A ratiometric chemodosimeter for highly selective naked-eye and fluorogenic detection of cyanide

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HIGHLIGHTS

- A simple indole-based chemodosimeter specific for CN^- has been developed.
- The sensor exhibits colorimetric and ratiometric fluorescent response to CN^-.
- An ESICT mechanism plays a key role in the sensing properties.

GRAPHICAL ABSTRACT
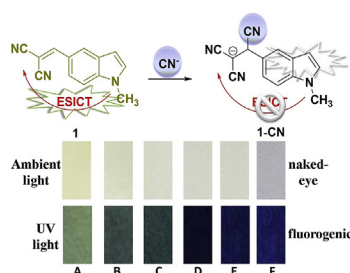
ABSTRACT

A simple indole-based chemosensor (**1**) with a very low molecular weight of 207 g mol^{-1} has been synthesized for the highly reactive and selective detection of CN^- in aqueous media, even in the presence of other anions, such as F^-, Cl^-, Br^-, AcO^-, S_2^-, SCN^-, NO_2^-, NO_3^-, CO_3^-, BzO^-, $H_2PO_4^-$, and HSO_4^-. The sensor achieves rapid detection of cyanide anion in 2 min, and the *pseudo*-first-order rate constant is estimated as 1.576 min^{-1}. The colorimetric and ratiometric fluorescent response of the sensor to CN^- is attributable to the addition of CN^- to the electron-deficient dicyanovinyl group of **1**, which prevents intramolecular charge transfer. The sensing mechanism is supported by density functional theory and time-dependent density functional theory calculations. Moreover, sensor **1** exhibits both high accuracy in determining the concentration of CN^- in real samples and **1**-based test strips can conveniently detect CN^- without any additional equipment. The detection limit of the sensor **1** (1.1 μM) for cyanide is lower than the maximum permissible level of CN^- (1.9 μM) in drinking water.

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1. Introduction

The recognition and sensing of anions is an area of growing interest in supramolecular chemistry due to its important role in a wide range of chemical, biological, environmental, and clinical applications [1]. Among various anions, cyanide (CN^-) is one of the most studied anions because of its lethal effect on living organisms

and the environment [2]. Nevertheless, CN^- is widespread in industrial processes, such as gold mining, electroplating, metallurgy, and the synthesis of nylon, fibers, and resins [3]. Thus, it is highly desirable to develop selective, sensitive, simple, low-cost, colorimetric and fluorometric chemosensors for detecting CN^- [4].

Optical sensors for CN^- [5,6], in which a change in the absorption and/or fluorescence spectra is monitored, have been continually investigated due to their desirable features including simplicity, high sensitivity, and potential for *in vivo* imaging [7]. Fluorescence-based detection normally depends on the intensity change at a single wavelength, which is considered more efficient

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than absorption spectroscopy due to its high sensitivity and easy implementation under diverse environmental conditions. However, the signal output could be easily overshadowed by the background noise of the sample media. To overcome this shortcoming, ratiometric fluorescent sensing has been used, enabling measurement of the relative emission intensities at two different wavelengths, which can serve as an internal reference for self-correction; hence, the reliability of the measurements is significantly enhanced [8].

Many different mechanisms for detecting CN⁻ have been developed, including those based on excited-state intramolecular charge transfer (ESICT) [9,10], excited-state intramolecular proton transfer (ESIPT) [11,12], ESICT—ESIPT switching [13], supramolecular self-assembly [14], hydrogen-bonding interactions [15], complex formation with metal ions and boron derivatives [16], and attachment with quantum dots [17]. Furthermore, reaction-based chemosensors [18,19] for CN⁻ have been used due to their high selectivity over other anions, as well as because they can effectively reduce the interference of hydrogen bonding and acidity of the media. Effective optical sensors that are based on this method have been synthesized using oxazines [20,21], squaraine [22], acridium salts [23], dicyanovinyl derivatives [24—28], calix[4]pyrrole derivatives [29], coumarin derivatives [30,31], benzyl derivatives [32,33], and trifluoroacetophenone derivatives [34]. However, sensors—especially those with dual colorimetric and ratiometric fluorescent signal outputs—have complicated structures with high molecular weights [4,5,35—40]. For practical applications, it is necessary to develop CN⁻ sensors that are simple, affordable and possess selective and sensitive signaling mechanisms. Therefore, we are the first to report a simple low-cost 1-methylindole-malononitrile conjugate, **1** (Mw = 207 g mol⁻¹), as a colorimetric and ratiometric fluorescent probe, which can sense CN⁻ with specific selectivity and high sensitivity in aqueous media based on ESICT. To the best of our knowledge, this probe is the simplest colorimetric and ratiometric fluorescent cyanide-selective chemodosimeter with the lowest molecular weight that has ever been reported [4,5].

