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Version: Post-print

Publisher's version: Beh, Michael; Douglas, Katherine; House, Kelsey; Murphy, Alexandra;
Sinclair, Jackson; and Thompson, Alison. Robust Synthesis of F-BODIPYs. Org. Biomol. Chem. 2016, 14,
11473-11479. DOI: 10.1039/c6ob02238c

Robust Synthesis of *F*-BODIPYs

Michael Helmut Reynolds Beh, Katherine Isabelle Biehn Douglas, Kelsey Taylor Elver House, Alexandra Celeste Murphy, Jackson Scott Testemale Sinclair and Alison Thompson*

Department of Chemistry, Dalhousie University, P.O. Box 15000, Halifax, NS, B3H 4R2, Canada
Alison.Thompson@dal.ca
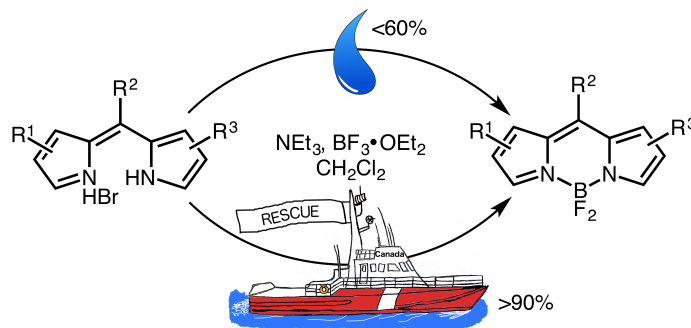
Abstract: *F*-BODIPYs are widely used in applications that rely upon their highly tunable optical properties. A protocol is established for the high-yielding synthesis of *F*-BODIPYs involving non-anhydrous reagents and not requiring precautions to exclude moisture. This simple and robust strategy simply requires a second addition of NEt_3 and $BF_3 \bullet OEt_2$, midway through the reaction period. The ratio and amounts of NEt_3 and $BF_3 \bullet OEt_2$ used in each aliquot are critical to success. The protocol can be completed using bench-dry apparatus, without need to achieve and maintain anhydrous conditions or solvents.

Introduction

Compounds built on the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (*F*-BODIPY) framework have a wide range of uses stemming from their highly tunable electronic properties.[1] The versatility of this class of compound encompasses applications as probes in biological systems, as dyes, as materials in electroluminescent devices, and as light harvesting materials.[2-6] The study of

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F-BODIPYs is a longstanding area of research in the Thompson lab.[7-13] We have recently demonstrated that some *F*-BODIPYs are quantitatively converted into their parent dipyrrins through treatment with $BF_3 \bullet OEt_2$[7] and subsequent addition of thrice stoichiometric amounts of water. As such, the preparation of *F*-BODIPYs under anything less than rigourously anhydrous conditions lends the possibility that successful complexation will be followed by immediate decomplexation, and thus recovery of dipyrrin starting material alongside lower product yields. However, we herein report a practical approach to the synthesis of *F*-BODIPYs that results in high yields without the need for careful exclusion of moisture.

Results and Discussion

Using the traditional reaction conditions involving $BF_3 \bullet OEt_2$ and NEt_3 in CH_2Cl_2,[14] we investigated the synthesis of *F*-BODIPY **1BF₂** from salt **1HBr** (Scheme 1). Previously the effect of varying the equiv of $BF_3 \bullet OEt_2$, while the stoichiometry of NEt_3 remained constant, was determined.[12] Working further, we explored how varying the amount of NEt_3 and keeping $BF_3 \bullet OEt_2$ constant would affect the yield of **1BF₂**, ultimately concluding that the traditional 6:9 ratio of NEt_3 and $BF_3 \bullet OEt_2$ provided optimum yields (Supporting Information, Table S1).
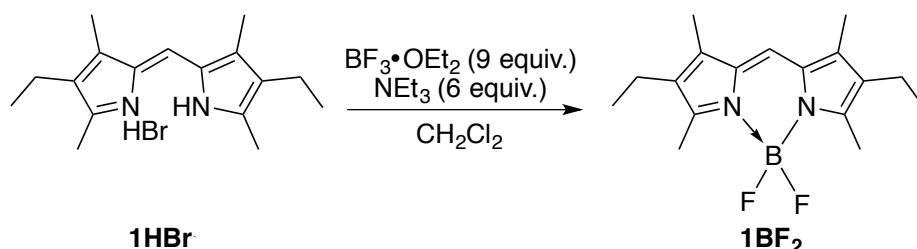
Scheme 1. Synthesis of *F*-BODIPY 1BF₂ from dipyrrin salt 1HBr

