Synthesis and Characterisation of the Unsubstituted Dipyrrin and 4,4-Dichloro-4-bora-3a,4a-diaza-*s*-indacene: Improved Synthesis and Functionalization of the Simplest BODIPY Framework

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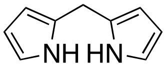
1.1 General Information

^{1}H NMR, ^{13}C NMR and ^{11}B NMR spectra were recorded using either 500 or 300 MHz spectrometers. Chemical shifts are expressed in parts per million (ppm) using the solvent signal [$CDCl_3$ (^{1}H 7.26 ppm; ^{13}C 77.16 ppm); MeOD-*d4* (^{1}H 3.31 ppm, ^{13}C 49.00 ppm)] as an internal reference for ^{1}H and ^{13}C, and $BF_3{\bullet}OEt_2$ as an external reference for ^{11}B at 0 ppm. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. All coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were obtained using ion trap (ESI) instruments operating in positive mode. Column chromatography was performed using 230-400 mesh ultra pure silica or Brockman (III) basic alumina, as indicated. Reagents and anhydrous solvents were purchased from Sigma-Aldrich and used as received, with the exception of starting material di(1H-pyrrol-2-yl)methane, which was purchased from Frontier Scientific (Logan, Utah, USA). Anhydrous dichloromethane for use in the formation of **2** was further dried with the use of molecular sieves. Di(1H-pyrrol-2-yl)methane,[1] **1**[2-4] and **3** have been previously reported in the literature.

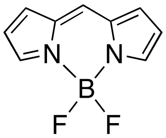
1.2 Experimental Procedures and Characterization Data

Di(1H-pyrrol-2-yl)methane



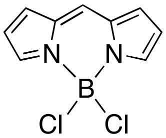
Di(1H-pyrrol-2-yl)methane was obtained either using Wang's method[5] as a crystalline, colourless solid, or as purchased from Frontier Scientific (the purchased sample contained grease impurities). δ_H (500 MHz, $CDCl_3$): 3.95 (s, 2H), 6.05 (s, 2H), 6.17 (q, *J* = 2.9 Hz, 2H), 6.63 (q, *J* = 2.1 Hz, 2H), 7.74 (bs, 2H); δ_C (125 MHz, $CDCl_3$): 26.4, 106.6, 108.4, 117.5, 129.2. HR-MS (ESI^{+}): [M+Na]$^{+}$ calcd. for: $C_9H_{10}N_2Na$: 169.0742; found: 169.0736. These data correspond with literature values.[5]

4,4-Difluoro-4-borato-3a-azonia-4a-aza-*s*-indacene (1)



To a slurry of *p*-chloranil (925 mg, 3.7 mmol) in CH_2Cl_2 (70 mL) at -40 °C under nitrogen, a solution of a di(1H-pyrrol-2-yl)methane (500 mg, 3.4 mmol) in CH_2Cl_2 (100 mL) under N_2 was added drop-wise over several minutes. The reaction was stirred for 3 hours, during which the colour of the mixture turned from brown to bright yellow. After DIPEA (3.5 mL, 20.5 mmol) were added, the solution was stirred for 30 minutes. $BF_3{\bullet}OEt_2$ (3.4 mL, 30.6 mmol) was then added slowly over several minutes, and the mixture was stirred for 18 hours, during which time the temperature was allowed to rise to 22 °C. The fluorescent solution was sonicated for 30 minutes and then filtered through Celite to remove insoluble oxidation products: it was then washed with sat aq. $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed *in vacuo*. Purification using basic Brockman III alumina (ethyl acetate/hexanes, 1:9 V/V) gave the title compound as a dark red solid (468 mg, 72 %). δ_H (500 MHz, $CDCl_3$): 6.55 (d, J = 4.0 Hz, 2H), 7.15 (d, J = 4.0 Hz, 2H), 7.42 (s, 1H), 7.90 (s, 2H); δ_C (125 MHz, $CDCl_3$): 118.9, 131.4, 131.5, 135.3, 145.2; δ_B [^1H] (160 MHz, $CDCl_3$): -75.6 (t, $J_{B\text{-}F}$ = 29 Hz). HR-MS (ESI$^+$): $[M+H]^+$ calcd. for: $C_9H_7BF_2N_2Na$: 215.0586; found: 215.0563. These data correspond with literature values.[4]

4,4-Dichloro-4-borato-3a-azonia-4a-aza-*s*-indacene (2)

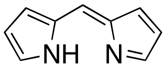


To a solution of **1** (200 mg, 1.02 mmol) in CH_2Cl_2 (20 mL) under a nitrogen environment, a 1 M solution of BCl_3 (1.14 mL, 1.14 mmol) in $CH_2Cl_2$was added drop-wise. The mixture was stirred for 30 minutes, during which time the dark red colour lightened significantly. The solution was filtered through Celite, and the solvent removed *in vacuo* to produce **2** as a pure, brick-red solid

(216 mg, 99%). δ_H (500 MHz, $CDCl_3$): 6.61 (s, 2H), 7.19 (d, *J* = 2.8 Hz, 2H), 7.48 (s, 1H), 8.10 (s, 2H); δ_C (125 MHz, $CDCl_3$): 119.90, 131.41, 132.12, 133.90, 147.39; δ_B (160 MHz, $CDCl_3$): 2.28 (s). Mass spectral analysis was inconclusive, as is typical for 4,4-dichloroBODIPYs.[6]

Alternatively, to a solution of **3** in CH_2Cl_2under a nitrogen environment (**3** generated from **2**, as per the second method of formation for **3**), 5 equivalents of BCl_3 were added, and the mixture stirred for an hour. The solution was filtered through Celite, and the solvent removed *in vacuo*. Analysis via ^{1}H and ^{13}B NMR techniques revealed the presence of the **2**, as well as several unidentifiable impurities.

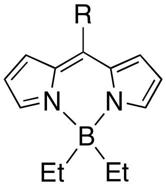
(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-1*H*-pyrrole (3)



To a slurry of *p*-chloranil (184 mg, 0.75 mmol) in CH_2Cl_2 (10 mL) at –40 °C under nitrogen, a solution of di(1H-pyrrol-2-yl)methane (100 mg, 0.68 mmol) in CH_2Cl_2 (10 mL) was added drop-wise over several minutes. The reaction was stirred for 3 hours, during which time the colour of the mixture turned from brown to bright yellow. The solvent was removed *in vacuo*, and the yellow material was characterized as a mixture of reaction products including **3** as its free-base according to ESI$^+$ mass spectral analysis.

Alternatively, to a solution of **2** (25 mg, 0.11 mmol) in CH_2Cl_2 (10 mL) under nitrogen, methanol (22 μL, 0.55 mmol) was added, and the mixture was then stirred for 30 minutes. The solvent was removed *in vacuo*, to give complete conversion to **3•HCl**. δ_H (500 MHz, $CDCl_3$): 6.66 (s, 2H), 7.33 (s, 2H), 7.49 (s, 1H), 8.01 (s, 2H), 14.63 (bs, 1H); δ_C (125 MHz, $CDCl_3$): 117.8, 130.0, 133.2, 137.2, 144.5. HR-MS (ESI$^+$): $[2M+H]^+$ calcd. for: $C_{18}H_{17}N_4$: 289.1448; found: 289.1443.

