Research article

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A colorimetric and fluorescent probe for fluoride ions based on 6-acetyl-2-naphthol

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ABSTRACT: A colorimetric and turn-on fluorescent probe for fluoride ions, *tert*-butyldimethylsilane 6-acetyl-2-naphtholate, was readily synthesized from 6-acetyl-2-naphthol and *tert*-butyldimethylchlorosilane (TBSCl). The probe exhibits high sensitivity and good selectivity for fluoride ions in acetonitrile. The inherent mechanism involves the cleavage of the Si–O bond in the probe, which induced yellow color formation and prominent fluorescence enhancement. Copyright © 2013 John Wiley & Sons, Ltd.

The following supporting information is available online.

Keywords: colorimetric; fluorescent probe; fluoride ion

Introduction

Because of the crucial roles of anions in biological systems and chemical processes, intensive research has been conducted on the design of signaling probes for anions (1–5). The fluoride ion has been widely used as an essential element in toothpaste and pharmaceutical agents to prevent dental caries and orthodontics (6–8). However, fluoride ions are poisonous to biological systems when levels exceed normal cellular values, and can cause fluorosis such as metabolic disorders and immunological damage in humans (9–13). Thus, it is very important to regulate the uptake of fluoride ions and the detection of fluoride ions has attracted considerable attention. Owing to its simplicity and exquisite sensitivity, fluorescent probes are highly attractive for the selective detection of fluoride ions. A number of fluorescent probes for fluoride ions have been developed in recent years (14–22). However, many of the reported probes suffer from complicated synthesis procedures, turn-off fluorescence response, slow response or low sensitivity. Therefore, there is still a high demand for probes for fluoride ions with good selectivity and high sensitivity.

It is well known that *tert*-butyldimethysilane (TBS) ether is a useful protective group for the hydroxy group and can be specifically and efficiently cleaved by fluoride ions. Therefore, TBS ether has been proven to be an attractive component for the design of fluoride probes (23–32). 6-Acetyl-2-naphthol, which has a pull–push electron structure, exhibits outstanding chemical and photophysical properties such as high fluorescent quantum yield, good photostability and a large Stokes shift induced by an intramolecular charge transfer process (ICT). Therefore, derivatives of 6-acetyl-2-naphthol have emerged as very promising fluorescent probes. Here, we report the design and synthesis of a TBS ether of 6-acetyl-2-naphthol, **1**, as a colorimetric and turn-on fluorescent probe for fluoride ions (shown in Scheme 1). In probe **1**, the ICT process was completely inhibited due to the protection of phenolate by TBS. However, upon the addition of fluoride ions, probe **1** can be quickly converted into 6-acetyl-2-naphthol, which leads to a marked color change and significant fluorescence enhancement.

Experimental

Materials

Acetonitrile was purchased from J&K Scientific Ltd. (Shanghai, China) Dry methylene chloride was obtained by distillation after refluxing with CaH_2 for 6 h. Unless otherwise stated, all chemicals were purchased from commercial suppliers and used as received. The investigated anions were F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, AcO^- and ClO_4^-, and tetrabutylammonium (TBA^+) was the counter cation.

Synthesis of probe 1

The synthetic route for probe **1** is shown in Scheme 1. Following to the literature, 6-acetyl-2-naphthol was obtained by refluxing 2-acetyl-6-methoxy-naphthalene with concentration hydrochloric acid for 2 h (33). To a mixture of 6-acetyl-2-naphthol (0.4 mmol, 74.5 mg), DMAP (0.16 mmol, 20 mg) and triethylamine (2 mmol, 202 mg) in 50 mL of dry CH_2Cl_2 was added *tert*-butyldimethylchlorosilane (2 mmol, 301.4 mg). After stirring the reaction mixture at room temperature for 1 h, 50 mL of water was added. The organic layer was separated and dried over anhydrous Na_2SO_4. The drying agent was removed by filtration and the solvent was removed by distillation. The obtained residue was purified by silica gel column chromatography (10:1 petroleum:ethyl acetate as

