ORGANIC LETTERS

2013
Vol. 15, No. 4
748–751

Spirosilane Derivatives as Fluoride Sensors

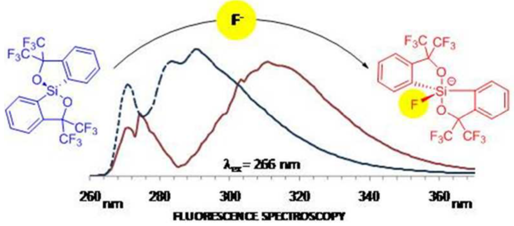
Hugo Lenormand, Jean-Philippe Goddard,* and Louis Fensterbank*

Institut Parisien de Chimie Moléculaire (UMR CNRS 7201)-FR 2769, Université Pierre et Marie Curie, Univ Paris 06, 4 place Jussieu, C. 229, 75005 Paris, France

jean-philippe.goddard@upmc.fr; louis.fensterbank@upmc.fr

Received December 2, 2012

ABSTRACT



Spirosilane derivatives have been investigated as fluoride sensors. The reactions between these compounds and different fluoride sources, which resulted in structural alterations, have been monitored and quantified by UV and fluorescence spectroscopy. The high selectivity of these probes for fluoride ions has been demonstrated in either organic or aqueous media.

The fluoride anion has beneficial effects on human health only if its concentration intake is controlled. Indeed, daily overdosage of fluoride has a serious pathological impact, for example by promoting tooth and skeletal fluorosis.[1] Other organ diseases have been assigned to an increased concentration, leading to dramatic side effects such as osteosarcoma.[2] Thus, the detection and quantification of fluoride in feeding and drinking water are considered of prime importance.

This still remains a challenging task. Different approaches have been reported to sense this anion.[3] Many are based on ion-selective electrodes or ion chromatography methods.[4] Nevertheless, molecular sensor-based strategies have appeared less expensive, more reliable, and often more sensitive in organic, aqueous, or mixed media.[3a,f] Often relying on H-bond formation between acidic protons of the probe and F^-, they imply structural modifications upon complexation that can be detected by UV–vis, fluorescence, or NMR spectroscopy.[5]

The formation of Lewis acid–base complexes represents another versatile alternative. For instance, organoboron compounds that are known to create strong B–F bonds which warrant selective, quantitative detection have been judiciously exploited as very sensitive receptors.[3d,6] Following the same consideration, silicon derivatives, which form Si–F bonds with comparable strength, should be good candidates for that purpose but interestingly have witnessed very limited developments. Two approaches have been followed. One includes the formation of coordination complexes, in some cases leading to hypervalent silicon species.[7] Tamao and Yamaguchi reported that trianthrylfluorosilane reacted with F^- to give pentavalent difluorosilicate with modified photophysical properties.[7b] Later,

---

(1) (a) Kleerekoper, M. *Endocrinol. Metab. Clin. North Am.* **1998**, *27*, 441. (b) Ayoob, S.; Gupta, A. K. *Crit. Rev. Environ. Sci. Technol.* **2006**, *36*, 433.

(2) (a) Bassin, E. B.; Wypij, D.; Davis, R. B.; Mittleman, M. A. *Cancer Causes Control.* **2006**, *17*, 421. (b) Singh, P. P.; Barjatiya, M. K.; Dhing, S.; Bhatnagar, R.; Kothari, S.; Dhar, V. *Urol. Res.* **2001**, *29*, 238.

(3) (a) Martinez-Máñez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419. (b) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486. (c) Cho, D.-G.; Sessler, J. L. *Chem. Soc. Rev.* **2009**, *38*, 1647. (d) Wade, C. R.; Broomsgrove, A. E. J.; Aldridge, S.; Gabbaï, F. P. *Chem. Rev.* **2010**, *110*, 3958. (e) Cametti, M.; Rissanen, K. *Chem. Commun.* **2009**, 2809. (f) Gunnlaugsson, T.; Glynn, M.; Tocci, G. M.; Kruger, P. E.; Pfeffer, F. M. *Coord. Chem. Rev.* **2006**, *250*, 3094. (g) Cametti, M.; Rissanen, K. *Chem. Soc. Rev.* **2013**, DOI: 10.1039/C2CS35439J.

