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meso-Triphenylamine-BODIPY Derivative for Optical Chemosensing of Metal Ions †

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Abstract: The design and synthesis of organic molecules for recognition of biologically/environmentally important metal ions have been emerging as a highly regarded research field. BODIPY core is a versatile signaling molecule that can be fine-tuned with functional groups to create selective binding sites and improve its optical properties. As an extension of the work developed in our research group, we report the synthesis and characterization of a BODIPY functionalized with triphenylamino and a formyl group at *meso* and 2-position, respectively, for a highly selective detection of Cu^{2+} and Fe^{3+}. The preliminary study of the BODIPY derivative as optical chemosensor was carried out in acetonitrile solution in the presence of different cations and interaction with Cu^{2+} and Fe^{3+} induced a perceptible color change. UV-visible titrations showed changes in the absorption spectra upon addition of 3 equivalents of each cation with the appearance of a new absorption band at 693 nm.

Keywords: BODIPY; metal ions; optical chemosensor; synthesis

1. Introduction

Great efforts have been devoted to developing organic molecules as optical chemosensors with application in fields of biomolecular analysis, medical diagnosis and environmental monitoring. In particular, metal ions became a prime target considering they are essential elements for biological systems but in uncontrolled amounts they might represent a critical issue. Classical chemosensors for metal ions contain molecular structures based on polyamines, polyethers, polysulfides, carboxylic acids, hydroxamic acids and open-chain or macrocyclic structures [1–4].

In the last two decades, BODIPY derivatives have emerged as a novel class of chemosensors for molecular recognition and biological fluorescent labelling. BODIPY shows remarkable optical properties, such as sharp absorption and emission patterns, high molar extinction coefficient of absorbance, high fluorescence quantum yield and good photostability under physiological conditions [5–7].

The functionalization of BODIPY framework enables the introduction of highly selective/sensitive binding sites and, simultaneously, modulate its photophysical properties. Modified BODIPYs at *meso*-position show greater stability than their *meso*-unsubstituted analogues. In fact, diverse aldehydes can be used to prepare *meso*-substituted derivatives which allows the design of innovative compounds bearing a large range of functional groups. Furthermore, BODIPY core is inherently an electron-rich heteroaromatic structure therefore very susceptible to regioselective electrophilic aromatic substitution reactions, with 2,6-positions undergoing preferential substitution [8,9].

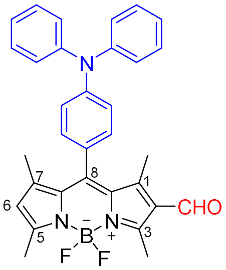
In continuation of our research group's work in the field of chromofluorogenic sensors [10–12], we report the synthesis, characterization and evaluation of a *meso*-triphenylamine-BODIPY derivative as optical chemosensor of Cu^{2+} and Fe^{3+} in acetonitrile solution.

2. Experimental Section

2.1. 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 shifts 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. BODIPY precursor 1 was synthesized as previously reported [13]. 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 determined by using a 1×10^{-5} M solution of Rhodamine 6G in ethanol as standard ($\Phi_F = 0.95$) [14,15].

2.2. Synthesis of BODPY Derivative **2**



A mixture of *N*,*N*-dimethylformamide (23 mmol) and $POCl_3$ (18.2 mmol) was stirred for 5 min at 0 °C under a N_2 atmosphere. The mixture was allowed to reach room temperature and stirred for additional 30 min. BODIPY precursor **1** (0.127 mmol) dissolved in dichloroethane (7 mL) was added dropwise while stirring. The reaction mixture was heated for 2 h at 50 °C. After cooling, the solution was poured slowly into 40 mL of saturated sodium bicarbonate solution at 0 °C and stirred during 30 min at room temperature. Ethyl acetate (5 mL) was added to the reaction mixture and the resulting organic layer was separated and washed with water (2 × 50 mL). The organic layer was dried with anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude residue was purified by a silica gel chromatography column, using dichloromethane as eluent. The final product was obtained as a dark red solid (6.8 mg, 15%).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 3H, CH_3-7), 1.89 (s, 3H, CH_3-1), 2.62 (s, 3H, CH_3-5), 2.83 (s, 3H, CH_3-3), 6.15 (s, 1H, H-6), 7.09–7.21 (m, 10H, Ar-H), 7.30–7.34 (m, 4H, Ar-H), 10.05 (s, 1H, CHO) ppm.

