Rationalizing the Photophysical Properties of BODIPY Laser Dyes via Aromaticity and Electron-Donor-Based Structural Perturbations

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Abstract

The absorption and fluorescence properties of six boron dipyrromethene (BODIPY) laser dyes with simple non-aromatic substituents are rationalized by relating them to observable structural perturbations within the molecules of the dyes. An empirical relationship involving the structure and the optical properties is derived using a combination of single-crystal X-ray diffraction data, quantum chemical calculations and electronic constants: i.e. the tendency of the pyrrole bond lengths towards aromaticity and the UV-vis absorption and fluorescence wavelengths correlate with the electron-donor properties of the substituents. The effect of molecular conformation on the solid-state optical properties of the dyes is also discussed. The findings in this study also demonstrate the usefulness and limitations of using crystal structure data to develop structure-property relationships in this class of optical materials, contributing to the growing effort to design optoelectronic materials with tunable properties via molecular engineering.

Keywords: X-ray diffraction, structure-property relationships, optoelectronics, absorption, fluorescence, DFT

1. Introduction

Since their initial development, reported in the late 1960s [1], boron dipyrromethene (BODIPY) derivatives (Figure 1) have been studied extensively due to their interesting optical and photophysical properties: in particular, their high fluorescence quantum yields and absorption coefficients [2–9]. These properties, coupled with their stability and low volatility, have led to their use in many applications across various disciplines, encompassing physics - solar energy conversion [10,11], photonic wires [12] and dye lasers [13–15]; chemistry - chemical probes/sensors [4,16–18]; biology – biolabels [19] and fluorescence markers [20], and medicine – cancer treatment [21].

Due to this widespread interest and the over 250 crystal structures of organic BODIPY derivatives for which atomic coordinates are available in the *Cambridge Structural Database* (CSD) [22], several studies have been published relating the photophysical properties of BODIPYs to their structure, providing useful insights into the effects of structural modification on these properties. These studies can be broken down into two groups: those investigating the effect of varying chemical substituents and those studying the effects of conformational perturbations.

The effects on photophysical properties resulting from varying the substituents attached to the BODIPY fragment are well documented. For example, longer fluorescence lifetimes and higher quantum yields can be achieved by increasing the electron donating power of substituents at the 3- and/or 5-positions [23]. Changing the substituent at the 8-position offers another useful method for modifying the absorption and fluorescence properties of BODIPYs. An example of this is the work of Kim *et al.*, detailing the changes in these characteristics observed upon altering the atomic number and position of the chalcogen atom of a heterocyclic substituent [24].

The conformation of BODIPY-based molecules has been shown to be of importance as well. Extending the π -system of the BODIPY chromophore has been shown to increase the wavelength and intensity of optical absorption and fluorescence. This can be observed in BODIPY derivatives where a freely-rotating aryl substituent is made rigid, bridging two positions on the pyrrole rings, to create this extended π -system and lower the energy of the corresponding excited states [25]. The conformation of aryl substituents in the 8-position can also affect photo-excitation, as the interplanar angle dictates the extent to which the π -systems of the BODIPY moiety and the substituent align [26]. This is manifest in the hypsochromic shift in absorption and fluorescence wavelengths observed in BODIPY derivatives, where the rotation of aryl substituents in the 8-position is restricted by methyl groups in the 1- and 7-positions, relative to those with unhindered substituents which are free to align with the BODIPY π -system [27].

While the effects of conformation and of substitution at various sites on the BODIPY skeleton have been investigated, it remains to be determined whether there is a *quantifiable* photophysical effect on the structure, owing, for example, to the bond-length patterns or a direct correlation of interplanar angles to properties. Using structural analysis techniques which have allowed us to use such characteristics manifest within the structure of molecules to predict photophysical properties in other families of photoactive compounds [28–31], we hope to develop similar structure-property relationships in BODIPYs. These relationships could herald the systematic design of BODIPY chromophores with the desired photophysical properties to match a given application through an accurate prediction algorithm.

To this end, six representative BODIPY dyes with various, simple, non-aryl substituents at the 8- and 2/6-positions are studied herein. Structural perturbations that correlate with the optical properties of these compounds are identified via analysis of bond geometry and molecular conformation as derived from single-crystal X-ray diffraction.

2. Experimental

2.1. Single-Crystal X-ray Diffraction. All BODIPY dyes [**1**: Pyrromethene 546, $C_{14}H_{17}BN_2F_2$, $R = H$, $R' = Me$; **2**: Pyrromethene 567, $C_{15}H_{25}BN_2F_2$, $R = Et$, $R' = Me$; **3**: Pyrromethene 567A, $C_{22}H_{33}BN_2F_2$, $R = Et$, $R' = C_5H_{11}$; **4**: Pyrromethene 580, $C_{22}H_{33}BN_2F_2$, $R = ^nBu$, $R' = Me$; **5**: Pyrromethene 597, $C_{22}H_{33}BN_2F_2$, $R = ^iBu$, $R' = Me$; **6**: Pyrromethene 605, $C_{20}H_{27}BN_2O_2F_2$, $R = Et$, $R' = CH_2OC(O)Me$; (R and R' refer to the substituent at the 2-/6-positions and the 8-position, respectively; Scheme S1)] were obtained from Exciton Inc. in a crystalline form suitable for single-crystal X-ray crystallography, except for **2**, **3** and **5**, which were crystallized *via* slow evaporation of the solvent from a solution of the compound in acetone at room temperature (**2** and **3**) or 276 K (**5**).