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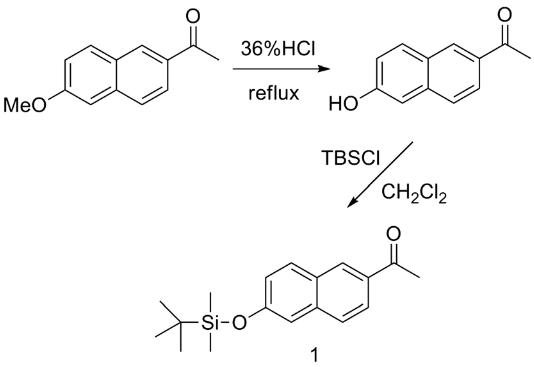


Scheme 1. Synthesis of probe **1**.

eluent) to yield the product, **1**, as a white solid (102 mg, 85%) (Fig. S1,S2). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 8.40 (*s*, 1H), 7.97 (*t*, *J* = 8.8 Hz, 1H), 7.85 (*d*, *J* = 9.2 Hz, 1H), 7.72 (*d*, *J* = 8.8 Hz, 1H), 7.21 (*d*, *J* = 2.0 Hz, 1H), 7.14 (*d*, *J* = 8.8 Hz, 1H), 2.70 (*s*, 3H), 1.03 (*s*, 9H), 0.27 (*s*, 6H). GCMS (*m/z*): 300.1.

Results and discussion

UV/vis absorption studies with fluoride ion

Prior to the reaction with fluoride ions, probe **1** is colorless in acetonitrile with an absorption maximum at 304 nm, as shown in Fig. 1. Upon the addition of 3 eq. of fluoride ions, an apparent 102 nm red-shift (from 304 to 406 nm) instantly appeared. With increasing addition amounts of fluoride ion, the absorption band at 304 nm progressively decreased and a new band centered at 406 nm gradually formed with a clear isosbestic point at 329 nm (Fig. 2). To demonstrate the selectivity of probe **1** as a colorimetric probe, titration experiments were carried out on probe **1** with other typical anions (Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, AcO^- and ClO_4^-) by observing the absorption spectral change. As shown in Fig. 3, only fluoride ions could induce the probe to form a yellow color with 102 nm a red-shift, whereas other typical anions have no influence on the absorption spectra. The above results proved that probe **1** could be used as a highly selective colorimetric probe for fluoride ion.

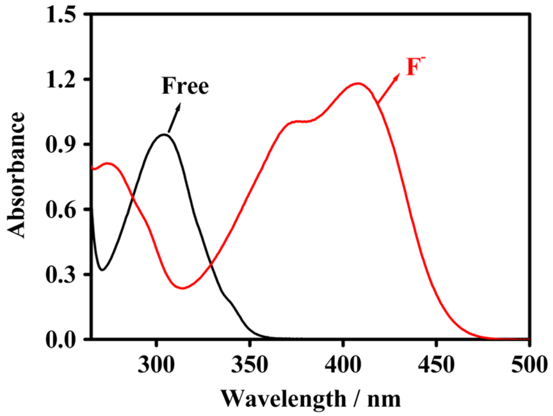


Figure 1. UV/vis absorption spectra of probe **1** (100 μM) in the absence and presence of TBAF (300 μM) in CH_3CN.

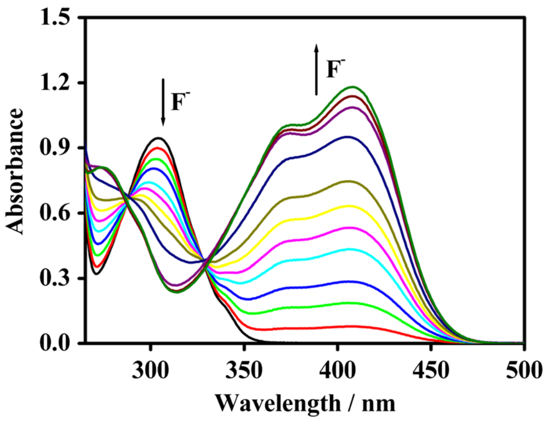


Figure 2. UV/vis absorption spectra of probe **1** (100 μM) in CH_3CN containing different amounts of TBAF (0, 10, 15, 20, 25, 30, 35, 40, 50, 100, 200, 300 μM).

