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Short communication

Novel furo[2,3-d] pyrimidine derivative as fluorescent chemosensor for HSO_4^-

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ABSTRACT

A class of novel heterocyclic compounds **1a–1c** has been designed and synthesized. And our initial discovery is that these compounds can effectively recognize HSO_4^-. With the addition of HSO_4^-, a new energy band appears at 360–390 nm in the absorption spectra. The emission spectrum (λ_{ex} = 328 nm) undergoes an important change in its fluorescent effect in the presence of HSO_4^-. All available data (absorption and emission) strongly support the formation of hydrogen-bonded complexes between **1a** and **1c** and HSO_4^-.

1. Introduction

The development of recognition and sensing systems for anions has received considerable attention in recent years [1–3] due to anions being ubiquitous in biological systems and playing significant roles in wide areas of biology, pharmacy, and environmental sciences [4–8]. Sensors based on anion-induced changes in fluorescence are particularly attractive because of the simplicity, high spatial and temporal resolution of fluorescence [9–17]. Among various important anions, HSO_4^-, an environmentally important anion, is attracting a great deal of interest because of its established role in biological and industrial areas. Recently, considerable efforts have been devoted to HSO_4^- ion sensing via UV–vis, fluorescence, or other methods [18–24]. For example, Wu and co-workers have succeeded in developing a colorimetric and fluorescent HSO_4^- ion chemosensor based on flavones quasi-crown ether–metal complex [18]. Tang and co-workers have performed studies on an HSO_4^- ion recognition by a zinc(π) xanthone–crown ether complex [19]. Furthermore Kim has synthesized a compound which can selectivity recognize HSO_4^- [20]; however, highly selective recognition of HSO_4^- is still questionable.

In the pursuit of HSO_4^- sensors with high binding affinity and selectivity, we designed and synthesized a class of compounds **1**, which have binding sites for anions and can discharge fluorescence. **1a–1c** can report the presence of HSO_4^- over other anions. **1d** has been synthesized to establish the mechanism of the fluorescence change in the presence of HSO_4^-.

2. Experiment

2.1. Reagents

All starting materials and catalysts were obtained commercially and used without further purification. Most of the solvents were distilled under N_2 over the appropriate drying reagents (sodium or calcium hydride). Column chromatography: silica gel 200–300 mesh.

2.2. Apparatus

Absorption spectra were determined on a UV-2501 PC spectrophotometer. Fluorescence spectra measurements were performed on a FluoroMax-P spectrofluorometer equipped with a 150 W xenon discharge lamp and 1 cm quartz cells at room temperature (about 298 K). Typical scanning parameters were integrated at a time of 0.1 s per point, intervals of 2 nm, and excitation/emission slits set at 3 nm. pH was determined using a DELTA320 pH meter. NMR spectra were measured on Varian Mercury 400 spectrometer operating at frequencies of 400 MHz for ^1H and 100 MHz for ^{13}C, while the Varian NMR System 600 MHz spectrometer operated at frequencies of 600 MHz for ^1H and 125 MHz for ^{13}C relative to tetramethylsilane as an internal standard. Mass spectrometry was carried out on a Finnigan Trace MS spectrometer. IR spectra were recorded on a Tensor 27 infrared spectrometer as KBr pellets with absorption reported in cm^{-1}. The X-ray crystal structure determination of **1c** was obtained on a Bruker SMART APEX CCD system.

