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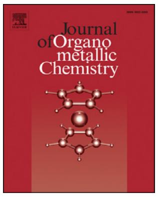

On the structure of *meso*-substituted F-BODIPYs and their assembly in molecular crystals: An experimental-theoretical approach

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ABSTRACT

Molecular crystals of *meso*-(5-((4-formylphenyl)ethynyl)thiophen-2-yl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene **4a** and *meso*-(4-((4-formylphenyl)ethynyl)phenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene **4b** were synthesized using palladium(0)-catalyzed Sonogashira cross coupling reactions and characterized using an experimental-theoretical approach. The crystal structures of F-BODIPYs **4a-b** are structurally analogous, yet their crystal packing motifs displayed remarkable differences due to contrasting hydrogen-bonding interactions. A CASTEP study of the unit cell for each compound provided the theoretical band structure and density-of-states (DOS) diagrams for each molecular crystal, suggesting a semiconductor character for both solids. Analysis of the computed electron density with Bader's QTAIM describes the intermolecular-contact network within each periodic system, while Natural Bonding Orbitals (NBO) display in-phase overlap between stacked units, denoting intermolecular delocalization of the electron density via stacking. TDDFT analysis of solution UV-Vis spectra gives insight into the nature of the observed excitations along with the effects derived from the relative rotation of π-subsystems in solution.

1. Introduction

The possibility to tailor fluorescent small-molecular compounds to display predefined features has been very useful for medicinal, molecular and materials applications. The progress in fluorescence and microscopy imaging techniques is intimately related to the evolution of dyes and small-molecular fluorophores. In this sense, 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene derivatives (*see* Fig. 1), typically named F-BODIPYs, have received particular attention due to their absorption and emission profiles, along with synthetic feasibility and chemical stability [1]. F-BODIPYs have been tested in DNA sequencing and bio-analysis [2], as fluorescent probes [3], as molecular sensors [4], in photodynamic therapy [5], and in organic light emitting diodes (OLEDs) [6]. Moreover, it is possible to tune their spectroscopic and photo-physical properties functionalizing the pyrrole core, the *meso* position and also the boron substituents, depending on the properties and the applications to achieve [7].

In general, there are various strategies to functionalize the F-BODIPY dyes at the *meso*-position. Particularly, the *meso*-aryl F-BODIPYs are readily prepared from commercial aromatic aldehydes; in this case, the *meso*-aryl substituent adopts an orthogonal conformation with respect to the F-BODIPY core which reflects in suboptimal electronic coupling between them. Alternatives to introduce substituents *via* nucleophilic aromatic substitution or by palladium-catalyzed cross-coupling reactions at *meso*-position are the use of *meso*-methylthio-F-BODIPYs [8] or *meso*-halogenated-F-BODIPYs [9]. Another strategy involves the introduction of electron-donor groups at *meso*-position bridged by an ethynyl group, which favors electronic coupling between the introduced

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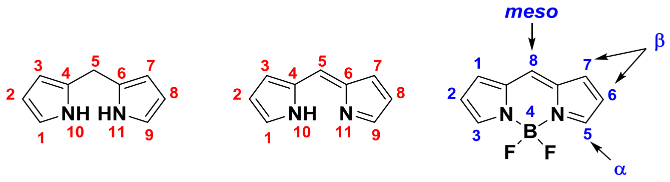

Fig. 1. Generic structural formulas for: dipyrromethane, dipyrromethene, and F-BODIPY cores.

substituent and the F-BODIPY core [10].

In contrast with these rotationally-unhindered systems, where molecular response to absorption may be fine-tuned by remote functionalization at the incorporated moiety, *meso*-aryl substituents display only very small responses to functional group introduction or structural decoration at distal positions. Due to sterically-hindered planarization, absorption and fluorescence bands arise mainly from transitions within the BODIPY core; only minute contribution from the staggered, vicinal aryl group are observed; electron-donor groups directly attached to this *meso*-position, however, have been found to significantly blue-shift absorption and emission maxima [11]. On the other hand, electron-acceptor substituents red-shift the spectral characteristics of the BODIPY core [12]. An appealing feature of *meso*-aryl F-BODIPYs is, hence, their potential application as molecular tags, whose introduction into larger systems embodied this partial disruption of π-electron delocalization, isolating the F-BODIPY core, and its properties as chromophore, from remote electronic effects.

Generally, the photophysics of F-BODIPYs is insensitive to solvent effects; *meso*-substitution with the adequate electron-donor or acceptor groups provokes, however, different photophysical processes in response to the environment. To achieve an efficient light-harvesting system, covering the broadest region within the visible spectrum, the adequate combination of electron-donor and electron-acceptor groups substituting the *meso*-position and F-BODIPY core must be met. Regrettably, detailed analysis about the influence of single substituents on the absorption and emission of these kinds of dyes is not present in the literature.