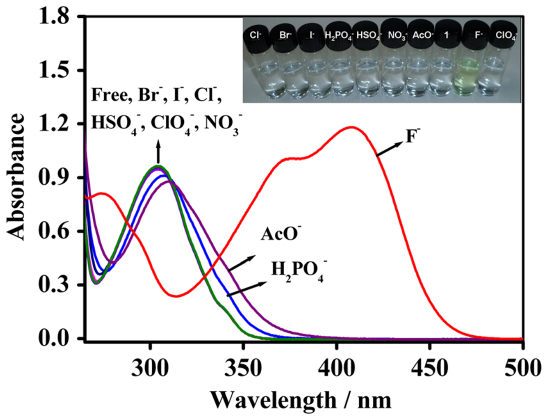


Figure 3. Absorption spectra of probe **1** (100 μM) in CH_3CN upon addition of various TBA salts (F^-, Cl^-, Br^-, I^-, AcO^-, HSO_4^-, $H_2PO_4^-$, ClO_4^- and NO_3^-; 300 μM each). (Inset) Color changes of the probe **1** (100 μM) in the presence of 3 eq. of TBA salts (F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, AcO^- and ClO_4^-) in CH_3CN.

Fluorescence studies with fluoride ion

As shown in Fig. 4, probe **1** in acetonitrile is essentially nonfluorescent in the absence of fluoride ions. By contrast, a dramatic fluorescence enhancement (9663-fold) was observed with a maximum at 488 nm upon treatment with 10 eq. of fluoride

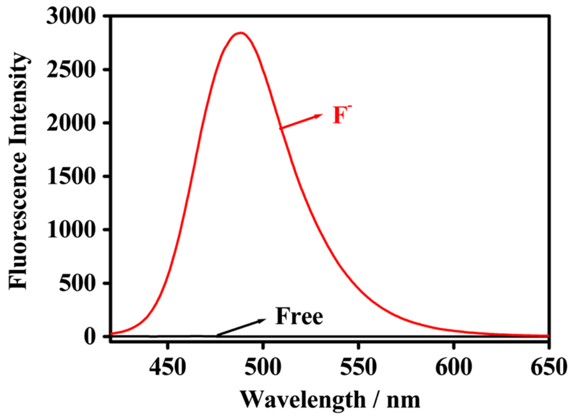


Figure 4. Fluorescence spectra of probe **1** (5 μM) recorded before and after reaction with TBAF (50 μM) in CH_3CN.

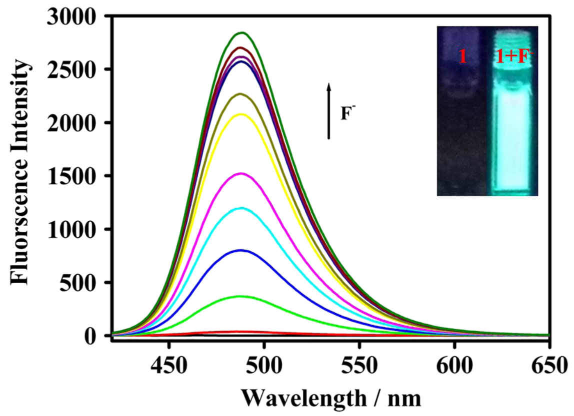


Figure 5. Fluorescence spectra of probe **1** (5 μM) in CH_3CN with different amounts of TBAF (0, 2, 3, 4, 5, 6, 8, 10, 20, 30, 40, 50 μM). The excitation wavelength was set at 406 nm.