Crystal structure data (Table 1) for **1** and **3-6** were collected on a Rigaku Saturn 724+ CCD diffractometer equipped with a molybdenum X-ray source ($\lambda_{Mo, K\alpha} = 0.71073 \text{ \AA}$) with SHINE Optics and an Oxford Cryostreams CryostreamPlus open-flow N_2 cooling device. Crystals of **2** were found to be unsuitable for data collection using the X-ray laboratory source owing to their small dimensions and narrow, needle-like morphology (negligible diffraction was observed beyond $\theta = 38^\circ$, even with an exposure time of 120 s). Accordingly, crystal structure data for **2** were collected on the I19 beamline ($\lambda = 0.68890 \text{ \AA}$) at the UK synchrotron, Diamond Light Source.

In all cases, cell refinement, data collection and data reduction were undertaken *via* the Rigaku *CrystalClear*-SM Expert 2.0 software [32]. The absorption correction was implemented using ABSCOR [33].

The structures were solved by direct methods and refined by full-matrix least-squares methods on F^2 values for all data, using SHELXL [34]. For **2-6**, hydrogen atoms were positioned geometrically and refined as riding on their parent atoms. For **1**, hydrogen atoms

were located from the Fourier difference map of electron density and refined freely, as geometrically-idealized hydrogen atoms manifest as disorder across the mirror plane, which is not representative of the actual electron density peaks.

While room temperature structure determinations are available for **1** [35] and **4** [36], it was necessary to collect structural data for these two compounds at low temperature (120 K) in order to provide a direct comparison to the other crystal structures that form part of this study.

2.2. Solution-State Optical Spectroscopy. The UV—vis absorption and fluorescence spectra of dilute solutions of **1-6** in sixteen solvents were tested on a Hewlett Packard G1103A UV—vis absorption spectrophotometer and a Varian Cary Eclipse fluorescence spectroscopy, respectively. These sixteen high-purity (> 99.5%) solvents used were acetic acid, acetone, acetonitrile, *n*-butanol, *tert*-butanol, diethyl ether, dimethylsulfoxide (DMSO), dioxane, ethanol, ethyl acetate, ethylene glycol, methanol, methyl-cyclohexane, *n*-pentane, propan-2-ol and tetrahydrofuran. The uncertainties in all peak UV-vis absorption wavelength (λ_{abs}) and peak fluorescence wavelength (λ_{em}) readings were ± 1 nm (Table S1; Figures S1—S6).

2.3 Density Functional Theory. Quantum-chemical calculations were performed using Gaussian 09 [37]. Becke's three-parameter and Lee-Yang-Parr hybrid functional (B3LYP) [38–40] and a 6-31+G(d,p) basis set [41] were used for the ground-state geometry optimization of **1-6** in ethanol and DMSO along with **7** (Pyrromethene 560, $\text{C}_{16}\text{H}_{21}\text{BN}_2\text{F}_2$, $\text{R} = \text{Me}$, $\text{R}' = \text{Me}$), for which absorption/fluorescence data were available but for which no crystal structure has been reported in the ground state [42]. The same functional/basis set combination was also employed in the first excited- state geometry optimization of **1—6** in ethanol (Tables S2—S15; Figures S7 and S8).

The solvent effect was accounted for using the polarizable continuum model (PCM) [43,44]. In all calculations, frequency checks were performed after each geometry optimization in order to ensure that minima on the potential energy surfaces were found.

3. Results and Discussion

3.1. Crystal Structures. The X-ray crystal structures of **1-6** (Figures 2-4) exhibit some interesting crystallographic features. The asymmetric unit of the structure of **1** is located about a mirror plane parallel to the BODIPY fragment such that it is completely planar as all non-hydrogen atoms comprising this fragment, as well as the carbon atoms of the methyl substituents, lie on the mirror plane.

The asymmetric units of both **3** and **4** comprise two crystallographically independent molecules unrelated by symmetry which adopt different molecular conformations (Figure 3). In the case of **3**, the conformations of the two independent molecules differ in the orientation of the pentyl substituent at the 8-position (Figure 4): in one molecule (**3^a**), the gauche relationship between the C14-C15 and C16-C17 bonds, expressed as the dihedral C14-C15-C16-C17 angle of $66.85(17)^\circ$, imparts a distinct twist to the pentyl group, whereas in the other molecule (**3^b**), all the C-C bonds are antiperiplanar to each other, resulting in a more linear carbon chain.

The two crystallographically independent molecules in the asymmetric unit of **4** are also differentiated by the conformation of alkyl chains, in this case the *n*-butyl groups at the 2/6-positions: in **4^a** (Figure 4), one of these chains exhibits antiperiplanar relationships between all C-C bonds while the other presents a twisted conformation, brought about by the gauche relationship between C18-C19 and C20-C21 ($\text{C18-C19-C20-C21} = 65.9(2)^\circ$); however, both *n*-butyl chains in **4^b** adopt the linear conformation. The presence of these different molecular conformations in the crystal structures of **3** and **4** will likely affect their photophysical properties [45,46]. As such, this structural variation is an important consideration when

discerning the lowest energy conformer for use in quantum-chemical calculations. As might be expected, those with more linear carbon chains exhibit the lowest energy geometry according to quantum calculations, while the twisted-chain conformers appear to form as a result of crystal packing forces.

