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A BODIPY dye as a reactive chromophoric/fluorogenic probe for selective and quick detection of vapors of secondary amines†

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A new reaction based fluorescence turn-off strategy for detection of secondary amines was developed. The probe shows fast response and high selectivity to secondary amines in solution/film at sub-ppm levels through chromogenic and fluorescent dual-mode signal changes.

Rapid and efficient detection of trace volatile organic amines in air is highly desirable. It is not only because of its high toxicity to human health but also because of its potential harm to the environment.[1] Traditional methods for detection of volatile organic amines, such as gas chromatography–mass spectrometry (GC-MS), are time-consuming and need complicated sample processing. Thus, the development of real-time sensitive analytical methods for amine vapors still remains challenging.[2]

Fluorescence sensing has gained considerable attention for vapor detection because of its high sensitivity, low cost and ease of fabrication.[3] However, it is found that the selectivity of most of the fluorescent sensory materials for amine vapor detection based on π–π interaction, H-bonding interaction, photo-induced electron transfer and other weak interactions is far from satisfaction, although an elaborate molecular design has been given special concern.[4] Most of such materials cannot distinguish the type of organic amine. Nevertheless, the recognition of secondary amines is significant in practical applications because the main ingredients of many famous medicaments and drugs are secondary amines. For instance, methamphetamine is the main component of ''ice'' and ephedrine is the main ingredient of cold cure. We reason that a reactive probe which possesses merits of specificity and cumulative signaling effects[5–7] is a possible tool to identify the organic secondary amines.

Generally, two major questions should be addressed to design a special reactive vapor probe: (1) can a selective and efficient reaction be used under mild solid-state conditions in a very short time? (2) Can a magic molecule be designed which will trigger a significant chromophoric and/or fluorescent response upon interaction with the target analyte?

It is known that phenyl boronate ester can be converted to phenol through the oxidation of H_2O_2 or other oxidative reagents in the presence of a catalyst, which has been used in biological systems or explosive detection,[8] but never been used for amine detection. Our consideration is that amine is a kind of Lewis base, and under the basic conditions the reducing capacity of phenyl boronate ester will increase. Hence organic amines may accelerate the photo-oxidation of arylboronates (or aryl boronic acids) to yield the corresponding phenols. Experiments were conducted with different arylboronates/aryl boronic acids and organic amines as reagents. The results indicate that the oxidative reactions can be carried out smoothly (Scheme S1, ESI†) with satisfactory yield (63–91%) within a few minutes in the presence of secondary amines. However, the primary amine and tertiary amine hardly induce this reaction which may be attributed to their weaker alkalescence compared with secondary amines. The proposed reaction mechanism is shown in Scheme S2 (ESI†). To the best of our knowledge, this is a new reaction to prepare phenols rapidly. Thus, the boronate ester can be chosen as the reactive recognition part in the fluorescent sensing of secondary amines.

4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) derivatives are famous fluorescent building blocks for the construction of sensory materials due to their high fluorescence quantum yields, good photochemical stability, low sensitivity to the environment, and easy functionalization.[9] Particularly, the absorption and emission properties of BODIPY-based dyes readily change when their donor and/or acceptor changed because of the intramolecular charge-transfer process.[10]

Herein, we report a simple BODIPY derivative as a probe for organic amine vapors with an aromatic boronate ester as the reactive unit. Probe **3** is prone to oxidative deboronation in the presence of secondary amines and shows instant chromogenic and fluorescent dual-mode response to secondary amine species. Probe **3** was synthesized conveniently through the incomplete palladium-catalyzed Suzuki cross-coupling reaction according to a known procedure (Scheme 1).[11]

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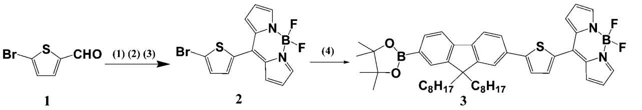


Scheme 1 Preparation of probe **3**: key: (1) pyrrole, TFA, CH_2Cl_2, rt; (2) DDQ, CH_2Cl_2, rt; (3) TEA, BF_3OEt_2, rt; (4) $Pd(PPh_3)_4$, K_2CO_3, 9,9-dioctylfluorene-2,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane), THF.

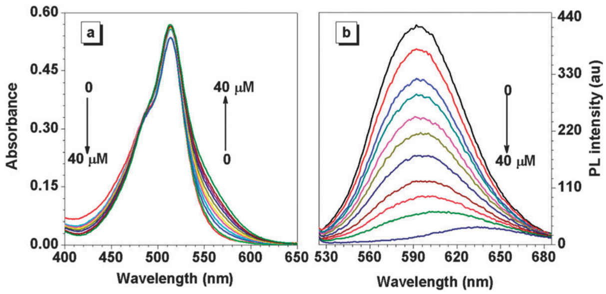


Fig. 1 Absorbance spectra (a) and fluorescence spectra (b) of **3** (10 μM) in the presence of increasing diisopropylamine concentrations (0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 μM) in a THF solution.

