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Synthesis of 3-aminoBODIPY dyes via copper-catalyzed vicarious nucleophilic substitution of 2-halogeno derivatives.

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2-Halogeno BODIPYs undergo copper catalysed nucleophilic substitution with alkyl amines and anilines and an amide to give the corresponding 3-aminoBODIPY derivatives. The substrates are readily prepared by the regioselective 2-halogenation of the chemically robust, preformed BODIPYs thus providing an alternative to direct nucleophilic substitution of the corresponding 3-halogenoBODIPYs which requires regioselective 3-halogenation of the more sensitive dipyrromethane intermediate. 2-Halogenation expands the scope of vicarious substitution of BODIPYs to include weaker nitrogen nucleophiles.

Introduction

Boron dipyrromethenes (BODIPY, Fig. 1)[1] are fluorescent dyes which display high molar absorption coefficients, high fluorescence quantum yields, narrow absorption and emission bandwidths, and excitation and emission wavelengths in the visible/near infra red region.[2] The absorption and emission characteristics can be fine-tuned by modification of the substituents on the periphery of the BODIPY core. These favourable photophysical properties are complemented by chemical and photochemical robustness, including stability to air, water, and irradiation, a low tendency for self-aggregation in solution, good solubility in many organic solvents, and good synthetic accessibility. As a result, they have found extensive use as biological markers and fluorescence probes for reporting on the intracellular environment,[3] organic light emitting diodes and laser dyes,[4] and as the photosensitizer for applications in photocatalysis,[5] photodynamic therapy[6] and dye-sensitized solar cells.[7]

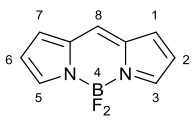


Figure 1. Numbering scheme for 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY).

BODIPYs containing a pendant amine which is able to act as an electron donor often display significant conjugative effects on the position of the absorption and emission maxima and/or fluorescence quenching due to intramolecular charge transfer. These effects can in principle be attenuated by co-ordination of the nitrogen lone pair to a Lewis or Brønsted acid, leading to restoration of the BODIPY fluorescence (switch on sensors).[8]

Although the majority of the reported amine-containing BODIPYs have the nitrogen appended to a substituent, there are a number of examples in which the amine is directly substituted onto the BODIPY core and these have recently been the subject of very detailed structural and photophysical investigations motivated by the high level of current interest in elucidating the effects of the nature of the substituents on the properties of these fluorophores.[9]

The introduction of amine substituents directly linked to the BODIPY core is normally achieved by nucleophilic substitution (S_NAr) of a BODIPY carrying a suitable nucleofuge (e.g. halogen, methylthio, or methoxy).[9,10] In principle, because of the electronic requirements for S_NAr, aminolysis of halogenoBODIPYs is expected only to be possible in the 1,3,5,7, and 8 (meso) positions because attack at these positions allows the resulting intermediate anion to be effectively delocalised onto one of the nitrogen atoms of the BODIPY core.

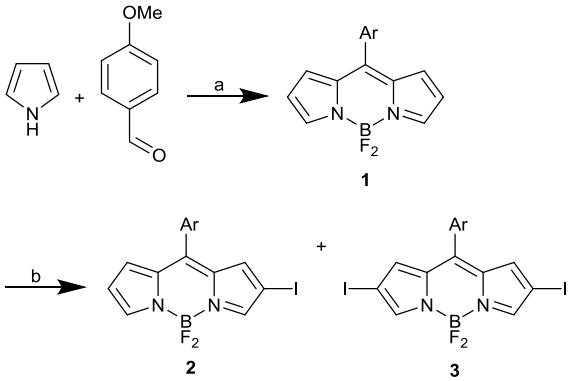
An interesting alternative to S_NAr displacement of 3-halogenoBODIPYs is the vicarious oxidative nucleophilic hydrogen substitution by amines which occurs in the 3-position of unhalogenated 8-arylBODIPYs in the presence of a stoichiometric oxidant (DDQ, CAN, permanganate, or O_2). This reaction is reported to be successful for primary and secondary alkyl amines but to fail in the case of anilines.[11]

We report here a related copper catalysed amination[12] of 2-halogenoBODIPYs which allows substitution at the 3-position to take place with a wider range of amine nucleophiles than the oxidative hydrogen substitution, to include more weakly nucleophilic anilines and even an amide.

Results and Discussion

Synthesis of the 2-iodoBODIPY 2

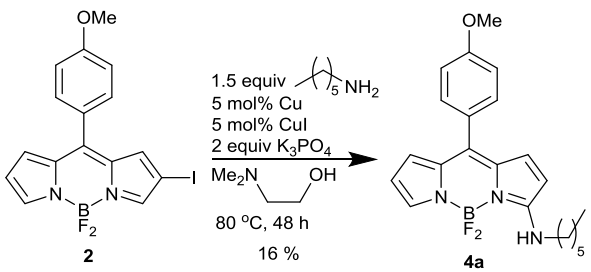
The 2-unsubstituted BODIPY **1** was prepared in good yield using a standard synthetic sequence[2b] from pyrrole and anisaldehyde via boron trifluoride-etherate catalysed condensation to the dipyrromethane,[13] DDQ oxidation to the corresponding dipyrromethene and reaction with boron trifluoride-etherate (Scheme 1). Regioselective iodination[10g] of **1** with ICl produced the 2-iodo-substituted BODIPY **2** together with a minor amount of the 2,6-diiodide **3** which were separable by column chromatography.



Scheme 1. *Reagents:* (a) $BF_3.OEt_2$, rt, 4 h (87%); DDQ, CH_2Cl_2, 0 °C, 30 min; $BF_3.OEt_2$, i-Pr_2NEt, rt, 2 h (77%); (b) ICl, CH_2Cl_2-MeOH, rt, 2 h (**2**, 65%; **3**, 15%). (Ar = 4-$MeOC_6H_4$).

Copper catalysed amination of 2-iodoBODIPY 2

Although there are many reports of copper catalysed amination of halogenobenzene derivatives, the amination of 3-halogeno-5-membered heteroaromatic compounds is much less well studied. We first attempted to couple the iodoBODIPY **2** with hexylamine using a mixture of copper:copper (I) iodide catalyst in dimethylaminoethanol; conditions reported by Twieg for the copper catalysed amination of halothiophenes (Scheme 2).[14]



Scheme 2. Cu/CuI catalysed amination of BODIPY **2**.

We were pleased to observe that amination had occurred, albeit in only 16% yield, but surprised to find that the product **4a** appeared to have been aminated in the 3-position. The structural assignment of **4a** was confirmed unambiguously by X-ray structure determination (Fig. S1, Electronic Supplementary Information).

In this amination, dimethylaminoethanol acts both as a ligand for the copper and also as the solvent. In order to optimise the yield of this reaction we screened a series of bidentate ligands **L1-L4** (Fig. 2). Buchwald has reported the use of the diketone **L1** for room temperature amination of aryl halides, including 3-iodothiophene,[15] Ding has reported the use of β-ketopyridine **L2**, which is prepared in one step from tetrahydroquinoline, for amination of aryl halides,[16] and *N,N'*-dimethyl ethylenediamine[17] **L3** and 1,10-phenanthroline[18] **L4** are commonly used ligands for copper catalysed aminations.

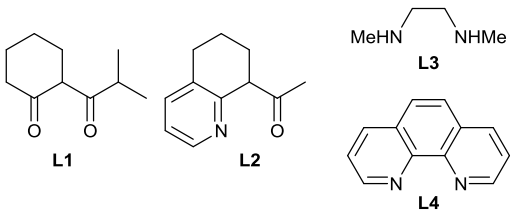
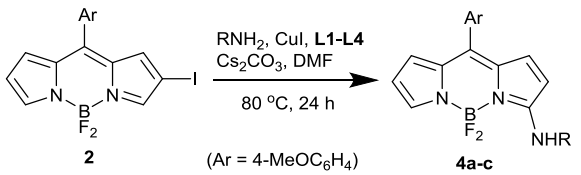


Figure 2. Ligands screened in the amination of 2-iodoBODIPY **2**.

