chemistry proceedings

MDPI

Proceeding Paper

Anion Colorimetric Chemosensor Based on a Benzimidazole-Functionalized BODIPY Derivative †

Raquel C. R. Gonçalves, Sónia C. S. Pinto, Susana P. G. Costa and Maria Manuela M. Raposo *

Centre of Chemistry, Campus of Gualtar, University of Minho, 4710-057 Braga, Portugal; raquelrainha10@hotmail.com (R.C.R.G.); spc@quimica.uminho.pt (S.C.S.P.); soniapinto4197@gmail.com (S.P.G.C.)

* Correspondence: mfox@quimica.uminho.pt

† Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

Abstract: A BODIPY derivative bearing a benzimidazole unit at position 2 and an electron donor group (anthracene) at the *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 a hydrogen sulfate anion (HSO_4^-).

Keywords: anions; benzimidazole; BODIPY derivative; colorimetric chemosensor

check for updates

Citation: Gonçalves, R.C.R.; Pinto, S.C.S.; Costa, S.P.G.; Raposo, M.M.M. Anion Colorimetric Chemosensor Based on a Benzimidazole-Functionalized BODIPY Derivative. *Chem. Proc.* **2022**, *8*, 90. https://doi.org/10.3390/ecsoc-25-11754

Academic Editor: Julio A. Seijas

Published: 18 July 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

The design and synthesis of optical chemosensors for the 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 that displays notable photophysical properties, such as sharp absorption and emission patterns, a high molar extinction coefficient, 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 [16–22].

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 an anthracene group at the *meso* position and a benzimidazole group at position 2, for a selective colorimetric response towards a hydrogen sulfate anion (HSO_4^-). The recognition behavior of the BODIPY derivative was studied in an 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 were obtained on a Bruker Avance III 400 at an operating frequency of 400 MHz, using the solvent peak as the internal reference. The solvents were 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 analyses 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 ($\Phi_F = 0.95$) [23,24].

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

where Φ_{ref} is the fluorescence quantum yield of the reference, A_{ref} and A_{cp} are the absorbances of the reference and compound, respectively, F_{ref} and F_{cp} are the areas of the reference and compound emission spectra, respectively, and 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. Figure 1 shows the structure of the resulting product after purification with a silica gel chromatography column using dichloromethane as the eluent, obtained as a red solid (0.012 g, 30%).

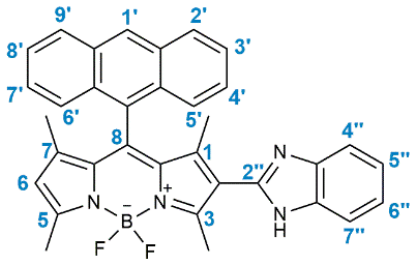


Figure 1. Structure of BODIPY derivative **2**.

^{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 (broad s, 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*: $[M + 1]^{+\bullet}$ calculated for $C_{34}H_{28}BF_2N_4$, 541.2370; found 541.2369.

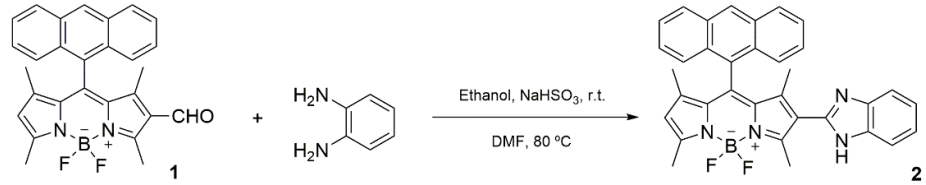
2.2. Chemosensing Studies of BODIPY Derivative **2** *in Aqueous Media*

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

The structure was confirmed with ^{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 broad 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*

Keeping in mind the possible application of the 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 a hydrogen sulfate anion. Figure 2 shows 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.