3.2. Substitution effects on bond geometry. For the purposes of this analysis, this set of compounds was sub-divided into two categories: a) where the chemical nature of the substituent at the 2- and 6-positions (R) is variable and the substituent at the 8-position (R') is constant *i.e.* **1**, **2**, **4** and **5** where R = H, Et, ⁿBu or ^tBu and R' = Me; and b) where R = Et and R' = Me, C₄H₁₁ or CH₂OC(O)Me *i.e.* **2**, **3** and **6**. Analyzing structural variations within each of these groups should enable the effects of chemical substitution at these positions to be isolated, with a view to correlating such variation with the optical properties of the dyes (Table 2).

In photo-active compounds, such as BODIPY dyes, the π -conjugated system is generally the absorption center; hence, the optical properties of the compounds are sensitive to the donor properties of chemical substituents adjacent to the conjugated system which affect the aromaticity of chromophore within the structure. Therefore, by investigating bond lengths within the common fragment of the structures and monitoring their variation with the donor properties of the substituents, it should be possible to observe changes in the structure which explain the differences in photophysical properties.

Within the series (a), the 2/6-position substituents exhibit variable electron-donating or withdrawing effects, eliciting a change in the optical properties of **1**, **2**, **4** and **5**. Increases in the absorption and fluorescence wavelengths in these compounds correlate with the increasing electron-donating effects of the substituents, as quantified by the corresponding Hammett values, a recognized measure of the electron donating power of chemical substituents (Table 3) [47].

Alkyl substituents are recognized electron-donating groups *via* induction and it is generally assumed that the more branched the chain, the greater the inductive donation. In this case, and as can be seen in the Hammett constants, the most branched substituent, ^tBu, is indeed the most donating. Little variation is observed in the donating power of Me, Et or ⁿBu substituents, and a hydrogen atom is regarded as neither donating or withdrawing with a Hammett constant of zero.

An electron-donating group at the 2/6-positions causes a bathochromic shift to the BODIPY spectra. The 2/6-positions exhibit a higher orbital population in the HOMO than in the LUMO (Figure 5). Consequently, the electron-donating substituents at these two positions destabilize the HOMO more substantially with respect to the LUMO and afford a lower bandgap in the resulting dyes (Figures S7).

It is easy to imagine that the donating/withdrawing abilities of the substituents would have not only an effect on the properties of the compounds, but also an effect on the structures; as the distribution of electrons is altered by substituent effects, this could manifest by changes in individual bond lengths and bond length patterns (Table 4).

A cursory examination of the bond lengths reveals that this is indeed the case. The bonds of the pyrrole ring directly adjacent to the 2/6-substituent do seem to lengthen as the donating power of the substituent increases, with the shortest bonds being observed for **1** and the longest for **5**, with intermediate values observed for **2** and **4**, where the bond lengths are essentially within error; this corresponds to the very similar Hammett constants given for Et and ⁿBu groups. Inductive effects are typically short-range and hence there is no significant trend in the bond lengths of the BODIPY fragment beyond these adjacent bonds. However, the bond length changes observed for the adjacent bonds correlate with the increasing absorption wavelengths, suggesting that the donor effects of the substituents perturb the conjugated system sufficiently to alter the optoelectronic properties (Figure 6a). The

correlation becomes even clearer when we use the theoretically optimized bond lengths, in which case the crystal packing effects and the associated distortion effects are eliminated (Figure 6b, c), and when the data set is expanded to include **7**. Note that in these DFT-optimized structures, the bond lengths of C1-C2 and C8-C9 are equal, owing to the symmetry of the molecular structures of the dyes in question. By the same token, the bond lengths of C2-C3 and C7-C8 are also the same.

Overall, as the electron-donating power of the chemical substituents increases, the bond lengths C1-C2, C2-C3, C7-C8, and C8-C9 also increase, reducing bond length variation within the pyrrole rings. The resulting increased aromaticity rationalizes the longer absorption and emission wavelengths in the order of **1** < **7** < **2** < **4** < **5**.

A similar structure-property relationship is also observed in other solvents, such as DMSO (Figure S9). This is not surprising, considering the symmetrical molecular structures and small dipole moments of **1**, **2**, **4**, **5**, and **7** in both the ground and the first excited state, and relatively weak interactions with solvents. Consequently, the solvatochromism effects on these dyes are very weak. For example, their λ_{abs} and λ_{em} values generally change by less than 10 nm, even though the solvent polarities have been greatly varied from methyl-cyclohexane to DMSO (Table S1). Their molecular geometry changes are also small (Tables S14 and S15). Hence, the aforementioned correlation also holds in other solvents.