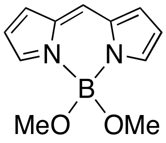
4,4-Diethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (4) and 4,4-diethyl-8-ethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (5)



4, R = H
5, R = Et

To a solution of **1** (50 mg, 0.26 mmol) in diethyl ether (20 mL) under nitrogen, a 3 M solution of ethyl magnesium bromide in diethyl ether (0.43 mL, 1.30 mmol) was added drop-wise and the reaction stirred for 10 minutes. TLC analysis indicated complete consumption of starting material, and the reaction was quenched with water. The product was extracted with CH_2Cl_2, and purified via flash chromatography on SiO_2 (ethyl acetate/hexanes, 2:8 V/V) to produce a brick-red solid. An inseparable mixture of products, **4** (11 mg, 22%) and **5** (7 mg, 10%) was isolated. Decomposition of the material was observed after several hours at room temperature, both in air and nitrogen environments. δ_H of **4** (500 MHz, $CDCl_3$): 0.42 (m, 6H), 0.60 (m, 4H), 6.56 (m, *J* = 4.2 Hz, 2H), 7.07 (dd, *J* = 4.2, 0.9 Hz, 2H), 7.45 (s, 1H), 7.56 (d, *J* = 0.9 Hz, 2H); δ_H of **5** (500 MHz, $CDCl_3$): 0.42 (m, 6H), 0.60 (m, 4H), 1.45 (t, *J* = 7.7 Hz, 3H), 3.01 (q, *J* = 7.7 Hz, 2H), 6.56 (m, 2H), 7.23 (d, *J* = 4.2 Hz, 2H), 7.52 (s, 2H) (note that peaks at 0.42, 0.60 and 6.56 contain signals from both **4** and **5**); δ_C of **4** and **5** (125 MHz, $CDCl_3$): 8.7, 8.8, 18.2, 24.8, 116.7, 117.5, 123.3, 127.0, 131.1, 134.2, 134.6, 141.2, 142.7, 151.4 (note that dipyrrins-type peaks were not resolved; boron-substituted ethyl carbon peaks overlap in spectrum); δ_B (160 MHz, $CDCl_3$) 1.71 (**4**) and 1.04 (**5**).

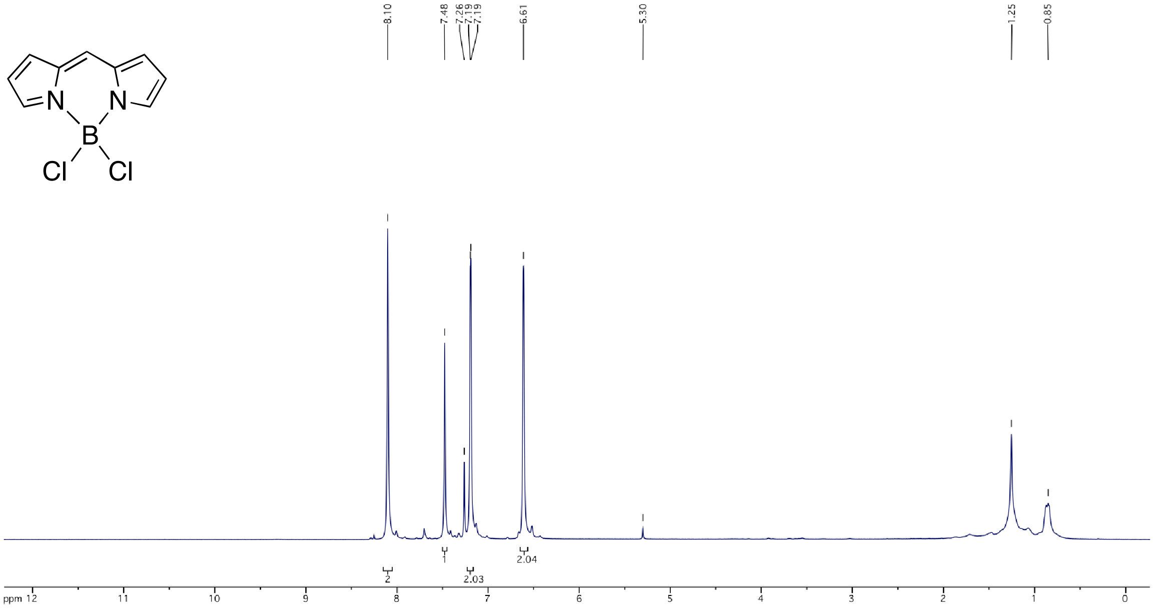
4,4-Dimethoxy-4-borato-3a-azonia-4a-aza-*s*-indacene (6)



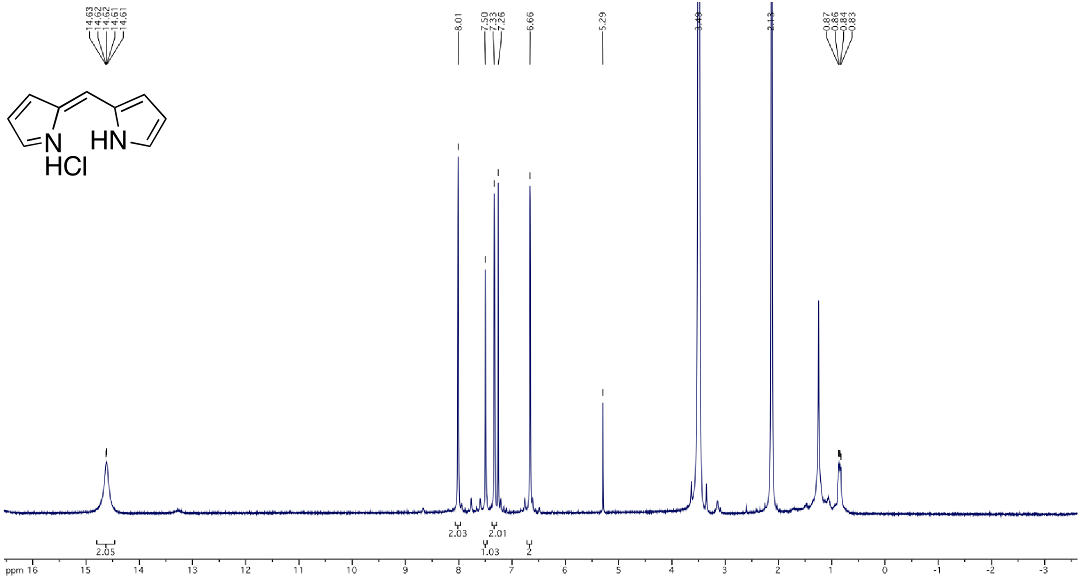
To a solution of **1** (50 mg, 0.26 mmol) in methanol (10 mL) under nitrogen at 65 °C, NaOMe (117mg, 1.56 mmol) was added, and the reaction stirred. After an hour, TLC analysis indicated complete consumption of starting material. The rapidly decomposing mixture was filtered through a plug of alumina, and the solvent removed *in vacuo* to produce a dark, red solid. The 4,4-dimethoxyBODIPY **6** was isolated (10 mg, 6%) with two unidentified side-products. δ_H (500 MHz, $CDCl_3$): 3.01 (s, 6H), 6.54 (m, *J* = 3.9 Hz, 2H), 7.12 (d, *J* = 3.9 Hz, 2H), 7.38 (s, 1H), 7.83 (s, 2H). δ_B (160 MHz, $CDCl_3$) 5.20 (impurity), 2.45 (**6**), 1.29 (impurity). Product instability limited further characterization.

