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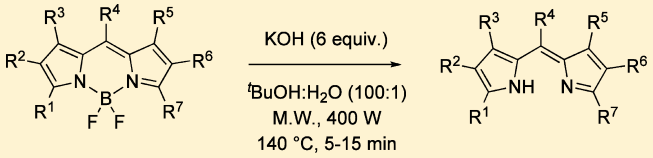
Use of *F*-BODIPYs as a Protection Strategy for Dipyrrins: Optimization of BF_2 Removal

Deborah A. Smithen, Alexander E. G. Baker, Matthew Offman, Sarah M. Crawford, T. Stanley Cameron, and Alison Thompson*

Department of Chemistry, Dalhousie University, P.O. Box 15000, Halifax, Nova Scotia, Canada, B3H 4R2

Supporting Information

ABSTRACT: We recently reported the first general method for the deprotection of 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes (*F*-BODIPYs) involving a microwave-assisted procedure for the removal of the BF_2 moiety, and liberation of the corresponding free-base dipyrrin. Further optimization of the reaction has resulted in a more convenient and accessible protocol. The availability of this new methodology enables BF_2-complexation to be used as a dipyrrin protection strategy. Herein lies a detailed examination of the deprotection reaction, with a view to optimization and gaining mechanistic insight, and its application in facilitating a multistep synthesis of pyrrolyldipyrrins.



INTRODUCTION

Dipyrrins (**1**, Figure 1), consisting of a pyrrole ring and an azafulvene moiety linked via an sp^2 hybridized carbon center, are a common motif, particularly for the synthesis of porphyrins and related structures and, more recently, within coordination chemistry.[1−4] These compounds have a wide range of interesting properties, not least their high molar absorptivities.[3−5] While synthesis of dipyrrins is often facile, generally involving either the acid-catalyzed condensation of a 2-formyl pyrrole with an α-free (2-unsubstituted) pyrrole,[6] or oxidation of a dipyrromethane with DDQ,[7] the resulting free-bases are frequently unstable, particularly when lacking substituents in the α-positions (i.e., 1 and 9-positions, **1**, Figure 1) or in the absence of deactivating groups, and are usually isolated as their crystalline HBr salts. Surprisingly, there are limited reported examples of the chemical manipulation of dipyrrins themselves.[3,4]

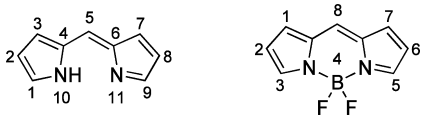


Figure 1. Skeletal structures of dipyrrins (**1**) and *F*-BODIPYs (**2**).

To overcome this inherent instability, dipyrrins may be isolated as neutral complexes of the respective dipyrrinato ligands coordinated to a transition metal center[8] or as the corresponding 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (boron difluoride dipyrrinato complex, *F*-BODIPY,[9,10] **2**, Figure 1). Although these strategies enable purification and have certain synthetic advantages, lability and stability, respectively, limit their utility: (i) lability of the dipyrrinato ligands from transition metals under acidic conditions results in untimely deprotection; and (ii) the high stability of *F*-BODIPYs under most reaction conditions, and so removal of the BF_2 moiety has been previously unavailable.

First reported in 1968,[11] *F*-BODIPYs are widely used as labeling dyes in biological systems,[12,13] courtesy of intense absorption and fluorescence spectroscopic properties.[9,10,14] Furthermore, their high quantum yields and tunable structure-based fluorescence properties facilitate their utility in areas as diverse as electroluminescent films,[15−17] dye lasers,[18−20] fluorescent switches,[21] sensitizers for solar cells,[22] and electron-transfer reagents.[23] Unlike dipyrrins or their transition metal complexes, *F*-BODIPYs exhibit low sensitivity to solvent polarity and pH,[9,12] and possess other desirable chemical properties, such as good solubility plus high thermal and photochemical stability.[24]

The conversion of dipyrrins to the corresponding *F*-BODIPYs is thus an ideal protecting group strategy, particularly as *F*-BODIPYs are typically facile to isolate owing to their distinct fluorescent properties and stability. However, for the use of boron difluoride complexes of dipyrrins to be considered as a viable protecting group strategy, facile removal of the BF_2 unit to reveal the parent dipyrrin is essential. We recently communicated the first general method for the decomplexation of *F*-BODIPYs using a microwave-assisted procedure: deprotection employed 6 equiv of potassium *tert*-butoxide in *tert*-butanol solvent, with heating at 92 °C in a sealed vessel for 40 min.[25] Good to excellent isolated yields were obtained for a range of substituted dipyrrins, both meso-substituted and unsubstituted, providing scope for BF_2-complexation to become a common protecting group strategy for the synthesis and manipulation of dipyrrins. We herein report the full scope of this deprotection, alongside simplified and further optimized reaction conditions, as well as the first application in the synthesis of pyrrolyldipyrrins.

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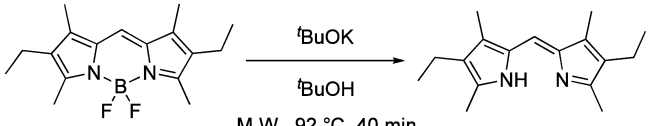
RESULTS AND DISCUSSION

Previous results[25] were obtained using a CEM Mars-X microwave digestion oven. We wished to evaluate the protocol using a standard robot microwave reactor, and we chose BODIPY **3** as our model substrate given its ease of synthesis and its full substitution pattern about the pyrrolic periphery. Furthermore, **3** features a meso-unsubstituted dipyrrin and we wished to work with this class of BODIPY since useful deprotection conditions must facilitate the isolation of free-base meso-unsubstituted dipyrrins, compounds that are rather less stable than meso-substituted dipyrrins. Using the robot microwave reactor, deprotection of **3** was successful using the original conditions and gave the corresponding dipyrrin (**4**) in an 85% yield (Scheme 1), comparable to that previously

Scheme 1. Assessment of Deprotection Reaction using Robot Microwave Reactor

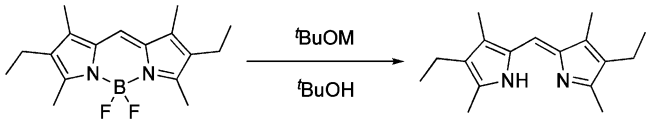


reported (90%).[25] Note that under these conditions, the solvent is heated past its boiling point inside the appropriate pressure-resistant microwave vial for the microwave reactor being used.

To optimize, and hopefully simplify, the reaction conditions for use in the robot microwave reactor, we investigated the role of each component of the reaction mixture.

Variation of Associated Cation. We first examined the influence of the cation associated with the *tert*-butoxide nucleophile. This showed a trend, with smaller and more strongly associated cations resulting in less effective deprotection and a decrease in isolated yield of product **4** (Table 1, entries 1–3).

Table 1. Effect of Cation[a]



entry	M	product **4** (%)[b]	recovered starting material **3** (%)[b]
1	K	85	0
2	Na	71	0
3	Li	21	68

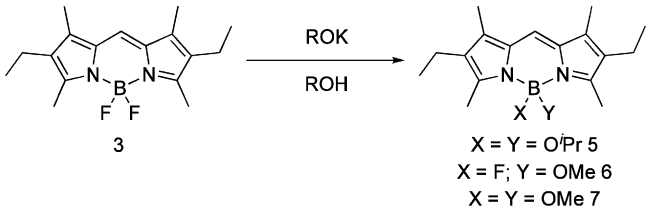
[a]Reactions carried out in a robot microwave reactor, with 6 equiv of ^{t}BuOM and heating at 92 °C for 40 min. [b]Isolated yield.

We concluded from this series of results that the ability of the alkoxide to dissociate from its counterion is a key factor for successful deprotection reactions, and so potassium remained our cation of choice.

Variation of Alkoxide. This study focused on the roles of steric effects and the nucleophilic nature of the reagent. To this end, isopropoxide and methoxide, alongside *tert*-butoxide, were selected for study.

In contrast to the success observed when using ^{t}BuOK, the use of isopropoxide as the base resulted in no deprotection of the starting *F*-BODIPY (**3**) to reveal the free dipyrrin. Instead, nucleophilic substitution of the two fluorine atoms at boron occurred to generate the diisopropoxide-BODIPY **5** in a 51% yield (Table 2, entry 2). The use of methoxide, also as its

Table 2. Effect of Alkoxide[a]



entry	R	product obtained	yield (%)[b]
1	^{t}Bu	**4**	85
2	^{i}Pr	**5**	51
3	Me	**6** + **7**	48 (**6**) and 52 (**7**)

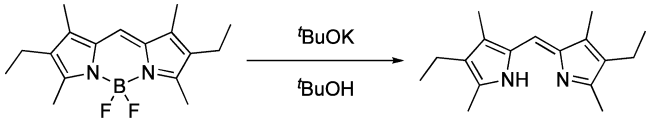
[a]Reactions carried out in a robot microwave reactor, with 6 equiv of ROK and heating at 92 °C for 40 min. [b]Isolated yield.

potassium salt, was then examined. Again, decomplexation of the BF_2 moiety was unsuccessful: this reaction resulted in two fluorescent compounds, which were isolated and identified as the previously reported mono- and dimethoxy substituted BODIPYs **6** and **7** in yields of 48 and 52%, respectively (Table 2, entry 3).[25] This study revealed that the use of a strong and bulky alkoxide base were key factors for successful removal of the BF_2 moiety from *F*-BODIPYs. Furthermore B–O bond formation, with concomitant B–F bond breakage, is preferred where sterically feasible under the reaction conditions, resulting in the corresponding *O*-BODIPY. As such, ^{t}BuOK is the reagent of choice.

Stoichiometry. We then examined the importance of the stoichiometry of ^{t}BuOK, with a view to gaining insight into the deprotection mechanism. On the basis of original observations[25] that the use of 3 equiv of ^{t}BuOK resulted in quantitative recovery of starting material, we suspected there to be a threshold for the amount of reagent required for effective deprotection. In the early screens, however, reactions were carried out for only 15 min.[25]

Results from reactions carried out over 40 min demonstrated a more linear trend between equivalents of ^{t}BuOK used and the effectiveness of the deprotection to give the dipyrrin **4** (Table 3).

Table 3. Variation of ^{t}BuOK Stoichiometry[a]



entry	equiv ^{t}BuOK	product **4** (%)[b,c]	recovered starting material **3** (%)[b]
1	8	74 (71)	0
2	6	85 (74)[d]	0
3	5	55 (57)	0
4[e]	4	26 (31)	0
5[e]	3	21	6
6[e]	2	trace	33
7[e]	1	0	70

[a]Reactions carried out in a robot microwave reactor, with heating at 92 °C for 40 min. [b]Isolated yield. [c]Repeat reaction in parentheses. [d]Repeat reaction carried out at 105 °C. [e]Intermediate **8** observed.