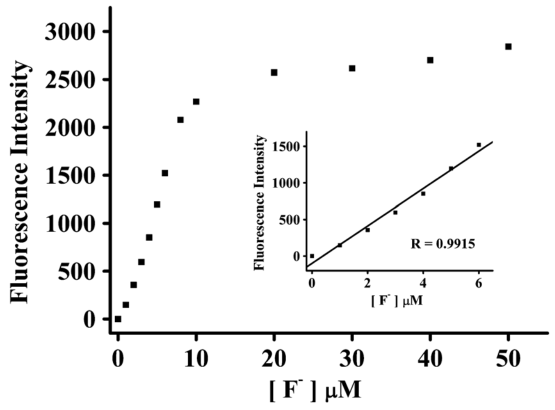


Figure 6. Fluorescence intensity at 488 nm of probe **1** (5 μM) in CH_3CN in the presence of TBAF. (Inset) Linear portion of the curve at low concentrations of TBAF.

ions. There was a good linear correlation between the fluorescence intensity and the concentration of fluoride ion in the range 0–50 μM (Fig. 5). The linear equation was expressed as $y = -734.4 + 379.8x$ ($R = 0.9915$, where y denotes the fluorescence intensity and x denotes the concentration of fluoride ion). The detection limit was determined to be 40 nM (Fig. 6).

In order to evaluate the selectivity of the probe for fluoride ions, we investigated the fluorescence behavior of probe **1** with other typical anions. The results presented in Fig. 7 show that other typical anions (Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^-, AcO^-, S^{2-}, SCN^- and ClO_4^-) have no effect on the fluorescence behavior of probe **1**, even at high concentrations (10 eq. of probe **1**). Therefore, it can be concluded that the fluorescent probe **1** displayed excellent selectivity for fluoride ions over other competing anions.

Time-dependent fluorescence studies of probe **1** with fluoride ions were also conducted. It can be seen in Fig. 8 that the fluorescence intensity was enhanced with increasing reaction time. Pronounced fluorescence enhancement was observed within 30 s and leveled off to a constant value after 3 min, which indicated that probe **1** showed rapid detection of fluoride ions.

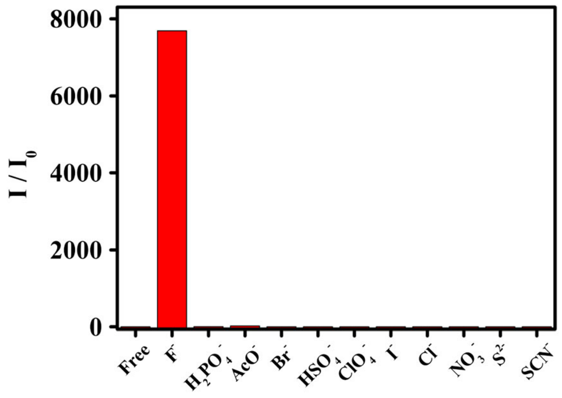


Figure 7. Ratio of emission intensity at 488 nm of probe **1** (5 μM) before (I_0) and after (I) the addition of TBAF (10 μM) and other TBA salts (Cl^-, Br^-, I^-, AcO^-, HSO_4^-, $H_2PO_4^-$, S^{2-}, SCN^- and NO_3^-; 50 μM, each).

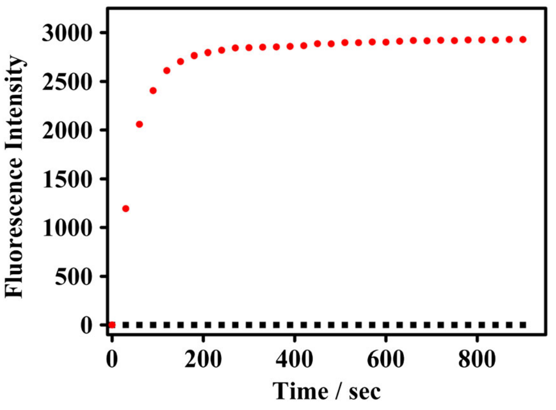
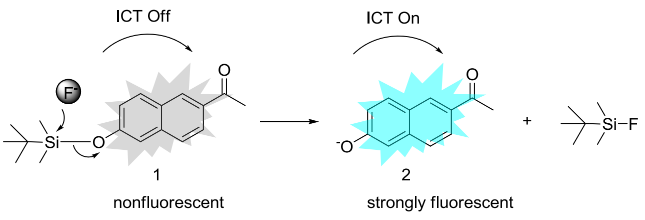


Figure 8. Time-resolved fluorescence spectra of probe **1** (5 μM) at 488 nm upon addition of TBAF (50 μM) in CH_3CN.



