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Cyclodextrin Supramolecular Complex as a Water-Soluble Ratiometric Sensor for Ferric Ion Sensing

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Heightened concern for human health and environmental protection has stimulated active research on the potential impact of transition-metal ions and their toxic effects, thus it is very demanding to design transition-metal ion detection methods that are cost-effective, rapid, facile, and applicable to the environmental and biological milieus. In this study, we demonstrated an alternative strategy for constructing a water-soluble FRET-based ratiometric sensor for ferric ion detection by forming a supramolecular β-cyclodextrin/dye complex. This water-soluble FRET system consists of a dansyl-linked β-cyclodextrin (β-CD-DNS) and a spirolactam rhodamine-linked adamantane (AD-SRhB). The dansyl moiety serves as the donor, and the spirolactam-rhodamine B derivative (SRhB) was chosen as a sensitive, selective chemosensor for Fe(III) ions and a very efficient ring-opening reaction induced by Fe(III) generates the long-wavelength rhodamine B fluorophore that can act as the energy acceptor. Moreover, the adamantyl (AD) group, which is known for its capability to form stable host−guest inclusion complexes with β-CD derivatives, was covalently linked to the spirolactam rhodamine, thus the adamantyl moiety of the ion-recognition element can be anchored inside the CD cavity. In this way, the donor−acceptor separation can be kept within the critical Förster distance; accordingly, energy transfer can take place from the donor (dansyl) to the acceptor (rhodamine derivative/Fe(III) complex), and thus ratiometric detection for Fe(III) in an aqueous medium can be fulfilled. This FRET-based supramolecular sensor can be readily formed via an inclusion process using the donor part and the acceptor part, hence this strategy could afford a robust approach for constructing a wide range of FRET-based water-soluble sensing systems simply by assembling a specifically predesigned donor-linked CD and acceptor-linked adamantane.

1. Introduction

Fluorescence detection has become a powerful tool for quantitative measurements of various analytes such as H^+,[1] metal ions,[2−4] and glucose[5] in environmental, industrial, medical, and biological applications because of its sensitivity, specificity, and real-time monitoring with fast response time.[1−9] In particular, a fluorescence resonance energy transfer (FRET)-based sensing technique, which does not directly produce redox-active ions that could lead to photodamage or other undesirable processes, has recently attracted considerable attention.[6−11] In addition, FRET can be utilized to realize ratiometric detection that can avoid external interference and/or ambiguities by the self-calibration of two emission bands.[12,13] The heightened concern for human health and environmental protection has stimulated active research on the potential impact of transition-metal ions and their toxic effects, thus it is very demanding to design transition-metal-ion detection methods that are cost-effective, rapid, facile, and applicable to the environmental and biological milieus.[14−17] In recent years, the spirolactam rhodamine derivatives have been found to be ideal for constructing off−on fluorescent chemosensors for transition-metal ions because of their particular structural property.[18,19] As is well known, rhodamine derivatives with spirolactam structure are nonfluorescent whereas ring-opening of the spirolactam gives rise to strong fluorescence emission.[18,19] To date, several rhodamine-modified chemosensors (including some rhodamine-based FRET sensors) for Hg^{2+} and Cu^{2+} ions have been developed.[18,19] In addition, some rhodamine-based sensors for Fe^{3+} via fluorescence enhancement have been reported.[20,21]

Traditionally, many of the FRET-based sensors are created in the form of a dyad or triad in which the donor and the acceptor

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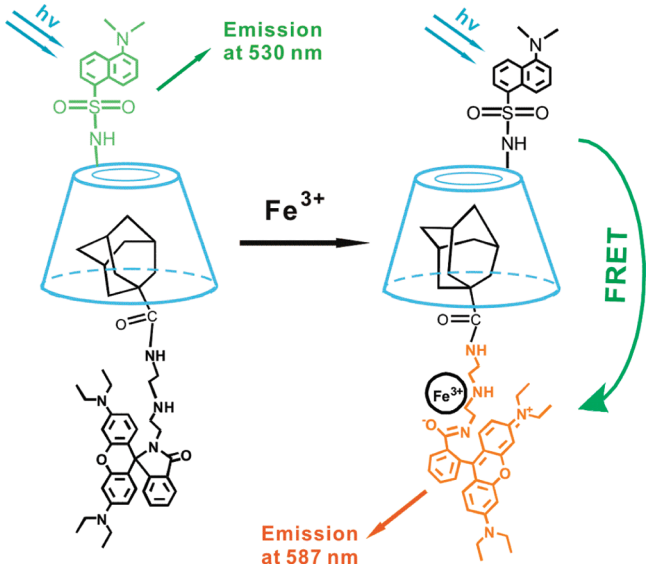
Scheme 1. Formation of the AD-SRhB/β-CD-DNS Supramolecular Complex and Its FRET-Based Ratiometric Sensing of the Ferric Ion in Aqueous Media



