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Colorimetric and ratiometric sensors derivated from natural building blocks for fluoride ion detection

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ABSTRACT

Three novel colorimetric and ratiometric probes (SH-1~3) for fluoride ion detection were designed and synthesized from nature small molecules. Obvious yellow-to-orange color change of these probes in the THF was achieved only in presence of F⁻ among the eight anions (F⁻, Cl⁻, Br⁻, I⁻, H₂PO₄⁻, HSO₄⁻, CH_3COO^- , ClO_4^-), along with the emission shifting from green to orange red. These three probes are 1:1 complexed with fluoride ions, with complexation constant of around $0.1 \times 10^4 \text{ M}^{-1}$. The detection limit of probes **SH-1~3** reached as low as around 1 μ M. ¹H NMR titration study suggested that the fluoride ion induced deprotonation of the probe through hydrogen bonding interaction between amino group of probe and fluoride ion.

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Introduction

The recognition and detection of ions have been received continuous attention due to their significance in biological and environmental fields [1,2]. Recently, the visual molecular recognition technology has been considered as a promising tool owing to its high sensitivity, good selectivity and practical operation, of which the concept is the change of the color and/or fluorescence of molecular probe caused by the structure change upon ion sensing [3,4]. The molecular design strategy of chemosensors should be dependent on the nature of the target ions [5-8]. Generally, the development of ratiometric sensors is crucial to improve the sensitivity and selectivity, involving the variations in the ratio of the intensities of the absorption or the emission peaks [9–18].

Fluoride is one of the essential trace elements in the human body, which is widely existed in nature in the form of fluorine ions [19–21]. Deficiency of fluoride in the human body can lead to dental caries, and the lack of fluoride in the elderly can lead to osteoporosis. However, excessive intake of fluoride in the human body can cause fluorosis and urolithiasis, and severe cases can lead to

https://doi.org/10.1016/j.tetlet.2019.151330 0040-4039/© 2019 Elsevier Ltd. All rights reserved. death [22–25]. So far, there are many types of molecular probes with the recognition mechanisms have been developed, involving F⁻-mediated desilylation of Si-O/Si-C bonds, B-F complexation, F⁻-induced deprotonation through H-bonding, intramolecular charge transfer, and so on [7,26-40]. Among them, molecular probes with acylhydrazone skeleton have been demonstrated to be promising due to their good sensitivity, high selectivity and a rapid response during the F⁻-induced deprotonation process [32,41-46].

Flavones are widely found in nature, which have been demonstrated to be possessing good biocompatibility and received considerable interest in pharmacological field [47,48]. However, only few molecular sensor has been developed based on flavones [49-51]. For example, Xu et al. designed a new flavone-based fluorescence probe for the detection of Al^{3+} and HSO_3^{-} [49]. Pina-Luis et al. reported a new fluorescent sensor for Cu²⁺ detection based on a flavone functional material [50]. On the other hand, nature *B*-phenylacrylic acids, such as erucic acid, caffeic acid and cinnamic acid, are also frequently used in the synthetic chemistry. We envisaged that the potential application of these nature molecules in molecular engineering of novel ion probes. Herein, we developed three novel highly selective naked-eye and fluorescent probe for fluoride ion detection based on functional acylhydrazones, which was constructed from nature molecules. Specially, β -phenylacrylic acid derivates (erucic acid, caffeic acid and cinnamic acid) were easily converted to corresponding acylhydrazines, which were fur-

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ther reacted with flavone to prepare the desired acylhydrazonetype probes **SH-1~3** in moderated yield, respectively (Scheme 1). These novel probes realized fast naked eye recognition of fluoride ion from yellow to orange in tetrahydrofuran with low detection limits around 1 μ M.

Results and discussion

Naked eye sensing and selectivity of probes SH-1~3

The interactions between probe **SH-1~3** and other anions (F^- , CI^- , Br^- , I^- , $H_2PO_4^-$, HSO_4^- , CH_3COO^- , CIO_4^-) were firstly checked by naked eye and UV–vis absorption upon the addition of 3 equiv tetrabutyl salt solution (F^- , CI^- , Br^- , I^- , $H_2PO_4^-$, HSO_4^- , CH_3COO^- , CIO_4^-) in THF solutions. As shown in Figs. 1 and S31, with the addition of fluoride ion salt, the color of the solution of probes in THF change from pale yellow to orange, along with the obvious enhancement of the absorption intensity in the peak around 480 nm. However, upon adding same mole amount of the other ions (CI^- , Br^- , I^- , $H_2PO_4^-$, HSO_4^- , CH_3COO^- , CIO_4^-), almost no color change shown in the solution of probes in THF. The results indicated that the present novel probes **SH-1~3** exhibit naked-eye sensitivity and good selectivity for fluoride ion detection.

UV-vis absorbance of probe SH-1 studies in THF

In order to further investigate the effect of fluoride ion concentration on the absorption spectra of these probes SH-1~3 solution, UV-vis absorption titration test was performed. As shown in Fig. 2a, with the adding amount of fluoride ion increasing, the intensity of the maximum absorbance peaks of pristine probe SH-1 in the UV region around 370 nm decreased, while a new absorption band in visible region around 480 nm appeared and its intensity was enhanced gradually. When 3 equiv. of fluoride ion was added, the intensity of new absorption peak in visible region reached the maxima, which suggested that the absorbance reached the saturated value (Fig. S32a). As a result, a naked-eve color of the probe SH-1 in THF changed from yellow to dark orange upon F⁻ sensing, while a weak fluorescence from green to orange was observed (Fig. S33) under 365 nm UV irradiation. When the concentration of fluoride ion increased from 0 to 300 µmol/L, the absorbance ratio (A480nm/A350nm) increased linearly from 0.008 to



Fig. 1. The intensity of the maximum absorption peak of probe **SH-1** $(1 \times 10^{-4} \text{ M})$ in the presence of 3 equiv. of various anions in THF at room temperature. (Inset: Color changes of probe **SH-1** with the addition of 3 equiv of various anions under ambient light.)