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We observed a gradual increase in isolated yield of the dipyrrin (**4**) and a concurrent decrease in the amount of starting material (**3**) recovered as the number of equivalents of ^{t}BuOK was increased (entries 2−7). Addition of 8 equiv of ^{t}BuOK (entry 1) did not serve to provide dipyrrin **4** in a greater yield than the use of 6 equiv of ^{t}BuOK, neither did increasing the temperature to 105 °C (entry 2, repeat).

During the course of our studies regarding the stoichiometry of reactants (Table 3), several milligrams of an unknown fluorescent compound were isolated from reactions involving 1−4 equiv of ^{t}BuOK (entries 4−7). Following analysis, this compound was identified as the mono-*tert*-butoxide BODIPY (**8**, Figure 2) in a yield of <4% in each case. Isolation of this

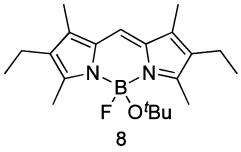

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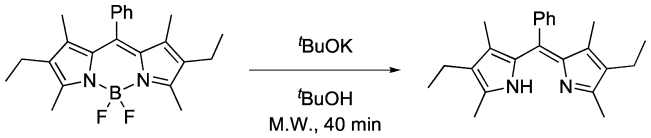
Figure 2. Isolated intermediate.

intermediate was significant as it indicated the role of *tert*-butoxide as a bulky nucleophile able to form B−O bonds. This finding provides key mechanistic insight into the deprotection reaction, and supports a step-wise substitution process whereby the accommodation of two *tert*-butoxy substituents is unviable for maintaining N−B−N chelation (unlike for OMe and O^{i}Pr derivatives), and so deprotection thus ensues.

In the original study, the BF_2-deprotection reaction was optimized for the *meso*-phenyl substituted BODIPY **9**.[25] A trial deprotection of this complex using the robot microwave reactor resulted in complete consumption of the starting material (**9**), according to analysis using TLC, but only 9% isolated yield of free dipyrrin **10** was obtained (Table 4, entry 1). This did not

Table 4. Re-examination of Deprotection of 9[a]



entry	equiv base	temp. (°C)	**10** (%)[b]
1[c,d]	6	92	9
2[e]	6	140	82

[a]Reactions carried out in a robot microwave reactor, with heating for 40 min. [b]Isolated yield. [c]15 mL of solvent. [d]Byproduct **11** isolated in 40% yield. [e]10 mL of solvent.

match with the previous success (92% of **10** isolated)[25] using the same conditions (time, temperature, and equivalents of ^{t}BuOK) using the Mars-X microwave oven. In addition, a previously unobserved fluorescent compound was isolated, analysis of which indicated the dihydroxy BODIPY **11** (Figure 3) in a 40% isolated yield after aqueous workup between ethyl acetate and saturated aqueous sodium bicarbonate solution, and purification via column chromatography over basic alumina, eluting with 0−5% methanol in ethyl acetate.

There are limited reports of the isolation of boron complexes of this type,[26−28] in which the boron atom bears two hydroxyl substituents, most likely owing to their relative instability and

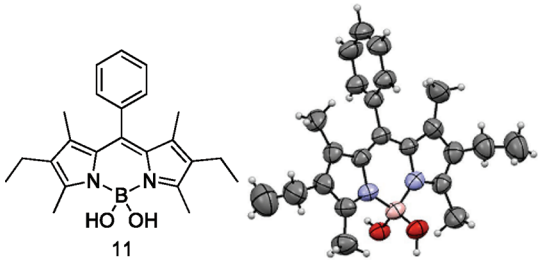


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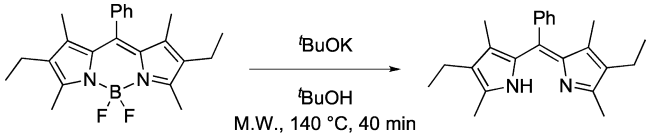
Figure 3. Isolated dihydroxy BODIPY **11**, with X-ray crystal structure.

their propensity to decompose to yield boric acid under aqueous/acidic conditions.[27,29] However, we obtained a crystal structure of this unexpected byproduct, which confirmed the presence of two boron-hydroxyl substituents. Solving the structure also revealed stabilizing solvent bonding interactions (see Supporting Information). To the best of our knowledge, this is the first X-ray-confirmed structure of a dihydroxy-*O*-BODIPY.

Returning to the deprotection of **9**, we decided to re-examine the reaction conditions. In the original trials, the reactions were carried out at 600 W.[25] However, the power of the robot microwave model only reached 300 W during the reaction. It was suspected that while this lower power is sufficient for the *meso*-H BODIPY **3**, additional energy may be required for the efficient deprotection of the *meso*-phenyl BODIPY **9**. The reaction was therefore repeated at 140 °C (Table 4, entry 2). As hoped, this resulted in a more effective deprotection and a higher yield of dipyrrin **10**.

Effect of Water. We then investigated the water content of the solvent. Results from this series of reactions, using a new bottle of HPLC grade solvent so as to be sure of the analytical constitution, showed a correlation between the amount of water present and the amount of product isolated (Table 5): a

Table 5. Investigation of the Effect of Water on the Deprotection of 9[a]



entry	solvent grade	equiv water added	**10** (%)[b]
1	HPLC	0	62
2	HPLC	20	71
3	HPLC	50	71
4[c]	HPLC	100	59

[a]Reactions carried out in a robot microwave reactor, using 10 mL of solvent, with heating at 140 °C for 40 min. [b]Single isolated yields. [c]Byproduct observed.

yield of 71% was obtained following the addition of both 20 and 50 equiv of water, with respect to the stoichiometry of *F*-BODIPY **9** (Table 5, entries 2 and 3). Further increasing the amount of water present resulted in a lower isolated yield (Table 5, entry 4), along with the observed formation of the corresponding dihydroxy-BODIPY (<5%), similar to that previously encountered (**11**, Table 4, entry 1).

Examination of KOH. With such a large quantity of water present in the reaction, we believed that potassium hydroxide could be an equally effective reagent as it would undoubtedly

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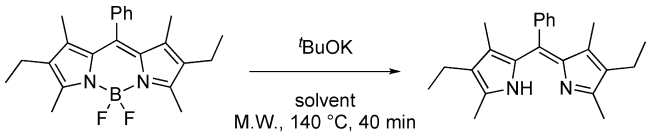
be forming in situ in the *tert*-butanol. A trial reaction was thus carried out in which 10 equiv of potassium hydroxide were used instead of the usual potassium *tert*-butoxide, and without the addition of water (Table 6, entry 1). This modification resulted in complete decomplexation, with an 80% isolated yield of the product (**10**).

Table 6. Examination of KOH as a Base for the Deprotection of 9[a]



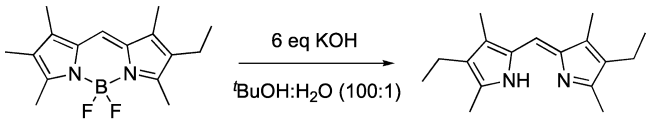
entry	solvent	equiv. KOH	Temp (°C)	**10** (%)[b,c]
1	^{t}BuOH	10	140	80 (75)
2	DMSO	10	140	0[d,e]
3	^{t}BuOH	6	140	83
4	^{t}BuOH	3	140	78[d]
5	^{t}BuOH	6	92	43[d]

[a]Reactions carried out in a robot microwave reactor in 10 mL of HPLC grade solvent, with heating for 40 min, unless otherwise stated. [b]Isolated yield. [c]Repeat reaction in parentheses. [d]Decomposition products observed. [e]Sixteen percent of **9** recovered.

Recalling the isolation of intermediate **8** in earlier studies, we believe that *tert*-butoxide is still the reactive species and is formed in situ. To test this theory, the reaction was repeated using DMSO as the solvent (Table 6, entry 2); no signs of deprotection were observed. The optimum amount of KOH was assessed and found to be 6 equiv (Table 6, entry 3), comparable to earlier results stemming from the use of potassium *tert*-butoxide (Table 3). The effect of temperature upon the reaction was probed, whereby higher temperatures were still found to be essential using the lab robot microwave, which operated at a lower power rating compared to that obtainable in the original Mars-X microwave oven.

The use of KOH was also assessed in the deprotection of **3**, whereby initial reactions carried out under the same conditions, at temperatures of both 92 and 140 °C, were disappointing, resulting in yields of 38 and 59% of dipyrrin **4**, respectively (Table 7, entries 1 and 2). Modification of the conditions to include the presence of water, in a convenient 100:1 (v/v) ratio of ^{t}BuOH/H_2O, and maintaining the higher temperature of 140 °C resulted in a significantly improved isolated yield (88%) of the decomplexed product **4** (Table 7, entry 3). Excellent yields were also attainable after reaction times of 15 and 5 min (Table 7, entries 4 and 5), suggesting that microwave irradiation during the first few minutes of the reaction is sufficient to disrupt B–N bonding. Very short reaction times would also prove to be of use with less stable substrates. Unsurprisingly, conducting the reaction in water, in the absence of *tert*-butanol, again resulted in no observed formation of dipyrrin **4** (Table 7, entry 6), with a 54% recovery of starting material (**3**) resulting instead.

Table 7. Modified BF_2-Deprotection of 3 Using KOH[a]

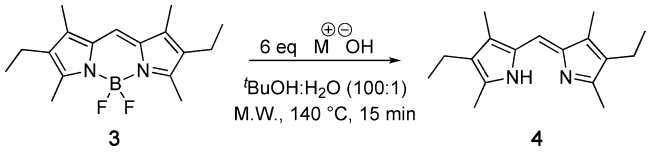


entry	temp (°C)	time (min)	**4** (%)[b,c]
1[d]	92	40	38[e]
2[d]	140	40	59
3	140	40	88 (88)
4	140	15	95
5	140	5	97
6[f]	140	15	0[e,g]

[a]Reactions carried out in a robot microwave reactor in 10 mL of HPLC grade solvent. [b]Isolated yield. [c]Repeat reaction in parentheses. [d]Without the addition of water. [e]Decomposition products observed. [f]One hundred percent water solvent used. [g]Fifty-four percent of **3** recovered.

We then determined the influence of the cation used in conjunction with hydroxide. Sodium and lithium hydroxide were thus employed in separate reactions, the outcome of which was very similar to that seen previously: slight reduction in yield going from potassium to sodium counterion (Table 8, entries 1 and 2), then a significant decrease in yield, along with a considerable amount of recovered starting material, when using the lithium salt (entry 3). The similarity between these results (Tables 1 and 8) suggest that the same mechanism is in operation in both cases.

Table 8. Effect of Hydroxide Counterion[a]



entry	M^+	**4** (%)[b]	**3** (%)[b]
1	K	95	0
2	Na	83	0
3	Li	33	44

[a]Reactions carried out in a robot microwave reactor in 10 mL of HPLC grade solvent. [b]Isolated yield.

Now satisfied with our optimized set of reaction conditions, we applied them to a series of substituted *F*-BODIPYs to examine the scope of the reaction (Table 9).