The correlations among the substituent electron-donating/withdrawing power of the substituent at the 8-position, the bond lengths of C4-C5 and C5-C6, and the spectral properties of **2**, **3**, and **6**, are less strong, owing partially to the more diverse nature of the substituents and the different solvent effects associated with them (the experimental spectral data are measured in ethanol). Overall, as the electron-donating power of the substituent becomes stronger, the bond lengths C4-C5 and C5-C6 increase (Table 4; Supporting Information); and the spectra of the dyes exhibit a blue shift (Table 2).

3.3. Conformational variations and solid-state properties. In addition to the electron-donating power of the substituents, the optical properties of photo-active compounds are sensitive to structural perturbations which affect the π -orbital overlap of the conjugated system within the molecule. Therefore, by identifying the parameters which best describe the molecular conformations of these dyes, it should be possible to predict changes in optical properties going from solution to the solid-state.

Regarding the optimal alignment of π -orbitals within the BODIPY fragment, the conformational criterion for an ideal conjugated system is that the fragment should be perfectly planar. A measure of this planarity is given by calculating the root-mean-square (RMS) deviation of atoms from the mean plane of the atoms involved. The mean plane should include both the atoms in the BODIPY fragment and the atoms of the substituents that are directly attached to it. These substituent atoms are herein included as the hybridization of the atoms in the BODIPY fragment, as well as the geometry of the BODIPY π -system itself, should be considered: if the atoms of the aromatic system deviate from ideal aromatic sp^2 hybridization this will result in reduced π -overlap. This deviation would not be apparent if only the core atoms within the π -system were considered; indeed, no noticeable trend in values is observed when planarity is calculated in this way.

Within the series (a), where R is variable, the RMS deviation of fitted atoms from the plane of the BODIPY fragment and directly-bonded substituent atoms increases in the order **1** < **2** < **4** < **5** (Table 5; using an average of the deviation of the two crystallographically independent molecules for **4**). This increasing order correlates with the monotonic rise in Taft constant of the 2/6-substituent (Table 3, Figure 7) [47], which is a measure of the steric influence of these substituents [48–50]. This correlation can be rationalized by the commensurate increase in steric interactions between the 2/6-substituent and the adjacent methyl groups, which are forced more and more out-of-plane by the increasing steric bulk of the substituent.

These non-planar molecular conformations within the crystal environment deviate from the relatively planar structures in the solution-state, afforded *via* quantum-chemical calculations. Such a deviation from planarity constitutes a deleterious effect on the π -overlap within the conjugated system, reducing overall aromaticity, and hence, contributing to the hypsochromic shift of the absorption and fluorescence properties in the solid state (in addition to other factors, such as the absence of solvent effects). Given our earlier assertion that increasing the bond lengths adjacent to the 2/6-substituents contributes to increased aromaticity, this accounts for the shorter equivalent bond lengths observed in the crystal structures relative to the solution-phase simulations.

Given that the primary application of these results is to laser dye applications, one can consider the conclusions from solution-state (DFT) effects to preside. That said, the salient, non-terminal bond geometry is expected to be retained in the solid-state. Measuring solid-state optical properties is non-trivial, although recent studies have demonstrated the effect of crystal packing forces and solid-state conformation on optical properties [45,46]. Our future work will focus on quantifying the effect of the varying levels of planarity of the chromophores in the crystal structures of these BODIPY dyes by measuring the absorption and fluorescence in the solid state. Determining the properties of crystallographically-independent molecules with different conformations in the same crystal structure should prove especially interesting.

3.4. Concluding remarks. Through this work, we have demonstrated a relationship between the aromaticity of the pyrrole rings in these molecules and the Hammett values of the chemical substituents. These structural perturbations have been shown to correlate well with the optical properties of the dyes and are, consequently the likely molecular root of the absorption/fluorescence properties. To this end, a clear correlation is observed in the crystal structure data, backed-up by computational analysis and empirical parameters; the

introduction of more electron-donating substituents in the 2-/6-positions increases the aromaticity of the pyrrole rings in the molecule to produce a bathochromic shift in absorption and fluorescence wavelengths. Less clear is the role of the 8-position chemical substituents. Though the effect of aromatic substituents in this position is well-documented and understood, the link between the electron-donor properties of the simple substituents used in this study and their optoelectronic properties could not be satisfactorily rationalized.

It is also found that the planarity of the BODIPY π -conjugated system is perturbed by crystal packing forces in the solid state. This perturbation increases as the steric hindrance of the substituents increases.

In summary, this analysis helpfully illustrates both the inherent strengths and inherent weaknesses in using single-crystal X-ray crystallography to develop optoelectronic structure-property relationships in this class of dyes. By detailing the herein observable link between structure and property, development of molecular design strategies for laser dyes with tunable absorption/fluorescence properties should ultimately prove feasible.

Appendix A. Supplementary data

The theoretically optimized atomic coordinates of **1-7** in ethanol, selected bond lengths of the optimized molecular structures and their HOMO and LUMO plots; UV—vis and fluorescence spectra and crystallographic information files (CIFs) for **1-6**.

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Notes

The authors declare no competing financial interest.