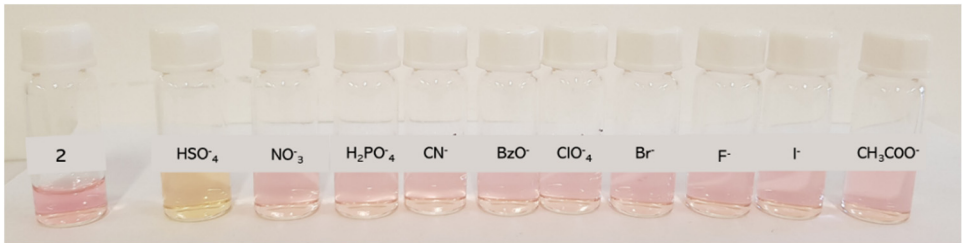


Figure 2. Color change observed for BODIPY derivative **2** in acetonitrile/water (75:25) upon addition of 50 equivalents of several anions.

The anion HSO_4^- is a relatively strong acid with pK_a 1.99 in an aqueous solution. Keeping this in mind, the chemosensing behavior of the BODIPY derivative towards this anion in an aqueous solution may be related to the protonation of the benzimidazole NH, since the anion's pK_a (1.99) was significantly lower than the compound's pK_a value (3.1, unpublished results).

4. Conclusions

In summary, we described the synthesis, photophysical properties and chemosensing studies of 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 the *meso* position. The selective detection of HSO_4^- in an 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 hydrogen sulfate anion in environmental and biological samples.

Funding: The authors acknowledge Fundação para a Ciência e Tecnologia-FCT (Portugal) for funding through CQUM (UID/QUI/00686/2020) and project PTDC/QUI-COL/28052/2017 and a PhD grant to. R. C. R. Gonçalves (SFRH/BD/05278/2020). The NMR spectrometer Bruker Avance III 400 was part of the National NMR Network and was purchased within the framework of the National Program for Scientific Re-equipment, contract REDE/1517/RMN/2005, with funds from POCI 2010 (FEDER) and FCT.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

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

References

1. Goshisht, M.K.; Tripathi, N. Fluorescence-Based Sensors as an Emerging Tool for Anion Detection: Mechanism, Sensory Materials and Applications. *J. Mater. Chem. C* **2021**, *9*, 9820–9850. [CrossRef]
2. Patil, A.; Salunke-Gawali, S. Overview of The Chemosensor Ligands used for Selective Detection of Anions and Metal Ions (Zn^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, Fe^{2+}, Hg^{2+}). *Inorg. Chim. Acta* **2018**, *482*, 99–112. [CrossRef]
3. Wu, D.; Sedgwick, A.C.; Gunnlaugsson, T.; Akkaya, E.U.; Yoon, J.; James, T.D. Fluorescent Chemosensors: The Past, Present and Future. *Chem. Soc. Rev.* **2017**, *46*, 7105–7123. [CrossRef] [PubMed]
4. Kaur, B.; Kaur, N.; Kumar, S. Colorimetric Metal Ion Sensors–A Comprehensive Review of the Years 2011–2016. *Coord. Chem. Rev.* **2018**, *358*, 13–69. [CrossRef]
5. Loudet, A.; Burgess, K. BODIPY Dyes and their Derivatives: Syntheses and Spectroscopic Properties. *Chem. Rev.* **2007**, *107*, 4891–4932. [CrossRef]
6. Boens, N.; Leen, V.; Dehaen, W. Fluorescent Indicators based on BODIPY. *Chem. Soc. Rev.* **2012**, *41*, 1130–1172. [CrossRef]
7. Bañuelos, J. BODIPY Dye, The Most Versatile Fluorophore Ever? *Chem. Rec.* **2016**, *16*, 335–348. [CrossRef]
8. Lu, H.; Shen, Z. BODIPYs and Their Derivatives: The Past, Present and Future. *Front. Chem.* **2020**, *8*, 290. [CrossRef]
9. Gonçalves, R.; Pina, J.; Costa, S.P.G.; Raposo, M.M.M. Synthesis and Characterization of Aryl-substituted BODIPY Dyes Displaying Distinct Solvatochromic Singlet Oxygen Photosensitization Efficiencies. *Dyes Pigm.* **2021**, *196*, 109784. [CrossRef]
10. Presti, M.L.; Martínez-Máñez, R.; Ros-Lis, J.V.; Batista, R.M.F.; Costa, S.P.G.; Raposo, M.M.M.; Sancenón, F. A Dual Channel Sulphur-containing Macrocycle Functionalised BODIPY Probe for the Detection of Hg(II) in Mixed Aqueous Solution. *New J. Chem.* **2018**, *42*, 7863–7868. [CrossRef]
11. Collado, D.; Casado, J.; González, S.R.; Navarrete, J.T.L.; Suau, R.; Perez-Inestrosa, E.; Pappenfus, T.M.; Raposo, M.M.M. Enhanced Functionality for Donor-Acceptor Oligothiophenes by means of Inclusion of BODIPY: Synthesis, Electrochemistry, Photophysics and Model Chemistry. *Chem. Eur. J.* **2011**, *17*, 498–507. [CrossRef] [PubMed]
12. Gonçalves, R.C.R.; Pinto, S.C.S.; Costa, S.P.G.; Raposo, M.M.M. *Meso*-Triphenylamine BODIPY Derivative for Optical Chemosensing of Metal Ions. *Chem. Proc.* **2021**, *3*, 8291. [CrossRef]
13. Gonçalves, R.C.R.; Pinto, S.C.S.; Costa, S.P.G.; Raposo, M.M.M. Synthesis, Characterization and Evaluation of a Novel BODIPY Derivative as a Colorimetric Chemosensor for Fe^{3+} Recognition. *Proceedings* **2019**, *41*, 6625. [CrossRef]
14. Gonçalves, R.; Nogueira, M.; Costa, S.P.G.; Raposo, M.M.M. BODIPY derivatives: Synthesis and Evaluation of their Optical Properties. *Proceedings* **2019**, *9*, 5700. [CrossRef]
15. Gonçalves, R.; Nogueira, M.; Costa, S.P.G.; Raposo, M.M.M. Functionalized BODIPY derivatives as Potential Fluorescent labels. *Proceedings* **2019**, *9*, 5701. [CrossRef]
16. Batista, R.M.F.; Ferreira, R.C.M.; Raposo, M.M.M.; Costa, S.P.G. Novel Optical Chemosensors for Anions and Cations based on an Amino Acid Core Functionalised with Benzimidazoles. *Tetrahedron* **2012**, *68*, 7322–7330. [CrossRef]
17. Alfonso, M.; Sola, A.; Caballero, A.; Tárraga, A.; Molina, P. Heteroditopic Ligands based on Ferrocenyl Benzimidazoles Fused to an Additional Diaza Heterocyclic Ring System. *Dalton Trans.* **2009**, *43*, 9653–9658. [CrossRef]
18. Moon, K.S.; Singh, N.; Lee, G.W.; Jang, D.O. Colorimetric Anion Chemosensor based on 2-Aminobenzimidazole: Naked-eye Detection of Biologically Important Anions. *Tetrahedron* **2007**, *63*, 9106–9111. [CrossRef]

