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A coumarin based chemodosimetric probe for ratiometric detection of hydrazine



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ABSTRACT

A coumarin-based sensor containing trifluoroacetyl acetonate moiety was designed, synthesized, and applied for hydrazine detection. Hydrazinolysis of the chemodosimeter results in a prominent chromogenic and fluorescence ratiometric response toward hydrazine within 3 min. The probe is highly selective toward hydrazine over other important amines and other biologically and environmentally abundant analytes. The limit of detection (LOD) of the probe is in 10^{-6} M range. The sensing mechanism was supported by NMR and HRMS analysis. The experimentally observed change in structure and electronic properties of the sensor after reaction with hydrazine was modeled by Density Functional Theory (DFT) and Time Dependent Density Functional Theory (TDDFT) computational calculations, respectively.

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In recent era, the development of chemosensors as well as chemodosimeters for the recognition of environmentally important and hazardous analytes has been receiving considerable attention.¹ Hydrazine pollution is a global problem and creates a significant damage to human health. Hydrazine is extensively used as a high energetic fuel in missile propulsion systems.^{2,3} It is a highly explosive base and a robust reducing mediator and is used as a key reactant in the preparation of pharmaceuticals, photography chemicals, pesticides, dyes, and emulsifiers.⁴ Nevertheless, hydrazine has considerable effects that can potentially lead to serious environmental pollution during its production, use, conveyance, and clearance. Hydrazine is routinely determined by electrochemical analysis⁵ and chromatography,⁶ including gas chromatography,⁷ HPLC,⁸ and capillary electrophoresis.⁹ Due to its extensive applications and poisonous effects, it is highly desirable to develop consistent and sensitive analytical methods for the selective detection of hydrazine. However, there are only a few reports regarding hydrazine-assisted fluorescent probes.¹⁰

In continuation of our research work in the development of fluorescence sensors¹¹ for important analytes, herein, we disclose the design and synthesis of a fluorescence sensor based on coumarin-trifluoroacetyl acetonate moiety (CTF; C = coumarin, TF = trifluoroacetyl acetonate) which can selectively detect hydrazine ratiometrically in acetonitrile media. Hydrazine plays here the

key role to affect the ICT distribution of CTF through the formation of a five-membered ring in its side chain, therefore a subsequent ICT-induced ratiometric response was observed both in absorption and fluorescence changes toward hydrazine. As depicted in Scheme 1, compound 1 [3-acetyl-7-(diethylamino)coumarin] was synthesized by following a similar procedure reported earlier.¹² Compound 1 was converted to the target sensor CTF [1-(7-(diethylamino)-2-oxo-2*H*-chromen-3-yl)-4,4,4-trifluorobutane-1,3-dione] by treatment with ethyl trifluoroacetate through Claisen condensation in 64% yield. The structure of CTF was confirmed by ¹H NMR, ¹³C NMR, (¹H-¹³C) HMBC NMR, and HRMS spectroscopy (Supplementary data Figs. S7–S11).

In this Letter, a new signaling probe (CTF) was devised for hydrazine, using selective hydrazinolysis at the carbonyl group of trifluoroacetyl acetonate moiety followed by cyclization to give ultimately a new fluorescent species (CTF $-N_2H_4$). We observed here that the sensor CTF can react with hydrazine to generate CTF $-N_2H_4$ (7-(diethylamino)-3-(3-(trifluoromethyl)-1H-pyrazol-5-yl)-2H-chromen-2-one) with a ratiometric fluorescence response as shown in Scheme 2.

The absorption and emission properties of the probe were investigated by addition of very small amount of hydrazine; it causes the signal to change rapidly. CH₃CN was selected as an analysis solvent to explore the optical response of CTF toward hydrazine at room temperature. UV–vis spectral studies of CTF (10 μ M, CH₃CN, 25 °C) exhibited the maxima around at 485 nm. Upon addition of hydrazine (2 × 10⁻⁴ M in CH₃CN), the absorption at 485 nm





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Scheme 1. Synthetic scheme of the probe (CTF). Reagents and conditions: (i) ethyl acetoacetate, EtOH, piperidine, reflux, 6 h; (ii) ethyl trifluoroacetate, NaOMe, DCM, reflux, 1 h.