are covalently linked through a spacer with a certain length.[22] However, FRET-based sensors can also be created within colloidal nanoparticles, such as capped quantum dots,[22−25] dye-doped silica[26,27] and polymeric nanoparticles,[28−34] and these particle-based FRET systems were found by some researchers[23−29] and our group[30−34] to exhibit high brightness and improved photostability. For the FRET systems to be used in biomedical and environmental applications, it is essential that they are nontoxic and water-soluble to prevent aggregation and precipitation and should have a substantial photoluminescence quantum yield in water.[35] However, it is well known that cyclodextrin (CD) has a unique configuration that makes its outer surface hydrophilic and its inner surface hydrophobic, thus it can form supramolecular inclusion complexes with hydrophobic small-molecule fluorophores that fit into its 5−8 Å cavity;[36−40] the fluorescence intensity, water solubility (and probably biocompatibility), and photostability of the guest fluorophores could be enhanced.[36−41]

Herein, we demonstrated a novel alternative strategy for constructing a FRET-based ratiometric sensor for ferric ion detection by forming a supramolecular β-cyclodextrin/dye complex, as shown in Scheme 1. This water-soluble FRET system consists of a dansyl-linked β-cyclodextrin (β-CD-DNS) and an adamantyl-linked spirolactam rhodamine (AD-SRhB). The dansyl moiety, with its fluorescence spectrum, well matches the absorption spectrum of rhodamine B and serves as the donor whereas the spirolactam-rhodamine B derivative (SRhB) was chosen as a sensitive and selective recognition element for Fe^{3+} and a highly efficient ring-opening reaction induced by Fe^{3+} generates the long-wavelength rhodamine B fluorophore, which can act as the energy acceptor. Moreover, the adamantyl (AD) group, which is known for its capability to form stable host−guest inclusion complexes with β-CD derivatives,[42−48] was covalently linked to the spirolactam rhodamine, thus the adamantyl moiety of the ion-recognition element (AD-SRhB) can be well anchored inside the cyclodextrin cavity. In this way, the donor−acceptor separation can be kept within the critical Föster distance; accordingly, energy transfer can take place from the donor (dansyl moiety covalently linked to β-CD) to the acceptor (rhodamine derivative/Fe^{3+} complex in the CD cavity). Consequently, the ratiometric detection of Fe^{3+} in an aqueous medium can be fulfilled.

2. Experimental Section

2.1. Materials. Rhodamine B (RhB), diethylenetriamine, β-cyclodextrin (β-CD), chloride salts of a metal ion (K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, and Hg^{2+}), the nitrate salt of a metal ion (Ag^+), tris(hydroxymethyl)-aminomethane (Tris), sodium acetate buffer concentrates, potassium hydrogen phthalate buffer concentrate, HEPES sodium salt buffer concentrate, hydrochloric acid/borax buffer concentrate, and sodium tetraborate/sodium hydroxide solution buffer concentrates were purchased from Sigma-Aldrich. Sodium azide (N_3Na), *p*-toluenesulfonyl chloride (TSO-Cl), triphenylphosphine (PPh3), dansyl chloride, *N*,*N*′-dicyclohexylcarbodiimide (DCC), *N*-hydroxysuccinimide (NHS), and triethylamine were obtained from Acros. 1-Adamantanecarboxylic acid (AD-CO-OH) was obtained from Alfa. *N*,*N*-dimethylformamide (DMF) was dried with CaH_2 and vacuum distilled. Triethylamine was dried over molecular sieves and vacuum distilled. Methanol, ethanol, and dichloroethane were analytically pure solvents and distilled before use.