1.4 ^{1}H Spectra

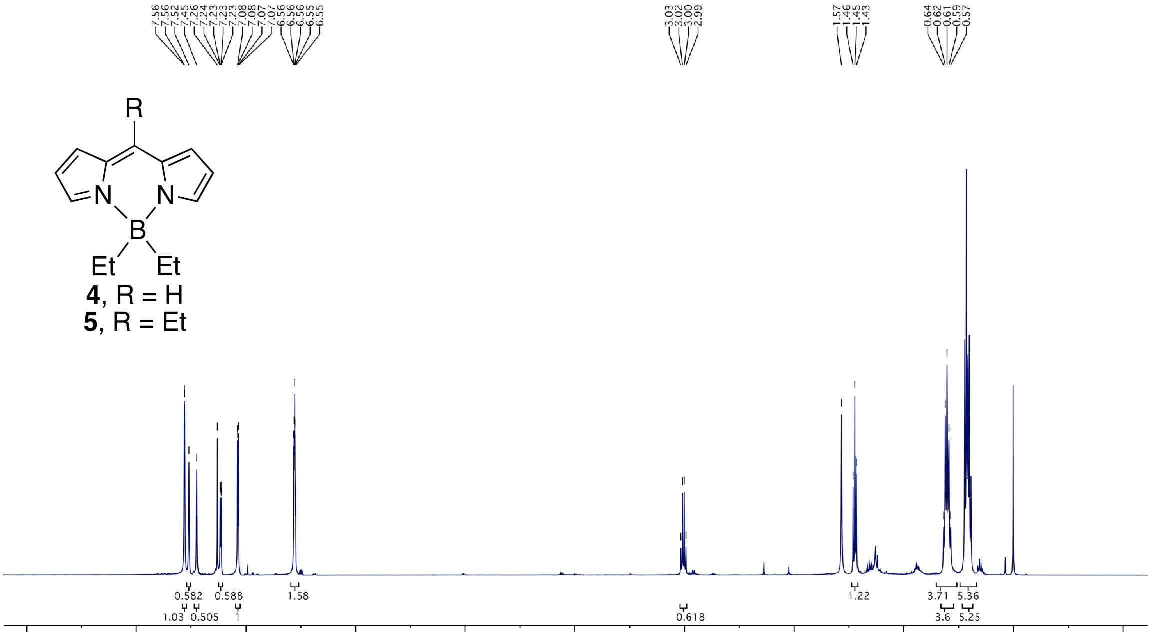
4,4-Dichloro-4-borato-3a-azonia-4a-aza-*s*-indacene (2)



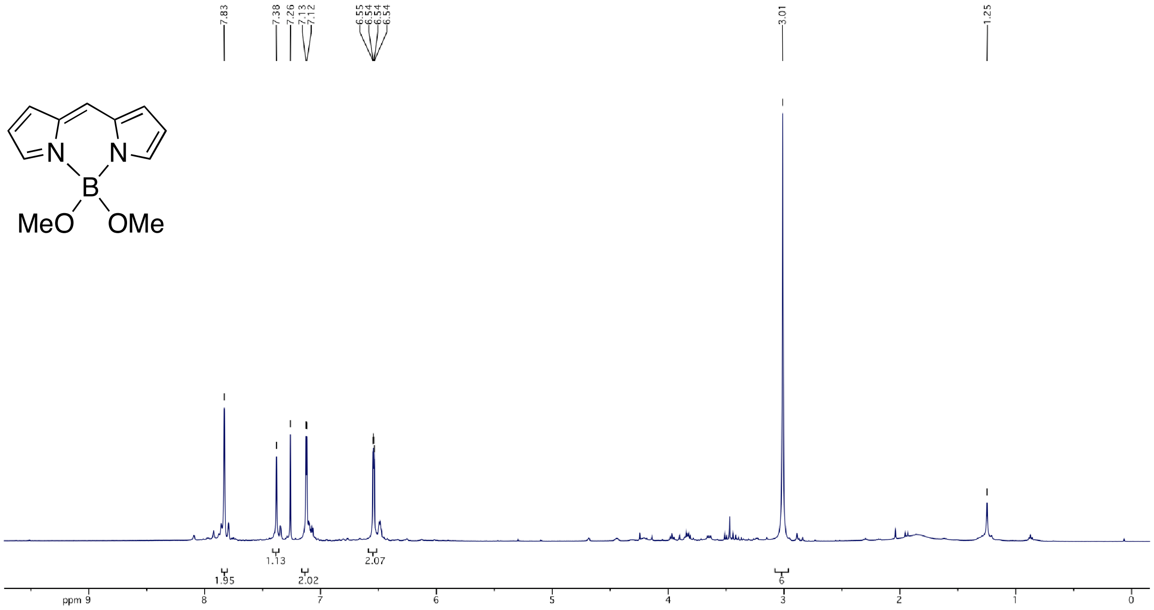
(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-1*H*-pyrrole (3•HCl)



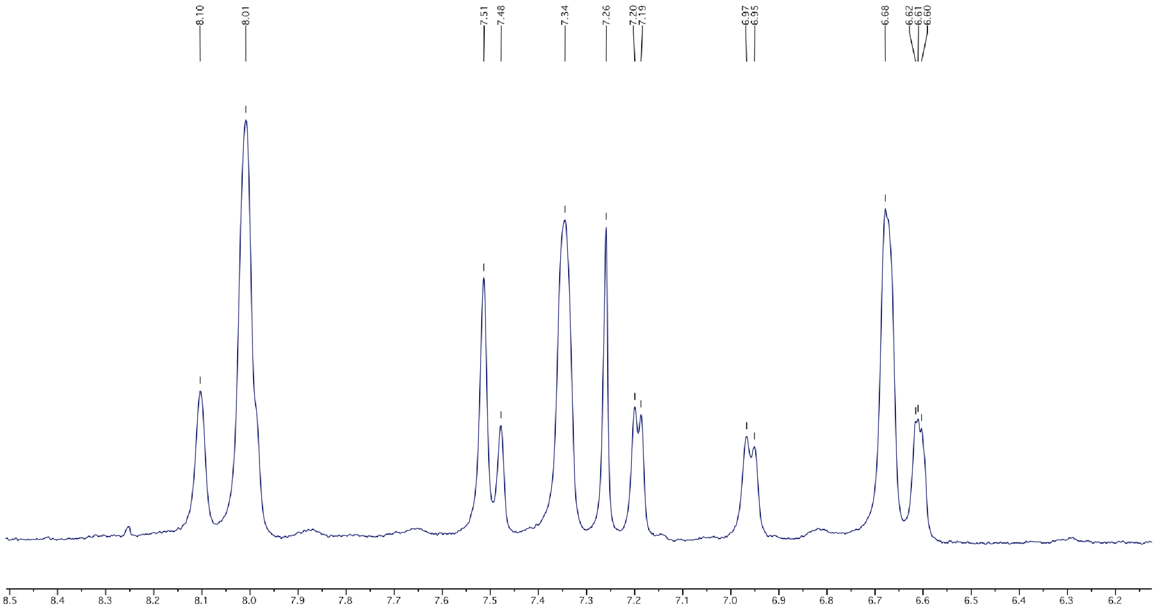
4,4-Diethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (4) and 4,4-diethyl-8-ethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (5)