(4) (a) De Marco, R.; Clarke, G.; Pejcic, B. *Electroanalysis* **2007**, *19*, 1987. (b) van den Hoop, M. A. G. T.; Cleven, R. F. M. J.; van Staden, J. J.; Neele, J. *J. Chromatogr. A* **1996**, *739*, 241.

(5) (a) Xu, Z.; Kim, S. K.; Yoon, J. *Chem. Soc. Rev.* **2010**, *39*, 1457. (b) Li, A. F.; Wang, J. H.; Wang, F.; Jiang, Y. B. *Chem. Soc. Rev.* **2010**, *39*, 3729. (c) Cho, E. J.; Moon, J. W.; Ko, S. W.; Lee, J. Y.; Kim, S. K.; Yoon, J.; Nam, K. C. *J. Am. Chem. Soc.* **2003**, *125*, 12376.

(6) (a) Galbraith, E.; James, T. D. *Chem. Soc. Rev.* **2010**, *39*, 3831. (b) Hudnall, T. W.; Chiu, C.-W.; Gabbaï, F. P. *Acc. Chem. Res.* **2009**, *42*, 388. For recent works, see: (c) Guliyev, R.; Ozturk, S.; Sahin, E.; Akkaya, E. U. *Org. Lett.* **2012**, *14*, 1528. (d) Fu, G.-L.; Pan, H.; Zhao, Y.-H.; Zhao, C.-H. *Org. Biomol. Chem.* **2011**, *9*, 8141. (e) Sung, W. Y.; Park, M. H.; Park, J. H.; Eo, M.; Yu, M.-S.; Do, Y.; Lee, M. H. *Polymer* **2012**, *53*, 1857.

10.1021/ol3033048

Gabbaï showed similar behavior with triarylfluorosilane bearing a sulfonium moiety as a stabilizing group.[7d] The second approach is the cleavage of a Si−O bond by fluoride activation which liberates a chromophore.[8]

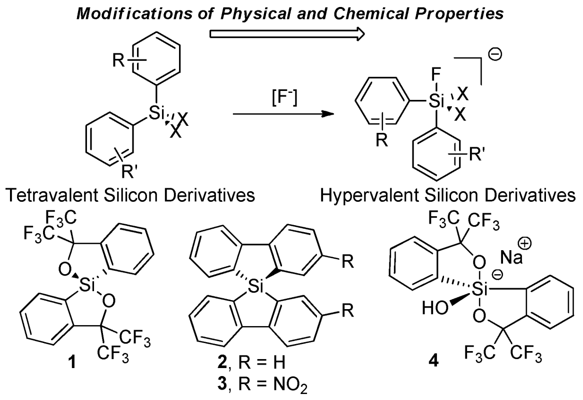
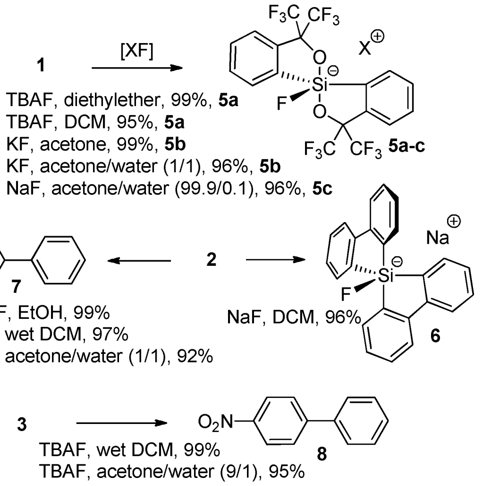


Figure 1. Fluoride sensors based on silicon derivatives.