A rationale for using this ratio of reagents to achieve optimum yields has yet to be provided amidst the complex equilibrium in effect between the Lewis acidic boron centre and the various species capable of Lewis basic behaviour. A detailed prior report[15] regarding the use of $BF_3 \bullet OEt_2$ as a catalyst for a condensation reaction specifically noted that $BF_3 \bullet OEt_2$ became less

effective in the presence of water. Assigning this observation to the complex equilibrium that must ensue, the formation of the less active $BF_3 \bullet H_2O$ was noted. In our case, several boron-containing byproducts,[7] alongside the $NEt_3 \bullet BF_3$ complex,[16] must inevitably form in solution as the reaction progresses. To shed some light on this complex equilibrium, we collected and analyzed ^{1}H NMR spectra relating to interactions between NEt_3 and $BF_3 \bullet OEt_2$ (Figure 1). In each case, samples for analysis were prepared by removing any reaction solvents or residual material *in vacuo*, followed by dissolving the residue in $CDCl_3$. The characteristics of the equilibrium, as reported through the ethyl signals originating with NEt_3, differ based upon the method of preparation (compare A and B), as well as upon the ratio of NEt_3 and $BF_3 \bullet OEt_2$ used (compare B and C). The ^{1}H NMR spectra corresponding to the crude reaction mixture for the conversion of **1HBr** to **1BF$_2$** reveal an equilibrium involving NEt_3 that evolves as the reaction progresses (compare D-F). Evidently, the unproductive interactions of $BF_3 \bullet OEt_2$ and NEt_3 complicate the conversion of dipyrrins to *F*-BODIPYs, yet an optimal 6:9 ratio of NEt_3 and $BF_3 \bullet OEt_2$ enables the reaction to render maximised yields.
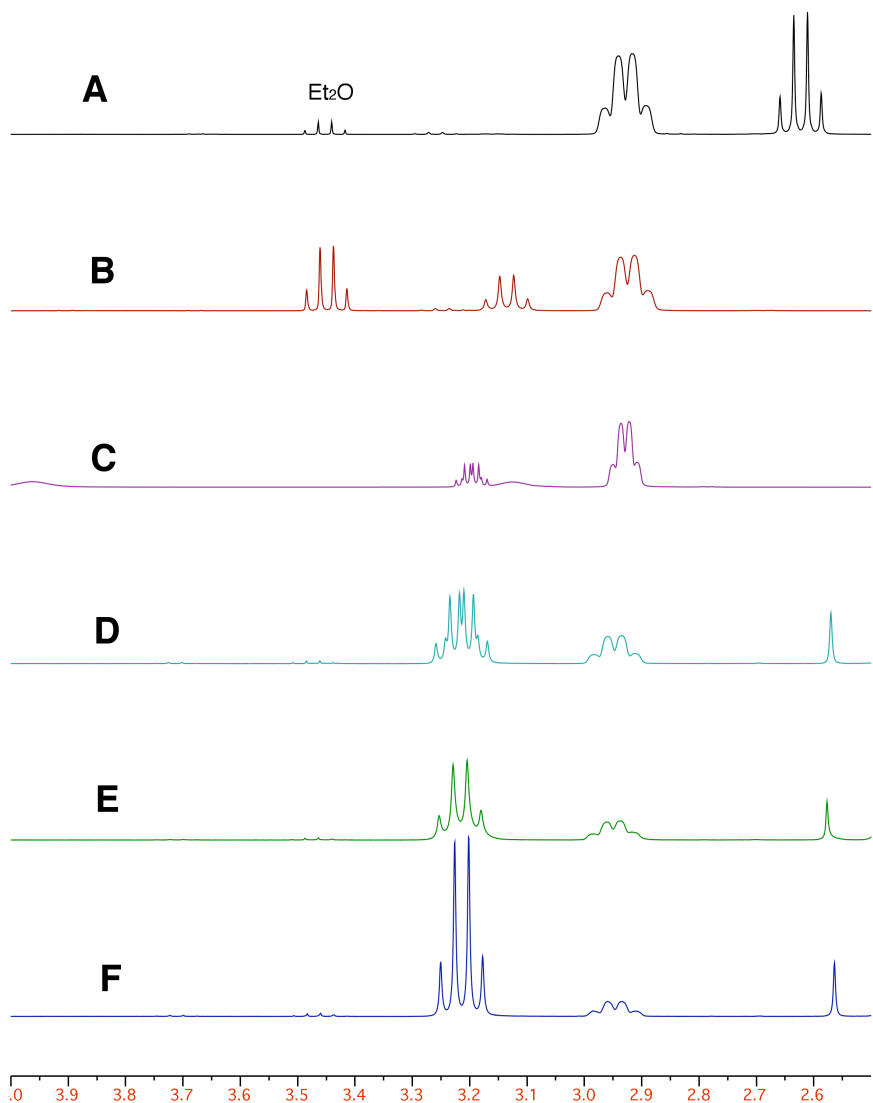
Figure 1: ^{1}H NMR spectra, recorded in CDCl$_3$, showing the ethyl signals arising from the presence of BF$_3$•OEt$_2$ and NEt$_3$. (A) NEt$_3$•BF$_3$ prepared neat; (B) NEt$_3$•BF$_3$ prepared in CH$_2$Cl$_2$ solution using 1:1 ratio of NEt$_3$ and BF$_3$•OEt$_2$; (C) NEt$_3$•BF$_3$ prepared in CH$_2$Cl$_2$ solution using 6:9 ratio of NEt$_3$ and BF$_3$•OEt$_2$; (D) crude reaction mixture for conversion of **1HBr** to **1BF$_2$** using 6:9 ratio of NEt$_3$ and BF$_3$•OEt$_2$, spectrum collected at 26 °C; (E) crude reaction mixture for conversion of **1HBr** to **1BF$_2$** using 6:9 ratio of NEt$_3$ and BF$_3$•OEt$_2$, spectrum collected at 50 °C; (F) crude reaction mixture of **1HBr** to **1BF$_2$** using 6:9 ratio of NEt$_3$ and BF$_3$•OEt$_2$, after warming to 50 °C and then cooling to 26 °C.

