# Robust Synthesis of *F*-BODIPYs

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# Supporting Information

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## Determination of yield of *F*-BODIPYs employing $^1$H NMR spectroscopy

The reaction mixture was evaporated to dryness, and the residue was dissolved in a known volume of deuterated chloroform ($CDCl_3$). A known volume of benzene was added as an internal standard. A known aliquot of the new mixture, containing benzene, was added to an NMR tube, and then diluted with a known amount of $CDCl_3$ to reach a volume suitable for $^1$H NMR analysis. Figure S1 compares $^1$H NMR spectra for starting material (**1HBr**, top), the corresponding product (**$1BF_2$**, middle) and the product mixture containing both **1HBr** and **$1BF_2$** (bottom).

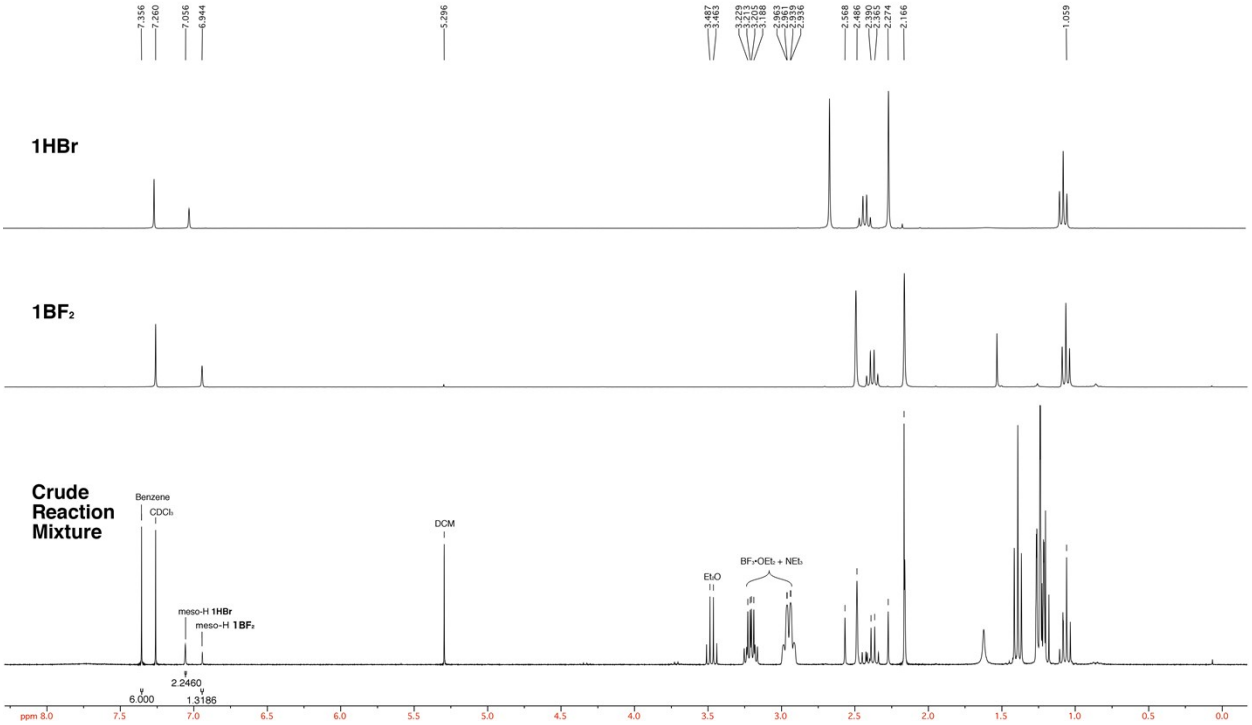



Figure S1: $^1$H NMR spectra, in $CDCl_3$, of **1HBr**, **$1BF_2$** and the crude reaction mixture containing **1HBr**, **$1BF_2$**, $NEt_3$, $BF_3$•$OEt_2$, $CH_2Cl_2$ and benzene.

