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Synthesis and characterization of cyclophane: The highly selective recognition of Fe^{3+} in aqueous solution and $H_2PO_4^-$ in acetonitrile solution

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ABSTRACT

In this work, we report a series of cyclophane fluorescent sensors based on acridine combining with imidazolium through ether linkages. X-ray crystal structures demonstrated the self-assembly behavior of these cyclophanes in the solid state driven by hydrogen bond and π–π interactions. Sensors showed excellent selectivity towards Fe^{3+} in aqueous solution ($H_2O/CH_3CN = 49:1$, v/v) and $H_2PO_4^-$ in acetonitrile solution with notable color change under UV light, evident changes were also noticed in fluorescence spectra. In fluorescence emission, the obvious turn-off was induced by Fe^{3+} in aqueous solution and the obvious turn-on as well as bathochromic-shift was induced by $H_2PO_4^-$ in acetonitrile solution.

Introduction

Design and synthesis of fluorescent chemosensors capable of selective recognition of ions is an active research field in supramolecular chemistry.[1–4] Ions play significant roles in chemical, biological, medical and environmental processes.[5,6] For example, Fe^{3+} is crucial to biological and environmental systems including cellular metabolism, oxidoreductase catalysis, oxygen transport, as well as DNA and RNA synthesis.[7] Abnormal Fe^{3+} fluctuations are often the cause of diseases, such as anemia, arthritis, heart failure, diabetes and cancer.[8,9] There are various analytical techniques such as atomic absorption spectroscopy, electrochemistry, spectrophotometry and inductively coupled plasma mass spectrometry that have been adopted for the determination of Fe^{3+}.[10–13] But these methods have self-defect factors such as sophisticated instrumentation, and complicated pretreatment procedures due to the poor anti-interference ability. Therefore, it is meaningful for us to design a specific ions sensor. Recently, fluorescence-based techniques have provided a simple, sensitive, selective, relatively low-cost method for online monitoring without any pretreatment of the sample, the analytical technique have gained increasing attention for the detection of Fe^{3+}.[14–19] Moreover, hydrophilicity of sensors is essential for interfacing with biological substrates such as proteins and DNA etc.[20] Therefore for practical applications especially in biological system, it is necessary to develop Fe^{3+} chemosensors that are selective, possess good hydrophilicity and sensitive fluorescence signal output.[20] For example, Wang and Liu[21] reported three macrocyclic fluorescent sensors for Fe^{3+} ion and Cu^{2+} ion in the $DMSO/H_2O$ solution, but the hydrophilicity and selectivity of sensors are not ideal.

From biological point of view, $H_2PO_4^-$ is considered to be essential in metabolic process, signal transduction, energy storage, and construction of the backbone of DNA and RNA.[22] $H_2PO_4^-$ have received extensive attention from chemists because of its unique properties, the response of the fluorescence employs a quenching or increase of the fluorescence for most of the reported $H_2PO_4^-$ fluorescent sensors.[23–25] Indeed, some variable factors such as photobleaching, sensor molecular concentration and the microenvironment around the sensor molecules could also cause fluorescence quenching or enhancement in practical applications.[23] In contrast, the turn-on as well as the bathochromic-shift/hypochromatic-shift of the fluorescence emission is a novel strategy for anion sensing.[26,27]

In these years, our group has been working hard at exploiting effective electrochemical and fluorescent detectors for ions.[28–32]

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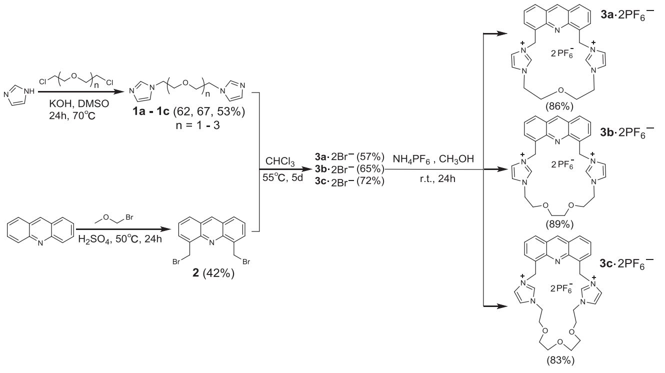
Most of our work focus on the design of imidazolium-based sensors, since this kind of functionalization sensors can be easily synthesized by reacting correspond imidazoles with a halogenate compound through the N atom of imidazole ring.[33,34] Additionally, imidazolium salt imply a higher hydrophilicity for the sensor, which means it's more likely to be applied in biological system.[35–37] During recent years, cyclophanes consist of a rigid aromatic unit and a flexible chain have become one of the most important kind of chemosensors due to their excellent performance in recognizing inorganic, organic cations, ions and neutral substrates selectively.[38,39]

The structure and rigidity of the sensors are important factors for ion sensing.[5,6] Cyclophane sensors performed better than their acyclic counterparts due to the well-preorganized topology.[23] In this work, we report a series of cyclophane fluorescent chemosensors **3a-3c**, which were constructed by acridine combining with imidazolium through ether linkages. The size of the sensors can be easily adjusted by changing the length of the ether linkage, and the oxygen atom can provide an recognition site for cations.[40,41] Moreover, the ether chain facilitates the hydrophilicity of sensor. As expected, sensors **3a**–**3c** showed specifical response to Fe^{3+} in aqueous solution (H_2O/CH_3CN = 49:1, v/v) with an apparent fluorescence quench. For $H_2PO_4^-$, sensors **3a**–**3c** showed an impressive bathochromic-shift behavior in their fluorescence spectra.

