A New Fluoride Chemodosimeter Based on 3-Ether-Substituted 1, 8-Naphthalimide Derivatives

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Abstract
We developed a new chromogenic and fluorescent “off–on” 1, 8-naphthalimide-derivated chemosensor 1 based on an F⁻-triggered desilylation reaction. It showed significant variations in UV/visible absorption (510 nm) and fluorescence emission wavelength (580 nm) for selective detection of fluorides in THF/H₂O system (v/v, 50:50). Moreover, chemodosimeter 1-loaded test strips were successfully fabricated to detect fluorides efficiently.

Keywords Colorimetric · Fluorescence · Chemodosimeter · Fluoride ion · 1, 8-naphthalimide

Introduction
Fluoride ions widely exist in the nature and organisms, and play an extremely important part in the metabolic process of organisms. It is widely used in dental treatment, disease surveillance, and drinking water health control [1–4]. Excessive fluoride ions leakage not only pollute the environment, but also cause irreversible harm to physiological condition, such as dental fluorosis, skeletal fluorosis, the acute reaction of gastrointestinal, and nephrotoxic lesions [5, 6]. Therefore, the development of new chemodosimeter to detect fluoride ions has attracted wide attention.

Among various fluorine ion detection technologies, the fluorescence method has been widely used in food detection, environmental monitoring, cell imaging, and other fields due to its high selectivity, rapid response, and strong anti-interference. Many sensor systems for fluoride detection have been developed to date for the detection of fluoride ions, including metal ion coordination [7, 8], Lewis acid base [9, 10], hydrogen bond 11–15[], and silicon-carbon bond cleavage [16, 17] sensing mechanisms.

The fluorescent sensor based on fluoride-induced desilylation reaction has attracted much attention. Especially, those fluorophore have been investigated extensively such as the skeleton of BODIPY, coumarin, and 1, 8-naphthalimide derivatives [18–20]. However, in contrast to those probes for detection of fluoride, the long wavelength responded chemodosimeter based on fluoride-induced desilylation reaction is limited (Table S1) [21–24]. In view of fluorescent probes with long emission wavelength have low light damage, low self-fluorescence as well as the better deep tissue penetration [25–28], it is very important to develop a new fluorescent chemodosimeter with the advantage of potential longer emission wavelength triggered by fluorine-induced desilylation reaction.

1, 8-naphthalimide fluorophore has a rigid planar skeleton and a large π-conjugated system, which can be used as a good chromophore. One particularly intriguing approach is based on the construction of a donor–acceptor-type skeleton that introduces the binding site such as OH or NH group in the 4-position of 1, 8-naphthalimide derivatives. The 4-silyl ethers of 1, 8-naphthalimide derivatives have been developed to fluoride anion sensor [29]. However, the 3-substituted 1, 8-naphthalimide derivatives as sensor are less investigated. The F⁻-triggered desilylation reaction in the 3-position of 1, 8-naphthalimide would be susceptible to take place by the introduction of cyano group in the 4-position of 1, 8-naphthalimide framework. Here, we reported a new colorimetric and fluorescent chemodosimeter 1...
coupled with 4-(tert-butyldiphenylsilyloxy)benzylbromide (3) and 3-hydroxy-4-cyano-1, 8-naphthalimide (2). The chemodosimeter showed significant color and fluorescent changes, highly selectivity and long wavelength response through the classical fluoride-induced desilylation reaction.

**Experimental**

**General Information**

Unless otherwise noted, solvents and reagents were choosed and purchased from commercial channels. They were analytical reagents that can be directly used. The column chromatography using silica gel (200–300 sights) was performed. The intermediate 2 was synthesized according to the reported literature [30, 31]. We used SHIMADZU UV-1800 spectrophotometer to determine UV–visible absorption spectra. We used the Hitach F-4600 Fluorescence spectrophotometer to determine the fluorescence emission spectra. We used Bruker AVANCE III instrument to obtain the 1H NMR and 13C NMR spectra. Mass spectra analyses were performed on SolanX 70 FT-MS electrospray ionization high-resolution mass spectra.

**Synthesis of Probe 1**

The synthesis of target chemodosimeter1 is shown in Scheme 1. The intermediates 3-hydroxy-4-cyano-1, 8-naphthaleneimide (2) and 4-(tert-Butyldiphenylsilyloxy) benzylbromide (3) were synthesized according to the literature [30, 31]. To a solution of 3-hydroxy-4-cyano-1, 8-naphthaleneimide (2, 0.20 g, 0.68 mmol) in CH3CN (20 mL) was added 3.0 equiv. of potassium carbonate (0.28 g, 2.04 mmol), and the mixture was stirred at 50 °C for 1 h. After adding 3.0 equiv. of 4-(tert-Butyldiphenylsilyloxy) benzylbromide (3, 0.87 g, 2.04 mol), then the mixture was further refluxed for 24 h. After cooling of the reaction mixture, the residue was poured into dilute hydrochloric acid, and then extracted with ethyl acetate (20 mL×3), then the organic layer was further washed with brine, then dried with Na2SO4 and filtered. After the removal of solvent in vacuo, the residue was purified by chromatography (PE:EA = 10:1) to afford the probe 1 (0.21 g, 48%) as a white solid. 1H NMR (500 MHz, CDCl3) δ8.51 (d, J = 7.0 Hz, 1H), 8.40 (d, J = 8.5 Hz, 1H), 8.34 (s, 1H), 7.88 (t, J = 8.0 Hz, 2H), 7.41 (t, J = 7.0 Hz, 4H), 7.36 (t, J = 7.0 Hz, 4H), 7.24 (s, 2H), 6.80 (d, J = 8.0 Hz, 2H), 5.34 (s, 2H). 1H NMR (125 MHz, CDCl3) δ 163.26, 162.79, 160.82, 156.09, 135.57, 132.73, 132.66, 130.07, 129.99, 129.96, 129.93, 129.87, 128.98, 127.91, 127.87, 127.57, 127.15, 123.04, 122.85, 120.24, 119.78, 117.25, 114.20, 101.44, 71.81, 40.74, 30.19, 27.00, 26.57, 20.44, 19.54, 13.94; HRMS-ESI (m/z): [M+H]+ Calcd. for (C40H38N2O4Si): 639.2674; Found: 639.2680.

