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Fluorescent and colorimetric detection of acid vapors by using solid-supported rhodamine hydrazides

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ABSTRACT

Rhodamine hydrazide-based chemosensors that can detect volatile acidic gases in solid state have been developed. The rhodamine hydrazide probes adsorbed on filter paper respond fluorescently and colorimetrically only to volatile acidic gases but not to organic bases nor to other volatile organic compounds (VOCs). Diethyl chlorophosphate (DCP), one of model compounds used for the studies of Chemical Warfare Agent (CWA), could also be detected by using this method.

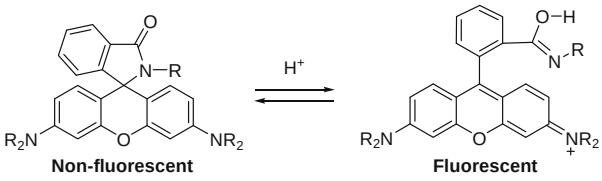
1. Introduction

The real-time sensing of volatile organic compounds (VOCs), such as amines,[1] hydrocarbons,[2] explosives,[3] and chemical warfare agents,[4] has been an active research area. Although much success has been achieved for the detection of VOCs by using various optical detection methods, the fluorescent probe-based sensing of VOCs still remains challenging, mainly because there are not many organic materials available which are sufficiently fluorescent in solid state and suitable for vapor detection.[5]

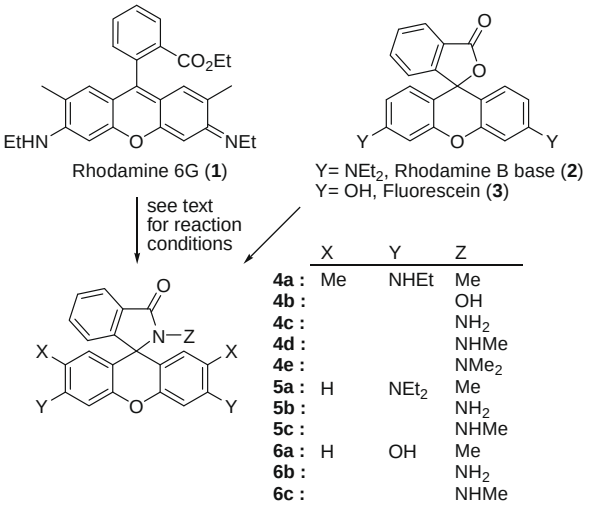
Recently, rhodamine amide derivatives are widely used as fluorescent probes for detection of various ions.[6] While the spirocyclic form of a rhodamine amide is non-fluorescent and colorless, the ring-opened form is strongly fluorescent and pink colored (Scheme 1).[7] This characteristic equilibrium is highly sensitive to the pH of the solutions. In acidic solutions, the ring-opened form is predominant, and therefore strongly fluorescent. Although this acid-sensitive equilibrium has been well known in solutions, its properties in solid states are not well examined. Herein, we report rhodamine hydrazide derivatives that respond to acid vapors in solid state.

We envisioned that the H^+-promoted ring-opening reaction of rhodamine amides could be utilized to detect volatile acids. Thus, we have prepared several rhodamine 6G (**4a**–**e**), rhodamine B (**5a**–**c**), and fluorescein (**6a**–**c**) amide derivatives to screen probes that are suitable for the detection of acid vapors in solid state (Scheme 2).

Compound **4a** was prepared from **1** in the presence of $MeNH_2{\cdot}HCl$ and Et_3N under refluxing EtOH solution in 88% yield. Compound **4b** was prepared from **1** in three steps: (1) NaOH, $EtOH–H_2O$, reflux; (2) $POCl_3$, CH_2Cl_2, rt; and (3) $NH_2OH{\cdot}HCL$, EtOH, Et_3N, reflux (34% yield for three steps). Treatments of **1**, **2**, and **3** with NH_2NH_2 or NH_2NHMe under refluxing EtOH solutions[8] produced compounds **4c** (75%), **4d** (78%), **5b** (42%), **5c** (74%), **6b**



Scheme 1. H^+-promoted ring opening of rhodamine amides.