The chromogenic and fluorometric signaling behaviors of **3** to secondary amines were investigated in a THF solution. As shown in Fig. 1a, with the addition of diisopropylamine (DIPA), the UV-vis absorption of **3** experienced a little red shift with a slight increase in its maximum absorption peak at 513 nm and an obvious enhancement of the tail between 540 and 600 nm. Simultaneously, the color of the solution turned from red to violet quickly. TLC (thin layer chromatography) monitoring suggested that a new product appeared in the solution. Fig. 1b shows the change in emission spectra upon addition of DIPA. Upon excitation at 513 nm, the emission intensity at 592 nm decreased 25-fold while the concentration of DIPA changed from 0 to 40 μM. A similar phenomenon was observed when the DIPA was displaced by diethylamine (DEA) (Fig. S1, ESI†). To demonstrate the selectivity to various amines in the solution, both visible color change and visual fluorescence change of **3** after addition of different amines are presented in Fig. 2. The free probe exhibited red color and red emission in the solution. After the addition of DEA or DIPA, the color of the solution turned violet and the fluorescence was quenched immediately. However, the addition of other amines such as *n*-propylamine, *n*-hexylamine, triethylamine, benzylamine and aniline had almost no effect on the color and fluorescence of the solution which indicated the high selectivity of this probe to secondary amines.

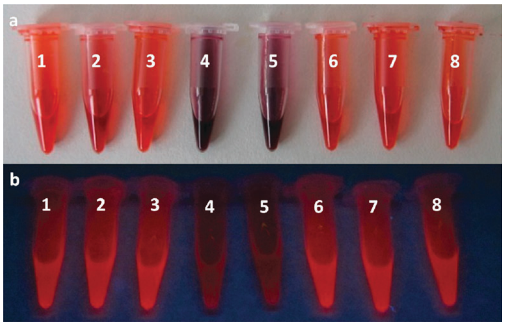
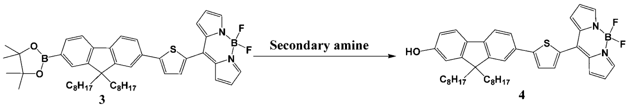


Fig. 2 Visible color (a) and visual fluorescence color change (b) of **3** (10^{-3} M) with representative amines after mixing for 5 minutes (100 equiv. for each amine in THF): (1) free **3**; (2) **3** + *n*-propylamine; (3) **3** + *n*-hexylamine; (4) **3** + diethylamine; (5) **3** + diisopropylamine; (6) **3** + triethylamine; (7) **3** + benzylamine; (8) **3** + aniline.

To identify the reaction products, we performed the reaction between **3** and several types of amines at a higher concentration in the solution (Scheme S3, ESI†). In the presence of primary amines and tertiary amines such as *n*-propylamine, *n*-hexylamine, triethylamine, benzylamine and aniline, only a trace amount of the new product was observed in the solution within half an hour. However, a new purple product formed in good isolated chemical yield (nearly 100%) within 5 minutes after adding DIPA or DEA. And the major product was identified to be 7-(8-(4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene))-2-hydroxyl-9,9-dioctylfluorene (**4**) according to its ^1H, ^{13}C-NMR spectra and the high resolution mass spectrum (Scheme 2). In ^1H-NMR spectra, resonances of the BODIPY moiety of probe **3** are observed at 7.93, 7.40 and 6.60 ppm. With the addition of 4 equiv. of DIPA, the resonances of the BODIPY moiety scarcely shifted. Nevertheless, as shown in Fig. 3, the chemical shifts of protons on the fluorene moiety and the thiophene moiety changed greatly owing to the effect of the newly formed hydroxyl group. In addition, a new peak centered at 5.29 ppm can be assigned to the hydroxyl proton of the –OH group. Thus, the NMR results further confirm that the interactive site should be at the boronate ester position, and no strong interaction exists between DIPA and BODIPY units because of no corresponding chemical shift of the protons.

To better understand the photophysical change before and after the addition of secondary amines, the optical properties of **3** and **4** were compared. The absorption peak positions of both **3** and **4** were observed at 513 nm, but **4** demonstrated a bigger absorbance with a broad and strong tail peak at around



Scheme 2 Signaling of secondary amines by **3**.

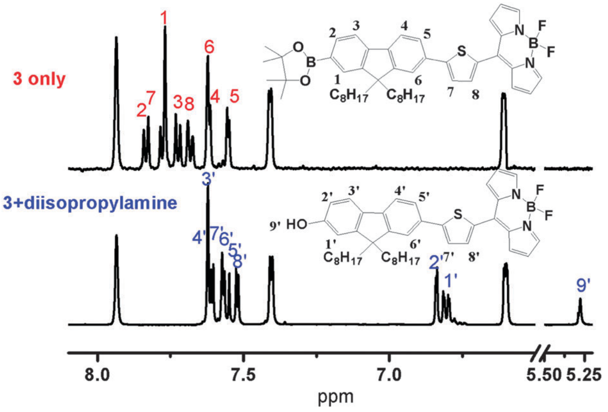


Fig. 3 Partial ^1H NMR spectra of **3** only, and **3** + diisopropylamine. [**3**] = 5.0×10^{-3} M, [diisopropylamine] = 2×10^{-2} M in $CDCl_3$.