4,4-Dimethoxy-4-borato-3a-azonia-4a-aza-*s*-indacene (6)



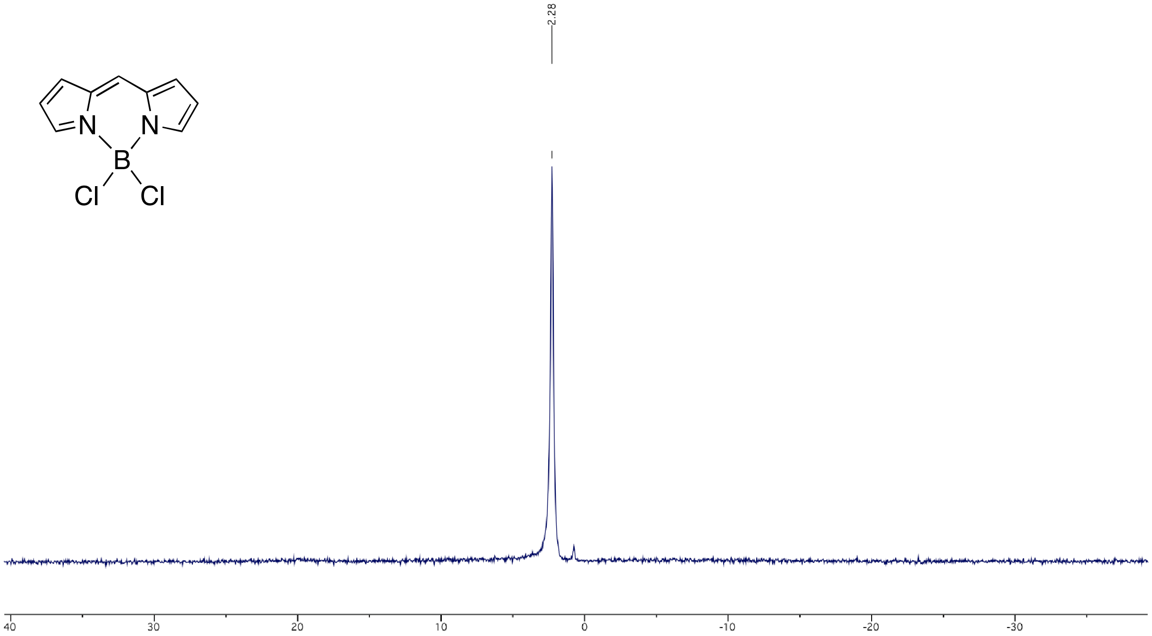
Aryl region corresponding to mixture of 2 and 3



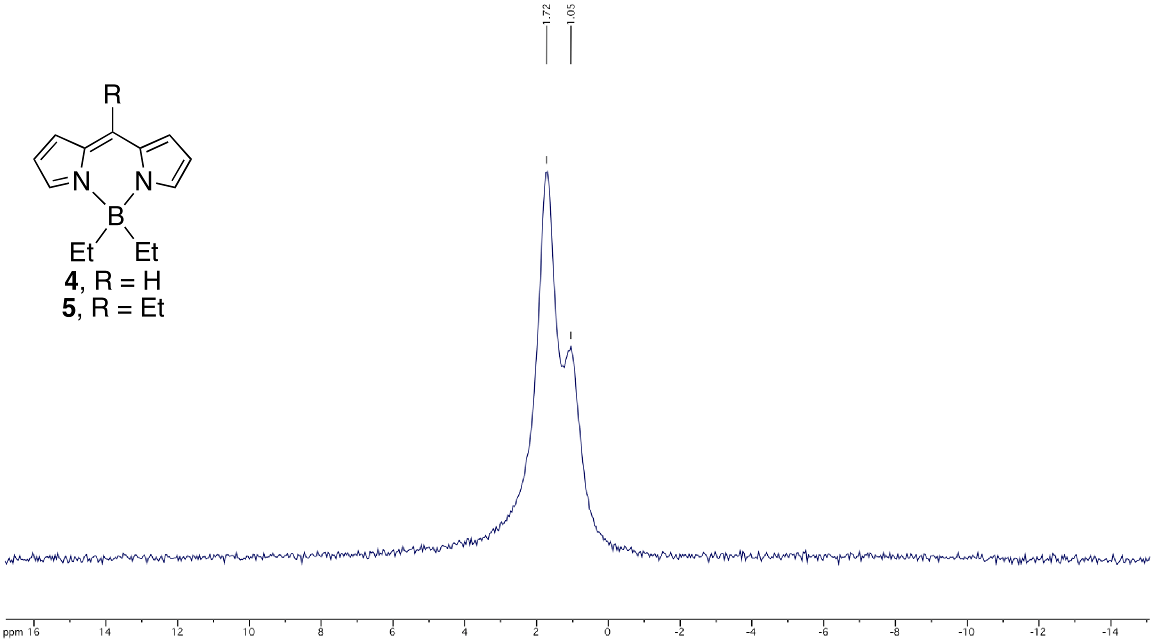
* Mixture synthesized via addition of BCl_3 to **3** (produced via deprotection of **2**)

1.5 ^{11}B Spectra

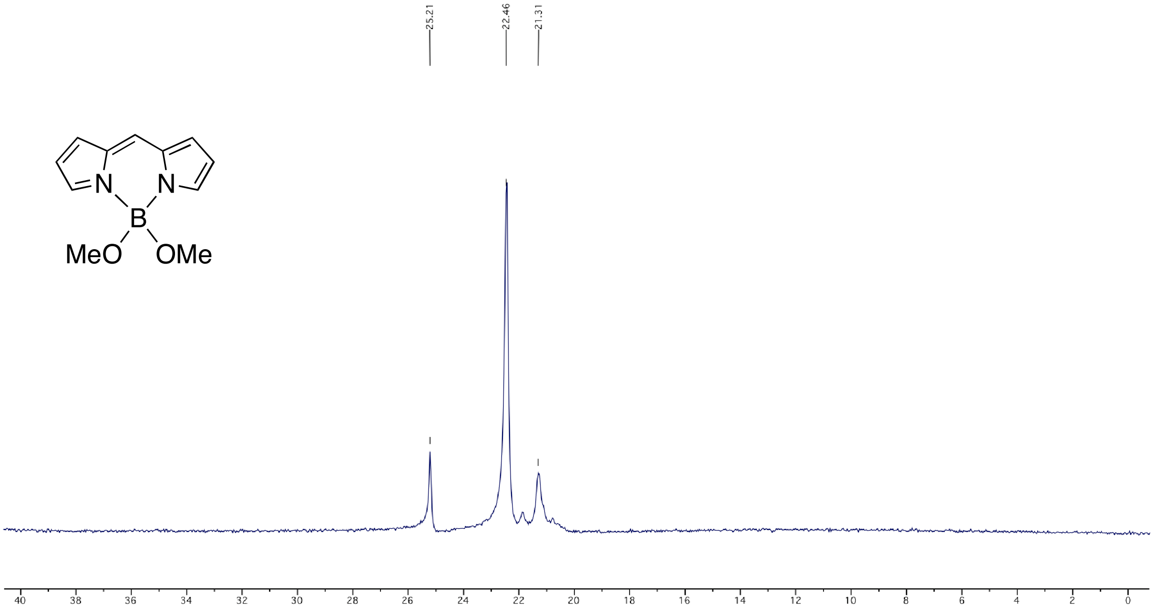
4,4-Dichloro-4-borato-3a-azonia-4a-aza-*s*-indacene (2)