2.2. Synthesis of the Dansyl-Containing β-Cyclodextrin (β-CD-DNS). First, mono-6-*O*-(*p*-tolylsulfonyl)-β-cyclodextrin (6-TSO-β-CD) was prepared according to the literature.[49] β-Cyclodextrin (5 g, 4.4 mmol) was dissolved in a solution of 2.5 g of sodium hydroxide in 150 mL of water. The solution was stirred

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at 0−5 °C in an ice−water bath, and *p*-toluenesulfonyl chloride (1.5 g, 7.90 mmol) was added in one portion. The reaction mixture was stirred vigorously for 1.5 h at 0−5 °C, and then another portion of *p*-toluenesulfonyl chloride (1.5 g, 7.90 mmol) was added and the reaction mixture was stirred at this temperature for another 1.5 h. Finally, the last portion of *p*-toluenesulfonyl chloride (2 g, 10.53 mmol) was added, and the reaction mixture was stirred at this temperature for another 2 h. The reaction mixture was filtered through Celite in a fritted glass funnel to separate unreacted tosyl chloride. The filtrate was cooled at 0−5 °C while 10% aqueous hydrochloric acid (HCl, 35 mL) was added to acidify to pH 1. The resulting solution was stored overnight in a refrigerator at 0 °C and then filtered. The product was dried in a vacuum to yield a white solid. This material was recrystallized (three times) by dissolving it in 20 mL of water at the boiling point and then cooling to room temperature. Storage in a refrigerator overnight provided 1.76 g (yield 31%) of 6-*O*-*p*-toluenesulfonyl-*β*-cyclodextrin as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.75 (d, 2H), 7.43 (d, 2H), 5.63−5.82 (m, 14H), 4.77−4.84 (m, 6H), 4.31−4.49 (m, 6H), 4.19 (m, 1H), 3.19−3.66 (m, 42H), 2.42 (s, 3H). ESI MS m/z $[M + H]^+$ 1287.5.

Second, mono-6-azido-6-deoxy-*β*-cyclodextrin was prepared. Mono-6-(*p*-tolylsulfonyl)-*β*-CD (1.73 g, 1.34 mmol) was dissolved in DMF (325 mL), and sodium azide (174 mg, 2.68 mmol) was added. The reaction mixture was heated to 105−110 °C and stirred for 4 h at this temperature. The almost-clear solution was treated with acetone at room temperature, and a white crystalline precipitate was formed. The crude product was recrystallized from 1:10 water−acetone. Yield: 1.56 g, 97%. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 5.68−5.80 (m, 14H, OH_2, OH_3), 4.87 (m, 1H, H_{1a}), 4.82 (m, 6H), 4.46−4.70 (m, 6H, OH_6), 3.33−3.83 (m, 42H).

Third, mono-6-deoxy-6-amino-*β*-CD (6-NH_2-*β*-CD) was synthesized as follows. A solution of mono-6-azido-6-deoxy-*β*-cyclodextrin (400 mg, 0.345 mmol) and Ph_3P (362 mg, 1.38 mmol) in DMF (5 mL) was stirred for 1 h under an N_2 atmosphere at room temperature. The reaction mixture was cooled to 0 °C, and concentrated aqueous ammonia (2 mL, approximately 28%) was added to the solution and the solution was stirred for 48 h. The resulting suspension was concentrated under reduced pressure, and the triphenylphosphin oxide was then precipitated by the addition of distilled water (100 mL) and filtered. After evaporation of the water, the crude product was washed with acetone and dried under vacuum to yield a white solid. Yield: 0.40 g, 95%. ^{1}H NMR (300 MHz, D_2O) δ: 5.00 (d, 7H, H1), 3.33−4.13 (m, 42H), 3.03−3.07 (m, 2H).

