

Proceedings

Synthesis, Characterization and Evaluation of a Novel BODIPY Derivative as a Colorimetric Chemosensor for Fe³⁺ Recognition †

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Abstract: A 4,4-difluoro-4-bora-3*a*,4*a*-diazas-indacene (BODIPY) derivative functionalized with a formyl group at position 2 was synthesized in 57% yield. The compound was characterized by ¹H and ¹³C Nuclear Magnetic Resonance (NMR) spectroscopy and mass spectrometry. The photophysical characterization was carried out by means of absorption and fluorescence spectroscopies in acetonitrile solutions. The BODIPY derivative showed an absorption band at 492 nm and an emission band at 506 nm. A preliminary evaluation of the recognition ability of the BODIPY derivative was investigated in the presence of several cations with environmental and biomedical relevance. A highly selective colorimetric response was obtained for Fe³⁺.

Keywords: BODIPY; colorimetric chemosensor; Fe³⁺; synthesis

1. Introduction

BODIPY derivatives have been proving to be a key class of compounds as a tool for a wide range of research fields. Among the diverse applications of BODIPYs, the development of derivatives owning the ability to recognize and detect small organic molecules and metal ions have received great attention in the last years. Moreover, the BODIPY core can be chemically modified in order to improve the optical properties or add new functionalities as chemosensors, for example, insertion of receptor groups selective to analytes. There are diverse cations with biological and environmental relevance, such as Fe³⁺ as an important metal ion in several physiological processes involving electron transfer and also as an enzymatic cofactor for oxygen transport, DNA synthesis, etc. On the other hand, the accumulation of iron in the central nervous system has been implicated in a number of diseases. Therefore, the design of molecular systems for recognition of cations with “naked-eye” detection is an attractive goal [1–4].

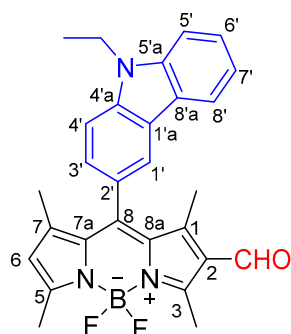
In continuation of our research group’s investigation developed in the field of chromofluorogenic sensors [5–8], we report in this work the synthesis, characterization, and evaluation of a novel BODIPY derivative as a colorimetric chemosensor for Fe³⁺ recognition in acetonitrile solution.

2. Experimental Section

2.1. Methods and Materials

NMR spectra were obtained on a Bruker Avance III 400 at an operating frequency of 400 MHz for ^1H and 100.6 MHz for ^{13}C , using the solvent peak as an internal reference. The solvents are indicated in parenthesis before the chemical shift values (δ relative to tetramethylsilane (TMS)). Peak assignments were made by comparison of chemical shifts, peak multiplicities, and J values, and were supported by spin decoupling-double resonance and bidimensional heteronuclear techniques. Mass spectrometry analyses were performed at the “C.A.C.T.I.—Unidad de Espectrometría de Masas” at the University of Vigo, Spain. All reagents were purchased from Sigma-Aldrich, Acros and Fluka and used as received. Precursor BODIPY **1** was synthesized as previously reported [8]. Thin-layer chromatography (TLC) analysis was carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel 60F254), and the spots were visualized under ultraviolet (UV) light. Chromatography on silica gel was carried out on Merck Kieselgel (230–400 mesh). The UV-visible absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer. Fluorescence spectra were collected using a FluoroMax-4 spectrofluorometer. The relative fluorescence quantum yields were determined by using a 1×10^{-5} M solution of Rhodamine 6G in ethanol as a standard ($\Phi_F = 0.95$) [9,10].

2.2. Synthesis of BODIPY Derivative **2**



A mixture of *N,N*-dimethylformamide (DMF) (23 mmol) and POCl_3 (18.2 mmol) was stirred for 5 min at 0°C under a N_2 atmosphere. Once the mixture reached room temperature, it was allowed to stir for 30 min. Then, BODIPY precursor **1** (0.127 mmol) dissolved in dichloroethane (7 mL) was added dropwise with stirring. The reaction mixture was then heated for 2 h at 50°C . After cooling, the solution was poured slowly into 40 mL of saturated sodium bicarbonate solution at 0°C and stirred for 30 min at room temperature. Ethyl acetate (5 mL) was added to the reaction mixture, and the resulting organic layer separated and 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 was obtained as a dark red solid (0.030 g, 57%).

^1H RMN (400 MHz, CDCl_3): δ = 1.37 (s, 3H, CH_3 -7), 1.37 (t, J = 7.2 Hz, 3H, $\text{N}(\text{CH}_2\text{CH}_3)$), 1.61 (s, 3H, CH_3 -1), 2.65 (s, 3H, CH_3 -5), 2.86 (s, 3H, CH_3 -3), 4.45 (q, J = 7.2 Hz, 2H, $\text{N}(\text{CH}_2\text{CH}_3)$), 6.15 (s, 1H, H-6), 7.27–7.35 (m, 2H, H-3' e H-4'), 7.52–7.58 (m, 3H, H-6', H-7' e H-8'), 8.00 (s, 1H, H-1'), 8.08 (d, J = 7.6 Hz, 1H, H-5'), 10.01 (s, 1H, CHO) ppm.

