

# A Fluorescein-based Fluorogenic Probe for Fluoride Ion Based on the Fluoride-induced Cleavage of *tert*-butyldimethylsilyl Ether

Xiao-Feng Yang · Si-Jie Ye · Quan Bai ·  
Xiao-Qing Wang

Received: 2 August 2006 / Accepted: 10 October 2006 / Published online: 2 December 2006  
© Springer Science+Business Media, LLC 2007

**Abstract** A highly sensitive and selective fluorogenic probe for fluoride ion, fluorescein di-*tert*-butyldimethylsilyl ether (FTBS), was designed and synthesized. FTBS was a colorless, non-fluorescent compound and was synthesized via the one-step reaction of fluorescein with *tert*-butyldimethylsilyl chloride. Upon incubation with fluoride ion in DMF-water solution (7 : 3, V/V), the Si-O bond of FTBS was cleaved, causing a large increase in fluorescence intensity and thereby allowing a selective detection of fluoride ion. The fluorescence increase is linearly with fluoride concentration in the range 0.1–2.0  $\mu\text{mol L}^{-1}$  with a detection limit of 0.041  $\mu\text{mol L}^{-1}$  ( $3\sigma$ ). The excellent selective signaling behavior of the proposed probe was found to originate from the high affinity of silicon toward fluoride ion. The method has been successfully applied to the fluoride determination in multi-trace elements injection and toothpaste samples, and the results are agreed well with those obtained by the fluoride-ion selective electrode method.

**Keywords** Fluoride ion · *tert*-butyldimethylsilyl ether · Fluorescein · Fluorescent probe

## Introduction

Fluoride, the smallest anion, has unique chemical properties and its recognition and detection are of growing interest because of its biologically important role in dental care and clinical treatment for osteoporosis. An acute intake of a large dose or chronic ingestion of lower doses of fluoride ions

can result in acute gastric and kidney disorders, dental and skeletal fluorosis, and even death [1]. For these reasons, it is important to develop new selective and sensitive methods for monitoring of fluoride concentration in environments that are not easily served by conventional ion selective electrodes.

Several methods have been developed for fluoride determination, including fluoride-ion selective electrodes (ISE) [2–4], spectrophotometry [5–8], ion chromatography [9–12], HPLC [13] and fluorimetry [14, 15]. Recently, some selective fluorescent chemosensors for fluoride ion have received considerable attention [16–18]. These chemosensors have enjoyed success and in some cases have resulted in the ability to visually detect fluoride ions [17, 18]. However, in most cases fluorescence changes can only be observed in non-aqueous solvent and there are relatively few chemosensors that can work in aqueous media, which greatly limits their analytical application in real samples.

Since the introduction of *tert*-butyldimethylsilyl (TBS) group by Corey in 1972 [19], the *tert*-butyldimethylsilyl ether has been extensively utilized as protecting group in organic synthesis for hydroxy functionality [20–23]. The resulting silyl ethers can be easily converted to their parent compounds under a variety of conditions [19, 24–26]. One of the most effective ways for the cleavage of silyl ethers is based on exploitation of the high affinity of silicon toward fluoride ion. And the treatment of silyl ethers with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) is the most popular condition for the removal of TBS group, which has been utilized in the synthesis of a variety of compounds [27, 28]. The strength of the Si-F bond has been claimed as the “driving force” of the reaction between silyl ethers and fluoride ion [19, 23].

Based on the above mechanism, Descalzo developed a new approach for fluoride determination based on the coupling between a MCM-41 silica matrix and a sensing

X.-F. Yang (✉) · S.-J. Ye · Q. Bai · X.-Q. Wang  
Department of Chemistry, Northwest University,  
Xi'an 710069, P. R. China  
e-mail: Xfyang@mail.china.com

molecule [29]. Zhu et al. synthesized a cyanine dye, 1-ethyl-4-(*p-tert*-butyldimethylsilane ether styryl) quinolinium iodide, and determined fluoride ion by colorimetric method [30]. Though optical probes for fluoride based on the fluoride-ion-triggered Si–O bond cleavage mechanism has been reported, some disadvantages can be cited about these probes, such as low sensitivity, longer reaction time, and cumbersome procedure to prepare [29].