Table 9. Investigations Regarding the Scope of the Newly Developed Reaction Conditions, As Applied to the Deprotection of Various *F*-BODIPYs[a]

entry	starting material	R^1	R^2	yield (%)[b]
1	**3**	Et	H	88 (97)[c] (**4**)
2	**9**	Et	Ph	94 (**10**)
3	**12**	Et	Me	89 (97)[c,d] (**16**)
4	**13**	H	H	79[e] (**17**)
5	**14**	Ac	Ph	45[f] (**18**)
6	**15**	$C(O)C_6H_{13}$	H	0[f] (**19**)

[a]Reactions carried out in a robot microwave reactor in 10 mL of HPLC grade solvent. [b]Isolated yield. [c]Repeat reaction in parentheses was carried out for 5 min. [d]Product isolated as the vinylic dipyrrole tautomer (see Experimental Section). [e]Product isolated as the zinc-complex to avoid handling the free-base dipyrrin, which is a powerful sternutator (see Experimental Section). [f]Decomposition products observed.

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A variety of symmetric *F*-BODIPYs were examined, for example, those bearing *meso*-H (**3**, **13**, **15**), alkyl (**12**), and aryl (**9**, **14**) substituents, and were generally found to undergo clean deprotection under the optimized conditions using 6 equiv KOH and the addition of water (100:1, ^{t}BuOH/H_2O). Furthermore, we looked at a β-unsubstituted BODIPY (**13**) and those bearing ketone substituents (**14**, **15**). Yields for these reactions were excellent in general, with the exception of the keto-substituted BODIPYs (**14** and **15**, Table 9, entries 5 and 6), to the extent that no product was isolated from the less stable substrate **15**. In these cases, side reactions between the ketone moiety and hydroxide reagent must be in operation. No starting material was recovered in either case, and the reactions were not improved upon reducing the duration of the reaction and/or temperature.

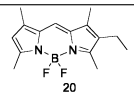
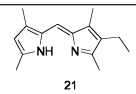
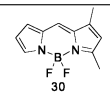
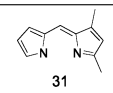
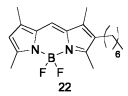
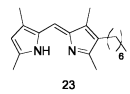
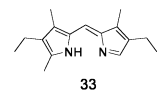
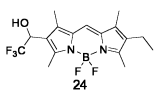
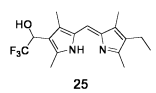
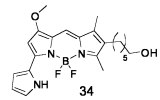
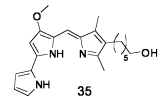
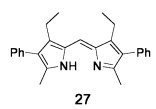
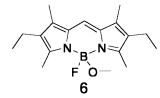
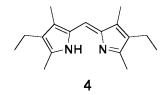
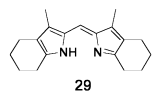
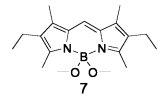
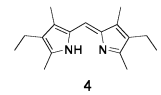
We wanted to test our improved deprotection protocol on more challenging substrates, to further address the question of substrate scope (Table 10). A wide range of *F*-BODIPYs were chosen, that were both symmetric (**26**, **28**) and asymmetric (**20**, **22**, **24**, **30**, **32**, **34**), with functionality that included one or multiple unsubstituted positions (**20**, **22**, **30**, **32**, **34**), long chain alkyl (**22**), aromatic (**26**), or hydroxy (**24**) substituents and increased steric crowding around the boron center (**28**). In almost all cases, the corresponding dipyrrin was obtained in excellent yield, demonstrating good functional group tolerance. Increasing the steric congestion around the boron center (**28**, Table 10, entry 5) resulted in a slight decrease in isolated yield of the product (**29**) compared to the open chain substrate (**3**) under the same reaction conditions (Table 8, entry 3). This was expected based on previous observations.[25]

The presence of α-H or β-H substituents in general were well tolerated, giving rise to acceptable product yields (Table 10, entries 1, 2, and 7). However, replacing one of the α-methyl groups of **3** with a proton resulted in a 16% decrease in yield under the same reaction conditions (Table 10, entry 7), and further reducing the substitution (**30**, Table 10, entry 6) resulted in a mere 26% yield of **31**. This trend in isolated yield was anticipated based on the knowledge that the completely unsubstituted dipyrrin is unstable above −40 °C,[30] and these lower yields are thus attributed to the relative instability of the forming dipyrrin.

A more structurally complex substrate examined in this series of deprotection reactions was *F*-BODIPY-protected pyrrolyldipyrrin **34** (Table 10, entry 8). Pleasingly, the deprotection proceeded smoothly, as hoped, giving the corresponding pyrrolyldipyrrin (**35**) in a 94% yield, with minimal purification required.

The deprotections of the mixed *F*-, *O*-BODIPY **6** and the *O*-BODIPY **7** were explored (Table 10, entries 9 and 10), whereby the former was found to be a viable substrate, giving the product (**4**) in a good yield of 89%. Dimethoxy BODIPY **7**, on the other hand, did not undergo decomplexation, the reaction instead resulting in only decomposition products. These results are comparable to those obtained in earlier studies,[25] and demonstrate the mechanistic need for the *F*-BODIPY boron center to accept an oxygen based nucleophile,

Table 10. Microwave-Assisted Deprotection of Further BODIPY Substrates[a]

entry	substrate	product	yield (%)[b]	entry	substrate	product	yield (%)[b]
1	 20	 21	98	6	 30	 31	26[c,d]
2	 22	 23	95	7	 32	 33	81[c]
3	 24	 25	96	8	 34	 35	94
4	 26	 27	83	9	 6	 4	89
5	 28	 29	72	10	 7	 4	<10[d]

[a]Reactions carried out in a robot microwave reactor in 10 mL of HPLC grade solvent for 15 min. [b]Isolated yield. [c]Reaction was carried out for 5 min. [d]Decomposition products observed.

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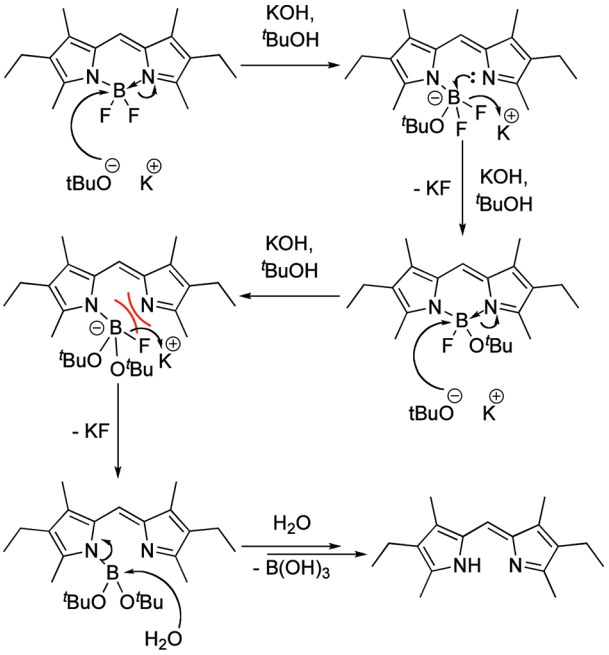
forming a stronger B−O bond. This is not advantageous for *O*-BODIPY **7** as it already has two such B−O bonds.

Proposed Deprotection Mechanism. Results to date have enabled us to propose a mechanism for the deprotection reaction (Scheme 2). On the basis of the observation that

Scheme 2. Proposed Mechanism for BF_2 Removal



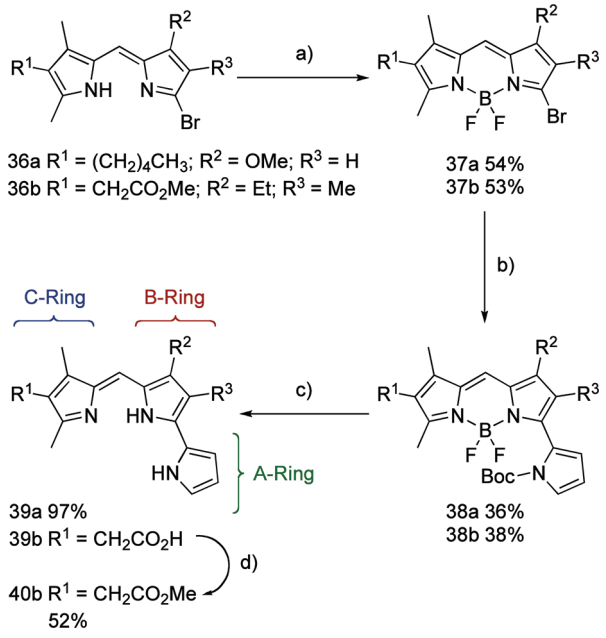
mixed *F*-, ^{t}BuO-BODIPY **8** (Figure 2) was formed as an intermediate during one study (Table 3), we believe that *tert*-butoxide is the active reagent, formed in situ from potassium hydroxide and *tert*-butanol.

This reagent is thought to attack the boron center, forming a strong B−O bond and temporarily disrupting one of the weaker boron nitrogen bonds.[31] This is followed by recomplexation of boron to nitrogen, with loss of fluoride, giving the observed BODIPY intermediate **8**. Attack of a second equivalent of *tert*-butoxide ensues, with the steric bulk of the two bulky pendant alkoxide groups preventing recomplexation. Loss of fluoride forms a charge-neutral species that undergoes further nucleophilic attack, presumably by a smaller hydroxide species to explain the need for water, resulting in complete dissociation of boron to give the free-base dipyrrin, which is stabilized by the basic reaction conditions. With bulky *tert*-butyl groups being key to the sterically inhibited reformation of the B−N bond, the isolation of *O*-BODIPYs when using the small alkoxides methoxide and isopropoxide as reagents can be appreciated (Table 2, compounds **6** and **7**).

