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# Development of Mono- and Di-AcO Substituted BODIPYs on the Boron Center

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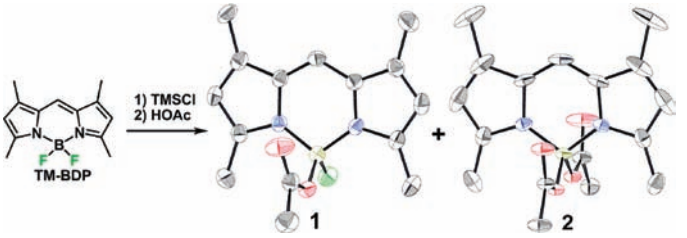
## ABSTRACT




**Mono- and di-AcO substituted BODIPYs (1 and 2) were synthesized from TM-BDP. The structures of 1 and 2 were supported by single crystal X-ray analysis. Both 1 and 2 possess a large absorption coefficient, high fluorescence quantum yield, and high light stability. Compound 2 has much improved water solubility which is highly desirable for biological applications. Theoretical calculation supports our observations in X-ray analysis, absorption, and cyclic voltammetry.**

In recent decades, 4,4′-difluoro-4-bora-3*a*,4*a*-diaza-*s*-indacene (abbreviated as F-BODIPY) dyes have received increased attention because of their high fluorescence quantum yields, high absorption coefficients, good solubility in organic solvents, and excellent thermal and photochemical stabilities. Various modifications on F-BODIPY dyes result in potential applications in probes and sensors, laser dyes, light harvesters, organic light emitting diodes, and sensitizers for solar cells.[1,2]

Apart from the various modifications on F-BODIPY cores,[2] very recently, modifications on the boron center became an active area. Modifications on boron not only generates a new series of fluorescent dyes but also opens up novel ways of functionalization of fluorescent dyes.[3−6] The replacement of fluoride atom(s) in F-BODIPY with ethynyl derivatives (leading to E-BODIPY),[3] and alkyl or aryl derivatives (formed C-BODIPY),[4] to modulate stability, solubility, Stokes shift, and electronic properties, was

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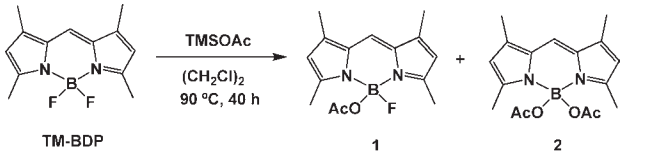
an important advance in BODIPY studies. The replacements of fluoride in F-BODIPY with alcohol or phenol affording alkoxy or aroxy BODIPYs,[5] as well as B, O-chelated BODIPYs,[6] were also reported to be useful strategies for adjusting fluorescence properties. F-BODIPY dyes are generally quite hydrophobic. For biological and medical applications, functionalized BODIPYs providing good water solubility are preferred. We have been interested in novel BODIPY and aza-BODIPY dyes.[7] Apart from modifications on the pyrrole moiety with water solubilizing functionalities, we are also interested in the novel replacement on the boron atom. Although many studies on boron substitution were documented,[3−6] the new type of boron modification is highly desired. Herein we wish to report novel BODIPY dyes with acetoxy (AcO) substituent(s) on the boron center of BODIPY dyes.

It is well-known that the electronic nature of the substituents on the BODIPY core and boron atom affects the fluorescent properties.[8,9] The reported replacement of F-BODIPYs on the boron atom with an alkoxy or aroxy group indicated that flexible alkoxy and electron-donating aroxy groups significantly diminished the fluorescent quantum yields of BODIPYs.[5c] It is noteworthy that a BODIPY dye with an electron-withdrawing aroxy group on the boron atom exhibited high fluorescent yield.[4g,5c] Inspired by the aforementioned reports, we are curious about the effect of an electron-withdrawing carboxylate on the boron atom in BODIPY. Herein we found that mono- and di-AcO substituted BODIPYs exhibited excellent fluorescence quantum yields and photostability. During preparation of this manuscript, a stability study of BODIPY dyes indicated that a 4,4′-dichloroacetoxy analog of BODIPY was formed when 4,4′-dimethoxy BODIPY was mixed with an excess of dichloroacetic acid in methylene chloride.[10] However, no fluorescence study of the 4, 4′-dichloroacetoxy BODIPY was explored.

