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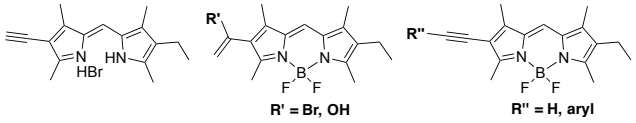
# Asymmetric dipyrrin and *F*-BODIPYs conjugated to terminal alkynes and alkenes

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

[a]*Department of Chemistry, Dalhousie University, PO BOX 15000, Halifax, NS, B3H 4R2, Canada*

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

**TOC graphic**




## Abstract

An asymmetric meso-*H* dipyrrin featuring a conjugated terminal alkyne substituent was converted to its corresponding difluoro boron complex and the extent of π-conjugation extended using Sonogashira cross-coupling. Treatment of the alkyne-substituted dipyrrin with $BF_3$•$OEt_2$ and $NEt_3$ revealed the reactivity of the conjugated terminal alkyne towards Lewis-activated electrophilic substitution, and led to the isolation of *F*-BODIPYs bearing terminal bromovinyl and enol substituents.

4,4′-Difluoro-4-bora-(3a,4a)-diaza-s-indacenes (*F*-BODIPYs)[1] are popular courtesy of their robustness in chemical and physiological environments, tunable nanosecond fluorescence lifetime, negligible triple-state population and high quantum yield.[2-7] Indeed, the electronic

properties of BODIPYs have recently been exploited in chromogenic and pH probes in biomolecular environments,[8,9], drug delivery agents,[10,11] fluorescent switches,[12] electro-luminescent films,[13,14] and photosensitizers in both solar cells and photodynamic therapy.[15-17] However, the emission wavelength of the BODIPY core (generally <600 nm) is outside of the 650-1000 nm biological window, where auto-fluorescence and light scattering are minimized.[18] Furthermore, conjugation of BODIPYs to large biomolecules is rather underdeveloped[19,20] and relies on synthetic methodology involving extended reaction times and harsh conditions. A bathochromic shift of the emission wavelength has been achieved by extending the π-conjugation of the dipyrrinato ligand of BODIPYs (Figure 1).[21] All eight positions of the dipyrrinato core can be substituted with groups such as aryl, ethynylphenyl, steryl and vinyl, as can the fluoro substituents at boron[21-28] (Figure 1). Particularly appealing is the incorporation of an acetelyne substituent on the β-positions of the dipyrrinato ligand with the goal of both extending π-conjugation and introducing a functional handle for linkage to other moieties.[29-43] Despite the large body of work concerning the synthesis and the reactions of alkene-substituted *F*-BODIPYs, systems substituted with terminal alkenes are scarce.[44]

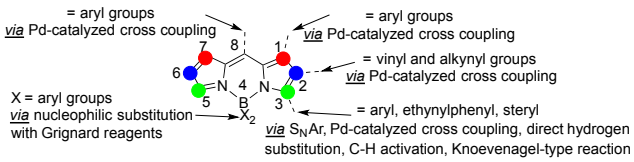
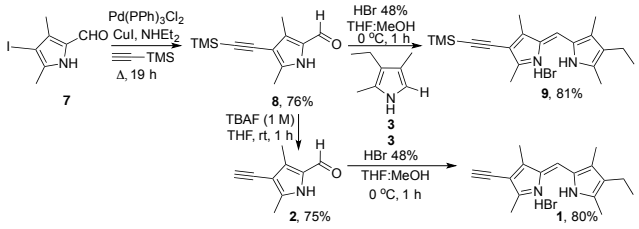



**Figure 1**. BODIPYs exhibiting a bathochromic shift through extension of the π-conjugation.

In an ongoing effort to synthesize new dipyrrole-based dyes and investigate their photochemical properties and reactivity,[45-50] we targeted the meso-*H* asymmetric dipyrrin **1** (Scheme 1), featuring a terminal alkyne directly conjugated to the dipyrrinato core, and complexed to $-BF_2$ to provide the *F*-BODIPY **4**. Furthermore, we report the generation and

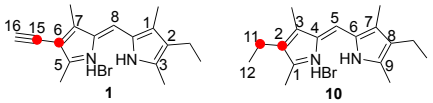
reactivity of the first bromovinyl- (**5**) and enol-substituted (**6**) *F*-BODIPYs (Scheme 2) bearing terminal alkenyl units. Our pre-functionalization synthetic approach to **1** (Scheme 1),[3] involving condensation of the corresponding alkyne-substituted 2-formyl pyrrole (**2)**[51] and krypto pyrrole (**3**), allows independent modification of the electronic and steric features of each pyrrole of the dipyrrin. Although *F*-BODIPYs have been isolated bearing alkynyl functionality at the β-position, most are symmetrical (with an alkynyl unit on each pyrrolic unit) and/or are synthesized in one pot from the requisite pyrroles, i.e. not isolated at the pre-ligand step.[29,30,41,51-55] Burgess reported the synthesis of an asymmetric *F*-BODIPY similar to **4** and bearing a terminal alkyne at the β-position of the dipyrrinato core, but the constituent dipyrrin was not isolated.[55]