Herein, we developed a new fluorogenic probe, fluorescein di-*tert*-butyldimethylsilyl ether (FTBS) for the selective determination of fluoride ion in aqueous media. Our strategy for the fluorescent detection of fluoride ion relies on the selective fluoride-mediated cleavage of Si–O bond to yield phenol, resulting in the formation of fluorescent compound and hence leading to a dramatic increase in fluorescence intensity. Based on the above mechanism, a new fluorimetric method for fluoride determination is developed. The fluorescence increase is linearly with fluoride concentration in the range 0.1–2.0  $\mu\text{mol L}^{-1}$  with a detection limit of 0.041  $\mu\text{mol L}^{-1}$ . The proposed method proves to be simple, sensitive and highly selective and has been successfully applied to the fluoride determination in multi-trace elements injection and toothpaste samples.

## Experimental

### Apparatus

The fluorescence spectra and relative fluorescence intensity were measured with a Sanco CRT-970 spectrofluorimeter (Shanghai, China) with a 10 mm quartz cuvette. The excitation and emission wavelength bandpasses were both set at 10 nm. Unless specific noted, the sensitivity of the spectrofluorimeter was set at “1.” The absorption spectra were recorded with a Shimadzu UV-1700 spectrophotometer. The pH was measured with a Model pHs-3B meter (Shanghai, China). Infrared spectrum was taken in KBr disks on a Bruker Tensor 27 FTIR spectrophotometer. Mass spectra were ob-

tained with AXIMA-CFR plus MALDI-TOF Mass Spectrometer. Uncorrected melting points were measured on an X-4 melting point apparatus (Beijing Tech Instrument Co., LTD).

### Chemicals

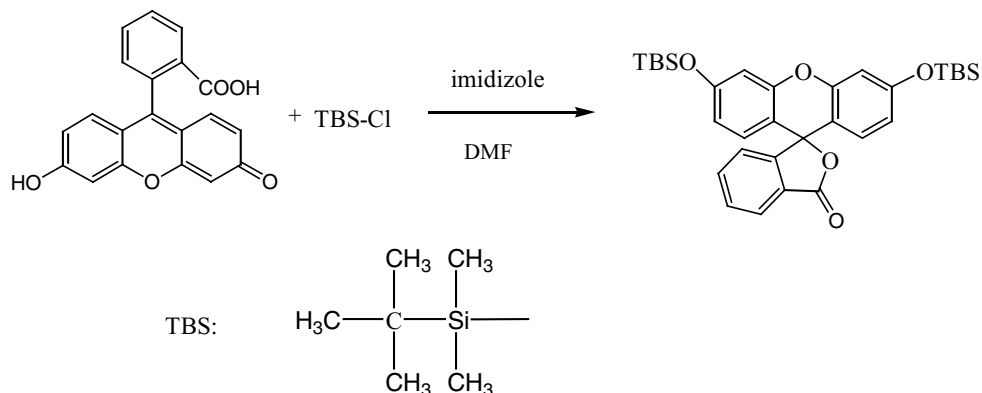
A stock solution of 0.01 mol L<sup>-1</sup> fluoride was prepared by dissolving 42.0 mg of sodium fluoride in 100 mL water. Standard test solutions were prepared by appropriate dilution of the stock solution. FTBS solution (0.5 mmol L<sup>-1</sup>) was prepared by dissolving 28.1 mg of the probe in 100 mL ethyl acetate. A 0.2 mol L<sup>-1</sup> Na<sub>2</sub>HPO<sub>4</sub>–NaH<sub>2</sub>PO<sub>4</sub> buffer solution (pH 7.0) was employed. The sources of reagents were as follows: Fluorescein was obtained from Xi'an Chemical Reagent Co.; *tert*-butyldimethylsilyl chloride was obtained from Shanghai Heqi Chemical Reagent Co.; Sodium fluoride was obtained from Beijing Chemical Reagent factory; Dimethylformamide (DMF) was obtained from Tianjin Chemical Reagent factory.

All the reagents were of analytical-reagent grade, and doubly distilled water was used throughout.

### Synthesis of FTBS

The synthesis of FTBS was employed a one-step reaction of fluorescein with *tert*-butyldimethylsilyl chloride by using imidazole as catalyst and DMF as solvent (Scheme 1). Fluorescein (1.6 g, 4.9 mmol) was combined with imidazole (1.72 g, 25.6 mmol) in 17 mL dry DMF and stirred. To the above solution was added *tert*-butyldimethylsilyl chloride (2.8 g, 18.6 mmol). The reaction mixture was stirred overnight at room temperature. The reaction mixture was then poured into saturated brine (~60 mL) and extracted with ethyl acetate. The combined organic extracts were washed with saturated brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent evaporated to dryness, giving 2.1 g of orange solid. After purification by column chromatography (200–300 mesh silica, 2.5:1 petroleum/ethyl acetate), the desired

