JOC The Journal of Organic Chemistry

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Asymmetric Dipyrrin and *F*-BODIPYs Conjugated to Terminal Alkynes and Alkenes

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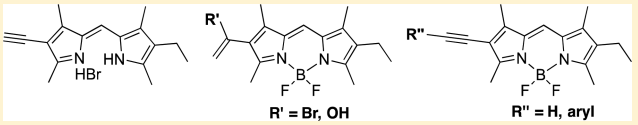
Supporting Information

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 was extended using Sonogashira cross-coupling. Treatment of the alkyne-substituted dipyrrin with $BF_3{\cdot}OEt_2$ and NEt_3 revealed the reactivity of the conjugated terminal alkyne toward Lewis-activated electrophilic substitution and led to the isolation of *F*-BODIPYs bearing terminal bromovinyl and enol substituents.



The 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] electroluminescent 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 autofluorescence 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]

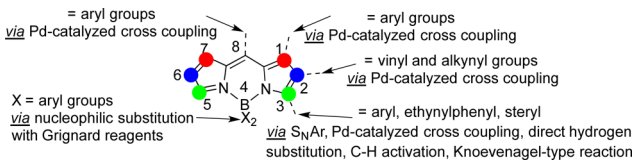
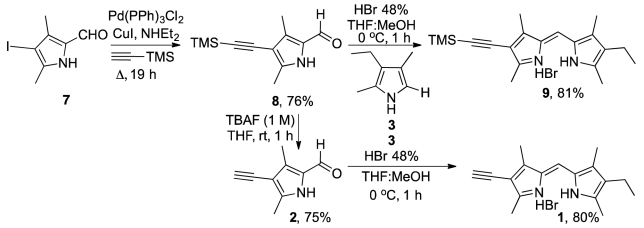


Figure 1. BODIPYs exhibiting a bathochromic shift through extension of the π-conjugation.

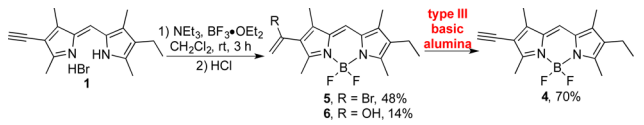
All eight positions of the dipyrrinato core can be substituted with groups such as aryl, ethynylphenyl, steryl, and vinyl, as can the fluoro substituents at boron[21−28] (Figure 1). Particularly appealing is the incorporation of an acetelyne substituent on the β-positions of the dipyrrinato ligand with 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]

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 it 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 prefunctionalization 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

Scheme 1. Synthesis of Dipyrrins Bearing Alkynyl Groups



Scheme 2. Reaction of Dipyrrin Hydrobromide 1 with $BF_3{\cdot}OEt_2$ and NEt_3



Received: May 11, 2017
Published: June 24, 2017

DOI: 10.1021/acs.joc.7b01129
J. Org. Chem. 2017, 82, 7059−7064

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 preligand 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 $BF_3{\cdot}OEt_2$, 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 toward Lewis acid activation.

Fortunately, TMS deprotection could be achieved earlier in the sequence using pyrrole **8**, followed by condensation of the resulting 2-formyl-4-alkynyl 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 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 dipyrrin

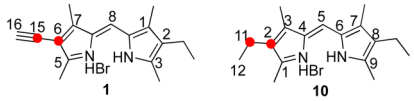


Figure 2. Comparison of bond length between dipyrrin hydrobromides **1** and **10**.

hydrobromide salt **10** (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 toward electrophilic attack.

Treatment of dipyrrin hydrobromide salt **1** with NEt_3 and $BF_3{\cdot}OEt_2$ did not initially afford the expected *F*-BODIPY **4** (Scheme 2). Instead, two new stable compounds, which were inseparable via chromatography over silica, were isolated. The ^{1}H NMR spectrum (Figure S3a) of the mixture contained two sets (4:1 ratio) of vinylic protons between 5.20 and 6.00 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.

Alongside two-dimensional NMR analysis, mass spectrometric analysis of the mixture enabled the identification of these

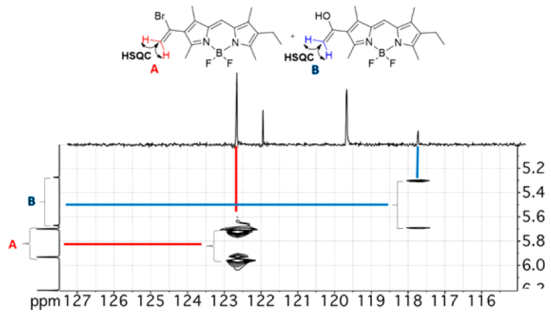


Figure 3. ^{1}H−^{13}C HSQC NMR spectra of the mixture of *F*-BODIPYs **5** and **6**.

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** forming as a result of exposure to water in the workup. To determine whether **5** was formed as the direct product of the reaction of **4** with NEt_3 and $BF_3{\cdot}OEt_2$, or during workup, the reaction was monitored through ^{1}H NMR spectroscopic analysis (Figures S3b and c). Analysis of the vinylic region revealed that bromovinyl analogue **5** dominates throughout the reaction with signals due to **6** becoming more prominent upon addition of aqueous acid in the workup. 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 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.