MS (ESI) *m*/*z* (%): 521 ($[M + 2]^{+\bullet}$, 35), 520 ($[M + 1]^{+\bullet}$, 100), 519 ($[M]^{+\bullet}$, 34), 453 (7), 232 (2); HRMS (ESI) *m*/*z*: $[M + 1]^{+\bullet}$ calcd for $C_{32}H_{29}BF_2N_3O$, 520.2366; found 520.2381.

2.3. Chemosensing Study of BODIPY Derivative 2 and UV-Visible Titrations

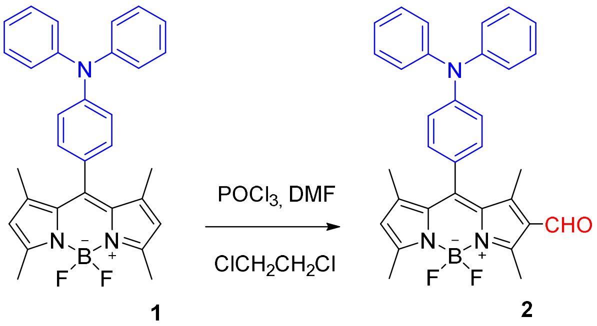
Evaluation of BODIPY derivative **2** as optical chemosensor was carried out in the presence of several cations (Ag^+, K^+, Li^+, Pb^{2+}, Mn^{2+}, Cd^{2+}, Cu^{2+}, Co^{2+}, Pd^{2+}, Ni^{2+}, Ca^{2+}, Hg^{2+}, Zn^{2+}, Fe^{2+}, Fe^{3+} and Al^{3+}) with environmental and biomedical relevance. Solutions of BODIPY derivative and cations were prepared in acetonitrile at 1×10^{-5} M and 1×10^{-2} M, respectively.

Preliminary study was carried out by addition of 50 equivalents of each cation to the solution of BODIPY derivative. UV-visible titration experiments were performed by the sequential addition of Cu^{2+} and Fe^{3+}, as a result of the previous study which revealed selectivity towards these cations. The stability constants were determined from UV−visible spectroscopic titration data, using the HypSpec software [16].

3. Results and Discussion

3.1. Synthesis of BODIPY Derivative **2**

BODIPY precursor **1** was prepared according to a procedure described previously [13]. The synthesis of BODIPY derivative **2** was obtained through Vilsmeier-Haack formylation of BODIPY precursor **1**, *meso*-substituted with a triphenylamino group, using *N*,*N*-dimethylformamide (DMF) and phosphorylchloride ($POCl_3$) as Vilsmeier reagent in dichloroethane (Scheme 1). The pure compound was obtained as a dark red solid in 15% yield.



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

The presence of a formyl group at position 2 of the BODIPY core was confirmed by ^1H NMR spectroscopy, with the appearance of a singlet at δ 10.05 ppm. As well, the obtained data from mass spectrometry was in agreement with the expected structure.

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 = 4.02) at 491 nm. Upon excitation at 460 nm, the compound exhibited an emission band at 515 nm. The relative fluorescence quantum yield, determined by using Rhodamine 6G in ethanol as standard ($\Phi_F = 0.95$), was found to be low ($\Phi_F = 0.010$). The small quantum yield measured could be ascribed to a carbonyl electron-withdrawing effect exerted by the formyl group linked to the BODIPY core [17].

