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Reversible Molecular Switch of Acridine Red by Triarylpyridine-Modified Cyclodextrin

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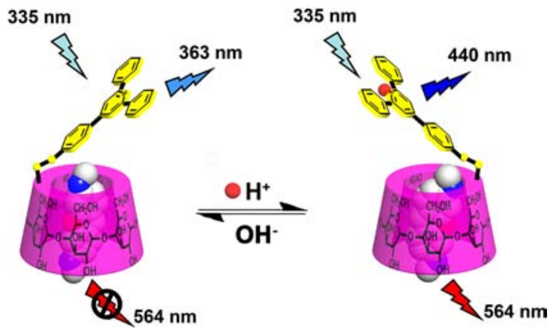
ABSTRACT



A novel molecular switch based on the supramolecular complex of 2,4,6-triarylpyridine modified β-cyclodextrin and acridine red was successfully constructed in aqueous solution, displaying the controlled photophysical behaviors by the effect of supramolecular positive cooperativity and fluorescence resonance energy-transfer process.

Stimuli-responsive supramolecular systems have stimulated considerable interest toward the construction of highly functional materials, mainly due to their immense advantages to achieve reversible and precise control of the photophysical properties and electronic communications in diverse nanoarchitectures through the cooperative contribution of noncovalent forces.[1] Among various components that are commonly involved in the molecular recognition and self-assembly, macrocyclic synthetic receptors as building blocks offer an alternative and even a more powerful strategy in the field of stimuli-responsive supramolecular systems.[2−6] Of which, cyclodextrins (CDs) as a class of cyclic oligosaccharides represent the superior candidates to construct the dynamically assembled nanomachines. However, the inventive developments of their reversible switching process with associated change in the spectroscopic behaviors still deserve our careful attention. Recently, Harada et al. have designed a [2]rotaxane comprising β-CD and oligothiophene units, implementing a

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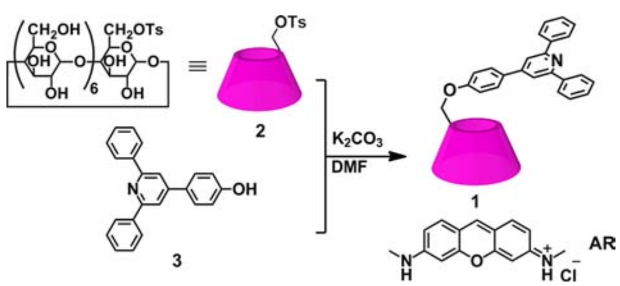
tunable intermolecular energy transfer process from the excited [2]rotaxane to the sexithiophene derivative.[7] Stoddart et al. have successfully elucidated a bistable [2]-rotaxane in which the redox-responsive movements of α-CD toward tetrathiafulvalene and triazole moieties were efficiently achieved under the control of external inputs.[8]

We have previously demonstrated a twisted intramolecular charge transfer (TICT) sensor for the magnesium ion (Mg^{2+}) based on triarylpyridine−crown ether conjugate.[9] These findings inspired us to hypothesize that a reversibly photophysical process may take place from the triarylpyridine moiety as a donor molecule to some appropriate guests as acceptor molecules. In the present work, one of the most commonly employed xanthene dyes,[10] acridine red (AR), was chosen as guest molecule to comprehensively study the cooperative noncovalent interactions in the host-enhanced molecular switch, taking both the binding affinity of β-CD with AR and the spectral complementarity of triarylpyridine and AR into account.

Scheme 1. Synthetic Routes of Compound **1** and Molecular Structure of Acridine Red (AR)



The synthetic route of 2,4,6-triarylpyridine modified β-CD (**1**) and molecular structure of AR were described in Scheme 1. 4-(4,6-Diphenylpyridin-2-yl)phenol (**3**) was prepared from 4-hydroxybenzaldehyde and acetophenone according to the reported literature.[11] Next, mono[6-*O*-(*p*-toluenesulfonyl)]-β-CD (**2**) reacted with the intermediate **3** under basic conditions to afford compound **1** in 60% yield (Figures S1−S3, Supporting Information). Benefiting from the CD unit as solubilizer, host compound **1** showed a satisfactory water solubility up to 0.2 M (i.e., 250.2 mg/mL). The good solubility of **1** was ascribed to the partial inclusion of triarylpyridine moiety into the cavity of CD in water (Figure S4, Supporting Information).

