DALHOUSIE UNIVERSITY

Synthesis and Characterization of Pyrrolyldipyrrin *F*-BODIPYs

Sarah M. Greening,[a] Katherine N. Robertson[b] and Alison Thompson[a]*

[a]*Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, B3H 4J3, Canada*

[b]*Department of Chemistry, Saint Mary's University, Halifax, NS, B3H 3C3, Canada*

Alison.Thompson@dal.ca

Abstract

A series of synthetic analogs of the tripyrrolic natural product prodigiosin were complexed with boron trifluoride to generate the corresponding *F*-BODIPYs. The maximum wavelengths of absorption and emission of the pyrrolyldipyrrin *F*-BODIPYs was tuned through variation of the substituents about the pyrrolyldipyrrinato core. The limited variation of substituents on the C-ring did not significantly affect absorption and emission. However, variation on the B-ring and A-ring resulted in a corresponding red-shift in absorption and emission reaching maximum wavelengths of 600 nm. The presence of electron donating substituents on the B-ring caused a decrease in the Stokes' shift, while the presence of electron-withdrawing substituents caused an increase, ranging from 3-25 nm. Stokes shifts were solvent-dependant for some compounds. The inclusion of a dimethylamino group resulted in photo-induced electron transfer and thus quenched fluorescence which was restored upon protonation.

Introduction

Tripyrrolic compounds that contain a dipyrrin and a pyrrolic unit, connected at the 9-position, constitute what are known as pyrrolyldipyrrins. The presence of this third pyrrolic unit extends the π-conjugation of the dipyrrinato ligand and causes red-shifted absorption maxima that have facilitated applications in the life sciences and materials chemistry.[1] The natural product prodigiosin and its synthetic analogues, termed prodigiosenes (**Figure 1**), belong to the pyrrolyldipyrrin family[2] and exhibit significant biological activity including immunosuppressive,[3] anti-malaria,[4] anti-microbial[5] and anti-cancer activity.[6, 7]

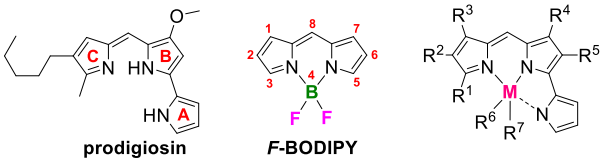


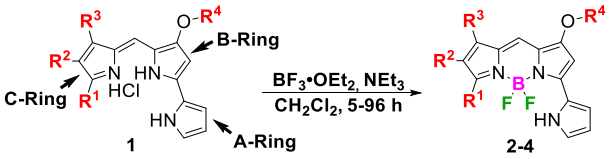
Figure 1. Prodigiosin, *F*-BODIPY and pyrrolyldipyrrin metal complexes

Dipyrrins coordinate to a variety of metals[1, 8] but the most prominent type of dipyrrinato complex features a $-BF_2$ unit to yield 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes (*F*-BODIPYs, **Figure 1**). *F*-BODIPYs are chemically robust, as well as thermally, photochemically and physiologically stable. They exhibit sharp fluorescence, with high molar extinction coefficients and quantum yields, making them useful in applications such as cell imaging, chemosensors and laser dyes.[9-12] Like dipyrrins, several metal complexes of pyrrolyldipyrrins have been reported, including those of cobalt, copper, tin, zinc and boron.[4, 13-17] Compared to boron complexes of dipyrrins, pyrrolyldipyrrinato complexes absorb and emit light at much longer wavelengths, due to the extended π-conjugation of the dipyrrinato ligand. As a result, these highly fluorescent complexes are useful as probes in biological applications, e.g., the commercially available fluorescent dyes BODIPY 576/589 and BODIPY 650/665 (absorption/emission, respectively).[16, 18-20] Other reported examples of boron difluoro pyrrolyldipyrrinato complexes include the unsubstituted pyrrolyldipyrrin[20] and those with substituted aromatics,[15, 17, 21-23] heterocycles[22] and alkyl groups[21] at the *meso*-position, phenyl substitution at the *meso*-

position with different functional groups present on the A-ring[24, 25] or the presence of halogens about the pyrrolyldipyrrin core[26, 27] and isoindole substitution of the B-ring.[16, 28] Boron difluoro complexes of prodigiosenes (pyrrolyldipyrrins bearing a methoxy substituent on the B-ring) have recently been reported. However, the purpose of the synthesis was to afford the desired synthetic natural products in a facile manner by removal of the $-BF_2$ protecting group.[29] Additionally, our group has recently synthesized two pyrrolyldipyrrin BF_2 complexes bearing ester functionality on the C-ring of the pyrrolyldipyrrin core.[4, 13, 30] To the best of our knowledge these are the only reported examples of pyrrolyldipyrrin *F*-BODIPYs. Despite these examples, a thorough study investigating how changing the substituents about the three rings of the pyrrolyldipyrrin core affects the photophysical properties is lacking. Herein, a series of pyrrolyldipyrrin *F*-BODIPYs with varying substituents on each of the pyrrolic rings, and their respective photophysical properties, are described.

Results and Discussion

To investigate the photophysical properties of prodigiosene-based *F*-BODIPYs, the pyrrolyldipyrrin HCl salts **1** bearing modifications to the A, B and C-rings were synthesized.[4, 6, 31] Modifications included conjugated carbonyl and alkyl substituents on the C-ring, electron-withdrawing and electron-donating groups on the B-ring, and indole substitution at the A-ring. The pyrrolyldipyrrin HCl salts **1** were complexed with boron trifluoride in the presence of base.[11, 32] Several additions of Lewis acid and base, plus extended reaction times, were required to afford the eighteen novel pyrrolyldipyrrin *F*-BODIPYs **2-4** in 38-95% yields after multiple purification attempts via column chromatography (**Scheme 1**).



Scheme 1. Synthesis of pyrrolyldipyrrin *F*-BODIPYs **2-4**

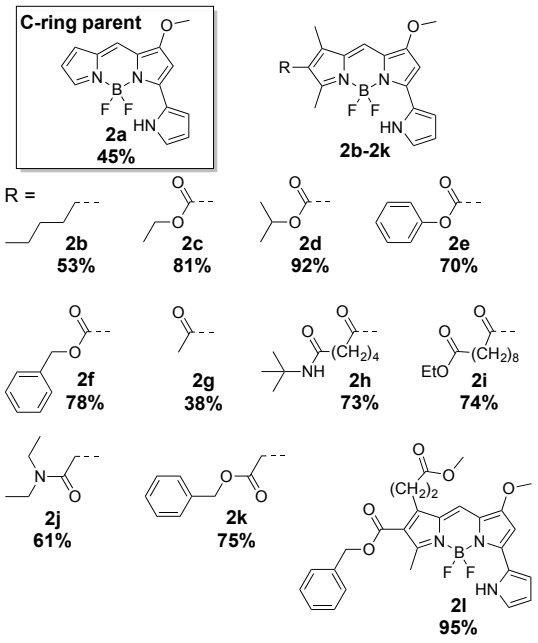


Figure 2. Pyrrolyldipyrrin *F*-BODIPYs (**2a-2l**) with C-ring modifications

A crystal suitable for x-ray analysis of pyrrolyldipyrrin *F*-BODIPY **2d** was obtained from the slow evaporation of a chloroform solution. The thermal ellipsoid diagram of **2d** is shown in Figure 3 and illustrates that the pyrrolyldipyrrin core is perpendicular to the plane of the coordinated F–B–F atoms. The B-N bond distances range from 1.54-1.56 Å indicating that the dipyrrinato unit is significantly resonance stabilized, as expected. The core structure of **2d** is essentially planar, with the uncoordinated pyrrolic unit slightly out of plane which may accommodate a hydrogen bond between the hydrogen atom of the pyrrolic nitrogen and a fluorine. The NH-F hydrogen bond distance ranges from 2.05-2.53 Å.

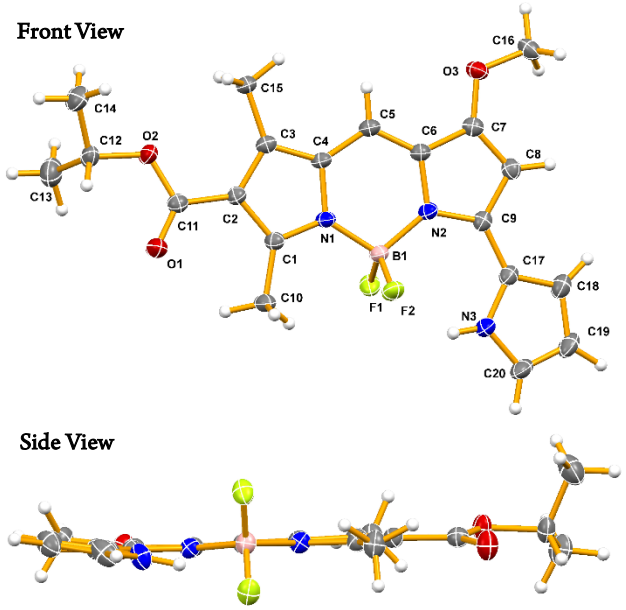


Figure 3. Thermal ellipsoid diagram of **2d** (50%). Selected bond distances (Å): B(1)-N(1), 1.5386(19); B(1)-N(2), 1.551(2); Selected bond angles (deg): N(1)-B(1)-N(2), 108.36(11); Selected torsional angles (deg): N(2)-C(9)-C(17)-N(3), -7.5(2); Hydrogen bond distance (Å): N(3)-H(3N)...F(1), 2.529(17), N(3)-H(3N)...F(2), 2.049(18).

