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Synthesis and Characterization of a *meso*-Anthracene-BODIPY Derivative for Colorimetric Recognition of Cu^{2+} and Fe^{3+} †

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Abstract: Ions exist widely in biological and environmental media, and the scarcity or excess of these species can have adverse consequences. BODIPY dyes appear as heterocyclic organic compounds capable of recognizing metal ions in solution and in cells, through optical signals (colorimetric and/or fluorimetric), and their photophysical properties can be adjusted through the functionalization of the BODIPY core. In continuation of the work developed recently, our research group reports the synthesis of a *meso*-anthracene-BODIPY derivative and the respective characterization by ^1H and ^{13}C nuclear magnetic resonance (NMR) and UV-Vis absorption spectroscopies. The preliminary study of the chemosensory capacity of the BODIPY derivative was also carried out in the presence of several cations in acetonitrile solution which shows a selective colorimetric response for Cu^{2+} and Fe^{3+}.

Keywords: synthesis; BODIPY; metal ions; optical chemosensor; colorimetric signal

1. Introduction

BODIPY has received great attention in the scientific world due to the combination of its remarkable physical-chemical characteristics and its ease of synthesis and functionalization. Also, it is an extremely versatile compound, as it can undergo structural changes to adjust its photophysical properties for the intended applications. In this sense, BODIPY derivatives have been widely applied in the area of chemical optical sensors, since they can detect various metal ions and organic molecules. Ions exist widely in biological and environmental media, however, any change in normal ion levels has adverse consequences. Copper (Cu^{2+}) and iron (Fe^{3+}) are examples of metallic cations essential for the proper functioning of the organ and metabolic processes and, consequently, the existence of changes in the normal levels of these ions in the body can be harmful to human health. Excess copper and iron in the body cause cell toxicity, cancer and several neurodegenerative diseases, including Alzheimer's, Parkinson's, Menkes and Wilson. Thus, in recent years, there has been interesting research in the field of the development of colorimetric and/or fluorimetric chemical sensors suitable for the quick and simple detection of important cations for the biological and environmental media [1–6].

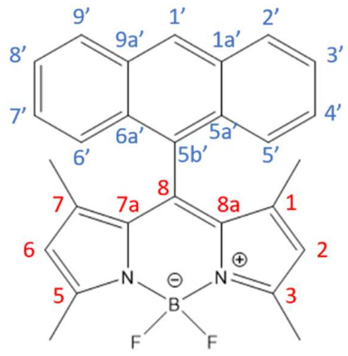
In continuation of the work of our research group in the field of chromofluorogenic sensors [7,8], we now report the synthesis, characterization and evaluation of the *meso*-anthracene-BODIPY derivative as a colorimetric chemosensor for recognition of Fe^{3+} and Cu^{2+} in acetonitrile solution.

2. Experimental Section

2.1. Methods and Materials

Dry flash chromatography was performed using silica gel 60 with a diameter between 230–400 mesh (Merck, Kenilworth, NJ, USA). All reagents were purchased from Sigma-Aldrich (St. Louis, MO, USA), Acros and Fluka and used as received. Thin-layer chromatography (TLC) analysis was performed on silica gel 60 plates with fluorescence indicator F254 (Merck). The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III device at 400 MHz and 100.6 MHz, respectively, using the solvent peak as an internal reference. The assignment of the ^{1}H and ^{13}C signals was performed using two-dimensional heteronuclear correlation techniques. Mass spectrometry analyses were performed at the "C.A.C.T.I.-*Unidad de Espectrometria de Massa*" 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 the emission spectra were obtained using a Horiba FluoroMax-4 spectrofluorimeter.

