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Anion Dual Mode Fluoro-Chromogenic Chemosensor Based on a BODIPY Core †

Raquel C. R. Gonçalves, Mathilde L. Boland, Susana P. G. Costa and M. Manuela M. Raposo *

Centre of Chemistry, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal
* Correspondence: mfox@quimica.uminho.pt
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Abstract: Herein, we report the synthesis and chromo-fluorogenic behavior of a BODIPY derivative. The BODIPY core was functionalized with a phenyl group at the *meso*-position and a formyl group at position 2 introduced through the Vilsmeier Haack reaction. The compound showed an absorption band at 492 nm and an emission band at 508 nm, with a $\Phi_F = 0.84$. The evaluation of the chemosensing ability of the BODIPY was investigated in the presence of several anions with environmental and biomedical relevance, and a simultaneous colorimetric and fluorimetric response was observed for cyanide and fluoride anions.

Keywords: colorimetric/fluorimetric probe; anion detection; BODIPY derivative; cyanide; fluoride

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1. Introduction

Numerous efforts have been devoted to the design of optical chemosensors for application in several research topics such as biochemistry, biomedical, food and environmental sciences. In particular, the recognition and detection of anions are of major interest considering their critical role in biological, environmental, and industrial fields, as they may become harmful and toxic at concentrations outside of the expected normal range [1–3].

BODIPY derivatives have emerged as a remarkable class of chemosensors for molecular recognition and biological fluorescent labeling. BODIPYs show notable properties, such as sharp absorption and emission patterns, high molar absorptivity, high fluorescence quantum yield, and good photostability under physiological conditions. The versatile chemical modification of the BODIPY core is a notable advantage that enables not only the optimization of its photophysical characteristics but also the introduction of selective recognition sites for a greater target-binding affinity [4–6].

As an extension of the work developed in our research group [7–11], we report a BODIPY derivative bearing a phenyl group at the *meso* position and a formyl group at position 2 of the BODIPY core for the simultaneous colorimetric and fluorimetric detection of CN^- and F^-. The recognition behavior of the BODIPY derivative was studied in an aprotic solvent (acetonitrile) in the presence of different anions, and the UV-vis and fluorescence spectroscopic titrations demonstrated a decrease in the absorption band intensity and a fluorescence quenching upon interaction with CN^- and F^-.

2. Materials and Method

All of the reagents were purchased from Sigma-Aldrich (St. Louis, MO, USA), Acros (Geel, Belgium) and Fluka (Buchs, Switzerland) and used as received. TLC analyses were carried out on 0.25 mm-thick pre-coated silica plates (Merck Fertigplatten Kieselgel $60F_{254}$) and the spots were visualized under UV light. Chromatography on silica gel was carried out on Merck Kieselgel (230–400 mesh).

NMR spectra were obtained on a Bruker Avance III 400 at an operating frequency of 400 MHz for ^1H at 25 °C, using the solvent peak as an internal reference. All of the chemical

shifts are given in ppm using δ_H Me_4Si = 0 ppm as a reference. The synthesis of BODIPY derivatives **1** and **2** has been reported earlier [12,13]. UV-visible absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer (Shimadzu Europa GmbH, Duisburg, Germany). Fluorescence spectra were collected using a Horiba FluoroMax-4 spectrofluorometer (HORIBA Europe GmbH, Darmstadt, Germany). The relative fluorescence quantum yield was calculated using a 1×10^{-5} M solution of Rhodamine 6G in ethanol as a reference (Φ_F = 0.95) [14,15].