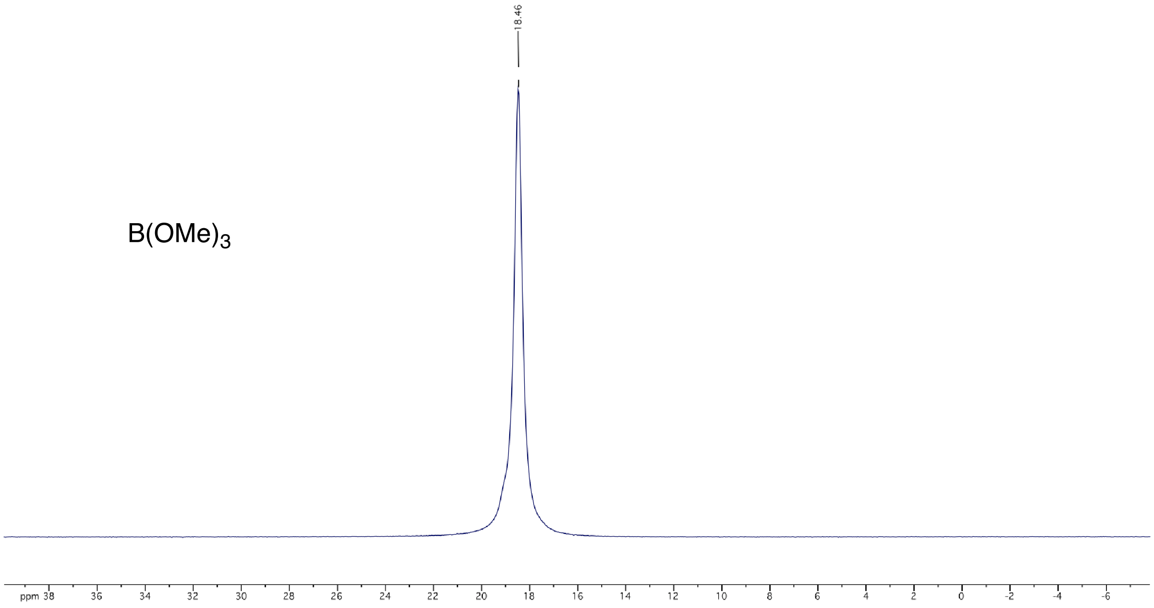
4,4-Diethyl-4-borato-3a-azonia-4a-aza-s-indacene (4) and 4,4-diethyl-8-ethyl-4-borato-3a-azonia-4a-aza-s-indacene (5)



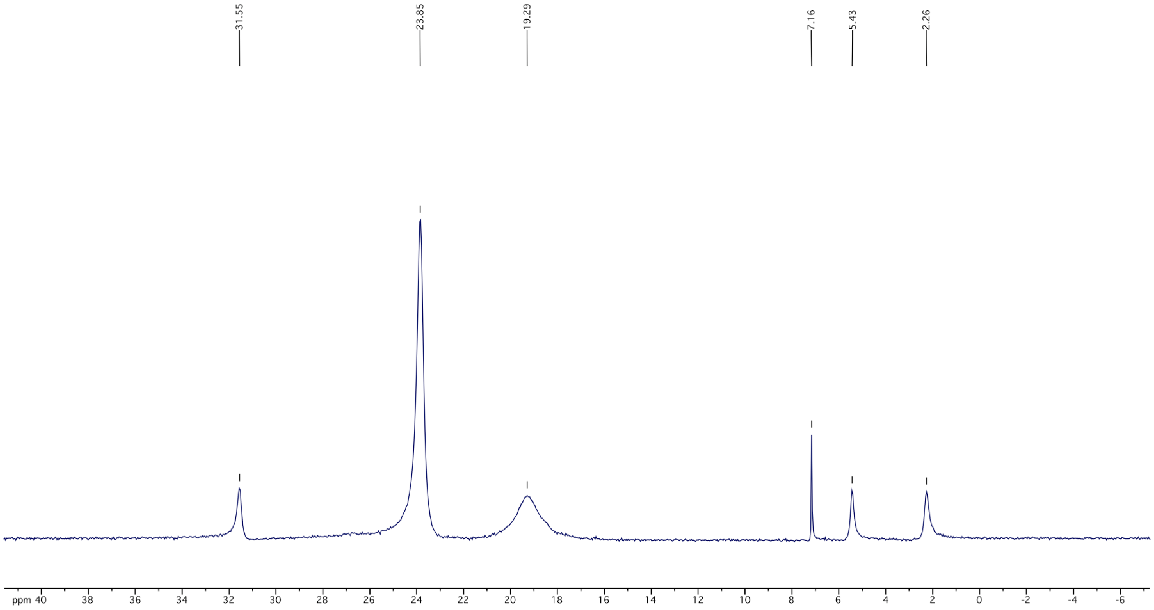
4,4-Dimethoxy-4-borato-3a-azonia-4a-aza-*s*-indacene (6, impure – unstable)



Trimethoxy borate (CDCl$_3$)



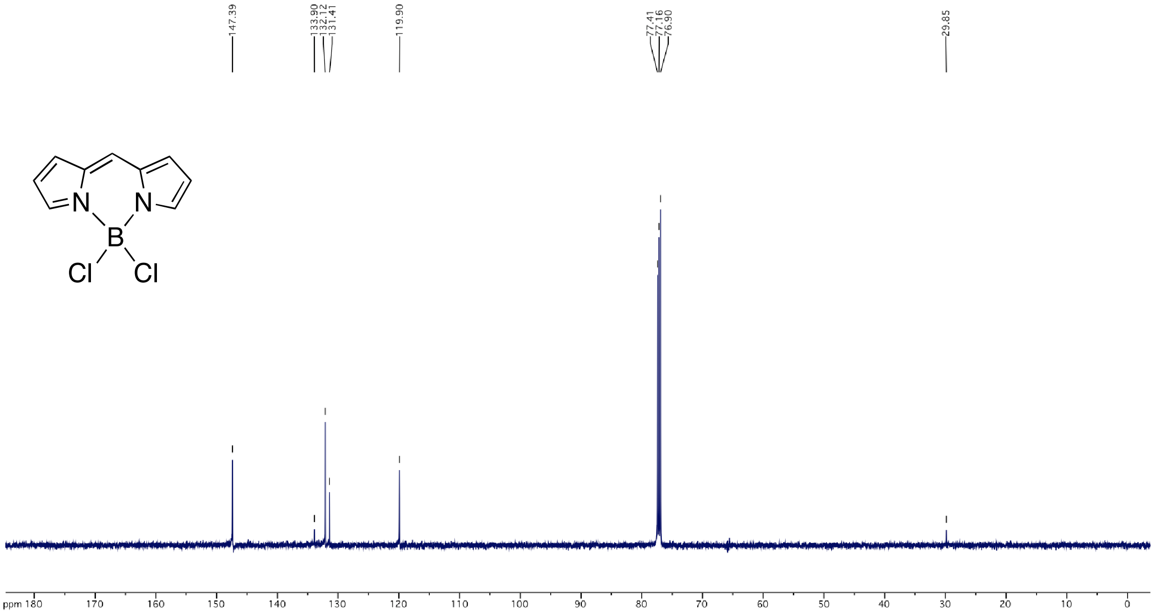
^{11}B Spectra depicting 2 as a reaction product



