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Photoresponsive Host−Guest Systems Based on a New Azobenzene-Containing Crytpand

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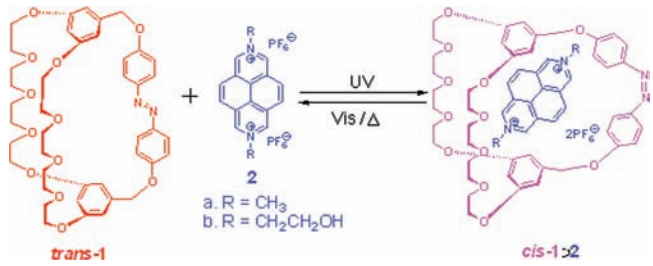
ABSTRACT



A new azobenzene-bridged cryptand was synthesized; it can be well controlled between *cis* and *trans* isomers by irradiation with different wavelengths or by being heated. It was found that this cryptand exhibits an ON−OFF binding ability with 2,7-diazapyrenium (DAP) derivatives. It binds DAP derivatives as the *cis* isomer only, as demonstrated by various methods. The fluorescence property of DAP derivatives endows these host−guest systems with detectable fluorescent output signals, which makes monitoring these photoresponsive systems convenient.

Of the different kinds of stimuli (chemical,[1] electrochemical,[2] heat,[3] and photo[4]) which can drive molecular machines or other supramolecular systems, photo stimulus[4] has acquired particular attention because of accessibility, instant action, and cleanness. Therefore, several efficient photoresponsive host−guest systems have been constructed and intensively studied in the past 30 years. The cyclodextrin (CD)−azobenzene system[5] has been widely used in the fabrication of molecular machines, supramolecular polymers, and drug-delivery materials. The cyclobis(paraquat-*p*-phenylene)-4,4′-azobiphenyloxy system[6] has been applied in a STOP−GO

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molecular shuttle recently. However, there are still only a few efficient photoresponsive host−guest systems.

2,7-Diazapyrenium (DAP) derivatives, which combine the features of pyrene, methylviologen, and nucleic acid intercalators, are attractive building units in supramolecular chemistry.[7] They have been incorporated in a variety of supramolecular systems as excellent π-electron-deficient units.[8] Furthermore, due to their luminescence properties, they have also been widely used as fluorescence probes for the detection of ions[9] and neurotransmitters,[10] both of which are important substances in life processes.

In our previous work on complexation of crown ether-based cryptands with *N*,*N*′-dimethyl-2,7-diazapyrenium bis(hexafluorophosphate), it was found that the cryptand cavity size has an important influence on the host−guest binding strength.[11] Therefore, we introduced a photoresponsive azobenzene unit into the third arm to make a new cryptand **1** (Figure 1). Acting as a "hinge", the azobenzene unit can

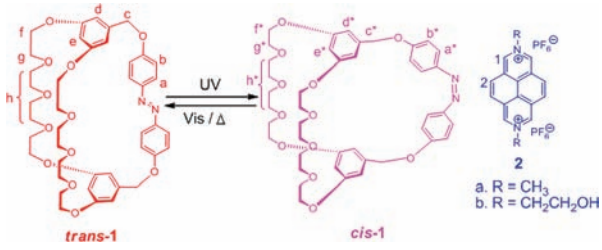

Figure 1. *Trans*−*cis* isomerism of cryptand **1** and the structures of 2,7-diazapyrenium derivatives **2**.

change the cavity size of **1** by its photocontrolled *trans*−*cis* isomerization process (Figure 1). It was expected that the change of the cavity size would influence the binding of cryptand **1** to DAP derivatives. Herein we report the synthesis of **1** and its application in the fabrication of photoresponsive host−guest systems with DAP derivatives **2** (Figure 1).