### Calculation of NMR-based yield

The crude reaction mixture was dissolved in 4.000 mL of $CDCl_3$ ($V_{CDCl3}$), to which 4 µL of benzene ($V_{benz}$) was added. The first step was to calculate the moles of benzene present ($n_{benz}$). This required using density ($d_{benz}$, 0.876 g/mL), mass ($m_{benz}$) and molar mass ($mm_{benz}$, 78.11 g/mol) of benzene as follows:

$$m = V_{benz} * d_{benz} = 3.50 \text{ x} 10^{-3} \text{ g}$$

$$n_{benz} = \frac{m_{benz}}{mm_{benz}} = 4.49 \text{ x}10^{-5} \text{ mol}$$

Thus, we knew the number of moles of benzene in the 4 mL solution. The concentration of benzene ($M_{benz}$) in this solution was calculated as follows:

$$M_{benz} = \frac{n_{benz}}{V_{CDCl3}} = 0.0224 \text{ mol/L}$$

A 200 µL aliquot of this solution ($V_{NMR}$) was added to an NMR sample tube and diluted to 600 µL for analysis. Using $M_{benz}$, the moles of benzene present in this aliquot ($n_{benz\ aliquot}$) could be calculated. The integral value for the *meso*-H signal of **1BF$_2$** ($\int 1BF_2$) was calculated when the integration of benzene was set to 6.000. Multiplying $n_{benz\ aliquot}$ by $\int 1BF_2$ allowed us to calculate the moles of **1BF$_2$** in the 200 µL aliquot ($n_{BF\ aliquot}$). This then allows us to calculate the concentration of **1BF$_2$** in the original 4 mL solution ($M_{BF}$):

$$n_{benz\ aliquot} = M_{benz} * V_{NMR} = 2.24 \text{ x}10^{-6} \text{ mol}$$

$$n_{BF\ aliquot} = n_{benz\ aliquot} * \int 1BF_2 = 2.96 \text{ x}10^{-6} \text{ mol}$$

$$M_{BF} = \frac{n_{BF\ aliquot}}{V_{NMR}} = 0.0148 \text{ mol/L}$$

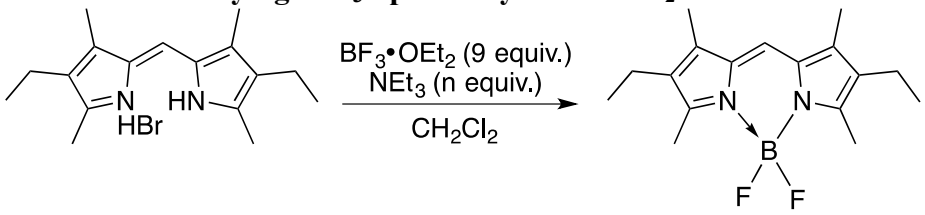
We were then able to work back and calculate the moles of **1BF$_2$** produced during the reaction ($n_{BF}$):

$$n_{BF} = M_{BF} * V_{CDCl3} = 5.92 \text{ x}10^{-5} \text{ mol}$$

The number of moles of **1BF$_2$** could now be used to calculate the yield. In this case 0.160 mmol of starting material was used and 0.0592 mmol of **1BF$_2$** were present, therefore the yield for this reaction was 37%.

## Effect of varying $NEt_3$ in the synthesis of *F*-BODIPYs

**Table S1: Effect of varying $NEt_3$ upon the yield of $1BF_2$**




**1•HBr** **$1BF_2$**

| Equiv. $NEt_3$ (n) | NMR yield (%) |
|---|---|
| 1 | 0 |
| 3 | 32 |
| 5 | 54 |
| 6 | 86 |
| 7 | 77 |
| 12 | 37 |