Acknowledgments

The authors thank Dr. Sarah Barnett and the rapid access service on the I19 beamline at Diamond Light Source, UK for collecting single-crystal X-ray diffraction data for **2**. X.L. is indebted to the Singapore Economic Development Board for a Clean Energy Scholarship. J.M.C. thanks the Fulbright Commission for a UK-US Fulbright Scholar Award; work done at Argonne National Laboratory was supported by DOE Office of Science, Office of Basic Energy Sciences, under Contract No. DE-AC02-06CH11357.

References

- [1] Triebs A, Kreuzer FH. Difluoroboryl Complexes of Di- and Tripyrrylmethenes. *Liebigs Ann* 1968;718:208–23.
- [2] Loudet A, Burgess K. BODIPY Dyes and their Derivatives: Syntheses and Spectroscopic Properties. *Chem Rev* 2007;107:4891–932.
- [3] Ulrich G, Ziessel R, Harriman A. The Chemistry of Fluorescent Bodipy Dyes: Versatility Unsurpassed. *Angew Chem Int Ed* 2008;47:1184–201.
- [4] Boens N, Leen V, Dehaen W. Fluorescent indicators based on BODIPY. *Chem Soc Rev* 2012;41:1130–72.
- [5] Falk H, Hofer O, Lehner H. Beiträge zur Chemie der Pyrrolpigmente, 1. Mitt.: Der Induzierte Circularichroismus einiger Pyrromethenderivate in Cholesterischer Mesophase. *Monatsh Chem* 1974;105:169–78.
- [6] Ulrich G, Ziessel R. Convenient and Efficient Synthesis of Functionalized Oligopyridine Ligands Bearing Accessory Pyrromethene-BF₂ Fluorophores. *J Org Chem* 2004;69:2070–83.
- [7] Mula S, Ray AK, Banerjee M, Chaudhuri T, Dasgupta K, Chattopadhyay S. Design and Development of a New Pyrromethene Dye with Improved Photostability and Lasing Efficiency: Theoretical Rationalization of Photophysical and Photochemical Properties. *J Org Chem* 2008;73:2146–54.
- [8] Hu R, Gómez-Durán CFA, Lam JWY, Belmonte-Vázquez JL, Deng C, Chen S, et al. Synthesis, Solvatochromism, Aggregation-Induced Emission and Cell Imaging of Tetraphenylethene-Containing BODIPY Derivatives with Large Stokes Shifts. *Chem Comm* 2012;48:10099–101.
- [9] Bartelmess J, Weare WW. Preparation and Characterization of Multi-Cationic BODIPYs and their Synthetically Versatile Precursors. *Dyes Pigments* 2013;97:1–8.
- [10] Erten-Ela S, Yilmaz MD, Icli B, Dede Y, Icli S, Akkaya EU. A Panchromatic Boradiazaindacene (BODIPY) Sensitizer for Dye-Sensitized Solar Cells. *Org Lett* 2008;10:3299–302.
- [11] Kolemen S, Bozdemir OA, Cakmak Y, Barin G, Erten-Ela S, Marszalek M, et al. Optimization of Distyryl-Bodipy Chromophores for Efficient Panchromatic Sensitization in Dye Sensitized Solar Cells. *Chem Sci* 2011;2:949–54.
- [12] Li F, Yang SI, Ciringh Y, Seth J, Martin CH, Singh DL, et al. Design, Synthesis, and Photodynamics of Light-Harvesting Arrays Comprised of a Porphyrin and One, Two, or Eight Boron-Dipyrrin Accessory Pigments. *J Am Chem Soc* 1998;120:10001–17.
- [13] Pavlopoulos TG, Shah M, Boyer JH. Laser Action from a Tetramethylpyrromethene-BF₂ Complex. *Appl Optics* 1988;27:4998–9.

