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A heptamethine cyanine-based colorimetric and ratiometric fluorescent chemosensor for the selective detection of Ag^+ in an aqueous medium†

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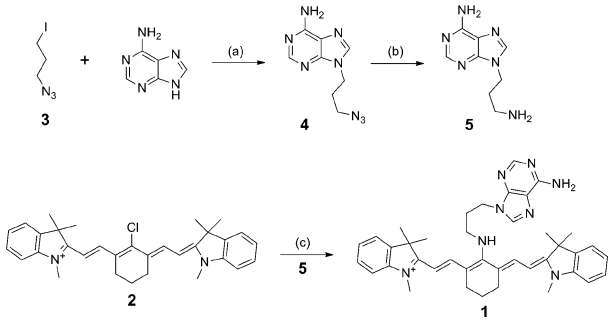
A highly selective and sensitive ratiometric fluorescent chemosensor for Ag^+ in aqueous solution was developed, in a linear range of 0.6×10^{-7} to 50×10^{-7} mol L^{-1}, based on a A–Ag^+–A binding mode with a heptamethine cyanine motif containing one adenine moiety.

Near-infrared (NIR) spectroscopic sensors are highly desirable in the study of biological or environmental samples because spectral interference caused by nonspecific absorption and fluorescence of the complex matrix is generally lower in the near-infrared range than in the visible range. Heptamethine cyanine, an important type of NIR dye, has a rigid chlorocyclohexenyl ring in the polymethine chain that can increase its photostability, enhance the fluorescence quantum yield, and provide an ideal site for further modification with amino or phenol substitutions. Very recently, applications of heptamethine cyanine dyes as NIR chemosensors for various inorganic and biological related species have been the subject of intensive interest, and various chemosensors based on heptamethine cyanine dyes have been reported.[1] The fluorescent signal export of these probes, however, is clearly based on two primary types of mechanisms namely photoinduced electron transfer (PET) and excited state intramolecular charge transfer. The self-association of dyes is a frequently encountered phenomenon, especially in many classes of dyes when used in aqueous solution. Such self-aggregation results in the maximum absorption band in dilute solution becoming weaker as the concentration is increased, and new bands appear at other wavelengths. These spectral changes can be attributed to the aggregation of the dye molecules in water to form dimers and higher-order aggregates in the "J-" or "H-" type aggregation state. In addition, the aggregation effect of dyes also exerts a strong influence on their spectroscopic characteristics.[2]

Though polymethine cyanines are among the best known self-associating dyes in aqueous solutions, and this self-association is clearly reflected by changes in the absorption spectra,[3] this behavior, to the best of our knowledge, has seldom been applied in the design of chemosensors. On the basis of these facts, we herein report a new probe for the efficient chromogenic and ratiometric fluorescent recognition of metal ions *via* modulation of the aggregation state of a heptamethine cyanine-based chromophore in aqueous medium. This modulation of the aggregation state leads to shifts in both the maximum absorption wavelength and the fluorescent emission. In our proposed approach, the manipulation of the aggregate state of a heptamethine cyanine probe is not accomplished by the classic method of increasing its concentration but by the specific binding with a metal center. To this end, based on the fact that adenine is an effective ligand for Ag^+,[4] we first introduced an adenine group into the cyclohexene bridgehead of the heptamethine cyanine, leading to the new adenine-modified heptamethine cyanine probe **1**. The synthetic procedures of **1** are given in Scheme 1, and its structural identification was confirmed by ^{1}H NMR, ^{13}C NMR, and ESI-MS spectroscopy (ESI†).



Scheme 1 Synthesis of the probe **1**.

Then, the spectroscopic characteristics in aqueous solution were studied. The absorption spectral traces of **1** upon coordination with Ag^+ in an optimized succinic acid–NaOH buffer solution at pH 5.4 ($MeOH/H_2O$ = 1/4, v/v) were monitored first. As shown in Fig. 1, the solution of **1** alone (2.0×10^{-5} M) exhibits an absorption maximum at 648 nm, which is responsible for the blue color of the solution. With increasing Ag^+ concentration, the absorbance at 648 nm decreased, while the absorbance at 511 nm increased accordingly. This pronounced hypsochromic shift of the maximum absorption

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† Electronic supplementary information (ESI) available: Synthesis and characterization of **1**, experimental details. See DOI: 10.1039/c2cc17388c

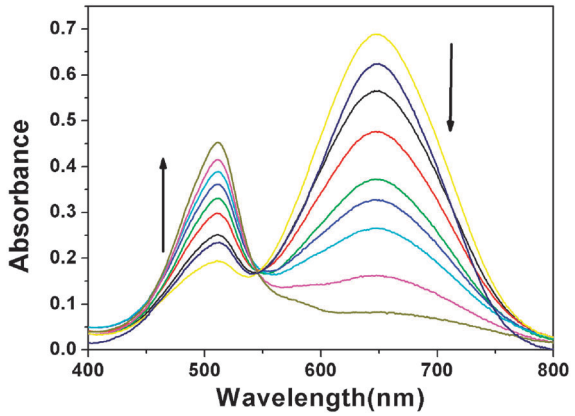

Fig. 1 Absorption spectra of **1** with Ag^+. [**1**] = 20.0 μmol L^{-1}, pH 5.40 (succinic acid–NaOH buffer) in MeOH–H_2O (1/4, v/v) solution. The concentrations of Ag^+ values ranged from 0 to 10 μmol L^{-1}.

