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Simple Michael acceptor type coumarin derived *turn-on* fluorescence probes to detect cyanide in pure water

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ABSTRACT

The present article describes design and synthesis of coumarin derived chemical reaction based chemodosimeter to recognize cyanide in aqueous medium. The Michael acceptor type coumarin derived probes **3** and **4** upon interaction with cyanide undergo Michael type nucleophilic addition reaction to form adducts in which fluorescence intensity was significantly enhanced, '*turn-on*' by the change in intramolecular charge transfer (ICT) mechanism. The nonfluorescent color of solutions changed to a naked-eye sensitive fluorescent blue (switched-on). Job's plot analysis revealed a 1:1 stoichiometry for the interaction between the probe and cyanide anion with a high detection limit.

Considering the importance of different anions in various chemical, industrial, and biological processes there is a considerable current interest in the development of anion sensing events that work in pure aqueous medium.[1,2] Among anions cyanide is highly toxic and its exposure to lungs, gastrointestinal track, and skin is responsible for various diseases in organisms.[3] The strong affinity of cyanide with the active site of cytochrome a_3 leads to eventual cell death.[4] Despite its acute toxicity cyanide finds common use in chemicals, polymers, and metal mining industries. The presence of cyanide in industrial waste is a matter of serious environmental concern to living beings.[3] Also cyanide is a chemical warfare agent which affects the ability of cells to utilize oxygen.[5] The World Health Organization (WHO) has set 0.07 mg/l (2.7 μM) as permissible level of cyanide in drinking water for a healthy life.[6]

While a variety of cyanide specific probes are known their use in aqueous solution is limited because the commonly known hydrogen bonding structural motifs fail to recognize cyanide more accurately in water.[5,7–11] In contrast to metal ions, structural feature and reactivity of anions play an important role to generate specific interactions with receptor molecules and the sensitivity of anions toward the micro environment makes their recognition more complex. Moreover, the charged cyanide anion has high solvation in water, so desolvation from nearby water molecules is a must to ensure strong anion-probe interaction, and a reversible chemosensor probe–cyanide complexation is thermodynamically less feasible.[12] As a result, there is considerable interest in the development of a readily available, simple-to-use, and an inexpensive method for the recognition of cyanide. Fluorescence based methods are promising because of added advantages of real-time low cost detection with high sensitivity and compatibility to biological systems.[14,15] Since, most of the known chemosensors for cyanide show fluorescence quenching in aqueous medium,[13a,13b] there is a great need of efficient systems which can detect cyanide through fluorescence enhancement, that is, '*turn-on*' response.

Several fluorescence based strategies have been explored[16] wherein chemical reaction based chemodosimeter[5] and displacement methods[17] have shown great success in detection of cyanide selectively in the environment of competitive anions, surpassing thermodynamic limitations for a cyanide–probe complexation in aqueous medium.[18] This can be easily achieved by using the inherent nucleophilicity and weak hydrogen bonding acceptability of cyanide.[8] Obviously, this would enhance cyanide-specific chemical response, and help to develop a desirable cyanide selective irreversible probe, a reaction-based chemodosimeter. Moreover, coumarin derived chemoreceptors exhibit structural specificity and their response toward various guests (like cation, anion, and biomolecules) varies in different microenvironments. So, one can plan a particular structural motif to recognize a specific target species.

Keeping these facts in mind we herein report the synthesis and characterization of a very simple, coumarin-derived intramolecular charge transfer (ICT) probe and its optoelectronic response toward different anions in aqueous medium. In the present design we have utilized the fluorescent coumarin molecule as a signaling unit and 2,4-dinitrophenyl hydrazine (DNP) moiety as a chromogenic

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charge modulator in which the presence of the electron withdrawing nitro (*–NO*$_2$) substituent is expected to facilitate relay of charge transfer upon interaction with anions. Secondly, the available conjugated *enone* function of the coumarin unit will encourage a Michael type nucleophilic addition reaction to induce a cyanide specific response in aqueous medium.

The synthetic route[19] to obtain coumarin-derived probes, **3** and **4** is shown in Scheme 1. Salicylaldehyde and ethylacetoacetate were refluxed in ethanol in the presence of a catalytic amount of piperidine. The intermediate 3-acetylchromen-2-one, **2** was isolated and was refluxed in ethanol subsequently with 2,4-dinitrophenyl hydrazine (DNP) and phenylhydrazine to afford compounds **3** and **4**, respectively, in good yields (~70%). Compounds were characterized by ^{1}H, ^{13}C NMR, IR, and ESI-Mass data (Figs. S1–S9). The compounds **3** and **4** are structurally different in the presence and absence of electron withdrawing nitro groups.