Table 1 shows the results of the amination of the 2-iodoBODIPY **2** catalysed by copper(I)iodide in the presence of ligands **L1-L4**. The choice of solvent, base, catalyst and ligand loading were taken from Buchwald's report[15] using **L1**. Selection of 80 °C was based on an initial screen of reaction temperature using **L3** which indicated that no reaction with hexylamine was observed at 25 or 50 °C. It was confirmed that no reaction with hexylamine occurred at room temperature for any of these ligands.

As shown in Table 1, reaction with *n*-hexylamine, *p*-toluidine and benzamide proceeded to give the corresponding 3-substituted products **4a**, **4b**, and **4c** respectively. Ligand **L4** (1,10-phenanthroline) proved to give the highest yield regardless of the nature of the nucleophile (entry 4, 8, 12). Good yields were obtained in the case of the primary alkyl amine (entry 4) and the aniline (entry 8) and the reaction was successful even using the much more weakly nucleophilic benzamide albeit in low yield (entry 12).

Table 1. Ligand variation in the amination of iodoBODIPY **2**.

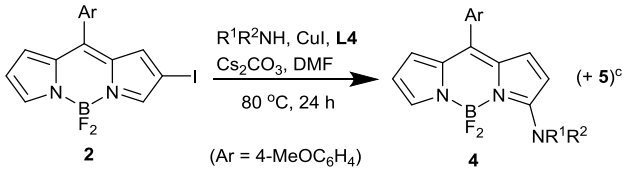


Entry[a]	R	Ligand	Product	Yield[b]
1	$CH_3(CH_2)_5$	**L1**	**4a**	30
2	$CH_3(CH_2)_5$	**L2**	**4a**	20
3	$CH_3(CH_2)_5$	**L3**	**4a**	35
4	*$CH_3(CH_2)_5$*	***L4***	***4a***	*60*
5	4-MeC_6H_4	**L1**	**4b**	6
6	4-MeC_6H_4	**L2**	**4b**	70
7	4-MeC_6H_4	**L3**	**4b**	30
8	*4-MeC_6H_4*	***L4***	***4b***	*84*
9	PhCO	**L1**	**4c**	6
10	PhCO	**L2**	**4c**	11
11	PhCO	**L3**	**4c**	10
12	*PhCO*	***L4***	***4c***	*15*

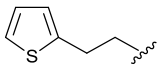
[a] *Reagents and conditions:* BODIPY **2** (0.235 mmol), amine/amide (0.470 mmol), CuI (5 mol%), ligand (20 mol%), Cs_2CO_3 (0.470 mmol), DMF (0.8 mL), 80 °C, 24 h. [b] Isolated yield of 3-substituted product **4**.

The substrate scope of this reaction was investigated by applying these conditions, using phenanthroline (**L4**), to the reaction of the 2-iodoBODIPY **2** with a range of alkyl amines and anilines (Table 2).

Table 2. Scope of the amination of iodoBODIPY **2**.



2 **4**

Entry[a]	R^1	R^2	Product	Yield[b]
1	$CH_3(CH_2)_5$	H	**4a**	60 (5)[c]
2	4-MeC_6H_4	H	**4b**	84 (5)[c]
3	PhCO	H	**4c**	15
4	$PhCH_2$	H	**4d**	64
5		H	**4e**	65
6	Cyclohexyl	H	**4f**	78 (4)
7	$O(CH_2CH_2)_2$		**4g**	85
8	$CH_2CH_2CH_2CH_2$		**4h**	87 (4)
9	2-MeC_6H_4	H	**4i**	60
10	4-$MeOC_6H_4$	H	**4j**	78 (6)
11	4-ClC_6H_4	H	**4k**	66 (13)[c]
12	4-NCC_6H_4	H	**4l**	77 (15)[c]
13	2-pyridyl	H	**4m**	60 (14)[c]
14	Ph	Me	**4n**	40

[a] *Reagents and conditions:* BODIPY **2** (0.235 mmol), amine/amide (0.470 mmol), CuI (5 mol%), phenanthroline (**L4**) (20 mol%), Cs_2CO_3 (0.470 mmol), DMF (0.8 mL), 80 °C, 24 h. [b] Isolated yield of 3-substituted product **4**. [c] Yield of 6-Iodo-3-amino by-product **5** (see later).

The reaction works well with primary alkyl amines (entry 1 and 4-6) and the yields were also good with the secondary alkyl amines morpholine (entry 7) and pyrrolidine (entry 8). Yields were high for electron rich (entry 2, 10) primary anilines but were slightly lower in the cases of the less nucleophilic electron deficient anilines (entry 11, 12, 13), the more sterically hindered *ortho*-methylaniline (entry 9) and a secondary aniline (entry 14). In several cases the product **4** was accompanied by formation of a small amount of the corresponding 3-amino-6-iodoBODIPY **5** (Table 2, yields in parenthesis, Fig. 3). The structure of this by-product was confirmed unambiguously by X-ray structure determination in the case of the hexylamine derivative **5a** (Fig. 3).

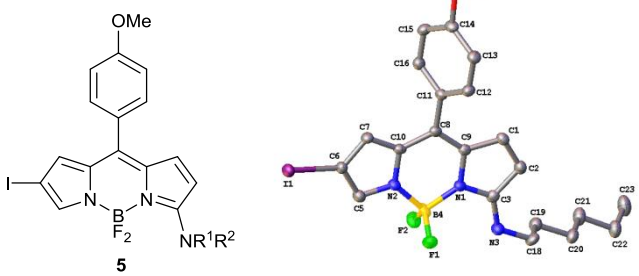
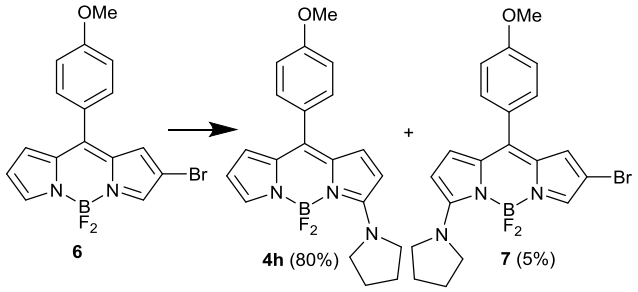


Figure 3. Structure of 3-amino-6-iodoBODIPY by-product **5** and molecular structure of **5a**. Hydrogen atoms have been omitted for clarity. The asymmetric unit comprises four independent molecules; one is shown here as the rest are similar.

The reaction is equally successful from the 2-bromoBODIPY **6** which was prepared by treatment of the unsubstituted BODIPY **1** with NBS (73%). The 2-bromo derivative **6** reacted with pyrrolidine to give the 3-amino product **4h** in 80% yield, together with a minor amount (5%) of the corresponding 3-amino-5-bromo byproduct **7** (Scheme 3).

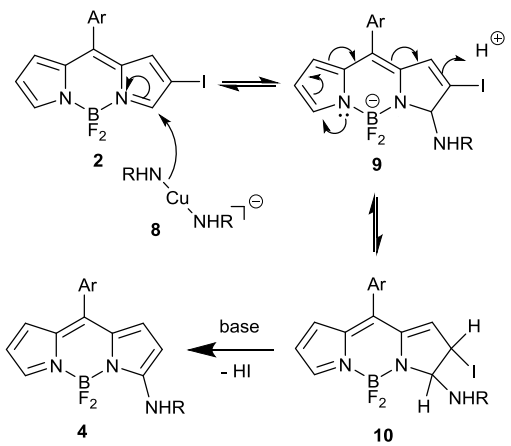


Scheme 3. *Reagents and conditions:* pyrrolidine (2.0 eq.), CuI (5 mol%), **L4** (20 mol%), Cs_2CO_3 (2.0 eq.), DMF, 80 °C, 24 h.