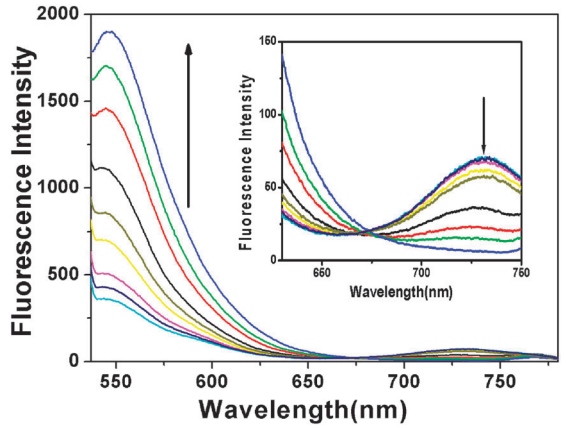

Fig. 2 Fluorescence emission spectra of **1** with Ag^+. [**1**] = 20.0 μmol L^{-1}, pH 5.40 (succinic acid–NaOH buffer) in MeOH–H_2O (1/4, v/v) solution. The concentration of Ag^+ ranged from 0 to 10 μmol L^{-1}. $\lambda_{ex}/\lambda_{em}$ = 512 nm/546 nm, 731 nm; slit: ex/em = 10.0/20.0 nm.

wavelength can be ascribed to the H-aggregation state of the cyanine dye[3] resulting from the coordination of Ag^+. Meanwhile, an isosbestic point was clearly observed around 541 nm, indicating the conversion of the free molecules into aggregation molecules. In addition, such a large blue-shift of 137 nm in the absorption behavior changes the color of the resultant solution from blue to pink, allowing "naked-eye" detection (Fig. S2, ESI†).

We also noticed that the reaction of **1** with Ag^+ produced obvious fluorescence emission changes (Fig. 2). A solution of **1** displayed two emission peaks, at 546 nm and 731 nm, when excited at 512 nm. When Ag^+ was added to the solution of **1**, a distinct decrease in the 731 nm emission and an increase in the fluorescence at 546 nm were observed, with a clear isoemission point at 673 nm. The emission intensity ratio, F_{546}/F_{731}, increases with the increasing Ag^+ concentration, which allows the Ag^+ concentration to be determined.

Then, the ratiometric fluorescence response of **1** was analyzed to determine its selectivity. As shown in Fig. 3, the solution of **1** alone exhibits a very low fluorescence intensity ratiometric value (F_{546}/F_{731}), but upon the addition of 1.0 equiv. of Ag^+, there is a prominent enhancement of this value.

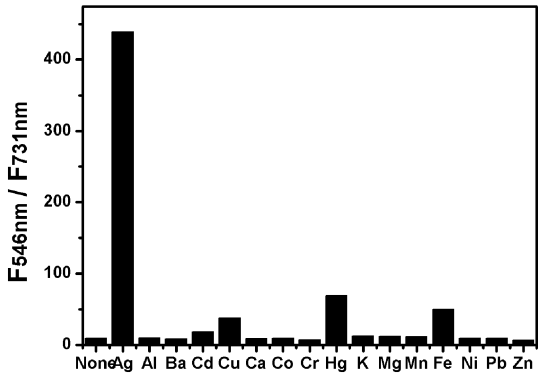

Fig. 3 Fluorimetric responses of **1** to 10.0 μmol L^{-1} of various cations. [**1**] = 20.0 μmol L^{-1}, [metal ion] = 10.0 μmol L^{-1}, pH 5.40.

The addition of Cu^{2+}, Hg^{2+}, and Fe^{3+} resulted in smaller increases in this value, and the remainder of the tested metal ions did not greatly alter the ratiometric value relative to **1** alone. A competitive experiment revealed that all of the tested foreign metal ions had minor or no interference with the ratiometric signal response to Ag^+, therefore, these results suggest that **1** has a high selectivity for Ag^+ in the presence of these tested foreign metal ions (Fig. S3, ESI†).