Dansyl chloride (71.2 mg, 0.265 mmol) was added to a stirred solution of 6-NH_2-*β*-CD (300 mg, 0.265 mmol) and triethylamine (1.5 mL) in 5 mL of dry DMF. The reaction was stirred at room temperature for 24 h in the dark. The solvent was evaporated mostly under reduced pressure. Acetone was poured into the residue, and the precipitate was collected and dried in vacuo. Then the residue was recrystallized from water/ethanol (1:1) and dried in vacuo to give *β*-CD-DNS (206.4 mg). Yield: 206.4 mg, 57%. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.41−8.43 (d, 1H), 8.27−8.30 (d, 1H), 8.01 (t, 1H),7.56 (q, 2H), 7.23 (d, 1H), 5.64−5.85 (m, 14H), 4.79−4.83 (m, 6H), 4.45−4.50 (m, 6H), 4.27 (m, 1H), 3.13−3.63 (m, 42 H), 2.83 (s, 6 H). ESI m/z $[M + H]^+$ 1365.2.

2.3. Synthesis of AD-SRhB. First, the spirolactam-rhodamine derivative (SRhB) was prepared. Under nitrogen, rhodamine B (1 g, 1.717 mmol) was dissolved in 20 mL of anhydrous methanol, and then diethylenetriamine (4.5 mL) was added as soon as possible at 40 °C and the temperature was slowly raised to 70 °C. After 10 h, the solvent was evaporated under reduced pressure and then CH_2Cl_2 (50 mL) and water (100 mL) were added and the organic layer was separated, washed five times with water, and dried over anhydrous Mg_2SO_4. After the filtration of sodium sulfate, the solvent was removed under reduced pressure to give an orange powder and purified by silica gel column chromatography (CH_2Cl_2/MeOH/Et_3N 40:2:1) to give SRhB. Yield: 0.87 g, 79%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.88−7.85 (m, 1H), 7.45−7.42 (m, 2H), 7.09−7.07 (m, 1H), 6.44−6.37 (m, 4H), 6.30−6.26 (m, 2H), 3.37−3.26 (m, 13H), 2.83−2.79 (t, 2H), 2.61−2.57 (t, 2H), 2.33−2.38 (t, 2H), 1.18−1.14 (t, 12 H). ESI m/z $[M+H]^+$ 528.5 .

Second, AD-NHS was synthesized as follows. Under nitrogen, adamantane-1- carboxylic acid (1.0961 g, 6.085 mmol) and *N*-hydroxysuccinimide (NHS) (0.7 g, 6.085 mmol) were dissolved in 10 mL of anhydrous DMF and then dicyclohexylcarbodiimide (DCC) (2.36 g, 12.17 mmol) was added and the solution soon became turbid. The suspension was stirred for 12 h. The reaction mixture was processed by DCU byproduct removal via filtration, and then the solvent was evaporated under vacuum and the residue was recrystallized from CH_2Cl_2/hexane to give purified ester AD-NHS. Afterwards, SRhB (0.248 g, 0.471 mmol) was dissolved in 5 mL of anhydrous DMF and then 1 mL of triethylamine was added. The solution was stirred for 10 min under nitrogen, and AD-NHS (0.16 g, 0.614 mmol) in 10 mL of anhydrous DMF was added. The reaction mixture was stirred for 12 h at 50 °C. The solvent was then evaporated, and the residue was redissolved in CH_2Cl_2 and extracted with water (3 × 50 mL) and dried with anhydrous Mg_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography using 24:1 CH_2Cl_2/CH_3OH as the eluent to give AD-SRhB. Yield 83%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.89−7.86 (m, 1H), 7.46−7.44 (m, 2H), 7.11−7.08 (m, 1H), 6.47 (s, 1H, amide), 6.44−6.37 (m, 4H), 6.29−6.26 (m, 2H), 3.37−3.27 (m, 10 H), 3.20−3.19 (q, 2H), 2.58−2.54 (t, 2H), 2.42−2.38 (t, 2H), 2.27−1.70 (16H, adamantyl, imine), 1.19−1.14 (t, 12H). ESI m/z $[M + H]^+$ 690.2.