Surprisingly, the 2,6-diiodoBODIPY **3** is unchanged under the reaction conditions and does not produce any singly or doubly aminated products.[19]

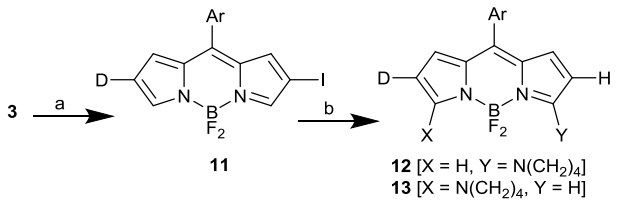
Mechanism of reaction

No reaction occurs between the iodide **2** and pyrrolidine in the absence of copper iodide and, as Table 1 indicates, the nature of the ligand influences the amination yield. In the absence of any added ligand the amination product **4h** was formed in 50% yield (together with a trace of **5h**). If the base (Cs_2CO_3) is omitted then the product **4h** is formed in low yield (14%) together with **5h** (10%). Thus copper is obligatory for the amination to occur and the ligand and base improve the conversion.[20] Scheme 4 shows a mechanism which is similar to that proposed for the oxidative hydrogen displacement of non-halogenated BODIPYs with alkyl amines.[11] The necessity for copper catalysis suggests that the nucleophile might be an amido copper species such as **8**.[21] Initial nucleophilic attack at C-3 leads to an anion **9** which could be copper-bound, corresponding to an amidocupration, but may be delocalised over the BODIPY π-system. In order to produce the product, iodide must be lost and this requires protonation at C-2 to give **10** followed by base-mediated elimination of HI. There are reports of the acid- or Lewis-acid-catalysed reaction of nitrogen nucleophiles with 3-haloindoles in which substitution occurs at the adjacent 2-position[22] and although these are proposed to be initiated by protonation the mechanism otherwise resembles that in Scheme 4.[23,24]



Scheme 4. Suggested mechanistic pathway initiated by nucleophilic attack.

Isotopic labelling was employed to support the proposed mechanistic scheme. The 2,6-diiodoBODIPY **3** was converted to the 6-deuterio-2-iodoBODIPY **11** by palladium catalysed reduction with dideuterium (Scheme 5). A minor amount (17%) of the 2,6-dideuteriated BODIPY (2,6-$^2H_2$-**1**) was also formed but was easily separated by column chromatography. Amination of the iodide **11** with pyrrolidine produced a 70:30 ratio of the 3-amino-6-deuterioBODIPY **12** together with the regioisomeric 3-amino-2-deuterioBODIPY **13** (Scheme 5).



Scheme 5. *Reagents:* (a) D_2, Pd/C, CH_2Cl_2, rt, 5 h (60%); (b) pyrrolidine (2.0 eq.), CuI (5 mol%), **L4** (20 mol%), Cs_2CO_3 (2.0 eq.), DMF, 80 °C, 24 h (95%; **12:13** = 70:30). (Ar = 4-$MeOC_6H_4$).

Formation of 3-amino-6-deuterioBODIPY **12** as the major product is consistent with the straightforward nucleophilic substitution mechanism (as shown in Scheme 4), but the presence of the regioisomeric 2-deuteriated product **13** indicates a minor pathway involving nucleophilic attack by the amine at C-5 in the iodoBODIPY **11** (and **2**). The unequal ratio of products **12**:**13** rules out any mechanisms involving prior dehalogenation to generate the unsubstituted BODIPY **1** in situ. Two other potential mechanisms, one based on a redox cycle[23] and one on a Base Catalysed Halogen Dance[24] were discounted on the basis of the results above.

Photophysical properties of the 3-aminoBODIPYs 4

The absorption and fluorescence data for the 3-aminoBODIPY compounds **4a-n** and the parent unsubstituted compound **1** are summarized in Table 3.

Table 3. Absorption and fluorescence data for compounds **1**, **4a-n** in THF.

BODIPY	λ_{abs} (max) /nm	ε /10^4 $M^{-1}cm^{-1}$	λ_{em} (max) /nm	Φ_f[b] (λ_{ex})
1	494	4.59	508	0.075 (479)
4a	493	3.51	525	0.026 (484)
4a[c]	508[c]	2.09[c]	524[c]	0.058[c] (484)
4b	500	4.34	—[d]	—[d]
4c	522	4.69	534	0.050 (492)
4d	498	3.43	525	0.030 (484)
4e	496	3.09	528	0.033 (485)
4f	496	3.56	525	0.015 (484)
4g	484	3.23	—[d]	—[d]
4h	476	4.15	540	0.005 (490)
4i	500	3.07	—[d]	—[d]
4j	501	1.99	—[d]	—[d]
4k	508	4.53	565	0.007 (475)
4l	533	5.34	557	0.015 (500)
4m	527	0.97	549	0.022 (497)
4n	500	1.95	—[d]	—[d]

[a] All spectra were recorded in THF. [b] Φ_f determined vs rhodamine 6G in ethanol (Φ_f = 0.95)[27] as reference. Excitation wavelength (λ_{ex}/nm) shown in brackets. [c] Value determined in cyclohexane. [d] Virtually non-fluorescent.

Figure 4 shows the absorption and fluorescence spectra for the parent 8-(4-methoxyphenyl)BODIPY **1**, and for the representative amine and aniline derivatives **4a** and **4l** respectively.

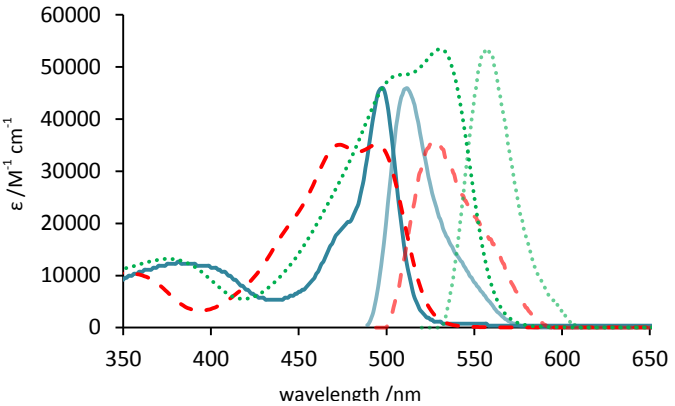


Figure 4. Absorption spectrum (heavy lines) in terms of the molar absorption coefficient (ε) and normalised fluorescence spectrum (feint lines) for **1** (—), **4a** (----), and **4l** (·····) in THF.

The photophysical properties of amino-substituted BODIPYs have previously been reported in detail.[9,10] As shown in Table 3, all of the compounds have low quantum yields, and some are essentially non-fluorescent which can be attributed in part to the free rotation of the aryl substituent in the 8-position and partly due to the influence of the amine. Although low fluorescence of this type of BODIPY might be considered detrimental it is in fact a key feature in their use as 'switch-on' fluorescent probes and this has recently been demonstrated to good effect.[8,9g,10f,10i] The red-shift in the absorption maximum, relative solvent insensitivity of the emission maximum, and slight increase in quantum yield in cyclohexane compared to the more polar THF for the hexylamine derivative **4a** (Table 3) are all in accord with reports on other 3-aminoBODIPYs.[4d,9f,10b,10n,10o,11]

Conclusions

2-Halogeno BODIPYs undergo copper catalysed vicarious nucleophilic substitution with alkyl amines and anilines to give the corresponding 3-aminoBODIPY derivatives. The corresponding reaction with a less nucleophilic amide also proceeded albeit in low yield. The observation that the 2,6-diiodoBODIPY does not react under these conditions allows straightforward separation of this byproduct after the amination. There are two existing approaches to these products, but both have limitations:

(i) Direct nucleophilic substitution of the corresponding 3-halogenoBODIPYs, which requires regioselective introduction of the halogen into the 3-position which must be performed either on the somewhat sensitive dipyrromethane intermediate[28,10h] or involves lengthier synthesis of a halogenated acylpyrrole;[29]

(ii) Direct oxidative hydrogen substitution of a 3,5-unsubstituted BODIPY is known[11] but this method cannot be used with weak nitrogen nucleophiles such as anilines or amides.