- [14] Pavlopoulos TG, Boyer JH, Shah M, Thangaraj K, Soong M-L. Laser Action from 2,6,8-position Trisubstituted 1,3,5,7-tetramethylpyrromethene-BF₂ Complexes: Part 1. *Appl Optics* 1990;29:3885–6.
- [15] Boyer JH, Haag AM, Sathyamoorthi G, Soong M-L, Thangaraj K. Pyrromethene-BF₂ Complexes as Laser Dyes: 2. Heteroatom Chem 1993;4:39–49.
- [16] Lee C-H, Yoon H-J, Shim J-S, Jang W-D. A Boradiazaindacene-Based Turn-On Fluorescent Probe for Cyanide Detection in Aqueous Media. *Chem Eur J* 2012;18:4513–6.
- [17] Coskun A, Akkaya EU. Signal Ratio Amplification via Modulation of Resonance Energy Transfer: Proof of Principle in an Emission Ratiometric Hg(II) Sensor. *J Am Chem Soc* 2006;128:14474–5.
- [18] Hudnall TW, Gabbaï FP. A BODIPY Boronium Cation for the Sensing of Fluoride Ions. *Chem Comm* 2008:4596–7.
- [19] Haugland RP. *Handbook of Fluorescent Probes and Research Chemicals*, 6th Ed. 1996.
- [20] Niu SL, Massif C, Ulrich G, Ziessel R, Renard P-Y, Romieu A. Water-Solubilisation and Bio-Conjugation of a Red-Emitting BODIPY Marker. *Org Biomol Chem* 2011;9:66–9.
- [21] Morgan LR, Chaudhuri A, Gillen LE, Boyer JH, Welford LT. Pentamethylpyrromethene Boron Difluoride Complexes in Human Ovarian Cancer Photodynamic Therapy. *Photodynamic Therapy: Mechanisms II* 1990;1203:253–65.
- [22] Allen FH. The Cambridge Structural Database: A Quarter of a Million Crystal Structures and Rising. *Acta Crystallogr, Sect B: Struct Sci* 2002;58:380–8.
- [23] Qin W, Leen V, Dehaen W, Cui J, Xu C, Tang X, et al. 3,5-Dianilino Substituted Difluoroboron Dipyrrromethene: Synthesis, Spectroscopy, Photophysics, Crystal Structure, Electrochemistry, and Quantum-Chemical Calculations. *J Phys Chem C* 2009;113:11731–40.
- [24] Kim K, Jo C, Easwaramoorthi S, Sung J, Kim DH, Churchill DG. Crystallographic, Photophysical, NMR Spectroscopic and Reactivity Manifestations of the “8-Heteroaryl Effect” in 4,4-Difluoro-8-(C(4)H(3)X)-4-bora-3a,4a-diaza-s-indacene (X = O, S, Se) (BODIPY) Systems. *Inorg Chem* 2010;49:4881–94.
- [25] Leen V, Qin W, Yang W, Cui J, Xu C, Tang X, et al. Synthesis, Spectroscopy, Crystal Structure Determination, and Quantum Chemical Calculations of BODIPY Dyes with Increasing Conformational Restriction and Concomitant Red-Shifted Visible Absorption and Fluorescence Spectra. *Chem Asian J* 2010;5:2016–26.
- [26] Kee HL, Kirmaier C, Yu L, Thamnyongkit P, Youngblood WJ, Calder ME, et al. Structural Control of the Photodynamics of Boron-Dipyrrin Complexes. *J Phys Chem B* 2005;109:20433–43.

- [27] Chen Y, Wan L, Zhang D, Bian Y, Jiang J. Modulation of the Spectroscopic Property of Bodipy Derivates through Tuning the Molecular Configuration. *Photochem Photobiol Sci* 2011;10:1030–8.
- [28] Liu X, Cole JM, Waddell PG, Lin T-C, Radia J, Zeidler A. Molecular Origins of Optoelectronic Properties in Coumarin Dyes : Toward Designer Solar Cell and Laser Applications. *J Phys Chem A* 2012;116:727–37.
- [29] Merz TA, Waddell PG, Cole JM. Systematic Molecular Design of p -Phenylene Lasing Properties. *J Phys Chem C* 2013;117:8429–36.
- [30] Liu X, Cole JM, Waddell PG, Lin T, McKechnie S. Molecular Origins of Optoelectronic Properties in Coumarins 343, 314T, 445, and 522B. *J Phys Chem C* 2013;117:14130–41.
- [31] Liu X, Xu Z, Cole JM. Molecular Design of UV – vis Absorption and Emission Properties in Organic Fluorophores : Toward Larger Bathochromic Shifts , Enhanced Molar Extinction Coefficients , and Greater Stokes Shifts. *J Phys Chem C* 2013;117:16584–95.
- [32] Rigaku. CrystalClear-SM Expert. CrystalClear-SM Expert, The Woodlands Texas 2009.
- [33] Higashi T. ABSCOR. ABSCOR, Rigaku Corporation, Tokyo, Japan 1995.
- [34] Sheldrick GM. A Short History of SHELX. *Acta Crystallogr, Sect A: Found Crystallogr* 2008;64:112–22.
- [35] Picou CL, Stevens ED, Shah M, Boyer JH. Structure of 4,4-Difluoro-1,3,5,7,8-pentamethyl-3a,4a-diaza-4-bora-s-indacene. *Acta Crystallogr, Sect C: Cryst Struct Comm* 1990;46:1148–50.
- [36] Jasinski JP, Crosby DJ. 4,4-Difluoro-1,3,5,7,8-pentamethyl-2,6-dibutyl-3a,4a-diaza-4-bora- s -indacene. *Acta Crystallogr, Sect E: Struct Rep Online* 2007;63:o1832–o1833.
- [37] Frisch AN, Trucks GW, Schlegel GW, Scuseria GE, Robb MA, Cheeseman JR, et al. Gaussian 09. Gaussian 09, Gaussian Inc, Wallingford, Connecticut 2009.
- [38] Stephens PJ, Devlin FJ, Cabalowski CF, Frisch MJ. Ab Initio Calculation of Vibrational Absorption and Circular Dichromism Spectra Using Density Functional Force Fields. *J Phys Chem* 1994;98:11623–7.
- [39] Becke AD. Density-Functional Thermochemistry. III. The Role of Exact Exchange. *J Chem Phys* 1993;98:5648–52.
- [40] Lee C, Yang W, Parr RG. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys Rev B* 1988;37:785–9.
- [41] Rassolov VA, Ratner MA, Pople JA, Redfern PC, Curtiss LA. 6-31G* Basis Set for Third-Row Atoms. *J Comput Chem* 2001;22:976–84.