Herein, we report the use of new silicon-based fluoride sensors that, upon capture of F^-, undergo structural alteration which provides useful spectroscopic signatures (Figure 1). For this study, we selected silanes **1**−**3** and also examined the behavior of hypervalent species **4** for ligand exchange. Bis(α,α-bis(trifluoromethyl)benzenemethanolato-(−2)C_2,O) silane **1** has been reported for the first time by Martin in 1979 and is easily accessed from the reaction of the dilithiated 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol with $SiCl_4$.[9] This stable 8-Si-4 spirosilane derivative has been reported to be a versatile precursor of 10-Si-5 hypervalent species subsequently to the addition of a nucleophile. This is illustrated by the easy formation of **4** resulting from the reaction of **1** with sodium hydroxide.[10] They usually adopt a trigonal bipyramidal (TBP) geometry with the formation of a three-center four-electron hypervalent bond that is stabilized by the most electronegative ligand at the apical position (Figure 1).[11]

Scheme 1. Reactivity of Sensors **1**−**3** with Fluoride (1 equiv)



Spirobisilafluorene **2** was prepared from 2,2′-dibromobiphenyl that was easily transformed into the dilithiated-biphenyl intermediate by halogen−metal exchange and reacted with $SiCl_4$.[12] Dinitro derivative **3** was obtained by nitration of **2** with $Cu(NO_3)_2$ in acetic anhydride and purified by flash chromatography.[13] With these four substrates in hand, we observed their behaviors in the presence of fluoride sources under different experimental conditions.

As anticipated, reaction of silane **1** with inorganic and organic sources of fluoride proved to be highly efficient either in pure organic solvents or in the presence of water (Scheme 1). Tetrabutylammonium fluoride (TBAF) allowed the almost quantitative formation of silicate **5a** in diethyl ether and dichloromethane (DCM) in <1 h. Potassium fluoride has also been used in acetone to afford **5b** in only 20 min and quantitative yield. This transformation was also highly efficient in a 1/1 acetone/water medium (96% yield). With 0.1% of water in acetone, sodium fluoride showed comparable results with a 96% yield in 15 min. In anhydrous DCM, silane **2** reacted with sodium fluoride to generate silicate **6** in 96% yield. In the presence of water (wet DCM or acetone/water 1/1), fast protodesilylation occurred in <15 min and biphenyl **7**, presumably via the formation of **6**, was obtained in 97% and 92% yield respectively.[14,15] When TBAF was used in a protic solvent (ethanol), the quantitative formation of **7** was observed. This protodesilylation pathway was also followed when silane **3** was reacted with TBAF in wet

---

(7) (a) Tamao, K.; Hayashi, T.; Ito, Y. *J. Organomet. Chem.* **1996**, *506*, 85. (b) Yamaguchi, S.; Akiyama, S.; Tamao, K. *J. Am. Chem. Soc.* **2000**, *122*, 6793. (c) Jung, M. E.; Xia, H. *Tetrahedron Lett.* **1988**, *29*, 297. (d) Kim, Y.; Kim, M.; Gabbaï, F. P. *Org. Lett.* **2010**, *12*, 600. For a review on photophysical properties of main group based compounds according to their coordination numbers, see: (e) Yamaguchi, S.; Akiyama, S.; Tamao, K. *J. Organomet. Chem.* **2002**, *652*, 3.