We first synthesized the asymmetric dipyrrin hydrobromide salt **9**, bearing a TMS-protected alkynyl unit (Scheme 1). The β-iodo pyrrole **7**[55] underwent Sonogashira cross-coupling reaction conditions with TMS-acetylene to afford pyrrole **8**.[51] Condensation of **8** and the α-free pyrrole **3** afforded the TMS-protected dipyrrin hydrobromide salt **9**. However, upon treatment of **9** with $NEt_3$ and $BF_3{\bullet}OEt_2$, loss of the TMS-group was accompanied by decomposition rather than formation of the corresponding *F*-BODIPY. At this point, we began to appreciate the unusual susceptibility of the β-alkynyl unit towards Lewis acid activation.




**Scheme 1.** Synthesis of dipyrrins bearing alkynyl groups.

Fortunately, TMS-deprotection could be achieved earlier in the sequence using the pyrrole **8**, followed by condensation of the resulting 2-formyl-4-alkynynl pyrrole **2** with **3** to provide the desired dipyrrin hydrobromide salt **1** (Scheme 1). The structure of **1**, featuring a terminal alkyne directly conjugated to the dipyrrinato core, was confirmed using X-ray crystallography (see Supporting Information, Figure S1). The ability of the alkynyl unit to extend the π-conjugated system of the dipyrrinato core is demonstrated by the C(6)-C(15) bond length of 1.438 Å, intermediate between the expected length of C–C single and double bonds (Figure 2). In contrast, the structure of the dipyrrin hydrobromide salt **10** (Supporting Information, Figure S2),[56] with only ethyl groups substituting the β-positions of the dipyrrinato core, features a C(2)-C(11) bond length of 1.503 Å. The short C(6)-C(15) bond length within **1** suggests that the triple bond π-system participates in the delocalization of electrons originating within the dipyrrinato core, and is thereby activated towards electrophilic attack.




| **Bond length (Å)** | 1.438 | 1.503 |
|---|---|---|

**Figure 2.** Comparison of bond length between dipyrrin hydrobromides **1** and **10**.

Treatment of dipyrrin hydrobromide salt **1** with $NEt_3$ and $BF_3{\bullet}OEt_2$ did not initially afford the expected *F*-BODIPY **4** (Scheme 2). Instead, two new stable compounds, that were inseparable via chromatography over silica, were isolated. The $^{1}H$ NMR spectrum (Supporting Information, Figure S3a) of the mixture contained two sets (4:1 ratio) of vinylic protons between 6.00 and 5.20 ppm. Although the $^{11}B$ NMR triplet diagnostic was too broad to reveal detailed information beyond confirming the presence of *F*-BODIPYs, the $^{19}F$ NMR spectrum clearly displayed two overlapping quartets, thereby also suggesting the presence of two *F*-BODIPYs in

the mixture. $^{1}H–^{13}C$ HSQC NMR analysis showed distinct correlations between peaks due to each set of vinylic protons (A and B in Figure 3) and signals due to their respective carbon atoms, implying that both compounds in the mixture feature a terminal vinyl group at the β-position.

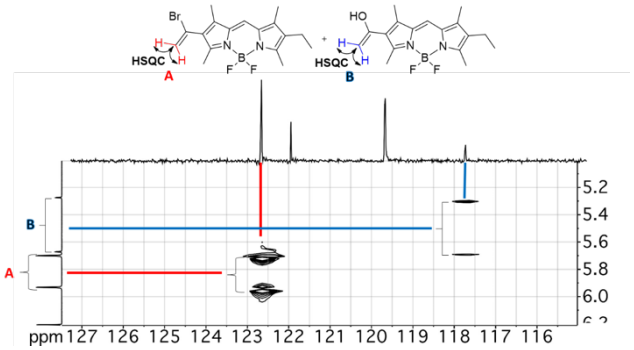
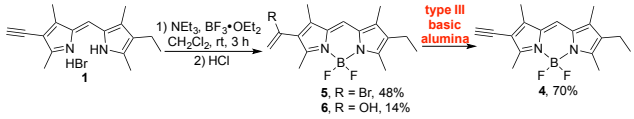