Experimental

General

All manipulations involving air-sensitive materials were carried out using standard Schlenk line techniques under an atmosphere of nitrogen in flame-dried glassware. $CHCl_3$, CH_2Cl_2 and NEt_3 were distilled from CaH_2; MeOH and EtOH from magnesium; 1,4-dioxane, Et_2O and THF from Na/benzophenone; toluene from sodium; and MeCN from K_2CO_3, under an atmosphere of nitrogen. DMF was dried over activated 4 Å molecular sieves and stored under nitrogen. All other chemicals were purchased from commercial suppliers and used without further purification. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on either a JEOL ECS 400 or a Bruker Avance 300 instrument. All NMR were referenced relative to $CDCl_3$ (δ_H = 7.26, δ_C = 77.16). IR spectra were recorded on a Varian 800 FT-IR Scimitar Series infrared spectrometer. Mass spectra were recorded on Waters ACQUITY UPLC LCT premier MS in positive ion mode. UV-vis and fluorescence spectra were recorded at 20 °C on a Shimadzu UV-1800 and Hitachi F2500 machines respectively. Relative fluorescence quantum yields (Φ_f) were determined using dilute solutions with an absorbance below 0.1 at the excitation wavelength and using Rhodamine 6G (Φ_f = 0.95)[27] in ethanol as standard. TLC was carried out on glass plates pre-coated with silica gel 60F_{254} and flash column chromatography was performed on Fluorochem LC3025 (40-63 μm) silica gel. Compounds **1**,[30] and **6**[10h] were prepared by modifications to the reported procedures (see Electronic Supplementary Information)

X-ray crystal structure analysis

Single crystals were prepared by slow diffusion of hexane into a solution of the compound in chlorofom. Crystal structure data was collected at 150 K on an Oxford Diffraction (Agilent Technologies) Gemini A Ultra using MoKα radiation (λ = 0.71073 Å) and equipped with an Oxford Cryosystems Cryostream open-flow N_2 cooling device. Cell refinement, data collection and data reduction were carried out using Oxford Diffraction CrysalisPro.[31] The intensities were corrected for absorption semi-empirically based on repeated, symmetry-equivalent reflections in the case of **4a** and analytically using a multi-faceted crystal model in the case of **5a**.[32]
The structures were solved *via* direct methods and refined on F^2 values for all unique data. Refinements were performed using SHELXL[33] within the Olex2 program.[34] Hydrogen atoms were positioned geometrically and defined as riding on their parent atoms.

Materials

2-Iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 2 and 2,6-diiodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 3. 8-(4-Methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene **1** (0.200 g, 0.67 mmol) was taken in dry CH_2Cl_2/MeOH (1:1, 48 mL). A solution of ICl (0.11 g, 0.67 mmol) in MeOH (5 mL) was added to the mixture dropwise. The mixture was stirred at room temperature for 2h. The solvent was then removed under reduced pressure and the crude product was dissolved in CH_2Cl_2 (50 mL) and washed with H_2O (2 x 100 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The resulting red crude product was purified by column chromatography (CH_2Cl_2:petroleum ether 1:1) to give:
First eluted, the 2,6-diiodide **3** as a pink solid (0.055 g, 15%), mp 246-248 °C. Rf = 0.4 (CH_2Cl_2 /petrol, 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.52 (d, J = 8.5 Hz, 2H), 7.13 (s, 2H), 7.06 (d, J = 8.5 Hz, 2H), 3.91 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 162.86, 147.74, 145.96, 137.50, 135.93, 132.64, 125.62, 114.57, 72.07, 55.75. ^{11}B NMR (128 MHz, $CDCl_3$) δ -1.27 (t, J_{BF} = 28.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.63 (q, J_{FB} = 28.0 Hz). IR (neat): υ_{max}/cm^{-1}: 3113, 2930, 1725, 1596, 1566, 1528, 1466, 1342, 1246, 1074, 984, 896, 707. HRMS-ES Calcd for $C_{16}H_{11}BN_2OF_2I_2 + Na^+$: 572.8920. Found: 572.8920.
Second eluted, the monoiodide **2** as a red solid (0.185 g, 65%), mp 206-208 °C. Rf = 0.3 (CH_2Cl_2/petrol, 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.81 (s, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 4H), 6.59 (d, J = 4.3 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.51, 146.73, 146.11, 145.22, 135.99, 135.78, 135.08, 133.00, 132.57, 125.95, 119.46, 114.36, 70.73, 55.69. ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.72 (q, J_{FB} = 28.0 Hz). ^{11}B NMR (128 MHz, $CDCl_3$) δ -1.26 (t, J_{BF} = 28.0 Hz). IR (neat): υ_{max}/cm^{-1}: 3109, 2849, 1721, 1603, 1573, 1532, 1470, 1400, 1349, 1250, 1062, 982, 706. HRMS-ES Calcd for $C_{16}H_{12}BN_2OF_2I + Na^+$: 446.9953. Found: 446.9961.

General procedure for copper catalysed amination. 2-Iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene **2** (0.100 g, 0.235 mmol), the amine (0.470 mmol), CuI (2.2 mg, 0.01 mmol, 5 mol%) Cs_2CO_3 (0.154 g, 0.470 mmol), and 1,10-phenanthroline (8.5 mg, 0.047 mmol, 20 mol%) were taken in a flame-dried Schlenk tube and flushed with N_2 several times. Dry DMF (0.8 mL) was then added and the mixture was stirred at 80 °C for 24 h. The mixture was dissolved in ethyl acetate (30 mL) and washed with water (2 × 100 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography. In all cases the 3-amino-6-iodo byproduct **5** eluted from the column first and the 3-amino compound **4** second.

3-(Hexylamino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4a. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark yellow solid (0.056 g, 60%); mp 202-204℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 3H), 6.97 (dd, J = 6.7, 4.7 Hz, 2H), 6.94 (s, 1H), 6.44 (d, J = 3.5 Hz, 1H), 6.33 (dd, J = 3.6, 2.4 Hz, 1H), 6.23 (s, 1H), 6.16 (d, J = 5.0 Hz, 1H), 3.86 (s, 3H), 3.38 (dd, J = 13.5, 6.8 Hz, 2H), 1.75 – 1.62 (m, 2H), 1.45 – 1.35 (m, 2H), 1.34 – 1.25 (m, 4H), 0.89 (dd, J = 9.0, 4.5 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.67, 160.49, 136.12, 133.40, 132.80, 132.75, 131.75, 130.84, 127.15, 119.78, 113.74, 113.39, 110.06, 55.47, 44.82, 31.44, 30.18, 26.32, 22.59, 14.08. ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.01 (t, J_{BF} = 33.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -149.24 (q, J_{FB} = 33.5 Hz). IR (neat): υ_{max}/cm^{-1}: 3413, 3127, 2923, 1606, 1524, 1471, 1397, 1372, 1243, 1178, 1021, 977, 759. HRMS-ES Calcd for $C_{22}H_{26}BN_3OF_2 + Na^+$: 419.2071. Found: 419.2060.

3-(Hexylamino)-6-iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5a. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark yellow solid (0.006 g, 5%), ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 3H), 7.01 – 6.93 (m, 3H), 6.47 (s, 1H), 6.31 (s, 1H), 6.23 (d, *J* = 5.0 Hz, 1H), 3.40 (q, *J* = 6.8 Hz, 2H), 1.68 (p, *J* = 7.3 Hz, 2H), 1.43 – 1.28 (m, 6H), 0.93 – 0.86 (m, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 162.04, 160.65, 136.78, 134.61, 134.21, 133.74, 131.67, 131.05, 126.57, 124.84, 113.92, 111.30, 65.08,

55.51, 44.97, 31.41, 30.19, 26.30, 22.57, 14.07. HRMS-ES Calcd for $C_{22}H_{25}BN_3OF_2 + Na^+$: 546.1001. Found: 546.1005.