Because silver and its derivatives are widely used in electrical, pharmaceutical, photographic and imaging industries, and because these substances have adverse biological effects, such as the inactivation of sulfhydryl enzymes and reactions with amine, imidazole, and carboxyl groups of various metabolites, when it bioaccumulates,[5] the development of sensitive and selective methods for the determination of trace amounts of silver ions in various media is of considerable importance to environmental and human health. Sensitive and selective optical sensors with simple and easy instrumental implementation have received a lot of attention, however, to date, there are few reports that describe fluorescent chemosensors for Ag^+ ions in organic solvents,[6] and examples of sensors with significant selectivity for Ag^+ in aqueous solution are even more rare.[7] Reports of ratiometric fluorescent sensors remain rare[7a–c] as well. In this work, with the aid of the A–Ag^+–A binding mode, we carried out the ratiometric fluorescent sensing of Ag^+ in aqueous solution in the range of 0.6×10^{-7} to 50×10^{-7} M (R = 0.9985), with a detection limit of 34 nM (*ca.* 4 ppb)[8] at an S/B ratio of 3 (Fig. S4, ESI†).

The binding stoichiometry of **1** to Ag^+ was also determined using a Job's plot[9] and the results showed that the ratiometric values of both the absorbance (A_{511}/A_{648}) and the fluorescence (F_{546}/F_{731}) of the system (**1** + Ag^+) reached a maximum value when the molecular fraction of Ag^+ was close to 0.3 (Fig. S5, ESI†). These experimental facts are indicative of the formation of a 2 : 1 (**1** : Ag^+) complex, and this binding stoichiometric result also agrees well with the known A–Ag^+–A mode. The results of the ^{1}H NMR titration in deuterated DMSO solution also confirmed the binding of Ag^+ to the adenine group of probe **1** (Fig. 4). The data revealed that the proton signals of the adenine moiety in probe **1** (protons of δ 7.217, singlet, 2H; δ 8.091, singlet, 1H; and δ 8.097, singlet, 1H were assigned to the protons of the $-NH_2$ groups and that of the condensed ring of the adenine group, respectively) are shifted significantly

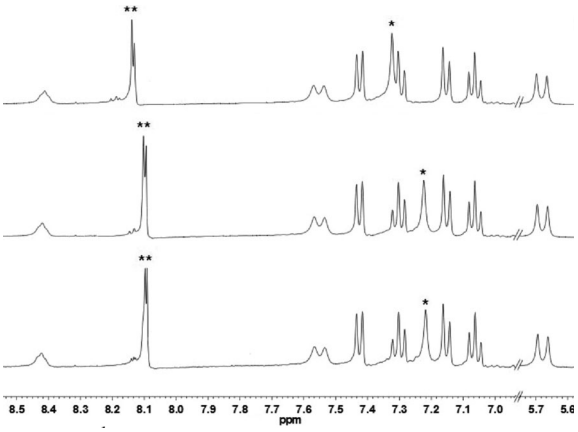

Fig. 4 Partial ^{1}H NMR spectra of **1** only and **1** in the presence of $AgClO_4$ in deuterated DMSO. The equiv. of Ag^+ with respect to **1**: 0, 0.5, 1.3, respectively (from bottom to top).

downfield to δ 7.324, 8.132 and 8.139, respectively. These obvious downfield shifting effects suggest that there is a decrease in the charge density of the adenine moiety, strongly implying that Ag^+ is bound to the adenine group. In addition, the chemical shifts of the unsaturated protons in the heptamethine cyanine moiety and the proton of –NH (δ 8.424, 1H) at the bridgehead of the cyclohexenyl ring did not show any significant changes in the ^{1}H-NMR spectrum, which can exclude the interaction of the heptamethine cyanine chromophore with Ag^+.

From the above experimental evidence of both the binding stoichiometry and the ^{1}H NMR analysis of the Ag^+ titrations, we can conclude that, in aqueous solutions, the binding of Ag^+ with the adenine moiety in probe **1** results in the formation of the **1**–Ag^+–**1** complex, bringing the inner two heptamethine cyanine chromophores of this complex into proximity, and this conformation is similar to that of "H"-aggregates, leading to a change in the solution color from blue to pink and to changes in the ratiometric fluorescence behavior.[10]

In summary, compound **1** was designed for use in a new fluorescent sensor by making use of the binding of adenine with Ag^+ to induce cyanine aggregation in aqueous solution. The fluorescent spectral results clearly indicate that compound **1** can be used as a ratiometric fluorescent sensor for Ag^+ with good selectivity and extraordinarily high sensitivity, and it is likely that the experimental results of this study will provide the basis for a new strategy for the design of various heptamethine cyanine based fluorescent chemosensors.

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10 The reversibility of **1** to Ag^+ was preliminary investigated by adding I^- to the **1** + Ag^+ solutions. It was found that even addition of 100 equiv. of I^- relative to Ag^+ could not obviously change the fluorescent behavior of **1**–Ag^+ solution. Since the interaction of the adenine group with Ag^+ is by coordination, therefore, these I^- experiments implied the far more stronger binding of **1** to Ag^+, and this stronger binding is also responsible for our higher sensitivity of **1** to Ag^+.