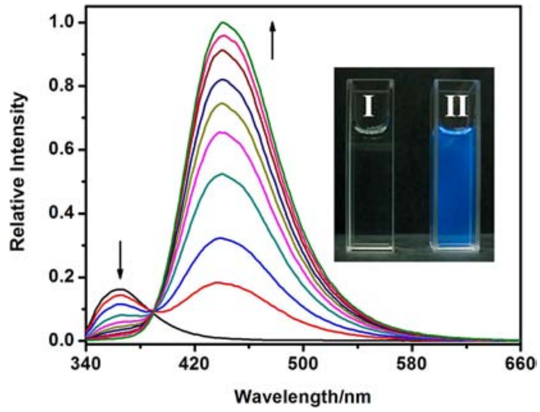


Figure 1. Emission spectral changes of **1** (5.0×10^{-5} M) upon addition of 0−150 equiv of $HClO_4$ in aqueous solution at 25 °C (λ_{ex} = 335 nm). Inset: visible emission of **1** in the absence (I) and presence (II) of $HClO_4$.

It is well-established that the 2,4,6-triarylpyridine signaling unit is an attractive chromophore featuring visible emission from a locally excited state and a charge transfer state induced by the coordination of an ion to pyridyl nitrogen.[12] Therefore, the quantitative investigation of intramolecular charge transfer (ICT) property of compound **1** in the presence of perchloric acid was examined by means of the absorption and fluorescence spectroscopy titration. As shown in Figure S5 (Supporting Information) with the stepwise addition of $HClO_4$ to a solution of **1**, the absorption peak of **1** at 270 nm gradually declined while the absorption peak at 333 nm increased in proportion, accompanied by an isosbestic point at 304 nm. In addition, the protonation of nitrogen atoms on triarylpyridine moiety led to a significant bathochromic shift from 363 to 440 nm with an enhancement of emission intensity (Figure 1). Obviously, these new absorption and emission bands in the long-wavelength region originate from the ICT process from the phenoxyl to pyridyl moiety.[9] It was noteworthy that this ICT process could be readily distinguished by not only spectroscopic experiments but also the naked eye upon irradiation with 365 nm light. That is, **1** (5.0×10^{-5} M) alone exhibited no obvious fluorescence but gave a strong blue fluorescence in the presence of $HClO_4$ (Figure 1, inset photos). Furthermore, as shown in Figure S6 (Supporting Information), deprotonation of $\mathbf{1}\cdot H^+$ system with NaOH could restore the original emission of **1**, which facilitates the proton-triggered reversible molecular switch by the addition of acid and base as described below.

Subsequently, the photophysical behaviors accompanied by the formation of a supramolecular complex between **1** and AR were further verified by fluorescence spectral titration. As seen in Figure S7 (Supporting Information),

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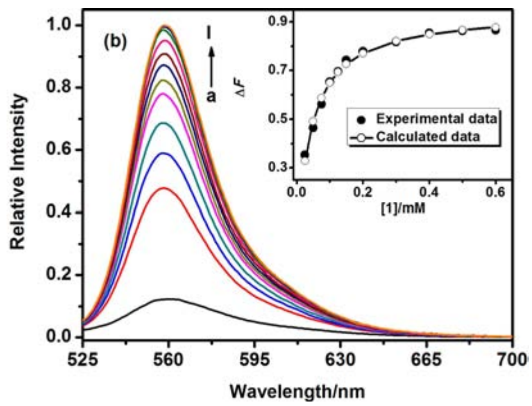

Figure 2. Emission spectral changes of AR upon addition of **1** in the presence of $HClO_4$ at 25 °C ([AR] = 5.0×10^{-6} M, [$HClO_4$] = 6.0×10^{-2} M, [**1**] = 0−6.0×10^{-4} M, respectively, from a to l). Inset: The nonlinear least-squares analysis of the differential spectral changes (ΔF) at 557 nm to calculate the stability constant (K_S) of **1** and AR (λ_{ex} = 520 nm).