^{13}C NMR (100.6 MHz, CDCl_3): δ = 11.85, 13.04, 13.8, 15.06, 15.14, 37.87, 108.94, 109.16, 119.50, 119.88, 120.62, 122.46, 123.59, 123.75, 124.15, 124.91, 126.30, 126.56, 130.65, 134.88, 135.82, 140.18, 143.13, 145.15, 147.52, 156.22, 161.09, 185.96 ppm.

MS (ESI) m/z (%): 471 ($[\text{M} + 2]^{+}$, 31), 470 ($[\text{M} + 1]^{+}$, 100), 469 ($[\text{M}]^{+}$, 23), 437 (9), 393 (8), 349 (6), 305 (3), 242 (52); HRMS (ESI) m/z : $[\text{M} + 1]^{+}$ for $\text{C}_{28}\text{H}_{27}\text{BF}_2\text{N}_3\text{O}$ calcd. 470.2210; found 470.2225.

2.3. Chemosensing Studies of BODIPY Derivative 2 and Spectrophotometric Titration

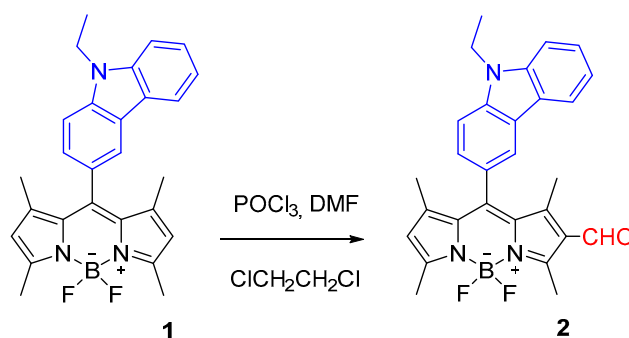
Evaluation of BODIPY derivative **2** as a colorimetric chemosensor was carried out in the presence of several cations (Ag^+ , K^+ , Li^+ , Pb^{2+} , Mn^{2+} , Cd^{2+} , Cu^{2+} , Co^{2+} , Pd^{2+} , Ni^{2+} , Ca^{2+} , Hg^{2+} , Zn^{2+} , Fe^{2+} , Fe^{3+} and Al^{3+}) with environmental and biomedical relevance. Solutions of the compound (1×10^{-5} M) and solutions of cations under study (1×10^{-2} M) were prepared in acetonitrile. A preliminary study was carried out by addition of up to 50 equivalents of each cation to the solution of BODIPY derivative in acetonitrile.

The spectroscopic study of BODIPY derivative **2** was performed in the presence of Fe^{3+} as a result of the preliminary study, which revealed the selectivity towards this cation. The solution of the BODIPY derivative (1×10^{-5} M) and the solution of the cation under study (1×10^{-2} M) were prepared in acetonitrile. The spectrophotometric titration was performed by the sequential addition of Fe^{3+} solution to the BODIPY derivative solution.

3. Results and Discussion

3.1. Synthesis of BODIPY Derivative 2

The synthesis of BODIPY derivative **2** was obtained through Vilsmeier–Haack formylation of BODIPY precursor **1**, *meso*-substituted with a carbazole group, using dimethylformamide and phosphorylchloride as Vilsmeier reagent in 1,2-dichloroethane (Scheme 1). The pure BODIPY derivative functionalized with a formyl group was obtained as a dark red solid in 57% yield.



Scheme 1. Synthesis of BODIPY derivative **2**.

The presence of a formyl group at position 2 of the BODIPY core was confirmed by ^1H NMR spectroscopy, with the appearance of a singlet at δ 10.01 ppm.

3.2. Photophysical Characterization of BODIPY Derivative 2

The photophysical properties of the BODIPY derivative **2** were investigated in acetonitrile solutions. The compound showed an intense absorption band ($\log \epsilon = 4.89$) at 492 nm. Upon excitation at 460 nm, the compound showed an intense emission band at 506 nm (Figure 1). The relative fluorescence quantum yield, determined by using Rhodamine 6G in ethanol as standard ($\Phi_F = 0.95$), was found to be low ($\Phi_F = 0.024$). The small quantum yield measured could be ascribed to a carbonyl electron-withdrawing effect exerted by the formyl group linked to the BODIPY core [11].