3-((4-Methylphenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4b. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.080 g, 84%); mp 186-188 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.43 (s, 1H), 7.39 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.89 (s, 1H), 6.47 (d, *J* = 3.3 Hz, 1H), 6.35 – 6.30 (m, 1H), 6.28 (d, *J* = 4.9 Hz, 1H), 3.81 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.74, 158.94, 136.20, 135.72, 135.01, 134.70, 133.13, 132.91, 132.17, 131.83, 130.38, 126.96, 122.89, 121.24, 113.97, 113.85, 111.16, 55.50, 21.08. IR (neat): υ_{max}/cm^{-1}: 3368, 2914, 2839, 1606,1580,1523,1489, 1397, 1293, 1241, 1175, 1032, 973, 787. ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.37 (q, J_{FB} = 33.0 Hz). ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.06 (t, J_{BF} = 33.0 Hz).HRMS-ES Calcd for $C_{23}H_{20}BN_3OF_2$ $+H^+$: 404.1742. Found: 404.1740.

6-Iodo-3-((4-methylphenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5b. Eluted with CH_2Cl_2:petroleum ether (1:1). Purple solid (0.007 g, 5%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.42 (d, *J* = 3.8 Hz, 2H), 7.40 (s, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.99 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.56 (s, 1H), 6.37 (d, *J* = 4.9 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 1H), 2.37 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.88, 159.64, 136.79, 136.39, 135.70, 134.56, 134.26, 133.53, 132.88, 131.73, 130.44, 126.43, 126.06, 123.28, 114.00, 112.47, 65.60, 55.52, 21.10. IR (neat): υ_{max}/cm^{-1}: 3374.918, 2934.681, 1712.014, 1604.078, 1519.013, 1477.763, 138.029, 1250.856, 1031.766, 733.380. HRMS-ES Calcd for $C_{23}H_{19}BN_3OF_2I + Na^+$: 551.0568. Found: 551.0565.

3-(*N*-Benzamido)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4c. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.015 g, 15%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H), 7.97 (d, *J* = 7.8 Hz, 2H), 7.67 (s, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 4.7 Hz, 1H), 7.09 (d, *J* = 4.7 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 3.8 Hz, 1H), 6.53 – 6.40 (m, 1H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.04, 161.68, 152.47, 142.51, 137.46, 135.05, 133.70, 133.35, 132.55, 132.22, 131.26, 129.28, 127.61, 127.01, 126.29, 116.29, 114.09, 113.34, 55.60.^{11}B NMR (128 MHz, $CDCl_3$) δ -0.15 (t, J_{BF} = 33.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -146.81 (q, J_{FB} = 33.1 Hz). IR (neat): υ_{max}/cm^{-1}: 3402, 2919, 1692, 1588, 1503, 1444, 1348, 1287, 1250, 1176, 1057, 1033 977, 699. HRMS-ES Calcd for $C_{23}H_{18}BN_3O_2F_2 + Na^+$: 440.1358. Found: 440.1360.

3-(Benzylamino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4d. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark orange solid (0.061 g, 61%); mp 132-134 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.42 (d, *J* = 8.7 Hz, 2H), 7.40 – 7.36 (m, 1H), 7.34 (d, *J* = 6.6 Hz, 2H), 7.33 – 7.28 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 4.9 Hz, 1H), 6.64 (s, 1H), 6.48 (d, *J* = 3.6 Hz, 1H), 6.34 (dd, *J* = 3.5, 2.5 Hz, 1H), 6.11 (d, *J* = 4.9 Hz, 1H), 4.60 (d, *J* = 6.3 Hz, 2H), 3.86 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.71, 160.60, 136.81, 136.14, 133.85, 133.28, 132.85, 131.78, 131.51, 129.15, 128.16, 127.02, 126.93, 120.55, 113.78, 113.68, 110.04, 55.48, 48.22.^{11}B NMR (128 MHz, $CDCl_3$) δ 0.02 (t, J_{BF} = 33.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.95 (q, J_{FB} = 33.5 Hz). IR (neat): υ_{max}/cm^{-1}: 3360, 2970, 1705, 1619, 1466, 1379, 1160, 1128, 951, 816. .HRMS-ES Calcd for $C_{23}H_{20}BN_3OF_2 + Na^+$: 426.1565. Found: 426.1584.

3-((2-(Thiophen-2-yl)ethyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4e. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.065 g, 65%); mp 119-120 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 9.0, 2.4 Hz, 3H), 7.18 (dd, J = 5.1, 1.3 Hz, 1H), 6.96 (t, J = 7.1 Hz, 3H), 6.91 (dd, J = 2.9, 2.2 Hz, 2H), 6.46 (d, J = 3.5 Hz, 1H), 6.36 (s, 1H), 6.33 (dd, J = 3.7, 2.3 Hz, 1H), 6.06 (d, J = 5.0 Hz, 1H), 3.86 (s, 3H), 3.65 (q, J = 6.6 Hz, 2H), 3.18 (t, J = 6.7 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.45, 160.55, 139.31, 136.06, 133.32, 132.79, 131.78, 131.21, 127.53, 127.04, 126.43, 124.69, 120.20, 113.77, 113.58, 109.73, 55.50, 46.23, 30.84. ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.04 (t, J_{BF} = 33.2 Hz), ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.47 – -149.21 (m). IR (neat): υ_{max}/cm^{-1}3361, 2923, 178, 1606, 1401, 1293, 1257, 1025, 792. HRMS-ES Calcd for $C_{22}H_{20}BN_3OF_2S$ $+H^+$: 424.1466. Found: 424.1456

3-(Cyclohexylamino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4f. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.073 g, 78%); mp 130-131 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 5.0 Hz, 1H), 6.43 (d, *J* = 3.3 Hz, 1H), 6.32 (dd, *J* = 3.6, 2.4 Hz, 1H), 6.19 (s, 1H), 6.16 (d, *J* = 5.0 Hz, 1H), 3.86 (s, 2H), 3.43 (d, *J* = 8.8 Hz, 1H), 2.02 (d, *J* = 10.2 Hz, 2H), 1.81 (d, *J* = 13.3 Hz, 2H), 1.63 (d, *J* = 16.3 Hz, 1H), 1.53 – 1.14 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.76, 160.45, 136.09, 133.34, 132.78, 132.47, 131.73, 130.67, 127.19, 119.56, 113.74, 113.29, 110.49, 55.47, 53.79, 33.62, 25.21, 24.53. ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.01 (t, J_{BF} = 30.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -149.24 (q, J_{FB} = 30.0 Hz) IR (neat): υ_{max}/cm^{-1}: 2931, 2858, 1718, 1604, 1511, 1293, 1253, 1175, 1062, 1027, 839, 795. HRMS-ES Calcd for $C_{22}H_{24}BN_3OF_2$ + Na^+: 418.1878. Found: 418.1879.

3-(Cyclohexylamino)-6-iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5f. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark yellow solid (0.005 g, 4%), ^{1}H NMR (400 MHz, $CDCl_3$) δ7.35 (s, 1H), 7.37 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 2H), 6.97 (s, 1H), 6.46 (s, 1H), 6.23 (s, 2H), 3.86 (s, 3H), 3.52 – 3.38 (m, 1H), 2.08 – 1.98 (m, 2H), 1.86 – 1.75 (m, 2H), 1.65 (d, *J* = 12.8 Hz, 1H), 1.50 – 1.21 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.11, 160.61, 136.72, 134.45, 134.21, 133.70, 131.66, 130.77, 126.62, 124.63, 113.91, 111.71, 65.00, 55.51, 54.04, 33.64, 25.14, 24.53. IR (neat): υ_{max}/cm^{-1}: 3372.915, 2916.489, 1608.145, 1573.648, 1518.964, 1480.453, 1392.344, 1251.759, 1101.075. HRMS-ES Calcd for $C_{22}H_{23}BN_3OF_2I + Na^+$: 544.0845. Found: 544.0850.

