ORIGINAL PAPER

Detection of HSO₄⁻ Ion Based on the Hydrolysis of Diketopyrrolopyrrole-derived Schiff Base with Chromogenic and Fluorogenic Dual Signals

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Abstract A new diketopyrrolopyrrole-based Schiff base L was synthesized and its anion sensing behavior was explored. L showed exclusive response toward HSO_4^- ion and also distinguished HSO_4^- from other anions by color changes (from dark red to orange) and 21 fold fluorescence enhancement at 370 nm in aqueous solution (THF/H₂O=8/1, v/v). The sensing mechanism was suggested to proceed via a hydrolysis process. The results provided colorimetric and fluorimetric assays to selectively detect the presence of a HSO_4^- over a wide range of other interfering anions. The results could potentially be used as a dual colorimetric-fluorescent probe for monitoring HSO_4^- levels in physiological and environmental systems.

Keywords $HSO_4^- \cdot Schiffbase \cdot Colorimetric \cdot Fluorescent \cdot Hydrolysis$

Introduction

The recognition of biologically important anions has received great attention, owing to their fundamental roles in biology, pharmacology and environmental sciences [1–4]. Among various important anions, hydrogensulfate anion (HSO₄⁻) is of particular interest owing to its established role in biological and industrial areas and can be found in agricultural fertilizer, industrial raw materials as pollutants due to their deleterious effect. For example, HSO_4^- anion is present in nuclear fuel

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L. Wang (\boxtimes) · L. Yang · D. Cao School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, China 510640 e-mail: lingyun@scut.edu.cn waste along with other oxoanions, which eventually get into the environment. Moreover, amphiphilic HSO_4^- anion eventually dissociates at high pH to generate toxic sulfate ion $(SO_4^{2^-})$, causing irritation of the skin and eyes and even respiratory paralysis. For these reasons, an improved method for the detection and sensing of HSO_4^- ions with high selectivity is of current interest.

On the other hand, in biological and environmental systems, anion-receptor interactions commonly occur in aqueous media. Therefore, much attention has been paid to develop anion sensors that work in the aqueous phase. Given that HSO_4^- anion has a large standard Gibbs energy of hydration (-1,080 kJ mol⁻¹), the recognition and separation of the HSO_4^- anion from an aqueous media is a challenging task.

To date, many of the reported HSO₄⁻ anion receptors have relied on hydrogen-bonding motifs and, as a consequence, have displayed poor selectivity in aqueous media [5-19]. To overcome this limitation, reaction-based HSO₄⁻ indicators form the irreversible formation of chemical bonds that can provide chemodosimetric information and develop ratiometric fluorescent probes. Because of their excellent selectivity and sensitivity, Schiff bases based chemodosimeters have proven attractive in this regard [1]. The mechanisms of hydrolysis of Schiff bases by acids and amines have been investigated in great detail [2]. It is well known that the pKa value of $HSO_4^$ is 1.99 (in aqueous medium) and it behaves as a hydrogen (H⁺) donor in aqueous/semi-aqueous medium instead of accepting H⁺ as for basic anions such as F⁻ and CH₃COO⁻. A few Schiff base-based probes due to HSO₄⁻-promoted hydrolysis have been developed for detection of HSO₄⁻ [20-22]. In 2012, Virendra et al. clearly demonstrated for the first time that the acidic nature of HSO_4^- gave rise to hydrolysis of the Schiff base, which led to the optical changes observed in this family of receptors [21]. Recently, Lin et al. reported selective colorimetric and fluorescent chemodosimeter for HSO₄⁻ based on hydrolysis of Schiff base [22]. However, these two chemodosimeters available are restricted to the detection of tetrabutylammonium hydrogensulfate, although water-soluble potassium hydrogen sulfate (KHSO₄) is more widespread in biological and industrial areas. Thus, realization of colorimetric and fluorescent measurements for KHSO₄ is still a challenge. In addition, the selectivity for only HSO_4^- has been a problem; especially, for the two tetrahedral oxyanions, HSO_4^- and $H_2PO_4^-$, which are too much alike [23].

Diketopyrrolopyrrole (DPP) dyes have been chosen as fluorophore signaling units because of their widely accepted superiority e.g., high fluorescence quantum yields, high molar absorptivity, high photostability, visible wavelength absorption and modular nature enabling facile functionalization, etc.. These favorable features have made it possible for DPP dyes to be widely used as fluorophore cores for the construction of fluorescent sensors/labels [24-29], polymer solar cells, field effect transistor and dye sensitizing solar cell [30, 31]. However, to the best of our knowledge, there are no reports on colorimetric and fluorescent probe to detect the presence of a target anion based on a DPP Schiff base platform using hydrolysis mechanism. Here, we have developed a new DPP Schiff base based probe L, which enables naked eye and dual channel (absorption and fluorescence) detection of HSO₄⁻.