4-AcO-4′-F-BODIPY **1** and 4,4′-$(AcO)_2$-BODIPY **2** were successfully obtained by utilizing TMSOAc generated in situ from acetic acid and TMSCl (Scheme 1).[11] With 5 equiv of TMSOAc, **1** (12%) and **2** (13%) were isolated. With 20 equiv of TMSOAc, 18% of **1** and 37% of **2** were obtained.

**Scheme 1.** Synthesis of BODIPY Analogs **1** and **2**




Both compounds **1** and **2** are highly fluorescent. The properties of **1** and **2** were evaluated in comparison with **TM-BDP** ($\lambda_{abs}$ = 509 nm; $\lambda_{em}$ = 516 nm; $\varepsilon$ = 80 000 $M^{-1}$ $cm^{-1}$; $\Phi_f$ = 0.92 in $CHCl_3$).[4a] The spectra of absorption and fluorescence of **1** and **2** are shown in Figure 1. Both **1** and **2** absorb at 510 nm and emit at 517 nm, which are very similar to those of the parent **TM-BDP**. Both **1** and **2** possess an identical Stokes shift to **TM-BDP** (7 nm). Monosubstituted species **1** possesses an almost identical extinction coefficient ($\varepsilon$ = 73 600 $M^{-1}$ $cm^{-1}$) to the parent **TM-BDP** and a slightly higher quantum yield ($\Phi_f$ = 0.96), compared to disubstituted **2** ($\varepsilon$ = 72 500 $M^{-1}$ $cm^{-1}$; $\Phi_f$ = 0.86). Replacement of an F-atom with AcO functionality provides a narrower full width at half-maximum (fwhm = 14 nm for **1**; fwhm = 16 nm for **2**) compared with the parent **TM-BDP** (fwhm = 19 nm).

Both **1** and **2** were found to be fully stable to air and moisture. When pH-dependence experiments were explored, we found that **1** and **2** were less degraded in basic conditions than the parent **TM-BDP**; however, they were more susceptible to lose boron and to generate dipyrrin in acidic conditions (Figure 2).[4h,10]

The dyes **1** and **2** are more polar than the parent **TM-BDP** and, thus, have improved water solubility. While

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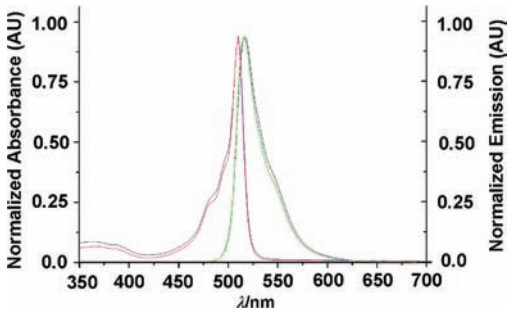


**Figure 1.** Normalized absorption and emission spectra of **1** (blue color for absorption and green for emission) and **2** (red color for absorption and black for emission) in $CHCl_3$ at 298 K.

