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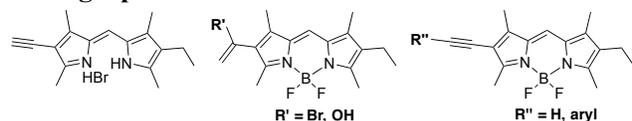
Asymmetric dipyrin and *F*-BODIPYs conjugated to terminal alkynes and alkenes

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TOC graphic



Abstract

An asymmetric meso-*H* dipyrin 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 dipyrin with $\text{BF}_3 \cdot \text{OEt}_2$ 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)-diazas-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 dipyrinato ligand of BODIPYs (Figure 1).²¹ All eight positions of the dipyrinato core can be substituted with groups such as aryl, ethynylphenyl, steryl and vinyl, as can the fluoro substituents at boron²¹⁻²⁸ (Figure 1). Particularly appealing is the incorporation of an acetylene substituent on the β -positions of the dipyrinato 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

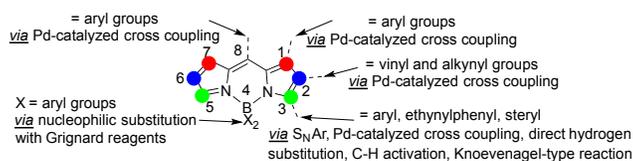
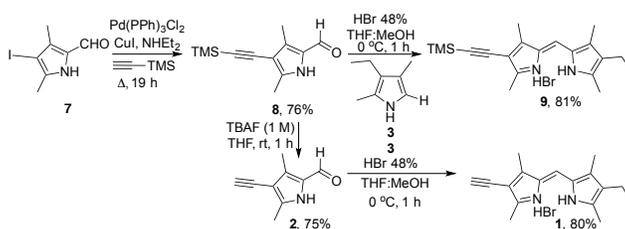


Figure 1. BODIPYs exhibiting a bathochromic shift through extension of the π -conjugation.

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 dipyrin **1** (Scheme 1), featuring a terminal alkyne directly conjugated to the dipyrinato core, and complexed to $-\text{BF}_2$ 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 dipyrin. 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 dipyrin core, but the constituent dipyrin was not isolated.⁵⁵

We first synthesized the asymmetric dipyrin 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 dipyrin hydrobromide salt **9**. However, upon treatment of **9** with NEt₃ and BF₃•OEt₂, 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 dipyrins 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 dipyrin hydrobromide salt **1** (Scheme 1). The structure of **1**, featuring a terminal alkyne directly conjugated to the dipyrin 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 dipyrin 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 dipyrin hydrobromide salt **10** (Supporting Information, Figure S2),⁵⁶ with only ethyl groups substituting the β -positions of the dipyrin 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 dipyrin core, and is thereby activated towards electrophilic attack.

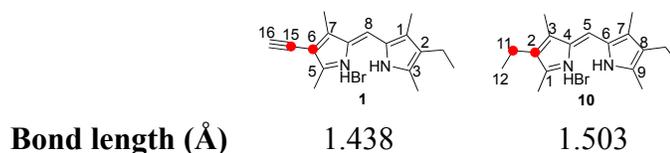


Figure 2. Comparison of bond length between dipyrin hydrobromides **1** and **10**.

Treatment of dipyrin hydrobromide salt **1** with NEt_3 and $\text{BF}_3 \cdot \text{OEt}_2$ 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 ^1H 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. ^1H - ^{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.

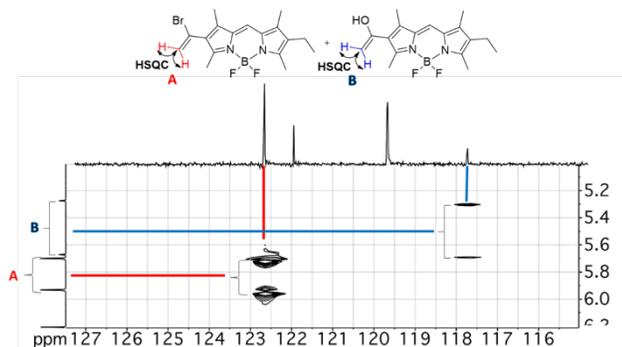
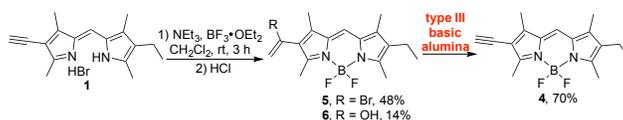


Figure 3. ^1H - ^{13}C HSQC NMR spectra of the mixture of *F*-BODIPYs **5** and **6**.