Experimental

Chemicals and Instruments

All reactants were commercially available and used without further purification. KHSO₄, NaF, NaCl, KBr, KI, Na₂CO₃,

Scheme 1 Synthesis of DPP Schiff base L

NaHCO₃, NaHSO₃, Na₃PO₄, Na₂HPO₄, NaH₂PO₄, Na₂S, NaHS, CH₃COONa, KCN, KNO₃, KSCN and Na₂SO₄ were purchased from Guangzhou Chemical Reagent Company. Compound **5** was prepared according to previous method [32]. Nuclear magnetic resonance was recorded on Bruker Avance III 400 MHZ and chemical shifts were expressed in ppm using TMS as an internal standard. The UV–vis absorption spectra were recorded using a Helios Alpha UV–vis scanning spectrophotometer. Fluorescence spectra were obtained with a Hitachi F-4500 FL spectrophotometer with quartz cuvette (path length= 1 cm).

The recognition between DPP-derived Schiff base compound L and different anions was investigated by UV-vis and fluorescent spectroscopy in aqueous solution (THF/H₂O=8/1, v/v) at room temperature. The stock solutions of L and anions were at a concentration of 10.0 mM.

Synthesis of DPP-Derived Schiff Base L

A portion of **5** (0.284 g, 0.5 mmol), *p*-methoxyaniline (compound **6**, 0.493 g, 4 mmol) were combined in hot absolute ethanol (20 mL). The solution was stirred under reflux for 6 h to yield a dark red precipitate. The precipitate was filtrated, washed with hot absolute ethanol three times, then recrystallized with ethanol to yield scarlet compound L (0.313 g, 0. 040 mmol) in 80.5 % yield. m.p. 190–191 °C. ¹H NMR (CDCl₃, 400 MHz, δ , ppm): 8.54 (s, 2H, -CH=N), 8.04–7.92 (m, 8H, ph-H),7.28 (d, 2H, ph-H), 7.26 (d, 2H, ph-H), 6.96 (d, 4H, ph-H), 4.00 (t, 4H, N-CH₂), 3.85 (s, 6H, -OCH₃), 1.59–0.85(m, 30H, - CH₂, - CH₃). ¹³C-NMR (CDCl₃, 100 MHz, δ , ppm):





(b)



Fig. 1 a UV–vis absorption spectra of L (10.0 μ M) with gradual addition of HSO₄⁻ [0, 2, 4, 6, 8 and 10 equiv., respectively] in THF-H₂O (8/1, v/v); b Color changes of L (1×10⁻⁴ M) upon addition of different anions in aqueous solution (THF/H₂O=8/1, v/v)

162.52, 158.71, 156.59, 147.92, 144.25, 138.64, 310.13, 129.12, 128.76, 122.47, 114.42, 110.36, 55.48, 41.84,

31.73, 29.11, 29.02, 26.73, 22.62, 14.12. ESI-MS m/z: 779.4532 [M+H]⁺.

Fig. 2 UV–vis absorption spectra of L (10.0 μ M) upon addition of various anion (10 equiv.) in THF-H₂O (8/1, v/v)



Fig. 3 Fluorescence spectra of L $(5.0 \ \mu M)$ with gradual addition of HSO₄⁻ in THF-H₂O (8/1, v/v) with excitation at 366 nm



Results and Discussion

The Design and Synthesis of Compound L

A convenient synthetic route to chemodosimeter L was developed as shown in Scheme 1. 2,5-Dioctyl-3,6-bis(4'formylphenyl)pyrrolo[3,4-c] pyrrole-1,4-dione (compound 5) was prepared from *p*-cyanobenzaldehyde as a starting material in four steps. L was obtained by condensation of 5 with *p*-methoxyaniline (8 equiv.) in anhydrous ethanol (yield: 80.5 %). The structures of the intermediates and final product were confirmed by NMR spectroscopy (Fig. S1), MS (ESI) analysis (Fig. S2). The ¹H NMR spectrum of **1** showed one singlet at 3.85 ppm corresponding to methoxyl protons, one triplet at 4.00 ppm corresponding to methylene protons (-CH₂-N), three doublets at 7.28, 7.26 and 6.96 ppm, one





v/v)



Fig. 5 Relative fluorescent of L (5 μ M, emission intensity at 366 nm) with 50 equiv. of HSO₄⁻ and 50 equiv. of anion stated

multiplet at 8.04–7.92 ppm corresponding to aromatic protons, and one singlet at 8.54 ppm corresponding to imino protons (N=CH). The mass spectrum of **1** showed the parent ion peak at m/z 779.4532, $[1+H]^+$.

