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Synthesis, Characterization and Evaluation of a Carbazolyl-BODIPY as a Fluorimetric Chemosensor for F^{-} †

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Abstract: BODIPY dyes have received great attention in the last years as chemical optical sensors since they can recognize metal ions in solution through optical signals (colorimetric and/or fluorimetric). In this sense, our research group reports the synthesis of a carbazolyl-BODIPY derivative and the respective characterization by ^{1}H NMR spectroscopy and mass spectrometry. Furthermore, a preliminary study of the chemosensory capacity of this BODIPY derivative was carried out in acetonitrile solution in the presence of several anions and a highly selective fluorimetric response was obtained for F^{-}.

Keywords: BODIPY; carbazole; fluorimetric chemosensor; fluoride anion; synthesis

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1. Introduction

The development of compounds capable of recognizing ions with biological and environmental importance through optical signals (colorimetric and/or fluorimetric) is an attractive goal nowadays. Fluoride is an example of an anion harmful to human health at certain levels since its high intake can lead to chronic diseases such as dental and skeleton fluorosis, and metabolic dysfunctions [1–2]. Thus, simple and rapid sensing tools to monitor fluoride levels in biological samples are of great importance. Boron-dipyrromethene (BODIPY) derivatives have received great attention for chemosensory applications due to their remarkable physical-chemical properties, such as high molar absorption coefficients, high quantum fluorescence yields, intense and narrow absorption/emission bands in the visible region of the electromagnetic spectrum, and good photochemical stability. Additionally, the BODIPY core can be easily functionalized to be used as selective chromo-fluorogenic chemosensor for various analytes [3–5].

In continuation of the work developed in our research group [6-12], regarding the synthesis and evaluation of optoelectronic properties of BODIPY derivatives for several applications, namely as chromofluorogenic chemosensors, we report the synthesis, spectroscopic characterization, and evaluation of the chemosensory ability of a novel BODIPY derivative functionalized with a carbazolyl group at the *meso* position as a fluorimetric chemosensor for the selective detection of fluoride.

2. Experimental Section

2.1. Methods and Materials

All reagents were purchased from Sigma-Aldrich, Acros, and Fluka and used as received. Thin-layer chromatography (TLC) analysis were carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel 60F254) and the spots were visualized under UV light. Dry flash chromatography was performed using silica gel 60 with a diameter between 230–400 mesh (Merck, Kenilworth, NJ, USA). The ^{1}H NMR spectra was recorded on a Bruker Avance III device at 400 MHz, using the solvent peak as an internal reference. Mass spectrometry analyses were performed at the "C.A.C.T.I.-Unidad de Espectrometria de Masas" at the University of Vigo, Spain. The deuterated solvent used in nuclear magnetic resonance spectroscopy was $CDCl_3$ with 99.8% deuteration degree, containing 0.03% v/v TMS (Sigma Aldrich). The absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer and fluorescence spectra were collected using a Horiba FluoroMax-4 spectrofluorometer.

2.2. Synthesis of BODPY Derivative **1**

2,4-Dimethylpyrrole (170 mg, 1.8 mmol) and *N*-ethylcarbazolyl-4-carbaldehyde (200 mg, 0.89 mmol) were dissolved in dry DCM (100 mL) and this reaction mixture was stirred for 50 min after adding a drop of TFA. Subsequently, a solution of DDQ (406 mg, 1.8 mmol) dissolved in dry DCM (100 mL) was added and the stirring time was extended for another 50 min. Then, triethylamine (2 mL, 15 mmol) was added and, after 15 min, was added $BF_3.OEt_2$ (3 mL, 25 mmol) to the reaction mixture, which was stirred for 30 min. The crude product obtained after evaporation of the solvent under reduced pressure was purified by dry flash chromatography using a petroleum ether/AcOEt (4:1) mixture as eluent. The pure BODIPY derivative **1** (Figure 1) was obtained as a dark red solid (65 mg, 17%).

