Robust Synthesis of F-BODIPYs

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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 ($^{1}$HBr, top), the corresponding product ($^{1}$BF$_2$, middle) and the product mixture containing both $^{1}$HBr and $^{1}$BF$_2$ (bottom).

![Figure S1: $^1$H NMR spectra, in CDCl$_3$, of $^{1}$HBr, $^{1}$BF$_2$ and the crude reaction mixture containing $^{1}$HBr, $^{1}$BF$_2$, NEt$_3$, BF$_3$•OEt$_2$, CH$_2$Cl$_2$ 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:

$$m = V_{benz} \cdot d_{benz} = 3.50 \times 10^{-3} \text{ g}$$
\[ n_{benz} = \frac{m_{benz}}{mm_{benz}} = 4.49 \times 10^{-5} \text{ mol} \]

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 \( (n_{benz \text{ aliquot}}) \) 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 \( n_{benz \text{ aliquot}} \) by \( \int 1BF_2 \) allowed us to calculate the moles of 1BF_2 in the 200 μL aliquot \( (n_{BF \text{ aliquot}}) \). This then allows us to calculate the concentration of 1BF_2 in the original 4 mL solution \( (M_{BF}) \):

\[ n_{benz \text{ aliquot}} = M_{benz} \cdot V_{NMR} = 2.24 \times 10^{-6} \text{ mol} \]

\[ n_{BF \text{ aliquot}} = n_{benz \text{ aliquot}} \cdot \int 1BF_2 = 2.96 \times 10^{-6} \text{ mol} \]

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

We were then able to work back and calculate the moles of 1BF_2 produced during the reaction \( (n_{BF}) \):

\[ n_{BF} = M_{BF} \cdot V_{CDCl3} = 5.92 \times 10^{-5} \text{ mol} \]

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$_2$

<table>
<thead>
<tr>
<th>Equiv. NEt$_3$ (n)</th>
<th>NMR yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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</tr>
<tr>
<td>3</td>
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<td>7</td>
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<td>12</td>
<td>37</td>
</tr>
</tbody>
</table>
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 CH₂Cl₂ (13 mL, lab grade, non-anhydrous) under air with stirring at room temperature NEt₃ (6 equiv, lab grade, non-anhydrous) was added, and the reaction was stirred for 10 minutes. Anhydrous BF₃•OEt₂ (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 NEt₃ (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 BF₃•OEt₂ (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 Na₂SO₄, and concentrated in vacuo. The resulting residue was purified via column chromatography on silica, using CH₂Cl₂ 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 CH₂Cl₂ (13 mL) under N₂, with stirring at room temperature until the water micelle was no longer visible (~45 min for 2 equiv). Anhydrous NEt₃ (6 equiv) was added, and the reaction was stirred for 10 minutes. BF₃•OEt₂ (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 CDCl₃ (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 CDCl₃ (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$_2$SO$_4$, and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, using CH$_2$Cl$_2$ 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$_2$Cl$_2$ (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$_2$SO$_4$, and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, using CH$_2$Cl$_2$ 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$^{10}$ 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 ($5$BF$_2$)

$^1$H NMR; 500 MHz, CDCl$_3$

$^{13}$C NMR; 125 MHz, CDCl$_3$
$^{11}\text{B NMR; 160 MHz, CDCl}_3$

$^{19}\text{F NMR; 470 MHz, CDCl}_3$
4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethoxycarbonyl-8-H-4-bora-3a,4a-diaza-s-indacene (6BF₂)

1H NMR; 500 MHz, CDCl₃

13C NMR; 125 MHz, CDCl₃
$^{11}\text{B NMR; 160 MHz, CDCl}_3$

$^{19}\text{F NMR; 470 MHz, CDCl}_3$