We continued our investigation through using the optimum 6:9 ratio of NEt$_3$ and BF$_3$•OEt$_2$ and studied the synthesis of *F*-BODIPY **1BF$_2$** under various humidity levels, with the

ultimate goal of developing a robust procedure that would enable the synthesis of *F*-BODIPYs

without the need to use rigourously anhydrous conditions. As shown in Table 1, the 84% yield of

1BF$_2$ (entry 1) determined using ^{1}H NMR analysis of the crude reaction mixture aligns, given

reasonable variations when working on a 50 mg scale of starting material, with the isolated yield

of 80% obtained subsequent to work-up and purification via chromatography over silica. This

reaction was conducted in a period of low relative humidity (0.4-0.5 kPa).[17] As a comparison,

entry 2 reveals NMR-based and isolated yields of **1BF$_2$** obtained when the relative humidity level

was much higher (1.3-1.7 kPa).[17] These seasonally-variable yields are reproducible, and were

obtained by the same researcher using identical equipment and protocols with the only variable

being humidity levels. Despite attempts to provide rigorous anhydrous conditions, i.e. inert

atmosphere, oven-dried glassware, heated purge cycles, and anhydrous reagents and solvent, it is

evident that yields of **1BF$_2$** are significantly affected by atmospheric humidity levels.

Table 1: Efficacy of NMR-based determination of yield, according to Scheme 1

Humidity	Entry	NMR yield (%)	Isolated yield (%)
Low	1	84	80
High	2	65	61

To gauge the effect of moisture content on the synthesis of **1BF$_2$**, the reaction according

to Scheme 1 was performed several times with variation in the rigour dedicated to securing

anhydrous conditions. The reactions were performed in our laboratory (not air-conditioned)

during December-March when the relative humidity was low.[17] As benchmark, we established

the yield for a control reaction using anhydrous and inert conditions, as well as anhydrous

reagents – each control reaction ran side-by-side with the reaction(s) of interest. Unless otherwise

stated, glassware was pre-dried in an oven (110 °C) for 18 hours and then further heat-dried, using a heat gun, during purge cycles containing the starting material **1HBr**. A dry and inert atmosphere was assured by equipping the nitrogen line with a flow-through desiccator filled with indicating desiccant. Anhydrous $BF_3 \bullet OEt_2$, NEt_3 and CH_2Cl_2 were used, and transferred using inert and moisture-free methods. The yield for this control reaction was 86%, as seen in Table 2. Repeating the reaction, but taking less care to assure anhydrous and inert atmospheric conditions, detrimentally affected the yield obtained. Indeed, taking glassware directly from the bench-top and submitting the vessel to a heated purge/fill cycle without any prior drying proved to reduce the yield slightly (entry 1). Following the same conditions but not performing any heated purge/fill cycles (entry 2) gave similar results. The impact of being remiss in ensuring rigourous anhydrous conditions can be best appreciated by considering the result when non-anhydrous CH_2Cl_2 was used (solvent exposed to air overnight before reaction commenced): the desired product **1BF$_2$** was not obtained even though the reaction glassware and set-up adhered to strict anhydrous protocols.