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 (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 $BF_3{\cdot}NEt_3$ Lewis pair,[45,57] which was reported unreactive toward the 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 $BF_3{\cdot}OEt_2$, 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 $BF_3{\cdot}OEt_2$ (1 equiv) under anhydrous conditions, and the mixture was 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

DOI: 10.1021/acs.joc.7b01129
J. Org. Chem. 2017, 82, 7059−7064

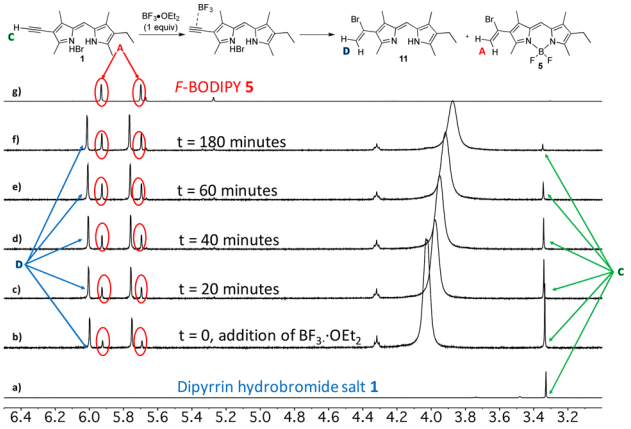
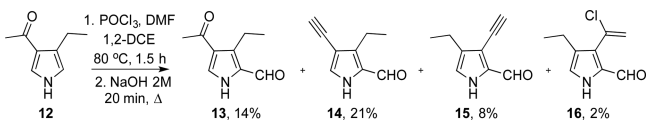


Figure 4. Treatment of a solution of dipyrrin **1** in $CDCl_3$ (0.1 M) with 1 equiv of $BF_3{\cdot}OEt_2$.

corresponded to our previous characterization of **5** (Figure 4, spectrum g). The other set of vinylic peaks was assigned to free-base **11**. The broad peak in the range of 4.20 and 3.90 ppm corresponds to the ethyl groups originating from $BF_3{\cdot}OEt_2$. 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 dipyrrin **1** clearly enables addition of HBr (from the original dipyrrin hydrobromide salt) across the exocyclic 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 $CDCl_3$ (Figure S5), but ^1H NMR spectroscopy revealed no reaction over 3 h, thus confirming the surprising sensitivity of the terminal alkyne of dipyrrin hydrobromide **1**. Treatment of the free-base of **1**, prepared by washing the hydrobromide salt with 2 M NaOH, with 1 equiv of $BF_3{\cdot}OEt_2$ resulted in the dark green solution producing a dark purple color and then a black polymerized precipitate. Attempts to solubilize the precipitate in organic solvents, including DMSO-d_6, were unsuccessful. Similar polymerization occurred when *F*-BODIPY **4** was treated with stoichiometric $BF_3{\cdot}OEt_2$. It is curious that the alkynyl functionality of 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 readily converted to alkyne **4** upon treatment with base.

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 desired product **13**, alkynes **14** and **15** were isolated (note that initial formylation suffers from poor regioselectivity). Furthermore, chlorovinyl-pyrrole **16** was also isolated, presumably as a consequence of HCl addition to alkyne **14** under the reaction conditions (Scheme 3). The contribution of the pyrrolic nitrogen lone pair to the reactivity of substituents has

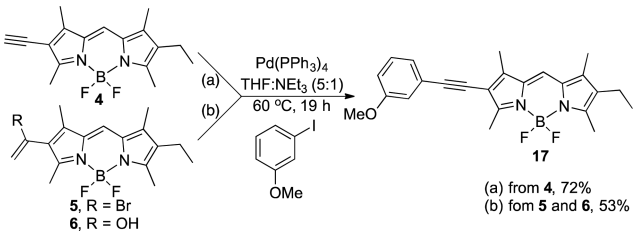
Scheme 3. Formylation of Pyrrole 12 using Vilsmeier–Haack Reaction Conditions



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.

With the goal of extending the π-conjugation, the chemical reactivities of *F*-BODIPYs **4**–**6** were investigated. First, alkyne-containing *F*-BODIPY **4** was reacted with 3-iodoanisole under Sonogashira cross-coupling conditions (a, Scheme 4).[55] The

Scheme 4. Sonogashira Cross-Coupling Reaction between *F*-BODIPYs 4–6 and 3-Iodoanisole



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). Enol **6** again remained unreacted and was isolated in a mixture alongside the excess 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

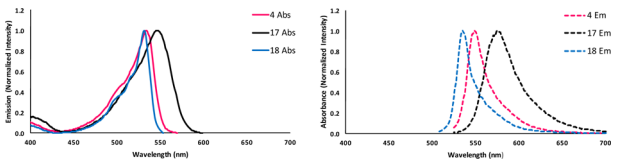


Figure 5. Absorbance and emission of *F*-BODIPYs **4**, **17**, and **18**.

wavelengths are significantly red-shifted courtesy of an increased Stoke's shift for both **4** (14 nm) and **17** (29 nm) compared to just 4 nm for per-alkyl analogue **18**. However, the *F*-BODIPY **17** exhibits a slightly lower quantum yield (ϕ_{fluo} = 0.60) compared to those of the simpler analogues (near quantitative, see Supporting Information).