UV-vis Spectroscopic Studies

The interaction of probe L with anions was investigated through spectrophotometric titrations by adding a standard aqueous solution of anions to a 8:1 THF:H₂O solution of L. Free L displayed an intense absorption band at 504 nm and a moderate absorption at 366 nm.

Fig. 6 The linear relation for concentration of HSO_4^- in the range of 0–0.8 μ M. I₀ and I are the emission intensities at 370 nm of 1 in the absence and presence of HSO_4^- , respectively

The main band at 504 nm was the typical absorption band of DPP dyes. With gradual addition of KHSO₄ aqueous solution, the absorption intensity at 366 and 504 nm decreased, as shown in Fig. 1a. Notably, the absorption peak at 366 nm completely disappeared in presence of 10 equiv. of HSO_4^- . The dark red color of the probe solution turned orange at the same time, as shown in Fig. 1b. Interestingly, the absorption spectrum of **L** in the presence of 10 equiv. HSO_4^- aqueous solution exhibited a similar pattern as that of compound **5** (Fig. S3) and *p*-methoxyaniline (Fig. S4). This led us to speculate if HSO_4^- may induce the hydrolysis of **L** to yield compound **5** and *p*-methoxyaniline.

To examine the feasibility of **L** as a HSO₄⁻ probe, analogous investigations were carried out on a variety of anions such as F⁻, Cl⁻, Br⁻, l⁻, CO₃²⁻, HCO₃⁻, HSO₃⁻, PO₄³⁻, HPO₄²⁻, H₂PO₄⁻, S²⁻, HS⁻, CH₃COO⁻, CN⁻, NO₃⁻, SCN⁻ and SO₄²⁻. As shown in Fig. 2, other anions did not cause significant absorption spectral changes of **L**. However, under the same conditions, only HSO₄⁻ resulted in obvious changes, indicating **L** had stronger UV–Vis absorption response toward HSO₄⁻ than other surveyed metal ions.

Fluorescent Spectroscopic Studies

The photophysical properties of L in presence of anions were then studied in 8:1 THF:H₂O solution by emission spectroscopy. The results obtained were in good agreement with those of UV-vis absorption spectroscopy. Upon excitation at 366 nm, free L displayed weak



Fig. 7 Partial ¹H NMR changes upon the addition **a** 0 equiv.; **b** 0.5 equiv.; **c** 1.0 equiv.; **d** 1.5 equiv.; **e** 2.0 equiv. of HSO_4^- in $THF-d_8/D_2O(8:1, v/v)$



emission bands at 370 and 597 nm, due to a photoinduced charge transfer process (from the electrondonating C=N moiety to the DPP ring), which quenched the excited state emission of the DPP fluorophore. As shown in Fig. 3, upon progressive addition of HSO_4^- , the intensity at 370 nm gradually increased, and a small hypsochromical shift (7 nm) of the maximum could be observed at 590 nm. What caught our attention was that the emission spectra of L after the addition of HSO₄⁻ were similar to that of compound 5, since 5 showed emission maxima at 370 nm and 590 nm (Fig. S5), Finally, a plateau with the addition of 500 μ M (100 equiv.) of HSO₄⁻ ions was achieved, resulting in 21 fold fluorescence enhancements at 370 nm and slightly increased emission at 590 nm. As the changes in fluorescence intensity are significant, it may be considered that the fluorescence emission is "switched off" in L and "switched on" upon the addition of HSO₄⁻. To gain insight into the whole process, we recorded the absorption and emission spectra of aldehyde 5 and pmethoxyaniline in presence of HSO₄⁻ (Figs. S6-S8).

Interestingly, the absorption/emission spectrum of 1 in the presence of HSO_4^- ions in mixed aqueous media exhibited a similar pattern as that of the absorption/ emission spectrum obtained in the case of aldehyde 5 and amine 6. From this result, we proposed that 1 was hydrolyzed in the presence of HSO_4^- ions aqueous media, generating fluorescent aldehyde 5 and *p*methoxyaniline.