Table 2: Synthesis of 1BF$_2$ according to Scheme 1, using varying set-up protocols

| Entry	Reaction Conditions	Yield (%)[a]	Control (%)[a]
1	No oven; flame dry, purge	78	86
2	No oven; flame dry	73	86
3	Non-anhydrous CH_2Cl_2; oven, flame dry, purge	0	86

[a]yields determined using NMR-based method

In an attempt to develop a procedure that would be reliable year-round and in circumstances where reaction conditions do not meet anhydrous standards, we first devised a protocol that enabled us to controllably mimic the detrimental effects of either high laboratory humidity levels or improper execution of anhydrous reaction conditions. As such, measured

amounts of distilled water were added to the reaction (Table 3). The yields of $1BF_2$ were recorded alongside a control that was identical in all aspects (except no water added), and run side-by-side with each reaction of interest. All reactions were set up using strict anhydrous and inert conditions as described above. Water was then added to a solution of $1HBr$ in CH_2Cl_2. The mixture was stirred for 30-90 minutes, depending on the amount of water added, so that a homogeneous solution was obtained and a water droplet was no longer visible. If the reaction was performed while the added water was still visible the influence of the water on the reaction was either diminished or sporadic (sometimes having great effect, other times very little). This experimental detail, i.e. allowing sufficient opportunity for the added water to disperse, was thus extremely important to ensuring consistency in our work and thus enabling us to compare the outcomes of each experiment, and has been alluded to previously.[15] The required amounts of $BF_3 \bullet OEt_2$ and NEt_3 were then added, according to Scheme 1, and the reaction mixtures stirred for 3 hours. Upon removal of the solvent and other material *in vacuo*, the crude product mixtures were analyzed to provide the NMR-based yield in each case.

The addition of 0.25 equiv of water (entry 1, Table 3) made little noticeable difference to the yield, unsurprising given the period of high relative humidity at the time (control yield of 70%). However, the addition of increasing amounts of water served to significantly reduce the yield of $1BF_2$ (entries 2-6). The final column of Table 3 shows the yield of each experiment as a percentage of that obtained in the control experiment run alongside (period of high laboratory humidity, hence modest yield for the control experiments). It is again clear from these results that the yield for the synthesis of $1BF_2$ decreases as the moisture content of the reaction mixture increases.

Table 3: The effect of water on the synthesis of 1BF$_2$
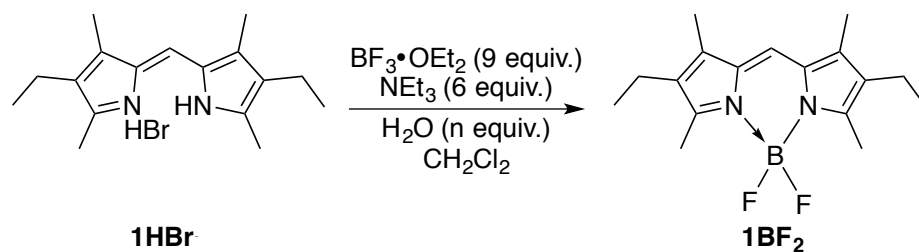
Entry	Equiv water (n)	Yield (%)[a]	Control (%)[a]	Yield/control[a]
1	0.25	71	70	101
2	0.5	64	70	91
3	1.0	49	74	66
4	1.5	36	72	50
5	2	23	74	31
6	3	0	70	0

[a]yields determined using NMR-based method

With these results in hand, we took the protocol involving the addition of 2 equiv water

and used it to mimic reactions inadvertently featuring significant amounts of moisture. This

enabled us to develop a procedure to "rescue" reactions such that acceptable yields could be

obtained. Our experiments employed the anhydrous set-up described earlier, and involved use of

6:9 equiv ratio of NEt$_3$ and BF$_3$•OEt$_2$, followed by a second aliquot of NEt$_3$ and/or BF$_3$•OEt$_2$

added after the reaction had been stirred for 1.25 hours. Each reaction mixture was then stirred

for a further 1.25 hours before work-up and the subsequent determination of yield. Such attempts

featuring a second full addition of *either* NEt$_3$ *or* BF$_3$•OEt$_2$ to a mixture containing 2 equiv of

dispersed water proved fruitless (Table 4, entries 1 and 2). However, a second addition of NEt$_3$

and BF$_3$•OEt$_2$ (6:9 ratio equiv) proved to be much more successful (entry 3), and resulted in near

quantitative yields despite the presence of 2 equiv water. Interestingly, reducing the quantities of

the reagents used for the second addition of NEt$_3$ and BF$_3$•OEt$_2$ was met with only a moderate

increase in yield (entry 4). This observation is of significance, as it means that salvage attempts

