Tetrahedron Letters 50 (2009) 5139–5141

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Cyanide sensing via metal ion removal from a fluorogenic BODIPY complex

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ARTICLE INFO

Article history:
Received 21 May 2009
Revised 16 June 2009
Accepted 26 June 2009
Available online 2 July 2009

ABSTRACT

We report a highly selective and sensitive reversible cyanide sensor operating in the ‘turn-off-on’ mode via decomplexation of Cu(II) ions from a brightly fluorescent boradiazaindacene derivative. The sensor is reversible as the emission signal originates from the dynamic equilibration of dipicolylamine–Cu(II) and tetracyanocuprate complex ions.

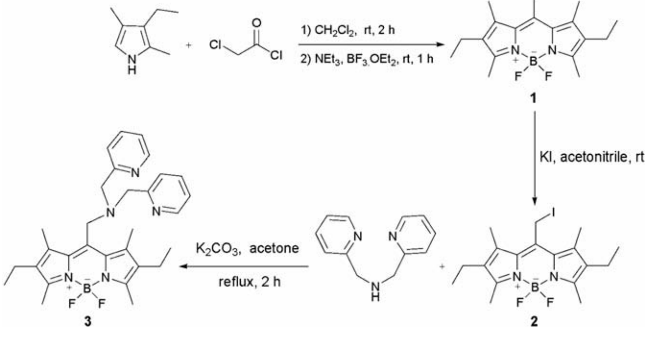
Fluorescent chemosensors capable of detecting toxic and lethal anionic species are of significant interest in chemistry, biology, medicine and in relation to environmental issues.[1] Cyanide is one of the most lethal poisons known. The highest level of cyanide ions allowed in drinking water is lower than 1.9 μM.[2] As assessed by recent studies, victims of fire disasters have 20–30 μM blood cyanide levels.[3] Due to its widespread use in the chemical industry in the synthesis of nitrile derivatives, nylon and acrylic polymers, and in electroplating and gold mining, the development of highly selective chemosensors for detection of cyanide concentrations lower than 30 μM in water or water-organic solvent mixtures is an important task in supramolecular photochemistry. There have been a number of fluorescent chemosensors and chemodosimeters reported for selective sensing of cyanide.[4] In addition to these coordination or covalent bond-based sensors, there are a few systems which utilize the strong affinity of cyanide ions for transition metals.[5] In such systems, complexation of cyanide with a transition metal results in a change in the photophysical properties of the dye and provides a method for detection.

Boradiazaindacene (BODIPY) dyes, due to the emergence of new synthetic strategies for their derivatization, have received much attention in recent years.[6] High quantum yields (typically 0.6–1.0), large extinction coefficients (60,000–80,000 M^{-1} cm^{-1}) and the photostability of these fluorophores insure their diverse applications in the fields of chemosensors,[7] logic gates,[8] light harvesting systems,[9] energy transfer cassettes,[10] photodynamic therapy,[11] and dye-sensitized solar cells.[12] 8-Halomethyl-BODIPY dyes, among other members of this class, can be easily converted into new derivatives via a simple nucleophilic substitution reaction at the *meso* position.

Based on these derivatives, several ‘turn-on’ metal ion and pH sensors have been designed and studied in recent years.[7b,13]

Herein we report the design and synthesis of a new BODIPY derivative operating in ‘turn-off-on’ mode for selective and sensitive detection of cyanide ions in a water-organic solvent mixture. The synthesis of our target molecule is shown in Scheme 1. 4,4-Difluoro-8-chloromethyl-1,3,5,7-tetramethyl-2,6-diethyl-4-bora-3a,4a-diaza-*s*-indacene **1** was obtained in 16% yield by reaction of 3-ethyl-2,4-dimethylpyrrole with chloroacetyl chloride at room temperature in dichloromethane and subsequent addition of triethylamine and boron trifluoride diethyletherate.[7b] The more reactive 8-iodomethyl-BODIPY **2** was prepared by treatment of compound **1** with KI in acetonitrile at room temperature. Compound **2** was then reacted with di(2-picolyl)amine in the presence of K_2CO_3 in acetone at reflux to afford the target molecule **3** in 48% isolated yield (see Supplementary data for the structural characterization of **3**).

Unlike related 8-aminomethyl-BODIPY derivatives,[13] compound **3** is a fluorescent molecule having a relatively high quantum yield ($\varphi_F = 0.24$) (Supplementary data). This new probe shows an absorption wavelength-ratiometric response to Cu(II) ions. Upon addition of Cu(II) ions (0.2–2.0 μM in THF) to a solution of **3** (1.0×10^{-6} M



Scheme 1. Synthesis of chemosensor **3**.