Cryptand **1** was made from bis(5-bromomethyl-*m*-phenylene)-32-crown-10 and 4,4′-dihydroxyazobenzene via a ring-closing reaction. As expected, cryptand **1** exhibited good photoresponsive properties as investigated by UV−vis spectroscopy (Figure S4, Supporting Information). Upon irradiation with UV light at 350 nm for 30 s, the absorption band at around 359 nm of **1** in CH_3CN decreases remarkably, and concomitantly the band at around 442 nm increases slightly. The absorption bands of the azobenzene unit at 359 and 442 nm are ascribed to $\pi-\pi^*$ and $n-\pi^*$ transitions, respectively.[12] The change of the absorption bands induced by UV irradiation is indicative of the photoisomerization of **1** from the *trans* to the *cis* state. When irradiated by visible light ($\lambda = 450$ nm), the $\pi-\pi^*$ absorption increased with a slight decrease in the $n-\pi^*$ absorption, indicating that **1** underwent a change from the *cis* form to the *trans* form. The photoisomerization process of **1** was also investigated by ^{1}H NMR spectroscopy. Compound **1** prefers the *trans* form in CD_3CN under normal conditions; the resonances of both isomers can be observed in the ^{1}H NMR spectrum at a ratio of 78:22 (*trans*/*cis*). After the irradiation ($\lambda = 350$ nm) of its CD_3CN solution for 5 min at room temperature, the ratio changed to 57:43 (*trans*/*cis*). Based on proton NMR characterization, almost all *cis*-**1** molecules changed to the *trans*-**1** molecules when the solution was heated in the dark for about 1 h.

The complexation of **1** with **2** was studied by ^{1}H NMR spectroscopy. As shown in Figure 2, when equivalent **2a** was

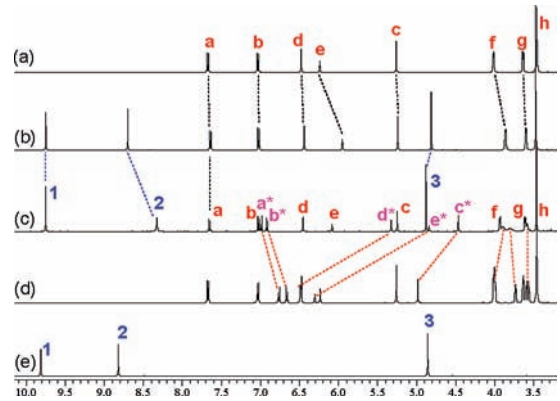

Figure 2. Partial ^{1}H NMR spectra (500 MHz, MeCN-d_3, 295 K) of (a) *trans*-**1**, (b) a 1.00 mM equivalent mixture of *trans*-**1** and **2a**, (c) irradiation of b with light at 350 nm for 1 min, (d) irradiation of *trans*-**1** with light at 350 nm for 1 min, and (e) **2a**.

added into *trans*-**1**, the signals of protons on the guest **2a** changed slightly and only the signals of H_e and H_f, which are positioned at one side of the cryptand, changed significantly. We cannot judge whether *trans*-**1** can form an inclusion complex with **2a** only from these chemical shift changes. In the ESI-MS there were not any signals related to complex *trans*-**1**⊃**2a**. The same situation was found for *trans*-**1** and **2b**. These results indicated that *trans*-**1** did not form inclusion complexes with DAP derivatives **2** or at least had only weak interactions with them, which was also