**Figure 3**. $^{1}H–^{13}C$ HSQC NMR spectra of the mixture of *F*-BODIPYs **5** and **6**.

Alongside two-dimensional NMR analysis, mass spectrometric analysis of the mixture enabled the identification of these two products as the bromovinyl- and enol-containing *F*-BODIPYs **5** and **6**, respectively, with the bromovinyl- derivative as the major constituent (Scheme 2). Both materials presumably formed as a result of addition across the triple bond, with **6** as a result of exposure to water in the work-up. To determine whether **5** was formed as the direct product of the reaction of **4** with $NEt_3$ and $BF_3{\bullet}OEt_2$, or during work-up, the reaction was monitored through $^{1}H$ NMR spectroscopic analysis (Supplementary Information, Figures S3b and S3c). Analysis of the vinylic region revealed that the bromovinyl analog **5** dominates throughout the reaction, with signals due to **6** becoming more prominent upon addition of aqueous acid in work-up. Although the use of silica did not enable the chromatographic separation of **5** and **6**, the use of basic alumina was effective in that it resulted in elimination of HBr from **5** to produce the desired *F*-BODIPY **1** (Scheme 2, yields based on the amount of **5** in the mixture). However, the remarkably stable enol *F*-BODIPY **6** was recovered. The mixture of

**5** and **6** was reacted with either TsCl or MeI in the presence of a base (DIPEA and $NEt_3$, respectively). However, in both cases, only starting materials were recovered.




**Scheme 2**. Reaction of dipyrrin hydrobromide **1** with $BF_3$•$OEt_2$ and $NEt_3$.

The elimination of HBr from **5** to form the alkynyl-substituted *F*-BODIPY **4** was investigated spectroscopically via treatment of a solution of the mixture of **5** and **6** in $CD_3CN$ with $NEt_3$ (Supporting Information, Figure S4). Two sets of vinyl peaks were clearly apparent until 1 equiv. of $NEt_3$ was added whereupon the alkynyl peak at 3.60 ppm of **4** appeared. Further additions of $NEt_3$ resulted in increasing conversion to **4** at the expense of only the bromo-vinyl substituted *F*-BODIPY **5**, as determined through monitoring the vinyl protons. The vinyl proton peaks of the enol-containing *F*-BODIPY **6** remained constant, matching the previous observation following chromatography over basic alumina. Presumably, the conversion of **5** to **4** does not occur in the original complexation reaction, despite the presence of excess $NEt_3$, due to equilibria involving $NEt_3$ preferably interacting with HF and $HBF_4$, as well as forming the $BF_3$•$NEt_3$ Lewis pair,[45,57] which was reported unreactive towards terminal alkyne.[58]

Cognizant that activation of terminal alkynes can occur in the presence of Lewis acids, including those involving boron species,[53,54,58-64] dipyrrin hydrobromide salt **1** was reacted with stoichiometric $BF_3$•$OEt_2$ whereby formation of the *F*-BODIPY would not be expected.[45] A solution of **1** in $CDCl_3$ (Figure 4, spectrum a) was treated with $BF_3$•$OEt_2$ (1 equiv.), under anhydrous conditions, and the mixture analyzed using $^1$H NMR spectroscopy. Immediately after the addition, the intensity of the signal due to the alkynyl proton of **1** diminished and two sets of vinyl peaks appeared (Figure 4, spectrum b). One of the sets of signals due to vinyl protons

corresponded to our previous characterization of **5** (Figure 4, spectrum g). The other set of vinylic peaks was assigned to the free-base **11**. The broad peak in the range of 4.20 and 3.90 ppm corresponds to the ethyl groups originating from $BF_3 \bullet OEt_2$. Sequential $^1H$ NMR analysis (Figure 4, spectra c-f), revealed conversion of **1** to the mixture of **5** and the corresponding free-base **11**. Stoichiometric activation of the triple bond of the dipyrrin **1** clearly enables addition of HBr (from the original dipyrrin hydrobromide salt) across the exo-cyclic π-system. To the best of our knowledge, this is the first report whereby the HX unit of a dipyrrin salt reacts with the substituents about the dipyrrinato core. The same experiment was repeated using 1-hexyne in $CDCl_3$ (Supporting Information, Figure S5), but $^1H$ NMR spectroscopy revealed no reaction over 3 hours thus confirming the surprising sensitivity of the terminal alkyne of dipyrrin hydrobromide **1**. Treatment of the free-base of **1**, prepared through washing the hydrobromide salt with 2 M NaOH, with 1 equiv. $BF_3 \bullet OEt_2$ resulted in the dark green solution producing a dark purple colour and then a black polymerized precipitate. Attempts to solubilize the precipitate in organic solvents, including DMSO-$d_6$, were unsuccessful. Similar polymerization occurred when the *F*-BODIPY **4** was treated with stoichiometric $BF_3 \bullet OEt_2$. It is curious that the alkynyl functionality of the salt **1** is essentially protected upon reaction with HBr, yet this unit of HBr was introduced with the intention of protecting the dipyrrinato unit. The HBr addition product **5** essentially masks the triple bond, yet can be ready converted to the alkyne **4** upon treatment with base.