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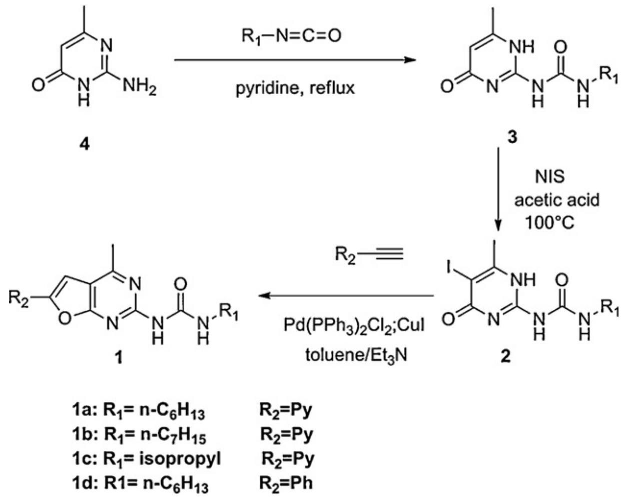

Scheme 1. Synthesis of compound **1**.

2.3. *Synthesis of compounds **1***

The synthetic route of compounds was shown in Scheme 1. The reaction of 6-methylisocytosine **4** with isocyanate in dry pyridine under reflux gave **3** an 87–90% yield [25–27]. Subsequently with NIS in acetic acid at a temperature of 100 °C gave **2** a 78–82% yield [28]. For the preparation of **1**, we conducted the Pd-catalyzed Sonogashira coupling reactions between **2** and **4**-ethynylpyridine (phenylacetylene), then base-catalyzed self-cyclization reactions in 39–45% [29–31].

2.4. *X-ray diffraction analysis of compound **1c***

The crystal of **1c** that was suitable for X-ray crystal structure analysis was grown by the slow evaporation of solutions of the compound in $CHCl_3$–CH_3OH (10:1, v/v). The detail of the crystal data has been deposited with Cambridge Crystallographic Data Centre as Supplementary Publication CCDC No. 823403.

2.5. *Binding titration*

The stock solutions of **1** (1.0×10^{-5} M) were prepared by dissolving **1** respectively in $CHCl_3$–MeOH (9:1, v/v). The anions stock solutions were prepared in $CHCl_3$–MeOH (9:1, v/v) with a concentration of 3.0×10^{-3} M for fluorescence spectral analysis. Each time a 3 mL solution of **1** was filled in a quartz cell of 1 cm optical path length, we increased concentrations of anions by the stepwise addition of different equivalents using a micro-syringe. An excitation wavelength of 328 nm and room temperature were employed in all experiments.

2.6. *UV–vis spectrophotometric titrations*

Anion solutions in $CHCl_3$–MeOH (9:1, v/v) were added to a solution of 1.0×10^{-5} M of **1** in $CHCl_3$–MeOH. Spectra in the range of 450–280 nm were recorded upon the addition of 50 equiv. of different anions at room temperature.

3. Results and discussion

3.1. *Synthesis and structural characteristics of **1***

We first synthesized compounds **1** by Pd-catalyzed coupling reactions of 4-ethynylpyridine or phenylacetylene with **2**, then base-catalyzed self-cyclization reactions with reference to the methods of other people [32,33].

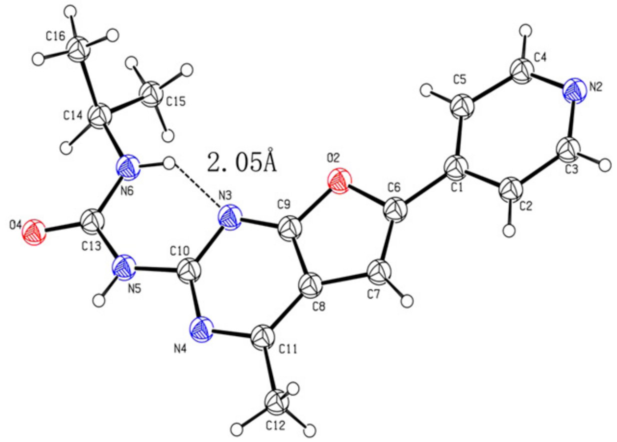

Fig. 1. Crystal structure of **1c** (some disordered parts were omitted for clarity).