Scheme 2. Probable sensing mechanism of CTF with N₂H₄.

eventually decreased, whereas two new absorption peaks gradually appeared at 445 and 395 nm with two isosbestic points arising at 273 and 335 nm. Such a blue shift (most prominent one) of 90 nm causes a change in the absorption behavior showing the change in the color of the solution from orange yellow to light green, which allows a colorimetric detection of hydrazine to the naked eye (Fig. 1). Now, the experimental data showed that in the presence of 1.5 equiv of hydrazine ratiometric value increases (A_{395}/A_{485} , from 0.7315 to 1.9094), which was observed with respect to CTF itself and ratio of two absorbance intensities (A_{395}/A_{485}) maintained a good linear relationship with the concentration of hydrazine ($R^2 = 0.994$).

Fluorogenic studies of CTF were investigated in CH₃CN solution. Here also the spectral property of CTF was found to perturb only by hydrazine. Upon excitation at 450 nm CTF (10 µM, CH₃CN, 25 °C) shows a maxima at 545 nm (φ = 0.01) in the absence of any analyte. Upon incremental addition of hydrazine the peak at 545 nm decreases regularly and a new peak at 500 nm increases (φ = 0.11) rapidly and consequently it leads to a blue-shift from 545 to 500 nm (Fig. 2). The experimental data showed that the emission intensity ratio (I_{500}/I_{545}) of CTF after addition of hydrazine fits linearly with hydrazine concentration, having a good R^2 value of 0.995. The detection limit was found to be 3.38×10^{-6} M. The



Figure 1. (a) Change of UV-vis spectra of CTF ($10 \ \mu$ M) upon gradual addition of hydrazine (0–2 equiv). Inset: Visible color change observed in CTF in absence and presence of 2 equiv of hydrazine.



Figure 2. (a) Change of fluorescence spectra of CTF (10 μ M) upon gradual addition of hydrazine (0–2 equiv). Inset: Visible emission observed from CTF in absence and presence of 5 equiv of hydrazine after irradiation under UV light.

mechanism of this type of change may be explained by the addition of hydrazine. After reaction with hydrazine the conjugation is being hampered, that is, ICT (intramolecular chargetransfer) turning off, which is accompanied by the blue-shift in fluorescence. In contrast, only an insignificant change was observed upon the addition of different amines, for example, ethylenediamine, dimethylamine, triethylamine, NH₂OH, piperazine, phenylhydrazine, etc. Noteworthy is that it gains much importance that even after addition of about 10 fold excess of these test amines, there was no perturbation of the hydrazine-induced fluorescence response. The effect of environmentally as well as biologically important ions such as Na⁺, Zn²⁺, Cu²⁺, Mn²⁺, Fe³⁺, Hg²⁺, Cd²⁺ (as their chloride salts), S^{2–}, HSO⁻₃, SO²₄⁻, NO⁻₃ and N⁻₃ (as their sodium salts) was also examined and there was no significant change observed both in UV–vis and fluorescence titration experiments.

Now the reaction of CTF with hydrazine might proceed through the formation of a five-membered cyclized product (CTF $-N_2H_4$) (Scheme 2, Figs. 3 and 4). Here the trifluoroacetyl acetone moiety



Figure 3. Partial HRMS spectra (a) of CTF and (b) [CTF-N₂H₄] the product resulting from reaction of CTF with hydrazine.



Figure 4. Partial ¹H NMR spectra of (a) CTF and (b) $[CTF-N_2H_4]$, the product resulting from reaction of CTF with hydrazine.

plays a key role in the chemodosimetric approach of hydrazine in our design.

Noticeably the inhibition in the fluorescence signature was caused only by hydrazine and not by any other tested amines. This indicates that the five-membered ring formation was assisted only by hydrazine induced chemodosimetric approach. The proposed product (CTF– N_2H_4) was isolated and it was observed that the dehydrated product was formed simultaneously and its structure was characterized by ¹H NMR, ¹³C NMR, and HRMS spectroscopic analyses (Supplementary data, Figs. S12–S14).

Time dependent fluorescence change of CTF upon addition of hydrazine and its reaction kinetics was studied in acetonitrile solution. To understand this time dependent experiment with CTF-N₂H₄ system, the fluorescence spectra of this system were



Figure 5. Change of emission spectra of CTF (10 μ M) after addition of hydrazine (2 equiv) with time interval.

recorded with change in time (Fig. 5). These results are satisfactory to indicate that CTF is an efficient sensor for hydrazine and it reacts chemodosimetrically with the probe. This experiment showed a rapid decrease in the fluorescence intensity at 545 nm within 50 s and a new peak at 500 nm increased regularly. The hydrazine induced reaction was completed within 180 s. We also studied the reaction kinetics of this reaction (Supplementary data, Fig. S1). The time vs. emission ratio (I_{500}/I_{545}) plot was obtained by using first order rate equation. We get the rate constant = k = slope × 2.303 = 20 × 10⁻³ s⁻¹.