(8) For recent studies, see: (a) Zhu, C.-Q.; Chen, J.-L.; Zheng, H.; Wu, Y.-Q.; Xu, J.-G. *Anal. Chim. Acta* **2005**, *539*, 311. (b) Kim, T.-H.; Swager, T. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4803. (c) Hu, R.; Feng, J.; Hu, D.; Wang, S.; Li, S.; Li, Y.; Yang, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 4915. (d) Kim, S. Y.; Park, J.; Koh, M.; Park, S. B.; Hong, J.-I. *Chem. Commun.* **2009**, 4735. (e) Zhu, B.; Yuan, F.; Li, R.; Li, Y.; Wei, Q.; Ma, Z.; Du, B.; Zhang, X. *Chem. Commun.* **2011**, *47*, 7098. (f) Bao, Y.; Liu, B.; Wang, H.; Tian, J.; Bai, R. *Chem. Commun.* **2011**, *47*, 3957. (g) Sokkalingam, P.; Lee, C.-H. *J. Org. Chem.* **2011**, *76*, 3820. (h) Jiang, X.; Vieweger, M. C.; Bollinger, J. C.; Dragnea, B.; Lee, D. *Org. Lett.* **2007**, *9*, 3579. (i) Kim, S. Y.; Hong, J.-I. *Org. Lett.* **2007**, *9*, 3109. (j) Zhang, J. F.; Lim, C. S.; Bhuniya, S.; Cho, B. R.; Kim, J. S. *Org. Lett.* **2011**, *13*, 1190. (k) Ke, B.; Chen, W.; Ni, N.; Cheng, Y.; Dai, C.; Dinh, H.; Wang, B. *Chem. Commun.* **2012** DOI: 10.1039/C2CC37270C.

(9) (a) Perozzi, E. F.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1591. (b) Perozzi, E. F.; Michalak, R. S.; Figuly, G. D.; Stevenson, W. H.; Dess, D.; Ross, M. R.; Martin, J. C. *J. Org. Chem.* **1981**, *46*, 1049.

(10) Stevenson, W H., III; Wilson, S.; Martin, J. C.; Farnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340.

(11) Farnham, W. B.; Harlow, R. L. *J. Am. Chem. Soc.* **1983**, *103*, 4608.

(12) (a) Gilman, H.; Gorsich, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 3243. (b) Couzijn, E. P. A.; van den Engel, D. W. F.; Slootweg, J. C.; de Kanter, F. J. J.; Ehlers, A. W.; Schakel, M.; Lammertsma, K. *J. Am. Chem. Soc.* **2009**, *131*, 3741.

(13) Xiao, H.; Leng, B.; Tian, H. *Polymer* **2005**, *46*, 5707.

(14) Johnson, S. E.; Dieters, J. A.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 3250.

DCM or acetone/water (9/1) since *p*-nitrophenyl benzene **8** was formed in high yields in only 15 min. Two equivalents of biphenyl derivatives **7** and **8** were obtained, resulting from the cleavage of the four C$-$Si bonds.[16]

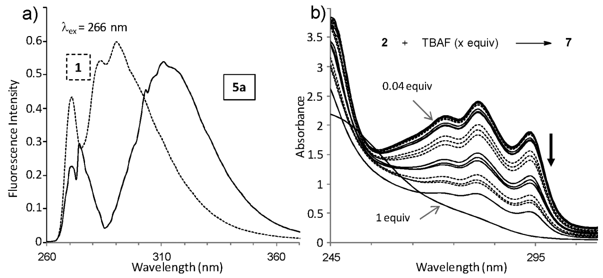


Figure 2. (a) Fluorescence spectra (λ_{ex} = 266 nm) of **1** (100 μM, dashed curve) and **5a** (100 μM, solid curve) in DCM. (b) UV spectra from successive additions of TBAF (0.04, 0.12, 0.2, 0.4, 0.6, 0.8, 1 equiv) into a solution of **2** (125 μM) in DCM. Three measurements have been done for each addition at 5, 10, and 15 min (represented by blocks of three curves, alternatively solid and dashed).