Single crystal of **1c** suitable for crystallography was obtained from the slow evaporation of a concentrated $CHCl_3/CH_3OH$ (9:1, v/v) solution of **1c** at ambient temperature. The structure of **1c** is depicted in Fig. 1. It should be noted here that there is a strong intramolecular hydrogen bond between the pyrimidine moiety and the urea group with a distance of 2.05 Å, due to a strong crystal packing interaction existing in the solid. Moreover, the crystal of **1c** packing exhibits intermolecular C—H· · ·N hydrogen bond with the distance of 2.06 Å and π–π interactions with the distance of 3.51 Å.

3.2. *Spectral characteristics*

As shown in Fig. 2, compound **1a** exhibited a strong absorption band centered at 328 nm in $CHCl_3$–CH_3OH (9:1, v/v), whereas the compound **1b**–**1d** showed a similar characteristic absorption peak (Figs. S2, S9 and S10). The high-energy peak around 328 nm was expected to $\pi \rightarrow \pi^*$ electronic transitions.

The fluorescence emission spectrum of chemosensor **1a** consists of a peak centered at 386 nm. It found a similar peak between **1a** and **1c**, which owns the same luminescent fragments. The fluorescent quantum yield of diastereomers was measured by comparing

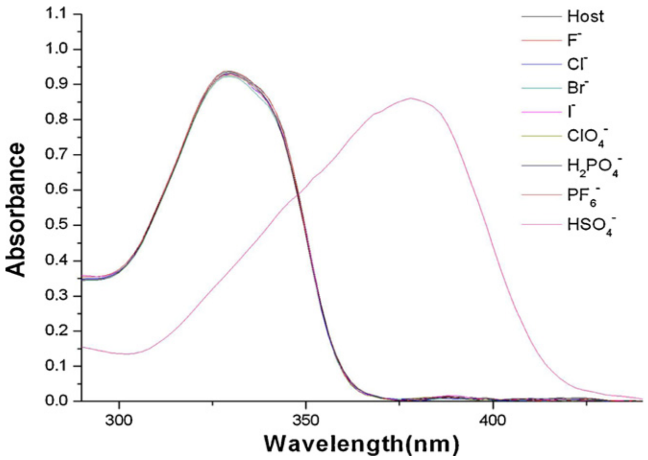

Fig. 2. Absorption spectra of compound **1a** (10 μM) in $CHCl_3/CH_3OH$ (9:1, v/v) upon addition of 50 equiv. of a particular n-tetrabutylammonium anion salt (500 μM).