Herein we report a synthetic route to obtain highly crystalline F-BODIPYs. These compounds display a reactive formyl group for covalent anchoring and derivatization. Through carbonyl chemistry, a wide chemical space may be readily covered, giving access to a diverse palette of increasingly-complex systems; introduction of molecular antennae to different structures may be performed as well. To delve deeper into the structural and electronic properties of the molecular crystals based on F-BODIPYs, the featured molecular structures were thoroughly studied using an experimental-theoretical approach. Electronic excitations were characterized for the highlighted compounds through UV–vis and time-dependent density-functional-theory (TDDFT) studies. The different degrees of electronic communication and conformational freedom were studied through this tandem strategy to describe the absorptive behavior of these chromophores in solution. The presented molecules readily provided molecular crystals which were solved within the P -1 group. Solid-state superstructures exhibited periodic networks of directionally-stacked subunits, as derived through analysis of the computed electron density for each experimental unit-cell within the Quantum Theory of Atoms in Molecules (QTAIM). Natural Bonding Orbitals (NBO) computed for these densities feature in-phase intermolecular overlap across the molecular crystal, evidencing electronic communication among molecules within the crystalline domain. CASTEP analysis of the periodic lattices suggests a semiconductor character for both molecular crystals.

2. Results and discussion

2.1. Synthesis and structural characterization of F-BODIPYs 4a-b

The F-BODIPYs **2a-b** were synthesized in good yields following classical methodologies reported for these compounds (*see* Supporting Information File), the spectroscopic data confirmed their presence and matched with the previously reported [13]. The brominated F-BODIPYs **2a-b** were reacted with 4-ethynylbenzaldehyde **3** under Pd(0)-catalyzed Sonogashira cross-coupling conditions [14] to produce the corresponding F-BODIPYs **4a** (80%) and **4b** (63%) in moderate yields (*see* Scheme 1).

The synthesis of F-BODIPYs was corroborated by solution NMR experiments, where the ^{1}H-NMR spectrum of **4a** showed a single signal at $\delta = 10.04$ ppm for (H-17) and two doublet signals at $\delta = 7.90$ (H-15) and 7.70 ppm (H-14), confirming the presence of the benzaldehyde fragment. The thiophene ring displayed two doublet signals at $\delta = 7.50$ (H-9) and 7.45 ppm (H-8). In the ^{1}H-NMR spectrum of **4b**, the aldehyde hydrogen appeared as a singlet signal at $\delta = 10.05$ ppm (H-17). The phenyl rings can be unambiguously distinguished: the two doublet at $\delta = 7.91$ (H-15) and 7.60 ppm (H-14) for the benzaldehyde fragment, and the doublet-doublet-doublet signal at $\delta = 7.72$ ppm (H-8, H-9) for the phenyl bridge. The characteristic signals for the benzaldehyde fragment at $\delta = 191.2$ (C-17), 136.0 (C-16), 132.0 (C-14), 129.7 (C-15), 128.2 ppm (C-13) for **4a** and 191.5 (C-17), 135.9 (C-16), 130.7 (C-14), 129.8 (C-15) and 125.4 ppm (C-13) for **4b,** were present in the ^{13}C-NMR spectra. The alkyne bridge appeared at $\delta = 96.0$, 91.2 (C-12) and 85.2, 92.1 ppm (C-11) for **4a** and **4b**, respectively. Evidence for the boron complexation was obtained through ^{11}B- and ^{19}F-NMR experiments; for both compounds, a triplet signal appeared at *ca.* $\delta = -0.27$ ppm, and a quartet at *ca.* $\delta = -145$ ppm, respectively. The observed peaks at *m/z* 403.0889 (**4a**) and 397.1321 (**4b**) from high resolution mass spectrometry analyses were in accordance with the expected molecular ions. The FTIR spectra for F-BODIPYs **4a-b** showed the characteristic band for the C=O stretch at *ca.* $\nu = 1699$ cm^{-1}, and the band for the $-$C≡C- stretching around $\nu = 2200$ cm^{-1} for both compounds.

Suitable single crystals for X-Ray diffraction of compound **4a** were grown by slow evaporation of acetone solutions in partially closed glass vials. The molecular structure of compound **4a** was solved in the triclinic space group P -1 with Z = 2 as shown in Fig. 2a.

The structure of **4a** in the crystalline phase is not planar; the values of dihedral angles, discussed below confirmed this statement. Hydrogen-bonding C2–H2···O1 (**2.64 Å**) and C14–H14···F1 (**2.68 Å**) interactions aligned the molecules in a *head to tail* fashion creating one-dimensional monolayers. These monolayers are self-assembled by complementary hydrogen-bonding interactions between the BODIPY cores, C3–H3···F1 (**2.54 Å**) and C3′-H3′···F2 (**2.47 Å**) (*see* Fig. 3).

Dihedral angles between selected planes: (1) BODIPY core, (2) aryl *meso*-substituent and (3) benzaldehyde ring are calculated using all non-hydrogen atoms through the graphical interface from SHELXL [15] and Mercury [16] programs; the results are summarized in Table 1. The dihedral angle values were 44° for **4a** and 55° for **4b** between planes 1 and 2, the result for **4a** is reasonable considering hindrance arising from a single H–H interaction and a, presumably favorable, H–S contact; the larger value for **4b** is expected for hindered rings (such as 85° for *o*-tolyl or 75° for mesityl *meso*-substituents), due to restricted motion around the pyrrole rings [17]. Obviously, smaller values for dihedral angles between the BODIPY core and aryl *meso*-substituents are expected to favor electron density delocalization over the π-conjugated system.

Crystals of F-BODIPY **4b** were obtained by slow evaporation of hexanes/methylene chloride solutions (3:2) in partially closed glass