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A BODIPY Derivative for Selective Fluorescent Chemosensing of Iron (III) †

Raquel C. R. Gonçalves, Mathilde L. Boland, Susana P. G. Costa and M. Manuela M. Raposo *

Centre of Chemistry, University of Minho, Campus of Gualtar, 4710-057 Braga, Portugal; (R.C.R.G.); (M.L.B.); (S.P.G.C.); (M.M.M.R.)

* Correspondence: mfox@quimica.uminho.pt

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Abstract: A BODIPY derivative functionalized with a phenyl group at *meso*-position was synthesized and characterized through ^{1}H NMR and UV-Vis absorption/emission spectroscopies. The compound showed an absorption band at 497 nm and a fluorescence band at 513 nm, with a Φ_F = 0.68 in acetonitrile. The evaluation of the chemosensing ability of the BODIPY was investigated in the presence of several ions with environmental and biomedical relevance. A highly selective fluorimetric response was observed for Fe^{3+} through a fluorescence quenching upon successive additions of this cation.

Keywords: BODIPY derivative; fluorimetric chemosensor; fluorescence-quenching; iron (III); metal ions

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1. Introduction

The development of molecular sensors for detection of metal ions is an active research field with great potential for biomedical applications. It is well-known that metal ions display a fundamental role in biochemical processes, including, cell metabolism regulation and cell signaling. Moreover, iron is a cofactor of several proteins and enzymes involved in important processes such as oxygen transport, neurotransmission, regulation of gene expression and energy production. However, its abnormal levels in human tissues had been related to diabetes mellitus and neurodegenerative disease, namely, Alzheimer's disease. Therefore, the efficient detection of these species is a timeless topic in several areas of investigation [1–4].

3-Difluoroborodipyrromethene (BODIPY) derivatives have become a cornerstone in the optical sensors field because of their advantageous features: high molar absorptivity, high quantum fluorescence yields, intense and narrow absorption/emission bands in the visible region of the electromagnetic spectrum and good photochemical stability. Moreover, the BODIPY core can be chemically modified to fine tune their optical properties and to attach suitable receptor groups selective to a particular target [5–7].

Considering the above-mentioned facts as well as our research interest in BODIPY derivatives for several applications [8–15], particularly as optical chemosensors, we report herein a BODIPY fluorophore functionalized with a phenyl group at *meso* position for a selective response towards Fe^{3+}. The chemosensory ability of the BODIPY derivative was investigated in acetonitrile in the presence of different ions, showing a selective fluorescence quenching upon Fe^{3+} interaction.

2. Materials and Method

All reagents were purchased from Sigma-Aldrich (St. Louis, MO, USA), Acros (Geel, Belgium) and Fluka (Buchs, Switzerland) and used as received. TLC analyses were carried out on 0.25 mm thick pre-coated silica plates (Merck Fertigplatten Kieselgel $60F_{254}$) and spots were visualized under UV light. Chromatography on silica gel was carried out on Merck Kieselgel (230–400 mesh).

NMR spectra were obtained on a Bruker Avance III 400 at an operating frequency of 400 MHz for ^1H at 25 °C, using the solvent peak as an internal reference. All chemical shifts are given in ppm using δ_H $Me_4Si = 0$ ppm as reference. The synthesis of BODIPY derivative **1** has been reported elsewhere [16]. UV-visible absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer. Fluorescence spectra were collected using a Horiba FluoroMax-4 spectrofluorometer in quartz cells. The relative fluorescence quantum yield was calculated using a 1×10^{-5} M solution of Rhodamine 6G in ethanol as reference ($\Phi_F = 0.95$) [17,18].

2.1. Synthesis of the BODIPY Derivative **1**

2,4-Dimethylpyrrole (3.0 mmol) and benzaldehyde (1.5 mmol) were dissolved in dry dichloromethane (80 mL). Two drops of trifluoroacetic acid were added and the mixture was allowed to stir for 50 min at room temperature, under nitrogen atmosphere. A solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (3.0 mmol) in dry dichloromethane (100 mL) was added to the mixture. Stirring was continued for another 50 min and then triethylamine (25.5 mmol) was added. After stirring for 15 min, $BF_3.OEt_2$ (43.3 mmol) was added and further stirred for 30 min. The solvent was evaporated under reduced pressure and the crude residue was purified by dry flash chromatography (petroleum ether/dichloromethane, 2:1). BODIPY **1** (Figure 1) was obtained as an orange solid (0.106 g, 21%).