**Scheme 1.** Synthesis of FTBS



product which was obtained as off-white solid (1.8 g, 67.6% yield). The product was shown to consist of only one substance by thin layer chromatography (TLC), and its  $R_f$  value was 0.75 (petroleum/ethyl acetate, 2:1). mp: 154–155°C; IR (KBr,  $\text{cm}^{-1}$ ) 2930.74, 2858.48, 1769.37, 1611.35, 1468.70, 1422.35, 1279.35, 1257.23, 1220.75, 1179.70, 1083.42. MS (MALDI-TOF): Calculated for  $\text{MH}^+$ , 561.87; Found 561.8.

#### Procedure

The fluorogenic reaction was performed in a 10-mL volumetric tube. Typically, to a test tube containing 3.5 mL of DMF and 40  $\mu\text{L}$  of 0.5  $\text{mmol L}^{-1}$  FTBS, different concentration of fluoride was added and the reaction mixture was diluted to 5.0 mL with water. The reaction solution was kept at room temperature for 30 min, then 1.0 mL of 0.2  $\text{mol L}^{-1}$   $\text{Na}_2\text{HPO}_4$ – $\text{NaH}_2\text{PO}_4$  buffer solution (pH 7.0) was added and the solution was diluted to 10 mL with water. The fluorescence intensity of the above solution was recorded at an emission wavelength of 532 nm with excitation wavelength set at 502 nm. In the meantime, a blank solution containing no fluoride ion was prepared and measured under the same conditions for comparison.

## Results and discussion

### Fluoride ion-induced cleavage of TBS from FTBS

Upon treatment with fluoride ion in DMF–water media, the TBS group would be cleaved from the probe and subsequently generated the open, colored and fluorescent fluorescein product. As FTBS has two TBS groups in its structure, there are two possible deprotection products can be generated according to the molar ratio of FTBS to fluoride ion (as shown in Scheme 2). If the amount of fluoride ion is less than FTBS, the moderately fluorescent fluorescein mono-*tert*-butyldimethylsilyl ether should be the major one. Conversely, if the amount of fluoride ion is in a large excess than FTBS, the parent dye, fluorescein, should be the fully returned. The similar reaction mechanism has been

described in the literature [31–33]. In the present study, fluorescein doubly protected with TBS group was chosen as fluorescent probe instead of the corresponding mono-protected one. This is not only because the former is much more easily synthesized than the latter but also because, after screening protective groups of choice, changing their protection mode from bis- to mono-protected type will provide an access to sensitive fluorogenic probe.

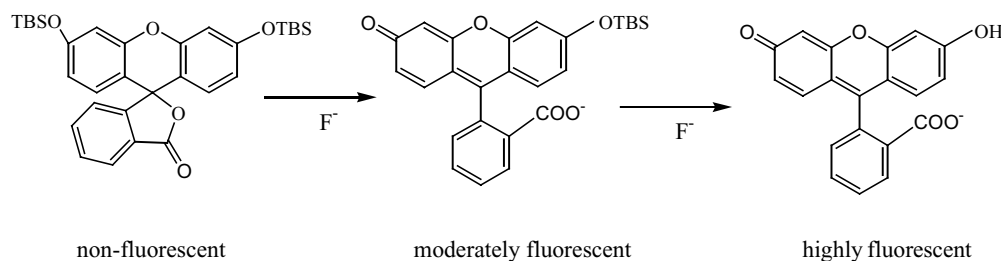
To ensure the single cleavage of TBS group from FTBS, FTBS concentration should be kept at a concentration large than that of fluoride ion. Under this experimental condition, only one major fluorescent product was generated, which greatly facilitated the quantitative measurement.

### Spectral characteristics

The installation of TBS groups at the 3' and 6' positions of a xanthenone scaffold would force this platform to adopt a closed, colorless, and non-fluorescent lactone form. Therefore, FTBS was a colorless solution showing no absorption at visible spectra range. Upon incubation with fluoride ion in DMF–water solution, a yellow green color was observed. Fig. 1 shows a color scale obtained upon addition of different concentrations of fluoride ion to FTBS solution. Furthermore, the absorption spectra of the above reaction solution were measured in pH 7.0 phosphate buffer and shown in Fig. 2. It can be seen that once one TBS group of FTBS was removed by fluoride ion, the characteristic absorption of initial fluorescein at about 496 nm was appeared. The fluorescence spectra of FTBS solution containing different concentrations of fluoride ion were measured, and a characteristic fluorescence emission maximum centered at about 532 nm was recorded (Fig. 3), consistent with the fluorescence emission maximum of fluorescein at the present conditions.