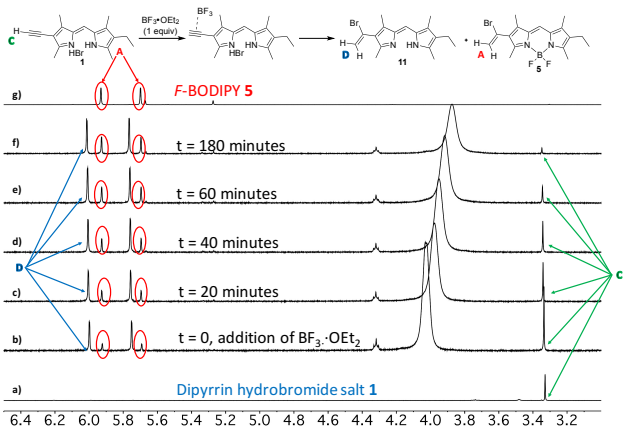
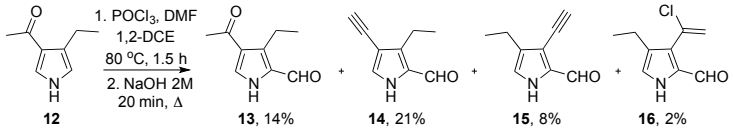



**Figure 4.** Treatment of a solution of dipyrrin **1** in $CDCl_3$ (0.1 M) with 1 equiv. $BF_3$•$OEt_2$.

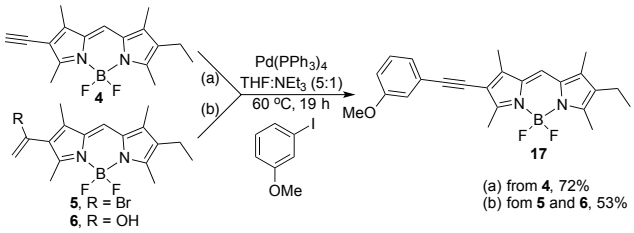
The susceptibility of a conjugated alkynyl-substituted pyrrole to addition reactions was similarly observed when pyrrole **12**[65] was subjected to Vilsmeier-Haack reaction conditions. Alongside the desired product **13**, the alkynes **14** and **15** were isolated (note that initial formylation suffers from poor regioselectivity). Furthermore, the chlorovinyl-pyrrole **16** was also isolated, presumably as a consequence of HCl addition to the alkyne **14** under the reaction conditions (Scheme 3). The contribution of the pyrrolic nitrogen lone pair to the reactivity of substituents has been well-documented,[66-69] and in the case of **4** and **15** is responsible for enabling a facile addition reaction across the triple bond.




**Scheme 3.** Formylation of pyrrole **12** using Vilsmeier-Haack reaction conditions.

With the goal of extending the π-conjugation, the chemical reactivity of *F*-BODIPYs **4**-**6** was investigated. First, alkyne-containing *F*-BODIPY **4** was reacted with 3-iodoanisole under Sonogashira cross-coupling conditions (a, Scheme 4).[55] The expected aryl-conjugated alkynyl *F*-BODIPY **17** was isolated in 72% yield. Interestingly, reaction of the mixture of **5** and **6** (4:1

ratio) with 3-iodoanisole, under the same conditions also gave the aryl-conjugated alkynyl *F*-BODIPY **17** (53% yield based on the amount of **5** in the mixture, reaction b in Scheme 4). The enol **6** again remained unreacted, and was isolated in a mixture alongside the excess 3-iodoanisole.




**Scheme 4.** Sonogashira cross-coupling reaction between *F*-BODIPYs **4**-**6** and 3-iodoanisole.

The absorbance and fluorescence exhibited by the new *F*-BODIPYs **4** and **17** were compared to those of the known *F*-BODIPY **18**, formed from **10**, with ethyl groups on each of the β-positions of the dipyrrinato core. The replacement of one of the β-ethyl groups of **18** with an alkynyl moiety (**4**), results in a negligible red-shift absorbance maximum of 3 nm whereas the extended conjugation seen in **17** results in a red-shift of 13 nm (Figure 5). Noteworthy is the fact that the emission wavelengths are significantly red-shifted courtesy of an increased Stoke's shift for both **4** (14 nm) and **17** (29 nm) cf. just 4 nm for the per-alkyl analog **18**. However, the *F*-BODIPY **17** exhibits a slightly lower quantum yield ($\phi_{fluo}$ = 0.60) compared to the simpler analogs (near quantitative, see Supporting Information).