1.773 (Fig. 2b), which demonstrated that **SH-1** can serve as a ratiometric sensor for F⁻ [52]. Moreover, we also investigated the properties of compound **SH-2** and **SH-3** by the same way (Figs. S32~S35). The results indicated that both **SH-2** and **SH-3** possessing similar sensing behavior for F⁻ with **SH-1**, which revealed that the successful design of probes from β -phenylacrylic acid derivates and flavone.

To determine the stoichiometric ratio of the present probes **SH-1~3** with fluoride ion, Job-plots of these probes with fluoride ion in THF were calculated from the continuous variation of the intensity of the absorption band during the titration process, respectively (Figs. 3a and S36). The results showed the maxima at 0.5 of $[F^-]/([F^-] + [probes])$, which suggested that the formation of a complex with a 1:1 stoichiometric ratio between probe **SH-1~3** and F⁻ during the initial stage of the reaction, respectively. We also calculated Benesi-Hildebrand equations of these probes. As shown in Fig. 3b and Fig. S37, the measured absorbance $[1/(A - A_0)]$ at 480 nm showed a linear relationship with the concentration of F⁻ (R = 0.998 for **SH-1**, R = 0.998 for **SH-2** and R = 0.990 for **SH-3**), which further indicated the 1:1 stoichiometry between F⁻ and



H. Shi et al./Tetrahedron Letters xxx (xxxx) xxx



Fig. 2. a) Absorbance spectra of probe SH-1 (10^{-4} M) in THF in the presence of different concentration of F⁻ ($0 \sim 3$ eq); b) Plot of A_{450nm}/A_{350nm} versus [F⁻].



Fig. 3. a) Benesi-Hilderbrand plot of probe **SH-1** with F⁻, b) UV-vis titration and calculation of banding constant of probe **SH-1** for F⁻, c) Absorbance of probe **SH-1** in the presence of F⁻ (from TBAF) at various concentrations in THF, d) The response time of probe **SH-1**.

these probes, respectively. The corresponding association constants between probes and F^- were $0.12\times10^4~M^{-1}$ for SH-1, $0.066\times10^4~M^{-1}$ for SH-2 and $0.18\times10^4~M^{-1}$ for SH-3, respectively. The limit of detection was calculated to be 0.91 μM for SH-1, $1.39~\mu M$ for SH-2 and $0.84~\mu M$ for SH-3, respectively (Figs. 3c and S38). Furthermore, probes SH-1~3 possessed good stability in THF (Fig. S39) and exhibited transient response to F^- sensing (Figs. 3d and S40).

We also investigated the influence of the water content on the sensing effect of these three probes. As shown in Figs. 4 and S41, with increasing the content of water in THF, the intensity of the absorption bands around 480 nm of probes **SH-1~3** in the presence of 3 eq TBAF decreased gradually, respectively. When the content of water increased over 1%, the absorption bands around 480 nm of these samples disappeared, which suggested that the present sensors **SH-1~3** are not effective for the F⁻ detection under high

H. Shi et al./Tetrahedron Letters xxx (xxxx) xxx



Fig. 4. Absorbance spectra of probe SH-1 in the presence of 3 eq F⁻ in THF with various content of water

water content. The phenomena was similar with other acylhydrazone-type sensors reported previously [41].

¹H NMR titration experiments

To gain further insight into the interaction between these probes and F⁻, we carried out ¹H NMR titration experiments in THF- d_8 solution with varied amount of F⁻ anion (0, 0.1, 1 equiv) by employing the sample of SH-1 with sufficient solubility. As shown in Fig. 5, the signal peak of N-H proton at 11.04 ppm decreased and broadened upon addition of 0.1 equiv of TBAF₄, which suggested the complexation between amino proton of SH-**1** and fluoride at low con centration, probably due to the hydrogen bond interactions. With further increase the concentration of TBAF₄, the resonance signal of the N–H active proton disappeared,



Fig. 5. ¹H NMR titration spectra of the probe SH-1 in THF-d₈ in presence of various equivalents of TBAF.

which implied that the probe SH-1 would be deprotonated at higher fluoride ion concentration. Hence, the result of ¹H NMR titrations proposed a similar mechanism with those probes with acylhydrazone backbone reported previously [44].

Conclusion

In summary, we have developed three novel new colorimetric and ratiometric sensors based on natural small molecules for fluoride ion detection. Probes SH-1, SH-2 and SH-3 showed good sensitivity and high selectivity to F⁻ with naked-eyes color change from yellow to orange, as well as weak fluorescence from green to orange under 365 nm irradiations. Moreover, all these three probes possessed good stability in THF and showed transient response to F^- sensing, with low detection limit around 1 μ M. This work provide enlightenment for further molecular design of ion probes by natural molecules. The biocompatibility of these probes will be expected and studied systematically in our future work.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2019.151330.

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ARTICLE IN PRESS

H. Shi et al./Tetrahedron Letters xxx (xxxx) xxx

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