2.4. Synthesis of Benzene-SRhB. SRhB (0.884 g, 1.52 mmol) was dissolved in 10 mL of CH_2Cl_2, and then Et_3N(1 mL) was added. The solution was stirred vigorously at 0 °C, and benzeneacetyl chloride (0.2 mL, 0.234 g) in 10 mL of CH_2Cl_2 was added dropwise over 1 h. The solution was allowed to rise to room temperature and stirred for 24 h at this temperature. The solvent was then evaporated, and the residue was purified by silica gel column chromatography using 30:1:0.5 (v/v/v) CH_2Cl_2/CH_3OH/Et_3N as the eluent to give benzene-SRhB. Yield: 0.86 g, 88%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.89 (m, 1H), 7.48−7.45 (m, 2H), 7.30−7.20 (m, 5H), 7.11−7.10 (m, 1H), 6.72 (s, 1H, amide), 6.41−6.37 (m, 4H), 6.27−6.23 (m, 2H), 3.57 (s, 2H), 3.37−3.19 (m, 12H), 2.60−2.58 (t, 2H), 2.37−2.27 (t, 3H), 1.18−1.14 (t, 12H). ESI MS m/z $[M + H]^+$ 646.6.

2.5. Preparation of the Supramolecular-Complex Aqueous Solution. The solution of *β*-CD-DNS (4×10^{-5} mol) in 40 mL of deionized water was prepared by being stirred at 45 °C until the solution was clear. Then, a solution of AD-SRhB (4×10^{-5} mol) in 10 mL of ethanol was added slowly. The solution was stirred for 5 days at room temperature. Then ethanol was evaporated under reduced pressure. Afterwards, the solution was fixed to a volume of 200 mL in a volumetric flask with deionized water to give the supramolecular-complex aqueous stock solution (2×10^{-4} M). When preparing the solutions for spectral measurement, we first added the supramolecular-complex aqueous stock solution to the flask containing buffer concentrates, and then ferric ion aqueous solution was added and the system was stirred for 10 min. Finally, fluorescence and absorption measurements were performed. The pH of the solution was adjusted as follows: sodium acetate buffer for pH 2.6, 3.8, 4.6, and 5.2; Tris/HCl for pH 7.0; potassium hydrogen phthalate buffer for pH 4.0; HEPES sodium salt buffer for pH 7.2; hydrochloric acid/borax buffer for pH 8.0; and sodium tetraborate/sodium hydroxide solution buffer for pH 9.0 and 10.0.

2.6. Measurements. ^{1}H NMR spectra were recorded on a Bruker Avance 300 MHz NMR spectrometer. UV−vis spectra were recorded on a Hitachi U-3010 UV−vis spectrophotometer. Fluorescence spectra were recorded on a Hitachi F-4600 fluorescence spectrophotometer. Mass spectra were obtained through a Bruker Esquire HCT Plus mass spectrometer. The fluorescence

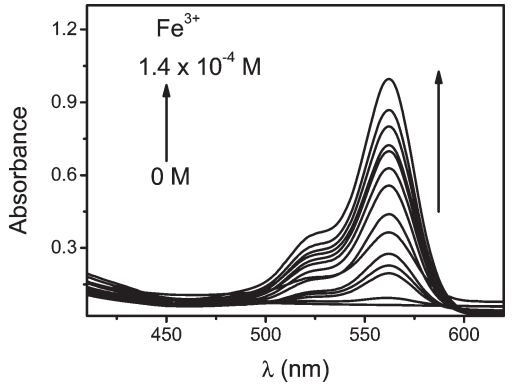

Figure 1. Absorption spectra of the AD-SRhB/β-CD-DNS supramolecular-complex aqueous solution upon addition of ferric ion (pH 7.0).

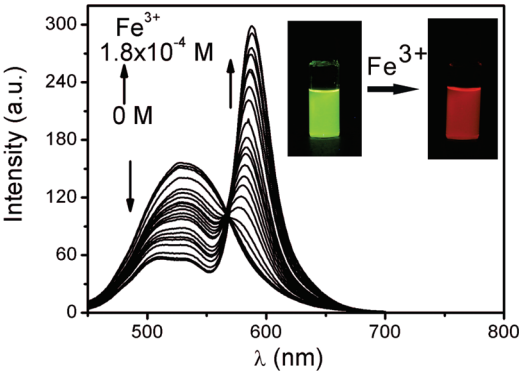

Figure 2. Fluorescence spectra (λ_{exc} 410 nm) of the AD-SRhB/β-CD-DNS supramolecular-complex aqueous solution (1×10^{-4} M) upon addition of ferric ion. (pH 7.0). (Inset) Photographs of the supramolecular-complex aqueous solution before and after the addition of ferric ion (1.4×10^{-4} M) under UV light irradiation.

emission lifetime was measured on an Edinburgh FL920 fluorescence lifetime spectrometer.