Scheme 2. Synthesis of rhodamine amide derivatives.

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(75%), and **6c** (75%). Dimethylhydrazine derivative **4e** was prepared from **4c** in the presence of MeI in acetone at room temperature (78%). Compound **5a** was prepared from **2** in two steps: (1) $POCl_3$, CH_2Cl_2, r.t. and (2) $MeNH_2$·HCl, Et_3N, EtOH, reflux (54% yield for two steps). And **6a** was prepared from **3** in two steps: (1) cat. c-H_2SO_4, MeOH, reflux and (2) $MeNH_2$·HCl, Et_3N, DMF, 100 °C (25% yield for two steps).[9]

Solid-adsorbed fluorescent probes were prepared by dipping a filter paper (d = 0.6 cm) into a CH_2Cl_2 solution of a fluorescent compound (1.0 mg of a probe in 10 mL of CH_2Cl_2) for 2–3 s.[10] Then, the filter paper was dried in high vacuum for 48 h in dark at room temperature. Fluorescent detection of an acid vapor is conducted using a glass chamber (volume = 100 mL, d = 5 cm) with a lid. The fluorescent-probe adsorbed filter paper is placed in the center of the chamber, and then a volatile acid (~5 μL) is dropped into the bottom of the chamber. After 15 s, the filter paper was removed from the chamber, and then the optical and the fluorescent images were taken.

Although rhodamine amides are known to be highly fluorescent in acidic solutions, the solid-supported rhodamine methyl amides **4a** and **5a** showed no apparent color changes and very weak fluorescence intensities in the presence of HCl and HNO_3 vapors (Fig. 1).[11] And the fluorescein amide derivatives (**6a**–**c**) were inert to acid vapors as expected. Strong color and fluorescence changes were observed for rhodamine hydrazine derivatives **4c**, **4d**, **5b**, and **5c**. However, the solid-supported rhodamine B hydrazides (**5b** and **5c**) were fluorescent even in the absence of acid vapors. Therefore, we selected rhodamine 6G hydrazide derivatives (**4**) for our further studies.

The solid-supported rhodamine hydrazides **4c** and **4d** uniformly displayed significant color and fluorescence intensity changes in response of volatile acids, such as HF, HCl, HBr, and HNO_3 (Fig. 2a and b). But the solid-supported rhodamine amide **4a** showed no apparent color and fluorescence changes in the presence of various volatile acids. Interestingly, the solid-supported **4c** and **4d** even responded to acid precursors (such as AcCl, $POCl_3$, $SOCl_2$, PBr_3, and acryloyl chloride), which could produce HCl or HBr indirectly by reaction with nucleophiles. This may imply that the nucleophilic hydrazide attacks the electrophilic acid precursors to produce HCl or HBr, which eventually induces the ring-opening reaction of rhodamine amide derivatives. Similarly, diethyl chlorophosphate (DCP), one of model compounds used for the studies of Chemical Warfare Agent (CWA), could also be detected by using these rhodamine 6G hydrazides (**4c** and **4d**) in solid state (Fig. 2, vapor e). On the other hand, volatile organic bases and other volatile organic compounds (VOCs) are completely silent to the rhodamine 6G hydrazides in solid state (Fig. 2c and d).

We further examined the concentration-dependent fluorescence response of **4d** to DCP and HCl in solid state (Fig. 3). As the amounts of DCP added increased from 5 to 20 μL, the fluorescence intensities increased accordingly. It seems that enough HCl vapors are generated even at 5 μL of c-HCl under the experimental conditions because we were not able to observe significant fluorescence intensity changes from 5 to 20 μL of c-HCl.