Scheme 2. TBAF-induced cleavage of the Si–O bond in probe **1**.

Proposed mechanism for the reaction of the probe with fluoride ion

It is known that fluoride can effectively cleave the Si–O bond. In our work, we expected that probe **1** was transferred into 6-acetyl-2-naphtholate in the presence of fluoride ion (Scheme 2). In comparison with probe **1**, the reaction product, 6-acetyl-2-naphtholate, has a more electron-donating group and possesses a push–pull electron structure, which can lead to a red-shift in its absorption spectrum and a strong fluorescence due to the ICT process. Absorption and fluorescence studies of probe **1** with fluoride ions are consistent with this. In order to further confirm the reaction mechanism, the resulting mixture of probe **1** with fluoride ion was subjected to ESI mass spectral analysis. The result in Fig. S3 shows a peak at $m/z = 185.3$, which clearly indicates the formation of 6-acetyl-2-naphtholate (calcd. 185.2 for $C_{12}H_9O_2$). The absorption, fluorescence (Fig. S4) and ESI spectral studies strongly support the proposed mechanism in Scheme 2.

Conclusions

In summary, on the basis of a specific reaction with fluoride and exploiting an ICT mechanism, we have developed a colorimetric and turn-on fluorescent probe based on 6-acety-2-naphthol moiety. The probe displayed extremely high sensitivity and good selectivity for the detection of fluoride ion.

SUPPORTING INFORMATION

The following supporting information is available online.