## Synthetic methods

### Optimised "rescue" procedure for the synthesis of *F*-BODIPYs (GP1)

Naturally air-dried glassware was used, without any provision to exclude air or moisture from the reaction vessel. To a solution of dipyrrin•HBr salt (0.16 mmol, 1 equiv) in $CH_2Cl_2$ (13 mL, lab grade, non-anhydrous) under air with stirring at room temperature $NEt_3$ (6 equiv, lab grade, non-anhydrous) was added, and the reaction was stirred for 10 minutes. Anhydrous $BF_3$•$OEt_2$ (9 equiv) was then added and the resulting solution was sealed with a septum and stirred for 1.25 h. The septum was then removed, and non-anhydrous lab-grade $NEt_3$ (6 equiv, lab grade, non-anhydrous) was added. The vessel was resealed and stirred for 5 minutes, after which the septum was again removed and anhydrous $BF_3$•$OEt_2$ (9 equiv) was added. The resulting solution was sealed again and then stirred for another 1.25 h. The reaction mixture was concentrated *in vacuo* to yield the crude product, which was dissolved in ether (20 mL) and washed with 1 M hydrochloric acid (4 x 20 mL) and 5 M hydrochloric acid (1 x 20 mL). The organic fraction was dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, using $CH_2Cl_2$ as eluent, to yield the desired *F*-BODIPY.

### General procedure for the synthesis of *F*-BODIPYs with added water (GP2)

Distilled water (2 equiv) was added to a solution of dipyrrin•HBr salt (0.16 mmol, 1 equiv) in anhydrous $CH_2Cl_2$ (13 mL) under $N_2$, with stirring at room temperature until the water micelle was no longer visible (~45 min for 2 equiv). Anhydrous $NEt_3$ (6 equiv) was added, and the reaction was stirred for 10 minutes. $BF_3$•$OEt_2$ (9 equiv) was then added and the resulting solution was stirred, under nitrogen, for 2.5 h. The reaction mixture was concentrated *in vacuo* to yield the crude product which was dissolved in $CDCl_3$ (4.000 mL) and benzene (4 μL) was added, with stirring. An aliquot (200 μL) of this solution was added to an NMR sample tube and diluted with $CDCl_3$ (400 μL). A $^1H$ NMR spectrum of the sample was collected and the NMR-

based yield was determined. To gain an isolated yield, the crude product was dissolved in ether (20 mL) and washed with 1 M hydrochloric acid (3 x 20 mL). The organic fraction was dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, using $CH_2Cl_2$ as eluent, to yield the desired *F*-BODIPY.

**General procedure for the synthesis of *F*-BODIPYs (GP3, anhydrous)**

These experiments used strictly anhydrous protocols, conditions and reagents (i.e. our control reactions). To a solution of dipyrrin•HBr salt (0.16 mmol, 1 equiv) in anhydrous $CH_2Cl_2$ (12 mL) under $N_2$, with stirring at room temperature, anhydrous $NEt_3$ (6 equiv) was added, and the reaction was stirred for 10 minutes. $BF_3$•$OEt_2$ (9 equiv) was then added and the resulting solution was stirred, under $N_2$, for 2.5 h. The reaction mixture was concentrated *in vacuo* to yield the crude product which was dissolved in ether (20 mL) and washed with 1 M hydrochloric acid (3 x 20 mL). The organic fraction was dried over anhydrous $Na_2SO_4$, and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, using $CH_2Cl_2$ as eluent, to yield the desired *F*-BODIPY.

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene ($1BF_2$)**

The title compound[24] was synthesised from **1HBr**[18] according to the GP3, and was isolated as a dark red solid (40 mg, 82%).

**4,4-Difluoro-1,2,3,5,6,7-hexamethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene ($2BF_2$)**

The title compound[18] was synthesised from **2HBr**[18] according to the GP3, and was isolated as a light orange solid (36 mg, 81%).

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-di-n-pentyl-8-H-4-bora-3a,4a-diaza-*s*-indacene ($3BF_2$)**

The title compound[25] was synthesised from **3HBr**[18] according to the GP3, and was isolated as a dark red solid (47 mg, 76%).

**4,4-Difluoro-1,3,5,7-tetramethyl-6-ethyl-2,8-H-4-bora-3a,4a-diaza-*s*-indacene ($4BF_2$)**

The title compound[10] was synthesised from **4HBr**[19] according to the GP3, and was isolated as a red solid (36 mg, 81%).

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-di(2-methoxy-2-oxoethyl)-8-H-4-bora-3a,4a-diaza-*s*-indacene ($5BF_2$)**

The title compound was synthesised from **5HBr**[20] according to the GP3, and was isolated as an orange solid (45 mg, 72%).

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethoxycarbonyl-8-H-4-bora-3a,4a-diaza-*s*-indacene ($6BF_2$)**

The title compound[26] was synthesised from **6HBr**[21] according to the GP3, and was isolated as a pale yellow/orange solid (33 mg, 53%).