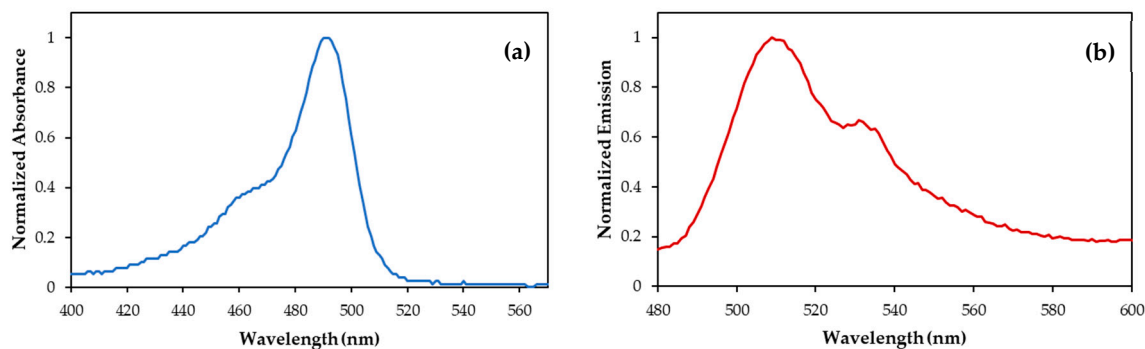


Figure 1. Normalized UV-visible spectrum (a) and fluorescence spectrum (b) of BODIPY derivative 2 in acetonitrile.

3.3. Chemosensing Studies of BODIPY Derivative 2 and Spectrophotometric Titration

Evaluation of the BODIPY derivative 2 as colorimetric chemosensor was carried out in acetonitrile solutions, in the presence of several cations. The preliminary study was carried out by the addition of up to 50 equivalents of each cation to the solution of the compound. It was observed that the BODIPY derivative displayed a color change only upon interaction with Fe³⁺, from light orange to light grey (Figure 2).

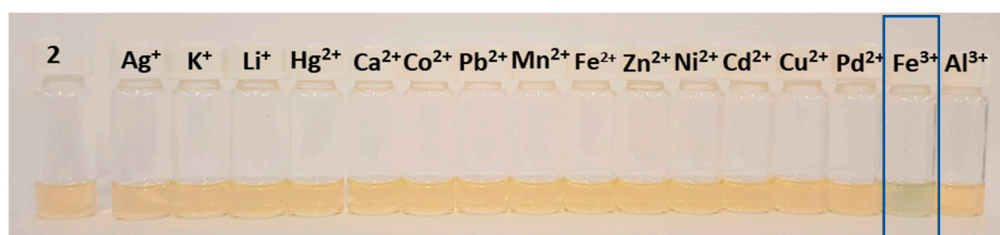


Figure 2. Color changes of BODIPY derivative 2 (1×10^{-5} M) in the presence of 50 equivalents of several cations, in acetonitrile.

The spectrophotometric titration of BODIPY derivative 2 was performed in acetonitrile with Fe³⁺ as a result of the preliminary study, which revealed the highly selective colorimetric response towards this cation. The UV-visible spectra revealed that the intensity of the absorption band at 491 nm decreased progressively upon the addition of the cation. The number of Fe³⁺ equivalents to achieve a plateau was at about 15 equivalents (Figure 3).

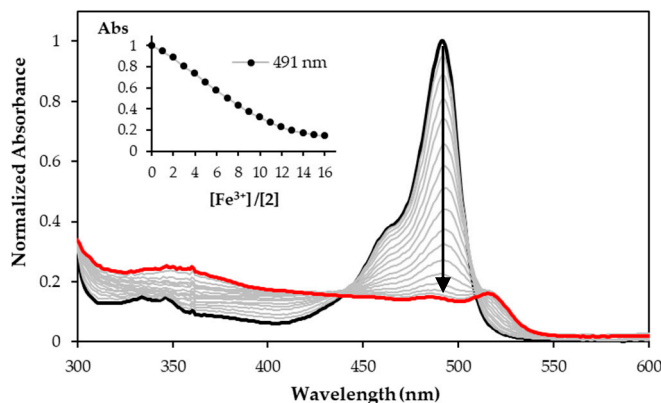


Figure 3. Spectrophotometric titration of BODIPY derivative 2 with addition of increasing amounts of Fe³⁺ in acetonitrile. The inset represents the normalized absorbance at 491 nm ($[2] = 1 \times 10^{-5}$ M).

4. Conclusions

The BODIPY derivative **2** functionalized at position 2 with a formyl group was synthesized in good yield (57%) through Vilsmeier–Haack reaction. The compound was characterized by the usual spectroscopic techniques, and the photophysical properties were also determined.

The selective recognition of Fe³⁺ in acetonitrile solution among several cations was obtained with the novel BODIPY derivative **2** through a color change from light orange to light grey, making this compound suitable as a colorimetric chemosensor for Fe³⁺.

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Conflicts of Interest: The authors declare no conflict of interest.

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