***F*-BODIPYs as a Protecting Group Strategy.** We were satisfied with the efficacy of our improved deprotection protocol and wished to evaluate the potential for BF_2 complexation to be used as a protecting group strategy in a multistep synthesis. The design and synthesis of C-ring modified pyrrolyldipyrrins is an ongoing area of interest, and this seemed like the perfect model for study. Our initial target was **39a**, chosen for the purpose of comparison to the traditional synthetic approach. Starting from 2,4-dimethyl-3-pentyl-1*H*-pyrrole-5-carboxaldehyde, the synthesis of 2-pentyl-9-bromodipyrrin **36a** followed a previously reported synthetic pathway.[32]

At this point, the synthesis deviated from the traditional route, with conversion of the dipyrrin **36a** to the protected BF_2 complex (**37a**) by reaction with boron trifluoride diethyl etherate, in the presence of triethylamine (Scheme 3). This proceeded in a 54% isolated yield of **37a**, after a slightly extended reaction time of 18 h, but without further optimiza-

Scheme 3. Application of BF_2 Protection to the Synthesis of Pyrrolyldipyrrins[a]



[a]Reaction conditions: (a) $BF_3.OEt_2$, NEt_3, CH_2Cl_2, N_2, rt, 18 h; (b) *N*-Boc pyrrole-2-boronic acid, LiCl, $Pd(PPh_3)_4$, 1,2-DME, 2 M aq Na_2CO_3, 85 °C, 24 h; (c) KOH, ^{t}BuOH·H_2O (100:1 v/v), MW, 140 °C, 15 min; (d) H_2SO_4, MeOH, Δ, 3 h.

tion of existing methods. This bromo-substituted *F*-BODIPY (**37a**) was then subjected to Suzuki coupling reaction with *N*-Boc-pyrrole-2-boronic acid, which completed the synthesis of the pyrrolyldipyrrin core, but surprisingly left the *N*-Boc group intact, as opposed to the in situ deprotection normally observed.[33] The enhanced stability of the *N*-Boc group is attributed to the electron withdrawing nature of the BF_2 moiety. The isolated yield for this reaction (**38a**, 36%) was slightly higher than that of the non-BF_2-protected bromo-dipyrrin (30% average yield). The final step of deprotection worked exceptionally well: decomplexing the BF_2 moiety and removing the *N*-Boc group under our new optimized conditions gave **39a** in an excellent 97% isolated yield following purification over neutral alumina.

The success of this synthesis (Scheme 3) demonstrated the use of a BF_2-protecting group strategy for the synthesis of pyrrolyldipyrrins as a viable alternative to the traditional synthesis. We thus turned our attention to a more challenging target to test the utility of this alternative approach. Bromo-dipyrrin **36b**, possessing an alkyl ester on the future C-ring and alkyl substituents on what was to become the B-ring, was chosen as a second trial starting material, which was protected with BF_2 under the same reaction conditions and in comparable yield (53%). *F*-BODIPY **37b** then underwent Suzuki coupling to give protected pyrrolyldipyrrin **38b**, again in comparable yield and still possessing the *N*-Boc group. Deprotection at this stage was further complicated by the presence of an additional ester group that would undoubtedly be hydrolyzed to give free carboxylic acid **39b**. The reaction mixture was thus concentrated and the crude product simply subjected to re-esterification

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conditions. This provided us with the corresponding methyl ester pyrrolyldipyrrin (**40b**) in an overall 52% isolated yield (from **38b**).

Previous attempts within the group to synthesize pyrrolyldipyrrins lacking the B-ring methoxy group have proved especially challenging, with the final Suzuki coupling reaction often proceeding in yields of <5%.[33] This is also true of certain bromo- and triflate-dipyrrins that lack a deactivating group (e.g., carbonyl) directly adjacent to the pyrrole ring. This work thus represents an important alternative for the synthesis of pyrrolyldipyrrins with diverse substitution patterns and represents just one example of the broad scope of BF_2 complexation for the protection and chemical manipulation of dipyrrins.

CONCLUSIONS

We have developed a microwave-assisted procedure for the removal of BF_2 from *F*-BODIPYs to reveal the free-base dipyrrin. Optimization of the protocol resulted in a general procedure for use in a standard lab robot microwave, with potassium hydroxide as an improved reagent and a shorter reaction time of 5 min. This method is effective for a wide range of *F*-BODIPYs, with studies also providing insight into the deprotection mechanism. Further work included the application of this methodology to the synthesis of both known and novel pyrrolyldipyrrins, whereby it was found that the use of a BF_2 moiety as a protecting group enables the synthesis of more challenging target compounds.

EXPERIMENTAL SECTION

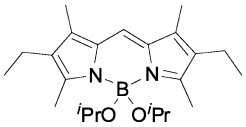
General Methods. All chemicals and reagents were purchased from commercial sources and were used as received, unless otherwise noted. Ethyl acetate, hexanes, dichloromethane, and *tert*-butanol were obtained crude and purified via distillation, under air and at 1 atm pressure, before use. HPLC grade methanol, chloroform, and *tert*-butanol were employed in reactions where stated. Anhydrous dichloromethane was purchased from EMD Chemicals. Column chromatography was performed using 230−400 mesh Silicycle Ultra Pure Silica Gel, 150 mesh Brockmann III activated neutral aluminum oxide, or 150 mesh Brockmann III activated basic aluminum oxide, as indicated. TLC was performed on silica gel or neutral aluminum oxide plates and visualized using UV light (254 and/or 365 nm) and/or developed with Vanillin stain. NMR spectra were recorded using a 500 or 250 MHz spectrometers. All ^{1}H, ^{11}B, and ^{13}C NMR 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); DMSO (^{1}H 2.50 ppm; ^{13}C 39.52 ppm)] as the internal reference or $BF_3.OEt_2$ (^{11}B 0.00 ppm) as an external reference. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; at, apparent triplet; q, quartet; m, multiplet; sep, septet. All coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were recorded using ion trap (ESI TOF) instruments. UV analysis was carried out using HPLC grade dichloromethane solvent, with the baseline manually corrected for the solvent, and the wavelength measured in nanometers (nm). Microwave reactions were carried out using a robot-type microwave reactor (in our case a Biotage Initiator 8 Microwave) with 0−400 W power at 2.45 GHz with an integrated internal probe by which to monitor the temperature of the reaction mixtures.

Synthesis of *F*-BODIPYs. *General Procedure for the Synthesis of F-BODIPYs (**GP1**).* Triethylamine (6 mmol, 6 equiv) was added dropwise to a solution of dipyrrin HBr salt (1 mmol, 1 equiv) in dry dichloromethane (65 mL) under nitrogen, with stirring at room temperature for 10 min. Boron trifluoride diethyl etherate (9 mmol, 9 equiv) was then added dropwise over 5 min and the resulting solution was stirred at room temperature, under nitrogen, for 2 h, before concentrating in vacuo and separating the residue between diethyl ether (80 mL) and 1 M aqueous HCl (80 mL). The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the organic extracts were combined and washed with brine, dried over anhydrous magnesium sulfate, filtered through a short pad of silica, washed with diethyl ether, and concentrated in vacuo. This gave the corresponding *F*-BODIPY without the need for further purification, unless otherwise stated.

*4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**3**).*[25]

Compound **3** was synthesized from the corresponding dipyrrin·HBr salt[34] using GP1 as a shiny reddish-brown solid (3.703 g, 82% yield). Mp 178−181 °C; ^{1}H NMR ($CDCl_3$, 500 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). NMR data matches that previously reported for this compound.[25]

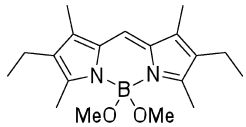
*4,4-Diisopropoxy-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**5**).*



Potassium isopropoxide (5% solution in isopropyl alcohol, 1.97 mL, 0.99 mmol) was added to a stirred suspension of **3** (50 mg, 0.16 mmol) in freshly distilled isopropoxide (15 mL) in a 20 mL capacity microwave vial. The vial was then sealed and placed in the microwave reactor, where it was heated at 92 °C for 40 min, at a maximum of 400 W power. After cooling, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (50 mL) and diethyl ether (50 mL). The aqueous phase was extracted with diethyl ether (2 × 50 mL) and the combined organic extracts were washed with brine (100 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was purified using column chromatography on basic alumina (Brockmann type III), eluting with 15% ethyl acetate in hexanes, to give the product **5** (32 mg, 51% yield) as an orange solid. Mp 135−138 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.90 (s, 1H), 3.21 (sep, 2H, J = 6.0 Hz), 2.54 (s, 6H), 2.38 (q, 4H, J = 7.5 Hz), 2.18 (s, 6H), 1.04 (t, 6H, J = 7.5 Hz), 0.80 (d, 12H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.6, 134.7, 133.4, 131.6, 118.3, 62.9, 24.9, 17.6, 15.0, 13.7, 9.6; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 1.63 (s); LRMS-ESI (m/z): 407.3 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{23}H_{37}N_2BO_2Na$ 407.2844; found, 407.2840; $\varepsilon_{529\ nm}$ = 86 000.

*4-Fluoro-4-methoxy-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**6**)*[25] *and 4,4-Dimethoxy-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**7**).*[25]

6



7

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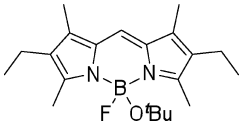
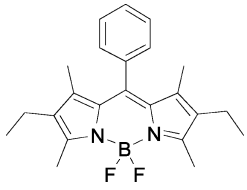
Potassium methoxide (69 mg, 0.99 mmol) was added to a stirred suspension of **3** (50 mg, 0.16 mmol) in methanol (15 mL) in a 20 mL capacity microwave vial. The vial was then sealed and placed in the microwave reactor, where it was heated at 92 °C for 40 min, at a maximum of 400 W power. After cooling, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (50 mL) and diethyl ether (50 mL). The aqueous phase was extracted with diethyl ether (2 × 50 mL) and the combined organic extracts were washed with brine (100 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was purified using column chromatography on basic alumina (Brockmann type III), eluting with 10−30% ethyl acetate in hexanes, to give **6** (25 mg, 48%) as a dark red solid; mp 140−143 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.93 (s, 1H), 2.89 (s, 3H), 2.49 (s, 6H), 2.39 (q, 4H, J = 7.5 Hz), 2.17 (s, 6H), 1.06 (t, 6H, J = 7.5 Hz); and compound **7** (28 mg, 52%) as a dark red solid. Mp 143−146 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.91 (s, 1H), 2.85 (s, 6H), 2.47 (s, 6H), 2.39 (q, 4H, J = 7.5 Hz), 2.17 (s, 6H), 1.07 (t, 6H, J = 7.5 Hz). NMR data matches that previously reported for these compounds.[25]

*4-Fluoro-4-^{t}butoxy-1,3,5,7-tetramethyl-2,6-diethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**8**).*



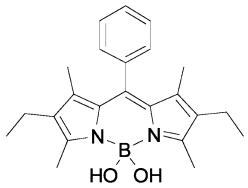
Potassium *tert*-butoxide (55 mg, 0.49 mmol) was added to a stirred suspension of **3** (75 mg, 0.25 mmol) in *tert*-butanol (15 mL) in a 20 mL capacity microwave vial. The vial was then sealed and placed in the microwave reactor, where it was heated at 92 °C for 40 min, at a maximum of 400 W power. After cooling, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (50 mL) and diethyl ether (50 mL). The aqueous phase was extracted with diethyl ether (2 × 50 mL) and the combined organic extracts were washed with brine (100 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was purified immediately using column chromatography on basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, to give the product **8** (2 mg, 2% yield) as a deep pink film. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.92 (s, 1H), 2.52 (s, 6H), 2.37 (q, 4H, J = 7.5 Hz), 2.16 (s, 6H), 1.03 (t, 6H, J = 7.5 Hz), 0.85 (s, 9H); ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.45 (d, J = 23.8 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ 151.0; LRMS-ESI (m/z): 381.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{21}H_{32}N_2BOFNa$ 381.2482; found, 381.2484. Starting material **3** (25 mg, 33%) was also recovered.

