

PAPER • OPEN ACCESS

Nir mono and bi 2-vinylthiophene substituted boron dipyrin dyes: from practice to theory to further practice

To cite this article: A.Yu. Shagurin *et al* 2021 *J. Phys.: Conf. Ser.* **1822** 012018

View the [article online](#) for updates and enhancements.

You may also like

- [Between life and death: strategies to reduce phototoxicity in super-resolution microscopy](#)
Kalina L. Tosheva, Yue Yuan, Pedro Matos Pereira et al.
- [Fluorescent probes for detecting cysteine](#)
Fanyong Yan, Xiaodong Sun, Fanlin Zu et al.
- [Three-dimensional live microscopy beyond the diffraction limit](#)
Reto Fiolka



ECS
The
Electrochemical
Society
Advancing solid state &
electrochemical science & technology

DISCOVER
how sustainability
intersects with
electrochemistry & solid
state science research

Nir mono and bi 2-vinylthiophene substituted boron dipyrin dyes: from practice to theory to further practice

A.Yu. Shagurin, E.E. Molchanov, D.A. Sbytov and Yu.S. Marfin

Russia Laboratory of Coordination and Supramolecular Chemistry of Linear Oligopyrroles, Department of Inorganic Chemistry, Ivanovo State University of Chemistry and Technology, Russian Federation

shagurin.A.Y@gmail.com

Abstract. Boron dipyrin (BODIPY) family is one of the most studied collection of fluorophores, many of which are specifically designed for vital medical uses, such as cell imaging. In this research area, near-infrared absorbing and emitting compounds play the key role. Because of their long wavelength of absorption, they can be effectively excited by taking advantage of therapeutic window of human tissues. Herein we report the repeat of the synthesis of two vinylthiophene-substituted derivatives with extended π -electron systems and their computational investigation. Those dyes were prepared starting from methyl-substituted ones via addition reaction of aldehyde-containing thiophene following the literature. Obtained experimental and theoretical data will allow us to design promising tools not only for cell imaging, but also for fluorescent detection of heavy cations via coordination and possibly more.

1. Introduction

Among all fluorophores, boron dipyrin (BODIPY) derivatives definitely stand out due to their evergrowing popularity. BODIPY dyes are characterized by narrow and intense [1] absorption and emission bands, good thermo- and chemostability as well as tunability of spectral properties. Main areas of their application include but are not limited to fluorescent live cell imaging [2, 3, 4] and fluorescent response to the molecular environment i.e. solution viscosity [5, 6], pH [7], etc. Much thought has been put into extending the bathochromic shift of absorption of BODIPY dyes to take better advantage of NIR therapeutic tissue window [8, 9]. Another area that deserves attention is functional modification of BODIPY core to allow sensoric activity towards specific ions [10]. There are a lot of available options when it comes to the design of a BODIPY dye, but not all of them are theoretically understood.

Quantum chemistry has become quite a widespread way to explain obtained experimental results and predict/design the properties of new compounds. Although methods such as DFT for ground state or TD-DFT for response have become de facto standard for many molecules and solids, BODIPY dyes present their unique challenges. Indeed, most applications of BODIPY derivatives are related to their spectral properties or band gaps. Brown and Momeni have shown [11] that there is no quick black-box method to get accurate spectral properties for cyanine-like compounds. Standard errors associated with TD-DFT range from 0.3 to 1.0 eV.

A promising approach for such molecular systems relies on the use of Green's functions. Blase and coworkers have shown [12] that reasonable compromise between speed and accuracy can be achieved



by using Bethe–Salpeter equation, a single-reference method, on top of preliminary GW with remarkable success. Although the cost is certainly more than that of the TD-DFT calculation, its accuracy rivals much heavier methods such as CC3 or MC-PDFT.