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confirmed by isothermal titration microcalorimety. Thus, we assumed that these chemical shift changes were due to the side-on interactions between electron-rich phenyl rings of *trans*-**1** and the electron-poor aromatic rings of **2a**.[13] On the other hand, when an equivalent *trans*-**1** and **2a** solution was irradiated by UV light for 5 min, the ratio of the *trans* to *cis* form changed to 48:52, higher than the situation when DAP salt **2a** was not added. This revealed that the existence of DAP salt **2a** could help the transformation of **1** from the *trans* state to the *cis* state and also implied that the *cis*-**1** isomer has some interactions with **2a**. As shown by spectrum d in Figure 2, the chemical shifts of some protons on *cis*-**1** changed dramatically. Signals of H_{d*} and H_{e*}, the protons on the π-electron rich benzene rings of *cis*-**1**, shifted upfield 1.16 and 1.46 ppm, respectively. Furthermore, the peak related to benzylic protons H_{c*} shifted upfield 0.52 ppm. At the same time, the signal of H_2 protons on the π-electron deficient units of **2a** shifted upfield 0.49 ppm. All these chemical shift changes indicated that π-donor/π-acceptor interactions exist between *cis*-**1** and **2a**. The ESI-MS experiments further demonstrated the formation of a 1:1 complex between **1** (obviously the *cis* isomer since the *trans* form was unable to bind **2a**) and **2a**. Two relavent peaks were found at *m*/*z* 504.5 (48%) and 1154.0 (100%) for *cis*-**1**⊃**2a** corresponding to $[cis\text{-}\mathbf{1}\supset\mathbf{2a} - 2\ PF_6]^{2+}$ and $[cis\text{-}\mathbf{1}\supset\mathbf{2a} - PF_6]^{+}$, respectively. No peaks related to complexes with other stoichiometries were found. A Job plot using ^{1}H NMR data confirmed the 1:1 stoichiometry of the complex between *cis*-**1** and **2a**. By fitting the chemical shift change of H_2 on the guest as a function of the initial concentration of *cis*-**1**, the association constant (K_a) of *cis*-**1**⊃**2a** was determined to be 3.33 ($\pm$1.26) $\times$ 10^4 M^{-1} in CH_3CN.

From the study of the thermal isomeriztion process from *cis*-**1** to *trans*-**1** in the dark,[14] we found that the rate constant of the thermal back-relaxation *cis*-*trans* transformation of **1** without DAP guests was 1.20 $\times$ 10^{-4} min^{-1} in MeCN, while it dropped to 8.04 $\times$ 10^{-5} min^{-1} when **2a** was added. This decreased rate also demonstrated that **2a** stabilized the *cis* form of **1** and delayed the *cis*−*trans* transformation process.

2D NOESY is a useful tool to study the relative postions of the components in host−guest inclusion complexes. From the 2D NOESY spectrum of a mixture containing *trans*-**1**, *cis*-**1**, and **2a** (1:1:2), it was found that only some protons on *cis*-**1** have NOE correlation signals with protons on the guest **2a** (Figure 3). Protons H_{f*}, H_{g*}, and H_{h*} on the ether chains of *cis*-**1** have NOE correlations with protons H_1 on **2a**. A NOE correlation was observed between H_{a*} on the azobenzene unit of *cis*-**1** and H_2 on **2a** (Figure S13, Supporting Information). Since ethyleneoxy protons H_{f*} and H_{g*} and azobenzene protons H_{a*} and H_{h*} are on different

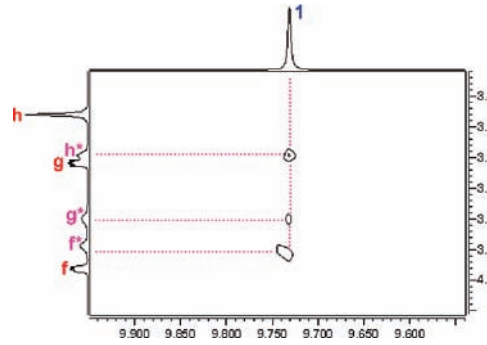

Figure 3. Partial NOESY NMR spectrum (500 MHz, MeCN-d_3, 295 K, 300 ms for the mixing time) of a mixture of *trans*-**1**, *cis*-**1**, and **2a** (1: 1: 2).

sides of *cis*-**1**, the above-mentioned correlations between *cis*-**1** and **2a** suggested that **2a** penetrates through the cavity of *cis*-**1**. On the other hand, no NOE signals were found between *trans*-**1** and **2a**. Similar NOESY results were obtained for the case of **1** and **2b** (Figure S10, Supporting Information). These observations further demonstrated that *cis*-**1** could form inclusion complexes with DAP salts **2**.