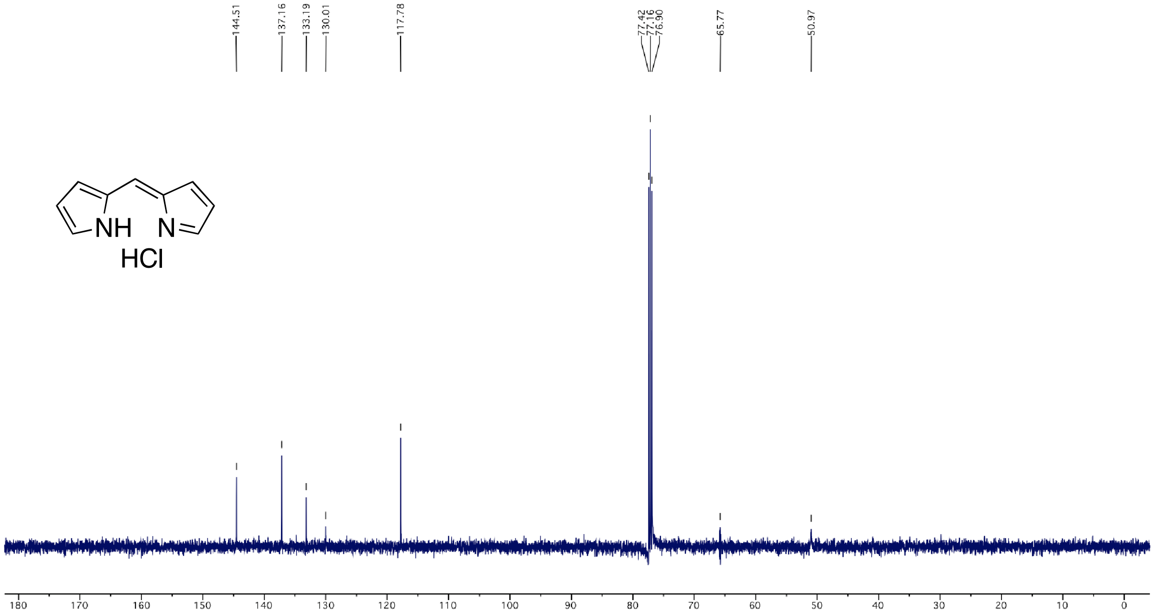
* Mixture synthesized via addition of BCl_3 to **3** (produced via deprotection of **2**)

1.6 ^{13}C Spectra

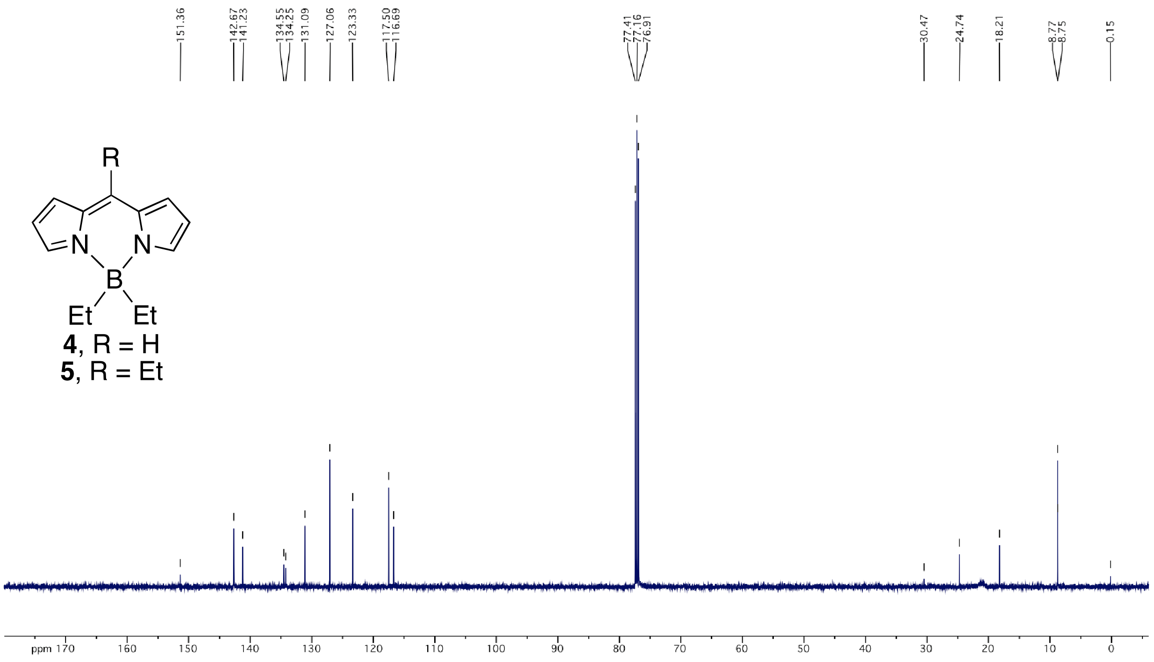
4,4-Dichloro-4-borato-3a-azonia-4a-aza-*s*-indacene (2)



(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-1*H*-pyrrole (3•HCl)



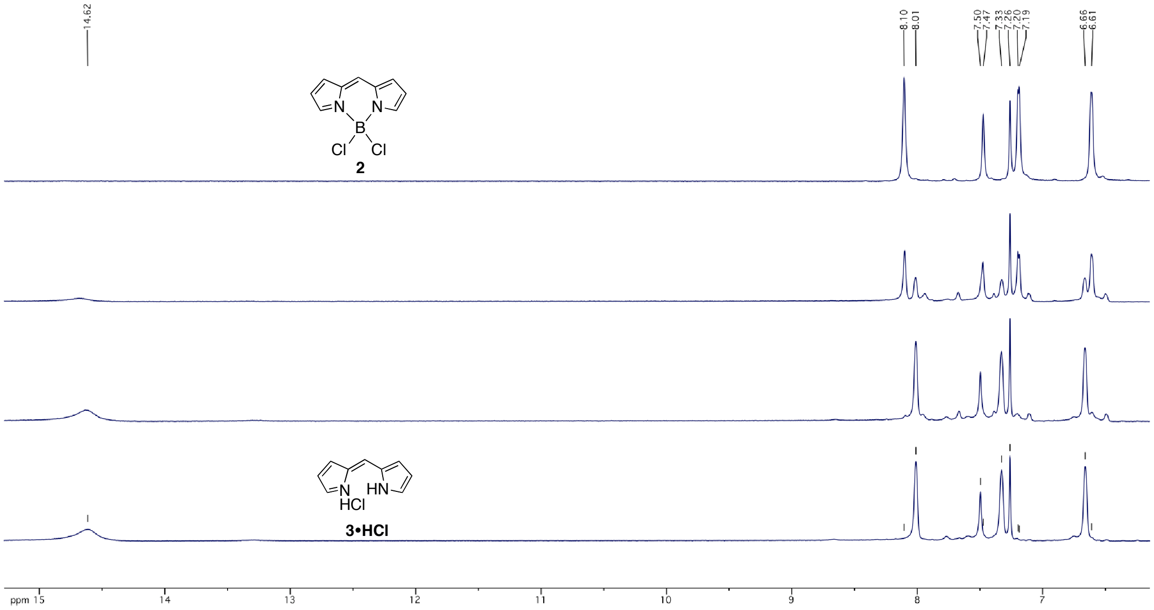
4,4-Diethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (4) and 4,4-diethyl-8-ethyl-4-borato-3a-azonia-4a-aza-*s*-indacene (5)