The optoelectronic behavior of **3** was examined in aqueous medium in the absence and presence of different anions. The electronic transition spectra of **3** (10 μM) in water exhibited a low energy (n→π*) intramolecular charge transfer (ICT) band at 380 nm ($\varepsilon = 1.85 \times 10^4\ M^{-1}\ cm^{-1}$) and a high energy band at ~265 nm ($\varepsilon = 2.0 \times 10^4\ M^{-1}\ cm^{-1}$) (Fig. 1, inset). The emission spectra of **3** ($\Phi_3 = 0.0023$) upon excitation at 380 nm displayed a very weak broad emission band at ~450–500 nm (Fig. 1). To examine the affinity of **3** toward different anions, absorption and emission spectra have been acquired. Probe **3** has shown relatively high affinity for cyanide in which the electronic transition band, centered at 380 nm decreased with a blue shift of ~10–17 nm to appear at 363 nm ($\varepsilon = 1.1 \times 10^4\ M^{-1}\ cm^{-1}$) (Fig. S18). Interestingly, emission spectra of **3** upon interaction with cyanide displayed enhanced fluorescence, '*turn-on*' at 495 nm, and nonfluorescent color of the solution changed to fluorescent blue. Similarly, the distinct low and high energy absorption bands of probe **4** (10 μM), at 377 nm ($\varepsilon = 3.0 \times 10^4\ M^{-1}\ cm^{-1}$) and 278 nm ($\varepsilon = 6.8 \times 10^4\ M^{-1}\ cm^{-1}$), respectively, upon interaction with different anions displayed hypochromic (at 372 nm) and blue shifts (appeared at 368 and 267 nm ($\varepsilon = 3.6 \times 10^4\ M^{-1}\ cm^{-1}$)) with CN$^-$ (Fig. S18). Moreover, probe **4** ($\Phi_4 = 0.0012$) upon excitation at 378 nm exhibited very weak emission, almost similar to probe **3** which upon interaction with tested anions showed high affinity for CN$^-$ in which relative fluorescence intensity enhanced, '*turn-on*' significantly (~10 times) at 473 nm and the color of the solution became fluorescent blue–green (switched-On) (Fig. 2). The other tested anions (100 equiv) such as F$^-$, Cl$^-$, Br$^-$, I$^-$, SO_4^{2-}, CO_3^{2-}, SCN$^-$, AcO$^-$, CN$^-$, N^{3-}, S^{2-}, and $H_2PO_4^-$ (as their sodium salt) failed to exhibit considerable change in the optoelectronic behavior of probes (Figs. 1 and S19). The interference studies were performed to understand the selectivity of probes toward CN$^-$. The absorption and emission spectra remained unchanged upon addition of the tested anions to a solution of probes containing CN$^-$. Thus, confirming the affinity of probes for CN$^-$ in aqueous medium (Fig. S18) through the chemodosimeter approach in which cyanide possibly reacted with the *enone* function of the probe to form Michael adducts, **6** and **7** (Scheme 2) in the medium.

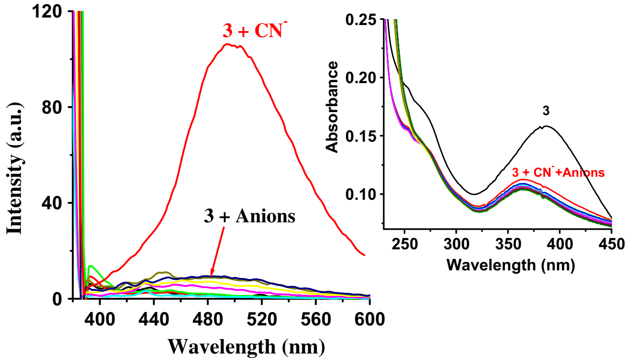


Figure 1. Emission spectra of **3** (10 μM) upon addition of different anions (100 equiv) in aqueous medium. Inset: Interference absorption spectra upon the addition of different anions (100 equiv) to a solution of **3-CN**$^-$.

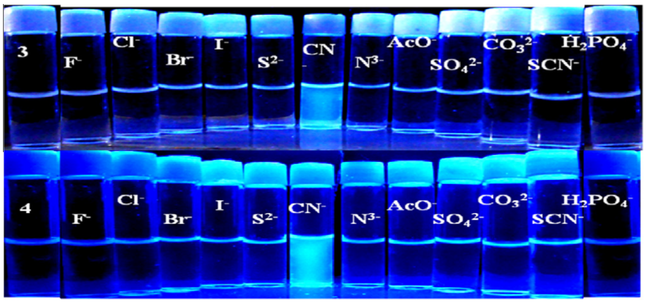
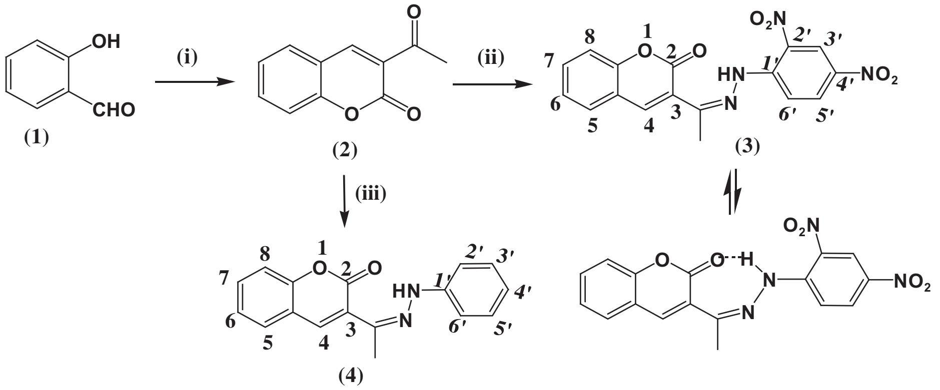


Figure 2. Fluorimetric color changes of **3** and **4** (10 μM) with different anions (0–100 equiv) in aqueous medium.

The binding affinities of **3** and **4** with CN$^-$ have been examined through the titration experiments. Upon gradual addition of CN$^-$ (0–100 equiv) to the solutions of both probes the absorption band of **3** centered at 380 nm decreased with hypsochromic shift and the molar absorptivity of the high energy band at 253 nm increased concomitantly. However, in the case of **4** the band at 377 nm decreased gradually while the band at 278 nm disappeared and a new band appeared at 267 nm concomitantly. Notably, an isosbestic point appeared at 266 nm in the case of **3** indicating the



Scheme 1. Reagents and conditions: (i) Ethylacetoacetate/piperidine/ethanol/reflux, (ii) 2,4-dinitrophenylhydrazine/ethanol/reflux, (iii) phenylhydrazine/ethanol/reflux.