Herein we report the synthesis, spectral properties and results of the quantum chemical investigation of 1,3,7-trimethyl-5-(2-vinylthiophene)-8-(2,4-dimethylphenyl)-BODIPY (later referenced as MONO) and 1,7-dimethyl-3,5-di(2-vinylthiophene)-8-(2,4-dimethylphenyl)-BODIPY (later referenced as BI) (figure 1). Thiophenyl substituted BODIPY and Aza-BODIPY dyes have recently been shown to possess NIR absorption and emission [13, 14] and good power conversion efficiency [15]. By using ethylene linking units between thiophene and BODIPY fragments we were able to further extend the pi-electron conjugation.

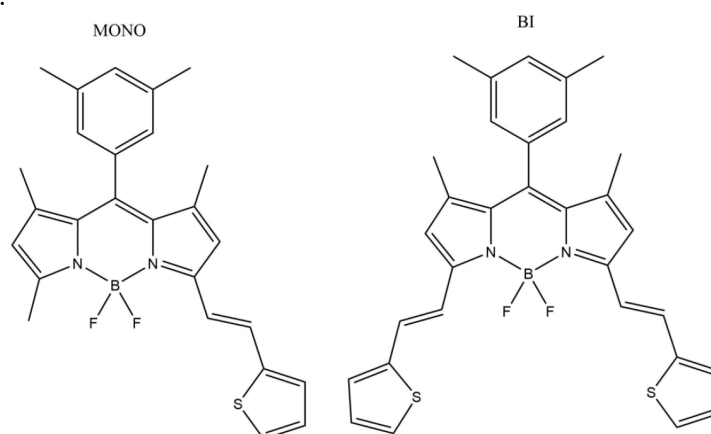


Fig. 1. Objects of the current study and nomenclature used throughout this paper.

2. Materials and methods

2.1. Synthesis

In a round bottom flask equipped with a Dean-Stark apparatus, a mixture of BODIPY (64 mg, 0.2 mmol), 2-thiophene-carboxaldehyde (40 mg, 0.4 mmol), glacial acetic acid (0.4 mL, 7.0 mmol), and piperidine (0.8 mL, 8 mmol) in toluene (20 mL) was refluxed for 10 h. The solution was heated at reflux for 12 h. After cooling to room temperature, the mixture was washed three times with water. MgSO_4 was added to dry the organic phase, and the solvent was evaporated under the reduced pressure. The crude residue was purified by silica-gel column chromatography (eluent: hexane/ethyl acetate (3:1)).

2.2. Experimental spectra

Absorption spectra were recorded on the Avantes AvaSpec-2048 spectrometer and emission spectra were recorded on the Cary Eclipse fluorescence spectrometer. Both compounds were dissolved in tetrachloromethane. To measure fluorescence, excitation wavelengths of 560 nm and 640 nm were used for MONO and BI compounds respectively.

2.3. Quantum chemistry

Conformational analysis was done by meta-dynamical simulations and automatic conformer-rotamer finding algorithm of the CREST program [16] using semi-empirical tight-binding GFN2-xTB [17]. All obtained conformers were resorted based on the Gibbs free energy. Relaxed potential energy surface scans were also performed with GFN2-xTB with a step of 1° .

DFT calculations were done using ORCA [18] software package. B3LYP/N07D model [19] was chosen for its good performance [20] and relatively small size. All optimized structures were confirmed to be minima based on vibrational analysis.

G0W0/B3LYP/6-31G and subsequent BSE calculations were done with the MOLGW [21] suit. RI approximation was employed together with the frozen core approximation wherever possible. BSE was used to obtain only the first seven roots instead of full diagonalization to save computational time.

No solvent model was used throughout the calculations for consistency as MOLGW does not have PCM implementation.

3. Results and discussion

3.1. Synthesis

The synthesis was controlled primarily by monitoring spectral properties of reaction mixture. As a result of chromatography two compounds were isolated and purified (MONO and BI). As a result of the introduction of thiophene substituents through the methene bridge there is a strong shift of absorption and fluorescence bands in the longer wavelength region (figure 2). Introduction of each such functional group leads to a bathochromic shift of spectral bands approximately by 0.3 eV. The low Stokes shift and intense fluorescence are preserved from the precursor.