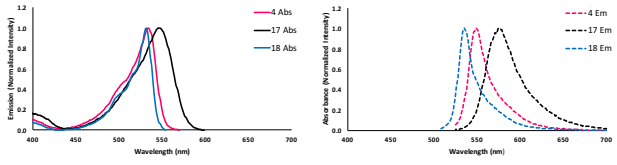



**Figure 5.** Absorbance and emission of *F*-BODIPYs **4**, **17** and **18**

In conclusion, the synthesis, characterization and reactivity of the asymmetric meso-*H* alkyne-conjugated dipyrrin **1** are reported. The reaction of **1** with $BF_3$•$OEt_2$ and $NEt_3$ revealed that the conjugated terminal alkynyl unit undergoes electrophilic attack. Future work involving dipyrrins bearing terminal alkynes should take this unusual reactivity into consideration. Two new terminal alkene-substituted *F*-BODIPYs, **5** and **6**, were isolated after treating **1** with $BF_3$•$OEt_2$ and $NEt_3$. $^1$H NMR spectroscopic analysis suggests activation of the alkynyl unit by $BF_3$, and subsequent nucleophilic addition of HBr onto the triple bond. Basic conditions induced elimination of HBr from **5** and restoration of the conjugated triple bond. Extension of the π-conjugation of **4** and **5** give the new dye **17**. The absorption and emission spectra of *F*-BODIPYs **4** and **17** were compared to a per alkyl dipyrrin, thereby enabling the effect of the terminal and substituted alkynyl units to be assessed. The extension of the π-conjugation resulted in red shifted absorbance and a Stoke's shift of almost 30 nm.

**Experimental procedures**

All chemicals were purchased and used as received unless otherwise indicated. Moisture sensitive reactions were performed in oven-dried glassware and under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced via syringe or cannula through a rubber septum. Flash chromatography was performed using either ultra-pure silica (230-400 mm) or 150 mesh Brockmann III activated basic alumina oxide as indicated. The NMR spectra were recorded using a 500 MHz spectrometer instrument using $CDCl_3$ as solvent and is reported in parts per million (ppm). Internal solvent was referenced at 7.26 ppm for $^1$H and at 77.16 ppm for $^{13}$C when using $CDCl_3$. All chemical shifts regarding $^{11}$B and $^{19}$F were referenced using the absolute referencing procedure standard on digital spectrometers. For $^{11}$B chemical shifts the 0 ppm position corresponds to the chemical shift of $BF_3 \cdot Et_2O$ (15% in $CDCl_3$) whereas for $^{19}$F the

reference compound is $CCl_3F$. Coupling constants (*J*) are given in Hertz (Hz). Mass spectra were obtained using TOF and LCQ Duo ion trap instruments operating in $ESI^{+/-}$ or APCI mode, as indicated. Compounds **2**,[51] **3**,[55] **8**,[51] **10**,[70] **12**[65] and **18**[71] were prepared according to literature procedures.

**General Procedure for Absorbance and Emission Measurements**

A 10 mm quartz cuvette was used. For fluorescence experiments, a slit width of 3 nm was used for both excitation and emission. Each compound was dissolved in $CH_2Cl_2$.

**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 ($\phi$=0.94 in ethanol).[72] The excitation wavelength was 520 nm for rhodamine 6G, *F*-BODIPY **4** and *F*-BODIPY **17**. The excitation wavelength was 500 nm for the reference compound **18**, and compared to rhodamine 6G excited at 500 nm. Relative quantum yields were determined using Equation 1,[73] where $\Phi_{st}$ 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 $\eta$ is the refractive index of the solvent used. The subscripts "X" and "st" denote the unknown and standard compound, 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 ($\Phi_X$).

**3-Ethyl-5-((4-ethynyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole hydrobromide (1)**

2-Formyl pyrrole **2**[51] (0.10 g, 0.680 mmol) was dissolved in MeOH:THF (1:1.5 mL) and α-free pyrrole **3**[55] (0.08 g, 0.680 mmol) was added in one portion at room temperature. The reaction mixture was degassed (× 3) and 48% aq. HBr (0.18 mL, 0.680 mmol) was added at 0 °C. The reaction mixture was placed under an atmosphere of $N_2$ and stirred for 1 hour and then poured into $Et_2O$ (30 mL). The resulting precipitate was isolated *via* suction filtration and then washed with $Et_2O$ (10 mL × 3) to afford the title compound as a bright red solid (80%). M.p.: decomposition >170 °C. $^1$H NMR ($CDCl_3$, 500 MHz) 1.08 (t, $J$ = 7.6 Hz, 3H), 2.29 (s, 3H), 2.39 (s, 3H), 2.44 (q, $J$ = 7.6 Hz, 2H), 2.70 (s, 3H), 2.71 (s, 3H), 3.33 (s, 1H), 7.07 (s, 1H), 13.16 (br s, 1H), 13.29 (br s, 1H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz) 10.2, 11.4, 13.2, 13.4, 14.4, 17.4, 75.2, 83.8, 110.9, 119.8, 124.8, 127.8, 132.4, 143.6, 145.5, 155.3, 158.5 ppm. HRMS-ESI (m/z): $[M\text{-}Br]^+$ calcd for $C_{17}H_{21}N_2$, 253.1699; found, 253.1693.