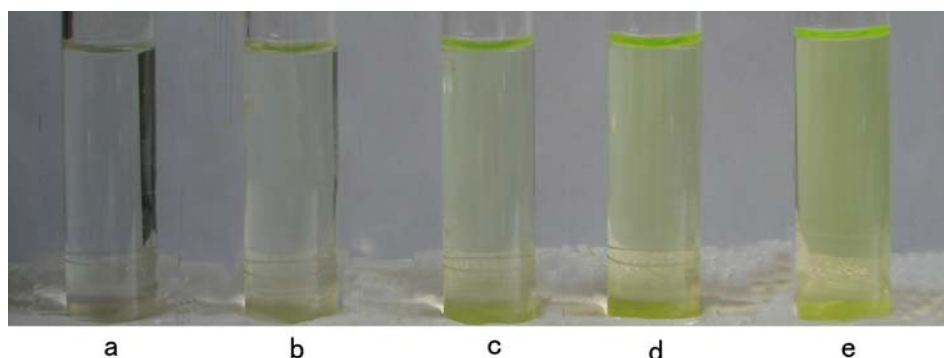
### Effect of the reaction media and detection pH

In general, the optimal conditions for the removal of silyl protecting group by fluoride ion was in aprotic medium [19]. However, non-aqueous reaction media was unpractical to



**Scheme 2.** Cleavage of Si–O bond in FTBS by fluoride ion.

**Fig. 1** Color changes of FTBS ( $20 \mu\text{mol L}^{-1}$ ) upon addition of different concentration of fluoride ion. Fluoride ion concentration: (a), 0; (b),  $2 \mu\text{mol L}^{-1}$ ; (c),  $5 \mu\text{mol L}^{-1}$ ; (d),  $10 \mu\text{mol L}^{-1}$ ; (e),  $20 \mu\text{mol L}^{-1}$ . Other reaction conditions were the same as those described in the procedure



real samples. In the present study, the organic solvent-water solution was selected as the fluorogenic reaction medium. The cleavage reaction performed at different organic solvent-water solution was studied, and results were shown in Table 1. It was found that organic solvent had greatly effects on the deprotection reaction. When the deprotection reaction was performed in DMF-water solution, a high  $F/F_0$  was obtained (where  $F$  and  $F_0$  were the fluorescence signal in the presence and absence of fluoride, respectively), indicating that the cleavage of silyl ether by fluoride ion was more efficient in DMF-water solution. Therefore, DMF-water solution was selected for the present cleavage reaction system.

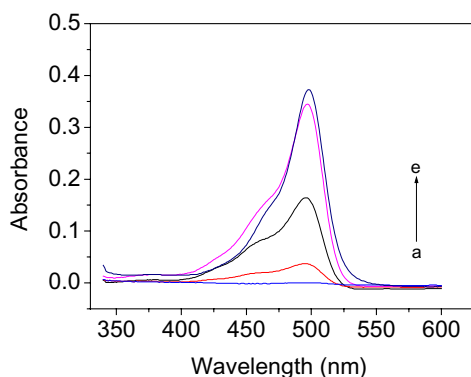
The effect of DMF concentration on the fluorescence emission of the system was further studied, and the results were shown in Fig. 4. It can be seen that  $F/F_0$  remains almost unchanged when DMF concentration in the range 0–40%, and increases dramatically when the concentration of DMF was above 40%. To facilitate the real sample analysis, 70% DMF-water solution was selected as the fluorogenic reaction media in the subsequent experiment.

The detection pH of the reaction solution was studied in the range 6.0–10.4, and it was found that FTBS was unstable

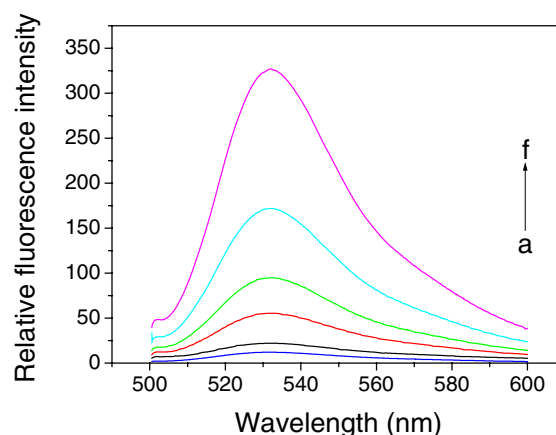
in high pH media and would cause a higher background signal. As the  $\text{pK}_{a,2}$  of fluorescein is 6.80 in aqueous solution [34], the fluorescent product is mainly present in its dianion form in pH 7.0 aqueous media, which has the most intense fluorescence among all the forms. Therefore, pH 7.0 phosphate buffer solution was selected as the detection media in the following study.