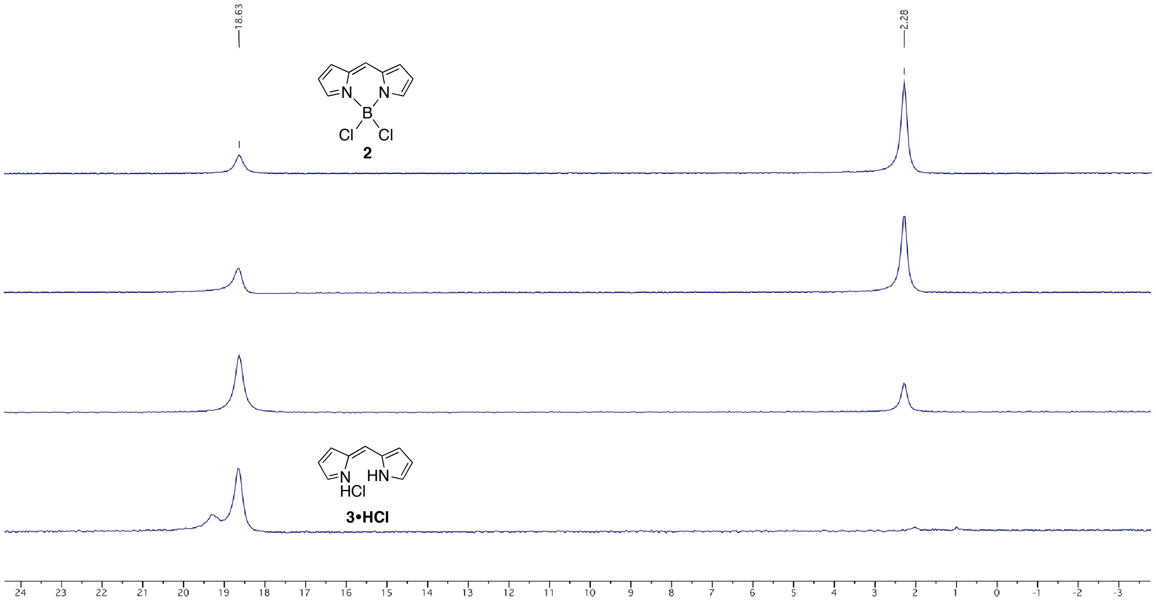
4, R = H
5, R = Et

1.8 NMR Stack Plots

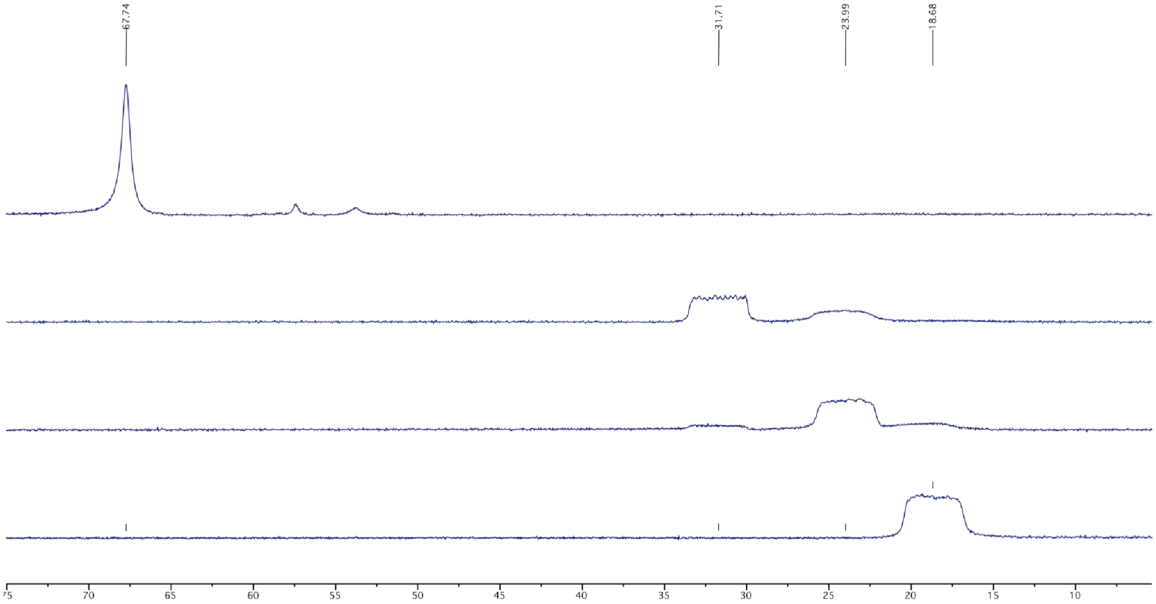
^{1}H NMR spectra depicting formation (top to bottom) of **3**•HCl from **2** via addition of 5 equivalents of methanol (3 times addition of 1.5 μL) over 30 minutes (spectrum obtained every 10 min).



