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Sensors

A Rapid Aqueous Fluoride Ion Sensor with Dual Output Modes**

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The development of sensors and receptors for biologically important anions is currently of great interest because of their indispensable roles in vital (or physiological) processes.[1] Among the anions, fluoride ions are one of the most attractive targets because of their considerable significance for health and environmental issues. As an essential element of the body, the U.S. Public Health Service affirmed the optimal level to be 1 mg of consumed fluoride per day. On the other hand, unnecessary and inappropriate fluoride ingestion can result in fluorosis, urolithiasis, or even cancer.[2] The EPA (United States Environmental Protection Agency) gives an enforceable drinking water standard for fluoride of 4 $mg L^{-1}$ to prevent osteofluorosis and a secondary fluoride standard of 2 $mg L^{-1}$ to protect against dental fluorosis. Hence, the accurate determination of the levels of fluoride in drinking water is necessary. To date, the ion-selective electrode, ion chromatography, and standard Willard and Winter methods are generally used for quantitative fluoride analysis.[3] However, all these methods involve disadvantages, such as complicated procedures, high costs, or low mobility. Therefore, it is important to develop highly selective, sensitive, convenient, and rapid fluoride detection methods.

Fluorescent chemosensors with high specificity and sensitivity, ease, and safety of handling have received considerable attention, and a number of fluorescence sensors have been reported that are capable of detecting fluoride ions.[4–6] The recognition proceeded mostly through hydrogen bonding or Lewis acid coordination, and the sensors could only be operated in organic solvents to detect tetrabutylammonium (TBA^+) fluoride rather than inorganic fluoride salts. This incompatibility with aqueous environments is one of the main drawbacks that restrict the application of these sensors. Unavoidable interference from $H_2PO_4^-$, AcO^-, or CN^- ions is the other disadvantage. To improve the performance of fluoride sensors, another strategy based on the chemical affinity between fluoride and silicon was developed. *tert*-Butyldimethylsilyl (TBDMS) and *tert*-butyldiphenylsilyl (TBDPS) were chosen as additional substituents for the dye molecule, and rendered the dye unreactive to potentially interfering compounds and thus sensitive only to fluoride ions. This approach was pioneered by Kim and Swager, who developed a fluorescent fluoride receptor in organic solvents.[7] Subsequently, several research groups reported different chemodosimeters that can probe NaF in mixtures of organic solvents and water or even pure water.[8] However, several tens of minutes or even hours are needed to complete the detection process because low concentrations of these chemodosimeters severely reduce the reaction rate between the fluoride ions and the silyl moieties. However, the low concentration is necessary for general organic dyes to avoid fluorescence quenching induced by concentration effects, such as self-absorption and self-quenching.[9]

To date, most fluorescent sensors were based on the specific fluoride ion dependence of the emission intensity and could be significantly influenced by the excitation power and the detector sensitivity. More importantly, fluorescence intensity changes are not suitable for direct observation with the naked eye. To develop a more convenient fluorescence sensor, it is essential to make use of other fluoride-dependent measurable signals other than intensity. The fluorescence color change, which can be measured directly with a colorimeter or even distinguished easily by eye, is thus a good choice.

Herein we describe a rapid and portable sensor for fluoride ions in aqueous solution. The sensor, which has a high sensitivity, operates through the special affinity between fluoride ions and silicon, and provides two independent modes of signal transduction based on fluoride-dependent changes of fluorescence color (color metric mode) or intensity (power metric mode), respectively. For the design of the sensor, we chose *N*-(3-(benzo[d]thiazol-2-yl)-4-(hydroxyphenyl) benzamide (3-BTHPB) as an excited-state intramolecular proton transfer (ESIPT) compound. Just like other ESIPT compounds, 3-BTHPB shows two emission bands, which originate from the enol and keto forms at 418 and 560 nm, respectively. The ratio of the two bands is determined by the number of molecules that could undergo ESIPT reactions.[10] We coupled the *tert*-butyldiphenylchlorosilane with the sodium salt of 3-BTHPB to afford a derivative *N*-(3-(benzo[d]thiazol-2-yl)-4-(*tert*-butyldiphenyl silyloxy)phenyl)-benzamide (BTTPB). As expected, BTTPB shows only blue-violet fluorescence, which was almost identical to the emission of the enol form of 3-BTHPB (see the Supporting