for the synthesis of *F*-BODIPYs should not consist of merely adding *some* additional amount of
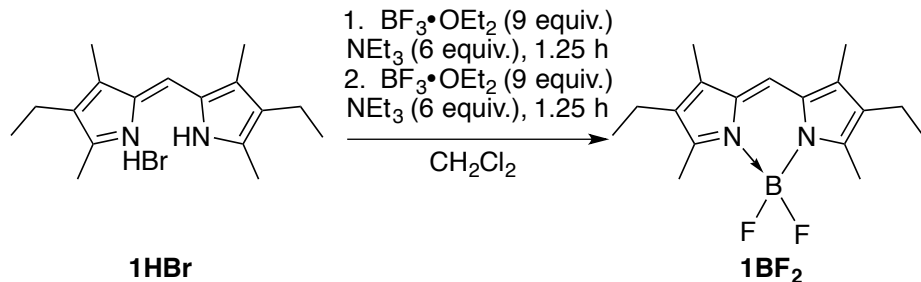
reagent(s) but rather that the specific ratio of 6:9 equiv NEt_3 and $BF_3 \bullet OEt_2$ is required for optimum results. Entry 5 shows that there is no detriment, in terms of yield, to adding a second portion of NEt_3 and $BF_3 \bullet OEt_2$ to the reaction mixture, regardless of moisture levels, as this reaction did not contain any additional water. Concluding, the use of a second aliquot of 6:9 equiv NEt_3 and $BF_3 \bullet OEt_2$ is clearly beneficial to yield, although the excess reagents require the implementation of a more comprehensive work-up procedure. Indeed, three washes with 1 M HCl plus a final wash with 5 M HCl were required.

Table 4: The effect of additional aliquots of reagents upon the synthesis of 1BF$_2$
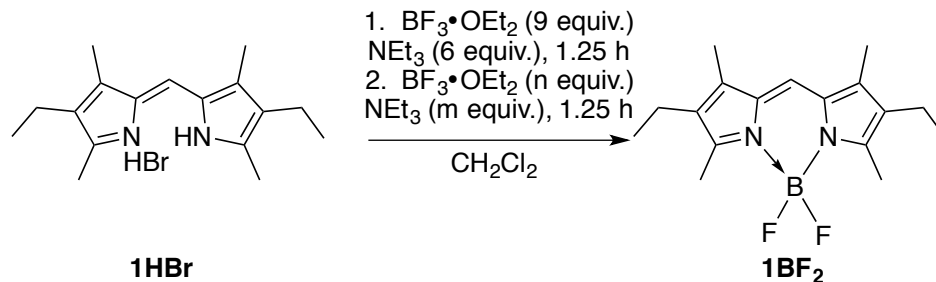
Entry	Equiv water	Second addition[a] (equiv)	Yield (%)[b]	Control (%)[b]
1	2	NEt$_3$ (6)	19	21[c]
2	2	BF$_3$•OEt$_2$ (9)	24	21[c]
3	2	NEt$_3$:BF$_3$•OEt$_2$ (6:9)	>95	23[c]
4	2	NEt$_3$:BF$_3$•OEt$_2$ (3:4.5)	82	23[c]
5	0	NEt$_3$:BF$_3$•OEt$_2$ (6:9)	>95[d]	69[e]

[a]second addition added after reaction mixture stirred for 1.25 hours; [b]yields determined using NMR-based method; [c]control reactions contained 2 equiv water and only the initial addition of 6:9 equiv NEt$_3$:BF$_3$•OEt$_2$; [d]isolated yield 90%; [e]control reaction contained 0 equiv water and only the initial addition of 6:9 equiv NEt$_3$:BF$_3$•OEt$_2$
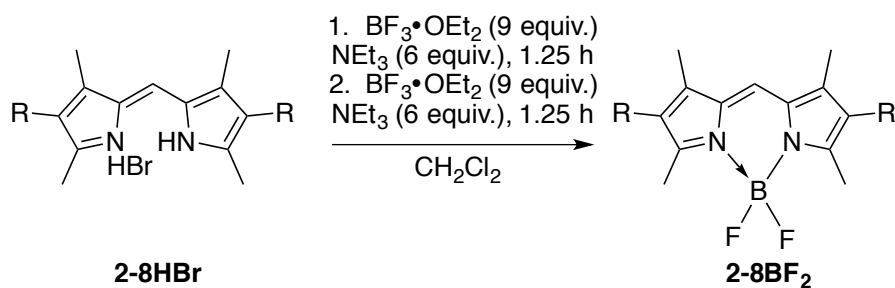
Given our success achieving high yields through the addition of a second aliquot of 6:9 equiv NEt$_3$ and BF$_3$•OEt$_2$ even in the presence of 2 equiv of added water, we were curious as to whether the reaction could be performed using "wet" lab-grade reagents and solvents (Table 5). NEt$_3$ of indeterminate vintage (lab grade, long-opened 4 L glass jug with screw-cap), non-anhydrous CH$_2$Cl$_2$ from three different sources, and anhydrous BF$_3$•OEt$_2$ were used. The atmosphere-distilled lab-grade CH$_2$Cl$_2$ (entry 1) had been stored in a bench-top squeeze-bottle for 1 week prior to these experiments. The reaction vessel and stir bar, although clean and naturally air-dried, were taken directly from the bench-top and used without any special consideration for drying. Each of the experiments was prepared in an open vessel under atmospheric conditions. The reaction was capped with a septum only after the addition of BF$_3$•OEt$_2$. To our delight, our modified reaction protocol involving a second aliquot of 6:9 equiv NEt$_3$ and BF$_3$•OEt$_2$ produced excellent yields of **1BF$_2$** (entry 1-3). Furthermore, the same conditions were employed on a larger scale, with equal success (entry 4).