To further understand the relationship between the structural changes of CTF and its complex with hydrazine and the optical response of CTF to hydrazine, a theoretical calculation was carried out by Density Functional Theory (DFT) and Time Dependent Density Functional Theory (TDDFT) with the B3LYP/6-31+G(d,p) method basis set using the Gaussian 03 program.

The optimized geometry and the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of CTF and its hydrazine complex are presented in Figure 6. UV– vis spectra of CTF and its hydrazine complex were calculated using



Figure 6. Energy diagrams of HOMO and LUMO orbitals of CFT and CTF-hydrazine complex calculated at the DFT level using a B3LYP/6-31+G(d,p) basis set.



Figure 7. Time-resolved fluorescence decay of CTF (Red), CTF+N₂H₄ (green), and prompt (black) (λ_{ex} = 450 nm).



Figure 8. Photographs of TLC plates after immersion in a CTF-acetonitrile solution (a and c) and after immersion in a CTF-N₂H₄-acetonitrile solution (b and d) taken in ambient light (left) and under hand-held UV light (right).



Figure 9. Change of absorbance of CTF after adding 2.0 equiv of each of the investigated guest analytes in CH₃CN at 485 nm.

the TDDFT method in acetonitrile medium. Calculated absorption peaks had agreed well with the experimentally observed peaks (Supplementary data, Table S1). In case of CTF, the transition from HOMO to LUMO and HOMO-2 to LUMO had contributed mainly to the excitation at 459 and 298 nm, respectively. For the CTF-N₂H₄, main absorption peaks in the short wavelength region were at 394 and 283 nm generated from the transition of HOMO to LUMO and HOMO-1 to LUMO, respectively (Supplementary data, Table S1).

A nano second time-resolved fluorescence technique has been adapted in order to examine the excited state behavior of our probe CTF sensor and its reaction based product with hydrazine in CH₃CN solvent (Fig. 7). According to the equations¹³ $\tau^{-1} = k_r + k_{nr}$, where $k_r = \Phi_f/\tau$, the radiative rate constant k_r and the total non-radiative rate constant k_{nr} of CTF and CTF–N₂H₄ species were

calculated. For CTF, $\tau = 0.646$ ns ($\varkappa^2 = 0.969$) and CTF+N₂H₄, $\tau = 2.867$ ns ($\varkappa^2 = 1.029$).

The fluorescence decay curves of CTF and the CTF–N₂H₄ compounds were fitted by utilizing the bi-exponential functions with the acceptable \varkappa^2 values (Supplementary data, Table S2). The changes in k_r and k_{nr} values are attributed to the reaction of hydrazine with CTF to form a new fluorescent compound CTF–N₂H₄.

Dip-stick is a very simple but very important experiment because it gives instant qualitative information without resorting to the instrumental analysis. In order to perform this experiment we prepared TLC plates which were further immersed into the solution of CTF (2×10^{-4} M) in acetonitrile, and then evaporating the solvent to dryness. We immersed the TLC plate in N₂H₄ (2×10^{-3} M) solution and then exposed it in air to evaporate the solvent. The color of the TLC plates changes from brownish-yellow to greenish yellow (Fig. 8). Now this experiment evokes a real time monitoring and it is devoid of using any instrumental analysis. Just by naked-eye detection and use of TLC plates we can easily investigate a qualitative instant detection of N₂H₄.

Selectivity and interference are the two very vital constraints to estimate the performance of a receptor. The interference of other competing analytes was investigated by the competition experiment which is demonstrated in Figure 9. When CTF is treated with 2.0 equiv of hydrazine in the presence of other analytes in the same concentration, the detection of hydrazine in the presence of other analytes is not troubled, that is, the interference in the detection of the hydrazine is not observed. So CTF can be used as a selective and sensitive sensor for the hydrazine.

In summary, in this Letter a coumarin functionalized fluorophore linked with trifluroacetyl acetone has been designed and synthesized for the chemodosimetric detection of hydrazine. The photophysical properties of CTF in CH₃CN solution were observed and the changes are remarkably different from those of other analytes. It shows a high selectivity toward hydrazine at the molecular level (solution) and in solid material (absorbed in TLC plates). The spectroscopic studies are further supported by DFT and TDDFT calculations. The detection limit of our probe CTF is in micro molar range.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.03. 041.

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