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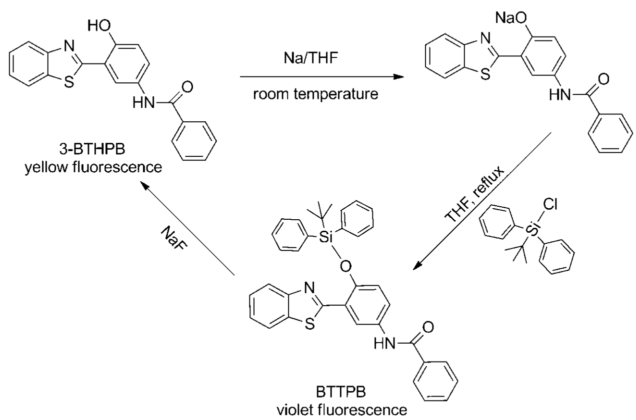
Information). Upon addition of fluoride ions, the Si–O bond of BTTPB is immediately cleaved, and 3-BTHPB, which exhibits a bright yellow emission in water, is simultaneously released. Therefore, it is logical to expect that the fluorescence color change from blue-violet to yellow upon addition of fluoride ions reflects the extent of the fluoride-induced Si–O bond cleavage. A schematic of the feasible fluorescence sensing mechanism in the fluoride ion detection is shown in Scheme 1.



Scheme 1. Synthesis and sensing mechanism of chemosensor BTTPB for the detection of NaF.

Both BTTPB and 3-BTHPB are not soluble in water; to apply them efficiently in an aqueous environment, cetyltrimethylammonium bromide (CTAB) was introduced into the aqueous phase. A stable sensor system was prepared by rapidly injecting a solution of BTTPB in THF (100 μL, 2.0 mM) into a micellar solution of CTAB in water (10 mL, 2.0 mM) under vigorous stirring for 30 seconds at 20 °C.

UV/Vis absorption and fluorescence spectra were recorded with different amounts of NaF to test the sensing ability of the BTTPB dispersions (Figure 1 a, b). As expected, the addition of fluoride ions to the dispersion resulted in gradual changes in the absorption and emission spectra. Figure 1 b shows the fluorescence spectra of the BTTPB dispersion 200 seconds after addition of NaF with the excitation wavelength at the isosbestic point (see Figure 1 a). The dispersion in the absence of fluoride ions exhibits only one emission band with a maximum at 418 nm, which is assigned to the BTTPB emission. Upon the addition of fluoride ions, the blue-violet emission band decreases and a new emission band located at 560 nm simultaneously appears and increases gradually. The fluorescence color change of BTTPB upon addition of one equivalent of fluoride ions (i.e., 0.38 ppm) is too small to be directly observed with the naked eye, but can be detected by fluorescence spectroscopy. When the fluoride ion concentration was further increased, the change can be seen with the naked eye. As shown in Figure 1 c, 0.95, 1.9, and 3.8 ppm of fluoride ions cause the dispersion fluorescence color to change from blue-violet to violet, pink-purple, and to pink-white, respectively. As mentioned above, the ideal and enforceable standards for fluoride in drinking water are 1–4 ppm. Therefore we conclude that the BTTPB/CTAB/water colorimetric sensing system is sufficiently sensitive for practical fluoride ion detection.

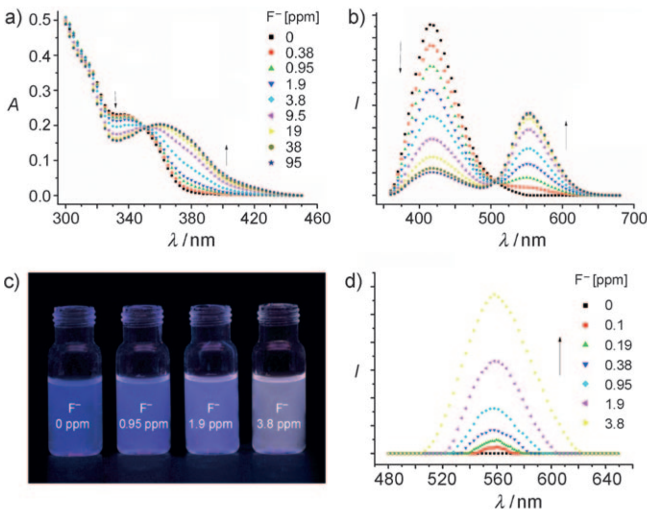


Figure 1. Absorption (a) and fluorescence spectra (b, d) of the BTTPB dispersions 200 s after addition of NaF, $\lambda_{ex} = 350$ nm (b) and 385 nm (d); pictures of BTTPB dispersions upon addition of NaF (c).

