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Coumarin-based fluorescent chemodosimeter for selective sensing of hydrazine in semi-aqueous medium

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A chemodosimeter based on 2,3,5,6-tetrafluoro benzoyl ester of 7-hydroxy-4-(trifluoromethyl)coumarin has been designed and synthesized for selective detection of hydrazine in semi-aqueous medium. The structure of the probe was confirmed by conventional spectroscopic techniques and single crystal X-ray analysis. The sensory system was found to be capable of sensing hydrazine in CH_3CN/H_2O (70:30, v/v) by showing turn-on type sensing behaviour accompanying distinct naked-eye colour change from colourless to greenish yellow in visible light as well as colourless to bright green under illumination of UV light. In the presence of hydrazine, 2,3,5,6-tetrafluoro benzoyl ester function gets cleaved resulting in the formation of highly fluorescent coumarin moiety. The sensing behaviour was followed by various spectroscopic techniques such UV-Visible, fluorescence, mass spectroscopy etc.

Keywords: Chemodosimeter, coumarin, fluorescence sensing, hydrazine sensor.

Introduction

Design and synthesis of fluorescent sensory system for biologically, chemically and environmentally important analyte is one of the important areas of research in field of supramolecular chemistry[1]. In recent years, numerous chemosensors, especially the fluorescent sensors (optical) have been used to detect different ions and molecules, elbowing their way to centre stage in the field of molecular recognition. An intense effort has been invested on the development of small molecule synthetic sensors that can selectively report the presence of such species. In this regard, hydrazine is of particular interest because of its wide applications in industrial, pharmaceutical, as well as space science[2–4]. For example, hydrazine is used as a corrosion inhibitor for boilers, catalyst, pharmaceutical intermediates, emulsifier, antioxidant agent and preservative in nuclear and electrical power plants[2]. It has wide application in the preparation pesticide, drug intermediates, dyes etc. due to its highly basic and reducing chemical nature[3]. Because of its combustible and detonable characteristics, it is also used as high-energy fuel in missiles, satellites and rocket-propulsion systems[4]. However, hydrazine can causes severe damage to the liver, lungs, kidneys, central nervous system and classified as carcinogenic substances with allowable threshold limit of 10 ppb[5,6]. Therefore, extensive use of hydrazine in different industries and laboratories is of great concern for the safety and health of human with long term exposure to this substance. Moreover, some nitrogen fixing bacteria, yeasts and anammox organisms synthesises hydrazine as a by-product[7]. Therefore, selective detection of hydrazine is highly demanding.

The various analytical techniques available for hydrazine detection include chromatography, mass spectroscopy, coulometry, potentiometry, colorimetry etc.[3,8-10]. But, most of these methods are not only time consuming and complex but are not applicable *in vivo* detection in live organisms. In this regard, fluorescence spectroscopic techniques has drawn much more attention due to its simplicity and high detection limit as well as it permits *in vivo* analysis of various species in their native environment with minimal perturbation of living organism[1,11]. To date, only a few fluorescent chemodosimeter for hydrazine have been reported in literature[12–20]. For example, Chang *et al.* employed levulinated coumarin that undergoes deportation in presence of hydrazine resulting increase in fluorescence intensity in DMSO-water[21]. Recently, Chen *et al*. prepared a pair of ESIPT-based benzothiazole derivatives for the detection of N_2H_2[22]. The

number of such chemodosimetric sensor system that selectively and specifically detects hydrazine is limited and remains still a challenge.

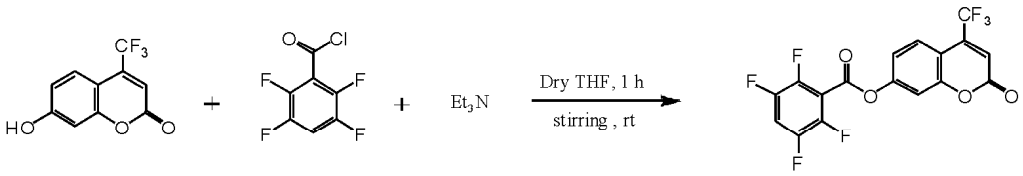
We herein devised a new hydrazine selective easy-to-make sensory system **1**, based on hydrazine mediated ester cleavage. A 2,3,5,6-tetrafluoro benzoyl ester of 7-hydroxy-4-(trifluoromethyl)coumarin gets deprotected under mild conditions and thus could be used as selective chromogenic and fluorogenic probe for hydrazine. The presence of four fluorine atom in the benzene ring makes the ester carbonyl carbon sufficiently electrophilic to be attacked easily by hydrazine resulting in the cleavage of ester function.