#### Effect of reaction time

The effect of the reaction time on the fluorescence emission of the system was studied and the results were shown in Fig. 5. It can be seen that the fluorescence signal of the system increased rapidly at the beginning, and increased slowly when the reaction time was above 20 min. Meanwhile, the blank signal remained almost unchanged at the same conditions. Though the sensitivity of the present method could be increased with increasing the incubation time, a



**Fig. 2** The absorption spectra of FTBS ( $20 \mu\text{mol L}^{-1}$ ) after incubation with increasing concentration of fluoride ion. Fluoride ion concentration: (a), 0; (b),  $2 \mu\text{mol L}^{-1}$ ; (c),  $10 \mu\text{mol L}^{-1}$ ; (d),  $20 \mu\text{mol L}^{-1}$ . (e),  $20 \mu\text{mol L}^{-1}$  of fluorescein. Other reaction conditions were the same as those described in the procedure



**Fig. 3** Fluorescence emission spectra (excitation at 480 nm) of FTBS ( $2.0 \mu\text{mol L}^{-1}$ ) after incubation with increasing concentration of fluoride ion. Fluoride ion concentration: (a), 0; (b),  $0.05 \mu\text{mol L}^{-1}$ ; (c),  $0.1 \mu\text{mol L}^{-1}$ ; (d),  $0.5 \mu\text{mol L}^{-1}$ ; (e),  $1.0 \mu\text{mol L}^{-1}$ ; (f),  $2.0 \mu\text{mol L}^{-1}$ . Other reaction and detection conditions are the same as those described in the procedure

**Table 1** Effect of solvent on the fluorescence signal of the system

Solvent <sup>a</sup>	F/F <sub>0</sub>
–	1.1
Methanol	1.2
Ethanol	1.5
Acetonitrile	2.2
Acetone	1.4
THF	1.3
DMF	20.3

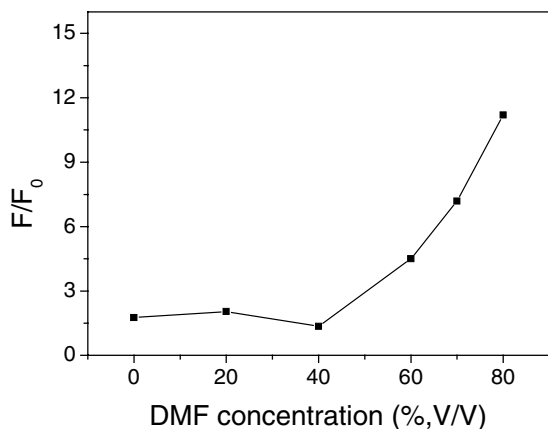
<sup>a</sup>Solvent concentration: solvent/water, 7:3 (V/V).

<sup>b</sup>F and F<sub>0</sub> was the fluorescence signal of the system in the presence and absence of 2.5 μmol L<sup>-1</sup> of fluoride ion, respectively.

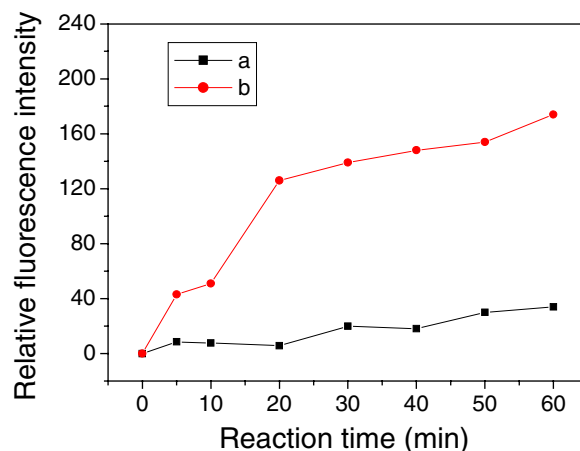
30-min reaction time was selected as a compromise of sensitivity and analytical frequency.