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0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.06.117

in THF), due to **3**+Cu(II) complex formation ($K = 5.35 \times 10^6\ M^{-1}$), the absorption peak at 537 nm decreased and a new absorption peak corresponding to the complex appeared at 565 nm (Supplementary data). This pronounced bathochromic shift is in accordance with previous literature, since electron-withdrawing substituents at the 8-position (*meso*) of the BODIPY chromophore results in red shifts in both the absorption and emission spectra. The transformation of an electron-donor aminomethyl substituent into a metal-complexed amine substituent, possibly with electron-withdrawing character, is expected to yield such a red shift. An isosbestic point at 548 nm clearly indicates the formation of single discrete species during the titration experiments. Complete quenching of the fluorescence takes place by the addition of Cu(II) ions (2 μM in THF) to the dye solution in THF (Supplementary data). The observed quenching by Cu(II) ions is hardly surprising, since Cu(II) is a redox-active, open-shell transition metal ion. The fact that the BODIPY derivative **3** demonstrates a bright fluorescence emission before metal-ion-induced quenching may require an explanation. Photoinduced electron transfer (PET) processes in BODIPY dyes have been studied previously.[14] It appears that the substituents on the BODIPY core have a very strong influence on the direction and magnitude of the PET process. We know that a BODIPY derivative which lacks ethyl substituents at the 2- and 6-positions, and otherwise identical to compound **3**, shows a very strong PET quenching. Ethyl substituents not only cause a red shift of the absorption spectrum by 30 nm, but apparently do so by raising the HOMO energy level significantly, such that there is no PET in compound **3**.

To determine its cyanide sensing ability, compound **3** was converted into its non-fluorescent 'off-mode' (**3**+Cu(II) complex) by the addition of 2.0 μM Cu(II) ions (20.0 μL, 3.0×10^{-4} M in THF, in the form of a triflate salt) to its solution (3.0 mL, 1.0×10^{-6} M in THF) in a quartz cell. A solution of NaCN (1.0×10^{-3} M in deionized water) was added in portions (total volume; 10.0–60.0 μL: 3.3–20.0 μM) and after each addition, the absorbance and emission spectra (λ_{ex} = 530 nm) were recorded. As expected from the very high stability constant of the tetracyanocuprate(II) complex ion, the addition of cyanide to the copper(II) complex form of **3** released the free, fluorescent 'on-mode' of the chemosensor and absorption wavelength-ratiometric behaviour in the reverse direction was observed including an isosbestic point at 549 nm (Fig. 1).

While the absorption band at 565 nm decreased, the absorption band due to the free form of **3** at 537 nm increased. To account for the quenching effect of the added water on the emission spectra during the titrations, we prepared a blank solution (3.0 mL, 1.0×10^{-6} M) in THF containing 60.0 μL of deionized water and obtained a reference emission spectrum (Fig. 2, top line).

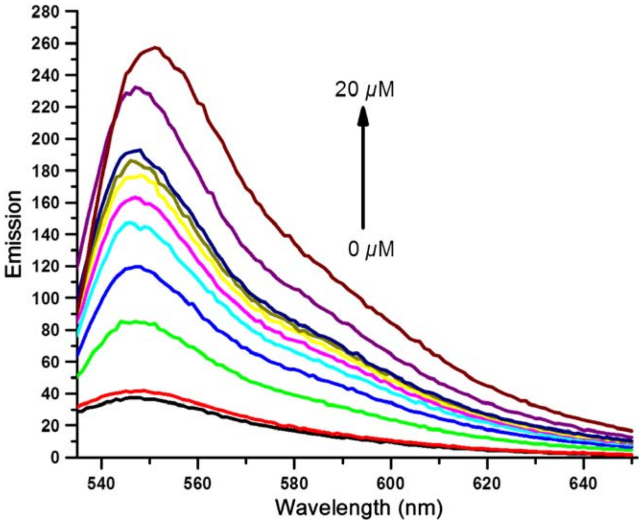

Figure 2. Emission spectra of compound **3**+Cu(II) in the presence of increasing CN⁻ concentrations (0, 3.3, 6.7, 10.0, 11.7, 13.3, 15.0, 16.7, 18.3 and 20.0 μM).

Figure 2 indicates that starting with very low concentrations of cyanide, an increase in the emission intensity occurred with a small hypsochromic shift (5 nm). Compared to the reference emission intensity, nearly 90% of the emission was recovered upon addition of 20.0 μM of cyanide and this result is the basis for the very sensitive 'turn-on' behaviour of our cyanide sensor at the lowest limit of blood cyanide concentrations found in fire victims. In order to ascertain the selectivity of our **3**+Cu(II) complex system for cyanide ions, we repeated the titration experiments with other, potentially interfering anions, including F^-, Cl^-, Br^-, I^-, AcO^-, NO_3^-, ClO_4^-, HSO_4^- and OH^- (Figs. 3 and 4).