*4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diethyl-8-phenyl-4-bora-3a,4a-diaza-s-indacene (**9**).*[25]



2,4-Dimethyl-3-ethylpyrrole (2.0 mL, 14.8 mmol) was added to a stirred solution of benzaldehyde (0.50 mL, 4.9 mmol) in 0.18 M aqueous HCl (50 mL), with stirring at room temperature for 4 h.[35] The precipitate formed during this time was then extracted into ethyl acetate (3 × 50 mL) and the combined organic extracts were washed with water (100 mL) and brine (100 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give the crude product, which was purified using column chromatography on silica, eluting with 15% ethyl acetate in hexanes to give the desired dipyrromethane (1.39 g, 84%) as a light brown solid. DDQ (0.87 g, 3.8 mmol) was then added to a solution of the preceding dipyrromethane (1.28 g, 3.83 mmol) in anhydrous dichloromethane (80 mL), with stirring under nitrogen for 1 h. After this time, no starting material remained according to analysis using TLC, and thus, triethylamine (3.20 mL, 23.0 mmol) and then boron trifluoride diethyl etherate (4.25 mL, 34.5 mmol) were added dropwise over 5 min, with continued stirring for 3 h. The reaction mixture was then diluted with dichloromethane (50 mL) and washed with 0.1 M NaOH (100 mL), 1 M HCl (100 mL), and brine (100 mL); dried over anhydrous sodium sulfate; and concentrated in vacuo to give the crude product, which was purified using column chromatography on silica, eluting with 20% ethyl acetate in hexanes, to give **9** (0.689 g, 47%) as a dark red/green solid. Mp 165−167 °C; ^{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 = 7.5 Hz), 1.27 (s, 6H), 0.98 (t, 6H, J = 7.5 Hz). NMR data matches that previously reported for this compound.[25]

*4,4-Dihydroxy-1,3,5,7-tetramethyl-2,6-diethyl-8-phenyl-4-bora-3a,4a-diaza-s-indacene (**11**).*



Potassium *tert*-butoxide (89 mg, 0.79 mmol) was added to a stirred suspension of **9** (50 mg, 0.13 mmol) in *tert*-butanol (15 mL) in a 20 mL capacity microwave vial. The vial was then sealed and placed in the microwave reactor, where it was heated at 92 °C for 40 min, at a maximum of 400 W power. After cooling, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (50 mL) and diethyl ether (50 mL). The aqueous phase was then extracted with diethyl ether (50 mL) and ethyl acetate (50 mL) and the combined organic extracts were washed with brine (100 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was purified immediately using column chromatography on basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, followed by 5% methanol in ethyl acetate, to give **11** as a dark red solid (20 mg, 40% yield). Mp 125−130 °C (mp/dp); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47−7.45 (m, 3H), 7.28−7.26 (m, 2H), 2.63 (s, 6H), 2.29 (q, 4H, J = 7.5 Hz), 1.25 (s, 6H), 0.97 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.8, 140.0, 136.8, 136.6, 132.7, 130.8, 129.0, 128.6, 128.5, 17.3, 14.9, 13.3, 11.7; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 1.29 (s); LRMS-ESI (m/z) 333.2 [free base dipyrrin **4** + H]$^+$. A crystal suitable for X-ray crystallography was obtained by recrystallization of a solution of compound **11** in 10% ether in hexanes by slow evaporation at room temperature. Data for **11**: $C_{101}H_{138}B_4N_8O_8$, M = 1635.49, deep orange plate, 0.03 × 0.09 × 0.14 mm^3, triclinic, space group $P\bar{1}$, a = 12.86150(10) Å, b = 19.9997(4) Å, c = 20.5839(2) Å, V = 5113.57(12) Å^3, Z = 2, T = 296.1 K, ρ = 1.062 g cm^{-3}, μ(Mo Kα) = 0.066 mm^{-1}, 146 260 reflections (6659 unique, R_{int} = 0.121), R = 0.0667, R_w = 0.0715, GOF = 1.065.

Compound **11** was also synthesized according to the following procedure. BCl_3 (1 M in hexanes, 0.37 mL, 0.37 mmol) was added

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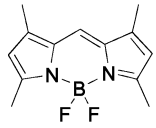
to a solution of **9** (70 mg, 0.18 mmol) in anhydrous dichloromethane (15 mL), with stirring at room temperature under nitrogen for 30 min. The reaction mixture was then partitioned between dichloromethane (50 mL) and saturated aqueous $NaHCO_3$ (50 mL) and the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to give the crude product, which was purified using column chromatography on basic alumina, eluting with 0−30% acetonitrile in dichloromethane, to give **11** (27 mg, 39%) as a shiny dark red solid.

*4,4-Difluoro-1,3,5,7,8-tetramethyl-2,6-diethyl-4-bora-3a,4a-diaza-s-indacene (**12**).*[25]

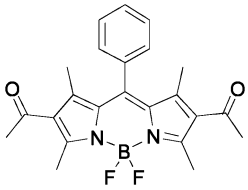
Compound **12** was synthesized from the corresponding dipyrrin·HCl salt[20] using GP1 as a dark red solid (285 mg, 92% yield). Mp 203−205 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.60 (s, 3H), 2.50 (s, 6H), 2.40 (q, 4H, J = 7.5 Hz), 2.33 (s, 6H), 1.04 (t, 6H, J = 7.5 Hz). NMR data matches that previously reported for this compound.[25]

*4,4-Difluoro-1,3,5,7-tetramethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**13**).*[25]



Compound **13** was synthesized from the corresponding dipyrrin·HBr salt[36] using GP1 as a dark red solid (208 mg, 94% yield). Mp 208−210 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.04 (s, 1H, *meso*-H), 6.04 (s, 2H), 2.53 (s, 6H), 2.24 (s, 6H). NMR data matches that previously reported for this compound.[25]

*4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diacetyl-8-phenyl-4-bora-3a,4a-diaza-s-indacene (**14**).*

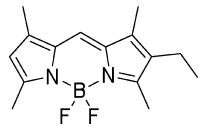


TFA (5 drops) was added to a solution of 3-acetyl-2,4-dimethylpyrrole[37] (1.50 g, 10.9 mmol) and benzaldehyde (0.56 mL, 5.5 mmol) in dichloromethane (200 mL), with stirring at room temperature under nitrogen for 24 h.[38] A solution of DDQ (1.24 g, 5.47 mmol) in dichloromethane (30 mL) was then added dropwise over 10 min, with continued stirring for 1 h. After this time, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (200 mL) and the aqueous phase was extracted with dichloromethane (2 × 150 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate, and concentrated to give the crude product, which was purified using column chromatography on basic alumina (Brockmann type III), eluting with 20−40% ethyl acetate in hexanes, to give the dipyrrin product (**18**, 540 mg, 27% yield) as a bright orange solid. Compound **14** was synthesized from the preceding dipyrrin (**18**) using GP1, followed by purification on neutral alumina, eluting with 10−30% ethyl acetate in hexanes to give the title compound as a bright orange solid (62 mg, 21% yield). Mp 190−195 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.55 (at, 3H, J = 3.3 Hz), 7.29−7.26 (m, 2H), 2.79 (s, 6H), 2.42 (s, 6H), 1.57 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 196.5, 158.0, 146.2, 144.8, 134.4, 130.0, 129.91, 129.86, 127.8, 127.7, 32.1, 15.2, 14.1; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.67 (t, J = 32.2 Hz); LRMS-ESI (m/z): 431.2 $[M + Na]^+$; HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{23}H_{23}N_2O_2BF_2Na$ 431.1706; found, 431.1713; $\varepsilon_{507\ nm}$ = 124 000.

*4,4-Difluoro-1,3,5,7-tetramethyl-2,6-diheptanoyl-8-H-4-bora-3a,4a-diaza-s-indacene (**15**).*

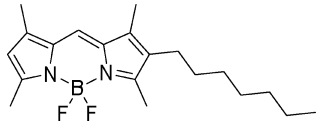
Compound **15** was synthesized from the corresponding dipyrrin using GP1, followed by purification on silica, eluting with 20% ethyl acetate in hexanes to give the title compound as a bright orange solid (235 mg, 61% yield). Mp 139−142 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (s, 1H), 2.80 (s, 6H), 2.75 (t, 4H, J = 7.3 Hz), 2.51 (s, 6H), 1.72−1.66 (m, 4H), 1.39−1.29 (m, 12H), 0.89 (t, 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 198.1, 160.5, 142.7, 133.3, 130.3, 123.4, 43.6, 31.9, 29.2, 24.2, 22.7, 15.8, 14.2, 12.7; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.81 (t, J = 32.2 Hz); LRMS-ESI (m/z): 495.3 $[M + Na]^+$; HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{27}H_{39}N_2O_2BF_2Na$ 495.2988; found, 495.2965; $\varepsilon_{511\ nm}$ = 155 000.

*4,4-Difluoro-1,3,5,7-tetramethyl-6-ethyl-2,8-H-4-bora-3a,4a-diaza-s-indacene (**20**).*



Compound **20** was prepared previously from the dipyrrin·HBr[39] salt using GP1 and repurified using column chromatography on silica, eluting with 5−10% ethyl acetate in hexanes. Mp 118−122 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (s, 1H), 6.00 (s, 1H), 2.51 (s, 6H), 2.39 (q, 2H, J = 7.7 Hz), 2.23 (s, 3H), 2.17 (s, 3H), 1.07 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.7, 155.4, 140.0, 137.7, 133.3, 133.0, 132.6, 119.4, 118.4, 17.5, 14.7, 14.6, 12.8, 11.3, 9.5; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.81 (t, J = 32.7 Hz); LRMS-ESI (m/z): 299.1 $[M + Na]^+$; HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{15}H_{19}N_2BF_2Na$ 299.1502; found, 299.1502; $\varepsilon_{519\ nm}$ = 95 000.

*4,4-Difluoro-1,3,5,7-tetramethyl-6-heptyl-2,8-H-4-bora-3a,4a-diaza-s-indacene (**22**).*

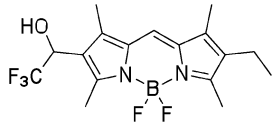


Compound **22** was synthesized from the corresponding dipyrrin·HBr salt using GP1, followed by purification on silica, eluting with 5−10% ethyl acetate in hexanes to give the title compound as a dark red solid (321 mg, 69% yield). Mp 68−72 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (s, 1H), 6.00 (s, 1H), 2.52 (s, 3H), 2.50 (s, 3H), 2.35 (t, 2H, J = 7.8 Hz), 2.23 (s, 3H), 2.16 (s, 3H) 1.45−1.39 (m, 2H), 1.32−1.26 (m, 8H), 0.89 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.9, 155.1, 139.9, 138.1, 133.2, 132.9, 131.3, 119.4, 118.3, 32.0, 30.2, 29.6, 29.3, 24.2, 22.8, 14.7, 14.3, 13.0, 11.4, 9.8; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.81 (t, J = 33.1 Hz); LRMS-ESI (m/z): 369.2

dx.doi.org/10.1021/jo3002003 | J. Org. Chem. 2012, 77, 3439−3453

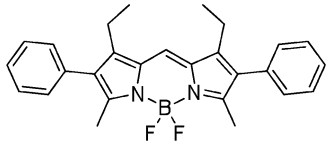
[M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{20}H_{29}N_2BF_2Na$ 369.2272; found, 369.2284; $\varepsilon_{520\ nm}$ = 81 000.