3. Results and Discussion

3.1. Synthesis and Characterization. The dansyl-containing cyclodextrin β-CD-DNS was synthesized by first preparing mono-6-O-(p-tolylsulfonyl)-β-cyclodextrin, then mono-6-deoxy-6-amino-β-CD was prepared, and finally dansyl chloride was reacted with mono-6-deoxy-6-amino-β-CD to render β-CD-DNS. The ion-recognition element AD-SRhB was synthesized from the reaction of 1-adamantane carboxylic acid with rhodamine B-modified amine. And then the chromophore formed supramolecular complex with the cyclodextrin β-CD-DNS, as shown in Scheme 1. The molecular structure of the AD-SRhB and β-CD-DNS were confirmed by NMR and MS spectra (Figure S1−S6).

3.2. Absorption Spectra. Ion-recognition element AD-SRhB is insoluble in water; however, when it formed a supramolecular complex with β-CD-DNS in water, the whole system was soluble in water. The supramolecular-complex aqueous solution is clear and transparent, and the UV/vis spectrum of the supramolecular-complex solution showed only the absorption profile of the donor (dansyl), which has absorptions at about 330, 380, and 410 nm (Figure S7). The addition of Fe^{3+} ions immediately induced an increase in the absorption intensity at about 560 nm, which corresponds to the absorption of rhodamine B, as shown in Figure 1. A significant color change from clear colorless to pink could be easily visually observed (Figure S8). This confirms that the addition of Fe^{3+} can promote the formation of the open-ring state of the SRhB moieties.

3.3. Emission Spectra and Detection. Figure 2 shows the fluorescence spectral changes in the supramolecular-complex aqueous solution upon addition of Fe^{3+}. In the absence of Fe^{3+}, excitation of the complex at 410 nm resulted in the emission profile of DNS at around 530 nm (Φ = 0.11, the spectroscopic data are shown in Table S1). Upon addition of Fe^{3+}, the DNS emission at 530 nm decreased and a new emission band with a maximum at 587 nm (rhodamine) gradually emerged (Figure 2). The ratio of the emission intensities at 587 and 530 nm (I_{587}/I_{530}) increased steadily as the concentration of ferric ion was increased (Figure S9), rendering the supramolecular complex a sensitive ratiometric fluorescent sensor for Fe^{3+} with a detection limit that can reach 1 μM Fe^{3+} (Figure 2 and Figure S9). Moreover, upon addition of Fe^{3+}, the fluorescence of the complex solution clearly changed from green to orange (Figures 2 and S8). It is explicit that the binding interaction between AD-SRhB/β-CD-DNS and Fe^{3+} induces the ring opening of spirolactam, which is responsible for the above dual color and fluorescence changes. It was clear that the FRET process was switched on by Fe^{3+} as the excitation of DNS at 410 nm resulted in the emission of rhodamine with a maximum of 587 nm. The calculated Förster radius R_0 (the distance at which the energy-transfer efficiency is 50%) was 29.9 Å (Table S1), and this distance is longer than the donor−acceptor separation (<20 Å) in this supramolecular complex, indicating that the excited energy of dansyl can transfer to rhodamine B. In addition, the emission lifetime of the supramolecular-complex aqueous solution (dansyl moiety) was measured, and the results showed that upon addition of ferric ion to the supramolecular-complex aqueous solution the emission lifetime of the donor decreased from 10.01 to 5.15 ns (Figure S10), thus providing additional evidence that in this system the FRET process was turned on by the ferric ion because the FRET process usually leads to a fluorescence lifetime decrease in the donor directly induced by energy transfer from the donor to the acceptor.[50,51]

This FRET system with the donor and acceptor located inside and outside the cyclodextrin cavity, respectively, can keep the donor and acceptor within the effective distance of the Förster energy transfer; therefore, it can be used for ratiometric sensing of the ferric ion. The FRET system can also avoid any undesirable interaction between the donor and acceptor, which might exist if they were in the unbound form, for example, the $\pi-\pi$ interactions between the donor and acceptor (both the donor and acceptor are aromatic), which could lead to dye aggregation through the stacking of aromatic units and accordingly changes in spectral properties.[52]