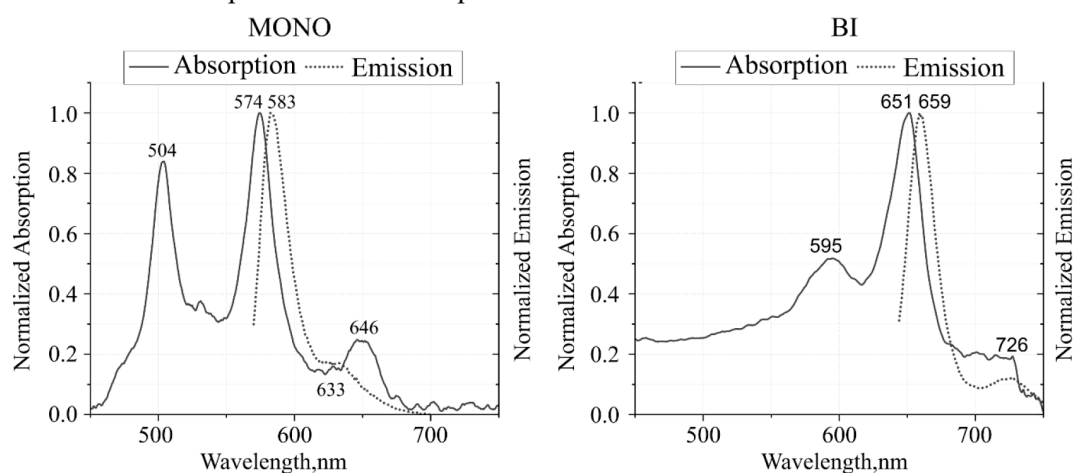


Fig. 2. Absorption and emission spectra of MONO and BI dyes obtained in CCl_4 .

3.2. Molecular geometry

Out of four possible MONO conformers and eight possible BI conformers the lowest energy corresponds to the inwards-facing sulfur atoms. Structures optimized at B3LYP/N07D level of theory are shown in figure 3. One immediately obvious advantage of ethenyl linkages is planar conjugation between thiophene and BODIPY core. Indeed, as was previously shown [14], direct bonding between those two fragments would result in steric hindrance (particularly between C2-H and thiophenyl's C-H hydrogens) and less than ideal pi-electron conjugation.

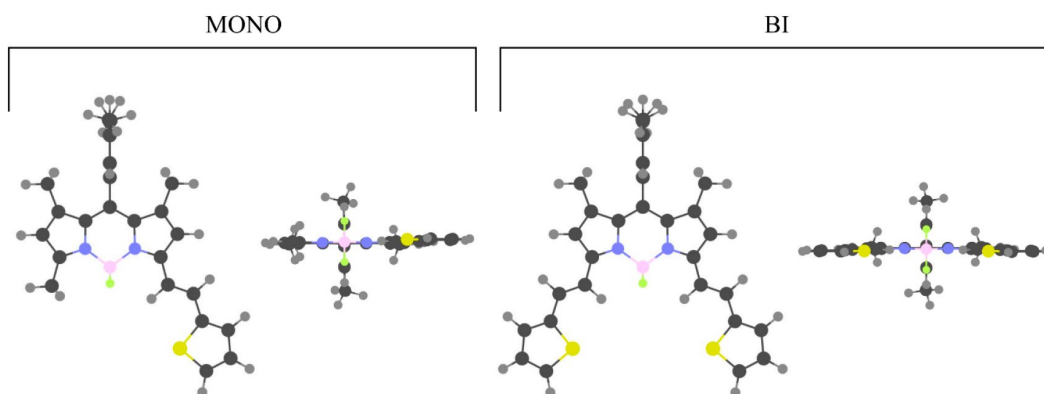


Fig. 3. Ground state geometries of MONO and BI dyes at the B3LYP/N07D level.