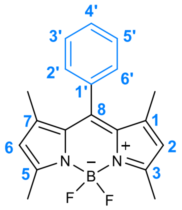


Figure 1. Structure of BODIPY derivative **1**.

^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.12$ (s, 6H, CH_3-1 and CH_3-7), 2.28 (s, 6H, CH_3-3 and CH_3-5), 5.73 (s, 2H, H-2 and H-6), 6.99–7.02 (m, 2H, H-3′ and H-5′), 7.21–7.24 (m, 3H, H-2′, H-4′ and H-6′) ppm.

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

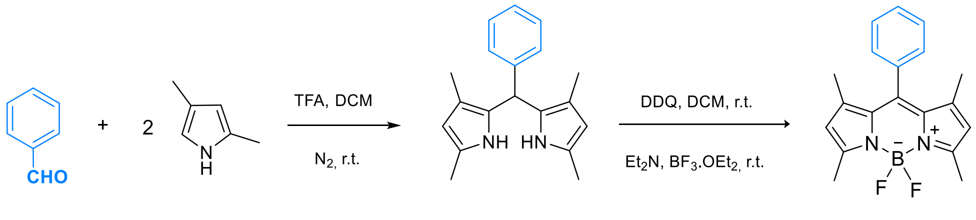
The evaluation of the BODIPY derivative **1** as optical chemosensor was carried out in the presence of several cations (Ag^+, K^+, Li^+, Na^+, Cu^+, TBT^+, Hg^{2+}, Ca^{2+}, Co^{2+}, Fe^{2+}, Zn^{2+}, Pb^{2+}, Mn^{2+}, Ni^{2+}, Cd^{2+}, Cu^{2+}, Pd^{2+}, Cs^{2+}, Fe^{3+}, Al^{3+}) and anions (HSO_4^-, 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 acetonitrile at a final concentration of 1×10^{-5} M and the solutions of ions were prepared in acetonitrile at a concentration of 1×10^{-2} M. The preliminary study was performed by the addition of 50 equivalents of each ion to the solution of BODIPY derivative.

The spectrofluorimetric titration was performed for the ion which induced a fluorimetric response in the preliminary study. The solution of BODIPY derivative **1** and the ion were prepared as in the previous study. A certain number of equivalents (eq) of the ion were successively added to the compound solution and the fluorescence spectra was plotted after each addition.

3. Results and Discussion

3.1. Synthesis and Photophysical Characterization of BODIPY Derivative **1**

The BODIPY derivative **1** was synthesized following the well-known Lindsey's method [18]. In the first step, benzaldehyde reacts with 2,4-dimethylpyrrole in presence of trifluoroacetic acid (TFA) as a catalyst, under nitrogen atmosphere. The oxidation of the dipyrromethane to dipyrromethene occurred through addition of a solution of 2,3-dichloro-5,6-diciano-1,4-benzoquinone (DDQ), followed by complexation with $BF_3.OEt_2$ in the presence of triethylamine, giving rise to BODIPY bearing a phenyl group at *meso*-position. The product was obtained after purification by chromatography as an orange solid in 21% yield (Scheme 1). The ^1H NMR of the compound was in accordance with the literature [16].



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Scheme 2. Synthetic route of BODIPY derivative **1.**

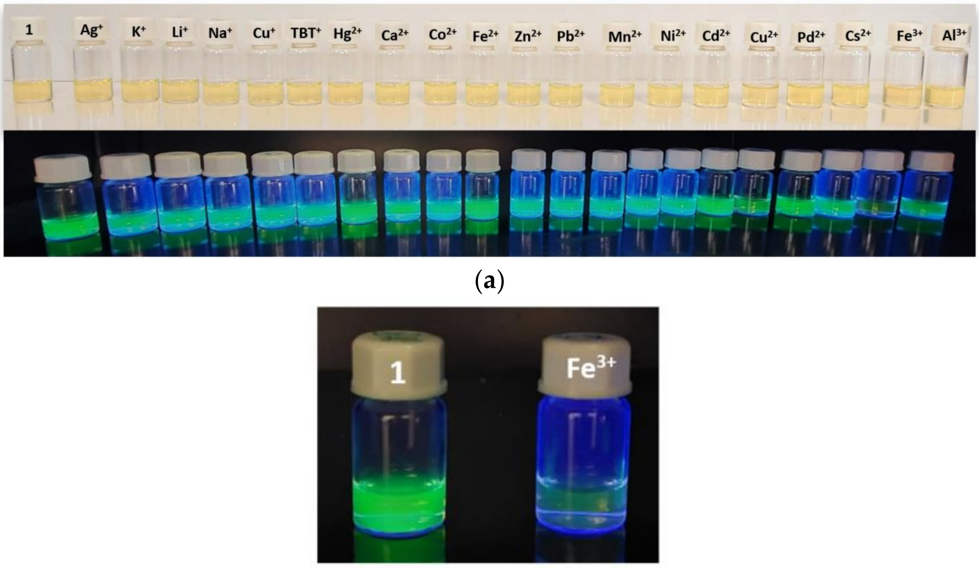
The photophysical features of BODIPY derivative **1** were studied in an aprotic solvent (acetonitrile). The compound exhibited an absorption band centered at 497 nm with a logarithmic molar absorption coefficient of 5.44 and an emission band with maximum at 513 nm. The relative fluorescence quantum yield was found to be 0.68.