Adamantyl is a well-known guest that forms a stable supramolecular inclusion complex with β-CD, and the association constant (binding constant or equilibrium constant) between the adamantyl group and β-CD can reach as high as 10^5 M^{-1}.[42−48] In this study, the binding constant for AD-SRhB and β-CD-DNS has been determined to be 3.88×10^4 M^{-1} (Figure S11), indicating that AD-SRhB bound strongly with β-CD-DNS, and the concentration for unbound AD-SRhB (dissolved in water) was very low, hence the contribution of singlet energy transfer

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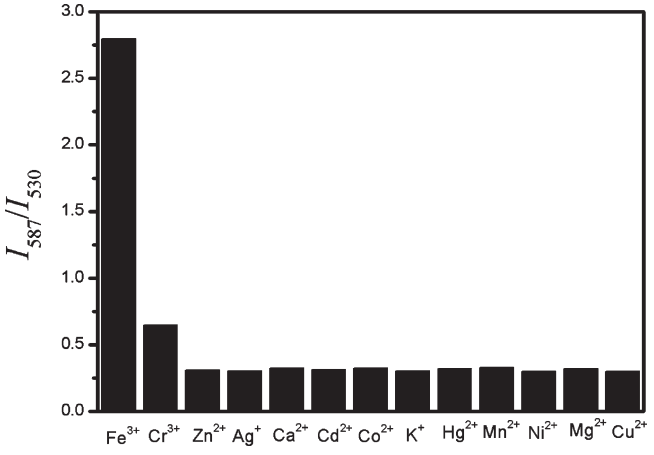

Figure 3. Fluorescence intensity changes (I_{587}/I_{530}) of the AD-SRhB/β-CD-DNS supramolecular-complex aqueous solution (1×10^{-4} M) upon addition of different metal ions (8×10^{-5} M) (λ_{exc} 410 nm, pH 7.0).

from the donor to the unbound AD-SRhB can be neglected in the spectral measurements. To verify further the role of the adamantyl moieties in forming a stable supramolecular inclusion complex and accordingly the efficient FRET process, we covalently linked the spirolactam rhodamine B to the phenyl group (instead of the adamantyl group) to form another ion-recognition element (benzene-SRhB, with characterization in Figures S12 and S13). The phenyl group is smaller than the adamantyl group, and the supramolecular complex formed by benzene-SRhB and β-CD-DNS is less stable than the supramolecular complex formed by AD-SRhB and β-CD-DNS because the phenyl group can get in and out of the cyclodextrin cavity more easily. The fluorescence spectra of the supramolecular-complex benzene-SRhB/β-CD-DNS aqueous solution in the presence and absence of ferric ion were measured (Figure S14). It can be seen that, compared with that in the AD-SRhB/β-CD-DNS system, benzene-rhodamine/Fe^{3+} in this complex system could not efficiently quench the fluorescence emission of dansyl, suggesting that some of the acceptors (benzene-SRhBs) were not within the effective energy-transfer distance but probably moved out of the CD cavity. In addition, the sensitivity of the supramolecular-complex benzene-SRhB/β-CD-DNS aqueous solution is much lower than that of the AD-SRhB/β-CD-DNS aqueous solution, as indicated in Figure S14.

3.4. Selectivity. The novel AD-SRhB/β-CD-DNS supramolecular-complex system showed high selectivity toward Fe^{3+}. From Figure 3, it is clear that Fe^{3+} induced a prominent fluorescence increment, whereas some metal ions such as K^+, Mg^{2+}, Ca^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Ag^+ gave a negligible response; only Cr^{3+} had a slight effect (Figure S15).

3.5. Antidisturbance. In addition, further experiments for Fe^{3+}-selective sensing were performed with the supramolecular-complex aqueous solution in the presence of multifarious cations including K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Ag^+ (1 equiv), as shown in Figure 4. The coexistence of most selected metal ions does not interfere with Fe^{3+} binding to the chromophore or the subsequent fluorescence turn on. The AD-SRhB/β-CD-DNS supramolecular-complex system showed very good antidisturbance.