In order to test whether L can be a fluorescent probe for HSO₄⁻, comparative fluorescence changes upon addition of various anions including F⁻, Cl⁻, Br⁻, I⁻, CO₃²⁻, HCO₃⁻, HSO₃⁻, PO₄³⁻, HPO₄²⁻, H₂PO₄⁻, S²⁻, HS⁻, CH₃COO⁻, CN⁻, NO₃⁻, SCN⁻and SO₄²⁻ to probe L are shown in Fig. 4. These anions gave no distinct response to the solution of L in fluorescence spectra, except HS⁻ induced 2.1 fold fluorescence enhancement at 370 nm. However, such a variation in fluorescence intensity by HS⁻ was relatively small compared with that of HSO₄⁻ (21-fold fluorescence enhancement at λ_{max} 370 nm, indicating that L showed the stronger response in fluorescence spectrum to HSO₄⁻ among these anions.

Fig. 8 Mass spectrum of L in the presence of HSO_4^-





Scheme 2 The possible hydrolysis of L in presence of $\rm HSO_4^-$ in THF-H_2O ($\rm 8/1,\,v/v)$

Competition Experiment

Competition experiment was carried out to test whether L can selectively recognize HSO_4^- in the presence of other anions. L was treated with 50 equiv. of HSO_4^- and 50 equiv. of other surveyed anion. As shown in Fig. 5, miscellaneous competitive anions did not cause significant effect on the sensing of HSO_4^- . HSO_4^- still exhibited similar fluorescent changes in the presence of various other anions, indicating that there was no interference from other surveyed anions.

The detection limit of **L** for HSO_4^- was calculated based on the fluorescence titration data according to a reported method [33]. Under optimal conditions, calibration graphs for the determination of HSO_4^- were constructed (Fig. 6). The detection limit for HSO_4^- were determined as 6.45×10^{-9} M based on S/N=3.

Proposed Mechanism for Interaction of L with HSO₄⁻

Schiff bases are prone towards hydrolysis in acidic medium as well as through a few metal ions [34-36]. pKa value of HSO₄⁻ is 1.99 (in aqueous medium) and it behaves as a hydrogen (H⁺) donor in aqueous/ semiaqueous medium [20]. In order to understand the mode of interaction between HSO_4^- and L in solution and hence to explore the mechanism behind the observed UV-vis absorption and fluorescence response, we carried on ¹H NMR spectral studies to investigate whether HSO₄ caused the cleavage of L. As shown in Fig. 7, free L had a singlet at δ 8.53 ppm assigned to imino protons (N=CH). After addition of 2 equiv. HSO_4^- , the singlet at δ 8.53 ppm disappeared and a new singlet at δ 10.06 ppm corresponding to aldehyde protons (-CHO) appeared. The ¹H NMR spectral studies clearly showed that L was hydrolyzed in the presence of HSO₄⁻ in mixed aqueous media to yield compound 5.

More direct evidence was obtained by comparing the mass spectra of compound L and L- HSO_4^- . In Fig. S2, the unique peak at m/z=779.4532 (calcd=779.4531) corresponding to [L + H]⁺ was observed. While in Fig. 8, with 10 equiv. of HSO_4^- added to L, the peak at m/z=779.4532 disappeared. Meanwhile, the mass spectral analysis showed peaks corresponding to aldehyde 5 (at m/z 568.5667, [5+ H]⁺) and *p*-methoxyaniline 6 (at m/z 124.0755, [6+H]⁺). The MS studies suggested that compound L underwent hydrolytic cleavage at the C=N bond in presence of HSO_4^- , thus generating aldehyde 5 and *p*-methoxyaniline.

In our case, the distinct color change and large fluorescence enhancement of L was due to HSO_4^- -promoted hydrolysis. The acid catalyzed mechanism, involves the attachment of a proton on the imino nitrogen followed by the attack of a H_2O molecule on the imine carbon eventually leading to the cleavage of the imine bond to generate aldehyde and amine, as depicted in Scheme 2.

Conclusions

In conclusion, we have developed a new DPP Schiff base L based colorimetric and fluorimetric probe for HSO_4^- anions in aqueous solution (THF/H₂O=8/1, v/v) with good selectivity. The system provides chromogenic and fluorogenic dual signals by displaying (i) a orange color and (ii) a strong orange fluorescence from an initially dark red and weak orange fluorescent solution, upon exposure to HSO_4^- . The drastic color change and strong fluorescence change of L are driven by hydrolysis of L in presence of HSO_4^- . The results could potentially be used as a dual colorimetric-fluorescent probe for monitoring HSO_4^- levels in physiological and environmental systems.

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