Results and discussion

The synthesis of probe **1** was achieved in one step according to Scheme 1. This involves the reaction of commercially available starting materials 7-hydroxy-4-(trifluoromethyl) coumarin and 2,35,6-tetrafluorobenzoyl chloride in dry THF (yield: 95%). Compound **1** was characterized by conventional spectroscopic means.

Table 1. Atomic coordinates and isotropic thermal parameters of **1**

Chemical formula	$C_{17}H_5F_7O_4$
Formula weight	406.21
Crystal system	Monoclinic
Space group	P21/n (No. 14)
a (Å)	9.1042(8)
b (Å)	6.0489(5)
c (Å)	27.955(2)
α (deg)	90
β (deg)	93.22
γ (deg)	90
λ (Å)	0.71073
V (Å^3)	1537.1(2)
F(000)	808
Z	4
T (K)	296
D (mg/m^{-3})	1.755
μ (mm^{-1})	0.179
*R*1 (all data)	0.0488
*wR*2 [$I > 2\sigma(I)$]	0.1134
GOF	1.09



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

Structure of **1** was further confirmed by single crystal X-ray analysis. A diffraction grade crystal was obtained by slow evaporation of chloroform solution of **1**. Fig. 1 shows the ORTEP of **1**. The crystallographic data of **1** is given in Table 1[23].

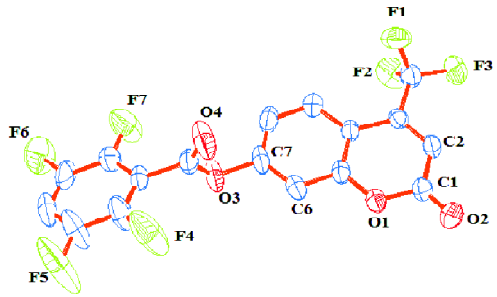


Fig. 1. Single-crystal X-ray structure of **1.** Displacement ellipsoids are scaled to the 30% probability level (C = blue, O = red, F = green).

We have investigated the optical sensing properties of the probe **1** by the UV-Vis absorption and fluorescence spectral changes upon the addition of hydrazine and other analytes (such as NH_4OH, NH_2OH, CH_3NH_2, urea, thiourea, cysteine, diaminopropane, and Na^+, K^+, Ca^{2+}, Mg^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+}, Zn^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Fe^{3+} and Al^{3+} as chloride or nitrate salt, and CH_3COO^-, F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^- and ClO_4^- as tetrabutylammonium salts) in aqueous acetonitrile (CH_3CN:H_2O; 70:30, v/v) at room temperature. The electronic spectra of **1** displayed absorption band at 280 and 320 nm (Fig. 2a). The absorption profile of **1** was significantly perturbed only in the presence of hydrazine along with a prominent colour change from colourless to greenish yellow that allowed a colorimeric detection of hydrazine through naked eye (Fig. 2a, inset).

Fig. 2a demonstrates the change absorption profile of **1**

with increase concentration hydrazine. Other environmentally and biologically relevant species (such as NH_4OH, NH_2OH, CH_3NH_2, urea, thiourea, cysteine, diaminopropane, and Na^+, K^+, Ca^{2+}, Mg^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+}, Zn^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Fe^{3+} and Al^{3+} as chloride nitrate salt, and CH_3COO^-, F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^- and ClO_4^- as tetrabutylammonium salts) did not affect absorption spectra of **1** significantly and remains non-responsive to probe **1** under identical experimental conditions (Fig. 2b).

