B$_2$:α-CD:Pd of 1:1.2:1.5:0.08, and we isolated the rotaxane α-CD-NPSI in 7.6% yield by chromatography (silica gel, 1:2:5 acetic acid/*n*-butanol/water as the eluent). The "dumbbell" NPSI was also synthesized by using the same conditions as those for the synthesis of α-CD-NPSI but in the absence of α-CD (yield 37%). The chemical structure of the rotaxane was confirmed by ^{1}H NMR and ^{1}H ROESY NMR spectroscopies, and TOF-MS. The NOEs spectra shown in Figure 2 and Figure 3 observed from the aromatic protons H$_e$, H$_f$, H$_g$, and H$_h$ (no H$_i$) of the dumbbell to the internal proton 5-H of the α-CD, from H$_f$, H$_g$, H$_h$, and H$_i$ (no H$_e$) to 3-H, and from the H$_e$, H$_d$ to 6-H, indicate that the 2, 3-OH rim of the α-CD is near to the isophthalic acid stopper, and that the α-CD ring sits over the stilbene unit. It is to our surprised that only one isomer was obtained, in which the orientation of α-CD was confirmed as shown in Figure 1.

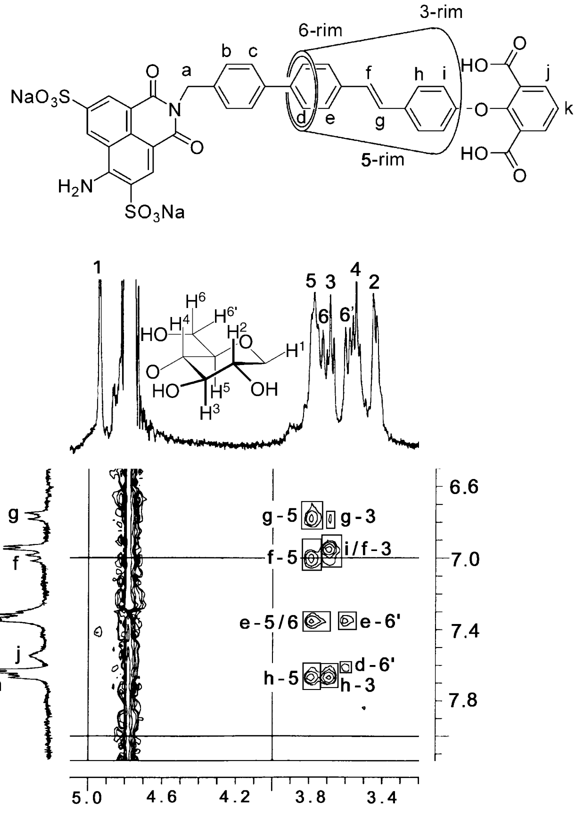

Figure 2. ^{1}H ROESY NMR (500 MHz) spectrum of α-CD-NPSI in D$_2$O recorded at 298 K.

The *E*/*Z* photoisomerism of the [2]rotaxane α-CD-NPSI in aqueous solution was investigated by monitoring the changes in ^{1}H NMR spectra as shown in Figure 4 and Figure 5. Efficient photoisomerization was found in a stilbene-based rotaxane set up by Anderson and co-workers, in which the *E*/*Z* isomerization was accompanied by the shuttling motion of the α-CD ring from the stilbene unit to the biphenyl unit.[9] But to our surprise, after the irradiation of α-CD-NPSI (5.0 mM in D$_2$O) at 335 nm for 65 min, no change in ^{1}H NMR signals was found,[10] which indicates that no *E* isomer was converted to *Z* isomer. This fact is probably due to

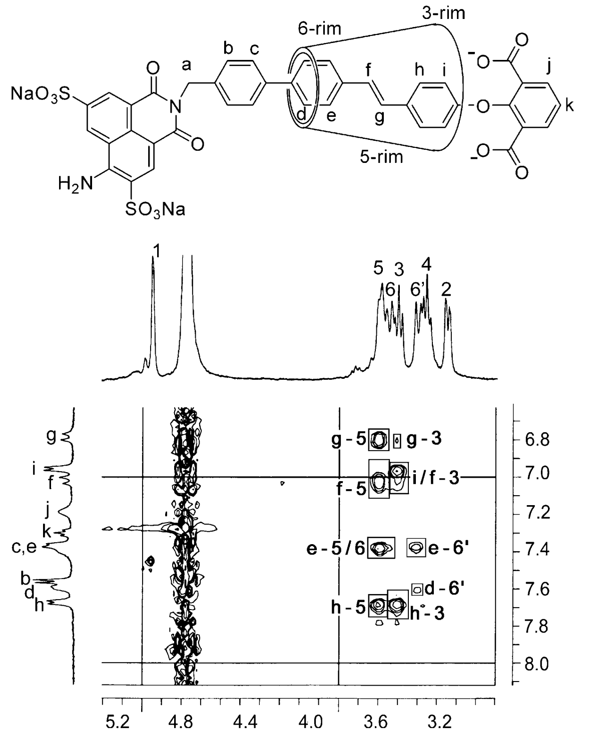

Figure 3. ^1H ROESY NMR (500 MHz) spectrum of [α-CD-NPSI]$^{2-}$ in D_2O recorded at 298 K.