2.1. Synthesis of the BODIPY Derivative **2**

A mixture of DMF (22 mmol) and $POCl_3$ (18 mmol) was stirred for 5 min at 0 °C under a N_2 atmosphere. Once the mixture reached room temperature, it was stirred for 30 min. Then, BODIPY precursor **1** (0.139 mmol) dissolved in 1,2-dichloroethane (13.5 mL) was added dropwise. The reaction mixture was then heated for 2 h at 50 °C. After cooling, the solution was poured slowly into 50 mL of saturated sodium bicarbonate solution at 0 °C and stirred for 30 min at room temperature. Ethyl acetate (20 mL) was added to the reaction mixture, and the resulting organic layer was washed with water (2×50 mL). The organic layer was dried with anhydrous $MgSO_4$, filtered, and the solvent was evaporated. The crude residue was purified through a silica gel chromatography column, using dichloromethane as eluent. The product (Figure 1) was obtained as a dark red solid (0.045 g, 91%).

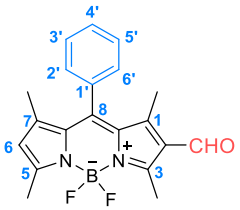


Figure 1. Structure of BODIPY derivative **2**.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 3H, CH_3-7), 1.66 (s, 3H, CH_3-1), 2.62 (s, 6H, CH_3-5), 2.83 (s, 3H, CH_3-3), 6.16 (s, 1H, H-6), 7.27–7.31 (m, 2H, H-3′ and H-5′), 7.53–7.55 (m, 3H, H-2′, H-4′ and H-6′), 10.01 (s, 1H, CHO) ppm.

2.2. Preliminary Chemosensing Studies of BODIPY Derivative **2**

The evaluation of the BODIPY derivative **2** as an optical chemosensor was carried out in the presence of several anions (HSO_4^-, NO_3^-, $H_2PO_4^-$, CN^-, BzO^-, ClO_4^-, Br^-, F^-, I^-, and $CH_3CO_2^-$) with environmental and biomedical relevance. The solution of the BODIPY derivative was prepared in acetonitrile at a final concentration of 1×10^{-5} M, and the solutions of the anions were prepared in acetonitrile at a concentration of 1×10^{-2} M. The preliminary study was performed by the addition of 50 equivalents of each anion to the solution of the BODIPY derivative.

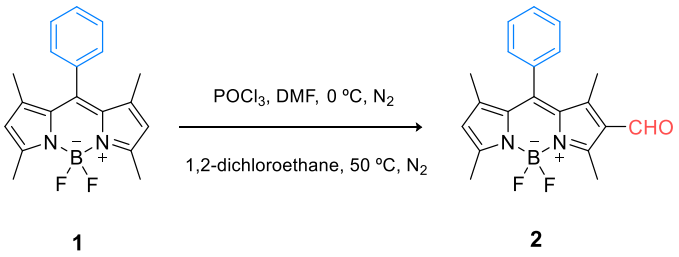
The spectrophotometric and spectrofluorimetric titrations were performed for the anions, which induced a colorimetric and/or fluorimetric response in the preliminary study. The solution of BODIPY derivative **2** and the anions was prepared as in the previous study. A certain number of equivalents (eq) of each anion were successively added to the compound's solution, and the absorption and/or fluorescence spectra were plotted after each addition.

3. Results and Discussion

3.1. Synthesis and Photophysical Characterization of BODIPY Derivative **2**

The BODIPY derivative **2** was synthesized through the Vilsmeier–Haack formylation reaction of the BODIPY precursor **1**, *meso*-substituted with a phenyl group, using dimethylformamide (DMF) and phosphorylchloride ($POCl_3$) as Vilsmeier reagent in 1,2-

dichloroethane (Scheme 1). The pure BODIPY derivative functionalized with a formyl group at position 2 was obtained as a dark red solid with 91% yield after chromatography.



Scheme 1. Synthetic route for BODIPY derivative **2.**

The ^{1}H spectrum of the compound was in accordance with the literature [13] and confirmed the presence of a formyl group at position 2 of the BODIPY core, with the appearance of a singlet at δ = 10.01 ppm due to the C*H*O proton.

The photophysical properties of BODIPY derivative **2** were investigated in acetonitrile solution. The compound showed an intense absorption band (log ε = 4.91) at 492 nm and an emission band at 508 nm. The relative fluorescence quantum yield determined using Rhodamine 6G as a reference was found to be 0.84.