*4,4-Difluoro-1,3,5,7-tetramethyl-2-(2,2,2-trifluoroethanol)-6-ethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**24**).*[40]



Compound **24** was prepared previously from the dipyrrin·HBr salt[40] using GP1. Mp 177−180 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.04 (s, 1H), 5.08−5.03 (m, 1H), 2.55 (s, 3H), 2.53 (s, 3H), 2.47 (d, 1H, J = 3.5 Hz), 2.39 (q, 2H, J = 7.7 Hz), 2.28 (s, 3H), 2.18 (s, 3H), 1.07 (t, 3H, J = 7.7 Hz). NMR data matches that previously reported for this compound.[40]

*4,4-Difluoro-1,7-diethyl-2,6-diphenyl-3,5-dimethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**26**).*



Compound **26** was synthesized from the corresponding dipyrrin·HBr salt using GP1, followed by purification on silica, eluting with 10% ethyl acetate in hexanes to give the title compound as a bright orange solid (54 mg, 78% yield). Mp 190−195 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.44 (t, 4H, J = 7.5 Hz), 7.36 (t, 2H, J = 7.5 Hz), 7.27−7.25 (m, 4H), 7.17 (s, 1H), 2.64 (q, 4H, J = 7.5 Hz), 2.51 (s, 6H), 1.12 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.5, 144.2, 133.9, 132.2, 131.8, 129.8, 128.6, 127.3, 120.4, 18.2, 17.1, 13.5; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 1.0 (t, J = 34.1 Hz); LRMS-ESI (m/z): 451.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{27}H_{27}N_2BF_2Na$ 451.2140; found, 451.2128; $\varepsilon_{535\ nm}$ = 74 000.

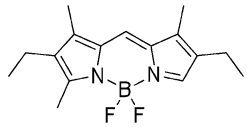
*6,6-Difluoro-12,14-dimethyl-2,3,4,6,8,9,10,11-octahydro-1H-[1,3,2]diazaborinino[1,6-a:3,4-a′]diindol-5-ium-6-uide (**28**).*

Compound **28** was synthesized from the corresponding dipyrrin·HBr salt using GP1, followed by purification on silica, eluting with 10% ethyl acetate in hexanes to give the title compound as a dark red solid (59 mg, 59% yield). Mp 250−255 °C (d.p.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (s, 1H), 2.98 (t, 4H, J = 6.0 Hz), 2.42 (t, 4H, J = 6.0 Hz), 2.13 (s, 6H), 1.84−1.79 (m, 4H), 1.77−1.72 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.7, 136.1, 133.0, 126.9, 119.1, 24.7, 22.8, 22.5, 21.7, 9.5; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.66 (t, J = 33.0 Hz); LRMS-ESI (m/z): 351.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{19}H_{23}N_2BF_2Na$ 351.1801; found, 351.1815; $\varepsilon_{538\ nm}$ = 67 000.

*4,4-Difluoro-5,7-dimethyl-1,2,3,6,8-H-4-bora-3a,4a-diaza-s-indacene (**30**).*[41]

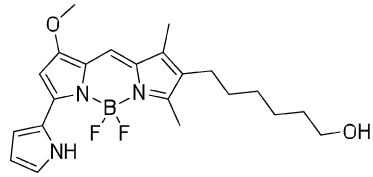
Compound **30** was synthesized from the corresponding dipyrrin·HBr salt[30] using GP1 as a metallic green solid (235 mg, 68% yield). Mp 132−135 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.64 (s, 1H), 7.20 (s, 1H), 6.93 (d, 1H, J = 3.5 Hz), 6.43 (s, 1H), 6.16 (s, 1H), 2.59 (s, 3H), 2.28 (s, 3H). NMR data matches that previously reported for this compound.[41]

*4,4-Difluoro-1,3,7-trimethyl-2,6-diethyl-5,8-H-4-bora-3a,4a-diaza-s-indacene (**32**).*



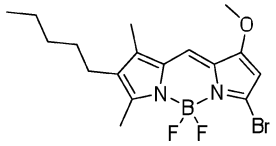
Compound **32** was synthesized from the corresponding dipyrrin·HBr salt[42] using GP1, followed by purification on silica, eluting with 15% ethyl acetate in hexanes to give the title compound as a dark red solid (142 mg, 79% yield). Mp 118−122 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42 (s, 1H), 7.06 (s, 1H), 2.52 (s, 3H), 2.44−2.37 (m, 4H), 2.19 (s, 3H), 2.18 (s, 3H), 1.18 (t, 3H, J = 7.5 Hz), 1.07 (t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.4, 139.3, 138.5, 135.4, 134.5, 133.3, 132.5, 132.2, 120.6, 18.3, 17.4, 14.5, 14.3, 13.1, 9.62, 9.60; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.41 (t, J = 31.9 Hz); LRMS-ESI (m/z): 313.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{16}H_{21}N_2BF_2Na$ 313.1652; found, 313.1658; $\varepsilon_{526\ nm}$ = 61 000.

*4,4-Difluoro-1-methoxy-3-pyrrolyl-5,7-dimethyl-6-(hexan-1-ol)-2,8-H-4-bora-3a,4a-diaza-s-indacene (**34**).*



Compound **34** was synthesized from the corresponding prodigiosene·HCl salt using GP1, with stirring for 48 h. Purification was carried out on neutral alumina, eluting with 20−50% ethyl acetate in hexanes to give the title compound as a dark purple solid (33 mg, 39% yield). Mp 71−76 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.42 (brs, 1H), 7.08 (s, 1H), 7.05 (s, 1H), 6.85 (s, 1H), 6.33 (s, 1H), 6.10 (s, 1H), 3.95 (s, 3H), 3.65 (t, 2H, J = 6.0 Hz), 2.48 (s, 3H), 2.37 (t, 2H, J = 7.0 Hz), 2.15 (s, 3H), 1.65−1.50 (m, 2H), 1.50−1.40 (m, 2H), 1.40−1.29 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.7, 150.1, 148.0, 134.3, 130.7, 129.2, 126.4, 124.3, 124.2, 115.7, 114.8, 110.9, 96.5, 63.2, 58.4, 33.0, 30.5, 29.5, 25.8, 24.3, 12.6, 9.7; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 1.31 (t, J = 36.7 Hz); LRMS-ESI (m/z): 438.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{22}H_{28}N_3O_2BF_2Na$ 438.2138; found, 438.2135; $\varepsilon_{565\ nm}$ = 116 000.

*4,4-Difluoro-1,3-dimethyl-2-pentyl-5-bromo-7-methoxy-6,8-H-4-bora-3a,4a-diaza-s-indacene (**37a**).*

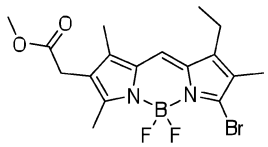


Compound **37a** was synthesized from the corresponding dipyrrin using GP1 and a reaction time of 18 h, followed by purification on basic alumina, eluting with 10−20% ethyl acetate in hexanes to give the title compound as a dark orange solid (122 mg, 54% yield). Mp 105−108 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.08 (s, 1H), 5.89 (s, 1H), 3.88 (s, 3H), 2.49 (s, 3H), 2.34 (t, 2H,

dx.doi.org/10.1021/jo3002003 | J. Org. Chem. 2012, 77, 3439−3453

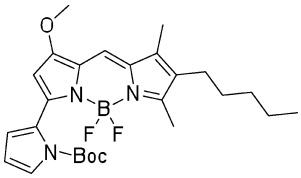
J = 7.5 Hz), 2.13 (s, 3H), 1.45−1.39, (m, 2H), 1.35−1.27, (m, 4H), 0.89 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.8, 158.5, 138.9, 133.0, 132.1, 126.2, 123.5, 117.2, 101.4, 58.6, 31.8, 29.8, 24.2, 22.7, 14.2, 13.2, 9.7; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.56 (t, J = 32.0 Hz); LRMS-ESI (m/z): 421.1 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{17}H_{22}N_2OBrBF_2Na$ 421.0858; found, 421.0869; $\varepsilon_{514\ nm}$ = 95 000.

*4,4-Difluoro-1,3,6-trimethyl-2-(methylethanoate)-5-bromo-7-ethyl-8-H-4-bora-3a,4a-diaza-s-indacene (**37b**).*



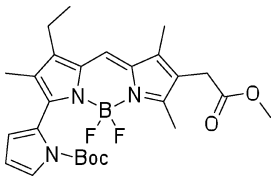
Compound **37b** was synthesized from the corresponding dipyrrin·HBr salt using GP1 and a reaction time of 18 h, followed by purification on silica, eluting with 20−40% ethyl acetate in hexanes to give the title compound as a dark brown solid (135 mg, 53% yield). Mp 137−142 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.00 (s, 1H), 3.69 (s, 3H), 3.40 (s, 2H), 2.61 (q, 2H, J = 7.7 Hz), 2.53 (s, 3H), 2.22 (s, 3H), 2.01 (s, 3H), 1.17 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 159.1, 143.4, 140.9, 133.7, 132.3, 130.4, 126.0, 123.9, 119.7, 52.4, 30.1, 18.5, 16.1, 13.2, 10.02, 9.98; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.56 (t, J = 29.6 Hz); LRMS-ESI (m/z): 435.1 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{17}H_{20}N_2O_2BrBF_2Na$ 435.0650; found, 435.0661; $\varepsilon_{529\ nm}$ = 78 000.