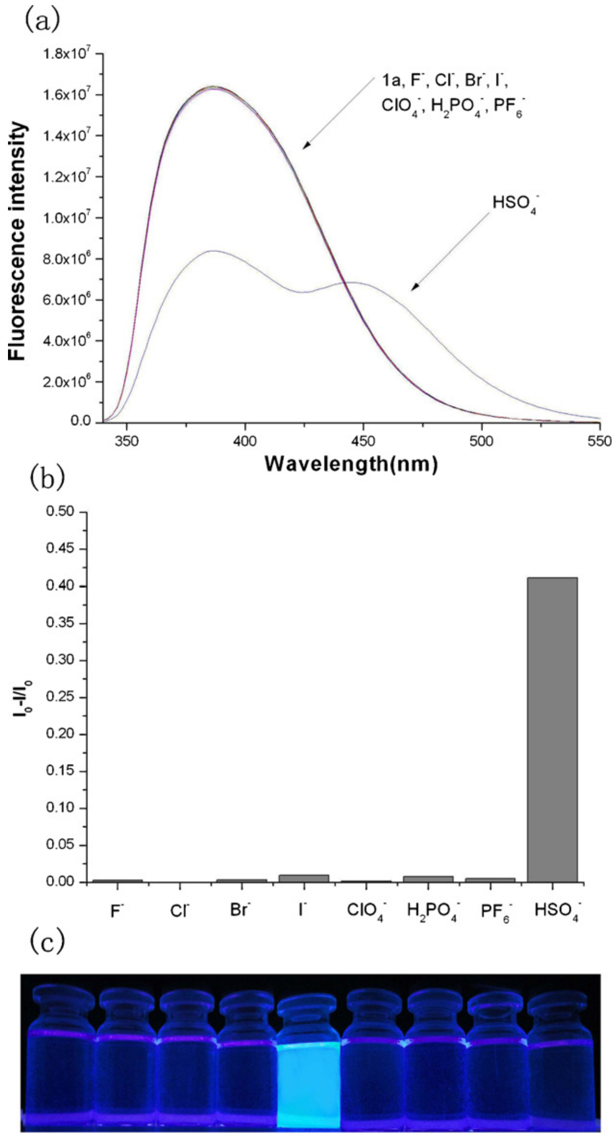

Fig. 3. (a) Fluorescence spectra of compound **1a** (10 μM) in $CHCl_3/CH_3OH$ (9:1, v/v) upon addition of 50 equiv of a particular n-tetrabutylammonium anion salt (500 μM) with excitation at 328 nm. (b) Fluorescence ratio ($I_0 - I/I_0$) of **1** (10 μM) at 328 nm upon addition of 50 equiv. of a particular n-tetrabutylammonium anion salt in $CHCl_3/CH_3OH$ (9:1, v/v). (c) The photograph shows the fluorescent responses of compound **1a** (10 μM) in $CHCl_3/CH_3OH$ (9:1, v/v) after the addition of 50 equiv. of anion (from left to right: no anion, ClO_4^-, $H_2PO_4^-$, PF_6^-, HSO_4^-, F^-, Cl^-, Br^- and I^-).

it with quinine sulphate as the standard compound in sulphuric acid according to the following equation [34,35]:

$$\Phi_u = \frac{\Phi_s \times A_s \times F_u \times n^2}{A_u \times F_s \times {n_0}^2}$$

where Φ_u and Φ_s are quantum yield for the sample and reference, F_u and F_s are the integrated area under the corrected fluorescence spectra for the sample and reference, A_u and A_s are the absorbance for the sample and reference, n and n_0 are the refractive indexes of the solvents used for samples and reference. The quantum yield for compound **1a** is 0.73, **1b** is 0.90, **1c** is 0.67 and **1d** is 0.38.

3.3. Selectivity

The titration of molecular **1a** with anions which included F^-, Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$, PF_6^- and HSO_4^- was conducted to examine the selectivity. As summarized in Fig. 3, the fluorescence of **1a** at around 380 nm which exits even at as high a concentration as 50 equiv. was not influenced by F^-, Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$ and PF_6^-. Under such conditions, HSO_4^- greatly quenched the emissions of **1a**–**1c** (Fig. 3, Figs. S3 and S4). Most interestingly, **1a**–**1c** did not sense $H_2PO_4^-$ when compared with some of the other compounds [18,19], which could sense HSO_4^-, although $H_2PO_4^-$ would compete with HSO_4^-. The relatively strong quenching by HSO_4^- when comparing it to other anions seems to be related to more electron deficiency. The fluorescence spectra of **1a** did not change upon addition of 10 equiv. of K_2SO_4 (Fig. S13). These mean the other anions, which except HSO_4^-, could not combine with **1a**.