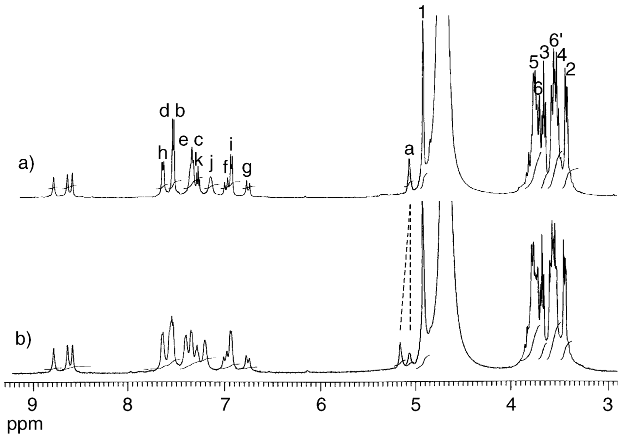

Figure 4. ^1H NMR spectra (500 MHz in D_2O at 298 K) of [α-CD-NPSI]$^{2-}$ a) before irradiation and b) after irradiation at 335 nm for 65 min (b).

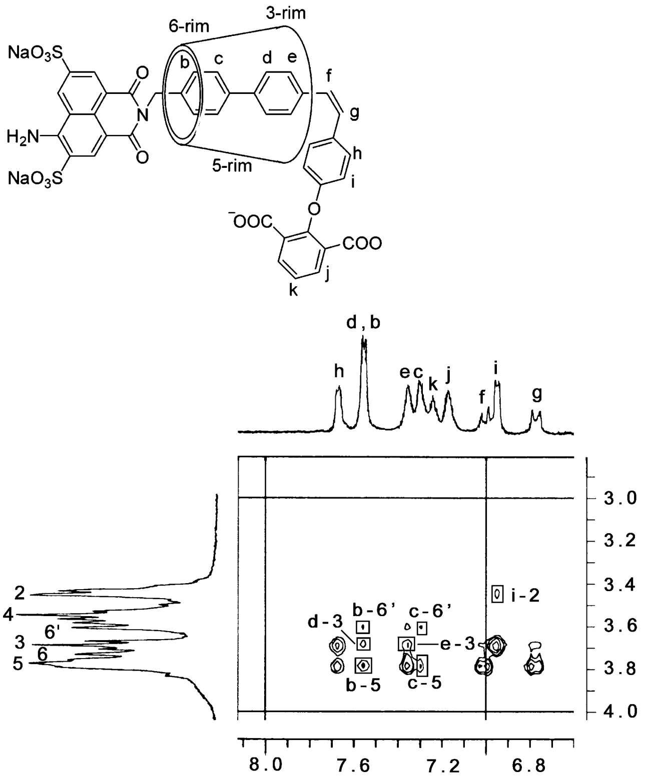

Figure 5. ^1H ROESY NMR (500 MHz) spectrum of [α-CD-NPSI]$^{2-}$ in D_2O recorded at 298 K afte irradiation at 335 nm for 65 min.

the strong hydrogen bonding between the OH groups in α-CD and the two carboxyl groups in the isophthalic acid unit, which consequently prevent the α-CD ring from shuttling away to the biphenyl unit, as illustrated in Figure 6. Conversion of the carboxyl groups into the disodium salt by adding 10 moles of solid Na_2CO_3 to the solution (pH 10.5), which destroys the strong hydrogen bonds, enables the photoisomerization of [α-CD-NPSI]$^{2-}$. Before irradiation, the same NOEs between the aromatic protons and 3-H, 5-H and 6-H protons on the interior of the α-CD annulus were found, as shown in Figure 3, which indicates that the ring is still found over the stilbene unit. Irradiation of the product at 335 nm for 65 min leads to new sets of NOEs from H_b, H_c to 5-H and 6-H, from H_d, H_e to 3-H, and from H_i to 2-H, on the external surface of the α-CD, as shown in Figure 5. These results indicate that [α-CD-NPSI]$^{2-}$ undergoes photoisomerization and the α-CD ring shifts from the stilbene unit to the biphenyl unit, as shown in Figure 6. Significant signal broadening and a new signal at $\delta = 5.19$ ppm (H_a of the Z form) and a decrease in $\delta = 5.07$ ppm (H_a of the E form) was found in ^1H NMR spectra after irradiation, as illustrated in Figure 4. Integrals of the two signals at $\delta = 5.07$ ppm and $\delta = 5.19$ ppm appear with a ration of 3:5, which suggests that at the photostationary about 63% of [α-CD-NPSI]$^{2-}$ was transformed from the E form to the Z form.