**Results and Discussion**

**Sensing Property of Probe 1 for Fluoride Ions**

Initially, the selectivity of probe 1 was evaluated by measuring the changes of absorption spectra after the addition of different anions (Fig. 1). Only the addition of fluoride ions (1.8 equiv., TBAF), the new absorption peak at 510 nm was increased followed by the unique color change from colorless to yellow, indicating that fluoride-induced desilylation reaction take places and the potential 3-hydroxy-4-cyano-1, 8-naphthaleneimide was produced.

However, the introduction of other anions, such as CN−, AcO−, H2PO4−, Cl−, NO3−, HSO4−, ClO4−, BF4−, Br−, SCN−, S2−, GSH, OH− ions (as their TBA salts) did result in no significant difference in color change, indicating that fluoride-induced desilylation reaction take places and the potential 3-hydroxy-4-cyano-1, 8-naphthaleneimide was produced.
peaks at 273 and 510 nm. Three isotonic points appeared at 320 nm, 356 nm and 410 nm in THF (Fig. 2).

The most significant changes were observed in fluorescence titration studies. Upon excitation at 410 nm in THF, with the addition of F⁻, probe 1 showed strong emission at 570 nm (Fig. 3). However, the introduction of other anions, such as F⁻, CN⁻, AcO⁻, H₂PO₄⁻, I⁻, Cl⁻, NO₃⁻, HSO₄⁻, ClO₄⁻, BF₄⁻, Br⁻, SCN⁻, S²⁻, GSH, OH⁻ ions (as their TBA salt), did result in no change in the emission intensity of probe 1 (Fig. 4). The unique orange fluorescence emission induced by fluorides was observed, which further showed the excellent selectivity of probe 1 for fluoride ions. In addition, this selectivity of probe 1 was further confirmed by competitive experiments (Fig. 5). The unique absorption and fluorescence bands produced by adding fluoride ions were not affected by other existing anions (including CN⁻, AcO⁻, H₂PO₄⁻, I⁻, Cl⁻, NO₃⁻, HSO₄⁻, ClO₄⁻, BF₄⁻, Br⁻, OH⁻). The fluorescence detection limit of probe 1 was further determined to be 57.18 nM (Fig. S7).

The fluorescent response time of probe 1 was studied, and the 60 min was selected as the standard test conditions (Fig. 6). In order to demonstrate the application of probe 1 in water-containing conditions, similar fluorescence titration were investigated in THF/H₂O (v/v, 50:50, Fig. 7), which shows that the fluorine-induced desilylation reaction take
places in the presence of excessive fluoride ions. The detection limit was determined to 0.092 mg/L (Fig. S8).

To further demonstrate the practicability of this sensor, the test paper were prepared by immersing the test paper into THF solution of probe 1 (1.0 mM) and drying them in air. As shown in Fig. 8, when the probe-loaded strips were immersed into the solutions of $F^-$ with different concentrations, the remarkable fluorescence color change from green to orange was observed with an increase in $F^-$ concentration. The probe 1-loaded test paper with can be used as a ‘Practical monitor’ to detect $F^-$ in the solution with significant color changes in fluorescence. This application provides a strong basis for further development of sensors similar to ‘Practical monitor’ method.

**Possible Reaction Mechanism of Probe 1 with Fluorine Ions**

In order to confirm the sensing mechanism, the titration reaction of chemodosimeter 1 with $F^-$ was analyzed by $^1$H NMR spectra. $^1$H NMR spectra confirmed that compound 2 was obtained by treating compound 1 with fluoride ions (Fig. S8). The results showed that compound 1 could react with fluorine ions to generate the compound 2 by the classical desilylation reaction (Scheme 2). Therefore, a new colorimetric and fluorescent 3-hydroxy-4-cyano-1,8-naphthaleneimide-based probe 1 by the fluorine-triggered desilylation reaction was developed for the first time.
Conclusion

In general, a new and simply chemosensor 1 based on fluorine-triggered desilylation reaction was described, and the mechanism involving the cascade release reaction to obtain the fluoroephore of 3-hydroxy-4-cyano-1,8-naphthaleneimide was studied. The probe 1 was shown excellent selectivity and sensitivity to fluoride ions with significant changes in fluorescence. Further work on this framework with 3-hydroxy-4-cyano-1,8-naphthaleneimide working in the aqueous solution is expected to yield novel fluoride-sensing probes with practical utility.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10895-021-02871-5.

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Author Contribution All authors contributed to the study conception and design. Xi Chen carried out the experiments, Haibin Shao, Tingting Zhu, Zhihua Chen and Yan Hu conducted the data analyses, Hua Zhang and Chuanxiang Liu wrote and edited the paper.

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Code Availability Not applicable.

Declarations

Ethics Approval Not Applicable.

Consent to Participate Not Applicable.

Consent for Publication Not Applicable.

Conflicts of Interest There are no conflicts of interest to declare.

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