Because of the repulsion that 1, 7-methyl and 8-phenyl groups experience, dimethylphenyl fragment is exactly perpendicular to the rest of the molecule. From this we can expect essentially no conjugation between the two aromatic systems. Although this phenyl substitution helps to prevent attacks to the vulnerable 8-position via steric factors as well as stabilizes charged intermediates during the synthesis, its impact on the spectral properties is minimal. In fact, the depth of the PES at equilibrium geometry (figure 4) would render any rotational motion of phenyl fragment negligible. Thus, we can expect such derivatives to show high fluorescence quantum yield [22] and no viscosity sensitivity.

Quite big Sulfur-Sulfur distance of 7 Å would allow coordination of heavier metal cations and subsequent detection by changes in absorption/emission wavelengths.

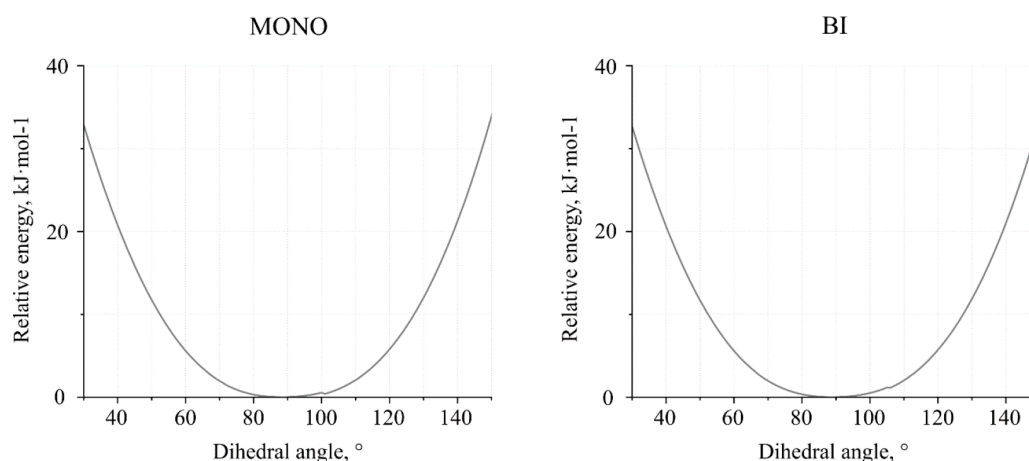


Fig. 4. Potential energy surfaces of MONO and BI dyes corresponding to the dimethylphenyl rotation at the GFN2-xTB.

3.3. Molecular orbitals

Figure 5 depicts frontier molecular orbitals isosurfaces and the respective G0W0 corrected energies. Introduction of a second vinylthiophenyl substituents results in the decrease of HOMO-LUMO gap by ca. 0.58 eV. Interestingly, along with the stabilization of the LUMO, a destabilization of the HOMO is observed. Spatial extent of the frontier molecular orbitals covers BODIPY core and 3, 5-substituents, but not the dimethylphenyl fragment, which is a direct consequence of geometries of MONO and BI.

