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Chromogenic and Fluorescent Chemodosimeter for Detection of Fluoride in Aqueous Solution

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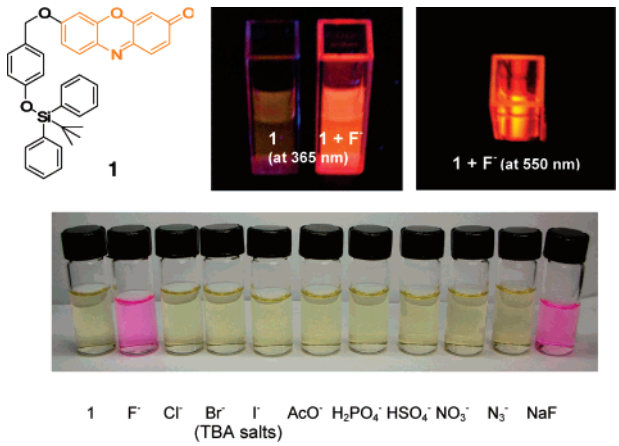
ABSTRACT



We have developed a chromogenic and fluorescent chemodosimeter 1 based on the release of resorufin for F^- (TBA^+ and Na^+ salts). This dosimeter 1 displayed drastic dual changes in UV–vis absorption and fluorescence emission intensities selectively for F^- over other anions in CH_3CN/H_2O (50:50, v/v) as well as in acetonitrile.

The development of sensors and receptors for anions has received considerable attention because of their roles in chemical and biological processes.[1] Among these anions, fluoride is primarily used for prevention of dental caries (decay),[2] enamel demineralization while wearing orthodontic appliances, and treatment for osteoporosis.[3] However, a high intake of fluoride can cause the most widespread side effect of fluoride, called fluorosis,[4] cause nephrotoxic changes in both humans and animals, and lead to urolithiasis. In addition, NaF functions as a potent G protein activator and Ser/Thr phosphatase inhibitor and affects plenty of essential cell signaling elements.[5] Therefore, there is a need to develop methods that can detect fluoride anions in aqueous solution.

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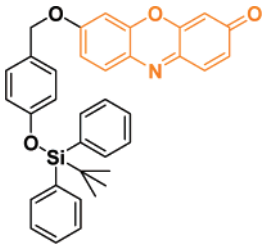
However, most fluoride sensors developed so far are operative only in organic solvents to detect tetrabutylammonium (TBA^+) fluoride.[6a,b,7,8,9a,c]

Even though many fluoride chemosensors have been developed over the past few decades, there are still difficulties in the detection of fluoride anions in polar or aqueous solution. For example, receptors using hydrogen-bonding find it difficult to detect fluoride efficiently in solvents with high dielectric constants such as acetonitrile, DMSO, and water,[6a,7] and in some cases, selective recognition of fluoride over oxygen-containing anions (e.g., AcO^-, $H_2PO_4^-$, $CH_3CO_2^-$) is restricted.[8] When Lewis acidic boron-based receptors bond with fluoride covalently, they cause fluorescence quenching due to intramolecular charge transfer between the boron p_π orbital and electrons from F^-.[9] Further, because most of the sensors and receptors above are poor at sensing fluoride (Na^+ salt) in aqueous media, they have problems in many bioanalytical applications.[5,10]

We have developed a dual chromogenic and fluorescent chemodosimeter **1** (Scheme 1), which is selective for F^-

Scheme 1. Structure of F^- Chemodosimeter **1**



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(TBA^+ and Na^+ salts). This dosimeter **1** shows a drastic change in UV−vis absorption and fluorescence emission upon fluoride addition over other anions in CH_3CN/H_2O (50:50, v/v), as well as in acetonitrile. Because of the high affinity of fluoride for silicon, silyl ethers (e.g., TBDMS, TBDPS ethers) are easily cleaved by fluoride.[11] Resorufin is a strong pink fluorescent dye with maximal emission at 585 nm upon excitation at 550 nm and is used to analyze intracellular processes without cell damage. The alkylation of the 7-hydroxy group of resorufin effectively quenches its fluorescence emission.[12] Dual spectroscopic changes are caused by release of resorufin through a fluoride-induced Si−O bond cleavage.