Results and discussion

Design and synthesis of the cyclophane sensors

As shown in Scheme 1, the synthesis of 4,5-bis(bromomethyl) acridine **2** was achieved by the reaction of acridine and bromomethylether at 50 °C in H_2SO_4 with a 42% yield.[23] Bisimidazoles **1a**–**1c** were prepared by the reaction of 1,1′-oxybis(2-chloroethane), 1,2-bis(2-chloroethoxy)ethane and bis[2-(2-chloroethoxy)ethyl]ether with imidazole in the presence of KOH in DMSO at 70 °C for 24 h.[42,43] Then bisimidazoles **1a**–**1c** reacted with **2** in $CHCl_3$ under high dilution conditions for 5 days to afford the bromide salts of sensors **3a**–**3c** in the yields of 57, 65 and 72%, respectively. Finally, a counterion exchange reaction using NH_4PF_6 in methanol gave the desired hexafluorophosphate salts of sensors **3a**–**3c**. All the sensors **3a**–**3c** were characterized by ^1H NMR, ^{13}C NMR and HRMS.



Scheme 1. Synthesis of cyclophane sensors **3a**–**3c**.

Crystal structures

Crystals of **3a**·$2PF_6^-$, **3b**·$2PF_6^-$ and **3c**·$2PF_6^-$ suitable for X-ray diffraction studies were obtained from slow evaporation of concentrated solutions of the corresponding sensors in $CH_3OH–CH_3COCH_3–CH_3CN$.

The crystal structure of **3a** reveals that cyclophane adopts a cave-like conformation (Fig. 1). Two hydrogen atoms of the two imidazoliums pointed upward outside of the cavity and formed hydrogen bonds with fluorine atoms of one $[PF_6]^-$ (2.30 Å). Adjacent molecules were connected by π stacking: π–π between two malposed acridine rings (3.653 Å). The crystal packing structure revealed the self-assembly nature of sensor **3a** in the solid state. Hydrogen bond and π–π stacking are major interactions for this assembly behavior. **3b** and **3c** is similar to that of **3a**, with the increase of the length of ether, the cavity size of **3b** is bigger than **3a** and ether structure of **3c** become distorted. From these crystal structures of sensors, some interesting points could be easily noticed. First, all the C(2) protons of the imidazoliums in these sensors were involved in hydrogen bonds with counterions, indicating their potential binding abilities for other competitive anions. Then, all the sensors **3a–3c** presented a cave-like conformation in which two C(2)–H of imidazoliums pointed upward outside of the cavity. This conformation would facilitate the two imidazoliums binding an anion which has two bifurcated electronegative atoms, such as $H_2PO_4^-$, with a good preorganization.[23] Finally, all the sensors showed a self-connected network in the solid state driven by hydrogen bond and π–π interactions. Especially, we observed the obvious but different extent π–π interactions between two acridine rings in the crystal structures of these sensors. The formation of the acridine dimers to a different extent could result in different

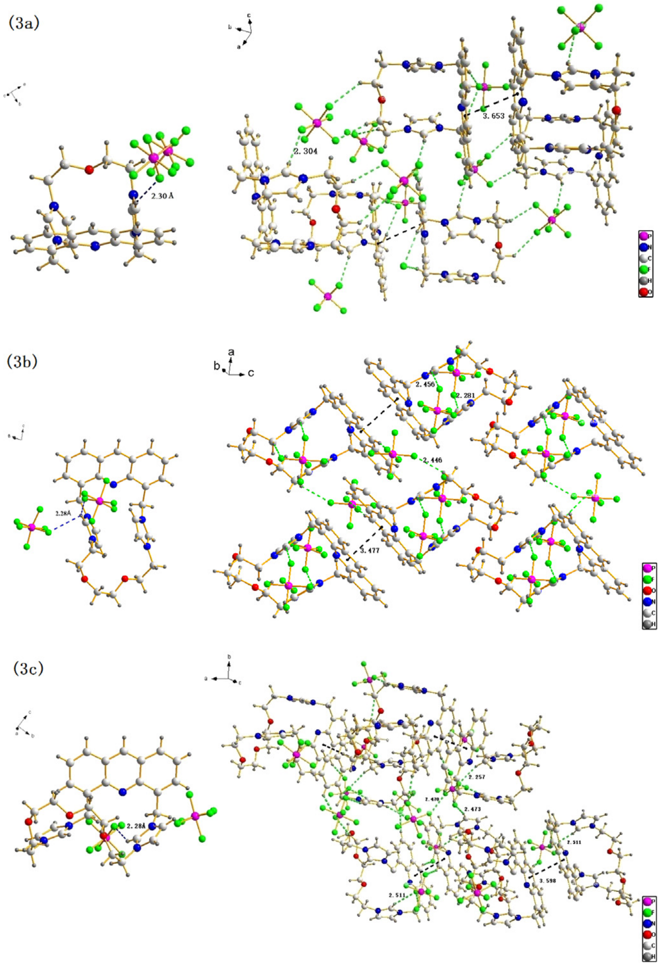


Fig. 1. Crystal structure and the self-assembly network of **3a**–**3c**·$2(PF_6^-)$. Dashed lines represent hydrogen bonds and π–π interactions.