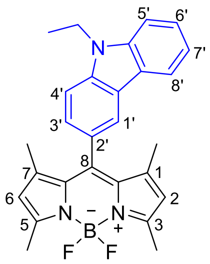


Figure 1. Structure of BODIPY derivative **1**.

^{1}H RMN (400 MHz, $CDCl_3$): δ =1.27 (s, 6H, CH_3-1 and CH_3-7), 1.51 (t, 3H, N($CH_2C\mathit{H}_3$)), 2.59 (s, 6H, CH_3-3 and CH_3-5), 4.45 (q, 2H, N($C\mathit{H}_2CH_3$)), 5.99 (s, 2H, H-2 and H-6), 7.26-7.30 (m, 1H, H6′ or H7′), 7.30 (dd, J=1.6 and 8.4 Hz, 1H, H3′), 7.48-7.56 (m, 3H, H8′, H4′, H6′ or H7′), 8.01 (d, J=7.6 Hz, 1H, H1′), 8.08 (dd, J=0.8 and 1.6 Hz, 1H, H5′), ppm.

MS (ESI) m/z (%): 443 ($[M+2]^{+\bullet}$, 33), 442 ($[M+1]^{+\bullet}$, 100), 441 ($[M]^{+\bullet}$, 29), 394 (54), 291 (3), 239 (8), 102 (6); HRMS (ESI) m/z : $[M+1]^{+\bullet}$ calcd for $C_{27}H_{27}BF_2N_3$, 442,2261; found 442,2263.

2.3. Photophysical Characterization of BODIPY Derivative **1**

The photophysical characterization of BODIPY derivative **1** in acetonitrile (1×10^{-5} M) was carried out using quartz cells. A 1×10^{-5} M Rhodamine 6G (Φ_F = 0.95) solution in ethanol was used as fluorescence standard [13]. Fluorescence was measured at an angle of 90 ° to the incident excitation radiation and the compound and the standard were excited at the maximum absorption wavelength of BODIPY **1**. After plotting the fluorescence spectrum of the compound **1** and Rhodamine 6G, the area under the curve was determined and the relative quantum fluorescence yield of BODIPY **1** was calculated through Equation (1).

$$\Phi_{F_{comp}} = \frac{A_s \times F_{comp} \times n_s^2}{A_{comp} \times F_s \times n_{comp}^2} \times \Phi_{F_s} \quad (1)$$

A_s and A_{comp}, F_s and F_{comp}, and n_s and n_{comp} correspond to the absorbances, areas under the fluorescence curve, and refractive index value of the solvent of the standard and compound **1**, respectively.

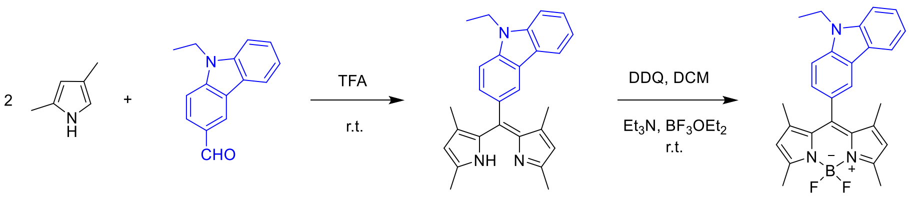
2.3. Chemosensing Studies of BODIPY Derivative **1**

The evaluation of BODIPY derivative **1** as optical chemosensor was carried out in the presence of several anions ($H_2PO_4^-$, HSO_4^-, CN^-, F^-, I^-, NO_3^-, CH_3COO^-, Br^-, ClO_4^-, BzO^-). For this study, solutions of the compound (1×10⁻⁵ M) and the various anions (1×10⁻² M) were prepared in acetonitrile, and the preliminary study was carried out by the addition of 50 equivalents of each anion to the BODIPY derivative **1** solution.