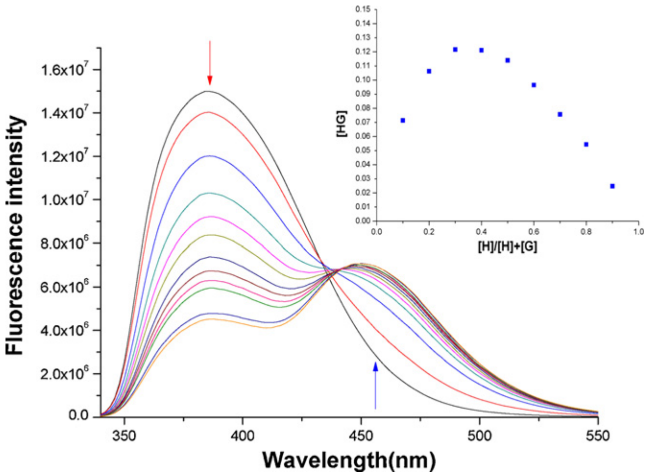

Fig. 4. Change of fluorescent emission spectra of compound **1a** (10 μM) in $CHCl_3/CH_3OH$ (9:1, v/v) upon addition of 0–110 equiv. of n-tetrabutylammonium anion salt. Excitation wavelength: 328 nm. Inset: Job's plot between the receptor **1a** and n-tetrabutylammonium anion salt. The concentration of [HG] was calculated by the equation $[HG] = \Delta I/I_0 \times [H]$.

3.4. Analytical figures of merit

In order to estimate the specific concentration for selective HSO_4^-, the fluorescence spectra of **1** in the presence of different concentrations of HSO_4^- were measured. A characteristic maximum fluorescence emission centered at about 386 nm was recorded and the fluorescence intensity of the **1a**–**1c** was significantly quenched with the increase in the HSO_4^- concentration (Fig. 3, Figs. S3 and S4). To know the stoichiometry between the quencher (HSO_4^-) and acceptor (**1a**–**1c**) molecule in $CHCl_3$–MeOH (9:1) solution, Job's plot (insets of Fig. 4, Figs. S7 and S8) has been drawn. It shows the maxima at 0.7 molar fraction for 1:2 stoichiometry between the two interacting species [36]. Stern–Volmer plots are a useful method of presenting data on emission quenching. The nature of the quenching process in quencher and acceptor was probed by the Stern–Volmer analysis [37,38]. Based on the fluorescence titration of **1a** in $CHCl_3$–MeOH with HSO_4^-, the association constants K_{11} and K_{21} of **1a** for HSO_4^- were determined by a nonlinear least-squares analysis of fluorescence intensity to be 1.07×10^3 and 2.55×10^3, the association constants K_{11} and K_{21} of **1b** were 1.57×10^3 and 9.97×10^3 and the association constants K_{11} and K_{21} of **1c** were 3.16×10^3 and 1.60×10^4 (see the supporting information).

3.5. Quenching mechanism of HSO_4^-

In contrast to the typical Stern–Volmer quenching behavior driven by a collision between the quencher and luminescent molecules, the fluorescence quenching of the hosts and guests is attributed to the complex formation between the electron deficient guest HSO_4^- anion and molecular **1a**–**1c** as shown in Fig. 5. As

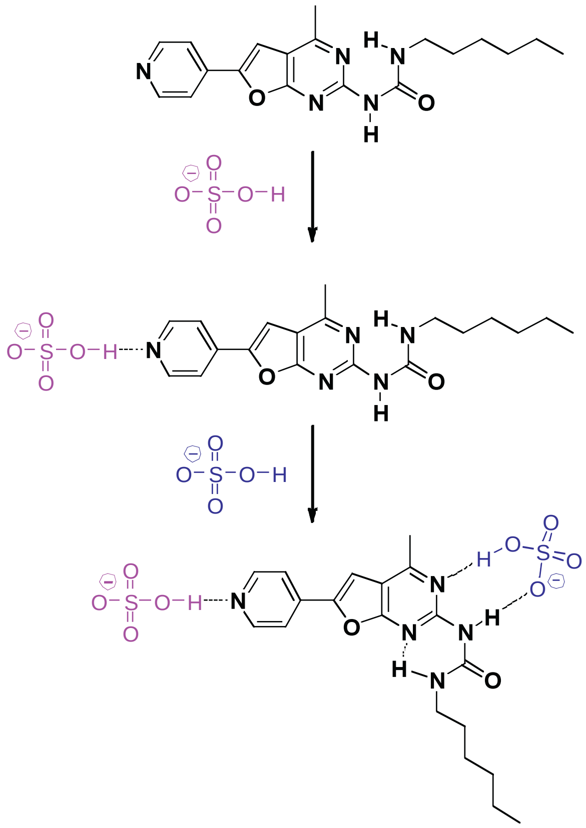

Fig. 5. Possible formation mechanism of **1a**·$2HSO_4^-$ complex.