- [42] Jones G, Kumar S, Klueva O, Pacheco D. Photoinduced Electron Transfer for Pyrromethene Dyes. *J Phys Chem A* 2003;107:8429–34.
- [43] Miertuš S, Scrocco E, Tomasi J. Electrostatic Interaction of a Solute with a Continuum. A Direct Utilization of Ab Initio Molecular Potentials for the Prevision of Solvent Effects. *Chem Phys* 1981;55:117–29.
- [44] Chipman DM. Reaction field treatment of charge penetration. *J Chem Phys* 2000;112:5558–65.
- [45] Coppens P, Sokolow J, Trzop E, Makal A, Chen Y. On the Biexponential Decay of the Photoluminescence of the Two Crystallographically-Independent Molecules in Crystals of [Cu(I)(phen)(PPh₃)₂][BF₄]. *J Phys Chem Lett* 2013;4:579–82.
- [46] Sylvester SO, Cole JM. Quantifying Crystallographically Independent Optical Switching Dynamics in RuSO₂ Photoisomers via Lock-and-Key Crystalline Environment. *J Phys Chem Lett* 2013;4:3221–6.
- [47] Speight JG. *Lange's Handbook of Chemistry*. 16th ed. McGraw-Hill; 2005.
- [48] Taft RW. Linear Free Energy Relationships from Rates of Esterification and Hydrolysis of Aliphatic. *J Am Chem Soc* 1952;74:2729–32.
- [49] Taft RW. Polar and Steric Substituent Constants for Aliphatic and o-Benzoate Groups from Rates of Esterification and Hydrolysis of Esters. *J Am Chem Soc* 1952;74:3120–8.
- [50] Taft RW. Linear Steric Energy Relationships. *J Am Chem Soc* 1953;75:4538–9.

Figure Captions:

Figure 1: Generic structure of the BODIPY fragment displaying the IUPAC position numbering of the core atoms.

Figure 2: Molecular structure of the asymmetric units of **1**, **2**, **5** and **6** with atomic displacement ellipsoids drawn at the 50% probability level.

Figure 3: View of the asymmetric units of **3** and **4** within their respective unit cells.

Figure 4: Structure of the crystallographically independent molecules of **3** and **4** with atomic displacement ellipsoids drawn at the 50% probability level.

Figure 5: The atomic contributions to (a) LUMO and (b) HOMO of **1**. The sizes of the blue/red circles represent the atomic contributions; only contributions greater than 0.02 are shown.

Figure 6: (a) Correlation of the crystal structure-derived C1-C2, C2-C3, C7-C8 and C8-C9 bond lengths and the maximum absorption wavelengths of **1**, **2**, **4** and **5** in ethanol. Note that

there are two asymmetric units in the crystal of **4**; hence, this compound contributes two data points in each series of plots. Correlation of the DFT geometrically-optimized (b) ground state C1-C2, C2-C3 bond lengths and the maximum absorption wavelengths of **1**, **2**, **4**, **5** and **7**; (c) the first excited state C1-C2, C2-C3 bond lengths and the maximum emission wavelengths of **1**, **2**, **4**, **5** and **7** in ethanol.

Figure 7: Monotonically increasing correlation of RMS deviation of fitted atoms from the plane of the BODIPY fragment and directly-bonded substituent atoms with the Taft constant of the 2/6-substituent in **1**, **2**, **4** and **5**.

Table Captions:

Table 1: Experimental and refinement details for the X-ray crystal structures of **1-6**

Table 2: Peak UV—vis absorption (λ_{abs}) and fluorescence wavelengths (λ_{em}) of **1-7**. All values are for dyes in ethanol.

Table 3: Hammett and Taft constants for the substituents observed in **1-6** [47].

Table 4: Selected BODIPY fragment bond lengths (Å) for the crystal structures of **1-6**.

Table 5: Selected interplanar angles (°) and root-mean-square deviations from planes for **1-6**.

Figure 1.

Figure 2.

Figure 3.

3

4

Figure 4.

3^a

3^b

4^a

4^b

Figure 5.

Figure 6.

Figure 7.

Table of Content Figure.

Table 1: Experimental and refinement details for the X-ray crystal structures of **1-6**