19. Molina, P.; Tárraga, A.; Otón, F. Imidazole Derivatives: A Comprehensive Survey of Their Recognition Properties. *Org. Biomol. Chem.* **2012**, *10*, 1711–1724. [CrossRef]
20. Esteves, C.I.C.; Ferreira, R.C.M.; Raposo, M.M.M.; Costa, S.P.G. New Fluoroionophores for Metal Cations based on Benzo[*d*]Oxazol-5-yl-Alanine Bearing Pyrrole and Imidazole. *Dyes Pigm.* **2018**, *151*, 211–218. [CrossRef]
21. Okda, H.E.; Sayed, S.E.; Ferreira, R.C.M.; Otri, I.; Costa, S.P.G.; Raposo, M.M.M.; Martínez-Máñez, R.; Sancenón, F. A Simple and Easy-to-prepare Imidazole-based Probe for the Selective Chromofluorogenic Recognition of Biothiols and Cu(II) in Aqueous Environments. *Dyes Pigm.* **2019**, *162*, 303–308. [CrossRef]
22. Li, Z.; Li, L.J.; Sun, T.; Liu, L.; Xie, Z. Benzimidazole-BODIPY as Optical and Fluorimetric pH Sensor. *Dyes Pigm.* **2016**, *128*, 165–169. [CrossRef]
23. Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M.T. *Handbook of Photochemistry*, 3rd ed.; CRC Press: Boca Raton, FL, USA, 2006.
24. Demas, J.N.; Crosby, G.A. Measurement of Photoluminescence Quantum Yields. *Review. J. Phys. Chem.* **1971**, *75*, 991–1024. [CrossRef]