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethyl-8-phenyl-4-bora-3a,4a-diaza-*s*-indacene ($7BF_2$)**

The title compound[10] was synthesised from free-base **7**[22] according to the GP3, and was isolated as a dark red solid (56 mg, 92%).

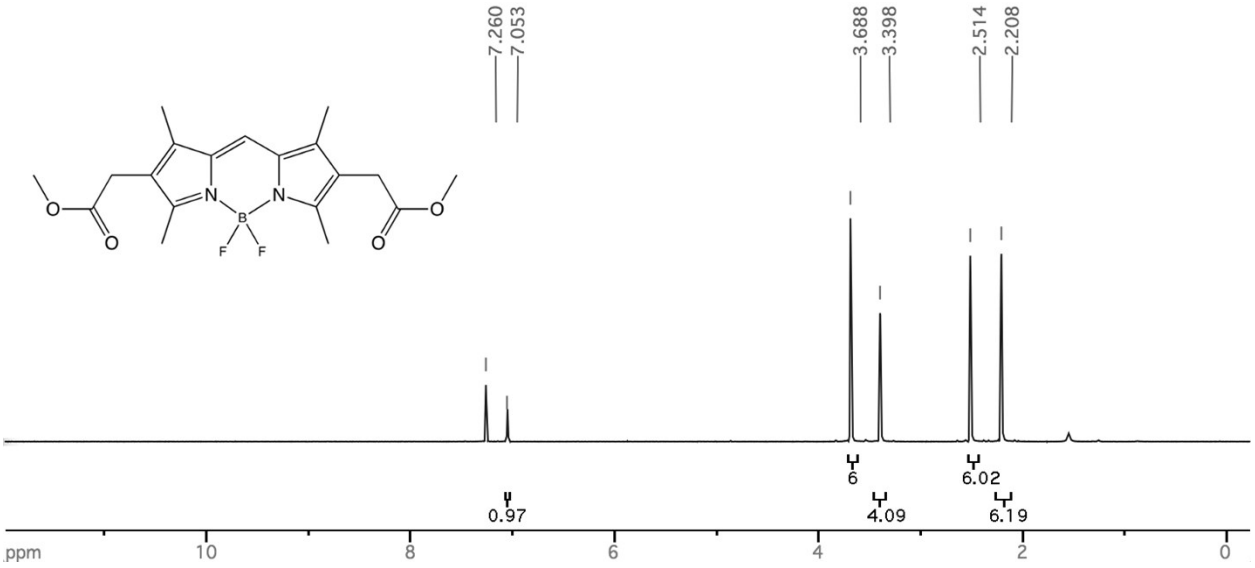
**4,4-Difluoro-1,3,5,7,8-pentamethyl-2,6-diethyl-4-bora-3a,4a-diaza-*s*-indacene ($8BF_2$)**

The title compound[10] was synthesised from **8HCl**[23] according to the GP3, and was isolated as a light orange solid (46 mg, 91%).