*4,4-Difluoro-1-methoxy-3-(N-Boc-pyrrolyl)-5,7-dimethyl-6-pentyl-2,8-H-4-bora-3a,4a-diaza-s-indacene (**38a**).*



N-Boc-pyrrole-2-boronic acid (91 mg, 0.43 mmol), lithium chloride (46 mg, 1.1 mmol), and tetrakis(triphenylphosphine)-palladium (41 mg, 0.036 mmol) were added to a solution of **37a** (143 mg, 0.358 mmol) in 1,2-dimethoxyethane (15 mL) and the resulting mixture was purged with nitrogen for 15 min. Sodium carbonate solution (2.0 M, 0.72 mL, 1.4 mmol), previously bubbled with nitrogen, was then added dropwise and the reaction mixture was heated to 85 °C, with stirring under nitrogen for 24 h. After cooling to room temperature, the reaction mixture was diluted with water (30 mL) and thoroughly extracted with ethyl acetate (3 × 30 mL). The organic extracts were combined and washed with water (50 mL) and brine (50 mL), then dried over anhydrous magnesium sulfate before filtering and concentrating to give the crude product, which was purified using column chromatography on silica, eluting with 10−30% diethyl ether in hexanes, to give the product **38a** as a dark red solid (62 mg, 36% yield). Mp 152−154 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42 (dd, 1H, J = 3.5, 1.5 Hz), 7.18 (s, 1H), 6.58 (dd, 1H, J = 3.5, 1.5 Hz), 6.27 (t, 1H, J = 3.5 Hz), 5.82 (s, 1H), 3.90 (s, 3H), 2.40 (s, 3H), 2.33 (t, 2H, J = 7.5 Hz), 2.15 (s, 3H), 1.44−1.38 (m, 2H), 1.41 (s, 9H), 1.34−1.26 (m, 4H), 0.89 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.9, 156.4, 149.0, 146.9, 137.5, 132.6, 131.1, 124.9, 123.7, 117.9, 117.6, 110.9, 100.2, 83.7, 58.4, 31.8, 29.9, 27.8, 24.2, 22.7, 22.6, 14.2, 13.0, 9.7; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.60 (t, J = 31.5 Hz); LRMS-ESI (m/z): 508.3 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{26}H_{34}N_3O_3BF_2Na$ 508.2531; found, 508.2553; $\varepsilon_{516\ nm}$ = 74 000.

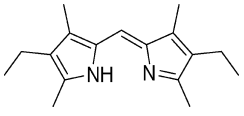
*4,4-Difluoro-1-ethyl-2,5,7-trimethyl-3-(N-Boc-pyrrolyl)-6-(methylethanoate)-8-H-4-bora-3a,4a-diaza-s-indacene (**38b**).*



N-Boc-pyrrole-2-boronic acid (83 mg, 0.39 mmol), lithium chloride (42 mg, 0.98 mmol) and tetrakis(triphenylphosphine)-palladium (38 mg, 0.033 mmol) were added to a solution of **37b** (135 mg, 0.327 mmol) in 1,2-dimethoxyethane (14 mL) and the resulting mixture was purged with nitrogen for 15 min. Sodium carbonate solution (2.0 M, 0.65 mL, 1.3 mmol), previously bubbled with nitrogen, was then added dropwise and the reaction mixture was heated to 85 °C, with stirring under nitrogen for 24 h. After cooling to room temperature, the reaction mixture was diluted with water (30 mL) and thoroughly extracted with ethyl acetate (3 × 30 mL). The organic extracts were combined and washed with water (50 mL) and brine (50 mL), then dried over anhydrous magnesium sulfate before filtering and concentrating to give the crude product, which was purified using column chromatography on neutral alumina, eluting with 5−20% ethyl acetate in hexanes, to give the product **38b** as a dark red solid (62 mg, 38% yield). Mp 52−54 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47 (dd, 1H, J = 2.0, 3.5 Hz), 7.10 (s, 1H), 6.46−6.45 (m, 1H), 6.32 (t, 1H, J = 3.5 Hz), 3.68 (s, 3H), 3.38 (s, 2H), 2.63 (q, 2H, J = 7.7 Hz), 2.43 (s, 3H), 2.23 (s, 3H), 1.85 (s, 3H), 1.33 (s, 9H), 1.21 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 156.7, 148.9, 142.8, 139.3, 133.1, 132.2, 127.1, 123.2, 122.6, 121.5, 120.3, 117.5, 110.9, 83.5, 60.5, 52.2, 30.1, 27.7, 18.1, 16.1, 13.0, 10.0, 9.3; ^{11}B {^{1}H} NMR ($CDCl_3$, 160 MHz) δ 0.52 (t, J = 30.6 Hz); LRMS-ESI (m/z): 522.2 [M + Na]$^+$; HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{26}H_{32}N_3O_4BF_2Na$ 522.2341; found, 522.2346; $\varepsilon_{533\ nm}$ = 60 000.

Microwave-Assisted Deprotection of *F*-BODIPYs. *General Procedure for the Deprotection of F-BODIPYs (**GP2**).* Potassium hydroxide (6 equiv) was added to a stirred suspension of BODIPY compound (50 mg, 1 equiv) in HPLC grade *tert*-butanol (10 mL) and distilled water (0.1 mL), in a 20 mL capacity microwave vial. The vial was then sealed and placed in the microwave reactor, where it was heated at 140 °C for 15 min, at a maximum of 400 W power. After cooling, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (30 mL) and diethyl ether (30 mL). The aqueous phase was extracted with diethyl ether (2 × 30 mL) and the combined organic extracts were washed with brine (50 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was purified immediately using column chromatography on basic alumina (Brockmann type III), unless otherwise stated.

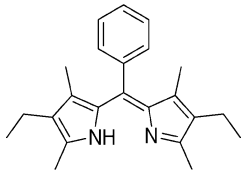
*(Z)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2H-pyrrol-2-ylidene)-methyl)-2,4-dimethyl-1H-pyrrole (**4**).*[25]



dx.doi.org/10.1021/jo3002003 | J. Org. Chem. 2012, 77, 3439−3453

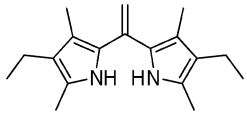
Compound **4** was synthesized from the corresponding *F*-BODIPY (**3**), using GP2 and a reaction time of 5 min, and purified over basic alumina (Brockmann type III), eluting with 5% ethyl acetate in hexanes, to give the title compound as a brown solid (41 mg, 97% yield). Mp 111−114 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.63 (s, 1H), 2.36 (q, 4H, J = 7.7 Hz), 2.29 (s, 6H), 2.12 (s, 6H), 1.05 (t, 6H, J = 7.7 Hz). NMR data matches that previously reported for this compound.[25]

*(Z)-3-Ethyl-5-((4-ethyl-3,5-dimethyl-2H-pyrrol-2-ylidene)-(phenyl)methyl)-2,4-dimethyl-1H-pyrrole (**10**).*[25]



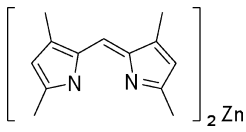
Compound **10** was synthesized from the corresponding *F*-BODIPY (**9**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, to give the title compound as a brown solid (41 mg, 94% yield). Mp 144−147 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 13.10 (brs, 1H), 7.42−7.40 (m, 3H), 7.32−7.30 (m, 2H), 2.32 (s, 6H), 2.27 (q, 4H, J = 7.6 Hz), 1.19 (s, 6H), 0.97 (t, 6H, J = 7.6 Hz). NMR data matches that previously reported for this compound.[25]

*5,5′-(Ethene-1,1-diyl)bis(3-ethyl-2,4-dimethyl-1H-pyrrole) (**16**).*[43]



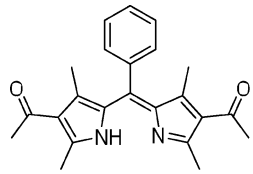
Compound **16** was synthesized from the corresponding *F*-BODIPY (**12**), using GP2 and a reaction time of 5 min, and purified over basic alumina (Brockmann type III), eluting with 6% ethyl acetate in hexanes, to give the title compound as a dark yellow oil (33 mg, 97% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.56 (brs, 2H), 5.04 (s, 2H), 2.41 (q, 4H, J = 7.5 Hz), 2.17 (s, 6H), 1.97 (s, 6H), 1.09 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 132.4, 125.6, 123.0, 122.4, 117.1, 108.3, 17.8, 15.8, 11.2, 10.3. NMR data matches that previously reported for this compound.[43]

*Zinc[κ2-(3,3′, 5,5′-tetramethyl-meso-H-dipyrrinato)] (**17**).*[25]



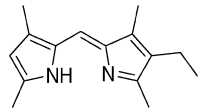
CAUTION! The free-base dipyrrin derived from **13** is a powerful sternutator and must be handled only under adequate ventilation.[25] Compound **17** was thus synthesized from the corresponding *F*-BODIPY (**13**), using GP2, followed by addition of $Zn(OAc)_2{\cdot}2H_2O$ (400 mg, 1.82 mmol, 9 equiv.) to the microwave vial following deprotection with stirring at room temperature for 30 min. The reaction mixture was then partitioned between saturated aqueous sodium bicarbonate solution (30 mL) and diethyl ether (30 mL). The aqueous phase was extracted with diethyl ether (2 × 30 mL) and the combined organic extracts were washed with brine (50 mL), dried over anhydrous magnesium sulfate, and concentrated to give the crude product, which was dissolved in pentane and filtered through a short pad of basic alumina (Brockmann type III), washing with 10% diethyl ether in pentane, to give the title compound as a pale brown solid (37 mg, 79% yield). Mp 208−212 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.02 (s, 2H), 5.99 (s, 4H), 2.32 (s, 12H), 1.95 (s, 12H). NMR data matches that previously reported for this compound.[25]

*(Z)-1-(2-((4-Acetyl-3,5-dimethyl-1H-pyrrol-2-yl)(phenyl)-methylene)-3,5-dimethyl-2H-pyrrol-4-yl)ethanone (**18**).*



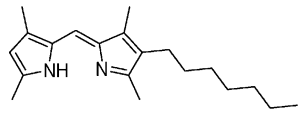
Compound **18** was synthesized from the corresponding *F*-BODIPY (**14**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 30% ethyl acetate in hexanes, to give the title compound as a bright orange solid (20 mg, 45% yield). Mp 152−154 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 13.93 (brs, 1H), 7.50−7.46 (m, 3H), 7.30−7.28 (m, 2H), 2.58 (s, 6H), 2.39 (s, 6H), 1.53 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 196.7, 154.5, 143.7, 143.6, 137.2, 137.1, 131.0, 129.4, 129.3, 129.2, 31.8, 18.1, 14.5; LRMS-ESI (m/z): 361.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{23}H_{25}N_2O_2$ 361.1916; found, 361.1911.

*(Z)-2-((4-Ethyl-3,5-dimethyl-2H-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1H-pyrrole (**21**).*[44]



Compound **21** was synthesized from the corresponding *F*-BODIPY (**20**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, to give the title compound as a yellow solid (41 mg, 98% yield). Mp 64−65 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.09 (brs, 1H), 6.64 (s, 1H) 5.85 (s, 1H), 2.36 (q, 2H, J = 7.5 Hz), 2.33 (s, 3H), 2.31 (s, 3H), 2.21 (s, 3H), 2.12 (s, 3H), 1.05 (t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.7, 143.6, 142.5, 136.9, 133.8, 133.4, 132.1, 115.7, 113.6, 18.1, 16.0, 14.9, 14.7, 11.4, 9.7; LRMS-ESI (m/z): 229.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{15}H_{21}N_2$ 229.1708; found, 229.1699.