Table 5: Synthesis of 1BF₂ using bench-top conditions

1. BF₃•OEt₂ (9 equiv.)
NEt₃ (6 equiv.), 1.25 h
2. BF₃•OEt₂ (9 equiv.)
NEt₃ (6 equiv.), 1.25 h

CH₂Cl₂

1HBr   **1BF₂**

Entry	Quality of CH₂Cl₂	Yield (%)[a]	Control (%)[a]
1	Distilled lab-grade	95	35[b]
2	HPLC-grade	95	32[b]
3	Non-distilled lab-grade	90	38[b]
4	Distilled lab-grade	98[c]	35[b]

[a]isolated yields; [b]control reactions used the same grade CH₂Cl₂ but featured only the initial addition of 6:9 equiv NEt₃ and BF₃•OEt₂; [c]2.8 g scale

With a protocol in hand that rendered high yields of **1BF₂**, no matter the moisture content within the reaction mixture, we moved to establish the scope of effectiveness in the production of other *F*-BODIPYs. Seven dipyrrins with varying substitution patterns were used to represent the broad classes of BODIPYs frequently synthesised. As shown in Scheme 2, our optimised procedure involved an initial addition of 6:9 equiv NEt₃ and BF₃•OEt₂. After stirring for 1.25 hours, a second aliquot of 6:9 equiv NEt₃ and BF₃•OEt₂ was followed by stirring for 1.25 hours before work-up of the reaction. Of note, these reactions featured non-anhydrous reagents (apart from BF₃•OEt₂) and were performed using the bench-top conditions described above, with no attempts made to dry glassware or otherwise ensure moisture-free conditions. In contrast, the control reactions (Table 6) each involved meticulous exclusion of moisture, via oven-drying of glassware, repeated hot purge cycles, inert conditions and the use of anhydrous solvents and reagents.
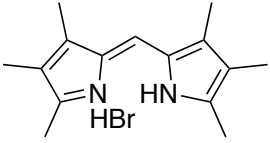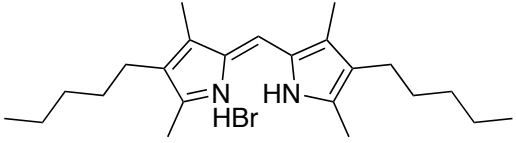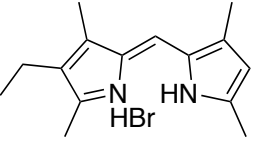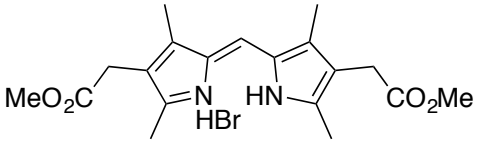
1. BF$_3$•OEt$_2$ (9 equiv.)
NEt$_3$ (6 equiv.), 1.25 h
2. BF$_3$•OEt$_2$ (9 equiv.)
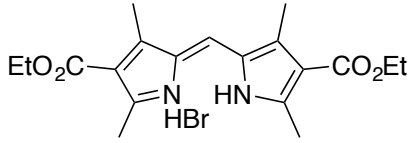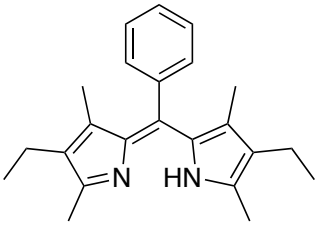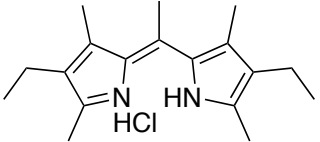NEt$_3$ (6 equiv.), 1.25 h