UV and fluorescence spectroscopy were investigated as analytical methods to detect the presence of fluoride ions. Unfortunately, UV spectra of **1** and **5a**$-$**c** do not differ sufficiently to allow the identification of an adduct formation between **1** and F^-. Fluorescence spectra of **1** (dashed curve) and **5a** (solid curve) have been recorded at λ_{ex} = 266 nm in DCM (Figure 2a). The maximum emission of fluorescence has been obtained at 290 nm for **1** and 311 nm for **5a**. By monitoring the disappearance of **1** and the formation of **5a**, we were able to detect fluoride ions to a 10 μM threshold which is close to the normal concentration in drinking water.[17]

Having shown that spirobisilafluorene **2** readily reacted with fluoride, either in protic solvent or in the presence of water, to afford biphenyl **7** in high yields (Scheme 1), we monitored the evolution of UV spectra after successive additions of TBAF into a solution of **2** (125 μM) in DCM. For each addition, three measurements were obtained at 5, 10, and 15 min. All seven sequences are represented by the alternation of solid and dashed curves (Figure 2b). This allowed us to conclude that, after 15 min, the total amount of fluoride has been consumed and the corresponding amount of **2** has been converted into **7**. As the concentration of fluoride increased, the intensity of the three characteristic absorption bands (λ_{max} = 271, 279, and 290 nm with respectively ε = 15490, 16367, and 12910 L mol^{-1} cm^{-1}) decreased until they completely disappeared with 1 equiv of fluoride. Then, only the UV spectrum of **7** was seen. Unfortunately, it was not possible to highlight a diagnostic signal that would allow for the quantification of the biphenyl **7** concentration.

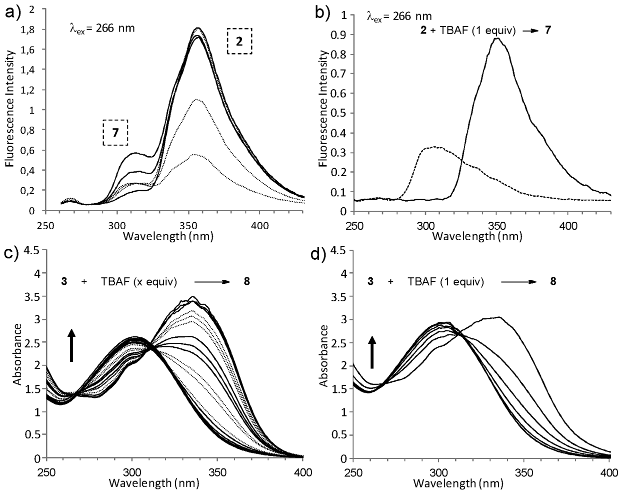


Figure 3. *Fluorescence spectra (*λ_{ex} = 266 nm). (a) **2**/**7** mixture solutions at different concentrations, dashed curve: *c* (**2**/**7**) = 50/12.5, 25/12.5, 10/12.5 μM; solid curve *c* (**2**/**7**) = 50/50, 50/25, 50/5 μM. (b) Reaction of **2** (47 μM) with TBAF (1 equiv) in DCM, *t* = 0 min (solid curve) and 5 min (dashed curve). *UV monitoring of the reaction of* ***3*** *with TBAF in DCM.* (c) Successive additions of TBAF (0.14, 0.28, 0.42, 0.56, 0.7, 0.84, 1 equiv) into a solution of **3** (85 μM). (d) UV spectra at various reaction times (*t* = 1, 5, 7, 10, 12, 17, 20 min) of an equimolar mixture of **3** (125 μM) and TBAF.

Upon excitation at 266 nm, sensor **2** showed an emission fluorescence signal at 348 nm while **7** emitted at 301 nm. Once again, the fluorescence spectroscopy was very helpful because of the possibility to detect the quantitative formation of the reaction product **7**. The fluorescence spectra of **2**/**7** mixture solutions recorded at different concentrations clearly showed that distinctive signals were obtained with a sufficient gap between the emission wavelengths of both compounds (Figure 3a). Moreover, no significant interaction between **2** and **7** has been found which allows the independent quantification of **7** and **2**. Thus, it was clear that sensor **2** is univocally suitable for fluoride detection and quantification. We then examined the reaction of **2** with 1 equiv of TBAF and monitored it by fluorescence spectroscopy (Figure 3b). After 5 min of reaction, the complete disappearance of the emission signal at 348 nm was observed together with the appearance of the signal at 301 nm. This indicated a very fast reaction and a quantitative transformation. These two properties are of primary importance in the development of an ion sensor, and this system allowed the detection of fluoride ions to as low as 10 μM.