The pyrrolyldipyrrin *F*-BODIPYs featured a variety of substituents on the C-ring (**2a-2l**, **Figure 2**) and B-ring (**3m-3p**, **Figure 4**). In addition, two analogues **4q** and **4r** (**Figure 5**) of Obatoclax,[33] bearing an indole moiety in lieu of the A-ring, were prepared. *F*-BODIPY **2a** (**Figure 2**), the unsubstituted pyrrolyldipyrrin bearing only the signature methoxy group on the B-ring, was chosen as a parent compound to which the properties of the C-ring substituted pyrrolyldipyrrin *F*-BODIPYs would be compared. Such substituents included a mimic of the natural product prodigiosin (**2b**), conjugated esters (**2c-2f**, **2l**), conjugated ketones (**2g-2i**) and derivatives of ethanoic acid (**2j** and **2k**). These substituents provide a wide scope to demonstrate the influence that C-ring substituents have on the photophysical properties of pyrrolyldipyrrin *F*-BODIPYs.

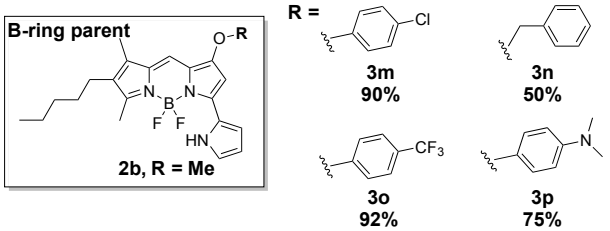


Figure 4. Pyrrolyldipyrrin *F*-BODIPYs (**3m-3p**) with B-ring modifications

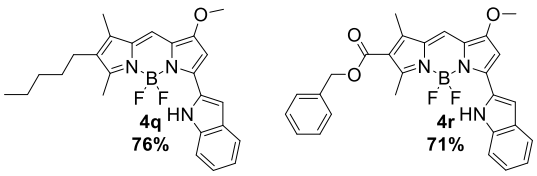


Figure 5. Pyrrolyldipyrrin *F*-BODIPYs (**4q-4r**) A-ring (indole) modifications

The synthetic analog **2b** of prodigiosin was selected as the parent compound by which substrates (**3m-3p**), bearing benzoxy or phenoxy substituents in lieu of the methoxy group, would be compared. In this regard, the effect that the methoxy substituent has upon the photophysical properties would be evaluated. The nature of this substituent is highly important to some aspects of the biological activity of prodigiosenes, yet substituting the methyl group for benzyl or phenyl groups does not diminish the anticancer properties of the compound.[6] Lastly, pyrrolyldipyrrin *F*-BODIPYs **4q** and **4r** feature an indole moiety which further extends the π-conjugation of the *F*-BODIPY core and as a result are expected to inherently absorb and emit at longer wavelengths. Compounds **2b** and **2f** (**Figure 2**) represent the parent compounds of the A-ring indole analogs, **4q** and **4r**.

The photophysical properties of solutions of pyrrolyldipyrrin *F*-BODIPYS (**2-4**) in CH_2Cl_2 were evaluated. All absorbance spectra exhibited a similar band structure in the visible region, with a peak and shoulder that are characteristic of BF_2 dipyrrin complexes. Additionally, all compounds emitted at wavelengths in the yellow/orange visible region, displaying high extinction coefficients (11 000 – 156 000 mol M^{-1} $cm^{-}1$) and have Stokes' shift in the range of 3-25 nm. As representative examples, the absorbance and emission spectra of *F*-BODIPY **2a** and **3o** (**Figure 6**) illustrate the increase in Stokes' shift observed for electron-withdrawing groups of the B-ring compared to the unsubstituted pyrrolyldipyrrin. A summary of the results is presented in Table 1.

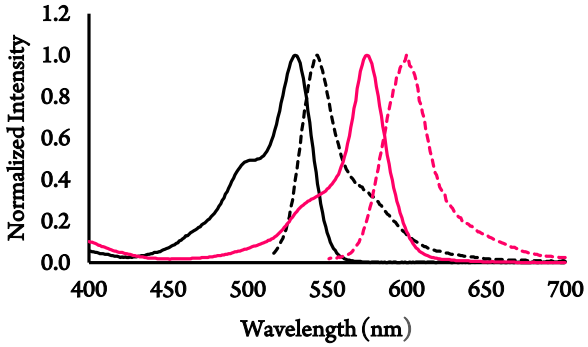


Figure 6. Normalized absorbance and emission spectra of **2a** (left, black, Stokes shift 13 nm) and **3o** (right, pink, Stokes shift 25 nm)

Table 1. Photophysical Propteries of *F*-BODIPYs **2-4** in CH_2Cl_2 at 22 °C

F-*BODIPY*	λ_{abs}*(nm)*	λ_{em} *(nm)*	*Stokes shift (nm)*	*log*ε	Φ_F
2a	530	543	13	4.57	0.95[b]
2b	565	578	13	4.69	0.84[b]
2c[34]	542	555	13	4.81	0.85[a]
2d	543	555	12	4.83	0.90[a]
2e	539	555	16	4.80	0.90[a]
2f[a]	542	553	11	5.20	1.00[a]
2g	544	557	13	4.04	0.78[a]
2h	545	557	12	4.85	0.85[a]
2i	546	559	13	4.93	0.90[a]
2j	561	574	13	4.65	0.81[b]
2k	558	571	13	5.10	0.79[b]
2l	540	559	19	4.74	0.70[a]
3m	573	597	24	4.88	0.89[b]
3n	566	572	6	4.74	0.98[a]
3o	575	600	25	4.41	0.74[b]
3p	567	570	3	4.69	0.55[b,c]
4q	579	591	12	4.73	1.00[b]
4r	562	574	12	4.87	0.95[b]

[a] Relative to Rhodamine 6G in EtOH ($\Phi_F = 0.94$). [b] Relative to Rhodamine 101 in EtOH ($\Phi_F = 0.96$). [c] Hexanes used instead of CH_2Cl_2 for quantum yield data

To evaluate the effects of C-ring substituents on the absorption maxima, each compound was compared to the parent (**2a**) bearing only the methoxy substituent on the B-ring. *F*-BODIPY **2a** itself has a maximum absorbance wavelength of 530 nm, which is hypsochromically shifted by 44 nm from the unsubstituted pyrrolyldipyrrin *F*-BODIPY.[16] This indicates that the electron-donating methoxy group causes a blue-shift in absorption. All modifications to the C-ring (**2b**-**2l**) bathochromically shifted the absorbance wavelength (9-35 nm) compared to the unsubstituted, methoxy bearing *F*-BODIPY **2a** (See **SI**, **Figures S3 and S4**). The greatest shift in absorption wavelength maxima of the C-ring modified pyrrolyldipyrrin *F*-BODIPYs occurred with the alkyl and ethanoic acid derivative substituents: **2b**, **2j** and **2k** bearing a $-CH_2CH_3$, $-CH_2C(O)NEt_2$ and $-CH_2CO_2Bn$ group, respectively. This trend is in agreement with that observed for *F*-BODIPYs whereby as the core becomes more alkyl substituted, the fluorophore absorbs at a higher wavelength.

The presence of electron-withdrawing groups on the B-ring (–Ph-*p*Cl, **3m** or –Ph-*p*CF_3, **3o**) resulted in a slight red-shift in absorption and emission wavelengths when compared to the parent compound **2b** (See **SI**, **Figures S5 and S6**) A similar trend has been reported for dipyrrin *F*-BODIPYs that contain electron-withdrawing groups in the *meso*-position.[35] Both *F*-BODIPYS **4q** and **4r** bearing the indole moiety in lieu of the A-ring pyrrole, exhibited significantly red-shifted absorbance maxima compared to the unsubstituted *F*-BODIPY **2a**. Furthermore, **4q** and **4r**, the A-ring indole analogs of **2b** and **2f**, respectively, exhibited a red shift in absorption of 14-20 nm of their A-ring pyrrole analogues, courtesy of the indole moiety. (See **SI**, **Figures S7 and S8).**

Unlike their constituent ligands, pyrrolyldipyrrin *F*-BODIPYs (**2-4**) exhibited considerable fluorescence with excellent relative quantum yields ($\Phi_F > 0.70$, Table 1) with the exception of *F*-BODIPY **3p**. Pyrrolyldipyrrin *F*-BODIPY **3p** did not display fluorescence when dissolved in CH_2Cl_2 (**Figure 7a**). However, when **3p** was dissolved in hexanes, an immediate display of fluorescence was evident (**Figure 7b**). The emission spectra of **3p** in CH_2Cl_2 and hexanes is shown in **SI Figure S9**. As well as a broader band structure for the emission of **3p** in

hexanes, compared to that of *F*-BODIPY **2a** (see **Figure 6**), **3p** exhibited a very narrow Stokes' shift of 3 nm and much lower quantum yield of 0.55.