**Interference study**

The effect of foreign ions was tested by analyzing a standard solution of fluoride ion (0.8 μmol L<sup>-1</sup>) to which increasing amounts of interfering species were added, using an error < 5% as the criterion. The results are shown in Table 3. It can be seen that most of ion have little interference with the determination of fluoride. The high selectivity of the present probe toward fluoride over Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup> can be explained by the specificity with which fluoride reacts with silicon atom. It was found that BF<sub>4</sub><sup>-</sup> can also lead to the cleavage of TBS from the proposed probe at the present conditions and may cause interference for fluoride determination, which was agreement with that reported in the literature [24].



**Fig. 4** Effect of DMF concentration on fluorescence intensity of the FTBS cleavage system by fluoride ion. F and F<sub>0</sub> were the fluorescence signal in the presence and absence of 0.8 μmol L<sup>-1</sup> fluoride ion, respectively. Other conditions are the same as those described in the procedure



**Fig. 5** Effect of reaction time on the fluorescence intensity of FTBS cleavage system by fluoride ion. Fluoride ion concentration: (a), 0; (b), 0.8 μmol L<sup>-1</sup>. Other reaction and detection conditions are the same as those described in the procedure

**Analytical characteristics of FTBS for fluoride ion**

Under the selected experimental conditions, the enhancement value of the fluorescence intensity in contrast to the blank solution without fluoride ion (ΔF) is directly proportional to the fluoride concentration (C) in a range of 0.1–2.0 μmol L<sup>-1</sup>. The linear regression equation was determined to be ΔF = 129.6 × 10<sup>6</sup>C [mol L<sup>-1</sup>] + 12.45 (n = 8, r = 0.9972). According to IUPAC, the detection limit was determined from three times the standard deviation of the blank signal (3σ) as 0.041 μmol L<sup>-1</sup>. The relative standard deviation (n = 7) was 3.1% for 0.8 μmol L<sup>-1</sup> of fluoride ion.

**Sample analysis**

The proposed method was applied to the determination of fluoride in multi-trace elements injection (Xi’an Anjian Pharmacy Co., LTD). The multi-trace elements injection samples were diluted appropriately with doubly distilled water and then analyzed by the proposed method. The results are shown in Table 3, which are in agreement with those obtained by fluoride ISE standard method.

**Table 2** Tolerance limits of some foreign ions on the determination of fluoride ion

Foreign ions	Molar ratio to fluoride ion <sup>a</sup>
Br <sup>-</sup> , I <sup>-</sup> , SO <sub>4</sub> <sup>2-</sup> , NO <sub>3</sub> <sup>-</sup> , SCN <sup>-</sup> , Cl <sup>-</sup> , Ba <sup>2+</sup> , Co <sup>2+</sup> , Mn <sup>2+</sup>	100
Ni <sup>2+</sup>	50
Pb <sup>2+</sup> , Cu <sup>2+</sup>	10
P <sub>2</sub> O <sub>7</sub> <sup>4-</sup>	5

<sup>a</sup>Fluoride concentration: 0.8 μmol L<sup>-1</sup>.

**Table 3** Results of determination of fluoride ion in multi-trace elements injection and toothpaste

Sample	Proposed method	ISE method
Injection 1	99.8 ± 4.1 μg mL <sup>-1</sup>	98.6 ± 2.6 μg mL <sup>-1</sup>
Injection 2	97.3 ± 3.2 μg mL <sup>-1</sup>	95.2 ± 1.8 μg mL <sup>-1</sup>
Toothpaste 1	0.992 ± 0.043 mg g <sup>-1</sup>	1.07 ± 0.015 mg g <sup>-1</sup>
Toothpaste 2	1.06 ± 0.034 mg g <sup>-1</sup>	1.10 ± 0.022 mg g <sup>-1</sup>

Note. Average of four measurements (± S.D.)

Furthermore, the proposed method was applied to the fluoride determination in toothpaste. An accurately weighed amount of the commercial toothpaste (Jiajieshi) sample (~ 1.0 g) was dispersed in 30.0 mL of double-distilled water, and stirred for 3 h at 70 °C in a polypropylene vessel at with a magnetic stirrer. The resulting solution was cooled to room temperature and then filtered to eliminate solids in suspension. The insoluble part was washed several times with water, and the resulting solution was diluted to 100 mL with water. This solution was diluted appropriately with water and was analyzed by the proposed method and fluoride ISE standard method, respectively, and the results are shown in Table 2. From the above results, it can be seen that the proposed was reliable.