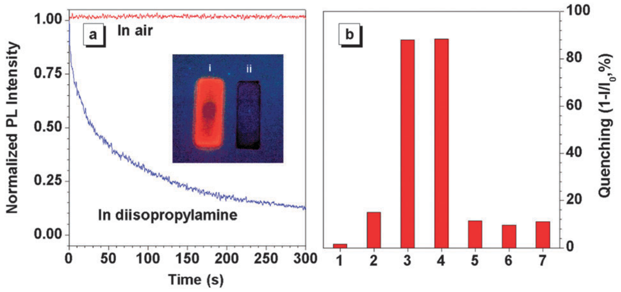


Fig. 4 (a) Changes in fluorescence intensity of **3** films exposed to air and the saturated diisopropylamine vapor for 300 s at 25 °C at their wavelength of the maximum emission. The inset picture was the fluorescence response of **3** films before (i) and after (ii) exposure in DIPA for 300 s. (b) Fluorescence quenching efficiency of **3** deposited on a quartz slide exposed to the saturated vapor of various organic amines for 300 s: 1. *n*-propylamine; 2. *n*-hexylamine; 3. diethylamine; 4. diisopropylamine; 5. triethylamine; 6. aniline; and 7. benzylamine.

570 nm (Fig. S2, ESI†). The molar absorption coefficients are 45 700 M^{-1} cm^{-1} and 50 500 M^{-1} cm^{-1} for **3** and **4**, respectively. The higher molar absorptivity of **4** indicated the higher sensitivity for secondary amines using a colorimetric technique. The relative fluorescence quantum yields (Φ_{FL}) of **3** and **4** were evaluated to be 2.6% and 0.14% in THF, with Rhodamine B as the standard. In addition, the Φ_{FL} of **3** and **4** in the solid state determined by a calibrated integrating sphere are 0.31% and 0.01%, respectively, which corresponded very well with the fact that the fluorescence of **3** was quenched rapidly when the secondary amines were added.

Solid-state fluorescence sensing for vapor detection is highly desirable *in situ* and real time detection. To further investigate the possibility of solid sensing, we also monitored the changes in the fluorescence intensity of **3** films upon exposure to air and DIPA vapors. A simple spin-coating method was used to fabricate the sensing film from the THF solution of **3** (10^{-2} M). As shown in Fig. 4a, the fluorescence of the sensing film of **3** is quite stable even after exposure to air for 300 s, which indicates its high photo-stability. Further monitoring of the photo-stability demonstrated that the fluorescence intensity remains almost unchanged after exposure to air for a week (Fig. S4, ESI†). In contrast, upon exposure to the DIPA vapor, its fluorescence was quenched by 34%, 43% and 88%, respectively, within 10 s, 50 s and 300 s, which indicated its high sensitivity to DIPA vapors. The detection limits of **3** for DEA and DIPA vapors can be estimated to be 1.85 ppb and 2.42 ppm, respectively (Fig. S5, ESI†). To facilitate this probe for more practical applications, we also prepared test papers of **3** by immersing a piece of filter paper (2×0.5 cm^2) into the THF solution of **3** (1.0×10^{-2} M) followed by drying it in air. Both color and fluorescence changes of the test paper were observed after it was placed in the saturated DIPA vapor for 5 minutes (Fig. S6, ESI†), indicating the great advantage of our test paper for real-time testing.

To examine the selectivity, the fluorescence responses of **3** films to various amine vapors were investigated by inserting the films into sealed vials (6.75 mL) containing cotton and analytes at room temperature. The fluorescence was quenched slightly for *n*-propylamine (1.6%), *n*-hexylamine (15%), triethylamine (11.5%), aniline (9.7%) and benzylamine (11%) due to the formation of trace **4**. While in DEA and DIPA vapors, the quenching efficiency was 87.9% and 88.3%, respectively. Obviously, this probe exhibited excellent selectivity to secondary amines in the solid films.

In summary, chemosensing of secondary amines was investigated by virtue of its particular characteristic that catalyzes the oxidation of boronate esters (or boronic acids) in air to yield the corresponding phenols. The BODIPY-based probe exhibits both color and fluorescence response to secondary amines either in solution or in solid films even in the form of test papers exhibiting its wide potential applications. Besides, the probe showed remarkably high selectivity to secondary amines over other amine species. This work offers a new strategy for solid-state fluorescence sensing, and also provides an efficient and quick method to synthesize some special phenols starting from the corresponding boronate esters. Endeavors to further modify the sensory materials so as to increase the sensitivity of BODIPY-based conjugates are in progress, and studies to expand the analytes based on different sensing mechanisms *via* various functionalizations of BODIPY are also underway in our laboratory.

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