It is crucial that the absorption wavelength of 3-BTHPB is slightly longer than that of BTTPB, so that 3-BTHPB is selectively excited above 380 nm. Figure 1 d shows fluoride ion dependent fluorescence spectra of the BTTPB dispersion 200 seconds after addition of NaF with the excitation wavelength at 385 nm. No emission was found in the absence of fluoride ions, and the intensity of the yellow emission increased drastically with fluoride ion concentration; this result is indicative of an "off–on" switch triggered by fluoride ions. As mentioned above, although the intensity change of the fluorescence alone is not appropriate for detection with the naked eye, it is still a very sensitive method. The detection limit was determined as the three-fold standard deviation of the fluorescence obtained from a blank sample, prepared as described above but without the addition of BTTPB. The detection limit of the BTTPB dispersion system for fluoride ions is measured to be about 100 ppb. This result shows that in power metric mode the dispersion system has a very good sensitivity for the detection of aqueous fluoride ions.

For further evaluation of the fluoride sensing ability of the system, the selectivity of the BTTPB dispersion was tested by addition of 500 equivalents of common anions (in the form of sodium salts), such as Cl^-, Br^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, and F^-. As shown in Figure 2, only NaF induced an immediate red shift in the fluorescence maximum from 418 nm to 560 nm. All other anions did not cause any emission intensity changes at 560 nm until 30 minutes after the addition of each anion. The slight disturbances at 418 nm probably originated from the interaction between micelles and highly concentrated ions. This result indicates that the system is a very good sensor for recognizing fluoride ions over other anions.

To confirm the mechanism shown in Scheme 1, ESI-MS was carried out on agglomerates that resulted from the demulsification of the dispersion by addition of small

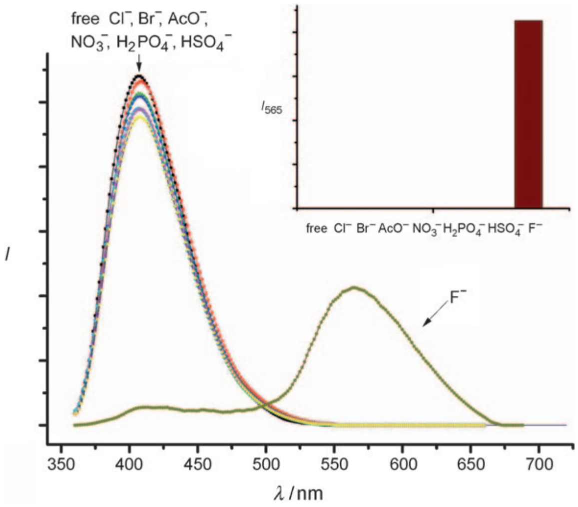


Figure 2. Luminescence spectra of BTTPB in CTAB micelles (2 mM) upon addition of 500 equivalents of sodium salts. The inset shows the selectivity for fluoride ions (monitoring the emission at 566 nm).

amounts of ethanol. The dispersion obtained by addition of 500 equivalents of fluoride ions was composed of three components, 3-BTHPB, BTTPB, and *tert*-butylfluorodiphenylsilane, thus confirming the postulated mechanism.

Aggregates of BTTPB and 3-BTHPB were also used as fluoride ion responsive materials. Two other factors—the aggregates' emission intensity and their reactivity with fluoride ions—are therefore crucial to ensure successful sensing. In general, most organic dyes have low luminescence efficiency or are even nonemissive in solutions with high concentrations or as aggregates, because of concentration-dependent quenching effects. Only very few compounds with specific structures maintain or even enhance the luminescence intensity in their aggregated state;[11] This is also the case for BTTPB as well as 3-BTHPB, as the emission efficiencies of their aggregates in pure water are 0.032 (BTTPB) and 0.21 (3-BTHPB). The intense emission of the aggregates makes it possible to employ the compounds as fluorescent sensors in water.