## Conclusions

In summary, a fluorescein-based fluorogenic probe for fluoride ion was prepared and its fluorogenic behavior was investigated. The method was based on the selective cleavage of Si-O bond in FTBS by fluoride, yielding highly fluorescent compound, and hence leading to a dramatic increase in fluorescence intensity of the reaction solution. Because of the specific affinity of fluoride for TBS group, the proposed probe shows excellent selectivity toward fluoride ion over other anions. The method is proved to be simple, selective and highly sensitive and can be broadly applicable to detection of fluoride ion in an aqueous environment. Moreover, the color changes of the proposed probe from colorless to yellow green would allow the “naked-eye” detection of fluoride without resorting to any spectroscopic instrumentation, which is of particular interest because of convenience.

**Acknowledgements** This work was supported by the Natural Science Foundation of Northwest University of China (04NW46). And the author thanks the Northwest University of China for startup funds.

## References

- Ekstrand J (1996) In Fejerskov O, Ekstrand J, Burt BA (ed.), Fluoride in Dentistry, 2nd ed. Munksgaard, Copenhagen, pp. 55
- Kazuyoshi I, Humio T (2001) Highly sensitive and rapid method for determination of fluoride ion concentrations in serum and urine using flow injection analysis with a fluoride ion-selective electrode. *Clin Chim Acta* 308:163–171
- Marian KM, Kjell B, Kåre J (2001) Determination of fluoride in food by the use of alkali fusion and fluoride ion-selective electrode. *Food Chem* 73:373–379
- Hirokazu H, Keiko Y, Mayumi H, Masahiro O (1998) Determination of free and total fluoride in rain water using a continuous-flow system equipped with a fluoride ion-selective electrode detector. *Anal Chim Acta* 364:117–123
- Arancibia JA, Rullo A, Olivieri AC, Nezio SD, Pistonesi M, Lista A, Band BSF (2004) Fast spectrophotometric determination of fluoride in ground waters by flow injection using partial least-squares calibration. *Anal Chim Acta* 512:157–163
- Khalifa ME, Hafez MAH (1998) Spectrophotometric and complexometric methods for the determination of thorium and fluoride using bromocresol orange reagent. *Talanta* 47(3):547–559
- Themelis DG, Tzanavaras PD (2001) Simultaneous spectrophotometric determination of fluoride and monofluorophosphate ions in toothpastes using a reversed flow injection manifold. *Anal Chim Acta* 429(1):111–116
- Themelis DG, Tzanavaras PD, Tzanavaras HD (2001) Simple, rapid reagent-injection spectrophotometric determination of fluorides in pharmaceutical formulations. *J Pharm Biomed Anal* 25:971–976
- Vasconcelos MTSD, Gomes CAR, Machado AASC (1994) Ion chromatographic determination of fluoride in welding fumes with elimination of high contents of iron by solid-phase extraction. *J Chromatogr A* 685:53–60
- Kalyakina OP, Dolgonosov AM (2003) Ion-chromatographic determination of fluoride ions in atmospheric precipitates and natural waters. *J Anal Chem* 58(10):951–953.
- Thangavel S, Dash K, Dhavile SM, Chaurasia SC, Mukherjee T (2005) Determination of traces of chloride and fluoride in H<sub>2</sub>SO<sub>4</sub>, H<sub>3</sub>PO<sub>4</sub> and H<sub>3</sub>BO<sub>3</sub> by in situ analyte distillation - ion chromatography. *J Chromatogr A* 1074(1–2):229–233
- Kapinus EN, Revelsky IA, Ulogov VO, Yu A (2004) Simultaneous determination of fluoride, chloride, nitrite, bromide, nitrate, phosphate and sulfate in aqueous solutions at 10<sup>-9</sup> to 10<sup>-8</sup>% level by ion chromatography. *J Chromatogr B* 800(1–2):321–323
- Xu XR, Li HB, Gu JD, Paeng KJ (2004) Determination of fluoride in water by reversed-phase high-performance liquid chromatography using F<sup>-</sup>-La<sup>3+</sup>-alizarin complexone ternary complex. *Chromatographia* 59(11–12):745–747
- Garrido M, Lista AG, Palomeque M, Band BSF (2002) Fluorimetric determination of fluoride in a flow assembly integrated on-line to an open/closed FIA system to remove interference by solid phase extraction. *Talanta* 58(5):849–853
- Nishimoto J, Yamada T, Tabata M (2001) Solvent extraction and fluorometric determination of fluoride ion at ppb level in the presence of large excess of aluminum(III) and iron(III) by using an expanded porphyrin, sapphyrin. *Anal Chim Acta* 428:201–208
- Cho EJ, Moon JW, Ko SW, Lee JY, Kim SK, Yoon J, Nam KC (2003) A new fluoride selective fluorescent as well as chromogenic chemosensor containing a naphthalene urea derivative. *J Am Chem Soc* 125(41):12376–12377
- Badugu R, Lakowicz JR, Geddes CD (2005) A wavelength-ratiometric fluoride-sensitive probe based on the quinolinium nucleus and boronic acid moiety. *Sens Actuators, B* 104:103–110
- Zhou G, Cheng Y, Wang L, Jing X, Wang F (2005) Novel polyphenylenes containing phenol-substituted oxadiazole moieties as fluorescent chemosensors for fluoride ion. *Macromolecules* 38:2148–2153
- Corey EJ, Venkateswarlu A (1972) Protection of hydroxyl groups as tert-butylidimethylsilyl derivatives. *J Am Chem Soc* 94:6190–6191