**3-Ethyl-5-((4-ethynyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole (free-base)**

A solution of dipyrrin **1** (0.10 g, 0.300 mmol) in $CH_2Cl_2$ (10 mL) was washed with 2 M NaOH (10 mL × 3). The organic layer was washed with water (10 mL × 2) and brine (10 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to give the title compound as a dark green solid (0.07 g, quant.). M.p.: decomposition >110 °C. $^1$H NMR ($CDCl_3$, 500 MHz) 1.06 (t, $J$ = 7.6 Hz, 3H), 2.13 (s, 3H), 2.27 (s, 3H), 2.31 (s, 3H), 2.37 (q, $J$ = 7.6 Hz, 2H), 2.40 (s, 3H), 3.30 (s, 1H), 6.66 (s, 1H), 8.84 (br s, 1H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz) 9.6, 10.7, 14.6, 14.8, 15.2, 17.9, 78.5, 81.9, 109.3, 116.3, 132.6, 134.2, 136.1, 138.1, 140.0, 151.1, 157.3 ppm. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{21}N_2$, 253.1699; found, 253.1707.

**4,4-Difluoro-1,3,5,7-tetramethyl-2-ethynyl-6-ethyl-8*H*-4-bora-3a,4a-diaza-s-indacene (4)**

$NEt_3$ (2.5 mL, 18.0 mmol) was added to a solution of dipyrrin hydrobromide **1** (1.00 g, 3.00 mmol) in anhydrous $CH_2Cl_2$ (313 mL) at room temperature under a $N_2$ atmosphere. The reaction mixture was stirred for 15 minutes and $BF_3{\bullet}OEt_2$ (3.3 mL, 27.0 mmol) was then added. After 2 hours, $NEt_3$ (2.5 mL, 18.0 mmol) and $BF_3{\bullet}OEt_2$ (3.3 mL, 27.0 mmol) were added and the reaction mixture stirred for an additional 2 hours. 5 M HCl (20 mL) was added and the two layers were separated. The organic layer was washed with 5 M HCl (20 mL × 4), water (50 mL × 2) and brine (50 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude mixture was purified using column chromatography over either $SiO_2$ or type III neutral $Al_2O_2$ (hexanes:EtOAc, 100:0, 95:5) and an inseparable mixture of compounds **5** and **6** was obtained as a bright purple powder (0.68 g). Purification of this mixture over type III basic $Al_2O_2$ (hexanes:EtOAc, 100:0, 99:1, 98:2, 95:5, 90:10) gave **4** as a dark red solid (70%). Data for **4**: m.p.: decomposition> 150 °C. $^1$H NMR ($CDCl_3$, 500 MHz) 1.08 (t, $J$ = 7.6 Hz, 3H), 2.19 (s, 3H), 2.29 (s, 3H), 2.40 (q, $J$ = 7.6 Hz, 2H), 2.53 (s, 3H), 2.59 (s, 3H), 3.30 (s, 1H), 7.01 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz) 9.5, 10.6, 13.1, 13.3, 14.4, 17.4, 76.8, 82.8, 111.5, 119.8, 130.7, 133.8, 134.6, 139.3, 140.6, 156.3, 159.7 ppm; $^{11}$B {1H} NMR ($CDCl_3$, 160 MHz) 0.74 (t, $J$ = 31 Hz) ppm; $^{19}$F NMR ($CDCl_3$, 470 MHz) -146.5 (q, $J$ = 31 Hz); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{17}H_{19}BF_2N_2Na$, 323.1502; found, 323.1492; UV/vis($CH_2Cl_2$): 534 nm (ε = 100280 L mol$^{-1}$ cm$^{-1}$); Data for the mixture of **5** and **6**, present in a 4:1 ratio: $^1$H NMR ($CDCl_3$, 500 MHz) 1.08 (t, $J$ = 7.6 Hz, (0.8 × 3H) + (0.2 × 3H), C$H_3$CH$_2$ of **5** and **6**), 2.19 (s, (0.8 × 3H) + (0.2 × 3H), C$H_3$ of **5** and **6**), 2.25 (s, 0.8 × 3H, C$H_3$ of **5**), 2.27 (s, 0.8 × 3H, C$H_3$ of **6**), 2.40 (q, $J$ = 7.6 Hz, (0.8 × 2H) + (0.2 × 2H), CH$_3$C$H_2$ of **5** and **6**), 2.53 (s, (0.8 × 3H) + (0.2 × 3H), C$H_3$ of **5** and **6**), 2.55 (s, 0.8 ×3H, C$H_3$ of **5**), 2.56 (s, 0.2 × 3H, C$H_3$ of **6**) 5.27 (s, 0.2 × 1H, C$H_2$COH of **6**), 5.67 (s, 0.2 × 1H, C$H_2$COH of **6**), 5.70 (s, 0.8 × 1H, C$H_2$CBr of **5**), 5.93 (s, 0.8 × 1H, C$H_2$CBr of **5**), 7.02 (s,