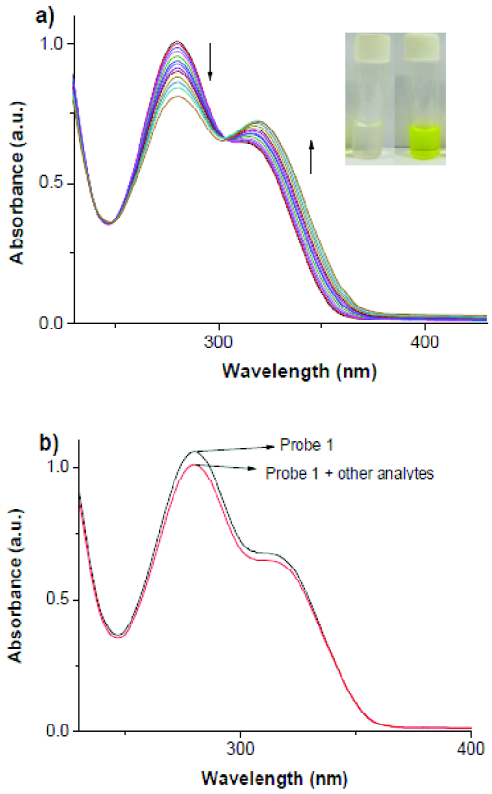


Fig. 2. Change in absorption spectra of **1** (c = 2.5×10^{-5} *M*) in aquous acetonitrile (**(**CH_3CN:H_2O; 70:30, v/v): (a) Upon gradual addition of hydrazine (c = 2.4×10^{-3} *M*) [Inset: Change in colour of **1** observed upon addition of hydrazine] and (b) upon addition of other analytes (c = 2.4×10^{-3} *M*).

The probe **1** itself showed very low fluorescence with an emission maxima at 415 nm upon excitation at 345 nm in aqueous acetonitrile (CH_3CN:H_2O; 70:30, v/v) at room temperature. In this regard, Fig. 3a represents the change in emission of **1** upon successive addition of hydrazine. Upon the addition of hydrazine the emission intensity at 415 nm increased significantly resulting in a turn-on type signalling system. Further the hydrazine sensing process was not only clearly seen by naked eye colour change but also by colour change under illumination with UV lamp from colourless nonfluorescent solution to bright green fluorescence (Fig. 3a, inset). Other metal ions and anions displayed almost no changes in emission spectra when they are exposed to probe **1** under similar experimental conditions (Fig. 3b). To address the specificity and selectivity of **1** towards N_2H_4 in presence of other analytes, we performed competitive experiments on the signaling of **1**-N_2H_4 system. When the deprotection reaction of **1** was carried out in the mixture of other analytes, no fluorescence appeared, but a strong fluorescence emission appeared only when hydrazine was added to this mixture (Fig. 3b). These observations led us to conclude that compound **1** is highly selective toward hydrazine even in the presence of the complex mixture of other relevant analytes.

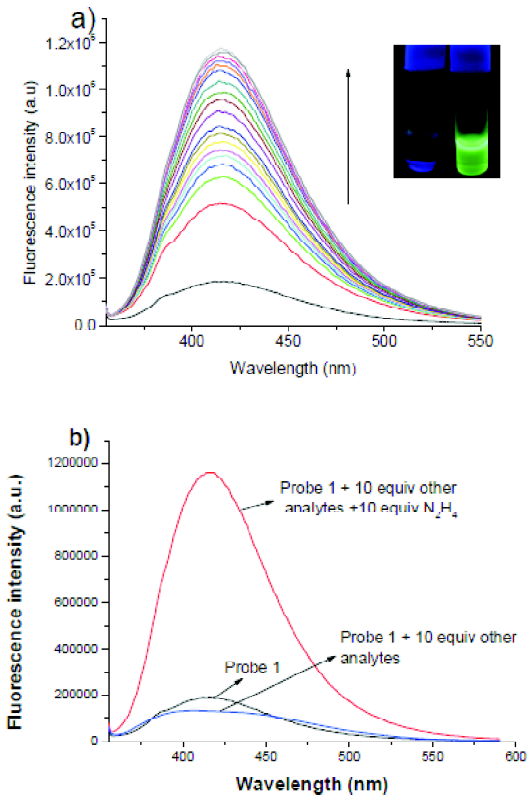
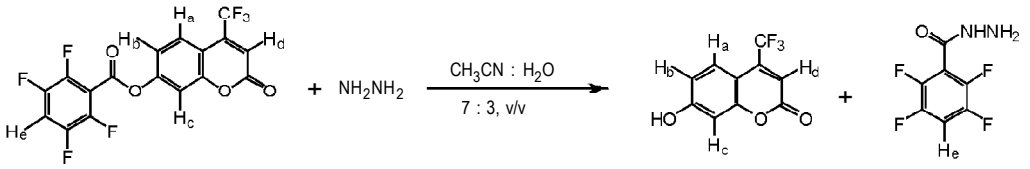