Following the same procedure as that reported for **2** (Figure 2b), we monitored by UV spectroscopy the

---

(15) The stability of hypervalent silicon species increases with the number of electronegative ligands. Thus, tetraorganylsilicates (e.g., **6**) are less stable than diorganylsilicates (e.g., **4** and **5**). For stability studies of pentacoordinate silicates, see: (a) Keijzer, A. H. J. F.; de Kanter, F. J. J.; Schakel, M.; Osinga, V. P.; Klumpp, G. W. *J. Organomet. Chem.* **1997**, *548*, 29. (b) Couzijn, E. P. A.; Slootweg, J. C.; Ehlers, A. W.; Lammertsma, K. *Z. Anorg. Allg. Chem.* **2009**, *635*, 1273. (c) Couzijn, E. P. A.; Ehlers, A. W.; Schakel, M.; Lammertsma, K. Z. *J. Am. Chem. Soc.* **2006**, *128*, 13634. (d) See also refs 12b and 10.

(16) We presumed fluoride acts as an activator in the protodesilylation process in the presence of water as a proton donor. Then, a hydroxide ion is formed and would play the same role as the fluoride for the second bond cleavage.

(17) Experiments have been carried out with authentic samples of spring water "Cristaline Isabelle"; see Supporting Information.

successive addition of TBAF into a solution of **3** (85 μM) (Figure 3c). Rapid, quantitative protodesilylation of **3** occurred to generate **8** when it was exposed to fluoride ions in the presence of traces of water (Scheme 1). We observed the decrease of the signal at 336 nm (ε = 28228 L mol^{-1} cm^{-1}) indicating the consumption of spiro silane **3**. At the same time, a signal quantitatively appeared at 305 nm (ε = 10228 L mol^{-1} cm^{-1}) that was characteristic of biphenyl **8**. The presence of two isosbestic points (267 and 310 nm) indicated that the stoichiometry of the reaction has been preserved without the formation of byproducts or intermediates. Then, we recorded the UV spectra of a sample containing an equimolar amount of **3** (125 μM) and TBAF in DCM (Figure 3d). The reaction was monitored by UV, and full conversion was observed before 17 min. The UV profile and the calibration curves (in agreement with Beer–Lambert law, see Supporting Information) confirmed **3** as another suitable sensor due to a measurable signal from **8** and allowed the detection of fluoride ions to as low as 5 μM.

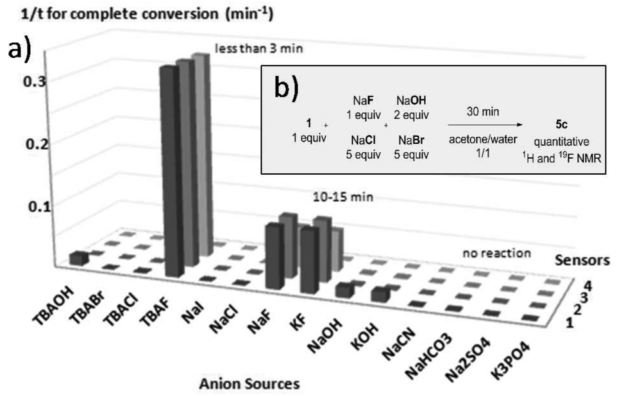


Figure 4. (a) Determination of the selectivity of sensors **1**–**4** toward various anions. (b) Selective reaction of **1** with fluoride contained in a mixture of OH$^-$, Cl$^-$, and Br$^-$ in excess.

