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Anion Colorimetric Chemosensor Based on a Benzimidazole Functionalized BODIPY Derivative †

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Abstract: A BODIPY derivative bearing a benzimidazole unit at position 2 and an electron donor group (anthracene) at *meso*-position was synthetized and characterized by the usual spectroscopic techniques. The evaluation of the compound as a colorimetric chemosensor was performed in solutions of acetonitrile/water (75:25) 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 biomedical and environmental relevance. The investigated BODIPY derivative demonstrated a selective color change from pink to yellow upon interaction with hydrogensulfate anion (HSO_4^-).

Keywords: anions; benzimidazole; BODIPY derivative; colorimetric chemosensor

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1. Introduction

The design and synthesis of optical chemosensors for recognition of anions is an essential research topic since these negatively charged species display an important role in biomedical and environmental fields [1–4].

Among chemosensors based on organic molecules, BODIPY is a multifaceted signaling scaffold which displays notable photophysical properties, such as sharp absorption and emission patterns, high molar extinction coefficient of absorbance, high fluorescence quantum yield and good photostability under physiological conditions. The BODIPY core can be modified through chemical functionalization to modulate its photophysical properties and to introduce selective recognition sites for a higher target binding affinity [5–15]. Moreover, (benz)imidazole and its derivatives have been investigated as anion and cation recognition systems that exhibit optical changes upon analyte complexation [16–21].

As an extension of the work developed in our research group concerning heterocyclic chromofluorogenic sensors [10,12,13,16,20,21], we report the synthesis and characterization of a BODIPY functionalized with anthracene group at *meso* position and a benzimidazole group at 2-position, for a selective colorimetric response towards hydrogensulfate anion (HSO_4^-). The recognition behavior of the BODIPY derivative was studied in aqueous solution of acetonitrile/water (75:25) in the presence of different anions and the results showed a specific color change of the solution upon HSO_4^- complexation.

2. Methods and Materials

NMR spectra was obtained on a Bruker Avance III 400 at an operating frequency of 400 MHz, using the solvent peak as internal reference. The solvents are indicated in parenthesis before the chemical shift values (δ relative to TMS). Mass spectrometry analyses were performed at the "C.A.C.T.I. -Unidad de Espectrometria de Masas" at the University of Vigo, Spain. All reagents were purchased from Sigma-Aldrich, Acros and Fluka and used as received. 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. Chromatography on silica gel was carried out on Merck Kieselgel (230-400 mesh). UV-visible absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer. Fluorescence spectra were collected using a Horiba FluoroMax-4 spectrofluorometer. The relative fluorescence quantum yield was calculated through equation 1, using a 1×10^{-5} M solution of Rhodamine 6G in ethanol as reference ($\Phi_F = 0.95$) [22,23].

$$\phi_{cp} = \phi_{ref} \times \frac{A_{ref}}{A_{cp}} \times \frac{F_{cp}}{F_{ref}} \times \frac{n_{ref}^2}{n_{cp}^2} \quad (1)$$

where Φ_{ref} is the fluorescence quantum yield of the reference, A_{ref} and A_{cp} are the absorbance of the reference and compound, respectively, F_{ref} and F_{cp} are the areas of the reference and compound emission spectra, respectively, n_{ref} and n_{cp} are the solvent refractive indices of the reference and compound, respectively.

2.1. Synthesis of BODIPY Derivative **2**

Formyl-BODIPY precursor **1** (0.11 mmol), ethanol (10 mL) and $NaHSO_3$ (0.10 mmol) were added in a round bottomed flask. The reaction mixture was stirred at room temperature for 4 h. Then, dry DMF (5 mL) and *o*-phenylenediamine (0.07 mmol) were added and the solution was heated for 2 h at 80 °C. The reaction mixture was cooled to room temperature, ethyl acetate was added (10 mL) and the mixture was washed with water (3 × 10 mL). The organic phase was dried with anhydrous $MgSO_4$ and the solvent was evaporated to dryness. In Figure 1 is represented the structure of the resulting product after purification by silica gel chromatography column using dichloromethane as eluent, obtained as a red solid (0.012 g, 30%).

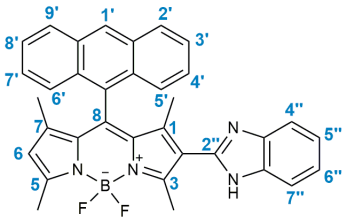


Figure 1. Structure of BODIPY derivative **2.**

^{1}H RMN (400 MHz, $CDCl_3$): δ =0.69 (s, 3H, CH_3-7), 0.83 (s, 3H, CH_3-1), 2.69 (s, 3H, CH_3-5), 2.84 (s, 3H, CH_3-3), 6.02 (s, 1H, H-6), 7.22-7.27 (m, 2H, H-5″ and H-6″), 7.42 (dt, *J*=1.2 and 8, 2H, H-4′ and H-7′), 7.48 (dt, *J*=1.2 and 8, H-3′ and H-8′), 7.56 (s large, 2H, H-4″ and H-7″) 7.88 (d, *J*= 8.8, 2H, H-2′ and H-9′), 8.03 (d, *J*=8.4, 2H, H-5′ and H-6′), 8.59 (s, 1H, H-1′) ppm.