CH$_2$Cl$_2$

2-8HBr

2-8BF$_2$

Scheme 2. Optimised procedure for synthesis of *F*-BODIPYs

In all cases, our optimised procedure involving two aliquots of NEt$_3$ and BF$_3$•OEt$_2$ met or exceeded the yields obtained under anhydrous conditions (Table 6). The revised method, requiring no special set-up, is successful for dipyrrins bearing alkyl substituents (**2HBr** and **3HBr**), as well as those featuring unsubstituted positions (**4HBr**) about the pyrrolic rings. Likewise, alkanoates (**5HBr**) are tolerated as are conjugated ester units (**6HBr**). The revised method was also effective in converting *meso*-phenyl (**7**) and *meso*-methyl (**8HCl**) dipyrrins into the corresponding *F*-BODIPYs in excellent yield. In these latter cases, although our modified protocol gives yields matching those of the anhydrous control reactions run on the same day, the experimental precautions and preparations required to achieve them were significantly less demanding.

Table 6. Modified two-aliquot protocol for the synthesis of *F*-BODIPYs according to Scheme 2

Dipyrrin	Yield (%)[a,b] Bench-top	Control (%)[c,d] Anhydrous
2HBr	92	81
3HBr	87	76
4HBr	98	81
5HBr	85	72
6HBr	96	53
7	92	92[a]
8HCl	96	91[a]

[a]isolated yields; [b]reactions conducted using non-anhydrous NEt$_3$ and CH$_2$Cl$_2$ and two aliquots of 6:9 equiv NEt$_3$ and BF$_3$•OEt$_2$; [c]control reactions conducted under anhydrous conditions with anhydrous reagents and solvent, and only using one addition of 6:9 equiv NEt$_3$ and BF$_3$•OEt$_2$; [d]yields determined using NMR-based method.

Conclusions

A robust method for the high yielding synthesis of *F*-BODIPYs has been developed that does not rely upon anhydrous conditions. In light of the complex equilibria[15] that must be present in

solution (including BX_n complexed to OEt_2, H_2O, amine and/or dipyrrin), the focus of this report

is on defining an optimised procedure rather than speculating on mechanisms. Certainly, the

beguiling thought that further aliquots of $BF_3 \cdot OEt_2$ serve merely to counter the effects of any loss

of active BF_3 upon reaction with water are stymied by note of the fact that addition of $BF_3 \cdot OEt_2$

alone fails to resurrect the reaction. Indeed, the optimised procedure reported herein involves

adding a second aliquot of 6:9 NEt_3 *and* $BF_3 \cdot OEt_2$ to the reaction mixture, after a period of initial

stirring. The ratio and amounts of the NEt_3 and $BF_3 \cdot OEt_2$ reagents are critical to producing high

yields, both with the initial addition and with the second addition. A second aliquot of 6 equiv of

NEt_3 and 9 equiv of $BF_3 \cdot OEt_2$ after 1.25 hours furnishes excellent yields of *F*-BODIPYs even

under non-anhydrous, or "wet", conditions, and even in the presence of 2 equiv of water (far

greater than would be present after careful reaction set-up in a humid climate). Thin layer

chromatography or ^{1}H NMR spectroscopy can both be used to easily determine the condition of

the reaction, i.e. progress towards completion, and whether or not a second addition of NEt_3 and

$BF_3 \cdot OEt_2$ is necessary. Although the yield can be significantly improved via this protocol, it

should be appreciated that the addition of twice the amount of NEt_3 and $BF_3 \cdot OEt_2$ requires a

more thorough work-up procedure. Although deceptively simple in conclusion, we publish this

work so as to unequivocally document robust and practical conditions to convert dipyrrins into *F*-

BODIPYs.

EXPERIMENTAL SECTION

All reagents and solvents were used as received. NMR spectra were recorded using 500 or 300

MHz spectrometers. All ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR chemical shifts are expressed in parts per

million (ppm). The solvent signal was used as the internal reference for ^{1}H and ^{13}C spectra

[$CDCl_3$ ([1]H 7.26 ppm; [13]C 77.16 ppm)]. For [11]B, the 0 ppm position corresponds to the chemical

shift of $BF_3 \cdot Et_2O$ (15% in $CDCl_3$), whereas for ^{19}F the 0 ppm position corresponds to the chemical shift of CCl_3F. Splitting patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qs, quartet of singlets ([11]B); m, multiplet. All coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were recorded using ion trap (ESI TOF) instruments. The dipyrrin salts were prepared according to literature procedures: **1HBr**,[18] **2HBr**,[18] **3HBr**,[18] **4HBr**,[19] **5HBr**,[20] **6HBr**,[21] **7**,[22] **8HCl**.[23]

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 $BF_3 \cdot OEt_2$ (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 $BF_3 \cdot OEt_2$ (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 (3 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.