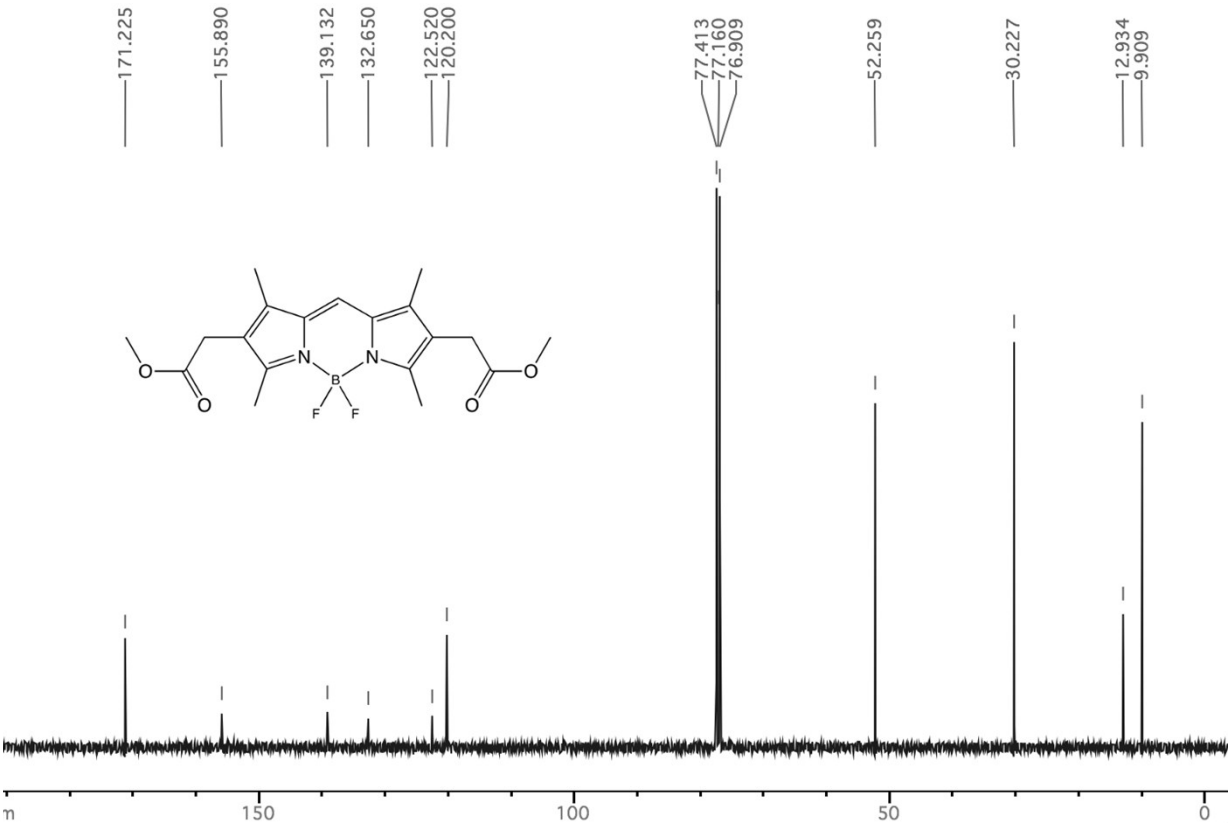
## $^{1}H$, $^{13}C$, $^{11}B$ and $^{19}F$ NMR spectra

**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-di(2-methoxy-2-oxoethyl)-8-H-4-bora-3a,4a-diaza-*s*-indacene ($5BF_2$)**