Acknowledgement

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References

1. Duke RM, Veale EB, Pfeffer FM, Kruger PE, Gunnlaugsson T. Colorimetric and fluorescent anion sensors: an overveiw of rescent developments in the use of 1,8-naphthalimide-based chemosensors. Chem Soc Rev 2010;39:3936–53.
2. Xu Z, Kim SK, Yoon J. Revisit to imidazolium receptors for the recognition of anions: highlighted research during 2006–2009. Chem Soc Rev 2010;39:1457–66.
3. Li AF, Wang JH, Wang F, Jiang YB. Anion complexation and sensing using modified urea and thiourea-based receptors. Chem Soc Rev 2010;39:3729–45.
4. Amendola V, Fabbrizzi L. Anion receptors that contain metals as structural units. Chem Commun 2009;5:513–31.
5. Chen S, Hou P, Wang J, Song X. A highly sulfite-selective ratiometric fluorescent probe based on ESIPT. RSC Adv 2012;2:10869–73.
6. Clarkson JJ, McLoughlin J. Role of fluoride in oral health promotion. Int Dent J 2000;50:119–28.
7. Horowitz HS. The 2001 CDC recommendation for using fluoride to prevent and control dental caries in the United States. J Public Health Dent 2003;63:3–8.
8. Todd MA, Staley RN, Kanellis MJ, Donly KJ, Wefel JS. Effect of a fluoride varnish on demineralization adjacent to orthodontic brackets. Am J Orthod Dentofac 1999;116:159–67.
9. Singh PP, Barjatiya MK, Dhing S, Bhatnagar R, Kothari S, Dhar V. Evidence suggesting that high intake of fluoride provokes nephrolithiasis in tribal populations. Urol Res 2001;29:238–44.
10. Matsui H, Morimoto M, Horimoto K, Nishimura Y. Some characteristics of fluoride-induced cell death in rat thymocytes: cytotoxicity of sodium fluoride. Toxicol in Vitro 2007;21:1113–20.
11. Barbier O, Arreola-Mendoza L, Del Razo LM. Molecular mechanisms of fluoride toxicity. Chem Biol Interact 2010;188:319–33.
12. Anuradha CD, Kanno S, Hirano S. Fluoride induces apoptosis by caspase-3 activation in human leukemia HL-60 cells. Arch Toxicol 2000;74:226–30.
13. Camargo JA, Fluoride toxicity to aquatic organisms: a review. Chemosphere 2003;50:251–64.
14. Wade CR, Broomsgrove AEJ, Aldridge S, Gabbaï FP. Fluoride ion complexation and sensing using organoboron compounds. Chem Rev 2010;110:3958–84.
15. Cametti M, Rissanen K. Recognition and sensing of fluoride anion. Chem Commun 2009;20:2809–29.
16. Wang Q, Xie Y, Ding Y, Li X, Zhu W. Colorimetric fluoride sensors based on deprotonation of pyrrole–hemiquinone compounds. Chem Commun 2010;46:3669–71.
17. Rochat S, Severin K. A simple fluorescence assay for the detection of fluoride in water at neutral pH. Chem Commun 2011;47:4391–3.
18. Mashraqui SH, Ghorpade SS, Tripathi S, Britto S. A new indole incorporated chemosensor exhibiting selective colorimetric and fluorescence ratiometric signaling of fluoride. Tetrahedron Lett 2012;53:765–8.
19. Sun H, Dong X, Liu S, Zhao Q, Mou X, Yang HY, Huang W. Excellent Bodipy dye containing dimesitylboryl groups as PET-based fluorescent probe for floride. J Phys Chem C 2011;115:19947–54.
20. Jia C, Wu B, Liang J, Huang X, Yang XJ. A colorimetric and ratiometric fluorescent chemosensor for fluoride based on proton transfer. J Fluoresc 2010;20:291–7.
21. Qu Y, Hua J, Tian H. Colorimetric and ratiometric red fluorescent chemosensor for fluoride ion based on diketopyrrolopyrrole. Org Lett 2010;12:3320–3.
22. Li S, Zhang C, Huang S, Hu F, Yin J, Liu SH. Highly selective colorimetric and fluorescent sensors for the fluoide anion based on imidazo[4,5-f]-1,10-phenanthroline metal-complexes. RSC Adv 2012;2:4215–19.
23. Kim TH, Swager TM. A fluorescent self-amplofying wavelength-responsive sensory polymer for fluoride ions. Angew Chem Int Ed 2003;42:4803–6.
24. Hu R, Feng J, Hu D, Wang S, Li S, Li Y et al. A rapid aqueous fluoride ion sensor with dual output modes. Angew Chem Int Ed 2010;49:4915–18.
25. Zhu B, Yuan F, Li R, Li Y, Wei Q, Ma Z et al. A highly selective colorimetric and ratiometric fluorescent chemodosimeter for imaging fluoride ions in living cells. Chem Commun 2011;47:7098–100.
26. Bao Y, Liu B, Wang H, Tian J, Bai R. A 'naked eye' and ratiometric fluorscent chemosensor for rapid detection of F^- based on combination of desilylation reaction and excited-state proton transfer. Chem Commun 2011;47:3957–9.
27. Dong M, Peng Y, Dong YM, Tang N, Wang YW. A selective, colorimetric, and fluorscent chemodosimeter for relay recognition of fluoride and cyanide anions based on 1,1′-binaphthyl scaffold. Org Lett 2012;14:130–3.
28. Ren J, Wu Z, Zhou Y, Li Y, Xu Z. Colorimetric fluoride sensor based on 1,8-naphthalimide derivatives. Dyes Pigment 2011;91:442–5.
29. Cao X, Lin W, Yu Q, Wang J. Ratiometric sensing of fluoride anions based on a Bodipy-coumarin platform. Org Lett 2011;13:6098–101.
30. Cao J, Zhao C, Feng P, Zhang Y, Zhu W. Acolorimetric and ratiometric NIR fluorescent turn-on fluoride chemodosimeter based on Bodipy derivatives: high selectivity via specific Si–O cleavage. RSC Adv 2012;2:418–20.
31. Cao J, Zhao C, Zhu W. A near-infrared fluorescence chemodosimeter for fluoride via specific Si–O cleavage. Tetrahedron Lett 2012;53:2107–10.
32. Bozdemir OA, Sozemen F, Buyukcakir O, Guliyev R, Cakmak Y, Akkaya EU. Reaction-based sensing of fluoride ions using built-in triggers for intramolecular charge transfer and photoinduced electron transfer. Org Lett 2010;12:1400–3.
33. Chang KW, Chen CC, Lee SY, Wang HE. Acute toxicity of two Alzheimer's disease radiopharmaceuticals: FDDNP and IMPY. Drug Chem Toxicol 2009;32:429–37.