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 $\text{BF}_3 \cdot \text{OEt}_2$, or during work-up, the reaction was monitored through ^1H 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 NEt₃, respectively). However, in both cases, only starting materials were recovered.



Scheme 2. Reaction of dipyrin hydrobromide **1** with BF₃•OEt₂ and NEt₃.

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 CD₃CN with NEt₃ (Supporting Information, Figure S4). Two sets of vinyl peaks were clearly apparent until 1 equiv. of NEt₃ was added whereupon the alkynyl peak at 3.60 ppm of **4** appeared. Further additions of NEt₃ 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 NEt₃, due to equilibria involving NEt₃ preferably interacting with HF and HBF₄, as well as forming the BF₃•NEt₃ 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} dipyrin hydrobromide salt **1** was reacted with stoichiometric BF₃•OEt₂ whereby formation of the *F*-BODIPY would not be expected.⁴⁵ A solution of **1** in CDCl₃ (Figure 4, spectrum a) was treated with BF₃•OEt₂ (1 equiv.), under anhydrous conditions, and the mixture analyzed using ¹H 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 $\text{BF}_3 \bullet \text{OEt}_2$. 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 dipyrin **1** clearly enables addition of HBr (from the original dipyrin 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 dipyrin salt reacts with the substituents about the dipyrinato 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 dipyrin hydrobromide **1**. Treatment of the free-base of **1**, prepared through washing the hydrobromide salt with 2 M NaOH, with 1 equiv. $\text{BF}_3 \bullet \text{OEt}_2$ 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 $\text{DMSO}-d_6$, were unsuccessful. Similar polymerization occurred when the *F*-BODIPY **4** was treated with stoichiometric $\text{BF}_3 \bullet \text{OEt}_2$. 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 dipyrinato unit. The HBr addition product **5** essentially masks the triple bond, yet can be readily converted to the alkyne **4** upon treatment with base.

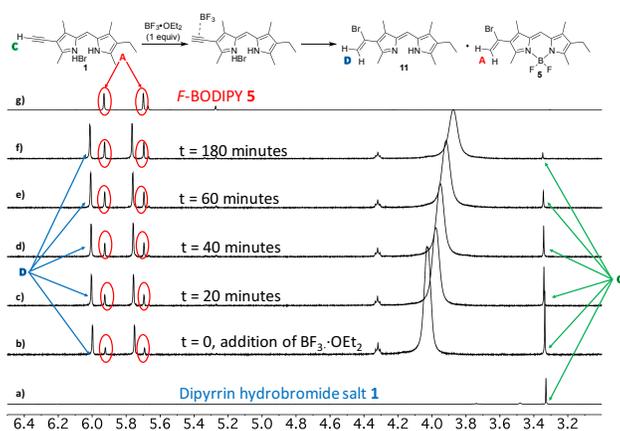
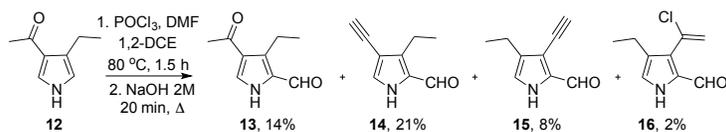


Figure 4. Treatment of a solution of dipyrin **1** in CDCl_3 (0.1 M) with 1 equiv. $\text{BF}_3 \cdot \text{OEt}_2$.

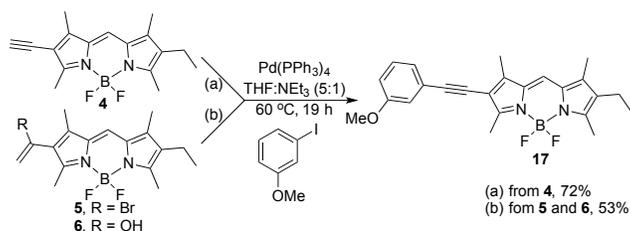
The susceptibility of a conjugated alkynyl-substituted pyrrole to addition reactions was similarly observed when pyrrole **12**⁶⁵ was subjected to Vilsmeier-Haack reaction conditions. Alongside the desired product **13**, the alkynes **14** and **15** were isolated (note that initial formylation suffers 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 dipyrinato 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 ($\phi_{\text{fluo}} = 0.60$) compared to the simpler analogs (near quantitative, see Supporting Information).