0.8 × 1H, meso-*H* of **5**), 7.03 (s, 0.2 × 1H, meso-*H* of **6**) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz) 9.6, 10.3 (×2), 13.1 (×2), 14.5, 17.4, 117.9, 120.0, 122.2, 122.9, 129.5, 131.0, 132.9, 133.7, 134.4, 136.2, 138.9, 151.9, 159.4 ppm; $^{11}$B {1H} NMR ($CDCl_3$, 160 MHz) 0.83 (t, $J$ = 31 Hz) ppm; $^{19}$F NMR ($CDCl_3$, 470 MHz) -146.1 (two overlapping q, $J$ = 33 Hz); HRMS-APCI (*m/z*): **5** $[M]^+$ calcd for $C_{17}H_{21}BBrF_2N_2$, 381.0944; found, 381.0948) and **6** $[M+H]^+$ calcd for $C_{17}H_{22}BF_2N_2O$, 319.1788; found, 319.1779).

**2-((3,5-Dimethyl-4-((trimethylsilyl)ethynyl)-2*H*-pyrrol-2-ylidene)methyl)-4-ethyl-3,5-dimethyl-1*H*-pyrrole hydrobromide (9)**

2-Formyl pyrrole **8**[51] (0.30 g, 1.37 mmol) was dissolved in MeOH:THF (1:1, 10 mL), and α-free pyrrole **3**[55] (0.20 g, 1.64 mmol) was added in one portion at room temperature. The reaction mixture was degassed (× 3) and 48% aq. HBr (0.75 mL, 1.37 mmol) was added at 0 °C. The reaction mixture was placed under an atmosphere of $N_2$ and stirred for 1.5 hours and then poured into $Et_2O$ (50 mL). The resulting precipitate was isolated *via* suction filtration and then washed with $Et_2O$ (× 3) to afford compound **13** as an orange solid (81%). M.p.: decomposition >220 °C. $^1$H NMR ($CDCl_3$, 500 MHz) 0.26 (s, 9H), 1.07 (t, $J$ = 7.6 Hz, 3H), 2.29 (s, 3H), 2.38 (s, 3H), 2.43 (q, $J$ = 7.6 Hz, 2H), 2.69 (s, 6H), 7.05 (s, 1H), 13.12 (br s, 1H), 13.22 (br s, 1H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz) 0.22, 10.2, 11.4, 13.2, 13.4, 14.4, 17.4, 96.1, 101.7, 112.3, 119.7, 124.9, 127.6, 132.2, 143.3, 145.2, 155.5, 158.0 ppm. HRMS-ESI (m/z): $[M-Br]^+$ calcd for $C_{20}H_{29}N_2Si$, 325.2095; found, 325.2096.

**4-Acetyl-3-ethyl-1*H*-pyrrole-2-carbaldehyde (13)**

$POCl_3$ (2.04 mL, 21.9 mmol) was added dropwise to DMF (16 mL) at 0 ºC and under a $N_2$ atmosphere. The mixture was allowed to warm to room temperature and then stirred for 15 minutes. A solution of pyrrole **12**[65] (2.00 g, 14.6 mmol) in 1,2-DCE (49 mL) was added at 0 ºC

under inert atmosphere. The resulting mixture was heated to 80 ºC and stirred for an additional 80 minutes. Aq. NaOH (2 M) was added to the reaction mixture until pH > 8, and the resulting emulsion was then heated at reflux temperature for 20 minutes. After cooling to room temperature, $H_2O$ (50 mL) was added and the reaction mixture was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude mixture was purified using column chromatography on $SiO_2$ (hexanes:EtOAc 80:20, 70:30) to afford the title compound as a brown solid (0.33 g, 14%), along with 2-fomyl pyrroles **14** (0.44, 21%), **15** (0.22 g, 10%) and **16** (0.05 g, 2%). The position of the formyl group was determined using 2D NMR (HSQC and HMBC). Data for **13**: M.p.: 119-123 ºC; $^1$H NMR (500 MHz; $CDCl_3$) 1.26 (t, *J* = 7.5 Hz, 3H), 2.44 (s, 3H), 3.11 (q, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 3.4 Hz, 1H), 9.74 (s, 1H), 10.03 (br s, 1H) ppm; $^{13}$C NMR (125 MHz; $CDCl_3$) 16.7, 17.9, 28.5, 125.0, 130.4, 130.7, 140.4, 179.1, 193.5 ppm; HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_9H_{11}NNaO_2$, 188.0682; found, 188.0680. **3-Ethyl-4-ethynyl-1*H*-pyrrole-2-carbaldehyde (14)**: M.p.: decomposition > 80 ºC, followed by melting at 119-120 ºC. $^1$H NMR ($CDCl_3$, 500 MHz) 1.30 (t, *J* = 7.6 Hz, 3H), 2.85 (q, *J* = 7.6 Hz, 2H), 3.10 (s, 1H), 7.22 (d, *J* = 3.0 Hz, 1H), 9.46 (br s, 1H), 9.64 (s, 1H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz) 16.4, 18.0, 76.3, 79.6, 106.8, 128.6, 129.6, 141.6, 177.9 ppm. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_9H_9NNaO_1$, 170.0576; found, 170.0575. **4-Ethyl-3-ethynyl-1*H*-pyrrole-2-carbaldehyde (15)**: M.p.: decomposition > 95 ºC, followed by melting at 104-105 ºC. $^1$H NMR ($CDCl_3$, 500 MHz) 1.23 (t, 3H, *J* = 7.6 Hz), 2.58 (q, 2H, *J* = 7.6 Hz), 3.35 (s, 1H), 6.86 (br s, 1H), 9.28 (br s, 1H), 9.68 (s, 1H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz) 14.5, 18.8, 75.2, 83.8, 114.7, 123.3, 132.5, 134.2, 178.5 ppm. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_9H_9NNaO_1$, 170.0576; found, 170.0578. **3-(1-Chlorovinyl)-4-ethyl-1*H*-pyrrole-2-carbaldehyde (16)**: M.p.: 65-66ºC. $^1$H