2.2. Synthesis of BODPY Derivative 1



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2,4-Dimethylpyrrole (181 mg, 1.9 mmol) and anthracene-9-carbaldehyde (200 mg, 0.97 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 (440 mg, 1.9 mmol) dissolved in dry DCM (100 mL) was added and the stirring time was extended for another 50 min. Then, triethylamine (2.2 mL, 16 mmol) was added and, after 15 min, was added $BF_3.OEt_2$ (3.3 mL, 26.8 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** was obtained as a dark red solid (108 mg, 26%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.64 (s, 6H, CH_3-1 e CH_3-7), 2.63 (s, 6H, CH_3-3 and CH_3-5), 5.89 (s, 2H, H-2 and H-6), 7.41 (dt, *J* = 1.2 and 8.2 Hz, 2H, H-3′ and H-8′), 7.48 (dt, *J* = 1.2 and 8 Hz, 2H, H-4′ and H-7′), 7.91 (dd, *J* = 0.8 and 8.8 Hz, 2H, H-2′ and H-9′), 8.04 (d, *J* = 8.8 Hz, 2H, H-5′ and H-6′), 8.57 (s, 1H, H-1′) ppm.

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.29 (C1-CH_3 and C7-CH_3), 14.67 (C3-CH_3 and C5-CH_3), 121.15 (C2 and C6), 125.07 (C2′ and C9′), 125.72 (C4′and C7′), 126,93 (C3′ and C8′), 128.20 (C1′a and C9′a), 128.25 (C5′ and C6′), 128.32 (C1′), 129.66 (C5′b), 131.28 (C5′a and C6′a), 132.35 (C7a and C8a), 138.94 (C8), 142.87 (C1 e C7), 155.74 (C3 e C5) ppm.

MS (ESI) *m*/*z* (%): 426 ($[M + 2]^{+\bullet}$, 29), 425 ($[M + 1]^{+\bullet}$, 92), 424 ($[M]^{+\bullet}$, 26), 405 (100), 291 (31), 209 (7), 147 (8), 102 (29); HRMS (ESI) *m*/*z*: $[M + 1]^{+\bullet}$ calcd for $C_{27}H_{24}BF_2N_2$, 425.1995; found 425.1989.

2.3. Photophysical Characterization of BODIPY Derivative 1

The photophysical characterization, UV-Vis absorption and fluorescence, of BODIPY derivative **1** in acetonitrile (1×10^{-5} M) was carried out using quartz cells and the fluorescence standard used was Rhodamine 6G ($\Phi_F = 0.95$) in ethanol, with concentration 1×10^{-5} M [9]. 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 and the standard, the area under the curve was determined to allow the calculation of the relative quantum yield of fluorescence.

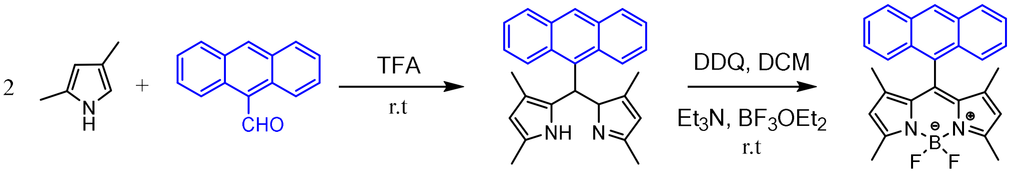
2.4. Chemosensing Studies of BODIPY Derivative 1

Through the preliminary study of the sensory capacity of the BODIPY derivative **1**, it is possible to verify in a simple and fast way the occurrence of interaction between the compound under analysis and different analytes through an optical signal. In this case, the analytes are several metal cations (Ag^+, K^+, Li^+, Hg^{2+}, Ca^{2+}, Co^{2+}, Pb^{2+}, Mn^{2+}, Fe^{2+}, Zn^{2+}, Ni^{2+}, Cd^{2+}, Cu^{2+}, Pd^{2+}, Fe^{3+} and Al^{3+}) with environmental and biomedical interest. For this study, solutions of the compound (1×10^{-5} M) and the various cations (1×10^{-2} M) were prepared in acetonitrile, and the study consisted in the addition of 50 equivalents of each ion to the BODIPY derivative **1** solution.