Fig. 3. Change in emission of **1** (c = 2.5×10^{-5} *M*) in aqueous acetonitrile (**(**CH_3CN:H_2O; 70:30, v/v): (a) Upon gradual addition of hydrazine (c = 2.4×10^{-3} *M*) [Inset: Change in colour of **1** observed under UV light illumination] and (b) upon addition of 10 equivalent N_2H_4 in the presence and absence of 10 equivalents amount of various other analytes (c = 2.4×10^{-3} *M*).

The chromogenic and fluorogenic signalling behaviour of **1** displaying greenish yellow colour and bright green fluorescence from an initially colourless and nonfluorescent solution, upon addition of hydrazine, is attributed to the hydrazine mediated ester cleavage of **1** to set free the coumarin dye. The kinetic behaviour of N_2H_4 (c = 5×10^{-2} *M*) to probe **1** (c = 1.5×10^{-3} *M*) 25°C was measured by plotting intensity versus time for the time dependant measurements. The plot clearly demonstrates first order kinetics and rate constant was determined to be 2.06×10^{-3} s^{-1}. As shown in scheme 2, hydrazine reacts with probe **1** at ester carbonyl carbon and subsequent amide bond formation leading to the cleavage of ester function release the coumarin moiety. 7-Hydroxy-4(trifluoromethy)coumrin thus generated is responsible for the observed chromogenic and fluorogenic signalling behaviour of probe **1**.

to removal of benzoyl function leading to the formation of **2** and **3**. In addition to this, a broad singlet observed at 9.25 ppm is assigned to amide NH (undergoes D_2O exchange) as coumarin -OH was not observed when ^1H NMR spectra of **2** recorded in $CDCl_3$ separately in pure state. Formation of **2** and **3** was further supported by mass spectrometry. In absence of hydrazine, probe **1** displays a molecular ion peak at 405.10 ($C_{17}H_5F_7O_4$, $[M-H]^+$). When mass spectra of **1** recorded after addition of 2.0 equivalent amount of hydrazine peaks corresponding to molecular ion **2** ($C_{10}H_5F_3O_3$, M^+) and **3** (**$C_7H_4F_4N_2O$**, M^+) at 229.00 ($[M-H]^+$) and 207.03 ($[M-H]^+$) were observed, respectively.

In conclusion we have demonstrated that 2,3,5,6-tetrafluoro benzoyl ester of 7-hydroxy-4-(trifluoromethyl)coumarin (**1**) can selectively report the presence of N_2H_4 in semi-aqueous medium by displaying turn-on type signalling



Scheme 2. Signaling of hydrazine by **1**.

We have also determined the detection limit to gain an insight about the sensitivity of the probe towards hydrazine. The detection limit was determined from the fluorescence titration data following the relation, detection limit = $3\sigma/K$, where σ is the standard deviation of blank measurement, and K is the slope between the fluorescence versus hydrazine concentration[24]. The detection limit for hydrazine was calculated to be 7.07×10^{-6} *M* (Fig. 4).

The proposed hydrazine induced cleavage of ester function was further verified by ^1H NMR spectral changes of **1** in absence and presence of hydrazine in $CDCl_3$. In the ^1H NMR spectroscopy, probe **1** displayed proton resonances at 7.83, 7.41, 7.32 and 6.84 ppm for coumarin moiety in $CDCl_3$. The multiplet centred at 7.35 ppm was assigned to H_e. Upon addition of 1.0 equivalent amount hydrazine all the signals corresponding to H_a, H_b, H_c, H_d, and H_e protons underwent large upfield shift as result of removal of 2,3,5,6-tetrafluorobenzoyl group from **1**. The observed upfield shift of all the proton signals is attributed to the increase in electron density into the π-conjugated framework through bond propagation due