The lack of emission of **3p** in CH_2Cl_2 can be attributed to the lone pair of the amino substituent transferring an electron to the *F*-BODIPY fluorophore to quench its fluorescence through photo-induced electron transfer (PET).[36, 37] This process can be effectively controlled by variation of the polarity of the solvent or by protonation of the amino substituent. To investigate the PET process observed for **3p**, a solution of this compound in hexanes was titrated with CH_2Cl_2 and indeed fluorescence quenching was observed (**Figure 8a**). Treatment of a CH_2Cl_2 solution of **3p**, using 5 μL of 1M HCl, restored fluorescence (Figure **7** and **Figure 8b**). The maximum wavelength of emission for **3p** in CH_2Cl_2 with the addition of 1M HCl is 597 nm with a Stokes' shift of 28 nm and a quantum yield of 0.41. The absorbance spectra of **3p** in CH_2Cl_2 shows a red-shift in the maximum wavelength of absorption (569 nm-574 nm) upon addition of 1M HCl (See **SI Figure S10**).

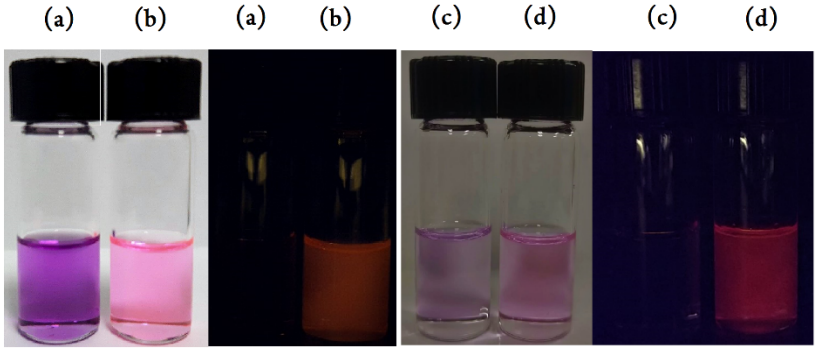


Figure 7 **3p** in CH_2Cl_2 **(a)**, hexanes **(b)**, CH_2Cl_2 without 1M HCl **(c)** and CH_2Cl_2 with 1M HCl **(d)** under ambient light and UV light.

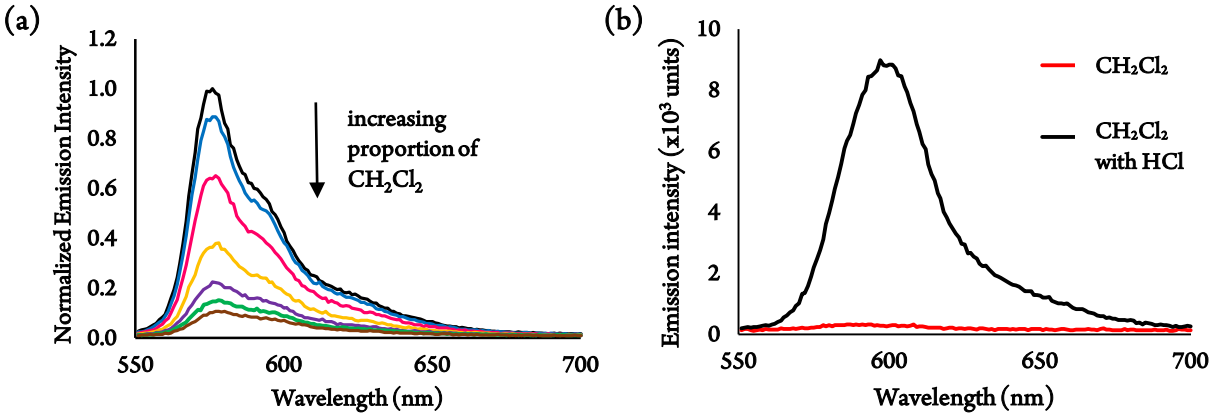


Figure 8 **(a)** Observed fluorescence quenching of **3p** in hexanes via titration with CH_2Cl_2; **(b)** Emission spectra of 3p dissolved in CH_2Cl_2 and in CH_2Cl_2 with addition of 1M HCl

Additionally, solvatochromatic effects of **2b** (**SI Figure S11** and **Figure S12**) and **3n**-**3p** were observed in hexane, toluene, dichloromethane, tetrahydrofuran, acetonitrile and methanol and is summarized in the Supporting Information **(Table S1)**. Interestingly, when **3p** was dissolved in polar solvents such as tetrahydrofuran, acetonitrile and methanol, the Stokes' shift was significantly increased from 3 nm (in hexanes) to 22-25 nm, yet with a lower quantum yield ranging from 0.22-0.30. Such an effect was not observed for **2b** and **3m**-**3o**, where the Stokes' shift and relative quantum yield did not vary amongst the different solvents. A slight blue-shift in absorption and emission wavelengths was observed for **2b** and **3m**-**3o** when dissolved in polar solvents (acetonitrile and methanol) compared to the wavelengths observed for these compounds dissolved in CH_2Cl_2.

The solvatochromatic effect on the emission of **3p** is illustrated by the Lippert-Mataga plot (**Figure 9**) of solvent orientation polarizability (Δf) versus Stokes' Shift (in cm^{-1}). There is a linear correlation between the solvent polarity and magnitude of the Stokes' Shift, with high polarity solvents exerting the greatest effect. It should be noted that Lippert-Mataga plots for compounds **2b** and **3m**-**3o** (**SI Figure 13**) do not illustrate such correlation, alluding that these compounds are not as sensitive to solvent polarity as **3p**. The larger Stokes' shift observed for **3p** dissolved in more polar solvents can be rationalized by considering the magnitude of the slope from the Lippert-Mataga plot, which gives an estimation of the change in dipole moment of the excited state and ground state of **3p**. In general, polar species can orient around the dipole of the excited state and thereby lower the energy of the excited state and shift emission maxima to longer wavelengths.

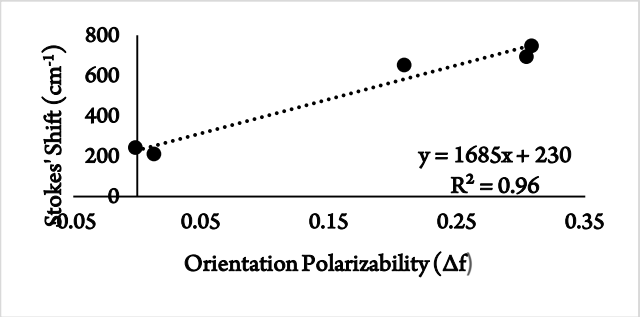


Figure 9. Lippert-Mataga plot of **3p** illustrating the Stokes' shift as a function of orientation polarizability (Δf). Solvents from left-right: hexane, toluene, tetrahydrofuran, acetonitrile and methanol. Dichloromethane is not represented on the plot as there was no measurable emission maximum for the compound in this solvent.

Conclusions

A series of pyrrolyldipyrrin *F*-BODIPYS with varying substituents on the A, B and C rings has been synthesized. Variation of substituents on the B-ring and A-ring result in the corresponding red-shift in absorption and emission reaching maximum emission wavelengths of 600 nm. Complexes bearing electron withdrawing substituents on the B-ring exhibited the largest Stokes' shift of 24-25 nm, while complexes bearing electron donating groups on the B-ring displayed the smallest Stokes' shift of only 3-6 nm. Extending the conjugation of the pyrrolyldipyrrin *F*-BODIPY core via placement of an indole substituent in lieu of the A-ring (**4q** and **4r**), results in the exhibition of a red-shift in absorption and emission wavelength (562-579 nm) with Stokes' shift comparable to that of C-ring substituents. Pyrrolyldipyrrin *F*-BOIPY **3p** exhibited interesting photophysical properties where the fluorescence is controlled depending on the polarity of the solvent. In hexanes, **3p** displays appreciable fluorescence, while in CH_2Cl_2 the fluorescence is effectively quenched. Additionally, the small Stokes' shift observed for **3p** could be enhanced when dissolved in polar solvents such as tetrahydrofuran, acetonitrile and methanol, or upon protonation with HCl. These data regarding the effects of substitution upon absorption and emission provide insight regarding how pyrrolyldipyrrin *F*-BODIPYs can be designed to match performance criteria.