Single-crystal X-ray analysis and molecular modeling were used to further validate our interpretation of the binding difference between the *trans* and *cis* forms of cryptand **1** to DAP salts **2**. Single crystals of *trans*-**1** were obtained by vapor diffusion of diisopropyl ether into a solution of **1** in CH_3CN, while single crystals of *cis*-**1** could not be obtained despite many attempts using different solvents and growing techniques. This is understandable considering that *cis*-**1** easily transforms to *trans*-**1** in the time required to form single crystals. However, the energy-minimized structures[15] which revealed the situation in solution are valuable. The energy-minimized structure (Figure S15b, Supporting Information) of *trans*-**1** is almost identical to its X-ray crystal structure (Figure 4a) in the solid state, showing the accuracy

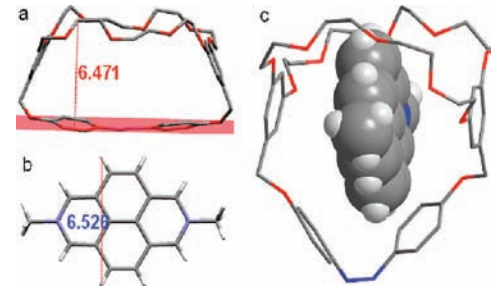

Figure 4. X-ray crystal structures of *trans*-**1** (a) and **2a** (b) and energy-minimized structure of *cis*-**1**⊃**2a** (c).

of the molecular modeling result to a certain degree. X-ray analysis and modeling of *trans*-**1** revealed a narrow cavity which is not big enough to include molecule **2a**.[16] What's more, the two π-electron-rich benzene rings of *trans*-**1** are

(13) (a) We also found this phenomenon previously. See: Li, S.; Liu, M.; Zhang, J.; Zheng, B.; Wen, X.; Li, N.; Huang, F. *Org. Biomol. Chem.* **2008**, *6*, 2103–2107. (b) It was reported that *trans*-azobenzene moiety could interact with DAP derivatives by π-electron donor−acceptor interaction: Balzani, V.; Credi, A.; Marchioni, F.; Stoddart, J. F. *Chem. Commun.* **2001**, *18*, 1860–1861. However, we didn't find obvious evidence for such kind of interaction between *trans*-**1** and DAP salts.

(14) The kinetic measurements of thermal isomerization of **1** were carried out according to the following reference: Wei, W.; Tomohiro, T.; Kodaka, M.; Okuno, H. *J. Org. Chem.* **2000**, *65*, 8979–8987.

nonparallel with a torsion angle of 47.96°. Therefore, good $\pi-\pi$ stacking and charge transfer between them and the π-electron-poor aromatic rings of **2a** can not be achieved. On the contrary, the cavity of *cis*-**1** in its energy-minimized structure (Figure S15c, Supporting Information) is spacious enough for the inclusion of **2a**. The two π-electron-rich benzene rings are nearly parallel, which will be good for the $\pi-\pi$ stacking and charge-transfer interactions between the host and guest. Finally, the energy-minimized structure of *cis*-**1**⊃**2a** (Figure 4c) showed a compact, well-stacked host−guest system. Besides π-donor/π-acceptor interactions, some hydrogen bonds (between H_2 and oxygen atoms on the ether chains of *cis*-**1**) and C−H···π interactions (between the protons on **2a** and the benzene rings of the azaobenzene unit) can also contribute to stabilize the complex structure.