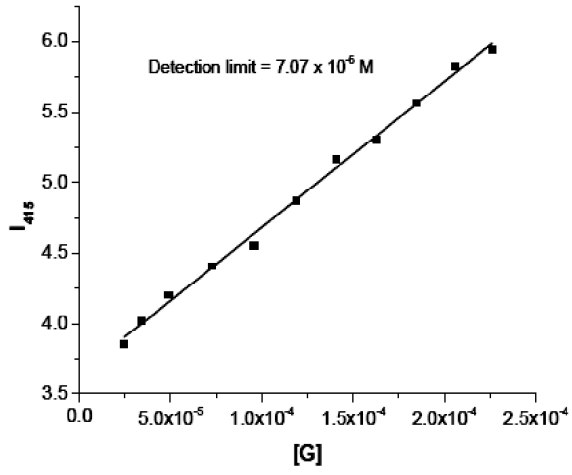


Fig. 4. Calculation of detection limits of **1** (c = 2.5×10^{-5} *M*) in aqueous acetonitrile (**$CH_3CN:H_2O$**; 70:30, v/v) for hydrazine.

behaviour. The probe is also capable to report the presence N_2H_2 through colour change from colourless to yellowish green in visible light as well as colorless nonflurescent to bright green fluorescent colour under illumination of UV-light

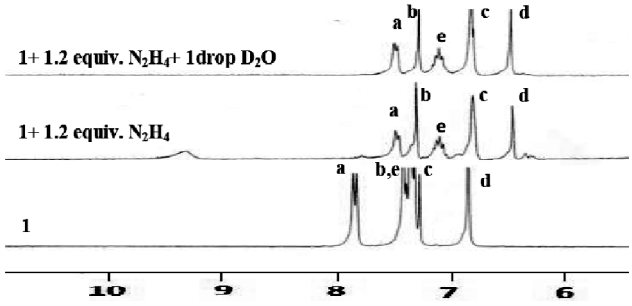


Fig. 4. Partial ^{1}H NMR spectra of **1** recorded in absence and presence of N_2H_4 in $CDCl_3$ solution.

that can be observed via naked eye. The change in colour of the probe solution in presence of wide range of other analytes is also sharp and reproducible. Hydrazine mediated deprotection of ester function has been exploited to construct the sensory system. Further work along this direction is under progress in the laboratory.

Experimental

*Synthesis of **1**:*

To the stirred solution of 2,3,5,6-tetrafluorobenzoyl chloride (0.332 g, 1.56 mmol) in dry THF (10 mL), 7-hydroxy-4-(trifluoromethyl)-2*H*-chromen-2-one **2** (0.300 g, 1.30 mmol) dissolved in dry THF was added dropwise followed by addition of Et_3N (0.160 g, 1.56 mmol). After stirring the reaction mixture for 1 h at room temperature, solvent was evaporated on a rotary evaporator. Aqueous $NaHCO_3$ solution (20 ml) was then added and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). Organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Crude mass was purified by column chromatography using 15% ethyl acetate in hexane as eluent to afford the receptor **1** in 95% yields (0.505 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (1H, dd, *J* 2 Hz), 7.41 (1H, d, *J* 2 Hz), 7.37–7.34 (1H, m), 7.32 (1H, dd, *J* 2 Hz), 6.84 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.2, 158.1, 156.0, 153.9, 147.0 (m), 145.9 (m), 141.9 (q, $J_{C\text{-}F}$ 33 Hz), 127.4, 122.0 (q, $J_{C\text{-}F}$ 276 Hz), 119.4, 116.6 (q, $J_{C\text{-}F}$ 6 Hz), 112.7, 112.5 (t, $J_{C\text{-}F}$ 15 Hz), 111.7, 110.9 (t, $J_{C\text{-}F}$ 23 Hz); Mass: 405.10 ($C_{17}H_5F_7O_4$, $[M\text{-}H]^+$).

General procedure of UV-Vis and fluorescence titration:

Stock solutions of the hosts and guests were prepared in CH_3CN-H_2O (70:30, v/v) and 2.5 ml of the individual host solution was taken in the cuvette. The solution was irradiated at the excitation wavelength maintaining the excitation and emission slits. Upon addition of guests, the change in fluorescence emission of the host was noticed. The corresponding emission values during titration were noted. For UV-Vis titration the receptors was dissolved in CH_3CN-H_2O (70:30, v/v) and 2.5 ml of the individual host solution was taken in the cuvette. Then, guests dissolved in CH_3CN-H_2O (70:30, v/v) were individually added in different amounts to the receptor solution and the corresponding absorbance values during titration were noted.

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