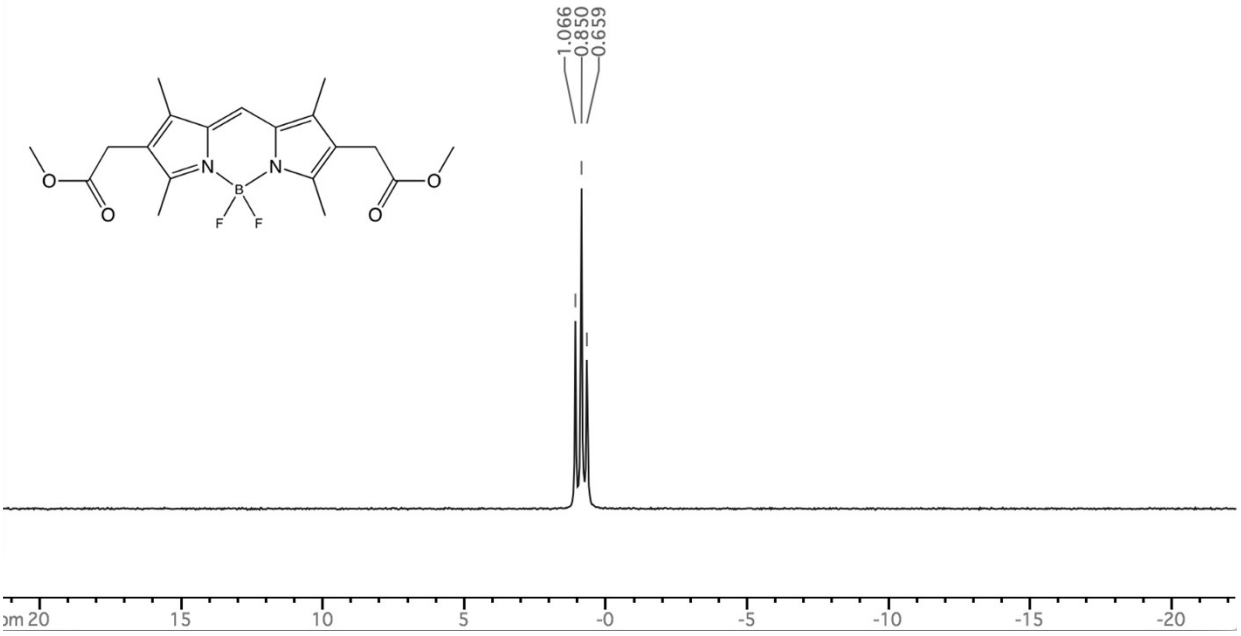
$^{1}H$ NMR; 500 MHz, $CDCl_3$



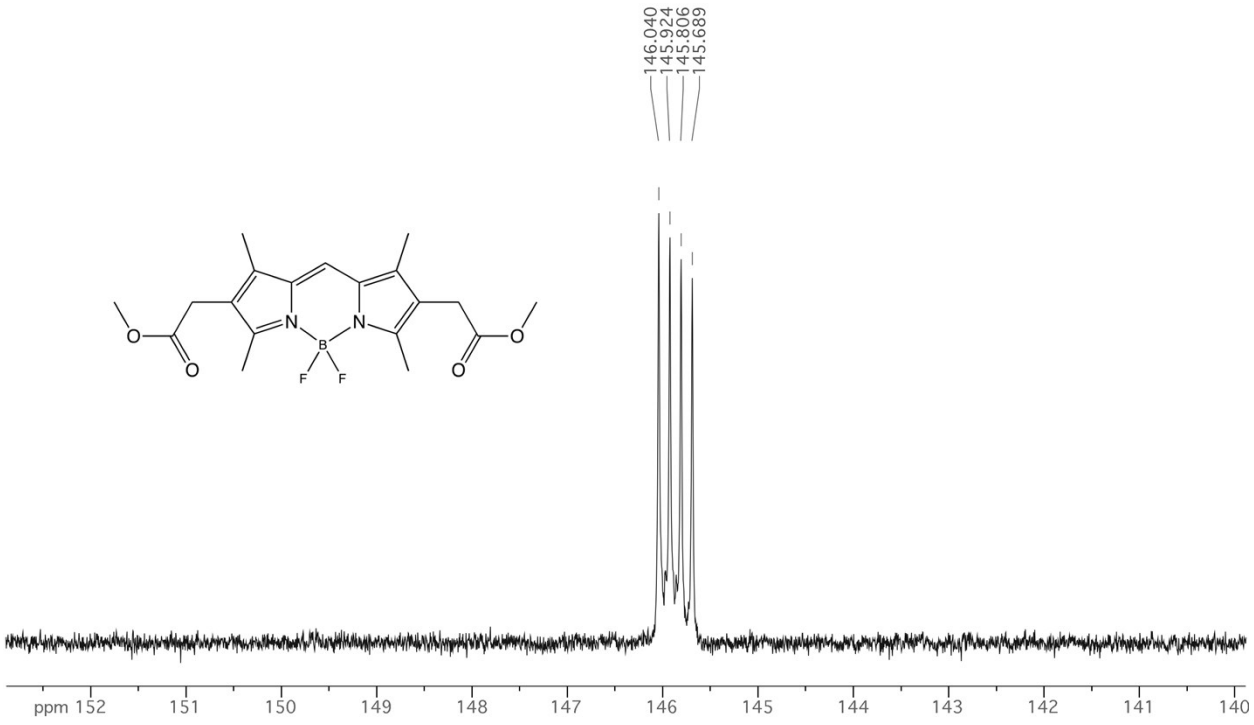

$^{13}C$ NMR; 125 MHz, $CDCl_3$



$^{11}B$ NMR; 160 MHz, $CDCl_3$