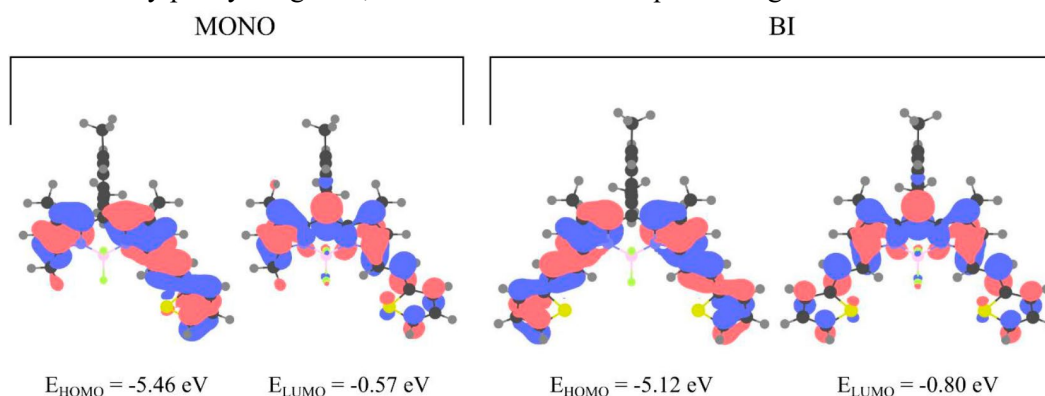


Fig. 5. Calculated HOMO and LUMO energies for MONO and BI dyes and corresponding isosurfaces visualized at 0.03 cutoff and calculated at BSE/G0W0/B3LYP/6-31G level.

3.4. Molecular orbitals

Vertical absorption spectra (figure 6) were calculated via BSE calculation on top of G0W0/B3LYP calculation. Obtained theoretical data is in a very good agreement with the experimental one. Here we can infer that the absorption peak at approximately 590 nm for BI is of vibronic structure - what is

usually called a “shoulder” and is characteristic for all BODIPY compounds. For the MONO dye the shoulder coincides with the precursors peak (500 nm. according to the literature [16]. Small peak at 650 nm for MONO is a BI fraction that could not have been prevented from forming.

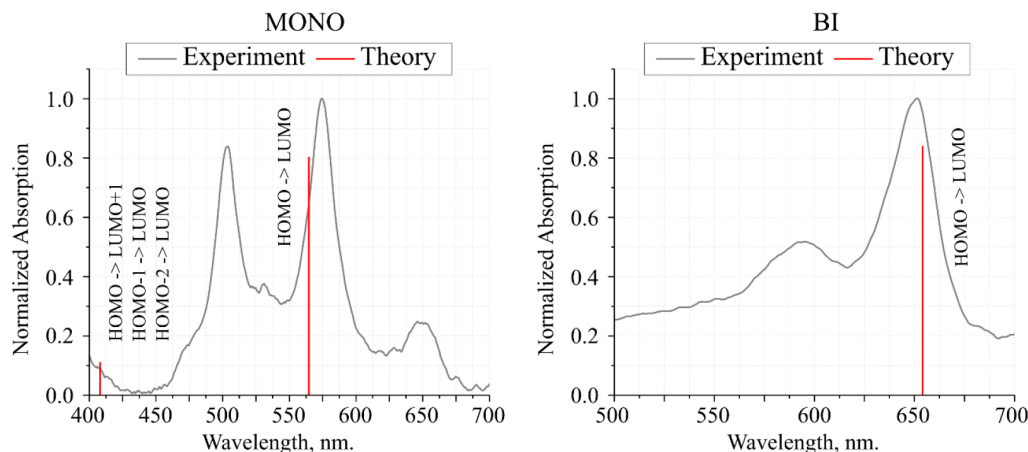


Fig. 6. Calculated vertical excitation spectra of MONO and BI dyes and corresponding transitions calculated at BSE/G0W0/B3LYP/6-31G level compared to the experimental absorption.

The main absorption band is dominated by a straightforward HOMO $\rightarrow$ LUMO transition, so the introduction of a second aromatic substituent results in a broader conjugation and further bathochromic shift.

4. Conclusions

In this research we report the successful synthesis of 3-(2-vinylthiophene) and 3,5-di(2-vinylthiophene) substituted BODIPY dyes. Used computational methods tested on those new structures proved to be quite effective. Remarkable agreement between theoretical and experimental absorption spectra will allow us to predict spectral properties of similar compounds before synthesizing them. One straightforward extension of this synthesis is to start from 8-methyl substituted BODIPY and introduce vinylthiophenyl or vinylfuranyl fragments [23] to obtain 3,5,8-trisubstituted dyes.