The absorption changes for the E/Z photoisomerism of systems in aqueous solution are shown in Figure 7. After irradiation at 335 nm of α-CD-NPSI (7.8×10^{-6} M) for 48 h, little change in absorption was found,[10] which is in accordance with the lack of photoisomerization found, as mentioned above. The conversion of α-CD-NPSI into its disodium salt [α-CD-NPSI]$^{2-}$ by adding 10 moles of Na_2CO_3 (pH 9.6) resulted in photoisomerization to give a E/Z mixture after irradiation at 335 nm for 48 min, characterized by an increase in the absorption at around 280 nm ($\Delta A = 0.040$), a decrease in the absorption at 335 nm ($\Delta A = 0.026$), and by the presence of two isobestic points at 317 nm and 370 nm as shown in Figure 7. Similarly, the irradiation on the disodium salt of dumbbell NPSI (Na^+_2[NPSI]$^{2-}$) for 15 min caused an increase in the absorption at around 280 nm ($\Delta A = 0.049$) and a

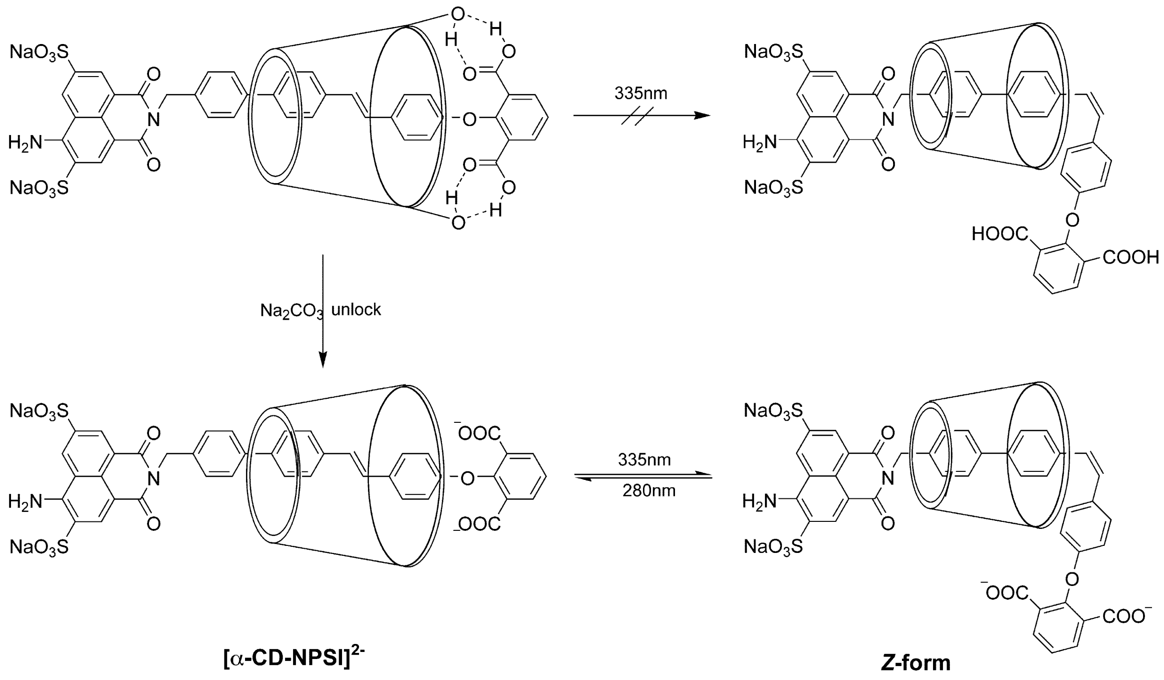

Figure 6. The strong hydrogen bonding between the OH groups in α-CD and the two carboxyl groups in the isophthalic acid unit locks the photo-driven motion of α-CD. The addition of Na_2CO_3 destroys the strong hydrogen bonds, thereby unlocking the shuttling motion.