Experimental procedures

General Experimental

All chemicals, including anhydrous solvents and reagents, were obtained from commercial sources and used as received unless otherwise noted. CH_2Cl_2 and hexanes for chromatography were obtained crude and distilled under air at 1 atm pressure before use. Column chromatography was performed using 150 mesh Brockman III, basic or neutral aluminum oxide. NMR spectra were obtained using a 500 MHz or 300 MHz instrument using $CDCl_3$ as solvent. Chemical shifts are reported in parts per million using the solvent signals as an internal ^{1}H and ^{13}C references. ^{11}B and ^{19}F chemical shifts were referenced using $BF_3 \bullet Et_2O$ (15% in $CDCl_3$) and CCl_3F defining the 0 ppm position as per the absolute referencing procedure standard for Bruker digital spectrometers. Coupling constants (*J*) are reported in Hertz. Mass spectra were recorded using ESI TOF ionization. UV-Vis and emission

analyses were performed using a UV-visible spectrophotometer and PTI spectrofluorometer, respectively. X-ray crystallography measurements were made on a CCD-equipped diffractometer (30 mA, 50 kV) using monochromated Mo Kα radiation (λ = 0.71073 Å) at 125 K. Compounds **1a-1r** were prepared according to literature procedures.[4, 6, 31]

General Procedure for Absorbance and Emission Measurements

In all measurements, a 10 mm quartz cuvette was used for solutions. For fluorescence experiments, a slit width of 3 nm was used for both excitation and emission.

Fluorescence Quantum Yield

Relative fluorescence quantum yields were obtained by comparing the area under the emission spectrum of the compound of interest to that of the standard, rhodamine 6G (ϕ=0.94 in ethanol) or rhodamine 101 (ϕ=0.96 in ethanol).[38] The excitation wavelength was 520 nm for rhodamine 6G and 546 nm for rhodamine 101. The excitation wavelength was 520 nm for **2c-2i**, **2l** and **3n** and compared to rhodamine 6G excited at 520 nm. The excitation wavelength for **2a-2b**, **2j-2k**, **3m**, **3o-3p** and **4q-4r** was 546 nm and compared to rhodamine 101 excited at 546 nm. Relative quantum yields were determined using equation 1,[39] where Φ_{st} is the reported quantum yield of the standard, I is the area of the integrated emission spectra, A is the absorbance at the excitation wavelength and η is the refractive index of the solvent used. The subscripts "X" and "st" denote the unknown and standard, respectively.

$$\Phi_X = \Phi_{st} \left(\frac{I_X}{I_{st}}\right)\left(\frac{A_{st}}{A_X}\right)\left(\frac{{\eta_X}^2}{{\eta_{st}}^2}\right)$$

Equation 1. Relative quantum yield (Φ_X)

General Procedure (GP1) for BF_2 complexation of pyrrolyldipyrrins

The corresponding pyrrolyldipyrrin HCl salt (1 equiv.) was dissolved in dry CH_2Cl_2 under a nitrogen atmosphere. Triethylamine (6 equiv.) was added and the reaction mixture then stirred for 10 minutes. $BF_3{\cdot}OEt_2$ (9 equiv.) was then added slowly, over a period of a few minutes. The reaction mixture was stirred until complete loss of starting material according to analysis using thin layer chromatography. Subsequent additions of base (6 equiv.) and $BF_3{\cdot}OEt_2$ (9 equiv.) were after a period of 8 hours. Reaction time and total amount of base and $BF_3{\cdot}OEt_2$ varied (5 h-96 h) depending upon the substrate. Upon completion, the reaction mixture was quenched via addition to 1 M HCl (15 mL) and then extracted with CH_2Cl_2 (25 mL). The organic phase was washed with 1 M HCl (1x15 mL) and brine (2x15 mL), dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting crude material was purified via column chromatography on basic or neutral alumina eluting with 5-20% ethyl acetate in hexanes, unless otherwise stated.

Boron, difluoro[(2*H*-pyrrol-2-ylidene)methyl]-4-methoxy-1*H*, 1'*H*-2,2'-bipyrrole] (2a) Following GP1, over a 72 hour period a solution of **1a** (20 mg, 0.07 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (233 μL, 1.89 mmol) and NEt_3 (176 μL, 1.26 mmol). The product was purified using column chromatography on basic alumina, eluting with 10-25% CH_2Cl_2 in hexanes, to provide *F*-BODIPY **2a** (9 mg, 45% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.61 (br s, 1H), 7.51 (s, 1H), 7.20-7.18 (m, 1H), 7.13 (s, 1H), 7.01-6.99 (m, 1H), 6.77-6.76 (m, 1H), 6.42-6.37 (m, 2H), 6.12 (s, 1H), 3.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) 165.3, 152.7, 134.1, 131.3, 130.5, 126.9, 123.5, 121.7, 119.2, 117.8, 114.9, 111.8, 97.1, 58.8; ^{11}B NMR ($CDCl_3$, 160 MHz) 1.23 (t, J = 35 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -139 (q, J = 34 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm) 530, ε 37000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{ex} (nm), 543, Φ_F: 0.95; LRMS: 310.1 $(M+Na)^+$; HRMS: 310.0925 Found, 310.0934 Calculated for $C_{14}H_{12}BF_2N_3NaO$.

Boron, difluoro[5-[(3,5-dimethyl-4-pentyl-2*H*-pyrrol-2ylidene)methyl]-4-methoxy-1*H*,1'*H*-2,2'-bipyrrole] (2b) Following GP1, over a 4 day period a solution of **1b** (18 mg, 0.05 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (278 μL, 2.25 mmol) and NEt_3 (167 μL, 1.20 mmol). The product was purified using column

chromatography on neutral alumina, eluting with 1%, 3%, 5% and then 10% ethyl acetate in hexanes, to provide *F*-BODIPY **2b** (10 mg, 53% yield). M.p. 124-126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 10.43 (br s, 1H), 7.08-7.07 (m, 1H), 7.05 (s, 1H), 6.84 (m, 1H), 6.33-6.31 (m, 1H), 6.10 (s, 1H), 3.95 (s, 3H), 2.49 (s, 3H), 2.37 (t, J = 7.7 Hz, 2H), 2.15 (s, 3H), 1.48-1.41 (m, 2H), 1.37-1.30 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 162.6, 150.2, 147.8, 134.3, 130.7, 129.5, 126.2, 124.2, 124.1, 115.6, 114.8, 110.8, 96.5, 58.4, 31.9, 30.2, 24.3, 22.7, 14.2, 12.6, 9.7; ^{11}B NMR (160 MHz, $CDCl_3$) 1.41 (t, J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -139 (q, J = 33 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 565, ε 49000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 578, Φ_F: 0.84; LRMS: 408.2 $(M+Na)^+$; HRMS: 408.2031 Found, 408.2029 Calculated for $C_{21}H_{26}BF_2N_3NaO$.

Boron, difluoro[ethyl 2-[(4-methoxy-1*H*,1'*H*-2,2'-bipyrrol-5-yl)-methylene]-3,5-dimethyl-2*H*-pyrrole-4-carboxylate] (2c)[13] Following GP1, over a 24 hour period a solution of **1c** (50 mg, 0.13 mmol) in CH_2Cl_2 (6 mL) was reacted with $BF_3{\cdot}OEt_2$ (610 μL, 4.94 mmol) and NEt_3 (544 μL, 3.90 mmol). The reaction mixture was quenched via addition of 5% citric acid and extracted with diethyl ether (20 mL). The product was purified using column chromatography on neutral alumina, eluting with 75% CH_2Cl_2 in hexanes, to provide *F*-BODIPY **2c** (42 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.50 (br s, 1H), 7.19-7.18 (m, 1H), 7.17 (s, 1H), 6.97-6.96 (m, 1H), 6.39-6.37 (m, 1H), 6.14 (s, 1H), 4.31 (q, J= 7.1 Hz, 2H), 3.99 (s, 3H), 2.81 (s, 3H), 2.43 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H); ^{11}B NMR (160 MHz, $CDCl_3$) 1.39 (t, J = 36 Hz); ^{1}HNMR and ^{11}B NMR chemical shifts were in agreement with literature values.[13] UV/vis (CH_2Cl_2) λ_{max} (nm): 542, ε 64000 mol L^{-1}cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 555, Φ_F: 0.85.