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

Having in mind the application of BODIPY derivative **1** as a chemosensor of ions with biological and environmental importance, a preliminary study was carried out in acetonitrile solution in the presence of selected cations (Ag^+, K^+, Li^+, Na^+, Cu^+, TBT^+, Hg^{2+}, Ca^{2+}, Co^{2+}, Fe^{2+}, Zn^{2+}, Pb^{2+}, Mn^{2+}, Ni^{2+}, Cd^{2+}, Cu^{2+}, Pd^{2+}, Cs^{2+}, Fe^{3+}, Al^{3+}) and anions (HSO_4^-, NO_3^-, $H_2PO_4^-$, CN^-, BzO^-, ClO_4^-, Br^-, F^-, I^- and $CH_3CO_2^-$).

As shown in Figure 2, although no color change was observed in the presence of the different cations (Figure 2a), the fluorimetric response of the compound was remarkably selective for Fe^{3+} (Figure 2b), showing a fluorescence quenching upon interaction between the compound and the cation.

On the other hand, the interaction with the anions did not induce any perceptible changes, neither colorimetric nor fluorimetric.



(**a**)

(**b**)

Figure 2. (**a**) Evaluation of BODIPY derivative **1** as colorimetric (**top**) and fluorimetric (**bottom**) chemosensor for several cations (50 equivalents) in acetonitrile solution**.** (**b**) Fluorescence quenching in the presence of Fe^{3+}.

The spectrofluorimetric titration of BODIPY derivative **1** was performed in acetonitrile with Fe^{3+}, as a result of the preliminary study, which revealed the highly selective response towards this cation. The fluorescence spectra demonstrated that the intensity of the emission band at 513 nm decreased progressively upon addition of the cation and the number of Fe^{3+} equivalents to achieve a plateau was around 15 equivalents.

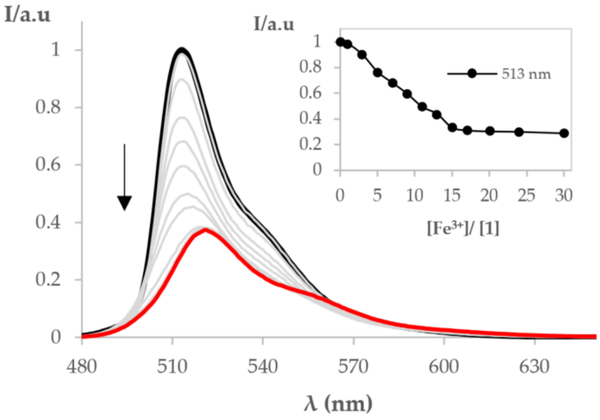


Figure 3. Spectrofluorimetric titration spectra of BODIPY derivative **1** upon addition of increasing quantities of Fe^{3+} (0–30 eq.) in acetonitrile. Inset: normalized emission intensity at 513 nm as a function of $[Fe^{3+}]/[$**1**$]$.

4. Conclusions

This work describes the photophysical properties and chemosensing studies toward several ions in acetonitrile of a BODIPY derivative bearing a phenyl unit at *meso*-position. The highly selective detection of Fe^{3+} in solution of acetonitrile among other ions was observed through a fluorescence quenching of the compound's emission band at 513 nm. This result might be of interest for applications of the BODIPY derivative **1** as a fluorimetric chemosensor of Fe^{3+}.

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