3. Results and Discussion

3.1. Synthesis of BODIPY Derivative 1

The synthesis of the *meso*-anthracene-BODIPY derivative **1** was accomplished in two reaction steps at room temperature. The first step consisted of the condensation reaction of 2,4-dimethylpyrrole and anthracene-9-carbaldehyde, in the presence of a catalytic amount of trifluoroacetic acid (TFA) to form the dipyrromethane core. The second reaction step consisted of the oxidation of dipyrromethane to dipyrromethene, through the addition of a solution of 2,3-dichloro-5,6-diciano-*p*-benzoquinone (DDQ). Then, the reaction mixture was subjected to the complexation reaction with $BF_3.OEt_2$ in the presence of triethylamine (Scheme 1). Finally, after purifying the product by dry flash chromatography, the pure BODIPY derivative **1** was obtained in the form of a dark red solid in 26% yield.



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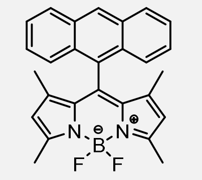
Scheme 1. Synthesis of a *meso*-anthracene-BODIPY derivative (**1**).

The interpretation of the ^1H NMR spectrum allowed to confirm the presence of the anthracene group at the *meso* position of the BODIPY core, with the characteristic proton signals appearing in the aromatic zone of the spectrum. The signals in the ^{13}C NMR spectrum and the obtained data from mass spectrometry were in agreement with the expected structure.

3.2. Photophysical Characterization of BODIPY Derivative 1

The photophysical characterization to evaluate the UV-Vis absorption and emission properties of the BODIPY derivative **1** was carried out in acetonitrile solution (1×10^{-5} M) (Table 1). BODIPY **1** exhibited an intense absorption band ($\log \varepsilon = 3.99$) at 502 nm and, after excitation, showed an intense emission band at 518 nm. A low relative quantum fluorescence yield was obtained for BODIPY 1 ($\Phi_F = 0.011$).

Table 1. UV-vis absorption and fluorescence of BODIPY derivative **1**, in acetonitrile (1×10^{-5} M).

Compound	UV-Vis		Fluorescence		
	λ_{max} (nm)	log ε	λ_{em} (nm)	Φ_F	Stokes' shift
	502	3.99	518	0.011	16

3.3. Preliminary Optical Chemosensing Studies of BODIPY Derivative 1

A preliminary chemosensing study of BODIPY derivative **1** was performed in acetonitrile solution (1×10^{-5} M) with various cations of interest, also in acetonitrile (1×10^{-2} M). The study was started by adding 50 equivalents of the solution of each cation to the compound's solution. It was observed that the BODIPY derivative showed a loss of color intensity after interaction with Cu^{2+} and intensification of orange coloration after interaction with Fe^{3+}. As for the fluorimetric behavior, the compound showed a loss of fluorescence in the presence of Cu^{2+} and a more intense quenching was observed in the presence of Fe^{3+} (Figure 1).