3-(Morpholino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4g. Eluted with CH_2Cl_2: petroleum ether (9:1). Orange solid (0.076 g, 85%); mp 214-215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.92 (d, *J* = 5.1 Hz, 1H), 6.42 (d, *J* = 3.3 Hz, 1H), 6.37 – 6.33 (m, 1H), 6.20 (d, *J* = 5.1 Hz, 1H), 3.93 (d, *J* = 5.1 Hz, 4H), 3.88 (d, *J* = 5.1 Hz, 4H), 3.87 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 162.07, 160.50, 135.83, 135.11, 133.61, 132.07, 131.87, 131.75, 127.37, 119.51, 113.91, 113.72, 112.44, 66.87, 55.49, 50.56. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.14 (t, J_{BF} = 33.5 Hz), ^{19}F NMR (376 MHz, $CDCl_3$) δ -135.24 (q, J_{FB} = 33.5 Hz).IR (neat): υ_{max}/cm^{-1}: 3361, 2923, 2852, 2360, 1590, 1536, 1512, 1408, 1287, 1244, 1178, 1019, 902, 760.. HRMS-ES Calcd for $C_{20}H_{20}BN_3O_2F_2 + Na^+$: 405.1551. Found: 405.1551.

3-(Pyrrolidin-1-yl)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4h. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark yellow solid (0.075 g, 87%); mp 171-173 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 1H), 7.39 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 5.1 Hz, 1H), 6.35 (d, *J* = 3.1 Hz, 1H), 6.34 – 6.32 (m, 1H), 6.15 (d, *J* = 5.1 Hz, 1H), 3.94 (br,s, 4H), 3.86 (s, 3H), 2.11 – 2.00 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.27, 160.17, 135.53, 135.37, 132.02, 131.83, 130.89, 129.96, 127.76, 117.46, 114.35, 113.60, 113.09, 55.46, 51.35, 25.68. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.01 (t, J_{BF} = 31.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -128.23 (q, J_{FB} = 31.0 Hz).IR (neat): υ_{max}/cm^{-1}: 3360, 2923, 1577, 1510, 1395, 2350, 1251, 1094, 1028, 908, 778. HRMS-ES Calcd for $C_{20}H_{20}BN_3OF_2$ + Na^+: 490.1565. Found: 490.1546.

6-Iodo-3-(pyrrolidin-1-yl)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5h. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark orange solid (0.005 g, 4%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 5.2 Hz, 1H), 6.39 (s, 1H), 6.21 (d, *J* = 5.1 Hz, 1H), 4.04 (s, 4H), 3.86 (s, 3H), 2.07 (t, *J* = 6.7 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.49, 160.33, 135.85, 133.82, 133.52, 132.53, 131.75, 129.11, 127.17, 122.68, 115.55, 113.77, 64.87, 55.50, 52.13, 25.75. IR (neat): υ_{max}/cm^{-1}: 2988.020, 2359.166, 1794.501, 1694.386, 1599.758, 1513.181, 1392.300, 1248.277, 1027.897, 779.549. HRMS-ES Calcd for $C_{20}H_{19}BN_3OF_2I$ + Na^+: 516.0532. Found: 516.0531.

3-((2-Methylphenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4i. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.057, 60%); mp 227-229 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 5.1 Hz, 1H), 6.41 (d, *J* = 3.4 Hz, 1H), 6.39 – 6.34 (m, 1H), 5.62 (d, *J* = 5.1 Hz, 1H), 3.96 (s, 2H), 3.85 (s, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 163.14, 160.34, 146.93, 135.59, 134.17, 132.93, 132.04, 131.82, 131.17, 130.20, 128.10, 127.57, 126.72, 118.74, 116.18, 113.65, 113.57, 55.45, 43.11. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.04 (t, J_{BF} = 33.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.10 (q, J_{FB} = 33.0 Hz). IR (neat): υ_{max}/cm^{-1}: 3378, 2925, 1620, 1578, 1489, 1398, 1258, 1085, 1021, 786. HRMS-ES Calcd for $C_{23}H_{20}BN_3OF_2$ + Na^+: 426.1565. Found: 426.1577.

3-((4-Methoxyphenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4j. Eluted with CH_2Cl_2:petroleum ether (9:1). Orange solid (0.077 g, 78%); mp 245-247 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.49 – 7.46 (m, 1H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.95 – 6.90 (m, 3H), 6.52 (d, *J* = 3.6 Hz, 1H), 6.36 (dd, *J* = 3.7, 2.3 Hz, 1H), 6.23 (d, *J* = 4.9 Hz, 1H), 3.87 (s, 3H), 3.85 – 3.80 (m, 3H). The compound was insufficiently soluble to determine ^{13}C NMR. ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.45 (q, J_{FB} = 32.5 Hz). ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.07 (t, J_{BF} = 32.5 Hz). IR (neat): υ_{max}/cm^{-1}: 3368, 2914, 1580, 1293, 1241. HRMS-ES Calcd for $C_{23}H_{20}BN_3O_2F_2$ + Na^+: 442.1514. Found: 442.1499.

6-Iodo-3-((4-methoxyphenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5j. Eluted with CH_2Cl_2:petroleum ether (9:1). Orange solid (0.008 g, 6%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.42 (s, 1H), 7.41 (d, *J* = 8.9 Hz, 2H), 7.21 (d, *J* = 6.9 Hz, 2H), 6.98 (d, *J* = 6.5 Hz, 2H), 6.96 (s, 1H), 6.93 (d, *J* = 6.9 Hz, 2H), 6.55 (s, 1H), 6.27 (d, *J* = 4.9 Hz, 1H), 3.87 (s, 3H), 3.83 (s, 3H). The compound was insufficiently soluble to determine ^{13}C NMR. IR (neat): υ_{max}/cm^{-1}: 3342.169, 3119.175, 2929.044, 1725.014, 1613.144, 1511.895, 1480.277, 1390.170, 1249.831, 1101.578. HRMS-ES Calcd for $C_{23}H_{19}BN_3OF_2I$ + Na^+: 568.0481. Found: 568.0489.

3-((4-Chlorophenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4k. Eluted with CH_2Cl_2:petroleum ether (1:1). Dark yellow solid (0.066 g, 66%); mp 178-180 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.51 (s, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.02 – 6.96 (m, 3H), 6.58 (d, *J* = 3.7 Hz, 1H), 6.39 (dd, *J* = 3.7, 2.4 Hz, 1H), 6.34 (d, *J* = 4.9 Hz, 1H), 3.88 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.90, 157.99, 136.36, 136.13, 135.74, 133.16, 132.97, 132.82, 131.86, 131.34, 129.95, 126.76, 123.72, 122.37, 114.42, 113.89, 110.26, 55.52. ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.01 (t, J_{BF} = 33.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -148.10 (q, J_{FB} = 33.0 Hz).IR (neat): υ_{max}/cm^{-1}: 3348, 2926, 2860, 1726, 1578, 1519, 1476, 1385, 1292, 1251, 1180, 1096 971, 784. HRMS-ES Calcd for $C_{22}H_{17}BN_3OF_2Cl$ + Na^+: 446.1019. Found: 446.1019.