To further confirm the potential of silicon-based probes **1**–**4** as fluoride sensors, we examined their selectivity of complexation toward various anions (OH$^-$, Cl$^-$, Br$^-$, I$^-$, CN$^-$, HCO$_3^-$, SO$_4^{2-}$, PO$_4^{3-}$). Compounds **1**–**3** reacted as described above while **4** could be involved in a ligand exchange process.[9a] Thus, an equimolar amount of anion was added to a solution of sensor in DCM (for tetrabutylammonium derivatives) or acetone/water 99/1 (for sodium and potassium salts). The transformations were monitored by ^{19}F and/or ^{1}H NMR, and full conversion times were recorded when sensors were reactive. To compare the different reactions, we plotted 1/t (min^{-1}) for each combination (Figure 4a). This evidenced the shorter reaction times and therefore the selectivity. In organic medium, silane **1** quantitatively reacted with tetrabutylammonium hydroxide to generate the corresponding hydroxyl silicate in 1 h while no conversion was observed with **2** and **3**. In contrast, probes **1**–**3** allowed very fast reactions with TBAF in < 3 min. The formation of **5a** from **4** proceeded quantitatively through the hydroxide/fluoride exchange in 36 h. None of the sensors were able to react with tetrabutylammonium bromide. The same trend was observed with tetrabutylammonium chloride except for **1** that afforded the corresponding chloro-silicate within 12 h.

Whatever the sensor, no conversion was observed with sodium iodide, sodium sulfate, and potassium phosphate. These interesting results, especially for sulfate that is very abundant in drinking water, allowed us to be confident in the ability of our probes to react selectively with fluoride. Only **1** reacted slowly with sodium cyanide and hydrogenocarbonate in 24 h. In the presence of sodium and potassium hydroxide, **1** was converted in 1 h while **2** and **3** needed 11 h to reach full conversion. Sodium chloride was only detected by **1** to obtain a complete conversion in 36 h. Once again, only fluoride was rapidly detected in 10 min by **1** and **2**, and 15 min by **3** by using sodium and potassium fluoride. With these two salts, the hydroxide/fluoride exchange on **4** to generate **5a** was slower than with TBAF.

The selectivity of fluoride capture has been illustrated when sensor **1** has been submitted to a mixture of NaF (1 equiv), NaOH (2 equiv), NaCl (5 equiv), and NaBr (5 equiv) in acetone/water (1/1) (Figure 4b). According to ^{1}H and ^{19}F NMR, only the fluoride adduct **5c** has been obtained in 30 min in a quantitative manner, even in the presence excess hydroxide, chloride, and bromide. All of these investigations demonstrated the high selectivity of our silicon-based sensors for F$^-$ toward other naturally abundant anions.

In conclusion, we have demonstrated the ability of silicon-based sensors to detect fluoride ions in solution. UV and fluorescence spectroscopy have been used for the observation and quantification of reaction products of fluoride with sensors. Detection limits as low as 5 μM have been obtained which is close to the residual concentration of fluoride in drinking water. Moreover, the reported sensors showed very high selectivity toward fluoride vs a set of other anions. Undoubtedly, this first set of silicon-incorporating sensors opens new perspectives in the complexation of anions.

Acknowledgment. L.F. thanks the Institut Universitaire de France. H.L. thanks the DGA for a Ph.D. grant. The authors thank E. Joubert (DGA), L. Sinault (DGA), and Prof. B. Hasenknopf (UPMC UMR 7201) for helpful discussions, Dr. S. Sagan (UPMC UMR 7203) and Prof. L. Julien (UPMC ENS UMR 8640) for providing access to a fluorimeter and helpful discussions. Technical assistance was generously offered through FR 2769.

Supporting Information Available. Full characterization data of all new compounds and experimental procedure for spectroscopy analysis are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.