Boron, difluoro[isopropyl 2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)-methylene]-3,5-dimethyl-2*H*-pyrrole-4-carboxylate] (2d) Following GP1, over a 72 hour period a solution of **1d** (23 mg, 0.08 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (133 μL, 1.08 mmol) and NEt_3 (100 μL, 0.72 mmol). The product was purified using column chromatography on neutral alumina, eluting with 5%, 10% and then 25% ethyl acetate in hexanes, to provide *F*-BODIPY **2d** (22 mg, 92% yield). M.p. 191-193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 10.50 (br s, 1H), 7.18-7.16 (m, 1H), 7.15 (s, 1H), 6.97-6.94 (m, 1H), 6.38-6.36 (m, 1H), 6.12 (s, 1H), 5.21 (sep, J = 6.2 Hz, 1H), 3.97 (s, 3H), 2.80 (s, 3H), 2.41 (s, 3H), 1.35 (d, J = 6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): 165.0, 164.4, 153.0, 151.4, 136.7, 129.5, 129.4, 126.4, 123.7, 118.6, 118.3, 115.1, 111.8, 97.3, 67.1, 58.8, 22.5, 14.5, 12.0; ^{11}B NMR (160 MHz, $CDCl_3$) 1.38 (t, J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138 (q, J = 34 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 543, ε 68000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 555, Φ_F: 0.90; LRMS: 424.2 $(M+Na)^+$; HRMS: 424.1607 Found, 424.1614 Calculated for $C_{20}H_{22}BF_2N_3NaO_3$.

Boron, difluoro[phenyl 2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)-methylene]-3,5-dimethyl-2*H*-pyrrole-4-carboxylate] (2e) Following GP1, over a 24 hour period a solution of **1e** (50 mg, 0.12 mmol) in CH_2Cl_2 (6 mL) was reacted with $BF_3{\cdot}OEt_2$ (267 μL, 2.16 mmol) and NEt_3 (201 μL, 1.44 mmol). The product was purified using column chromatography on neutral alumina, eluting with 60% CH_2Cl_2 in hexanes, to provide *F*-BODIPY **2e** (37 mg, 70% yield). M.p. 248-250 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 10.52 (br s, 1H), 7.41 (t, J = 7.93 Hz, 2H), 7.25-7.23 (m, 1H), 7.21-7.20 (m, 3H), 7.19 (s, 1H), 7.01-7.00 (m, 1H), 6.40-6.39 (m, 1H), 6.17 (s, 1H), 4.01 (s, 3H), 2.88 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 164.6, 163.6, 153.4, 152.0, 150.9, 136.4, 129.9, 129.6, 126.8, 125.6, 123.5, 122.2, 119.1, 114.8, 111.9, 97.4, 58.8, 14.6, 12.0; ^{11}B NMR (160 Hz, $CDCl_3$) 1.41 (t, J = 36 Hz); ^{19}F NMR (235 Hz, $CDCl_3$) -138 (q, 34 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 539, ε 63000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 555, Φ_F: 0.90; LRMS: 458.1 $(M+Na)^+$; HRMS: 458.1459 Found, 458.1458 Calculated for $C_{23}H_{20}BF_2N_3NaO_3$.

Boron, difluoro[benzyl 2-[(4-methoxy-1*H*,1'*H*-2,2'-bipyrrol-5-yl)-methylene]-3,5-dimethyl-2*H*-pyrrole-4-carboxylate] (2f) Following GP1, over a 24 hour period a solution of **1f** (22 mg, 0.05 mmol) in CH_2Cl_2 (8 mL) was reacted with $BF_3{\cdot}OEt_2$ (56 μL, 0.45 mmol) and NEt_3 (42 μL, 0.30 mmol). The product was purified using column chromatography on neutral alumina, eluting with 25% CH_2Cl_2 in hexanes, to provide *F*-BODIPY **2f** (6 mg, 26 % yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.49 (br s, 1H), 7.45-7.34 (m, 1H), 7.20-7.17 (m, 1H), 7.16 (s,

1H), 6.99-6.96 (m, 1H), 6.40-6.36 (m, 1H), 6.14 (s, 1H), 5.32 (s, 2H), 3.99 (s, 3H), 2,81 (s, 3H), 2.42 (s, 3H); ^{11}B NMR (160 MHz, $CDCl_3$) 1.35 (t, J = 36 Hz). ^{1}H and ^{11}B NMR chemical shifts were in agreement with literature values.[40] UV/vis (CH_2Cl_2) λ_{max} (nm): 542, ε 156000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 553, Φ_F: 1.00.

Boron, difluoro[1-[2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3,5-dimethyl-2*H*-pyrrol-4-yl]ethanone] (2g) Following GP1, over a 48 hour period a solution of **1g** (13 mg, 0.04 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (99 μL, 0.80 mmol) and NEt_3 (84 μL, 0.60 mmol). The product was purified using column chromatography on basic alumina, eluting with 25% ethyl acetate in hexanes, *F*-BODIPY **2g** (5 mg, 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.50 (br s, 1H), 7.20 (s, 1H), 7.18 (s, 1H), 6.99 (s, 1H), 6.39 (s, 1H), 6.15 (s, 1H), 4.00 (s, 3H), 2.80 (s, 3H), 2.48 (s, 3H), 2.44 (s 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 195.4, 164.4, 152.1, 151.8, 134.3, 129.5, 127.2, 126.7, 123.5, 118.9, 115.0, 114.8, 111.8, 97.3, 58.8, 31.7, 15.2, 12.5; ^{11}B NMR (160 MHz, $CDCl_3$) 1.41 (t, J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138 (q, J = 29 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 544, ε 11000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 557, Φ_F: 0.78; LRMS: 380.1 $(M+Na)^+$; HRMS: 380.1363 Found, 380.1352 Calculated for $C_{18}H_{18}BF_2N_3NaO_2$.

Boron, difluoro[N-tert-butyl-6-[2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3,5-dimethyl-2H-pyrrol-4-yl]-6-oxohexanamide] (2h) Following GP1, over a 60 hour period a solution of **1h** (21 mg, 0.04 mmol) in CH_2Cl_2 (3 mL) was reacted with $BF_3{\cdot}OEt_2$ (74 μL, 0.60 mmol) and NEt_3 (50 μL, 0.36 mmol). The product was purified using column chromatography on neutral alumina, eluting with 40% ethyl acetate in hexanes, to provide *F*-BODIPY **2h** (16 mg, 73% yield). M.p. 214-216 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 10.49 (s, 1H), 7.19-718 (m, 1H), 7.16 (s, 1H), 7.00-6.97 (m, 1H), 6.39-6.37 (m, 1H), 6.14 (s, 1H), 5.44 (br s, 1H), 3.99 (s, 3H), 2.79-2.76 (m, 5H, overlapping CH_3 and CH_2), 2.42 (s, 3H), 2.15 (t, J = 7.0 Hz, 2H), 1.73-1.68 (m, 4H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 197.9, 172.2, 164.4, 151.9, 151.7, 133.8, 129.7, 129.5, 127.3, 126.6, 123.5, 118.9, 114.8, 111.8, 97.3, 58.8, 51.3, 42.9, 37.8, 29.0, 25.6, 23.8, 15.2, 12.6; ^{11}B NMR (160 MHz, $CDCl_3$) 1.41 (t, J = 32 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138 (q, J = 34 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 545, ε 71000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 557, Φ_F: 0.85; LRMS: 521.3 $(M+Na)^+$; HRMS: 521.2517 Found, 521.2506 Calculated for $C_{26}H_{33}BF_2N_4NaO_3$.

Boron, difluoro[ethyl 10-[2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3,5-dimethyl-2*H*-pyrrol-4-yl]-10-oxodecanoate] (2i) Following GP1, over a 72 hour period a solution of **1i** (24 mg, 0.05 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (111 μL, 0.90 mmol) and NEt_3 (77 μL, 0.55 mmol). The product was purified using column chromatography on basic alumina, flushing first with 100% hexanes and then eluting compound with CH_2Cl_2, to provide *F*-BODIPY **2i** (20 mg, 74% yield) M.p. 138-140 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 10.50 (br s, 1H), 7.19 (s, 1H), 7.16 (s, 1H), 6.98 (s, 1H), 6.38 (s, 1H), 6.14 (s, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.98 (s, 3H), 2.78 (s, 3H), 2.74 (t, J = 7.4 Hz, 2H), 2.42 (s, 3H), 2.28 (t, J = 7.6 Hz, 2H), 1.72-1.54 (m, 4H), 1.33 (s, 8H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 198.5, 174.1, 164.4, 151.9, 151.6, 134.0, 129.7, 129.6, 127.6, 126.6, 123.6, 118.8, 114.9, 111.8, 97.3, 60.3, 58.8, 43.3, 34.6, 29.6, 29.4, 29.3, 25.2, 24.5, 15.2, 14.5, 12.5; ^{11}B NMR (160 MHz, $CDCl_3$) 1.41 (t, J = 30 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138, J = 36 Hz; UV/vis (CH_2Cl_2) λ_{max} (nm): 546, ε 85000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 559, Φ_F: 0.90; LRMS: 550.3 $(M+Na)^+$; HRMS: 550.2661 Found, 550.2659 Calculated for $C_{28}H_{36}BF_2N_3NaO_4$.