6-(Iodo)-3-((4-chlorophenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5k. Eluted with CH_2Cl_2:petroleum ether (1:1). Pink solid (0.013 g, 13%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.44 (d, *J* = 14.0 Hz, 2H), 7.39 (d, *J* = 9.0 Hz, 3H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.01 (d, *J* = 5.2 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.61 (s, 1H), 6.38 (d, *J* = 5.0 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.35, 156.52, 141.60, 138.11, 136.69, 136.47, 134.33, 133.96, 132.60, 131.81, 128.85, 125.88, 121.11, 118.24, 114.10, 110.82, 108.49, 66.93, 55.51. IR (neat): υ_{max}/cm^{-1}: 33762.294, 2970.918, 1581.968, 1524.811, 1397.159, 1250.096, 1113.533, 1028.771, 785.061. HRMS-ES Calcd for $C_{22}H_{16}BN_3OF_2ICl$ + Na^+: 571.9985. Found: 571.9990.

3-((4-Cyanophenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4l. Eluted with CH_2Cl_2:petroleum ether (9:1). Pink solid (0.075 g, 77%); mp 204-207 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.02 (dd, *J* = 10.7, 6.8 Hz, 3H), 6.67 (d, *J* = 4.6 Hz, 1H), 6.50 (d, *J* = 4.8 Hz, 1H), 6.43 (dd, *J* = 3.9, 2.3 Hz, 1H), 3.89 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.26, 155.54, 142.19, 138.61, 135.53, 135.12, 133.99, 133.21, 132.27, 131.97, 126.45, 124.45, 120.55, 118.55, 115.33, 114.01, 109.54, 107.74, 55.56. ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.09 (t, J_{BF} = 32.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ -147.61 (q, J_{FB} = 32.0 Hz).IR (neat): υ_{max}/cm^{-1}: 3383, 3072, 2224, 1599, 1560, 1524, 1476, 1396, 1251, 1175, 1113, 1024, 936, 780. HRMS-ES Calcd for $C_{23}H_{17}BN_4OF_2$+ Na^+: 437.1361. Found: 437.1367.

3-((4-Cyanophenyl)amino)-6-iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5l. Eluted with CH_2Cl_2:petroleum ether (9:1). Pink solid (0.019 g, 15%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.46 (s, 1H), 7.38 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 4.9 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.64 (s, 1H), 6.48 (d, *J* = 4.9 Hz, 1H), 3.83 (s, 3H). IR (neat): υ_{max}/cm^{-1}: 3366.735, 2995.752, 2227.815, 1597.598, 1566.083, 1474.928, 1394.394, 1253.863, 1101.720. HRMS-ES Calcd for $C_{23}H_{16}BN_4OF_2I$ + Na^+: 563.0328. Found: 563.0323.

3-(Pyridin-2-ylamino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4m. Eluted with CH_2Cl_2:petroleum ether (7:3). Pink solid (0.055 g, 60%); mp 213-215 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.34 (m, 2H), 7.71 – 7.63 (m, 1H), 7.54 (s, 1H), 7.52 (d, J = 4.9 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.04 (d, J =

4.9 Hz, 1H), 7.02 (d, J = 3.5 Hz, 1H), 7.00 (s, 2H), 6.95 (d, J = 8.9 Hz, 1H), 6.60 (d, J = 3.6 Hz, 1H), 6.39 (dd, J = 3.5, 2.3 Hz, 1H), 3.89 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 189.77, 160.98, 155.85, 151.33, 148.49, 138.37, 137.20, 135.35, 133.61, 133.11, 132.11, 131.98, 126.85, 122.93, 118.88, 114.51, 113.89, 113.03, 55.52. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.01 (t, J_{BF} = 33.2 Hz).^{19}F NMR (376 MHz, $CDCl_3$) δ -147.12 – -147.70 (m). IR (neat): υ_{max}/cm^{-1}: 3385, 3029, 2356, 1629, 1603,1562, 1496, 1393, 1340, 1297, 1247, 1097, 1028, 972, 769. HRMS-ES Calcd for $C_{21}H_{17}BN_4OF_2$ + H^+: 391.1542. Found: 391.1549.

6-Iodo-3-(pyridin-2-ylamino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 5m. Eluted with CH_2Cl_2:petroleum ether (7:3). Pink solid (0.017 g, 14%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.39 – 8.34 (m, 1H), 7.69 (td, *J* = 7.8, 1.9 Hz, 1H), 7.59 (d, *J* = 5.0 Hz, 1H), 7.47 (d, *J* = 1.1 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.07 (d, *J* = 5.1 Hz, 1H), 7.05 – 7.02 (m, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.66 – 6.60 (m, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.14, 156.70, 150.97, 148.57, 138.51, 136.88, 136.16, 135.34, 134.38, 132.49, 131.91, 127.54, 126.31, 119.36, 115.96, 114.06, 113.29, 66.24, 55.57. IR (neat): υ_{max}/cm^{-1}: 3384.942, 2997.326, 1629.610, 1604.071, 1563.166, 1496.334, 1393.697, 1248.697, 1029.204, 972.232, 769.562. HRMS-ES Calcd for $C_{21}H_{16}BN_4OF_2I$ + Na^+: 539.0328. Found: 539.0326.

3-(Methyl(phenyl)amino)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4n. Eluted with CH_2Cl_2:petroleum ether (1:1). Orange solid (0.038, 40%); mp 220-221 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 6.72 (d, *J* = 5.1 Hz, 1H), 6.52 – 6.16 (m, 1H), 5.62 (d, *J* = 5.1 Hz, 1H), 3.96 (s, 1H), 3.85 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.15, 160.34, 146.92, 135.59, 134.17, 132.92, 132.04, 131.82, 131.16, 130.20, 128.10, 127.56, 126.72, 118.73, 116.18, 113.65, 113.55, 55.45, 43.11. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.17 (t, J_{BF} = 32.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -129.68 (q, J_{FB} = 32.5 Hz). IR (neat): υ_{max}/cm^{-1}: 2962, 2919, 1681, 1603, 1513, 1298, 1258, 1020, 932, 794. HRMS-ES Calcd for $C_{23}H_{20}BN_3OF_2$ + Na^+: 425.1602. Found:425.1598.

6-Deuterio-2-iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene 11. 2,6-diiodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene **3** (0.38 g, 0.69 mmol) was dissolved in CH_2Cl_2 (31 mL). Et_3N (0.09 mL, 0.69 mmol), K_2CO_3 (0.31 g, 2.25 mmol) and 10% Pd/C (0.38 g) were added. The mixture was stirred under nitrogen for 15 min and the nitrogen line was replaced with a deuterium-filled balloon. The mixture was stirred at room temperature for 4 h and then filtered through Celite, washing with CH_2Cl_2. The solvent was removed under reduced pressure and the orange crude product was purified by column chromatography eluting with CH_2Cl_2:petroleum ether (1:1) to give, first eluted: the 6-deuterio-2-iodoBODIPY **11** as an orange solid (0.177 g, 60%) mp 214-215 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.75 (s, 1H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.05 – 6.93 (m, 4H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.45, 146.66, 146.03, 145.07, 135.90, 135.72, 135.01, 132.81, 132.49, 125.88, 119.19 (t, *J* = 27.07 Hz), 114.29, 70.65, 55.61. ^{19}F NMR (282 MHz, $CDCl_3$) δ -144.96 (q, J_{FB} = 28.5 Hz). ^{11}B NMR (96 MHz, $CDCl_3$) δ 0.45 (t, J_{BF} = 28.5 Hz). HRMS-ES Calcd for $C_{16}H_{11}{}^2HBN_2F_2IO$ + Na^+: 448.0115. Found: 448.0112.

Second eluted: **2,6-dideuterio-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene 2,6-^{2}H$_2$-1** as an orange solid (0.035 g, 17%) mp 133-135 ℃.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.89 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.11, 147.44, 143.31, 134.82, 132.44, 131.27, 126.30, 118.45, 118.12, 117.77, 114.08, 55.55. ^{11}B NMR (96 MHz, $CDCl_3$) δ 0.31 (t, J_{BF} = 29.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ -145.02 (q, J_{FB} = 29.0 Hz). HRMS-ES Calcd for $C_{16}H_{11}{}^2H_2BN_2F_2O$ + Na^+: 323.1112. Found: 323.1110.

