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Benzoselenadiazole Fluorescent Probes – Near-IR Optical and Ratiometric Fluorescence Sensor for Fluoride Ion

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Supporting Information

ABSTRACT: A highly selective and sensitive near-IR optical sensor, benzoselenadiazole based diarylamine (**TBS-HN**), for fluoride (F^-) has been designed and synthesized. **TBS-HN** also shows turn-on ratiometric fluorescence signaling in the presence of F^- by inhibiting the excited state intramolecular proton transfer (ESIPT) processes.

The design and synthesis of artificial receptors that are able to sense anions by the naked eye has currently been evolving as a forefront research topic because of the significant role of anions in the broad range of chemical and biological processes.[1] Among the anions, fluoride (F^-) is an attractive target for sensor design owing to its role in dental care, osteoporosis, skeletal fluorosis, etc.[2] So far the reported molecules that sense F^- can broadly be classified into four types based on the nature of molecular level interaction between the receptor and F^-: (1) suitably preorganized N–H, C–H, and O–H groups which are capable of sensing anions through hydrogen bonding interactions,[3] (2) recognition through anion–π interactions,[4] (3) Lewis acid–base interactions,[5] and (4) anion induced chemical reactions.[6] Notably, the H-bonding interactions between the N–H/O–H fragment of the receptor and the F^- ion are observed only at lower F^- concentrations; however an excess of F^- ion leads to deprotonation by means of Brønsted acid–base interactions, which is also an efficient and sensitive method.[7] In this case, the receptors generally are comprised of a highly acidic N–H proton, which is expected to facilitate spontaneous F^- induced deprotonation. On the other hand, diarylamine based receptors, to the best of our knowledge, have not been reported so far for this purpose. The N–H proton becomes weakly acidic due to the strongly electron-donating N-aryl groups, which eventually prevents F^- sensing through deprotonation.

The signaling mechanism for sensing could be the UV–visible absorption and fluorescence spectral changes upon modulations in the photoinduced electron transfer (PET),[8] intramolecular charge transfer (ICT),[9] excimer/exciplex formation,[10] metal-to-ligand charge transfer (MLCT),[11] and excited-state intramolecular proton transfer (ESIPT)[12] processes before and after F^- binding. Among the reported signaling pathways, the ESIPT based sensors have a significant advantage due to the larger Stokes shift, ratiometric fluorescence between the ESIPT and $S_0 \leftarrow S_1$ emission. Many F^- sensors have been reported using the inhibition of the ESIPT process previously.[13]

Although anion sensing by means of deprotonation of the N–H proton of diarylamine is rather difficult, appropriate modification of the aryl group with judicious choice of an electron-withdrawing substituent would probably increase the acidity of N–H proton, which in turn can be used for sensing applications. Hence, we have synthesized a diarylamine containing a strongly electron-withdrawing 2,1,3-benzoselenadiazole moiety, 7-(4-hexylthiophen-2-yl)-*N*-(4-nitrophenyl)-benzo[*c*][1,2,5]selenadiazol-4-amine (**TBS-HN**), as a receptor for F^-. Molecules with 2,1,3-benzoselena- and benzothiadiazoles are known to show intense fluorescence, large molar extinction coefficients, and good photostability.[14] Particularly, upon introduction of these electron-withdrawing moieties into the low band gap polymers, a clear ICT absorption band was observed in the visible region.[15] Hirao et al. demonstrated that benzothiadiazole-aniline oligomers have a hydrogen bonding interaction between the NH proton and nitrogen in the benzothiadiazole moiety.[16] Notably, in the presence of F^-, the oligomers undergo reduction followed by substitution and form the fluoride substituted polyaniline rather than the deprotonation of NH protons.[17] In the present investigation, we have shown that **TBS-HN** senses the F^- ion with high sensitivity and selectivity through the inhibition of the ESIPT process. Interestingly, it also shows ratiometric signaling of fluorescence for the fluoride ion.