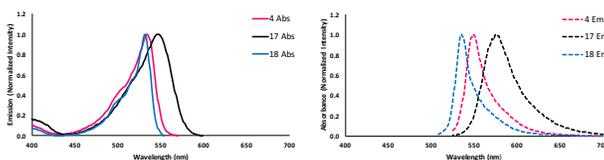


Figure 5. Absorbance and emission of *F*-BODIPYs **4**, **17** and **18**

In conclusion, the synthesis, characterization and reactivity of the asymmetric meso-*H* alkyne-conjugated dipyrin **1** are reported. The reaction of **1** with $\text{BF}_3 \cdot \text{OEt}_2$ and NEt_3 revealed that the conjugated terminal alkynyl unit undergoes electrophilic attack. Future work involving dipyrins 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 $\text{BF}_3 \cdot \text{OEt}_2$ and NEt_3 . ^1H 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 dipyrin, 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 ^1H 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 $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (15% in CDCl_3) whereas for ^{19}F the

reference compound is CCl₃F. 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 CH₂Cl₂.

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 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 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 (Φ_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 ($\times 3$) and 48% aq. HBr (0.18 mL, 0.680 mmol) was added at 0 °C. The reaction mixture was placed under an atmosphere of N₂ and stirred for 1 hour and then poured into Et₂O (30 mL). The resulting precipitate was isolated *via* suction filtration and then washed with Et₂O (10 mL $\times 3$) to afford the title compound as a bright red solid (80%). M.p.: decomposition >170 °C. ¹H NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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-Br]⁺ calcd for C₁₇H₂₁N₂, 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 dipyrin **1** (0.10 g, 0.300 mmol) in CH₂Cl₂ (10 mL) was washed with 2 M NaOH (10 mL $\times 3$). The organic layer was washed with water (10 mL $\times 2$) and brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure to give the title compound as a dark green solid (0.07 g, quant.). M.p.: decomposition >110 °C. ¹H NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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 C₁₇H₂₁N₂, 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)

NEt₃ (2.5 mL, 18.0 mmol) was added to a solution of dipyrin hydrobromide **1** (1.00 g, 3.00 mmol) in anhydrous CH₂Cl₂ (313 mL) at room temperature under a N₂ atmosphere. The reaction mixture was stirred for 15 minutes and BF₃•OEt₂ (3.3 mL, 27.0 mmol) was then added. After 2 hours, NEt₃ (2.5 mL, 18.0 mmol) and BF₃•OEt₂ (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 Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified using column chromatography over either SiO₂ or type III neutral Al₂O₃ (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 Al₂O₃ (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. ¹H NMR (CDCl₃, 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; ¹³C NMR (CDCl₃, 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; ¹¹B {1H} NMR (CDCl₃, 160 MHz) 0.74 (t, *J* = 31 Hz) ppm; ¹⁹F NMR (CDCl₃, 470 MHz) -146.5 (q, *J* = 31 Hz); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₁₉BF₂N₂Na, 323.1502; found, 323.1492; UV/vis(CH₂Cl₂): 534 nm (ε = 100280 L mol⁻¹ cm⁻¹); Data for the mixture of **5** and **6**, present in a 4:1 ratio: ¹H NMR (CDCl₃, 500 MHz) 1.08 (t, *J* = 7.6 Hz, (0.8 × 3H) + (0.2 × 3H), CH₃CH₂ of **5** and **6**), 2.19 (s, (0.8 × 3H) + (0.2 × 3H), CH₃ of **5** and **6**), 2.25 (s, 0.8 × 3H, CH₃ of **5**), 2.27 (s, 0.8 × 3H, CH₃ of **6**), 2.40 (q, *J* = 7.6 Hz, (0.8 × 2H) + (0.2 × 2H), CH₃CH₂ of **5** and **6**), 2.53 (s, (0.8 × 3H) + (0.2 × 3H), CH₃ of **5** and **6**), 2.55 (s, 0.8 × 3H, CH₃ of **5**), 2.56 (s, 0.2 × 3H, CH₃ of **6**) 5.27 (s, 0.2 × 1H, CH₂COH of **6**), 5.67 (s, 0.2 × 1H, CH₂COH of **6**), 5.70 (s, 0.8 × 1H, CH₂CBr of **5**), 5.93 (s, 0.8 × 1H, CH₂CBr of **5**), 7.02 (s,