Boron, difluoro[N,N-diethyl-2-[2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3,5-dimethyl-2*H*-pyrrol-4-yl]acetamide] (2j) Following GP1, over a 72 hour period a solution of **1j** (17 mg, 0.04 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (89 μL, 0.72 mmol) and NEt_3 (67 μL, 0.48 mmol).The product was purified using column chromatography on basic alumina, eluting with 25% and then 50% ethyl acetate in hexanes, to provide *F*-BODIPY **2j** (11 mg, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.44 (br s, 1H), 7.09 (s, 1H), 7.07 (s, 1H), 6.86 (s, 1H), 6.33 (s, 1H), 6.10 (s, 1H), 3.95 (s, 3H), 3.44 (s, 2H), 3.37 (dq, 22.4, 7.2 Hz, 4H), 2.49 (s, 3H), 2.17 (s, 3H), 1.14 (dt, J = 10.7, 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) 169.3, 162.9, 149.1, 148.4, 134.4, 130.1, 126.7, 124.4, 123.8, 121.8, 116.1, 114.7, 110.8, 96.4, 58.2, 42.1, 40.4, 30.1, 14.1, 13.0, 12.5, 9.7; ^{11}B NMR

(160 MHz, $CDCl_3$) 1.40 (t, J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -139 (q, J = 34 Hz) UV/vis (CH_2Cl_2) λ_{max} (nm): 561, ε 45000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 574, Φ_F: 0.81; LRMS: 451.2 $(M+Na)^+$; HRMS: 451.2081 Found, 451.2087 Calculated for $C_{22}H_{27}BF_2N_4NaO_2$.

Boron, difluoro[benzyl 2-[2-[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3,5-dimethyl-2*H*-pyrrol-4-yl]acetate] (2k) Following GP1, over a 48 hour period a solution of **1k** (12 mg, 0.03 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (100 μL, 0.81 mmol) and NEt_3 (75 μL, 0.54 mmol). The product was purified using column chromatography on basic alumina, eluting with CH_2Cl_2, to provide *F*-BODIPY **2k** (9 mg, 75% yield) ^1H NMR (500 MHz, $CDCl_3$): 10.46 (br s, 1H), 7.35-7.30 (m, 5H), 7.11-7.10 (m, 1H), 7.08 (s, 1H), 6.89-6.88 (m, 1H), 6.35-6.33 (m, 1H), 6.11 (s, 1H), 5.13 (s, 2H), 3.96 (s, 3H), 3.46 (s, 2H), 2.49 (s,*3*H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 171.0, 163.3, 149.1, 136.0, 135.3, 134.5, 131.0, 128.7, 128.2, 127.2, 124.9, 124.0, 120.5, 116.7, 115.0, 111.1, 106.1, 96.7, 66.8, 58.5, 30.6, 12.6, 9.8; ^{11}B NMR (160 MHz, $CDCl_3$) 1.39 (J = 36 Hz); ^{19}F (235 MHz, $CDCl_3$) -139 (J = 35 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 558, ε 127000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 571, Φ_F: 0.79; LRMS: 486.2 $(M+Na)^+$; HRMS: 486.1778 Found, 486.1771 Calculated for $C_{25}H_{24}BF_2N_3NaO_3$.

Boron, difluoro[benzyl 2[(4-methoxy-1H,1'H-2,2'-bipyrrol-5-yl)methylene]-3-(3-methoxy-3-oxopropyl)-5-methyl-2H-pyrrole-4-carboxylate] (2l) Following GP1, over a 48 hour period a solution of **1l** (19 mg, 0.04 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (89 μL, 0.72 mmol) and NEt_3 (67 μL, 0.48 mmol). The product was purified using column chromatography on basic alumina, eluting with 2%, 4%, 8%, 10% and then 25% ethyl acetate in hexanes, to provide *F*-BODIPY **2l** (18 mg, 95% yield). ^1H NMR (300 MHz, $CDCl_3$): 10.50 (s, 1H), 7.44-7.32 (m, 5H), 7.23-7.17(m, 2H), 6.99 (s, 1H), 6.38 (s, 1H), 6.12 (s, 1H), 5.30 (s, 2H), 3.98 (s, 3H), 3.61 (s, 3H), 3.12 (t, J = 7.5 Hz, 2H), 2.80 (s, 3H), 2.56 (t, J = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 173.4, 164.7, 152.7, 152.3, 137.6, 136.5, 130.3, 129.0, 128.7, 128.5, 128.2, 127.0, 123.4, 119.3, 114.9, 111.9, 97.4, 65.9, 58.8, 51.7, 35.4, 21.3, 14.6; ^{11}B NMR (160 MHz, $CDCl_3$) 1.34 (J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138 (J = 35 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 540, ε 55000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 559, Φ_F: 0.70; LRMS: 544.2 $(M+Na)^+$; HRMS: 544.1825 Found, 544.1826 Calculated for $C_{27}H_{26}BF_2N_3NaO_5$.

Boron, difluoro[4-(4-chlorophenoxy)-5-[(3,5-dimethyl-4-pentyl-2*H*-pyrrol-2-ylidene)methyl]-1H,1'H-2,2'-bipyrrole] (3m) Following GP1, over a 72 hour period a solution of **1m** (20 mg, 0.04 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (148 μL, 1.2 mmol) and NEt_3 (109 μL, 0.78 mmol). The product was purified using column chromatography on basic alumina, eluting with 20% CH_2Cl_2 in hexanes, to provide *F*-BODIPY **3m** (18 mg, 90% yield). M.p. °C 135-137 °C; ^1H NMR (500 MHz, $CDCl_3$) 10.35 (br s, 1H), 7.40-7.38 (m, 2H), 7.19-7.16 (m, 3H), 7.07-7.05 (m, 1H), 6.70-6.68 (m, 1H), 6.29-6.27 (m, 1H), 5.98 (s, 1H), 2.53 (s, 3H), 2.38 (t, J = 7.7 Hz, 2H), 2.18 (s, 3H), 1.46-1.41 (m, 2H), 1.35-1.30 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 158.3, 154.7, 153.3, 146.0, 136.2, 131.7, 130.7, 130.2, 130.1, 125.9, 124.1, 124.0, 120.9, 115.5, 115.4, 110.8, 100.4, 31.8, 30.1, 24.2, 22.7, 14.3, 12.9, 9.8; ^{11}B NMR ($CDCl_3$, 160 MHz) 1.37 (J = 31 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -140 (J = 33Hz); UV-vis (CH_2Cl_2) λ_{max} (nm): 573, ε 75000 mol L^{-1} cm^{-1}; Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 597, Φ_F: 0.89; LRMS: 504.2 $(M+Na)^+$; HRMS: 504.1793 Found, 504.1796 Calculated for $C_{26}H_{27}BClF_2N_3NaO$.

Boron, difluoro[4-(benzyloxy)-5-[(3,5-dimethyl-4-pentyl-2H-pyrrol-2-ylidene)methyl]-1H,1'H-2,2'-bipyrrole] (3n) Following GP1, over a 96 hour period a solution of **1n** (16 mg, 0.04 mmol) in CH_2Cl_2 (8 mL) was reacted with $BF_3{\cdot}OEt_2$ (160 μL, 1.3 mmol) and NEt_3 (120 μL, 0.86 mmol). The product was purified using column chromatography on basic alumina, eluting with 2%, 4%, 6% and then 8% ethyl acetate in hexanes, to provide *F*-BODIPY **3n** (9 mg, 50% yield). ^1H NMR (500 MHz, $CDCl_3$) 10.42 (br s , 1H), 7.46-7.38 (m, 5H), 7.10 (s, 1H), 7.07 (s, 1H), (6.81 (s, 1H), 6.33-6.31 (m, 1H), 6.14 (s, 1H), 5.16 (s, 2H), 2.49 (s, 3H), 2.36 (t, 2H), 2.14 (s, 3H), 1.48-1.40 (m, 2H), 1.37-1.29 (m, 4H), 0.90 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 161.4, 156.5, 147.6, 135.7, 134.6, 130.8, 129.6, 128.9, 128.8, 128.0, 126.4, 124.2, 124.1, 115.6, 115.0, 110.8, 97.4, 73.2,

31.9, 30.2, 24.3, 22.7, 14.2, 12.7, 9.7; ^{11}B NMR (160MHz, $CDCl_3$) 1.41 (J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -139 (J = 34Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 566, ε 55000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 520 (nm); λ_{max} (nm), 572, Φ_F: 0.98. LRMS: 484.2 $(M+Na)^+$; HRMS: 484.2339 Found, 484.2342 Calculated for $C_{27}H_{30}BF_2N_3NaO$.