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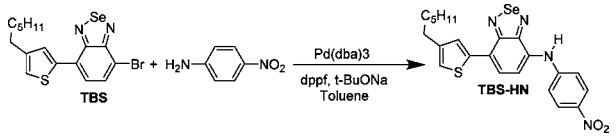
The **TBS-HN** was synthesized as shown in Scheme 1 by following the method previously reported for the preparation of

Scheme 1. Synthesis of TBS-HN



phenylenediamines.[18] Briefly, refluxing TBS with 4-nitroaniline in toluene in the presence of $Pd_2(dba)_3$, dppf, and *t*-BuONa afforded **TBS-HN** in quantitative yield. The **TBS-MN**, an *N*-methyl analogue of **TBS-HN**, was obtained in 96% yield through the reaction between **TBS-HN** and 7 equiv of *tert*-butylammonium fluoride in DMSO followed by the addition of 2 equiv of CH_3I. The structure of the **TBS-HN** and **TBS-MN** was confirmed by the ^1H and ^{13}C NMR and HRMS spectral techniques (Supporting Information (SI), Figures S12−S19).

The UV−visible absorption spectra of **TBS-HN** dissolved in toluene show intense peaks at 344, 383, and 520 nm (SI, Figure S1). The time-dependent density functional theory calculations using the Gaussian 09 program[19] at the B3LYP level with the PCM model suggest that the lowest electronic transition originated mostly from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) (Table S1). The major contribution to the absorptions at 383 and 520 nm originated through the charge transfer transition from the thiophene→nitro and thiophene→benzoselenadiazole groups, respectively. This feature suggests that **TBS-HN** possesses a substantial charge transfer character, which is a desired factor for anion sensing through alternations in PET processes. Further, the fluorescence spectra of **TBS-HN** measured in toluene solvent show two emission peaks at 662 and 705 nm (shoulder), which in fact do not have a mirror image relationship with the absorption spectrum (SI, Figure S1). The larger Stokes shift value ca. 4125 cm^{-1} (142 nm) suggests significant structural changes between the ground and excited states upon photoexcitation. Indeed, both of the above parameters suggest the possibility of intramolecular proton transfer processes from the Franck−Condon state. This interpretation has been further supported by the ^1H NMR data, which indicate the intramolecular hydrogen bonding between the amino-hydrogen with the imine nitrogen on the benzoselenadiazole moiety. This forms a strain-free, five-membered ring including the hydrogen bond, an ideal factor that facilitates the proton transfer processes.[20] In addition, the reduced electron density at the amino nitrogen in the LUMO weakens the NH bond, making the proton dissociation more facile, while the relatively higher electron density at the benzoselenadiazole nitrogen attracts the proton.

Since the ESIPT occurs in the femto- to picosecond time scale, the observed fluorescence from the ESIPT chromophore is expected to be from the zwitter ionic tautomer (SI, Scheme S2). Nonetheless, ESIPT strongly depends on conformations, the nature of the solvent medium, and its ability to form intermolecular hydrogen bonds between the chromophore.[21] To our surprise, the fluorescence spectrum changes with the excitation wavelength, particularly in the polar solvent acetonitrile: The emission band shifted from 667 to 617 nm, when the excitation wavelength changes from 380 to 440 nm. However further red-shifted excitation energy shifts the emission from 617 to 667 nm (SI, Figure S2). Notably, the emission peak at 709 nm remains quite insensitive to the excitation energy except the relative intensity. This feature suggests the presence of at least two species, viz. neutral and zwitter ionic tautomers that are responsible for the observed excitation energy dependent fluorescence in polar solvents. In contrast, in nonpolar solvent toluene, fluorescence from **TBS-HN** is independent of the excitation energy (SI, Figure S3). Further, replacing the NH proton by a methyl group (**TBS-MN**) in the diarylamino group resulted in the excitation energy independent fluorescence, both in polar, acetonitrile, and nonpolar, toluene, solvents (SI, Figure S4). A similar phenomenon has already been reported for *N*-(2-(benzo[*d*]-oxazol-2-yl)phenyl)-4-methyl benzene sulfonamide, which also shows the ESIPT process.[13a] Thus, based on the above facts we can conclude that the **TBS-HN** exhibits the ESIPT process and also possesses significant intramolecular charge transfer interactions.