Acknowledgments

The study was supported by a grant Russian Science Foundation (project No. 19-73-10107) in part of the computer modeling of geometry and spectral properties of BODIPY dyes. The results of BODIPY synthesis, isolation and characterization were obtained within the state assignment of Gran of the Russian Foundation for Basic Research (Grant No 19-33-90232).

References

- [1] Banakova E, Marfin Y, Molchanov E, Shipalova M, Rumiantsev E and Fomina N 2019 *J. Fluoresc.* **21** 41–51
- [2] Kowada T, Maeda H and Kikuchi K 2015 *Chem. Soc. Rev.* **44** 4953
- [3] Vodyanova O, Kochergin B, Usoltsev S, Marfin Y, Rumyantsev E, Aleksakhina E and Tomilova I 2018 *J. Photochem. Photobiol. A* **350** 44–51
- [4] Marfin Y, Aleksakhina E, Merkushev D, Rumyantsev E and Tomilova I 2015 *J. Fluoresc.* **26** 255–261
- [5] Toliautas S, Dodonova J, Žvirblis A, Čiplys I, Polita A, Devižis A, Tumkevičius S, Šulskus J and Vyšniauskas A 2019 *Chem. – A Eur. J.* **25** 10342
- [6] Banakova E, Bobrov A, Kazak A, Marfin Yu, Merkushev D, Molchanov E, Rumyantsev E, Shipalova M, Usoltsev S and Vodyanova O 2017 *J. Phys.: Conf. Ser.* **951** 012017
- [7] Marfin Y, Shipalova M, Kurzin V, Ksenofontova K, Solomonov A and Rumyantsev E 2016 *J.*

- Fluoresc.* **26** 2105–2112.
- [8] Ni Y and Wu J 2014 *Org. Biomol. Chem.* **12** 3774
- [9] Molchanov E, Marfin Yu, Ksenofontov A and Rumyantsev E 2019 *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.* **62** 13–18
- [10] Li Q, Guo Y and Shao S 2012 *Sensors Actuators, B Chem.* **872** 171–172
- [11] Momeni M and Brown A 2015 *J. Chem. Theory Comput.* **11** 2619
- [12] Boulanger P, Jacquemin D, Duchemin I and Blasé X 2014 *J. Chem. Theory Comput.* **10** 1212
- [13] Rihn S, Retailleau P, Bugsaliewicz N, De Nicola A and Ziessel R 2009 *Tetrahedron Lett.* **50** 7008
- [14] Zhang X, Yu H and Xiao Y 2012 *J. Org. Chem.* **77** 669
- [15] Mirloup A, Leclerc N, Rihn S, Bura T, Bechara R, Hébraud A, Lévêque P, Heiser T and Ziessel R 2014 *New J. Chem.* **38** 3644
- [16] Grimme S 2019 *J. Chem. Theory Comput.* **15** 2847
- [17] Bannwarth C, Ehlert S and Grimme S 2019 *J. Chem. Theory Comput.* **15** 1652
- [18] Neese F 2018 *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **8**
- [19] Barone V, Cimino P and Stendardo E 2008 *J. Chem. Theory Comput.* **4** 751
- [20] Ferrari B and Bennett C 2019 *J. Phys. Conf. Ser.* **1290** 12013
- [21] Bruneval F, Rangel T, Hamed S, Shao M, Yang C and Neaton J 2016 *Comput. Phys. Commun.* **208** 149
- [22] Gibbs J, Robins L, Zhou Z, Bobadova-Parvanova P, Cottam M, McCandless G, Fronczek F and Vicente M 2013 *Bioorganic Med. Chem.* **21** 5770
- [23] Shivran N, Mula S, Ghanty T and Chattopadhyay S 2011 *Org. Lett.* **13** 5870