0.8 × 1H, meso-*H* of **5**), 7.03 (s, 0.2 × 1H, meso-*H* of **6**) ppm; ¹³C NMR (CDCl₃, 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; ¹¹B {1H} NMR (CDCl₃, 160 MHz) 0.83 (t, *J* = 31 Hz) ppm; ¹⁹F NMR (CDCl₃, 470 MHz) -146.1 (two overlapping q, *J* = 33 Hz); HRMS-APCI (*m/z*): **5** [M]⁺ calcd for C₁₇H₂₁BBrF₂N₂, 381.0944; found, 381.0948) and **6** [M+H]⁺ calcd for C₁₇H₂₂BF₂N₂O, 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 N₂ and stirred for 1.5 hours and then poured into Et₂O (50 mL). The resulting precipitate was isolated *via* suction filtration and then washed with Et₂O (× 3) to afford compound **13** as an orange solid (81%). M.p.: decomposition >220 °C. ¹H NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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 C₂₀H₂₉N₂Si, 325.2095; found, 325.2096.

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

POCl₃ (2.04 mL, 21.9 mmol) was added dropwise to DMF (16 mL) at 0 °C and under a N₂ 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 °C

under inert atmosphere. The resulting mixture was heated to 80 °C 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, H₂O (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 Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified using column chromatography on SiO₂ (hexanes:EtOAc 80:20, 70:30) to afford the title compound as a brown solid (0.33 g, 14%), along with 2-formyl 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 °C; ¹H NMR (500 MHz; CDCl₃) 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; ¹³C NMR (125 MHz; CDCl₃) 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 C₉H₁₁NNaO₂, 188.0682; found, 188.0680. **3-Ethyl-4-ethynyl-1H-pyrrole-2-carbaldehyde (14)**: M.p.: decomposition > 80 °C, followed by melting at 119-120 °C. ¹H NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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 C₉H₉NNaO₁, 170.0576; found, 170.0575. **4-Ethyl-3-ethynyl-1H-pyrrole-2-carbaldehyde (15)**: M.p.: decomposition > 95 °C, followed by melting at 104-105 °C. ¹H NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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 C₉H₉NNaO₁, 170.0576; found, 170.0578. **3-(1-Chlorovinyl)-4-ethyl-1H-pyrrole-2-carbaldehyde (16)**: M.p.: 65-66°C. ¹H

NMR (CDCl₃, 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. ¹³C NMR (CDCl₃, 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 C₉H₁₀CINNaO, 206.0343; found, 206.0341.

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

A solution of **4** (56 mg, 0.187 mmol), 3-iodoanisole (27 μ L, 0.224 mmol) and CuI (7.0 mg, 0.037 mmol) in THF:NEt₃ (5:1, 3.4 mL) was degassed ($\times 3$) and placed under a N₂ atmosphere. Pd(PPh₃)₄ (22 mg, 0.019 mmol) was added to the solution and the resulting reaction mixture degassed ($\times 2$), placed under a positive pressure of N₂ 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 $\times 3$) and brine (10 mL), dried over Na₂SO₄, concentrated under reduced pressure and purified using column chromatography (SiO₂, 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 (CDCl₃, 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. ¹³C NMR (CDCl₃, 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. ¹¹B {1H} NMR (CDCl₃, 160 MHz) 0.76 (t, $J = 31$ Hz) ppm. ¹⁹F NMR (CDCl₃, 470 MHz) -146.5 (q, $J = 31$ Hz). HRMS-ESI (m/z): [M+Na]⁺ calcd for C₂₄H₂₅BF₂N₂NaO, 429.1920; found, 429.1918. UV/vis(CH₂Cl₂): 547 nm ($\epsilon = 141000$ 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.

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Notes

The authors declare no competing financial interest.

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