The fluorescence property of DAP salts enables monitoring these photocontrolled host−guest systems. When an equimolar amount of *trans*-**1** was added into an MeCN solution of **2a** (Figure 5a), the fluorescence intensity did not change

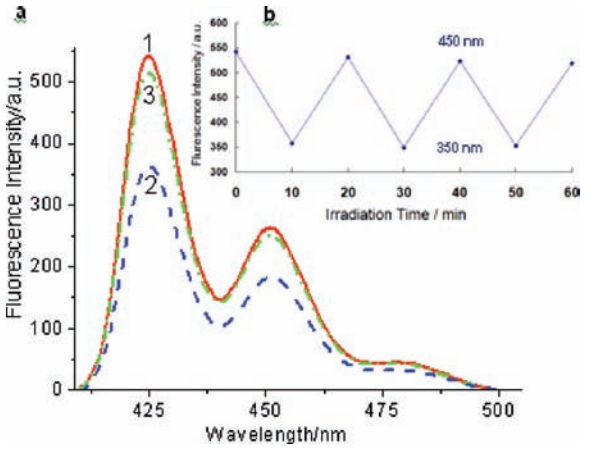

Figure 5. (a) Fluorescence spectra of (1) equimolar *trans*-**1** and **2a**, (2) irradiation with light at 350 nm for 1 min, (3) then irradiation with light at 450 nm for 10 min (MeCN, 25 °C). (b) Changes in the fluorescence intensity of equimolar *trans*-**1** and **2a** in CH_3CN along with changes in irradiation time and light source. Light sources of 350 and 430 nm light were alternated every 10 min.

appreciably,[17] once again indicating no interaction between *trans*-**1** and the DAP salt. However, after irradiation of this solution with UV light at 350 nm for 1 min, the fluorescence intensity decreased by 33%, implying that some **2a** molecules went into the cavities of the "newborn" *cis*-**1** molecules and that their fluorescence was quenched by charge transfer between the host and guest. Finally, the fluorescence intensity of the system was almost completely recovered after irradiation of the same solution with visible light at 450 nm for 10 min, transforming *cis*-**1** to *trans*-**1**. After several cycles being alternately irradiated with lights at 350 and 450 nm, this system showed very good recovery according to the fluorescence intensity changes (Figure 5b). From another point of view, the mixture of *trans*-**1** and **2a** can work as a chemical sensor for UV light. Its fluorescence intensity will decrease when exposed to UV light.

In summary, a new photoresponsive cryptand was synthesized. It is well controlled between the *trans* and *cis* isomers in solution by being irradiated with lights at different wavelengths or by being heated. It was found that this cryptand exhibits an ON−OFF binding ability to 2,7-diazapyrenium derivatives; it forms inclusion complexes with 2,7-diazapyrenium derivatives as a *cis*-isomer only, which has been well demonstrated by various characterization techniques. This new efficient photocontrolled host−guest recognition motif can be used in the fabrication of more complicated photoresponsive supramolecular systems. Furthermore, these derived supramolecular systems themselves will have easily detected fluorescence output, making it convenient to monitor their photocontrolled operation. Moreover, the robust interactions between DAP derivatives and nucleic acids or nucleotides imply that this new host−guest recognition motif has potential applications in the biological field.

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Supporting Information Available: Synthesis of **1**, kinetic measurements, crystal data for *trans*-**1**, and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) The energy-minimized structures of *trans*-**1**, *cis*-**1**, and *cis*-**1**⊃**2a** were calculated by GAUSSIAN 03 software, based on the arithmetic method B3LYP/6-31G(D): Frisch, M. J. et al. *Gaussian 03, revision D.01*; Gaussian, Inc.: Wallingford, CT, 2005. See the Supporting Information (ref S5) for the complete reference.

(16) The height, 6.526 Å, of guest molecule **2a** is bigger than the height, 6.471 Å, of *trans*-**1**'s cavity, indicating that **2a** cannot be included in the cavity of *trans*-**1** at a good stacking position.

(17) A slight decrease of the fluorescence intensity possibly resulted from some transformation of *trans*-**1** to the *cis* form, induced by the addition of **2a** guest.