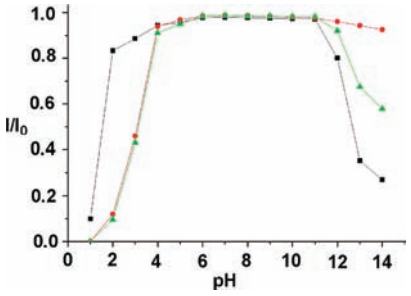


**Figure 2.** Normalized transmission ($I/I_0$) of **1** (red ●), **2** (green ▲), and **TM-BDP** (black ■) in response to pH range 1−14 in DMSO/$H_2O$ (1:1, v/v) after 24 h.

the parent hydrophobic **TM-BDP** has undetectable solubility in water, dye **2** exhibits 89 $\mu$g/mL solubility in water. The light stabilities of **1** and **2** were evaluated by monitoring the intensity changes of the emission with time of irradiation. The normalized intensities of emission of **1** and **2** in comparison with that of **TM-BDP** are shown in Figure 3. Compounds **1** and **2** have excellent light stability as in the case of the parent **TM-BDP**.

The structures of **1** and **2** were unambiguously confirmed by single crystal X-ray analysis (Figure 4). The bond lengths O1−C14 and C14−O2 in **1** were 1.323 and 1.191 Å, respectively, and close to those of acetic acid (*C*−*O*H: 1.31 Å; *C*═*O*: 1.25 Å). However, the distance of O1−B1 (1.484 Å) in **1** was found to be longer than that (1.437 Å) of BODIPY with dimethoxyl substituents by 0.04 Å[5c] and identical to that (CO*O*−*C*: 1.484 Å) of ester.[12] The $sp^3$ hybridized boron center in **1** appeared in a slightly distorted tetrahedron geometry with angles N1−B1−N2 of 107.8° and F1−B1−O1 of 104.5° compared with those (N1−B1−N2: 106.90°; F1−B1−C19: 111.63°) in mono-substituted perfluorinated aryl BODIPY.[4g] The bond lengths in **2** were similar to those in **1** (see Supporting

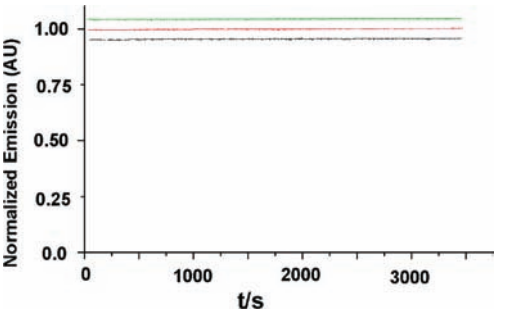


**Figure 3.** Intensity variations of **1** (red), **2** (green), and TM-BDP (black) under continuous irradiation with light (470 nm) in toluene (for clarity, the initial normalized intensities for compounds **1**, **2**, and **TM-BDY** are arbitrarily designated as 1.0, 1.05, and 0.95, respectively).

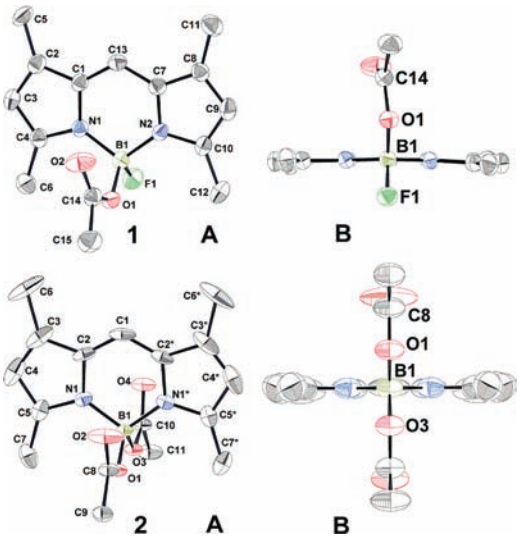


**Figure 4.** ORTEP view of **1** and **2** (displacement ellipsoids at the 30% probability level). All hydrogen atoms are omitted for clarity. Top view (A). Side view (B).