Boron, difluoro[5-[(3,5-dimethyl-4-pentyl-2*H*-pyrrol-2-ylidene)methyl]-4-[4-(trifluoromethyl)phenoxy]-1H,1'H-2,2'-bipyrrole] (3o) Following GP1, over a 48 hour period a solution of **1o** (12 mg, 0.02 mmol) in CH_2Cl_2 (8 mL) was reacted with $BF_3{\cdot}OEt_2$ (54 µL, 0.44 mmol) and NEt_3 (42 µL, 0.30 mmol). The product was purified using column chromatography on basic alumina, eluting with 5% ethyl acetate in hexanes, to provide *F*-BODIPY **3o** (12 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.34 (br s , 1H), 7.68 (d, J = 8.7 Hz, 2 H), 7.32 (J = 8.6 Hz, 2H), 7.13 (s, 1H), 7.07-7.05 (m, 1H), 6.72-6.70 (m, 1H), 6.30-6.28 (m, 1H), 6.11 (s, 1H), 2.54 (s, 3H), 2.39 (t, J = 7.7, 2H), 2.18 (s, 1H), 1.49-1.41 (m, 2H), 1.38-1.31 (m, 4H), 0.91 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$,) 159.2, 154.5, 145.8, 136.8, 131.2, 131.0, 129.0, 127.6, 126.1, 124.2, 124.0, 119.0, 115.7, 115.4, 110.9, 110.1, 101.6, 68.3, 31.9, 30.0, 24.3, 22.7, 14.2, 13.0, 9.8; ^{11}B NMR (160 MHz, $CDCl_3$) 1.27 (J = 35 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -62 (s, CF_3), -140 (q, J = 35 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 575, ε 26000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 600, Φ_F: 0.74. LRMS: 516.2 $(M+Na)^+$; HRMS: 516.2262 Found, 516.2240 Calculated for $C_{27}H_{28}BF_5N_3NaO$.

Boron, difluoro[4-[5-((3,5-dimethyl-4-pentyl-2*H*-pyrrol-2-ylidene)methyl)-1H,1'H-2,2'-bipyrrol4-yloxy]-N,N-dimethylaniline] (3p) Following GP1, over a 48 hour period a solution of **1p** (16 mg, 0.03 mmol) in CH_2Cl_2 (8 mL) was reacted with $BF_3{\cdot}OEt_2$ (67 µL, 0.54 mmol) and NEt_3 (50 µL, 0.36 mmol). The product was purified using column chromatography on basic alumina, eluting with 2%, 4%, 6%, and then 8% ethyl acetate in hexanes, to provide *F*-BODIPY **3p** (12 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.38 (br s, 1H), 7.21 (s, 1H), 7.10 (d, J = 9.0 Hz, 2H), 7.04 (t, J = 1.8 Hz, 1H), 6.75 (d, J = 9.0 Hz, 2H), 6.67 (t, J = 1.8 Hz, 1H), 6.26-6.25 (m, 1H), 5.87 (s, 1H), 2.98 (s, 6H), 2.51 (s, 3H), 2.38 (t, J = 7.7 Hz, 2H), 2.18 (s, 3H), 1.49-1.43 (m, 2H), 1.36-1.31 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 161.2, 150.3, 148.4, 146.6, 134.9, 131.1, 130.1, 126.0, 123.6, 120.6, 115.5, 115.2, 114.4, 113.4, 110.7, 99.6, 41.1, 31.9, 30.2, 24.3, 22.7, 14.2, 12.5, 9.7 (one carbon signal missing); ^{11}B NMR (160 MHz, $CDCl_3$) 1.41 (J = 35 Hz); ^{19}F NMR (235 MHz, $CDCl_3$,) -139 (q, J = 35 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 569, ε 55000 mol L^{-1} cm^{-1}. LRMS: 491.3 $(M+H)^+$; HRMS: 491.2803 Found, 491.2788 Calculated for $C_{28}H_{34}BF_2N_4O$.

Boron, difluoro[2-[5-((3,5-dimethyl-4-pentyl-2*H*-pyrrol-2-ylidene)methyl)-4-methoxy-1H-pyrrol-2-yl]-1H-indole] (4q) Following GP1, over a 5-day period a solution of **1q** (28 mg, 0.07 mmol) in CH_2Cl_2 (15 mL) was reacted with $BF_3{\cdot}OEt_2$ (273 µL, 2.21 mmol) and NEt_3 (205 µL, 1.47 mmol) toThe product was purified using column chromatography on basic alumina, eluting with 0%, 1%, 2% and then 4% ethyl acetate in hexanes, to provide *F*-BODIPY **4q** (22 mg, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 10.19 (br s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.28-7.24 (m, 1H), 7.13-7.09 (m, 3H), 6.30 (s, 1H), 3.95 (s, 3H), 2.56 (s, 3H), 2.39 (t, J = 7.7 Hz, 2H), 2.17 (s, 3H), 1.49-43 (m, 2H), 1.38-1.32 (m, 4H), 0.92 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 161.8, 153.5, 146.4, 138.2, 136.3, 131.8, 130.7, 129.5, 128.1, 126.0, 124.4, 121.2, 120.6, 116.0, 112.2, 107.9, 98.0, 58.4, 31.9, 30.0, 24.3, 22.7, 14.2, 13.0, 9.7; ^{11}B NMR (160 MHz, $CDCl_3$) 1.39 (t, J = 35 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -138 (q, J = 35 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 579, ε 54000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 591, Φ_F: 1.0; LRMS: 458.2 $(M+Na)^+$; HRMS: 458.2183 Found, 458.2186 Calculated for $C_{25}H_{28}BF_2N_3NaO$.

Boron, difluoro[benzyl 2-[(5-(1H-indol-2-yl)-3-methoxy-1H-pyrrol-2-yl)methylene]-3,5-dimethyl-4-pentyl-2H-pyrrol-4-carboxylate] (4r) Following GP1, over a 5 hour period a solution of **1r** (14 mg, 0.03 mmol) in CH_2Cl_2 (4 mL) was reacted with $BF_3{\cdot}OEt_2$ (48 µL, 0.39 mmol) and NEt_3 (38 µL, 0.27 mmol). The product was purified using column chromatography on basic alumina, eluting with CH_2Cl_2, to provide *F*-BODIPY **4r** (10 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$,) 10.24 (br s, 1H), 7.67 (d, J = 8 Hz, 1H), 7.54 (d, J = 8 Hz, 1H), 7.48 (d, J = 7 Hz, 2H), 7.43 (t, J = 7 Hz, 2H), 7.39-7.304 (m, 2H), 7.31 (s, 1H), 7.25 (s, 1H), 7.17 (t, J = 8 Hz, 1H),

6.38 (s, 1H), 5.37 (s, 2H), 4.05 (s, 3H), 2.90 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 164.8, 164.0, 155.3, 151.1, 139.1, 139.0, 136.6, 130.3, 130.2, 129.3, 128.7, 128.4, 18.2, 127.9, 125.9, 121.7, 121.2, 117.0, 112.5, 111.1, 98.6, 65.9, 58.8, 14.8, 12.1; ^{11}B NMR (160MHz, $CDCl_3$) 1.39 (J = 36 Hz); ^{19}F NMR (235 MHz, $CDCl_3$) -137 (q, J = 31 Hz); UV/vis (CH_2Cl_2) λ_{max} (nm): 562, ε 74000 mol L^{-1} cm^{-1}. Fluorescence (CH_2Cl_2) λ_{exci}, 546 (nm); λ_{max} (nm), 574, Φ_F: 0.95; LRMS: 522.2 $(M+Na)^+$; HRMS: 522.1762 Found, 522.1771 Calculated for $C_{28}H_{24}BF_2N_3NaO_3$.

Supporting Information

^{1}H, ^{13}C NMR, absorption/emission spectra for all new compounds and crystal data for **2d**.

ACKNOWLEDGMENTS

We thank Dr. Estelle Marchal for preparation of pyrrolyldipyrrin HCl salts, Pankaj Subedi for assistance with obtaining fluorescence spectra and Dr. Norman Schepp for spectrofluorometer access.