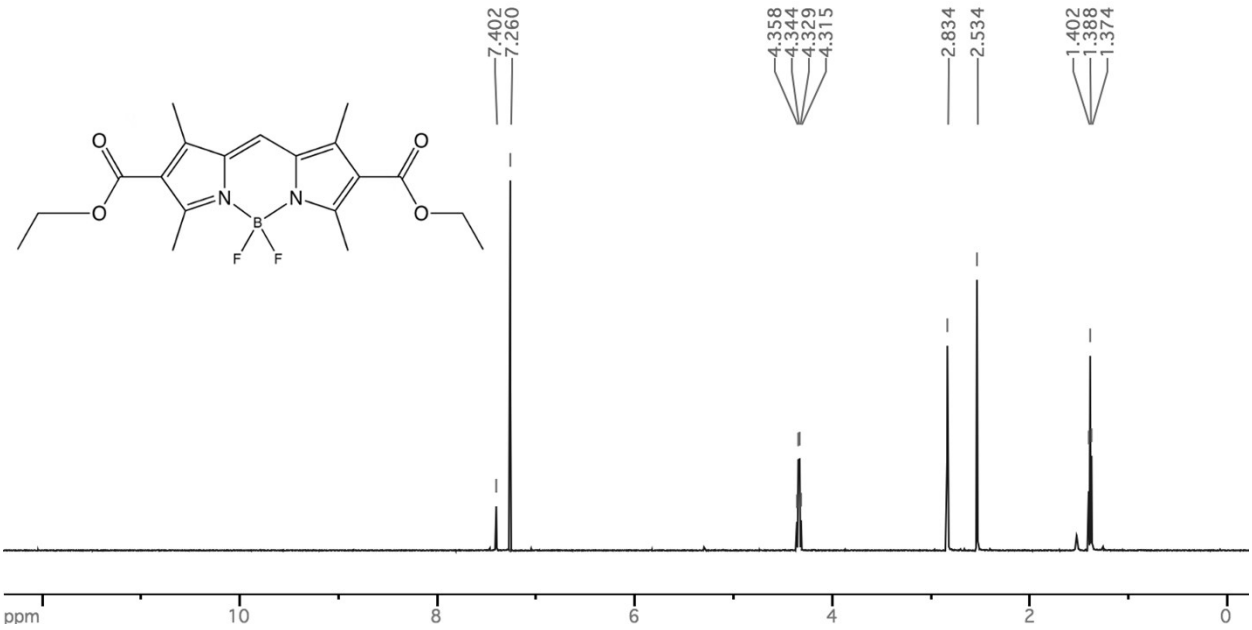



$^{19}F$ NMR; 470 MHz, $CDCl_3$

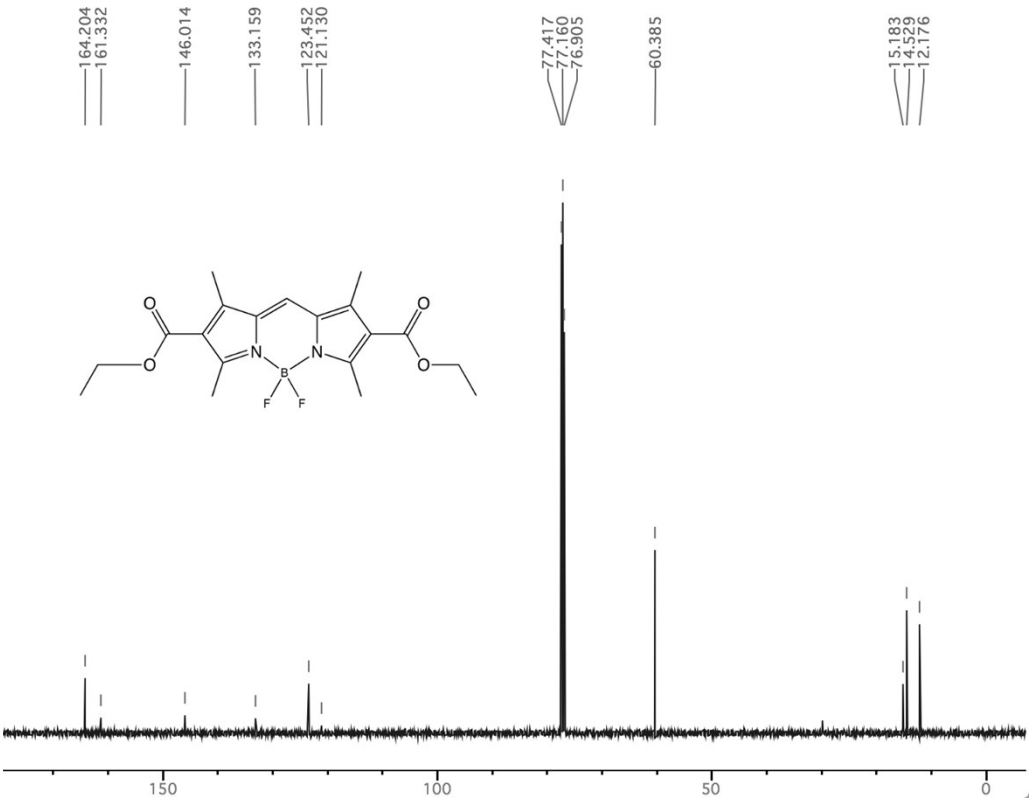


**4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethoxycarbonyl-8-H-4-bora-3a,4a-diaza-*s*-indacene ($6BF_2$)**

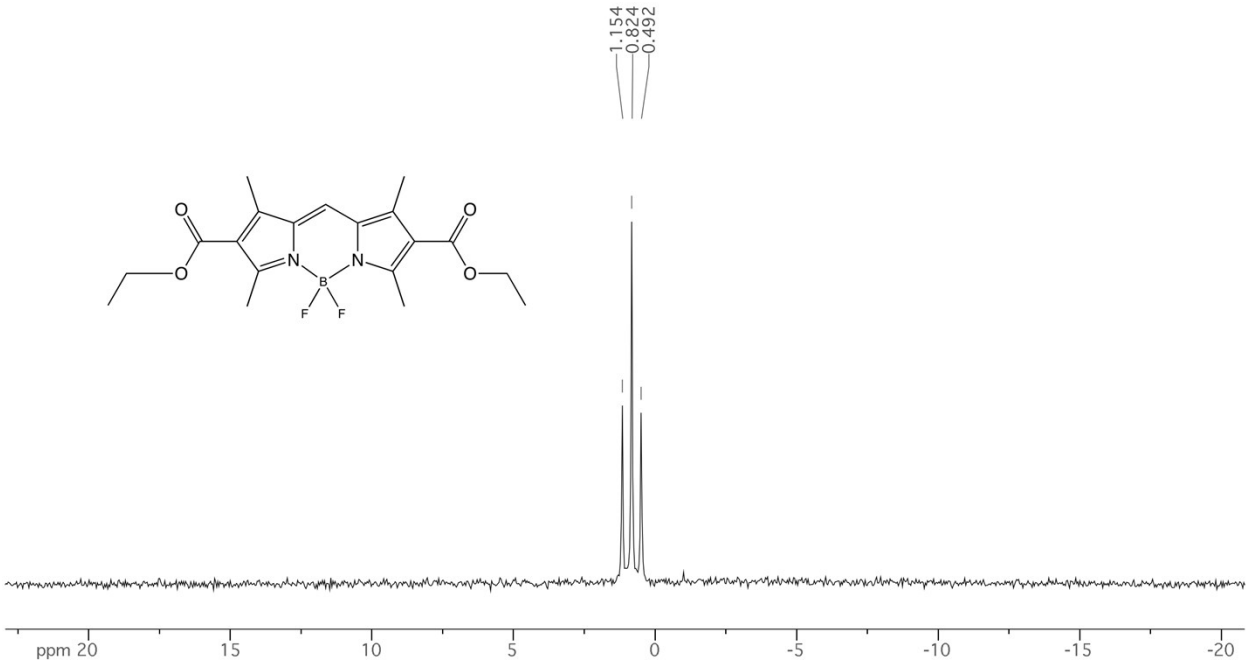
$^1$H NMR; 500 MHz, $CDCl_3$




$^{13}$C NMR; 125 MHz, $CDCl_3$



$^{11}B$ NMR; 160 MHz, $CDCl_3$




$^{19}F$ NMR; 470 MHz, $CDCl_3$