4-(*tert*-Butyldiphenylsilyloxy)benzyl bromide was synthesized according to the reported methods.[13] Dosimeter **1** was prepared by the coupling of 4-(*tert*-butyldiphenylsilyloxy)benzyl bromide with resorufin sodium salt in 52% yield (see the Supporting Information).

First, the effect of anions (TBA^+ salts) on the fluorescence emission spectrum (ex 550 nm) of dosimeter **1** (0.5 μM) was examined in acetonitrile (Figure 1). Upon the addition of

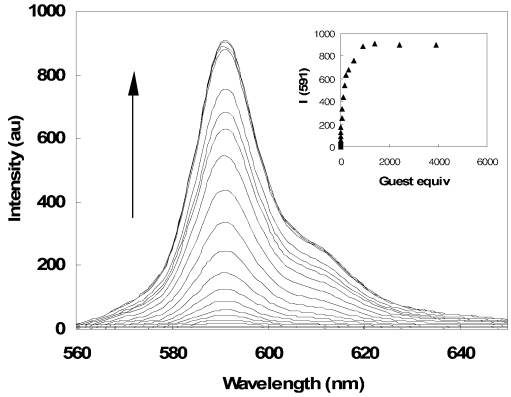

Figure 1. Fluorescence emission changes (ex 550 nm) of dosimeter **1** (0.5 μM) upon the addition of TBAF (50 μM) in acetonitrile: F^- (equiv) = 0, 0.5, 1, 2, 3, 4.5, 6.5, 10, 15, 22.5, 35, 55, 90, 140, 215, 315, 515, 900, 1400, 2400, 3900. (Inset: fluorescence emission change of dosimeter **1** vs TBAF equiv at 591 nm.)

F^-, the fluorescence emission intensity of dosimeter **1** increased drastically 500-fold at 591 nm, and was saturated with 1400 equiv of F^-. Over time, the color change of dosimeter **1** was observed from pale yellow to pink. However, each addition of 1400 equiv of $H_2PO_4^-$ or AcO^- caused only 3-fold or 2.5-fold emission enhancement, respectively. Other anions such as Cl^-, Br^-, I^-, HSO_4^-, NO_3^-, N_3^- did not affect the changes in emission intensity after the addition of 1400 equiv of each anion (Figure 2).

Upon the addition of F^-, the UV−vis absorption peak of dosimeter **1** (20 μM) decreased at 445 nm and increased at 586 nm in acetonitrile (Figure 3). The UV−vis absorbance (λ_{max} = 586 nm) of dosimeter **1** increased 250-fold and was saturated when 11 equiv of F^- was added to the acetonitrile

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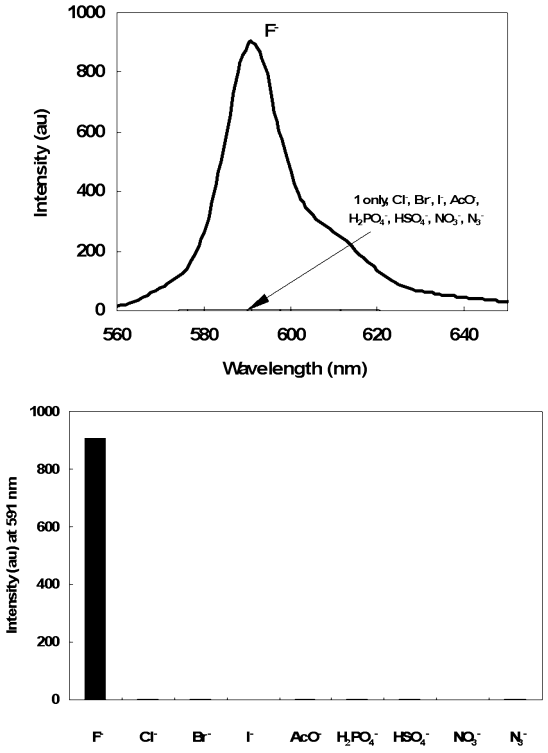


Figure 2. Comparison of fluorescence emission spectra of dosimeter **1** (0.5 μM) in acetonitrile after the addition of 1400 equiv of various anions (from left to right: F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, N_3^-) (TBA salt, 50 μM).

solution of dosimeter **1**. In the case of other anions, changes in UV−vis absorption were hardly observable after the addition of 11 equiv of each anion. As expected, other anions did not cause any color change.