2. Experimental

2.1. General information

The starting materials, including 1-methylindole-5-carboxaldehyde (**2**), malononitrile, triethylamine, tetrahydrofuran (THF) and methanol (MeOH) were purchased from Merck, ACROS and Sigma—Aldrich. Reagent grade solvents were used for synthesis, and spectroscopy grade solvents were used for spectra measurements. Column chromatography was performed using silica gel Merck Kieselgel *si* 60 (40—63 mesh). ¹H and ¹³C NMR spectra were recorded in deuterated tetrahydrofuran (THF-d_8) on a Bruker 400 MHz spectrometer. Mass spectra were recorded on a VG70-250S mass spectrometer. The absorption and emission spectra were measured using a Jasco V-570 UV—vis spectrophotometer and Hitachi F-7000 fluorescence spectrophotometer, respectively.

The kinetics of the reaction was followed by UV/Vis absorption spectroscopy. A freshly prepared cyanide solution was added in excess (25 equiv.) to the sensor (**1**) solution (THF/H₂O (9:1, v/v, containing 0.01 M HEPES, pH = 7.3)), and the absorbance was monitored with time. The rate constant was calculated from the following equation: $[A_t] = [A_0] e^{-kt}$, in which $[A_0]$ = initial concentration of A, $[A_t]$ = concentration of A at time t, k = rate constant, and t = elapsed time.

The test strips were prepared by immersing filter papers (2 × 1 cm²) in the THF/H₂O solution of **1** (1.0×10^{-6} M) and subsequently drying them in air. The tetrabutylammonium cyanide stock solution of 2.5×10^{-5} M was diluted to different

concentrations with deionized water, then, test strips coated with **1** were immersed in aqueous solutions of CN⁻ with different concentrations for colorimetric/fluorimetric response studies.

The Gaussian 03 program was used to perform the ab initio calculation of the molecular structure [41]. Geometry optimizations for compounds **1**, **1-CN**, and 1-methylindole were performed using density functional theory (DFT) at the B3LYP/6-31G** level. Vibrational frequencies were also performed to check whether the optimized geometrical structures for all compounds were at energy minima, transition states, or higher order saddle points. After obtaining the converged geometries, the TD-B3LYP/6-31G** was used to calculate the vertical excitation energies.

2.2. Synthesis and characterization

Compound **1** was synthesized via stirring a mixture of solution of **2** (159 mg, 1.0 mmol), malononitrile (330 mg, 5.0 mmol), a drop of triethylamine, THF (10 mL) and MeOH (5 mL) at room temperature for 2 h. The solution was extracted with ethyl acetate—water. Further purification via column chromatography (silica-gel column, hexane/ethyl acetate = 1/1) resulted in **1** (195 mg, 94%). Characterization data: **1**: ¹H NMR (400 MHz, C₄D₈O) δ 8.23 (s, 1H), 8.14 (d, J = 4.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 3.2 Hz, 1H), 6.64 (d, J = 3.2 Hz, 1H), 3.58 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.09, 139.76, 131.56, 128.79, 126.87, 123.78, 123.04, 115.00, 113.32, 110.40, 103.69, 33.17; MS (FAB) *m/z* (relative intensity) 208 (M + H⁺, 100); HRMS calcd. for C₁₃H₁₀N₃ 208.0875, found 208.0871.

3. Results and discussion

3.1. Design and synthesis of sensor **1**

Sensor **1** consists of an electron-donating 1-methylindole moiety, in which a dicyanovinyl group is attached to act as both an electron-accepting group to induce intramolecular charge transfer (ICT) and a cyanide sensing unit (Scheme 1). The electrophilic nature of the dicyanovinyl group can be modulated by CN⁻, which interrupts the π-conjugation, the role of which in the sensing mechanism can be clarified by a comparison with the spectrum of 1-methylindole [42]. The high yield synthesis of **1** is readily prepared through a condensation of aldehyde **2** with malononitrile in the presence of triethylamine. Detailed synthetic procedures and product characterizations are provided in the Experimental section and Supplementary data.

3.2. Optical properties of sensor **1**

The absorption and emission spectra of **1** in solvents of varying polarity are shown in Fig. 1 and pertinent photophysical data are given in Table S1. Sensor **1** shows two absorption bands at ~288 and 369 nm; the former is attributed to the π—π* transition and the latter to an ICT transition. This viewpoint can be further supported by a theoretical approach based on the density functional theory (Table S2). Unlike the small shift in absorption spectra, the fluorescence spectra of **1** are largely red-shifted with any increase in the solvent polarity, which indicates strong ICT characteristics for the excited states of **1** (Fig. S1). The fluorescence quantum yields of ICT emission in **1** are relatively high even in polar solvents (Φ > 0.1). This observation is attributed to the planarity and high rigidity of the compound as well as the change of the double bond in indole to the dicyanovinyl motif after the excitation, which gives rise to a rigid chromophore and decreases the likelihood of nonradiative relaxation pathways.