The sensing ability of the **TBS-HN** was tested in DMSO solvent using various anions as their tetrabutylammonium salt. Upon addition of about 100 equiv of F^- to the **TBS-HN** solution, the intense red color turned into dark blue as shown in Figure 1a, which in fact can be observed by the naked eye.

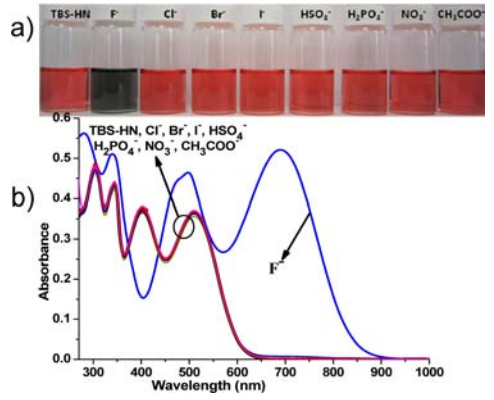


Figure 1. Visible color changes (a) and the corresponding absorption spectra (b) of **TBS-HN** (3×10^{-5} M) in the presence of 100 equiv of various anions (as their TBA salts) in DMSO.

Importantly, other anions Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$, NO_2^-, CH_3COO^- have no impact on the color of **TBS-HN**. We have further evaluated the sensing behavior using UV−visible absorption and fluorescence spectroscopy. As can be seen in Figure 1b, the addition of F^- to **TBS-HN** resulted in the appearance of intense new bands at 498 nm and at 691 nm at the expense of a peak at 402 nm. Addition of F^- to **TBS-HN** shifts the low-energy absorption band bathochromically by 181 nm. The observed excellent sensitive and selective detection of F^- over the other anions with a larger spectral shift and the appearance of a new peak close to the near-IR region are certainly advantageous for their applications in biological systems. To understand the nature of anion−receptor interaction, UV−visible titration experiments were carried out with the incremental addition of F^- to the DMSO solution of **TBS-HN**. Upon progressive addition of F^-, a new band at 691 nm appeared with clear isosbestic points at 369, 439, and 535 nm (SI, Figure S5). The appearance of an isosbestic point clearly defines the existence of only two species, i.e., a free and F^- bound receptor. The observed spectral changes are attributed to the interaction between the F^- ion with the amino proton of **TBS-HN** through hydrogen bonding

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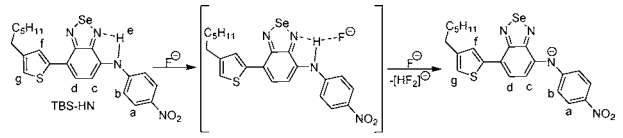
interactions. Since the N−H proton becomes strongly acidic as the amino nitrogen is bonded to the strongly electron-withdrawing 4-nitrophenyl and benzoselenadiazole moiety, the addition of excess F^- would lead to the deprotonation of the N−H proton (Scheme 2).

Scheme 2. Schematic Representation of Interaction of TBS-HN with F^- in DMSO



The charge transfer interactions such as thiophene→nitro and thiophene→benzoselenadiazole groups can be nullified after the deprotonation of the N−H proton due to the delocalization of the negative charge toward the acceptor end, but the absorption is tailing over the near-IR region. This can be explained on the basis of theoretical predictions that the shift in absorption maxima occurs only because of alternations in the electronic energy levels after deprotonation (SI, Table S2).