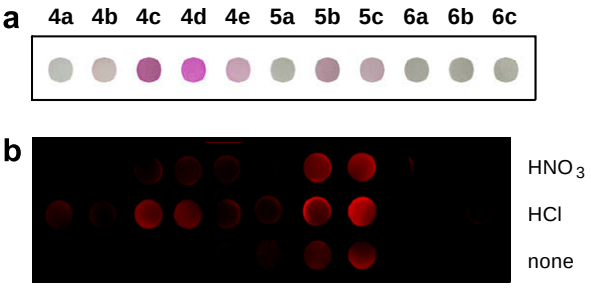


Figure 1. Responses of solid-supported **4**–**6** to acid vapors (5 μL in a 100 mL chamber). (a) Color changes in the presence of c-HCl. (b) Fluorescence changes in the presence of c-HCl and HNO_3.

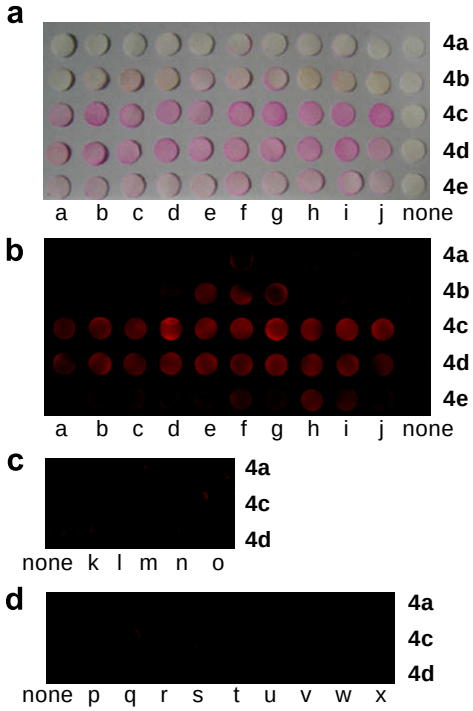


Figure 2. Responses of solid-supported **4a**–**e** to chemical vapors (5 μL in a 100 mL chamber). (a) Color changes and (b) Fluorescence changes in the presence of acid vapors: a. HF; b. AcCl; c. HBr; d. $POCl_3$; e. DCP (diethyl chlorophosphate); f. $SOCl_2$; g. HNO_3; h. c-HCl; i. PBr_3; j. H_2C=CHCOCl. (c) Responses to organic bases: k. pyridine; l. *i*-Pr_2NEt; m. Et_3N; n. *t*-$BuNH_2$; o. TMEDA (tetramethylethylenediamine). (d) Responses to other volatile organic compounds: p. PhSH; q. EtSH; r. CH_2Cl_2; s. $ClCH_2CH_2Cl$; t. hexane; u. pentane; v. Et_2O; w. EtOAc; x. MeOH.

The reason for the high sensitivity of rhodamine hydrazides (**4c** and **4d**), unlike other simple rhodamine amides (**4a** and **5a**), to acid vapors in solid state could be explained by the stabilized structure **7** as shown in Scheme 3. Protonation[12] of the rhodamine hydrazide

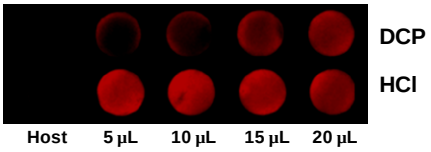
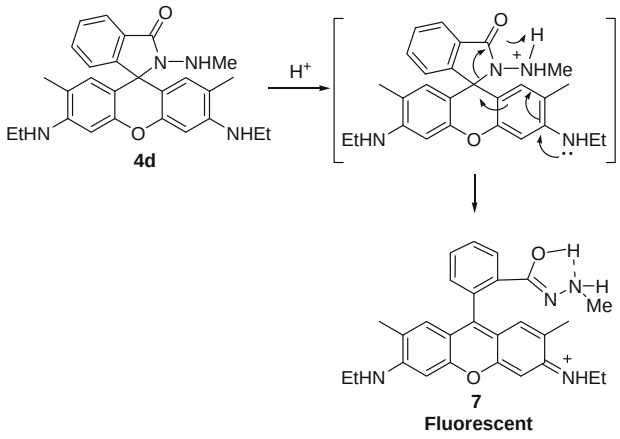


Figure 3. Concentration-dependent fluorescence changes of solid-supported **4d** in the presence of DCP and HCl vapors.