As indicated by the relative emission intensities (Fig. 4), the addition of I^- and NO_3^- resulted in some degree of emission recovery, however, they did not interfere significantly with the selective sensing of cyanide. To further explore the performance of our system, we ran interference experiments with some of the interfering ions. As expected, the fluorescence intensity in the presence of 20.0 μM cyanide did not change remarkably in the presence of 1.0×10^{-4} M solutions of other ions (Supplementary data). Thus,

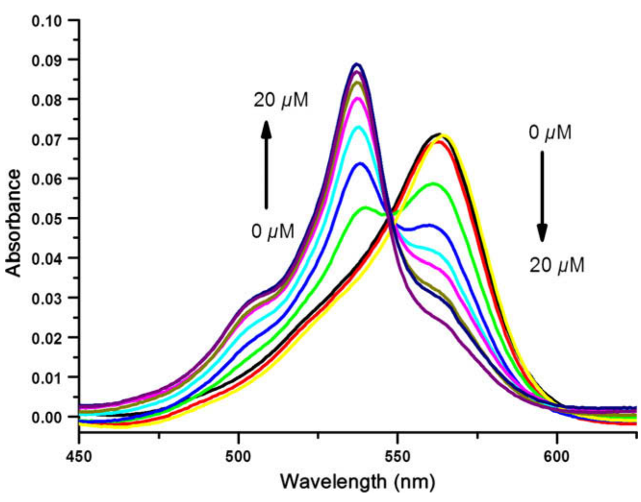

Figure 1. Absorbance spectra of compound **3**+Cu(II) in the presence of increasing CN⁻ concentrations (0, 3.3, 6.7, 10.0, 11.7, 13.3, 15.0, 16.7, 18.3 and 20.0 μM).

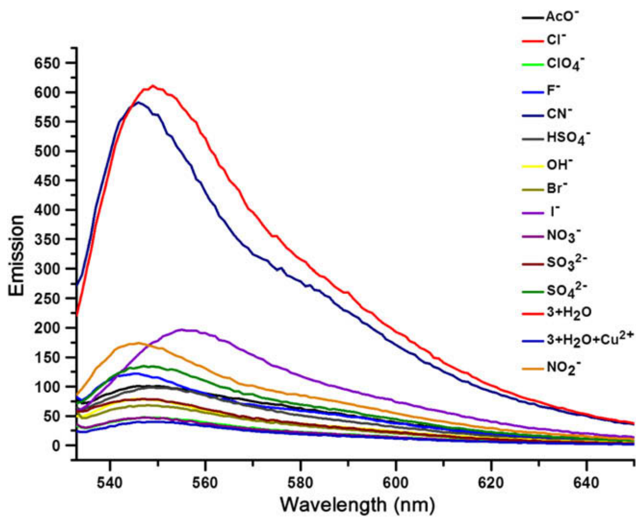

Figure 3. Emission spectra of compound **3**+Cu(II) in the presence of different anions [anion concentrations at 50 μM (λ_{ex} = 530 nm)].

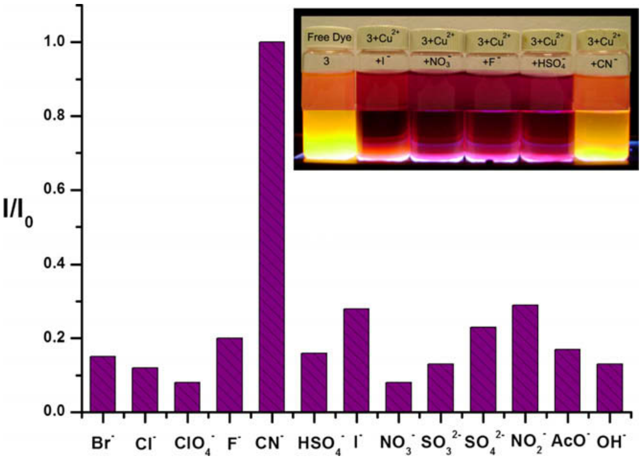

Figure 4. Emission ratios for compound **3**+Cu(II) obtained in the presence of different anions. The chemosensor was excited at 530 nm and the ratio of emission data at 547 nm was calculated. Inset shows the appearance of the solutions under ambient light (top) and under a hand-held UV-lamp (360 nm).

in this study, we have successfully employed the 'turn-off-on' sensing principle for the sensitive and selective probing of cyanide ions by using the ability of Cu(II) ions to quench the fluorescence of a novel BODIPY-dipicolylamine derivative. This simple system was shown to detect efficiently cyanide ion concentrations as low as 20.0 μM as an upper limit.

The sensor is reversible, as the emission signal originates from the dynamic equilibration of dipicolylamine–Cu(II) and tetracyanocuprate complex ions. While the sensor system described here requires co-solvents (THF-deionized water), as a reliable sensing method,[5e,f,j] it can detect cyanide concentrations as low as 0.66 μM in water. In addition to this apparently low detection limit, as can be seen from the inset in Figure 4, the absorption wavelength-ratiometric, hence colorimetric, response towards cyanide is another merit of the sensor. It is evident that the same sensing principle would be in effect in 100% aqueous solutions as long as the dye component is freely soluble in water.

Acknowledgements

The authors gratefully acknowledge support from the Turkish Scientific and Technical Research Council (TUBITAK). R.G. thanks TUBITAK for a graduate scholarship.

Supplementary data

Supplementary data (experimental details, ^1H and ^{13}C NMR spectra, additional spectroscopic data, absorbance and emission spectra of compound **3** in the presence of increasing Cu(II) concentrations) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.117.

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