To understand the interaction between the F^- and receptor further, ^{1}H NMR titration experiments were carried out in DMSO-d_6. Figure 2 shows the partial ^{1}H NMR spectra of **TBS-HN** upon addition of F^- as tetrabutylammonium fluoride (TBAF) in DMSO-d_6. The N−H signal completely disappears when the concentration of F^- is 0.4 equiv; however, the chemical shift values of aromatic protons remain unaltered (SI, Figure S9). Further gradual addition of F^- steadily shifts the aromatic protons to the upfield region until 6 equiv (Figure 2). Meanwhile, a new peak, characteristic of $[HF_2]^-$, started to appear at 16.5 ppm (triplet) in the presence of 2 equiv of F^- (SI, Figure S11). This indicates that F^- interacts with **TBS-HN** through hydrogen bonding at lower concentrations, but at higher concentrations it induces the deprotonation of the N−H proton. After deprotonation, the lone pair electron on the nitrogen has two possible ways to migrate as shown in Scheme S3 (SI). As shown in Figure 2, the magnitude of upfield shifting of protons in nitrobenzene is higher than that of the benzoselenadiazole ring, which suggests that the negative charge is favorably localized on the nitrobenzene rather than the benzoselenadiazole (SI, path B, Scheme S3). According to the NMR spectra of **TBS-HN** before and after the addition of F^-, the positions of the resonance signals of the protons were assigned (SI, Figures 20−25).

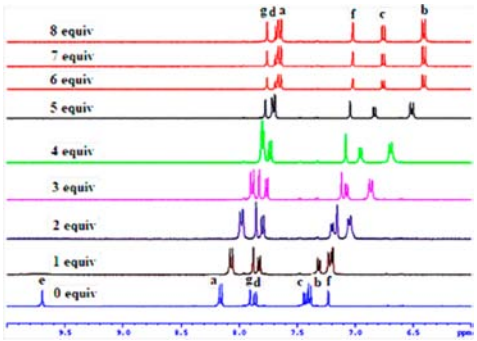


Figure 2. Partial ^{1}H NMR titration spectra of **TBS-HN** in DMSO-d_6 in the presence of various equivalents of TBAF.

TBS-HN can also act as a fluorimetric sensor as demonstrated by the fluorescence titration experiments in DMSO. In the absence of an anion, **TBS-HN** exhibited strong emission at 671 nm by exciting the solution at 440 nm. The gradual addition of F^- quenches the fluorescence at 671 nm with a concomitant, progressive, enhancement of a new band at 478 nm. The fluoride induced deprotonation induces the disappearance of normal and tautomer fluorescence and favors the new emission from the deprotonated state. Thus, the sensing mechanism in this case would be the inhibition of ESIPT processes. A ratiometric fluorescence response can be derived by plotting the intensities at two different wavelengths I_{478}/I_{671} which is calculated to be 25 ± 1 (Figure 3). The fluoride ion detection limit of **TBS-HN** was found to be in the range of the submillimolar level. Importantly, similarly to absorption spectral changes, the fluorescence spectra of **TBS-HN** remain unaltered by the other anions such as Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$, NO_3^-, and CH_3COO^-. From these observations it can be concluded that **TBS-HN** could sense F^- selectively by colorimetric and ratiometric fluorescence methods (SI, Figure S6).

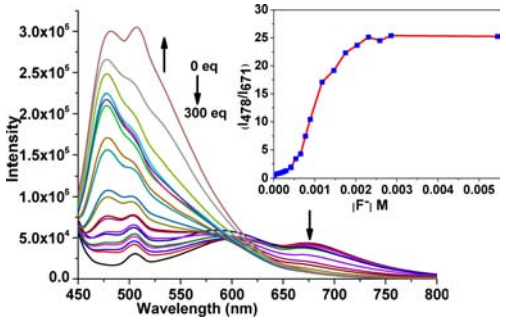


Figure 3. Fluorescence spectra of **TBS-HN** (3×10^{-5} M) in the presence of TBAF (0.06 M) in DMSO. Insets: ratios of fluorescent intensities at 478 and 671 nm as a function of F^- concentration.

We have synthesized **TBS-HN**, which exhibits ESIPT and CT processes. It senses the F^- with high sensitivity and selectivity by means of optical, and off-on, ratiometric, fluorescence methods. In the presence of F^-, **TBS-HN** develops a new absorption band in the near-IR region, which is beneficial in terms of using this sensor in a biological medium. We believe that the combination of near-IR optical, turn on, ratiometric fluorescence and the involvement of the ESIPT process in a single system is certainly a promising feature in the sensing of anions.

■ ASSOCIATED CONTENT

Supporting Information

The experimental details, synthetic procedures, characterization data, computational data, UV−vis and fluorescence data. This materials is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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