Information for details). However, the dihedral angle of F1−B1−O1−C14 in **1** was 171.3° and deviated from the ideal value of 180° from the side view. In stark comparison, the dihedral angle of O3−B1−O1−C8 in **2** was 180°.[13]

For cyclic voltammetry, the prototypic TM-BDP displayed a one-electron, reversible oxidation wave with a half-wave potential of +1.375 V (vs ferrocenium/ferrocene (Fc+/Fc)) (Figure 5). There was a corresponding one-electron, reversible reduction wave with a half-wave potential of 1.225 V (vs Fc+/Fc). In comparison, half-wave potentials for **1** and **2**, which lack one or both fluorine

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atoms, were 1.392 and 1.373 V for oxidization, and −1.208 and −1.232 V for the reduction, respectively. Both processes remained electrochemically reversible. It was interesting to note that the energy gap between HOMO and LUMO localized on the BODIPYs (2.600 V for **1**; 2.605 V for **2**) was identical to that (2.600 V) of the parent **TM-BDP**. The resemblance of energy gap resulted in the likeness of absorption and emission for **1**, **2**, and the parent **TM-BDP**.

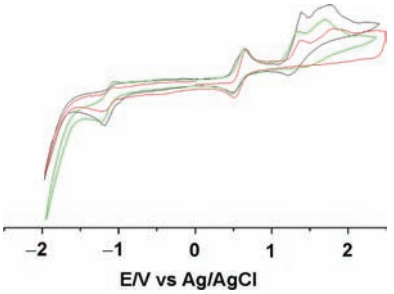


**Figure 5.** Cyclic voltammetry in $CH_2Cl_2$ at 20 °C using 0.1 M $n$Bu$_4$PF$_6$ as supporting electrolyte at a scan rate of 100 mV/s. **TM-BDP** (black), **1** (green), and **2** (red). Ferrocene is used as an internal standard ((half-wave potential) 0.65 V vs Ag/AgCl).[14]

MO calculations (Figure 6) revealed that the optimized structures of **1** and **2** were in good agreement with the crystal structures. The AcO groups are oriented essentially perpendicular to the dipyrromethene skeleton, and MO coefficients of all compounds are mainly localized on the dipyrromethene moiety. It means that the electronic substitution effect is negligible. Energy levels of frontier orbitals in **1**, **2**, and **TM-BDP** are almost identical, which suggests a similarity in absorption and cyclic voltammetry.

In conclusion, mono- and di-AcO substituted BODIPYs **1** and **2** were successfully prepared. The structures of **1** and **2** were supported by single crystal X-ray analysis. **1** and **2** possess the good characteristics of parent **TM-BDP** such as a large absorption coefficient, high fluorescence quantum yield, high light stability, etc. The AcO modification(s) on boron resulted in significantly improved water solubility

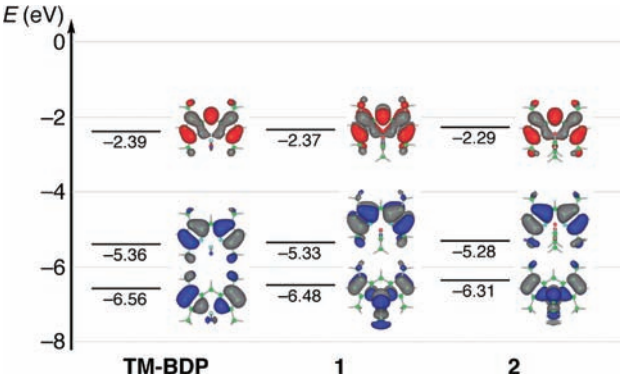


**Figure 6.** Energy levels of frontier molecular orbitals and their contour plots obtained from calculation. Blue plots indicate occupied orbitals, and red plots represent unoccupied orbitals. Calculations were performed at the B3LYP/6-31G* level (for details, see Supporting Information).

which is highly desirable for biological applications. MO calculations fit well with the observations in X-ray analysis, absorption, and cyclic voltammetry. Additional studies on further expansion of acid components, as well as modifications on boron with functionalized acids, are underway and will be reported in due course.

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**Supporting Information Available.** Experimental procedures, characterization data, the CIF files of compounds **1** and **2**, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.