20. Kendall PM, Johnson JV, Cook CE (1979) Synthetic route to an aromatic analogue of strigol. *J Org Chem* 44(9):1421–1424
21. Ronald RC, Lansinger JM, Lillie TS, Wheeler CJ (1982) Total synthesis of frustulosin and aurocitrin. *J Org Chem* 47:2541–2549
22. Liu AJ, Dillon K, Campbell RM, Cox DC, Huryn DM (1996) Synthesis of E-selectin Inhibitors: Use of an aryl-cyclohexyl ether as a disaccharide scaffold. *Tetrahedron Lett* 37:3785–3788
23. Corey EJ, Snider BB (1972) A total synthesis of ( $\pm$ )-fumagillin. *J Am Chem Soc* 94:2549–2550
24. Ranu BC, Jana U, Majee A (1999) A simple and efficient method for selective deprotection of t-butyldimethylsilyl ethers by zinc tetrafluoroborate in water. *Tetrahedron Lett* 40:1985–1988
25. Farras J, Serra C, Vilarrasa J (1998) Cleavage of tert-butyldimethylsilyl ethers by chloride ion. *Tetrahedron Lett* 39:327–330
26. Sartori G, Ballini R, Bigi F, Bosica G, Maggi R, Righi P (2004) Protection (and deprotection) of functional groups in organic synthesis by heterogeneous catalysis. *Chem Rev* 104:199–250
27. Burdette SC, Frederickson CJ, Bu W, Lippard SJ (2003) ZP4, An improved neuronal Zn<sup>2+</sup> sensor of the zinpyr family. *J Am Chem Soc* 125:1778–1787
28. Urano Y, Kamiya M, Kanda K, Ueno T, Hirose K, Nagano T (2005) Evolution of fluorescein as a platform for finely tunable fluorescence probes. *J Am Chem Soc* 127(13):4888–4894
29. Descalzo AB, Jiménez D, Haskouri JE, Beltrán D, Amorós P, Marcos MD, Martínez-Máñez R, Soto J (2002) A new method for fluoride determination by using fluorophores and dyes anchored onto MCM-41. *Chem Commun* 562–563
30. Zhu C-Q, Chen J-L, Zheng H, Wu Y-Q, Xu J-G (2005) A colorimetric method for fluoride determination in aqueous samples based on the hydroxyl deprotection reaction of a cyanine dye. *Anal Chim Acta* 539:311–316
31. Chen XQ, Sun M, Ma HM (2006) Progress in spectroscopic probes with cleavable active bonds. *Current Org Chem* 10:477–489
32. Chang MCY, Pralle A, Isacoff EY, Chang CJ (2004) A selective cell-permeable optical probe for hydrogen peroxide in living cells. *J Am Chem Soc* 126:15392–15393
33. Maeda H, Yamamoto K, Nomura Y, Kohno I, Hafsi L, Ueda N, Yoshida S, Fukuda M, Fukuyasu Y, Yamauchi Y, Itoh N (2005) A design of fluorescent probe for superoxide based on a nonredox mechanism. *J Am Chem Soc* 127:68–69
34. Mchedlov-Petrosyan NO, Kukhtik VI, Bezugliyz VD (2003) Dissociation, tautomerism and electroreduction of xanthene and sulfonephthalein dyes in N,N-dimethylformamide and other solvents. *J Phys Org Chem* 16:380–397