It is known that CTAB forms spherical micelles about 6 nm in diameter within the concentration range 0.9–100 mM in water.[12] In our system, the dispersions of BTTPB in 2 mM CTAB before and after addition of fluoride were transparent, thus implying that the sizes of the aggregates were smaller than half of the visible light wavelength. The small aggregate sizes were also confirmed by means of field emission scanning electron microscopy (FESEM) (see the Supporting Information), which illustrates the morphology of BTTPB aggregates before and 200 seconds after reaction with fluoride ions. Only a few 20–30 nm particles appear on the millipore filter surface (pore size of the filter is about 20 nm), but, by taking the emission of the filtrates into account, most aggregates should be below the pore size. In fact, the BTTPB molecules were concentrated in micelles and the fluoride ions were attracted to the micellar surface. The combination of small micelle sizes and the mobility of organic molecules in the micelles made the interaction between BTTPB and fluoride ions facile.

Fluorescence sensors for fluoride ion detection are usually solution-based. This approach is inconvenient since the sensors cannot be used as efficient tools under special circumstances, such as for in situ on-site detection. To facilitate the use of our system, we prepared test papers of BTTPB by immersing a filter paper ($2\times0.5\ cm^2$) in the solution of BTTPB in THF (2.0×10^{-3} M) and then drying it by exposure to air. For the detection of fluoride ions in water, the test paper was immersed in a fluoride-containing aqueous solution (containing 2 mM CTAB) and then exposed to air to remove water and to avoid further fluorescence color changes. The Commission Internationale de L'Eclairage (CIE) 1931 (x,y) chromaticity diagram of the test papers after immersion in solutions of NaF with different concentrations for three minutes are shown in Figure 3. When the

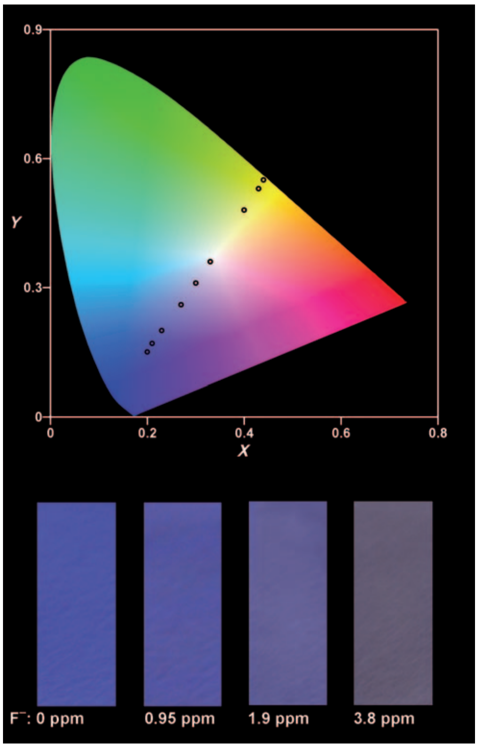


Figure 3. CIE 1931 (x,y) chromaticity diagram of the test papers for the detection of NaF at different concentrations derived from fluorescence spectra (black circles); NaF concentration from left to right: 0, 0.38, 0.95, 1.9, 3.8, 9.5, 19, 38, 95 ppm (top); images of the test papers after immersion into solutions with different concentrations of NaF (bottom).

fluoride ion concentration was increased, the color of the test paper changed from blue-violet to bright yellow. The immersion time was optimal for the detection of fluoride ions in the range of the enforced drinking water standard. According to the diagram, it can be easily seen if the fluoride ion concentration in drinking water exceeds the standard. Consequently, the easy-to-prepare test paper can be utilized to roughly and quantitatively detect and estimate the concentration of fluoride ions.

In summary, we have demonstrated a selective and sensitive method to detect aqueous fluoride ions based on the specific affinity between fluoride ions and silicon. The sensor system provides two independent modes of signal recognition in response to fluoride ions. In power-metric mode, fluoride ions can be detected at the ppb level, which relies on spectrometer sensitivity. In colorimetric mode, fluoride ion concentration is transformed to a fluorescence color signal that can be observed directly with the naked eye, and the sensitivity is still high enough at the level of drinking water standard. In both modes, the sensing process is rapid and takes only 200 seconds, and offers excellent differentiation from other common anions. The easy-to-prepare test paper based on the sensor system provides a convenient and reliable detection of fluoride ions in everyday applications.

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