3.6. Suitable pH Range. For practical applicability, we also investigated the suitable pH range for ferric ion sensing. In the absence of ferric ion, no remarkable fluorescence emission of the solution was observed between pH 3.8 and 10; at pH 2.6, the

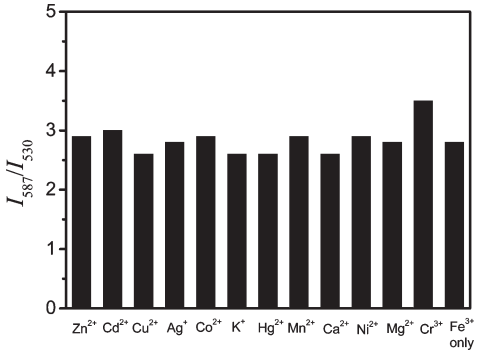

Figure 4. Fluorescence intensity changes (I_{587}/I_{530}) of the AD-SRhB/β-CD-DNS supramolecular-complex aqueous solution (1×10^{-4} M) upon addition of ferric ion (8×10^{-5} M) only, and the aqueous solution containing both ferric ion (8×10^{-5} M) and K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Ag^+ (8×10^{-5} M) (λ_{exc} 410 nm, pH 7.0).

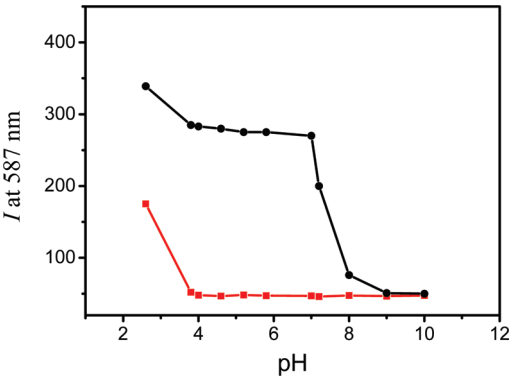

Figure 5. Variation of fluorescence intensity at 587 nm for the AD-SRhB/β-CD-DNS supramolecular-complex aqueous solution (1×10^{-4} M) with and without Fe^{3+} (1×10^{-4} M) as a function of pH (λ_{exc} 410 nm; black curve, with Fe^{3+}; red curve, without Fe^{3+}).

fluorescence emission intensity of the supramolecular-complex solution increased significantly because under highly acidic conditions protons may also induce the ring-opening reaction of spirolactam rhodamine. In the presence of ferric ion, the supramolecular-complex aqueous solution exhibits a higher fluorescence intensity, which remained fairly stable from pH 3.8 to 7, as shown in Figure 5. These data establish that the AD-SRhB/β-CD-DNS supramolecular-complex system could act as a fluorescent probe for Fe^{3+} over a pH span of 3.8−7.

4. Summary and Conclusions

We have developed a FRET-based cyclodextrin supramolecular-complex system as a ratiometric fluorescent probe that can selectively detect Fe^{3+} in an aqueous medium. The key to the successful formation of this FRET system is that the donor and acceptor can reside inside and outside the cyclodextrin cavity, respectively, because of its hydrophilic outer surface and hydrophobic cavity surface, thus not only keeping the donor and acceptor within the effective distance of the Förster energy transfer but also preventing any undesirable interaction between the donor and acceptor (e.g., $\pi-\pi$ interactions between donor and acceptor). This strategy provides a water-soluble ratiometric fluorescent sensor for Fe^{3+}, allowing for a large shift (> 100 nm) between donor excitation and acceptor emission, which rules out any influence of excitation backscattering effects on fluorescence detection. Moreover, this FRET-based supramolecular sensor

can be readily formed via an inclusion process using the donor part and the acceptor part, hence this strategy could afford a robust approach for constructing a wide range of FRET-based sensing systems for other analytes by preparing a variety of donor parts and acceptor parts in advance and then selecting a suitable donor−acceptor pair for a specific sensing purpose and assembling them according to the component assembly approach in industrial processes.

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Supporting Information Available: Characterizations, schemes, absorption and fluorescence spectra, photographs, and calculation of Förster critical radius. This material is available free of charge via the Internet at http://pubs.acs.org.