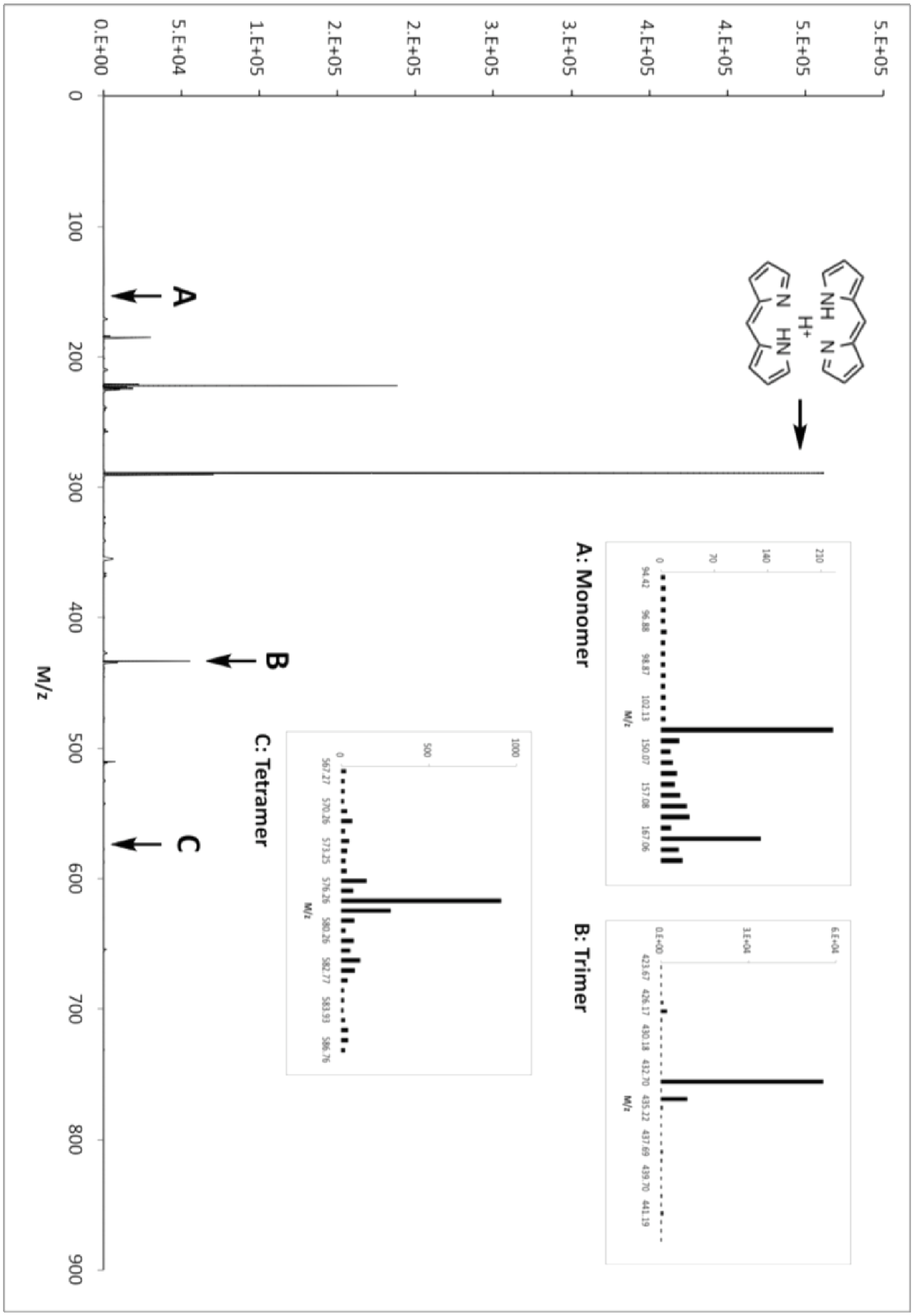
^{11}B NMR spectra depicting formation (top to bottom) of **3**•HCl and B(OMe)$_3$ from **2** via addition of 5 equivalents of methanol (3 times addition of 1.5 μL) over 30 minutes (spectrum obtained every 10 min).



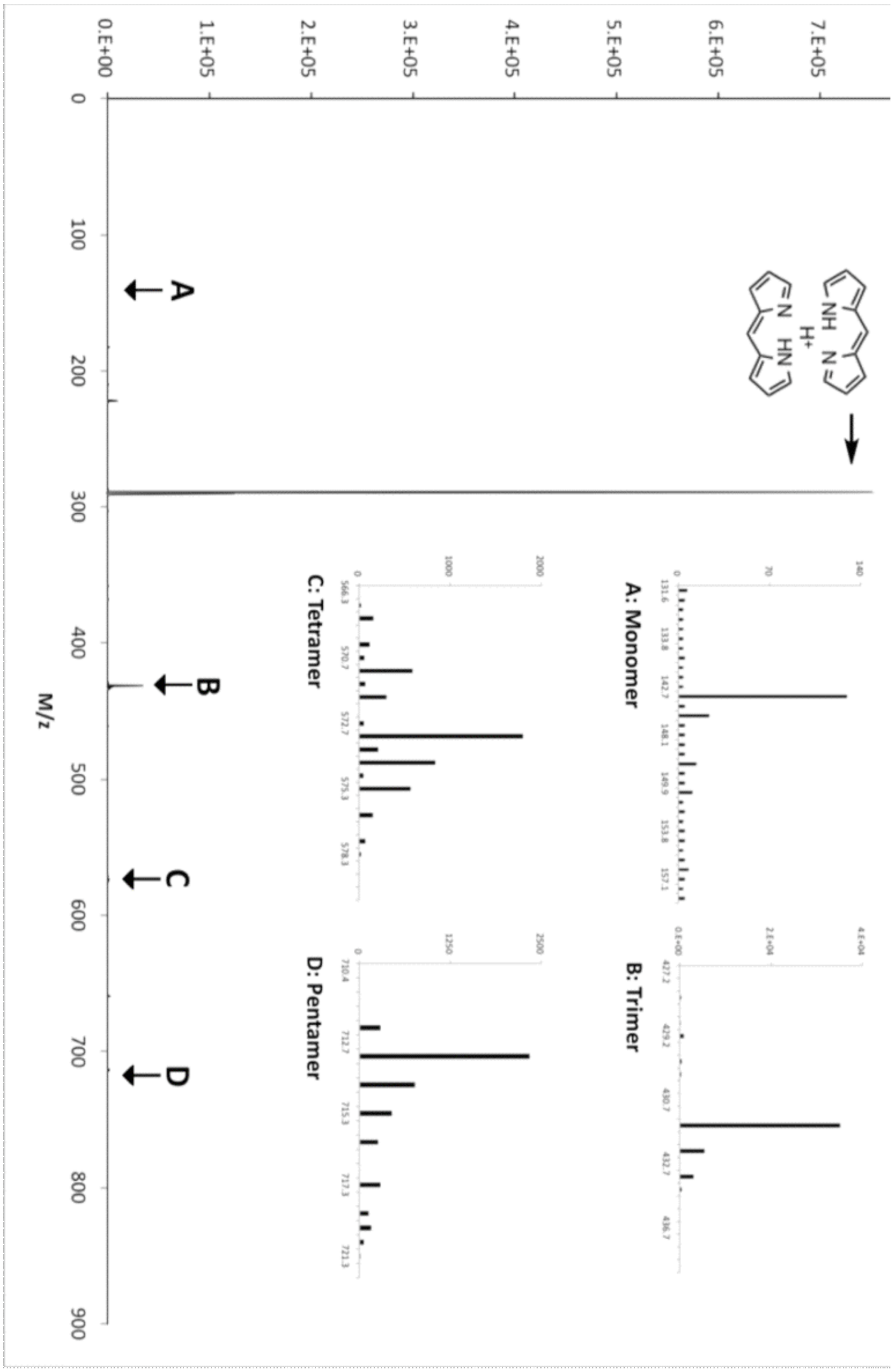
^{11}B NMR spectra depicting formation (top to bottom) of $B(OMe)_3$ from BCl_3 via stoichiometric addition of 3 eq. MeOH ($CDCl_3$).



1.7 Selected ESI$^+$ Spectra



Low resolution scan of (*Z*)-2-((2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole (**3**) produced via oxidation of di(1H-pyrrol-2-yl)methane



Low resolution scan of (*Z*)-2-((2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole (**3**) produced via deprotection from **2**

References

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