4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene (1BF₂)

The title compound was synthesised from **1HBr**[18] under non-anhydrous conditions according to GP1, and was isolated as a dark red solid (48 mg, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.95 (s,

1H), 2.49 (s, 6H), 2.38 (q, 4H, $J = 7.7$ Hz), 2.16 (s, 6H), 1.06 (t, 6H, $J = 7.7$ Hz), in accordance with the literature.[24]

4,4-Difluoro-1,2,3,5,6,7-hexamethyl-8-H-4-bora-3a,4a-diaza-*s*-indacene (2BF$_2$)

The title compound was synthesised from **2HBr**[18] under non-anhydrous conditions according to GP1, and was isolated as a light orange solid (52 mg, 92%). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 6.94 (s, 1H), 2.48 (s, 6H), 2.15 (s, 6H), 1.93 (s, 6H), in accordance with the literature.[18]

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 was synthesised from **3HBr**[18] under non-anhydrous conditions according to GP1, and was isolated as a dark red solid (49 mg, 87%). ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.94 (s, 1H), 2.48 (s, 6H), 2.34 (t, 4H), 2.15 (s, 6H), 1.46-1.40 (m, 4H), 1.34-1.30 (m, 8H), 0.90 (t, 6H), in accordance with the literature.[25]

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 was synthesised from **4HBr**[19] under non-anhydrous conditions according to GP1, and was isolated as a red solid (48 mg, 98%). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 6.99 (s, 1H), 6.00 (s, 1H), 2.51 (s, 3H), 2.49 (s, 3H) 2.39 (q, 2H, H, $J = 7.7$ Hz), 2.23 (s, 3H), 2.17 (s, 3H), 1.07 (t, 3H, $J = 7.7$ Hz), in accordance with the literature.[10]

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 for the first time from **5HBr**[20] under non-anhydrous conditions according to GP1, and was isolated as an orange solid (46 mg, 85%). Mp 214-218 °C; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.05 (s, 1H), 3.69 (s, 6H), 3.40 (s, 4H), 2.51 (s, 6H), 2.21 (s, 6H); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 171.2, 155.9, 139.1, 132.6, 122.5, 120.2, 52.3, 30.2, 12.9, 9.9; ^{11}B {^{1}H} NMR (CDCl$_3$, 160 MHz) δ 0.85 (t, $J = 33$ Hz); ^{19}F {^{1}H} NMR (CDCl$_3$, 470 MHz) δ 145.8

(qs, $J = 55$ Hz); HRMS-ESI (*m/z*): [M+Na]$^+$ calcd for $C_{19}H_{23}N_2O_4BF_2Na$ 415.1611; found 415.1626.

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 was synthesised from **6HBr**[21] under non-anhydrous conditions according to GP1, and was isolated as a pale yellow/orange solid (60 mg, 96%). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.40 (s, 1H), 4.33 (q, 4H, $J = 7.2$ Hz), 2.83 (s, 6H), 2.53 (s, 6H), 1.39 (t, 6H, $J = 7.2$ Hz); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 164.2, 161.3, 146.0, 133.2, 123.5, 121.1, 60.4, 15.2, 14.5, 12.2; ^{11}B (CDCl$_3$, 160 MHz) δ 0.83 (t, $J = 53$ Hz); ^{19}F (CDCl$_3$, 470 MHz) δ 143.2 (qs, $J = 38$ Hz). HRMS-ESI (*m/z*): [M+Na]$^+$ calcd for $C_{19}H_{23}N_2O_4BF_2Na$ 415.1611; found 415.1626. ^{1}H NMR data matches that previously reported for this compound.[26] ^{13}C NMR data have not been previously reported for this compound.

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 was synthesised from free-base **7**[22] under non-anhydrous conditions according to GP1, and was isolated as a dark red solid (56 mg, 92%). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.49-7.46 (m, 3H), 7.29-7.27 (m, 2H), 2.53 (s, 6H), 2.30 (q, 4H, $J = 4.5$ Hz), 1.27 (s, 6H), 0.98 (t, 6H, $J = 7.5$ Hz), in accordance with the literature.[10]

4,4-Difluoro-1,3,5,7,8-pentamethyl-2,6-diethyl-4-bora-3a,4a-diaza-*s*-indacene (8BF$_2$)

The title compound was synthesised from **8HCl**[23] under non-anhydrous conditions according to GP1, and was isolated as a light orange solid (46 mg, 96%). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 2.60 (s, 3H), 2.50 (s, 6H), 2.40 (q, 4H, $J = 7.5$ Hz), 2.33 (s, 6H), 1.04 (t, 6H, $J = 7.5$ Hz), in accordance with the literature.[10]

Supporting Information

Further experimental details, plus NMR spectral images for novel compounds.

Acknowledgments

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