MS (ESI) *m*/*z* (%): 542 ($[M + 2]^{+\bullet}$, 39), 541 ($[M + 1]^{+\bullet}$, 100), 540 ($[M]^{+\bullet}$, 24); HRMS (ESI) *m*/*z*: $[M + 1]^{+\bullet}$ calcd for $C_{34}H_{28}BF_2N_4$, 541.2370; found 541.2369.

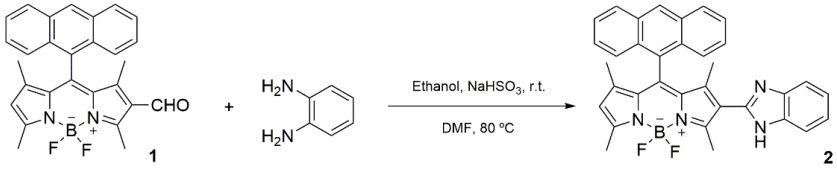
2.2. Chemosensing Studies of BODIPY Derivative **2** *in Aqueous Media*

Evaluation of BODIPY derivative **2** as 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 solutions of BODIPY derivative were prepared in mixtures of acetonitrile and water (75:25) at a final concentration of 1×10^{-5} M and the solutions of anions were prepared in acetonitrile 1×10^{-2} M. A preliminary study was performed by the addition of 50 equivalents of each anion to the solution of BODIPY derivative.

3. Results and Discussion

3.1. Synthesis of BODIPY Derivative **2**

As shown in Scheme 1, the BODIPY derivative **2** was synthesized through a condensation reaction between *o*-phenylenediamine and formyl-BODIPY precursor **1** in the presence of $NaHSO_3$ as the activating agent of the diamine. The pure BODIPY **2** functionalized with a benzimidazole group at position 2 of the core was obtained as a red solid in 30% yield after purification through column chromatography.



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

The structure was confirmed by ^{1}H NMR and mass spectrometry, as shown in the experimental section. It was possible to identify the signals corresponding to the aromatic protons of the benzimidazole moiety, with a multiplet at 7.22-7.27 ppm due to the 5″ and 6″ protons and a large singlet at 7.56 ppm due to the 4″ and 7″ protons.

3.2. Photophysical Characterization of BODIPY Derivative **2**

The photophysical properties of BODIPY derivative **2** were investigated in acetonitrile solution. The compound showed an intense absorption band (log ε = 4.80) at 515 nm. Upon excitation at 515 nm, the compound exhibited an emission band at 588 nm. The relative fluorescence quantum yield determined using Rhodamine 6G as reference was found to be 0.76.

3.3. Chemosensing Studies of BODIPY Derivative **2** *in Aqueous Media*

Having in mind the possible application of BODIPY derivative **2** as a chemosensor of anions with biological and environmental importance, a preliminary study of compound **2** was carried out in acetonitrile/ water (75:25) solutions in the presence of HSO_4^-, NO_3^-, $H_2PO_4^-$, CN^-, BzO^-, ClO_4^-, Br^-, F^-, I^- and $CH_3CO_2^-$.

The chromogenic response of the BODIPY derivative was remarkably selective and visible to the naked eye in the presence of hydrogensulfate anion. In Figure 2 is observed the color change of the solution of the compound, from pink to yellow upon addition of 50 equivalents of HSO_4^-. On the other hand, the interaction with other anions did not induce any perceptible changes.

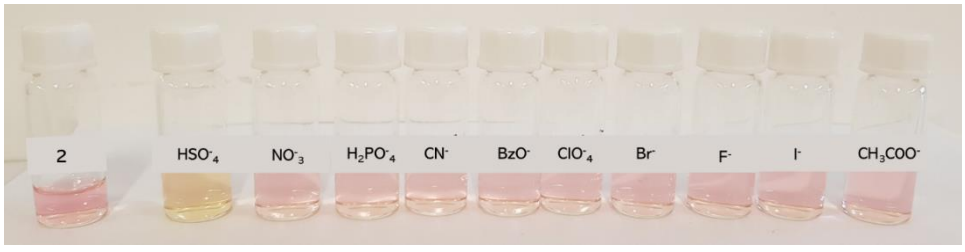


Figure 2. Color change observed for BODIPY derivative **2** in acetonitrile/water (75:25) upon addition of 50 equivalents of several anions.

4. Conclusions

In summary, we described the synthesis, photophysical properties and chemosensing studies toward several anions in acetonitrile/water (75:25) of a novel BODIPY derivative bearing a benzimidazole unit at position 2 and an electron donor group at *meso*-position. The selective detection of HSO_4^- in aqueous solution of acetonitrile among other anions was observed through a perceptible color change from pink to yellow. This result might be of interest for applications of the BODIPY derivative **2** as a colorimetric chemosensor of hydrogensulfate anion in environmental and biological samples.

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

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