*(Z)-2-((4-Heptyl-3,5-dimethyl-2H-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1H-pyrrole (**23**).*

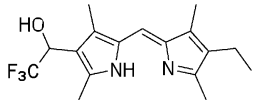


Compound **23** was synthesized from the corresponding *F*-BODIPY (**22**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, to give the title compound as a dark yellow oil (41 mg, 95% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.13 (brs, 1H), 6.65 (s, 1H), 5.85 (s, 1H), 2.34−2.32 (m, 5H), 2.31 (s, 3H), 2.21 (s, 3H), 2.11 (s, 3H), 1.45−1.41 (m, 2H), 1.31−1.27 (m, 8H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.0, 143.6, 142.5, 137.3, 133.3, 132.5, 132.1, 115.7, 113.6, 32.1, 30.3, 29.6, 29.4, 24.9, 22.8, 16.1, 15.0, 14.3, 11.4, 9.9; LRMS-ESI (m/z): 299.3

dx.doi.org/10.1021/jo3002003 | J. Org. Chem. 2012, 77, 3439−3453

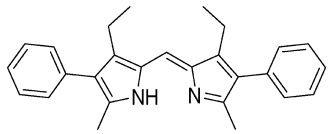
$[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{20}H_{31}N_2$ 299.2477; found, 299.2482.

*(Z)-1-(5-((4-Ethyl-3,5-dimethyl-2H-pyrrol-2-ylidene)-methyl)-2,4-dimethyl-1H-pyrrol-3-yl)-2,2,2-trifluoroethanol (**25**).*[25]



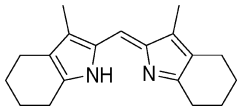
Compound **25** was synthesized from the corresponding racemic *F*-BODIPY (**24**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 30% ethyl acetate in hexanes, to give the title compound as a yellow solid (42 mg, 96% yield). Mp 160−163 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.65 (s, 1H), 5.03 (q, 1H, J = 7.3 Hz), 4.96 (brs, 1H), 2.39 (s, 3H), 2.36 (q, 2H, J = 7.6 Hz), 2.31 (s, 3H), 2.23 (s, 3H), 2.11 (s, 3H), 1.06 (t, 3H, J = 7.6 Hz). NMR data matches that previously reported for this compound.[25]

*(Z)-3-Ethyl-2-((3-ethyl-5-methyl-4-phenyl-2H-pyrrol-2-ylidene)methyl)-5-methyl-4-phenyl-1H-pyrrole (**27**).*



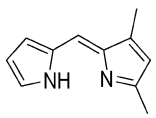
Compound **27** was synthesized from the corresponding *F*-BODIPY (**26**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 10% ethyl acetate in hexanes, to give the title compound as a brown solid (34 mg, 83% yield). Mp 129−131 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.34 (brs, 1H), 7.42 (t, 4H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 7.29−7.27 (m, 4H), 6.86 (s, 1H), 2.63 (q, 4H, J = 7.5 Hz), 2.34 (s, 6H), 1.14 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 151.8, 141.3, 136.5, 135.6, 130.0, 129.7, 128.4, 126.5, 117.3, 18.2, 17.4, 15.4; LRMS-ESI (m/z): 381.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{27}H_{29}N_2$ 381.2314; found, 381.2325.

*(Z)-3-Methyl-2-((3-methyl-4,5,6,7-tetrahydro-1H-indol-2-yl)methylene)-4,5,6,7-tetrahydro-2H-indole (**29**).*[45]



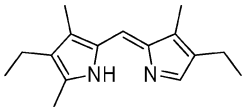
Compound **29** was synthesized from the corresponding *F*-BODIPY (**28**), using GP2, and purified over basic alumina (Brockmann type III), eluting with 10−30% ethyl acetate in hexanes, to give the title compound as a brown solid (30 mg, 72% yield). Mp 141−144 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.69 (s, 1H), 2.71 (t, 4H, J = 6.0 Hz), 2.43 (t, 4H, J = 6.0 Hz), 2.10 (s, 6H), 1.81−1.77 (m, 4H), 1.76−1.72 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.8, 137.2, 132.8, 125.4, 116.0, 26.3, 23.5, 23.4, 22.1, 9.5; LRMS-ESI (m/z): 281.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{25}N_2$ 281.2010; found, 281.2012.

*(Z)-2-((3,5-Dimethyl-2H-pyrrol-2-ylidene)methyl)-1H-pyrrole (**31**).*



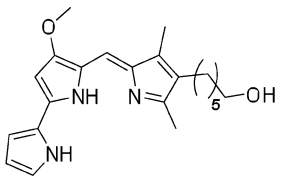
Compound **31** was synthesized from the corresponding *F*-BODIPY (**30**), using GP2 and a reaction time of 5 min, and purified over basic alumina (Brockmann type III), eluting with 0−5% ethyl acetate in hexanes, to give the title compound as a yellow film (8 mg, 26% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 (s, 1H), 6.73 (s, 1H), 6.62 (dd, 1H, J = 3.5, 1.0 Hz), 6.26 (dd, 1H, J = 3.5, 2.5 Hz), 6.12 (d, 1H, J = 1.5 Hz), 2.33 (s, 3H), 2.20 (s, 3H); LRMS-ESI (m/z): 173.1 $(M + H)^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{13}N_2$ 173.1067; found, 173.1073. This compound is very unstable and prone to decomposition; color change occurred from yellow to brown to black, beginning directly after the column.

*(Z)-3-Ethyl-5-((4-ethyl-3-methyl-2H-pyrrol-2-ylidene)-methyl)-2,4-dimethyl-1H-pyrrole (**33**).*



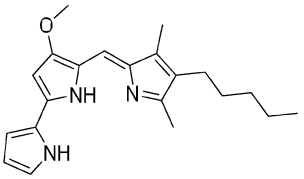
Compound **33** was synthesized from the corresponding *F*-BODIPY (**32**), using GP2 and a reaction time of 5 min, and purified over basic alumina (Brockmann type III), eluting with 5% ethyl acetate in hexanes, to give the title compound as a yellow solid (34 mg, 81% yield). Mp 50−51 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.90 (s, 1H), 6.63 (s, 1H), 2.43 (q, 2H, J = 7.5 Hz), 2.35 (q, 2H, J = 7.7 Hz), 2.30 (s, 3H), 2.16 (s, 3H), 2.11 (s, 3H), 1.17 (t, 3H, J = 7.5 Hz), 1.05 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.1, 146.3, 138.5, 135.8, 130.6, 127.9, 127.2, 126.0, 115.9, 18.5, 18.2, 16.7, 14.7, 14.6, 9.7, 9.4; LRMS-ESI (m/z): 243.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{16}H_{23}N_2$ 243.1860; found, 243.1856.

*(Z)-6-(2-((4-Methoxy-1H,1′H-[2,2′-bipyrrol]-5-yl)-methylene)-3,5-dimethyl-2H-pyrrol-4-yl)hexan-1-ol (**35**).*



Compound **35** was synthesized from the corresponding *F*-BODIPY (**34**), using GP2, and purified over neutral alumina (Brockmann type III), eluting with 60−80% ethyl acetate in hexanes, to give the title compound as a dark red solid (12.5 mg, 94% yield). Mp 56−60 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.89 (s, 1H), 6.642 (s, 1H), 6.635 (s, 1H), 6.13 (t, 1H, J = 3.0 Hz), 6.06 (s, 1H), 3.96 (s, 3H), 3.58 (t, 2H, J = 6.8 Hz), 2.22 (t, 2H, J = 7.5 Hz), 2.11 (s, 3H), 1.77 (s, 3H), 1.54−1.49 (m, 2H), 1.37−1.30 (m, 4H), 1.28−1.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.5, 132.3, 132.2, 132.1, 128.7, 128.6, 125.6, 123.0, 122.6, 113.5, 112.0, 109.8, 95.2, 63.1, 58.5, 32.8, 30.7, 29.4, 25.7, 24.2, 10.6, 9.8; LRMS-ESI (m/z): 368.2 $[M + H]^+$; HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{22}H_{30}N_3O_2$ 368.2327; found, 368.2333.

*(Z)-5-((3,5-Dimethyl-4-pentyl-2H-pyrrol-2-ylidene)methyl)-4-methoxy-1H,1′H-2,2′-bipyrrole (**39a**).*



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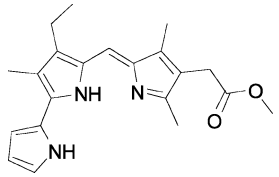
Compound **39a** was synthesized from the corresponding *F*-BODIPY (**38a**), using GP2, and purified over neutral alumina (Brockmann type III), eluting with 20% ethyl acetate in hexanes, to give the title compound as a dark red solid (10.4 mg, 97% yield). Mp 66−70 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.88 (s, 1H), 6.67 (s, 1H), 6.63 (s, 1H), 6.15 (s, 1H), 6.04 (s, 1H), 3.95 (s, 3H), 2.22 (t, 2H, J = 7.5 Hz), 2.11 (s, 3H), 1.83 (s, 3H), 1.34−1.30 (m, 2H), 1.28−1.22 (m, 4H), 0.85 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.6, 158.47, 158.45, 137.0, 129.8, 128.9, 125.7, 123.2, 122.3, 113.5, 111.7, 109.8, 95.2, 58.5, 31.9, 30.5, 24.3, 22.7, 14.2, 10.5, 9.7; LRMS-ESI (m/z): 338.2 [M + H]$^+$; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{21}H_{28}N_3O$ 338.2226; found, 338.2227.

*(Z)-Methyl 2-(2-((4-ethyl-3-methyl-1H,1′H-[2,2′-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetate (**40b**).*



Compound **40b** was synthesized from the corresponding *F*-BODIPY (**38b**), using GP2. The reaction mixture was then concentrated to dryness and the residue was dissolved in methanol (30 mL) and acidified with sulfuric acid (0.02 mL, 0.336 mmol, 7 equiv.) After heating at reflux temperature for 3 h, the reaction was cooled to room temperature and concentrated in vacuo. The residue was dissolved in ethyl acetate (30 mL) and washed with water (30 mL) and brine (30 mL). The aqueous phase was extracted with ethyl acetate (2 × 30 mL) and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated to give the crude product, which was purified over neutral alumina (Brockmann type III), eluting with 0−30% ethyl acetate in hexanes, to give the title compound as a dark red solid (8.8 mg, 52% yield). Mp 50−53 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.80 (s, 1H), 6.73 (s, 2H), 6.21 (s, 1H), 3.64 (s, 3H), 3.30 (s, 2H), 2.65 (q, 2H, J = 7.5 Hz), 2.27 (s, 3H), 2.18 (s, 3H), 1.90 (s, 3H), 1.18 (t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.4, 190.5, 172.3, 149.01, 148.97, 128.9, 128.2, 128.1, 127.0, 121.9, 115.0 (2 x C), 112.4, 110.3, 52.0, 30.2, 29.9, 18.2, 16.6, 11.8, 10.0. LRMS-ESI (m/z): 352.2 [M + H]$^+$; HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{21}H_{26}N_3O_2$ 352.2009; found, 352.2020.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra for all previously unpublished compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: Alison.Thompson@Dal.Ca

Notes

The authors declare no competing financial interest.

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