Dosimeter **1** (5 μM) upon the addition of TBAF (5 mM) also exhibited a large enhancement of fluorescence emission

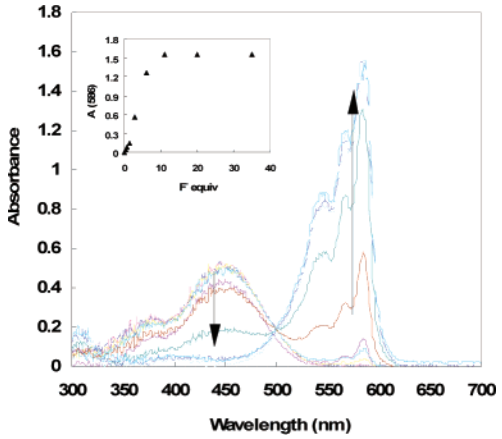


Figure 3. Changes of UV−vis absorption for dosimeter **1** (20 μM) upon the addition of TBAF (0.4 mM) in acetonitrile: F^- (equiv) = 0, 0.1, 0.3, 0.7, 1.5, 3, 6, 11, 20, 35. (Inset: UV−vis absorption change of dosimeter **1** vs TBAF equiv at 586 nm.)

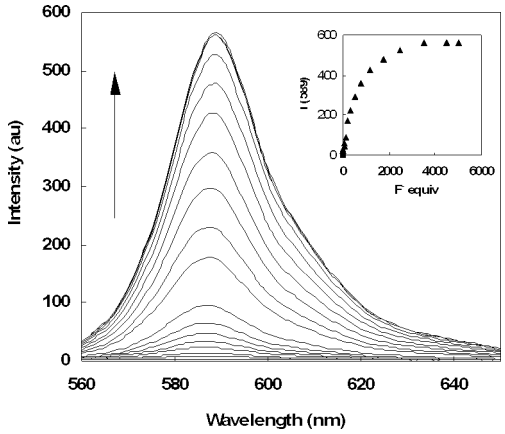


Figure 4. Change of fluorescence emission (ex 550 nm) of **1** (5 μM) upon the addition of TBAF (5 mM) in MeCN/H_2O (50:50, v/v): F^- (equiv) = 0, 0.5, 1, 2, 3, 4.5, 6.5, 10, 15, 22.5, 35, 55, 90, 140, 215, 315, 515, 900, 1400, 2400, 3900. (Inset: Fluorescence emission change of **1** upon the addition of F^- at 589 nm.)

in CH_3CN/H_2O (50:50, v/v) (Figure 4).[14] Upon the addition of F^-, the fluorescence emission intensity of dosimeter **1** increased drastically 200-fold at 589 nm and was saturated with 3000 equiv of F^-. Other anions did not cause the fluorescence emission to increase in the presence of each anion (3000 equiv) (see the Supporting Information). Likewise, dosimeter **1** turned from pale yellow to pink upon F^- addition in CH_3CN/H_2O (50:50, v/v) but other anions did not induce color changes (Figure 5a). To examine the possibility of application of dosimeter **1** to the biochemical analysis, the fluorescence emission and color changes (Figure 5) of dosimeter **1** were investigated in the presence of F^-