3.2. Chemosensing Studies of BODIPY Derivative **2**

The evaluation of the BODIPY derivative **2** as a chemosensor was carried out in acetonitrile in the presence of selected anions with biological and environmental relevance anions (HSO_4^-, NO_3^-, $H_2PO_4^-$, CN^-, BzO^-, ClO_4^-, Br^-, F^-, I^- and $CH_3CO_2^-$).

As shown in Figure 2, the solution of the BODIPY derivative **2** displayed a perceptible color change in the presence of fluoride (F^-) and cyanide (CN^-), from yellow to light pink, respectively.

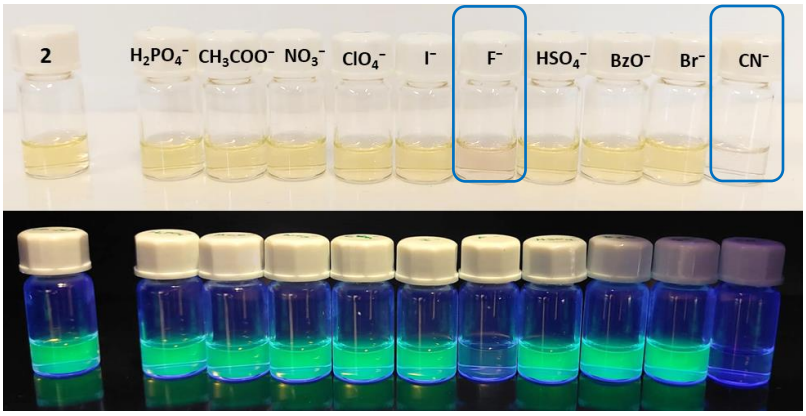


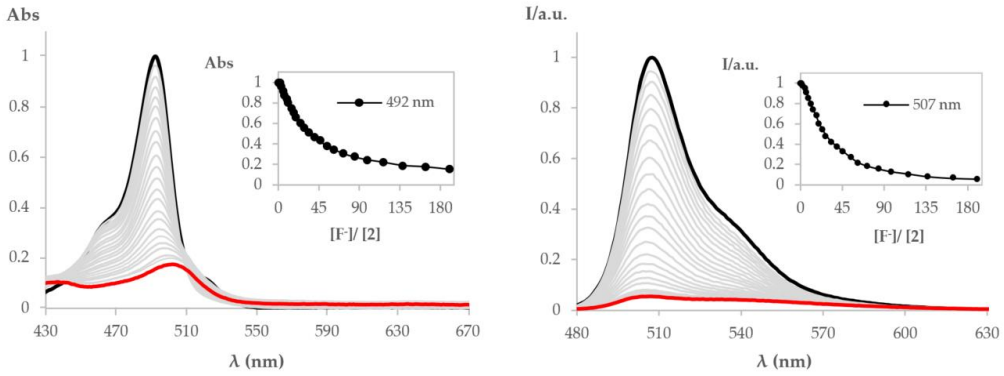
Figure 2. Preliminary evaluation of BODIPY derivative **2** as colorimetric (**top**) and fluorimetric (**bottom**, visualized under a UV lamp at 365 nm) chemosensor in the presence of several anions (50 equivalents) in acetonitrile solution.

Furthermore, analyzing the same solutions under a UV lamp at 365 nm, it was observed that the inherent BODIPY's fluorescence emission is quenched upon interaction only with F^- and CN^-.

Considering the preliminary results from the chemosensing study, where both colorimetric and fluorimetric responses were observed, spectrophotometric and spectrofluorimetric titrations were performed in acetonitrile with F^- and CN^-.