when excited at 520 nm to avoid any absorption of **1** and **1**·H^+, the fluorescence intensity of AR was significantly enhanced upon stepwise addition of **1** in the neutral solution, indicating that the guest molecule AR was encapsulated into the hydrophobic cavity of CD. According to the 1:1 binding stoichiometry in the supramolecular complex between native β-CD and AR,[13] the binding constant (K_S) in **1**/AR system was calculated to be 8.39×10^3 M^{-1} (Figure S7, Supporting Information, inset) by analyzing the sequential changes in fluorescence intensity (ΔF) of AR at varying concentrations of **1** by a nonlinear least-squares curve-fitting method. Moreover, using the similar fluorescence titration method, the K_S value between **1** and AR under acidic conditions was calculated to be 2.29×10^4 M^{-1} (Figure 2). Comparatively, lacking the 2,4,6-triarylpyridine moiety, the binding abilities of β-CD/AR complexes in neutral and acidic conditions were only 2.93×10^3 and 3.74×10^3 M^{-1}, respectively (Figures S8 and S9, Supporting Information). Considering that the fluorescence emission of AR was not sensitive to the addition of $HClO_4$ under our experimental conditions (Figure S10, Supporting Information), the significant enhancement in complex formation constants of **1**/AR and **1**·H^+/AR systems is contributed to the supramolecular cooperative contributions of protonated triarylpyridine substituent and β-CD cavity toward guest molecules.

It is well-documented that some criteria must be required to achieve a more effective fluorescence resonance energy transfer (FRET) process.[7,14] That is, the donor and acceptor chromophores should be located in close proximity, and the absorption spectrum of acceptor should sufficiently fall into the fluorescence emission spectrum of donor through long-range dipole−dipole interaction. As seen in Figure S11 (Supporting Information), no obvious spectral overlap could be observed between the fluorescence emission band of **1** and absorption band of AR, whereas there was appreciable overlap in the case of **1**·H^+ and dye molecule. Therefore, it is anticipated that the **1**·H^+/AR complex could exhibit the through-space energy transfer behaviors.

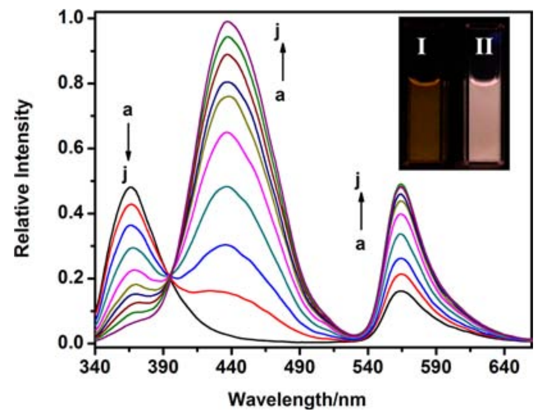

Figure 3. Emission spectral changes of **1**/AR complex upon addition of $HClO_4$ in aqueous solution at 25 °C ([**1**] = [AR] = 5.0×10^{-5} M, [$HClO_4$] = 0−15.0×10^{-4} M, respectively, from a to j, λ_{ex} = 335 nm). Inset: visible emission of **1**/AR complex in the absence (I) and presence (II) of $HClO_4$.

The fluorescence emission spectra of **1**·H^+/AR complex (1:1, 5.0×10^{-5} M) with increasing amounts of $HClO_4$ are shown in Figure 3. Through a calculation based on the binding constant between **1**·H^+ and AR as well as the concentrations of host and guest, more than 40% of **1**·H^+ could be converted to **1**·H^+/AR complex under our experimental conditions. When excited at 335 nm that corresponded to the absorption band of triarylpyridine moiety, the emission of **1** at 363 nm was gradually decreased upon addition of $HClO_4$, and the CT emission of **1**·H^+ at 440 nm and AR emission at 564 nm were synchronously increased (Figure 3, inset photos). In addition, the excitation spectrum of **1**·H^+/AR complex was recorded by monitoring the emission wavelength at 620 nm, in which the signals assigned to the absorptions of AR in the range from 430 to 580 nm and a strong band assigned to the absorptions qof **1**·H^+ around 350 nm appeared, giving further evidence for the energy transfer process (Figure S12, Supporting Information). Applying the absolute fluorescence quantum yield (Φ_F) of **1**·H^+ in the absence (0.157) and presence (0.113) of AR, the energy transfer efficiency (E) in 1:1 **1**·H^+/AR complex was calculated as 28.2%.[15] These phenomena clearly indicate that the protonation of triarylpyridine moiety may cause the charge transfer from