Job's plot indicated, the stoichiometric ratio of guests to hosts was proven to be 2:1. **1d** was synthesized to examine the role of pyridine in the fluorescence changes of **1a**–**1c**. The fluorescence spectrum of the compound **1d** upon addition of 50 equiv. of diverse anions was also carried out (Fig. S2). In contrast to that of **1a**–**1c**, the addition of HSO_4^- caused a slight change in the fluorescence spectrum of **1d**, and no saturation or isosbestic point was observed, implying that pyridine plays an important role in the high selectivity of **1a** for HSO_4^-.

Based on the above-described UV–vis and fluorescence studies, we proposed that the processes of recognition are to be as follows: upon addition of HSO_4^-, the pyridine group of **1a** bonds to 1.0 equiv. of HSO_4^- to change the electronic density of **1a**, then another 1.0 equiv. of HSO_4^- can combine with it to form a complex (**1a**·$2HSO_4^-$) which contains three hydrogen bonds, one between the pyridine and the hydrogen of the HSO_4^-, another between the oxygen of the HSO_4^- and the hydrogen (–NH) of **1a**, and a third between the hydrogen of the HSO_4^- and the nitrogen of **1a** [39] (Fig. 5). This conjecture has been supported by a UV–vis spectral study: the absorption spectrum change of compound **1a** induced by the addition of HSO_4^- is shown in Fig. 6. The addition of HSO_4^- caused the wavelength at 328 nm red to shift due to for the increase of electron density of **1a**. The concomitant high increase in the absorption intensity is relative to the formation of host–guest complexes which benefits from the OH···N H-bonds and NH···O H-bonds effect [40]. The UV–vis spectral study indicates that the direct interaction between HSO_4^- and host **1a** is strong.

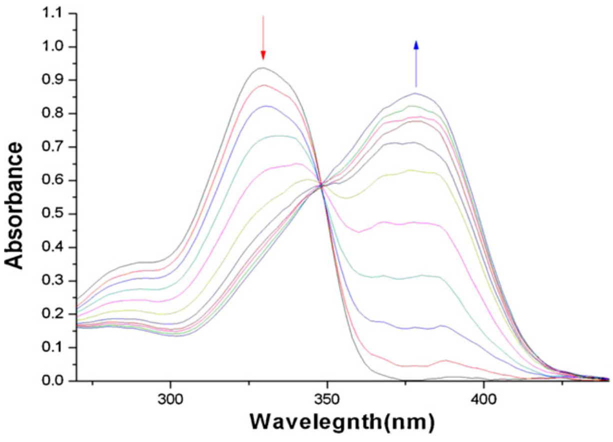

Fig. 6. Change of absorption spectra of compound **1a** (10 μM) in $CHCl_3/CH_3OH$ (9:1, v/v) upon addition of 0–100 equiv. of n-tetrabutylammonium anion salt.

4. Conclusion

In conclusion, compounds **1**, which possess pyridine, furan and pyrimidine, were designed and synthesized with a view to developing new fluorescent sensors for anions. The crystal structure of host **1c** was obtained from $CHCl_3/H_3OH$. Fluorescent spectral results clearly indicate that **1a**–**1c** can be used as fluorescent sensors for HSO_4^- with good selectivity and sensitivity in the $CHCl_3$–MeOH. Further studies include the design of new analogues of **1** with good solubility, which will enable the practical application of these types of HSO_4^- sensors to be implemented.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.talanta.2011.11.033.

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