In conclusion, the synthesis, characterization, and reactivity of asymmetric meso-*H* alkyne-conjugated dipyrrin **1** are reported. The reaction of **1** with $BF_3{\cdot}OEt_2$ 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 $BF_3{\cdot}OEt_2$ 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 new dye **17**. The

DOI: 10.1021/acs.joc.7b01129
J. Org. Chem. 2017, 82, 7059–7064

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 ultrapure 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 are 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 a 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$^{\pm}$ 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 (ϕ = 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 reference compound **18** and compared to rhodamine 6G excited at 500 nm. Relative quantum yields were determined using eq 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.

$$\Phi_X = \Phi_{st}\left(\frac{I_X}{I_{st}}\right)\left(\frac{A_{st}}{A_X}\right)\left(\frac{\eta_X^2}{\eta_{st}^2}\right) \quad (1)$$

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, stirred for 1 h, 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%). Mp: 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). ^{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. HRMS-ESI (m/z): $[M - Br]^+$ 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.). Mp: 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). ^{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. 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 min, and $BF_3{\cdot}OEt_2$ (3.3 mL, 27.0 mmol) was then added. After 2 h, NEt_3 (2.5 mL, 18.0 mmol) and $BF_3{\cdot}OEt_2$ (3.3 mL, 27.0 mmol) were added, and the reaction mixture was stirred for an additional 2 h. HCl (5 M, 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**: mp 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); ^{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; ^{11}B {1H} NMR ($CDCl_3$, 160 MHz) 0.74 (t, J = 31 Hz); ^{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), CH_3CH_2 of **5** and **6**), 2.19 (s, (0.8 × 3H) + (0.2 × 3H), CH_3 of **5** and **6**), 2.25 (s, 0.8 × 3H, CH_3 of **5**), 2.27 (s, 0.8 × 3H, CH_3 of **6**), 2.40 (q, J = 7.6 Hz, (0.8 × 2H) + (0.2 × 2H), CH_3CH_2 of **5** and **6**), 2.53 (s, (0.8 × 3H) + (0.2 × 3H), CH_3 of **5** and **6**), 2.55 (s, 0.8 × 3H, CH_3 of **5**), 2.56 (s, 0.2 × 3H, CH_3 of **6**) 5.27 (s, 0.2 × 1H, CH_2COH of **6**), 5.67 (s, 0.2 × 1H, CH_2COH of **6**), 5.70 (s, 0.8 × 1H, CH_2CBr of **5**), 5.93 (s, 0.8 × 1H, CH_2CBr of **5**), 7.02 (s, 0.8 × 1H, meso-*H* of **5**), 7.03 (s, 0.2 × 1H, meso-*H* of **6**); ^{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; ^{11}B {1H} NMR ($CDCl_3$, 160 MHz) 0.83 (t, J = 31 Hz); ^{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 h 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 **9** as an orange solid (81%). Mp: 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). ^{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. 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 °C and under a N_2 atmosphere. The mixture was allowed to warm to room temperature and then stirred for 15 min. A solution of pyrrole **12**[65] (2.00 g, 14.6 mmol) in 1,2-DCE (49 mL) was added at 0 °C

DOI: 10.1021/acs.joc.7b01129
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under inert atmosphere. The resulting mixture was heated to 80 °C and stirred for an additional 80 min. 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 min. 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-formyl pyrroles **14** (0.44, 21%), **15** (0.22 g, 8%), and **16** (0.05 g, 2%). The position of the formyl group was determined using 2D NMR (HSQC and HMBC). Data for **13**: mp 119−123 °C; ^{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); ^{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; 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**): mp decomposition >80 °C followed by melting at 119−120 °C; ^{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); ^{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; 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**): mp decomposition >95 °C followed by melting at 104−105 °C; ^{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); ^{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; 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**): mp 65−66 °C; ^{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); ^{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; 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 was degassed (× 2), placed under a positive pressure of N_2, and stirred at 60 °C in a sealed system for 19 h. 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). Mp: 192−193 °C. ^{1}H 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). ^{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. ^{11}B {1H} NMR ($CDCl_3$, 160 MHz) 0.76 (t, J = 31 Hz). ^{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: 10.1021/acs.joc.7b01129.

Crystallographic data for compound **1** (CIF)

X-ray structure and data for **1** and **10**, NMR spectroscopic analysis of reactions, absorption and emission data for **4**, **17**, and **18**, and NMR spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC). A.T. is a Faculty of Science Killam Professor at Dalhousie University.

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DOI: 10.1021/acs.joc.7b01129
J. Org. Chem. 2017, 82, 7059−7064