Scheme 3. Proposed structure of the protonated rhodamine hydrazide **4d**.

(**4d**) is expected to trigger opening of the non-fluorescent spirocyclic form to the highly fluorescent open form **7**, where the protonated hydrazide could be stabilized by intramolecular hydrogen bonding.

In summary, we have developed rhodamine hydrazide-based chemosensors that respond fluorescently and colorimetrically to acid vapors. The solid-supported rhodamine hydrazide probes are highly sensitive only to volatile acids, but not to organic bases nor to other volatile organic compounds. Diethyl chlorophosphate (DCP), one of model compounds used for the studies of chemical warfare agent (CWA), could also be detected by using this method.

2. Experimental procedures

2.1. General procedure for the synthesis of rhodamine hydrazide 4d

To a solution of rhodamine 6G (2.00 g, 4.18 mmol) in ethanol (4 mL) was added methylhydrazine (1.00 mL, 19.0 mmol). The solution was refluxed for 12 h, concentrated, and the residue was purified by column chromatography (hexanes/ethyl acetate = 1:2) to give 1.44 g of **4d** (78%) as a white solid.

Spectral data for **4**: mp decomposed at 254 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.94 (dd, J = 5.6 Hz, 3,2 Hz, 1 H), 7.45−7.48 (m, 2 H), 7.05−7.08 (dd, J = 5.6 Hz, 3.2 Hz, 1 H), 6.38 (s, 2 H), 6.25 (s, 2 H), 4.22 (br s, 1 H), 3.48 (br s, 2 H), 3.18−3.23 (q, J = 7.0 Hz, 4 H), 2.34 (s, 3 H), 1.90 (s, 6 H), 1.30–1.33 (t, J = 7.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.44, 152.25, 151.88, 147.45, 132.77, 130.52, 128.41, 128.22, 124.07, 122.88, 117.70, 106.39, 96.92, 65.51, 38.53, 38.50, 16.86, 14.91; IR (film, cm^{-1}) 3826, 1688, 1618, 1519, 1444, 1357, 1258, 1204, 1146, 1005; HRMS m/z calcd for $C_{27}H_{30}N_4O_2$ $(M + H)^+$ 443.2447; found 443.2455.

2.2. General procedure for the fluorescent detection of acid vapors using solid-supported rhodamine hydrazide

Filter papers (Advantec, 0.6 cm in diameter) were dipped in the CH_2Cl_2 (10 mL) solution of a rhodamine hydrazide (1.0 mg) for 2–3 s each. Then, the collected filter papers were dried in high vacuum for 48 h in dark at room temperature. The fluorescent-probe adsorbed filter paper is placed in the center of a glass chamber (volume = 100 mL, d = 5 cm). Then, a drop of volatile acid (~5 μL) is dropped into the bottom of the chamber using a micro–syringe, and the chamber was covered for 15 s. The filter paper was removed from the chamber and placed in a well of a 96-well assay plate. The fluorescent images were taken using a Typhoon 9210 fluorescence scanner (observed emission at 555 nm).

Acknowledgments

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Supplementary data

Experimental procedures for the synthesis, spectral data, of new compounds data are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.087.

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10. Using high concentrations of fluorescent materials or dipping longer time often resulted in colored filter papers.
11. In CH_2Cl_2 solutions, similarly, while **4a** induced very weak fluorescence intensity changes in the presence of HCl and DCP, the rhodamine hydrazide **4d** showed strong fluorescent responses under the same conditions (see Supplementary data).
12. The hydrazides of carboxylic acids are known to undergo protonation at the β-nitrogen atom in acidic media: *Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Oxford: Pergamon, 1979.