NMR ($CDCl_3$, 500 MHz) 1.22 (t, *J* = 7.6 Hz, 3H), 2.59 (q, *J* = 7.6 Hz, 2H), 5.45 (d, *J* = 0.6 Hz, 1H), 5.74 (d, *J* = 0.6 Hz, 1H), 6.87 (s, 1H), 9.56 (br s, 1H), 9.66 (s, 1H) ppm. $^{13}C$ NMR ($CDCl_3$, 125 MHz) 14.6, 18.6, 119.2, 123.1, 128.2, 129.7, 131.1, 131.3, 179.2 ppm. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_9H_{10}ClNNaO$, 206.0343; found, 206.0341.

**4,4-Difluoro-1,3,5,7-tetramethyl-2-(3-methoxyphenyl)ethynyl)-6-ethyl-8*H*-4-bora-3a,4a-diaza-s-indacene (17)**

A solution of **4** (56 mg, 0.187 mmol), 3-iodoanisole (27 μL, 0.224 mmol) and CuI (7.0 mg, 0.037 mmol) in THF:$NEt_3$ (5:1, 3.4 mL) was degassed (× 3) and placed under a $N_2$ atmosphere. $Pd(PPh_3)_4$ (22 mg, 0.019 mmol) was added to the solution and the resulting reaction mixture degassed (× 2), placed under a positive pressure of $N_2$ and stirred at 60 °C in a sealed system for 19 hours. The reaction mixture was diluted with EtOAc (5.0 mL), washed with water (10 mL × 3) and brine (10 mL), dried over $Na_2SO_4$, concentrated under reduced pressure and purified using column chromatography ($SiO_2$, hexanes:EtOAc, 80:20) to give the title compound as a dark pink solid (41%). Following the above procedure compound **17** was also obtained (56 mg, 53%) from the mixture of **5** and **6** (100 mg). M.p.: 192-193 °C. $^1H$ NMR ($CDCl_3$, 500 MHz) 1.08 (t, *J* = 7.6 Hz, 3H), 2.20 (s, 3H), 2.35 (s, 3H), 2.41 (q, *J* = 7.6 Hz, 2H), 2.54 (s, 3H), 2.65 (s, 3H), 3.83 (s, 3H), 6.88 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 7.02 (s, 1H), 7.10 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.24 (t, *J* = 8.3 Hz, 2H) ppm. $^{13}C$ NMR ($CDCl_3$, 125 MHz) 9.6, 10.8, 13.1, 13.6, 14.5, 17.4, 55.5, 82.1, 95.3, 112.8, 114.6, 116.3, 119.7, 124.1, 124.9, 129.5, 131.2, 133.7, 134.4, 139.0, 139.8, 156.4, 159.2, 159.4 ppm. $^{11}B$ {1H} NMR ($CDCl_3$, 160 MHz) 0.76 (t, *J* = 31 Hz) ppm. $^{19}F$ NMR ($CDCl_3$, 470 MHz) -146.5 (q, *J* = 31 Hz). HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{24}H_{25}BF_2N_2NaO$, 429.1920; found, 429.1918. UV/vis($CH_2Cl_2$): 547 nm (ε = 141000 L $mol^{-1}$ $cm^{-1}$).

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXX. X-ray structure and data for **1** and **10**. NMR spectroscopic analysis of reactions. Absorption and emission data for **4**, **17** and **18**. NMR spectra of all new compounds.

## AUTHOR INFORMATION


### Corresponding Author

*E-mail: Alison.Thompson@dal.ca

### ORCID

Alison Thompson: 0000-0003-4231-3446


### Notes

The authors declare no competing financial interest.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