3. Results and Discussion

3.1. Synthesis of BODPY Derivative 1

Carbazolyl-BODIPY **1** was synthesized in two reactional steps at room temperature. The first step consisted in the condensation reaction of 2,4-dimethylpyrrole and *N*-ethylcarbazolyl-4-carbaldehyde in dichloromethane (DCM) in the presence of trifluoroacetic acid (TFA) as catalyst. The second reactional step involved the oxidation of the dipyrromethane to dipyrromethene, through the addition of a solution of 2,3-dichloro-5,6-diciano-*p*-benzoquinone (DDQ) followed the complexation reaction with BF_3OEt_2 in the presence of triethylamine (Scheme 1). Finally, purification of the crude product by dry flash chromatography, using petroleum ether/ethyl acetate (4:1) as eluente, gave the pure BODIPY derivative **1** as a dark red solid in 17% yield.



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

Through the ¹H NMR spectrum, it was possible to confirm the presence of the carbazolyl group in *meso* position of the BODIPY core, with the characteristic proton signals appearing in the aromatic zone of the spectrum. Additionally, the data obtained by mass spectrometry agree with the expected structure.

3.2. Photophysical Characterization of BODIPY Derivative ***1***

The photophysical characterization of BODIPY derivative **1** was investigated in acetonitrile solution. The compound showed an intense absorption band (log ε = 4.9) at 496 nm. Upon excitation at 480 nm, the compound exhibited an emission band at 507 nm (Figure 2). The relative fluorescence quantum yield, determined by using Rhodamine 6G in ethanol as standard (Φ_F = 0.95), was found to be low (Φ_F = 0.019).

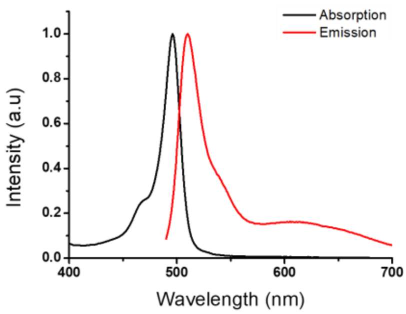

Figure 2. Normalized absorption and fluorescence spectra of BODIPY **1** in acetonitrile.

3.3. Chemosensing Studies of BODIPY Derivative **1**

Evaluation of the carbazolyl-BODIPY **1** as optical chemosensor was performed in the presence of several anions in acetonitrile solution. The study was carried out by addition of 50 equivalents of each anion to the compound's solution and as can be seen in Figure 3 there was a selective increase in the fluorescence of the compound upon addition of F^-.

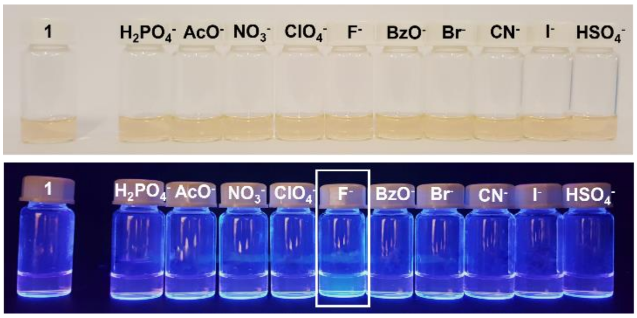

Figure 3. BODIPY derivative **1** solutions in the presence of various anions, in acetonitrile, under natural light (above) and UV radiation at λ_{max} = 365 nm (below).

4. Conclusions

The BODIPY derivative **1** functionalized at *meso* position with a carbazolyl group was synthesized through a condensation reaction between 2,4-dimethylpyrrole and *N*-ethylcarbazolyl-4-carbaldehyde, in 17% yield. This compound was characterized by the usual spectroscopic techniques and the photophysical properties were also determined. Additionally, the preliminary chemosensing study of BODIPY derivative **1** shows a selective recognition of F^- among several anions, through a perceptible enhancement of fluorescence of the solution of the compound. Therefore, BODIPY **1** could be a potential selective fluorimetric chemosensor for the detection of fluoride.

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

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