REFERENCES

1. Fluorescent indicators of metal ions based on dipyrromethene platform, E. V. Antina, N. A. Bumagina, A. I. V'yugin and A. V. Solomonov, *Dyes Pigm.*, 2017, **136**, 368-381.
2. Prodigiosene [5-(2-pyrryl)-2,2'-dipyrrylmethene] and some substitited prodigiosenes, W. R. Hearn, M. K. Elson, R. H. Williams and J. Medina-Castro, *J. Org. Chem.*, 1970, **35**, 142-146.
3. Synthesis and immunosuppressive activity of novel prodigiosin derivatives, R. D'Alessio, A. Bargiotti, O. Carlini, F. Colotta, M. Ferrari, P. Gnocchi, A. M. Isetta, N. Mongelli, P. Motta, A. Rossi, M. Rossi, M. Tibolla and E. Vanotti, *J. Med. Chem.*, 2000, **43**, 2557-2565.
4. Antimalarial activity of prodigiosenes, E. Marchal, D. A. Smithen, I. M. Uddin, A. W. Robertson, D. L. Jakeman, V. Mollard, C. D. Goodman, K. S. MacDougall, S. A. McFarland, G. I. McFadden and A. Thompson, *Org. Biomol. Chem.*, 2014, **12**, 4132-4142.
5. Antimicrobial activity of non-natural prodigiosenes, E. Marchal, M. I. Uddin, D. A. Smithen, L. A. Hawco, M. Lanteigne, D. P. Overy, R. G. Kerr and A. Thompson, *RSC Adv.*, 2013, **3**, 22967-22971
6. Influence of B-ring modifications on proton affinity, transmembrane anion transport and anti-cancer properties of synthetic prodigiosenes, E. Marchal, S. Rastogi, A. Thompson and J. T. Davis, *Org. Biomol. Chem.*, 2014, **12**, 7515-7522
7. Synthesis of prodigiosene-estrogen conjugates: optimization of protecting group strategies and anticancer properties, E. Marchal, M. I. Uddin, C. L. A. Hawco and A. Thompson, *Can. J. Chem.*, 2015, **93**, 526-535.
8. Advances in the chemistry of dipyrrins and their complexes, T. E. Wood and A. Thompson, *Chem. Rev.*, 2007, **107**, 1831-1861.
9. 4,4'-Difluoro-4-bora-3a,4a-diaza-s-indacenes (BODIPYs) as components of novel light active materials, M. Benstead, G. H. Mehl and R. W. Boyle, *Tetrahedron*, 2011, **67** 3573-3601.
10. Fluorescent indicators based on BODIPY, N. Boens, V. Leen and W. Dehaen, *Chem. Soc. Rev.*, 2012, **41**, 1130-1172.
11. BODIPY dyes and their derivatives: syntheses and spectroscopic properties, A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **107**, 4891-4932.
12. The chemistry of BODIPY: a new El Dorado for fluorescence tools, R. Ziessel, G. Ulrich and A. Harriman, *New. J. Chem.*, 2007, **31**, 496-501.
13. Synthesis and characterization of fluorescent pyrrolyldipyrrinato Sn(IV) complexes, S. M. Crawford, A. Al-Sheikh Ali, T. S. Cameron and A. Thompson, *Inorg. Chem*, 2011, **50**, 8207-8213.
14. Zinc and copper complexes of prodigiosin: implications for copper-mediated double-strand DNA cleavage, G. Park, J. T. Tomlinson, M. S. Melvin, M. W. Wright, C. S. Day and R. A. Manderville, *Org. Lett.*, 2003, **5**, 113-116.
15. Synthesis of BF2 complexes of prodigiosin type oligopyrroles, M. R. Rao, M. D. Tiwari, J. R. Bellare and M. Ravikanth, *J. Org. Chem.*, 2011, **76**, 7263-7268.
16. Red to near-infrared isoindole BODIPY fluorophores: synthesis, crystal structures, and spectroscopic and electrochemical properties, C. Yu, Q. Wu, J. Wang, Y. Wei, E. Hao and L. Jiao, *J. Org. Chem.*, 2016, **81**, 3761-3770.
17. Synthesis of pyrrolyldipyrrinato BF2 complexes by oxidative nucleophilic substitution of boron dipyrromethene with pyrrole, M. Zhang, E. Hao, J. Zhou, C. Yu, G. Bai, F. Wang and L. Jiao, *Org. Biomol. Chem.*, 2012, **10**, 2139-2145.
18. https://www.thermofisher.com/ca/en/home/brands/invitrogen.html.
19. Structural studies of C-ring substituted unnatural analogues of prodigiosin, S. Jenkins, C. D. Incarvito, J. Parr and H. H. Wasserman, *CrystEngComm*, 2009, **11**, 242-245

20. Synthesis and properties of meso-unsubstituted 3-pyrrolyl boron dipyrromethene, V. Lakshmi, M. S. Shaikh and M. Ravikanth, *J. Fluoresc.*, 2013, **23**, 519-525.
21. One-pot efficient synthesis of pyrrolylBODIPY dyes from pyrrole and acyl chloride, M. Zhang, E. Hao, Y. Xu, S. Zhang, H. Zhu, Q. Wang, C. Yu and L. Jiao, *RSC Adv.*, 2012, **2**, 11215-11218.
22. Effects of five membered aromatic heterocycles at the meso-position on the electronic properties of 3-pyrrolyl BODIPY, R. Sharma, V. Lakshmi, T. Chatterjee and M. Ravikanth, *New J. Chem.*, 2016, **40**, 5855-5860.
23. 3-/3,5-Pyrrole-substituted BODIPY derivatives and their photophysical and electrochemical studies, K. J. Kadassery, A. Nimesh, S. Raj and N. Agarwal, *J. Chem. Sci.*, 2016, **128**, 1435-1443
24. Functionalized 3-pyrrolyl boron-dipyrromethenes, T. Kaur, V. Lakshmi and M. Ravikanth, *RSC Adv.*, 2013, **3**, 2736-2745.
25. Synthesis, structure and spectral and electrochemical properties of 3-pyrrolyl BODIPY-metal dipyrrin complexes, V. Lakshmi, W.-Z. Lee and M. Ravikanth, *Dalton Trans.*, 2014, **43**, 16006-16014.
26. Synthesis and photophysics of BF2-rigidified partially closed chain bromotetrapyrroles: near infrared emitters and photosensitizers, E. Dai, W. Pang, X.-F. Zhang, X. Yang, T. Jiang, P. Zhang, C. Yu, E. Hao, Y. Wei, X. Mu and L. Jiao, *Chem. Asian J.*, 2015, **10**, 1327-1334.
27. Straightforward synthesis of oligopyrroles through a regioselective SNAr reaction of pyrroles and halogenated boron dipyrrins, T. Jiang, P. Zhang, C. Yu, J. Yin, L. Jiao, E. Dai, J. Wang, Y. Wei, X. Mu and E. Hao, *Org. Lett.*, 2014, **16**, 1952-1955.
28. Isoindole-BODIPY dyes as red to near-infrared fluorophores, C. Yu, Y. Xu, L. Jiao, J. Zhou, Z. Wang and E. Hao, *Chem. Eur. J.*, 2012, **18**, 6437-6442.
29. Metal-free and versatile synthetic routes to natural and synthetic prodiginines from boron dipyrrin, J. Li, Q. Zhang, J. Yin, C. Yu, K. Cheng, Y. Wei, E. Hao and L. Jiao, *Org. Lett.*, 2016, **18**, 5696-5699.
30. Use of *F*-BODIPYs as a protection strategy for dipyrrins: optimization of BF2 removal, D. A. Smithen, A. E. G. Baker, M. Offman, S. M. Crawford, T. S. Cameron and A. Thompson, *J. Org. Chem.*, 2012, **77**, 3439-3453.
31. Synthetic prodigiosenes and the influence of C-ring substitution on DNA cleavage, transmembrane chloride transport and basicity, S. Rastogi, E. Marchal, I. Uddin, B. Groves, J. Colpitts, S. A. McFarland, J. T. Davis and A. Thompson, *Org. Biomol. Chem.*, 2013, **11**, 3834-3845.
32. The chemistry of fluorescent BODIPY dyes: versatility unsurpassed, G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem. Int. Ed.*, 2008, **47**, 1184-1201.
33. Synthetic prodiginine Obatoclax (GX15-070) and related analogues: anion binding, transmembrane transport, and cytotoxicity properties, B. Díaz de Greñu, P. I. Hernández, M. Espona, D. Quiñonero, M. E. Light, T. Torroba, R. Pérez-Tomás and R. Quesada, *Chem. Eur. J.*, 2011, **17**, 14074-14083.
34. Investigations into the nucleophilic meso-substitution of *F*-BODIPYs and improvements to the synthesis of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene, S. M. Crawford and A. Thompson, *Heterocycles*, 2011, **83**, 311-322.
35. Effect of meso-substituents on the electronic transitions of BODIPY dyes: DFT and RI-CC2 study, I. K. Petrushenko and K. B. Petrushenko, *Spectrochim. Acta, Part A*, 2015, **138**, 623-627.
36. New BODIPY derivatives as OFF–ON fluorescent chemosensor and fluorescent chemodosimeter for Cu2+: cooperative selectivity enhancement toward Cu2+, X. Qi, E. J. Jun, L. Xu, S.-J. Kim, J. S. Joong Hong, Y. J. Yoon and J. Yoon, *J. Org. Chem.*, 2006, **71**, 2881-2884.
37. Novel optical pH-sensor based on a boradiaza-indacene derivative, T. Werner, C. Huber, S. Heinl, M. Kollmannsberger, J. Daub and O. S. Wolfbeis, *Fresenius' J. Anal. Chem.*, 1997, **359**, 150-154.
38. K. Rurack, in *Standardization and Quality Assurance in Fluorescence Measurements I: Techniques*, ed. U. Resch-Genger, Springer Berlin Heidelberg, Berlin, Heidelberg, 2001, p. 101.

39. S. Fery-Forgues and D. Lavabre, *J. Chem. Educ.*, 1999, **76**, 1260-1264.
40. Improved synthetic route to C-ring ester-functionalized prodigiosenes, M. I. Uddin, S. Thirumalairajan, S. M. Crawford, T. S. Cameron and A. Thompson, *Synlett*, 2010, 2561-2564.