3.3. Chemosensing Studies of BODIPY Derivative **2** *and Spectrophotometric Titration*

A preliminary evaluation of BODIPY derivative **2** as optical chemosensor was carried out in the presence of several cations in acetonitrile solution. The chromogenic response of BODIPY derivative was visible to the naked eye in the presence of Cu^{2+} and Fe^{3+}. In Figure 1 is observed the color modulation upon addition of 50 equivalents of each cation. As shown, a moderate color change from orange to blue-green exclusively occurred upon addition of Cu^{2+} and Fe^{3+}, while other cations were unable to induce a perceptible color change.

Figure 1. Color changes observed for BODIPY derivative **2** (1×10^{-5} M in acetonitrile) upon addition of 50 equivalents of different cations.

UV-visible titration of BODIPY derivative **2** was performed in acetonitrile with Cu^{2+} and Fe^{3+}, as a result of the previous study which revealed a selective chromogenic response towards these cations. As shown in Figure 2, a similar behaviour was observed upon addition of increasing quantities of Cu^{2+} and Fe^{3+}. The intensity of the absorption band at 298 nm decreased while a new red-shifted band appeared at 693 nm with a maximum absorbance reached at approximately 3 equivalents of each cation.

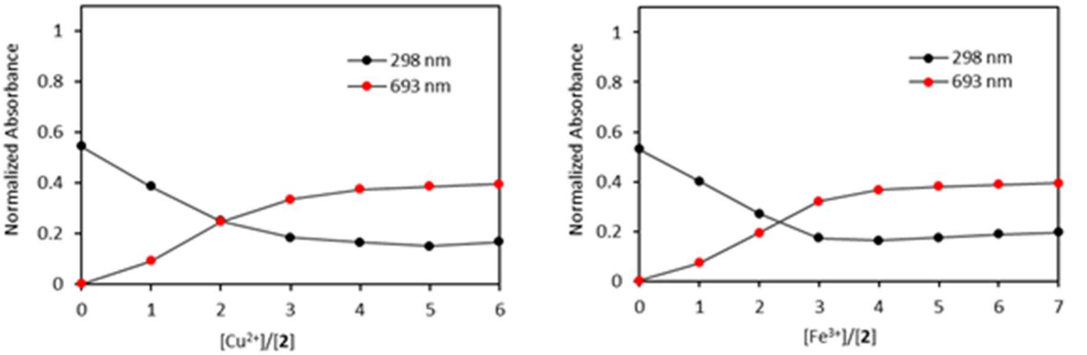


Figure 2. Absorbance at 298/693 nm as a function of the number of equivalents of each cation. Data was obtained from UV-visible titration spectra of BODIPY derivative **2** (1×10^{-5} M in acetonitrile) upon addition of increasing quantities of Cu^{2+} (left) and Fe^{3+} (right).

Moreover, the interaction between BODIPY derivative **2** with these cations was studied by the determination of the stability constants from UV−visible spectroscopic titration data, using the HypSpec software. The results suggested the formation of 2 : 1 cation–BODIPY stoichiometry complexes with a logarithm of the stability constant (log *K*) of 10.61 for Cu^{2+} and 10.19 for Fe^{3+}.

4. Conclusions

The BODIPY derivative **2** functionalized with triphenylamino and a formyl group at *meso* and 2-position, respectively, was synthesized by Vilsmeier-Haack formylation of the BODIPY precursor **1** and its molecular structure was confirmed by ^{1}H NMR and mass spectrometry. The recognition of both Cu^{2+} and Fe^{3+} in acetonitrile solution among several cations was observed through a perceptible color change from orange to blue-green. UV-visible titrations showed alterations in the absorption spectra upon addition of 3 equivalents of each cation with the appearance of a new absorption band at 693 nm, which clearly indicates that probe **2** can be used for detection of Cu^{2+} and Fe^{3+} ions in solution.

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

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