As shown in Figure 3a, BODIPY **2** has a characteristic absorption band centered at 492 nm in acetonitrile solution; however, the addition of increasing amounts of F^- induced a decrease in the BODIPY's absorption band. Simultaneously, the emission spectra (Figure 3b)

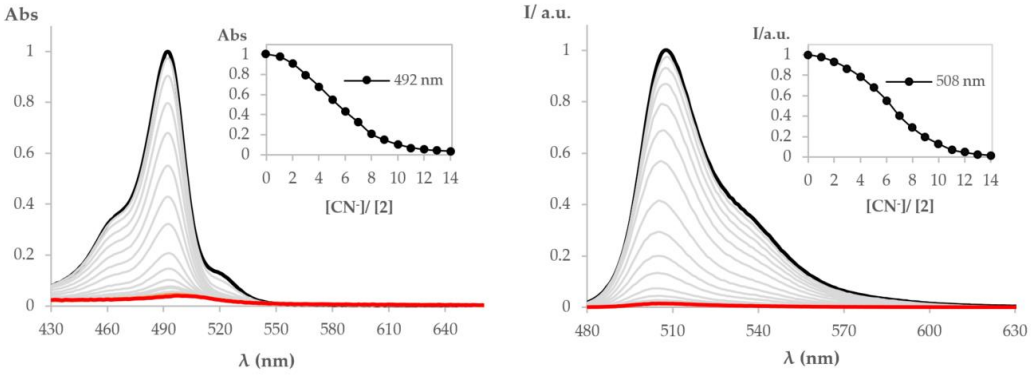
suffered considerable alterations, where the intensity decreased progressively upon the addition of the anion, achieving a plateau with 180 equivalents.



(**a**) (**b**)

Figure 3. (**a**) Spectrophotometric and (**b**) spectrofluorimetric titration spectra of BODIPY derivative **2** upon addition of increasing quantities of F^- (0 eq.—black line, to 190 eq.—red line) in acetonitrile. Inset: normalized absorbance and emission intensities at 492 nm and 507 nm, respectively, as a function of $[F^-]/[2]$.

In Figure 4a, it is shown that the absorbance with a maximum peak at 492 nm is progressively decreased with the gradual addition of CN^-. Moreover, it was observed that concurrently with the absorption variations, the strong emission band centered at 508 nm suffered a progressive decrease upon increasing amounts of CN^-.



(**a**) (**b**)

Figure 4. (**a**) Spectrophotometric and (**b**) spectrofluorimetric titration spectra of BODIPY derivative **2** upon addition of increasing quantities of CN^- (0 eq.—black line, to 14 eq.—red line) in acetonitrile. Inset: normalized absorbance and emission intensities at 492 nm and 508 nm, respectively, as a function of $[CN^-]/[2]$.

Additionally, comparing the chemosensing behavior of the BODIPY derivative **2** towards those anions, it was verified by the spectroscopic titrations that the number of equivalents necessary to achieve the absorbance and emission plateau was much lower for CN^- (14 equivalents for CN^- vs. 180 equivalents for F^-).

4. Conclusions

We reported the synthesis and characterization of BODIPY derivative **2**, bearing a phenyl moiety at the *meso*-position and functionalized with a formyl group at position 2 of the core. The recognition behavior of the BODIPY **2,** was investigated in the presence of different anions. The results from the spectrophotometric and spectrofluorimetric titrations demonstrated a decrease in the absorption band intensity at 492 nm and a strong

fluorescence quenching upon interaction with cyanide and fluoride. Moreover, compound **2** displayed a higher sensitivity towards CN^- than F^-, with a lower detection threshold for the former. This result might be of interest for application of the BODIPY **2** as a dual colorimetric and fluorimetric chemosensor of cyanide and fluoride.

Author Contributions: R.C.R.G.—Performed the synthesis of the compound, spectroscopic characterization, photophysical characterization, chemosensing studies, formal analysis, writing of original draft; M.L.B.—performed the synthesis of the compound, spectroscopic characterization, photophysical characterization, chemosensing studies; S.P.G.C.—methodology, supervision, formal analysis; M.M.M.R.—methodology, supervision, formal analysis, writing—original draft. All authors have read and agreed to the published version of the manuscript.

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