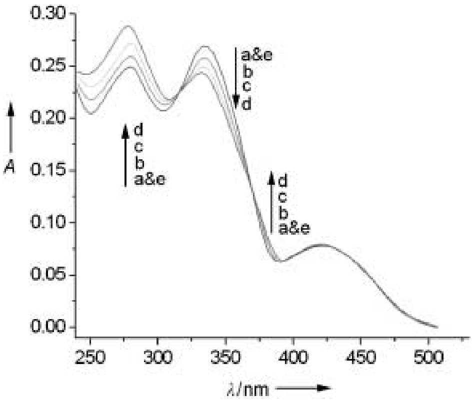

Figure 7. The absorption spectra of an aqueous solution of [α-CD-NPSI]$^{2-}$ a) before and b) after irradiation at 335 nm for 4 min, c) 16 min, d) 48 min. e) These changes in the absorption spectra can be reversed by irradiating the solution at 280 nm (25 min). The absorption changes of an aqueous solution of [NPSI]$^{2-}$ (7.8×10^{-6} M) at 25 °C after irradiation (335 nm) for 15 min were very similar.

decrease at 335 nm ($\Delta A = 0.032$). The fact that the spectral changes for [NPSI]$^{2-}$ are greater than for [α-CD-NPSI]$^{2-}$ indicates that [NPSI]$^{2-}$ undergoes $E\rightarrow Z$ photoisomerization more easily.[11] This is not surprising as the $E\rightarrow Z$ isomerization becomes more difficult in the presence of the α-CD ring.[9] The maximum absorption of 4-amino-3,6-disulfonic-1,8-naphthalimide disodium salt at around 422 nm changes little, because this unit is separated from the residues by the methylene group.

The absorption changes in [α-CD-NPSI]$^{2-}$ are accompanied by a parallel increase by about 46 % in the intensity of the fluorescence band at $\lambda_{max} = 530$ nm, as illustrated in Figure 8, while there is only a small increase by about 4 % in the intensity of the same fluorescence band in [NPSI]$^{2-}$.[10] This behavior is the result of the rigidity of the α-CD ring shifting away from the stilbene unit to the biphenyl unit, which hinders the vibration and the rotation of the bonds in the methylene and biphenyl units. This is confirmed by the finding of the weaker fluorescent intensity of dumbbell [NPSI]$^{2-}$,[10] in which the vibration and rotation modes more facile without the macrocycle.

When the photoisomerization of [α-CD-NPSI]$^{2-}$ from the E form to the Z form and the consequent α-CD shuttling have

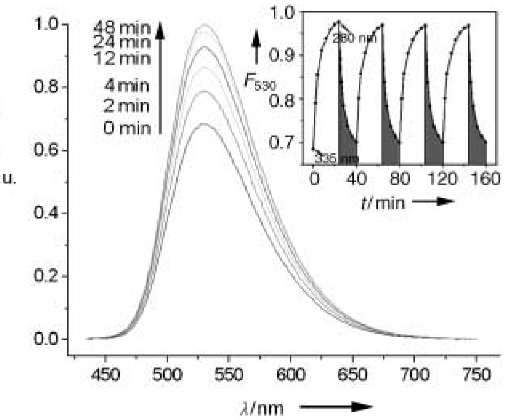

Figure 8. The increasing intensity of fluorescence (emission at 422 nm) of an aqueous solution of [α-CD-NPSI]$^{2-}$ (7.8×10^{-6} M) after irradiation at 335 nm (0 to 48 min). These changes in the absorption spectra can be reversed by irradiating the solution at 280 nm (25 min). Insert: Changes in fluorescence intensity at 530 nm (excited at 422 nm) for aqueous solution of [α-CD-NPSI]$^{2-}$ on alternating irradiation at 335 nm and 280 nm.

been performed, the equilibrium can be shifted back to the *E* form by irradiation at 280 nm. This process is accompanied by a decrease in the absorption at around 280 nm and a rise at 335 nm (Figure 7), as well as a decrease in the intensity of fluorescence at $\lambda_{max} = 530$ nm (Figure 8). Because of the full reversibility of the photoisomerization process, the photoinduced shuttling motion of the α-CD can be repeated (Figure 6) with reversible fluorescent output signals (Figure 8 insert). Thus, the photoinduced shuttling motion in α-CD-NPSI, which is a lockable molecular switch, can be easily detected by means of a fluorescent output signal at 530 nm.

In summary, a new [2]rotaxane, $[\alpha\text{-CD-NPSI}]^{2-}$, is a light-driven molecular shuttle, in which the α-CD macrocycle can shuttle back and forth between the stilbene unit and biphenyl unit by alternating the irradiation frequency. This shuttling is accompanied by obvious changes in the intensity of fluorescence at 530 nm. The shuttle can be locked by simple acidification. It also should be noted that the inputs (switching on at 335 nm and off at 280 nm) are photochemical.

Received: January 9, 2004
Revised: March 3, 2004 [Z53708]

Keywords: cyclodextrins · molecular devices · photochemistry · rotaxanes · supramolecular chemistry

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