	1	2	3	4	5	6
Molecular Formula	C ₁₄ H ₁₇ BN ₂ F ₂	C ₁₈ H ₂₅ BN ₂ F ₂	C ₂₂ H ₃₃ BN ₂ F ₂	C ₂₂ H ₃₃ BN ₂ F ₂	C ₂₂ H ₃₃ BN ₂ F ₂	C ₂₀ H ₂₇ BN ₂ O ₂ F ₂
Molecular weight	262.11	318.21	374.31	374.31	374.31	376.25
<i>T</i> /K	120	120	120	120	120	120
$\lambda/\text{\AA}$	0.71073	0.68890	0.71073	0.71073	0.71073	0.71073
Crystal System	Orthorhombic	Orthorhombic	Triclinic	Triclinic	Orthorhombic	Monoclinic
Space Group	Pnma	Pbca	P-1	P-1	Pbca	P2 ₁ /c
<i>a</i> /\AA	11.333(6)	17.029(6)	12.619(3)	7.971(3)	18.311(5)	10.876(5)
<i>b</i> /\AA	7.040(4)	7.729(3)	13.267(2)	14.639(7)	7.961(2)	11.325(4)
<i>c</i> /\AA	16.019(8)	25.154(8)	14.572(3)	19.238(9)	28.326(8)	16.446(7)
α (°)	90	90	69.115(11)	112.126(7)	90	90
β (°)	90	90	80.387(12)	91.183(3)	90	108.580(5)
γ (°)	90	90	67.375(9)	100.819(6)	90	90
<i>U</i> /\AA ³	1278.1(12)	3311(2)	2102.6(7)	2032.2(16)	4129.2(19)	1920.1(14)
<i>Z</i>	4	8	4	4	8	4
$\mu(\text{Mo-K}\alpha)$ mm ⁻¹	0.1	0.09	0.08	0.083	0.082	0.096
<i>D_c</i> /Mg m ⁻³	1.362	1.277	1.182	1.223	1.204	1.302
Total number of reflections	10693	26129	17262	17610	33050	14781
Independent reflections (<i>R</i> _{int})	1586 (0.054)	3711 (0.1129)	9519 (0.0334)	9152 (0.0426)	4720 (0.0664)	4391 (0.0416)
Max. and min. transmission	0.985, 0.982	0.996, 0.994	0.985, 0.973	0.985, 0.971	0.979, 0.973	0.975, 0.968
Final <i>R</i> , <i>wR</i> ₂	0.0513, 0.1325	0.0547, 0.1532	0.0500, 0.1268	0.0575, 0.1346	0.0570, 0.1388	0.0483, 0.1179
Largest Difference: Peak, hole/e. \AA ⁻³	0.392, -0.191	0.331, -0.341	0.296, -0.174	0.234, -0.212	0.348, -0.189	0.326, -0.165

Table 2: Peak UV—vis absorption (λ_{abs}) and fluorescence wavelengths (λ_{em}) of **1-7**. All values are for dyes in ethanol.

	1	2	3	4	5	6	7 [42]
$\lambda_{\text{abs}}/\text{nm}$	495	518	520	519	524	544	517
$\lambda_{\text{em}}/\text{nm}$	504	533	530	534	561	560	534

Table 3: Hammett and Taft constants for the substituents observed in **1-6** [47].

	σ_m	σ_p	σ^*
H	0.00	0.00	0.49
Me	-0.07	-0.17	0.0
Et	-0.07	-0.15	-0.10
ⁿ Bu	-0.07	-0.16	-0.13
^t Bu	-0.10	-0.20	-0.30
(CH ₂) ₄ CH ₃	-0.16 ⁱ	-	-0.25
OC(O)CH ₃	0.39	0.31	2.29 ⁱ
CH ₂ OC(O)CH ₃	0.07 ^{i,ii}	-	0.82 ^{i,ii}

i) calculated values using relationship: $\sigma_m = 0.217\sigma^* - 0.106$

ii) calculated values using the relationship: $\sigma_{(-R)}^* = 0.36\sigma_{(-CH_2-R)}^*$

Table 4: Selected BODIPY fragment bond lengths (Å) for the crystal structures of **1-6**.

	1	2	3^a	3^b	4^a	4^b	5	6
C1-C2	1.400(3)	1.407(2)	1.405(2)	1.406(2)	1.411(2)	1.410(3)	1.418(2)	1.405(2)
C2-C3	1.391(3)	1.394(2)	1.3918(19)	1.397(2)	1.390(2)	1.394(2)	1.414(2)	1.395(2)
C3-C4	1.434(3)	1.4302(19)	1.4307(18)	1.4312(19)	1.434(2)	1.431(2)	1.424(2)	1.4284(19)
C4-C5	1.402(3)	1.4075(19)	1.4054(18)	1.4104(18)	1.401(2)	1.400(2)	1.413(2)	1.408(2)
C5-C6	1.404(3)	1.4101(19)	1.4062(19)	1.4060(18)	1.404(2)	1.412(2)	1.405(2)	1.3976(19)
C6-C7	1.431(3)	1.4317(19)	1.4356(19)	1.4319(18)	1.429(2)	1.431(2)	1.435(2)	1.440(2)
C7-C8	1.394(3)	1.396(2)	1.391(2)	1.390(2)	1.390(2)	1.397(3)	1.401(2)	1.387(2)
C8-C9	1.399(3)	1.408(2)	1.410(2)	1.408(2)	1.405(3)	1.412(2)	1.425(2)	1.416(2)
N1-C1	1.352(3)	1.3526(18)	1.3493(17)	1.3526(17)	1.353(2)	1.353(2)	1.358(2)	1.3518(19)
N1-C4	1.404(3)	1.396(2)	1.4033(17)	1.3984(17)	1.403(2)	1.407(2)	1.3922(19)	1.3983(18)

Table 5: Selected interplanar angles (°) and root-mean-square deviations from planes for **1-6**.

	1	2	3^a	3^b	4^a	4^b	5	6
RMS dev. (BODIPY)	0.00	0.0222	0.0421	0.0159	0.0417	0.0282	0.0325	0.0210
RMS dev. (inc. Subst.)	0.00	0.0571	0.0565	0.0512	0.0678	0.0475	0.1165	0.0507