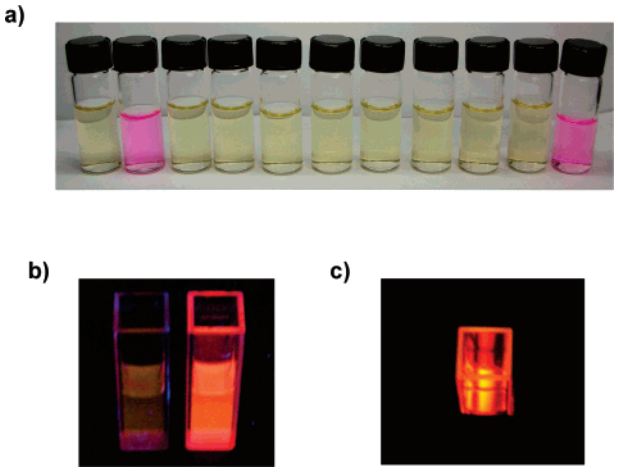
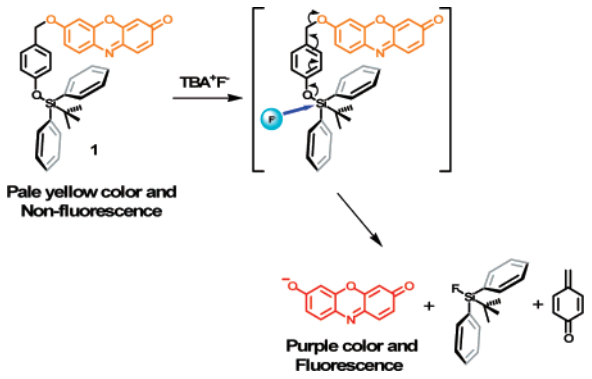


Figure 5. (a) Color changes of dosimeter **1** (5 μM) in CH_3CN/H_2O (50:50, v/v) after the addition of 3000 equiv of various anions (5 mM). From left to right: only dosimeter **1**, F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, N_3^- (TBA^+ salts), F^- (Na^+ salt). (b) Only **1** (left) and **1** + F^- (right) excited by UV lamp (ex. 365 nm). (c) **1** + F^- excited by spectrofluorometer (ex 550 nm).

Scheme 2. Feasible Mechanism for the Spectroscopic Changes of **1** in the Presence of F^-



(Na^+ salt) in CH_3CN/H_2O (50:50, v/v). Dosimeter **1** displayed a similar tendency for color change and an increase in fluorescence emission upon the addition of F^- as TBA^+ or Na^+ salt (see the Supporting Information).

A feasible mechanism for dual spectroscopic changes is shown in Scheme 2. When fluoride selectively attacks silicon atoms of the silyl ether group, an increased negative charge on the phenolate oxygen atom induces the release of resorufin through an extended conjugation system.[12] This mechanism is confirmed by identifying the same maximal emission wavelength of **1** + F^- as that of resorufin Na^+ salt in acetonitrile (see the Supporting Information).[15] Dosimeter **1** displays strong fluorescence and increased solubility in water owing to deprotonated resorufin formed after reaction with fluoride.

In summary, we have developed a novel chromogenic and fluorescent chemodosimeter **1** based on the release of resorufin upon addition of F^- (TBA^+ and Na^+ salts). This dosimeter **1** displayed drastic changes in UV−vis absorption and fluorescence emission intensities selectively for F^- in CH_3CN:H_2O (50:50, v/v) as well as in acetonitrile. Dual spectroscopic changes of **1** showed extreme selectivity for F^- over other anions not only in organic solvents but also in aqueous solution. The signal transduction occurs via a fluoride-triggered Si−O bond cleavage that results in the formation of a highly fluorescent resorufin.

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Supporting Information Available: Synthesis and spectra data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) A 10 mM aqueous HEPES buffer solution (pH 7.4) was used. Although the Si−O bond cleavage occurs instantly in CH_3CN, the cleavage reaction in aqueous solution shows a time-dependent dosimetric response. Each titration of **1** with the stock solution (**1** + TBAF: [**1**] = 5×10^{-6} M, [TBAF] = 5×10^{-3} or 5×10^{-2} M) in $MeCN/H_2O$ (50:50, v/v) was measured after mixing them for 3 min. Preparation of the saturated stock solution requires several hours (3−7 h) depending upon the concentration and temperature.

(15) The maximal emission wavelength (λ_{max} = 591 nm) of resorufin sodium salt (2 μM) appears to be the same as that of **1** after the addition of F^- (TBA salt).