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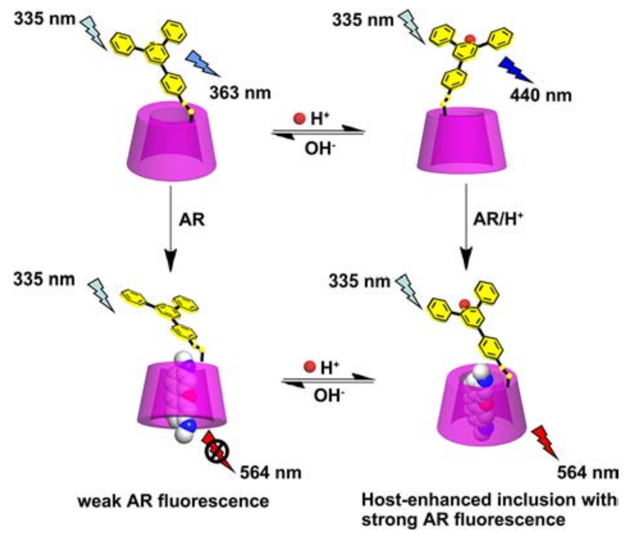
phenoxyl to pyridyl moiety followed by a FRET from the excited $\mathbf{1}\cdot H^+$ as donor to the included AR dye as acceptor.

To confirm the assumption of FRET mechanism in the formation of $\mathbf{1}\cdot H^+$/AR complex, some control experiments were carried out. The emission spectra of $\mathbf{1}\cdot H^+$ upon addition of AR in different molar ratios are shown in Figure S13 (Supporting Information). The CT emission of $\mathbf{1}\cdot H^+$ at 440 nm was decreased, whereas the fluorescence of emission AR at 564 nm was accordingly increased, undoubtedly demonstrating the energy transfer process from $\mathbf{1}\cdot H^+$ to AR in aqueous solution. Moreover, although the emission intensity of AR in the presence of $\mathbf{1}\cdot H^+$ was 0.5 times higher upon excitation at 525 nm, the one was 2.3 times higher upon excitation at 335 nm at the same concentrations (Figures S14 and S15,Supporting Information). Therefore, we can deduce that the effect of supramolecular positive cooperativity and intermoleczular FRET process jointly contribute to the proton-triggered fluorescence enhancement of dye molecule in $\mathbf{1}\cdot H^+$/AR complex.

Among the various external stimuli, it has been proven that pH change is a simple and accessible strategy to efficiently modulate the multicomponent assemblies in a precisely controlled manner. In our case, when NaOH was added to the solution of $\mathbf{1}\cdot H^+$/AR, the fluorescence emission at 363 nm of **1** was restored, suggesting that the triarylpyridine unit existed in neutral state. Meanwhile, the cooperative binding in host–guest complex and FRET process from $\mathbf{1}\cdot H^+$ to AR were completely suppressed. In addition, the enhancement of AR emission could be regenerated along with the reproduction of CT emission at 440 nm when adding another portion of $HClO_4$ to the same solution (Figure S16, Supporting Information). The reversibility can be repeated for several cycles (Figure S16, Supporting Information, inset). Consequently, a noncovalently connected conjugate of triarylpyridine-grafted CD and dye molecule based on the effect of positive supramolecular cooperativity and FRET mechanism was successfully constructed and the photophysical communications between donor and acceptor sites could be reversibly governed by adding acid and base in series. The schematic illustration of this reversible switching process via the acid–base input is illustrated in Scheme 2.

In conclusion, a newly synthesized β-CD derivative bearing a 2,4,6-triarylpyridine moiety (**1**) is found to form a stable supramolecular complex with AR, pronouncedly increasing about 1 order of magnitude in K_S value as compared with the corresponding native β-CD. Furthermore, an efficient molecular switch based on **1**/AR supramolecular complex has been represented. As investigated by fluorescence titrations, it is demonstrated that fluorescent enhancement in the supramolecular system could be modulated in a reversible way by adopting a proton-controlled binding and release strategy. We also envision that the triarylpyridine/AR couple as a new donor/acceptor system may find potential application in the biological system and construction of new molecule-based optical devices.

Scheme 2. Schematic Illustration of the Acid–Base-Modulated Molecular Switch



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Supporting Information Available. General experimental procedures and characterization data for **1**, as well as the fluorescence titrations in control experiments. This information is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.