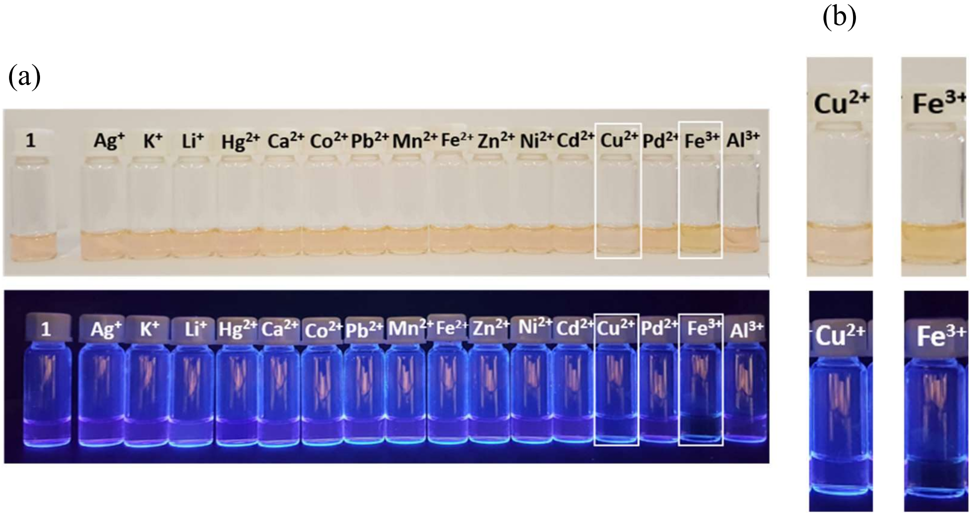


Figure 1. (**a**) BODIPY derivative **1** solutions in the presence of various cations, in acetonitrile, under natural light (above) and UV radiation at $\lambda_{max} = 365$ nm (below); (**b**) Expansion to highlight the color and fluorescence intensity changes in the presence of Cu^{2+} and Fe^{3+}.

4. Conclusions

The BODIPY derivative **1** functionalized at *meso* position with an anthracene group was synthesized through a condensation reaction between 2,4-dimethylpyrrole and anthracene-9-carbaldehyde, in 26% yield. This compound was characterized by the usual spectroscopic techniques and by the determination of its photophysical properties. Additionally, a preliminary chemosensing study of BODIPY derivative **1**, showed a colorimetric signal of this compound in the presence of Cu^{2+} and Fe^{3+}, through the loss of color and intensification of the orange coloration, respectively. The quenching of the fluorescence in the presence of these same ions was also observed. Therefore, BODIPY derivative **1** could be a potential selective colorimetric and fluorimetric chemosensor for Cu^{2+} and Fe^{3+}.

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

References.

1. Lakshmi, V.; Sharma, R.; Ravikanth, M. Functionalized Boron-Dipyrromethenes and Their Applications. *Rep. Org. Chem.* **2016**, *6*, 1–24, doi:10.2147/ROC.S60504.
2. Zlatić, K.; El Ayouchia, H.B.; Anane, H.; Mihaljević, B.; Basarić, N.; Rohand, T. Spectroscopic and Photophysical Properties of Mono- and Dithiosubstituted BODIPY Dyes. *J. Photochem. Photobiol. A Chem.* **2020**, *388*, 112206, doi:10.1016/j.jphotochem.2019.112206.
3. Suganya, S.; Naha, S.; Velmathi, S. A Critical Review on Colorimetric and Fluorescent Probes for the Sensing of Analytes via Relay Recognition from the Year 2012–17. *ChemistrySelect* **2018**, *3*, 7231–7268, doi:10.1002/slct.201801222.
4. Wu, D.; Chen, L.; Lee, W.; Ko, G.; Yin, J.; Yoon, J. Recent Progress in the Development of Organic Dye Based Near-Infrared Fluorescence Probes for Metal Ions. *Coord. Chem. Rev.* **2018**, *354*, 74–97, doi:10.1016/j.ccr.2017.06.011.
5. Okda, H.E.; El Sayed, S.; Otri, I.; Ferreira, R.C.M.; 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 Chromo-Fluorogenic Recognition of Biothiols and Cu(II) in Aqueous Environments. *Dyes Pigment*s **2019**, *162*, 303–308, doi:10.1016/j.dyepig.2018.10.017.
6. Udhayakumari, D.; Naha, S.; Velmathi, S. Colorimetric and Fluorescent Chemosensors for Cu^{2+}. A Comprehensive Review from the Years 2013–15. *Anal. Methods* **2017**, *9*, 552–578, doi:10.1039/c6ay02416e.
7. Lo Presti, M.; Martínez-Máñez, R.; Ros-Lis, J.V.; Batista, R.M.F.; Costa, S.P.G.; Raposo, M.M.; Sancenón, F. A Dual Channel Sulphur-Containing a Macrocycle Functionalised BODIPY Probe for the Detection of Hg(II) in a Mixed Aqueous Solution. *New J. Chem.* **2018**, *42*, 7863–7868, doi:10.1039/c7nj04699e.
8. 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 Pigment*s **2018**, *151*, 211–218, doi:10.1016/j.dyepig.2017.12.040.
9. Demas, J.N.; Crosby, G.A. The Measurement of Photolumineseence Quantum Yields. A Review. *J. Phys. Chem.* **1971**, *75*, 991–1024, doi:10.1021/j100678a001.