6-Deuterio-3-(pyrrolidin-1-yl)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene 12 and 2-Deuterio-3-(pyrrolidin-1-yl)-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene 13. Following the General Procedure for copper catalysed amination, 6-deuterio-2-iodo-8-(4-methoxyphenyl)-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene **11** (0.105 g, 0.247 mmol) was reacted with pyrrolidine (0.035 g, 0.494 mmol). Purification by column chromatography eluting with CH_2Cl_2:petroleum ether (1:1) gave a 70:30 mixture of the 6-deuterio and 2-deuterioBODIPYs **12** and **13** respectively as an orange solid (0.08 g, 88%). For the mixture: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (br,s, 1H), 7.41 (d, J = 8.7 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 6.93 – 6.88 (m, 1H), 6.48 – 6.25 (m, 1H), 6.16 (d, J = 5.1 Hz, 1H), 3.94 (br, s, 4H), 3.89 (s, 3H), 2.08-2.05 (m, 4H).^{11}B NMR (96 MHz, $CDCl_3$) δ 1.00 (t, J_{BF} = 32.5 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ -128.25 (q, J_{FB} = 32.5 Hz). HRMS-ES Calcd for $C_{20}H_{19}{}^2HBN_3F_2O$ + Na^+: 391.1628. Found: 391.1623. For the major product **12**: ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.22 (C3), 160.13 (C4'), 135.46 (C8a), 135.24 (C1), 131.94 (C7a), 131.75 (C2',C6'), 130.74 (C8), 129.74 (C5), 127.68 (C1'), 117.23 (C7), 114.35 (C2), 113.55 (C3',C5'), 112.97 (C6), 55.37 (OMe), 51.26, 25.58. For the minor product **13**: ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.17 (C3), 160.13 (C4'), 135.46 (C8a), 135.12 (C1), 131.94 (C7a), 131.75 (C2',C6'), 130.74 (C8), 129.82 (C5), 127.68 (C1'), 117.23 (C7), 114.35 (C2), 113.55 (C3',C5'), 112.97 (C6), 55.37(OMe), 51.26, 25.58.

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Notes and references

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Electronic Supplementary Information (ESI) available: modified synthetic procedures for previously reported compounds **1** and **6**, X-Ray crystal structure of compound **4a**, Schemes showing potential redox and Base Catalysed Halogen Dance mechanisms which were discounted by experiment, copies of NMR spectra for all compounds, and CIF files giving details of crystal data, structure solution, and refinement, atomic coordinates, bond distances, bond angles, and anisotropic displacement parameters for compounds **4a** and **5a**. See DOI: 10.1039/b000000x/

1. A. Treibs and F. H. Kreuzer, *Liebigs Ann. Chem.*, 1968, **718**, 208.
2. (a) G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem. Int. Ed.*, 2008, **47**, 1184; (b) A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **107**, 4891.
3. (a) K. Umezawa, D. Citterio and K. Suzuki, *Anal. Sci.*, 2014, **30**, 327; (b) Y. Ni and J. Wu, *Org. Biomol. Chem.*, 2014, **12**, 3774; (c) L. D. Lavis and R. T. Raines, *ACS Chem. Biol.*, 2008, **3**, 142.

4. (a) I. Esnal, I. Valois-Escamilla, C. F. A. Gõmez-Durán, A. Urías-Benavides, M. L. Betancourt-Mendiola, I. Lõpez-Arbeloa, J. Bañuelos, I. García-Moreno, A. Costela and E. Peña-Cabrera, *ChemPhysChem*, 2013, **14**, 4134; (b) Y. Yang, L. Zhang, B. Li, L. Zhang and X. Liu, *RSC Adv.*, 2013, **3**, 14993; (c) G. Duran-Sampedro, A. R. Agarrabeitia, I. Garcia-Moreno, A. Costela, J. Bañuelos, T. Arbeloa, I. López Arbeloa, J. L. Chiara and M. J. Ortiz, *Eur. J. Org. Chem.*, 2012, 6335; (d) M. Liras, J. B. Prieto, M. Pintado-Sierra, F. L. Arbeloa, I. García-Moreno, Á. Costela, L. Infantes, R. Sastre and F. Amat-Guerri, *Org. Lett.*, 2007, **9**, 4183.
5. (a) J. Zhao, W. Wu, J. Sun and S. Guo, *Chem. Soc. Rev.*, 2013, **42**, 5323; (b) S. Guo, L. Ma, J. Zhao, B. Küçüköz, A. Karatay, M. Hayvali, H. G. Yaglioglu and A. Elmali, *Chem. Sci.*, 2014, **5**, 489.
6. (a) A. Kamkaew, S. H. Lim, H. B. Lee, L. V. Kiew, L. Y. Chung and K. Burgess, *Chem. Soc. Rev.*, 2013, **42**, 77; (b) S. G. Awuah and Y. You, *RSC Adv.*, 2012, **2**, 11169.
7. (a) J. F. Lefebvre, X. Z. Sun, J. A. Calladine, M. W. George and E. A. Gibson, *Chemical Communications*, 2014, **50**, 5258; (b) A. M. Poe, A. M. Della Pelle, A. V. Subrahmanyam, W. White, G. Wantz and S. Thayumanavan, *Chem. Commun.*, 2014, **50**, 2913; (c) A. Bessette and G. S. Hanan, *Chem. Soc. Rev.*, 2014, **43**, 3342; (d) S. Erten-Ela, M. D. Yilmaz, B. Icli, Y. Dede, S. Icli and E. U. Akkaya, *Org. Lett.*, 2008, **10**, 3299; (e) S. Hattori, K. Ohkubo, Y. Urano, H. Sunahara, T. Nagano, Y. Wada, N. V. Tkachenko, H. Lemmetyinen and S. Fukuzumi, *J. Phys. Chem. B*, 2005, **109**, 15368.
8. For examples see: (a) R. Gotor, P. Gaviña, L. E. Ochando, K. Chulvi, A. Lorente, R. Martínez-Máñez and A. M. Costero, *RSC Adv.*, 2014, **4**, 15975; (b) X. Li, X. Gao, W. Shi and H. Ma, *Chem. Rev.*, 2014, **114**, 590; (c) H. Zhu, J. Fan, S. Zhang, J. Cao, K. Song, D. Ge, H. Dong, J. Wang and X. Peng, *Biomater. Sci.*, 2014, **2**, 89; (d) A. Nano, P. Retailleau, J. P. Hagon, A. Harriman and R. Ziessel, *Phys. Chem. Chem. Phys.*, 2014, **16**, 10187; (e) A. Barba-Bon, L. Calabuig, A. M. Costero, S. Gil, R. Martínez-Máñez and F. Sancenón, *RSC Adv.*, 2014, **4**, 8962; (f) W. Qin, M. Baruah, M. Van Der Auweraer, F. C. De Schryver and N. Boens, *J. Phys. Chem. A*, 2005, **109**, 7371.
9. (a) N. Boens, L. Wang, V. Leen, P. Yuan, B. Verbelen, W. Dehaen, M. Van Der Auweraer, W. D. De Borggraeve, L. Van Meervelt, J. Jacobs, D. Beljonne, C. Tonnelé, R. Lazzaroni, M. J. Ruedas-Rama, A. Orte, L. Crovetto, E. M. Talavera and J. M. Alvarez-Pez, *J. Phys. Chem. A*, 2014, **118**, 1576; (b) I. Esnal, J. Bañuelos, I. López Arbeloa, A. Costela, I. Garcia-Moreno, M. Garzón, A. R. Agarrabeitia and M. José Ortiz, *RSC Adv.*, 2013, **3**, 1547; (c) I. Esnal, I. Valois-Escamilla, C. F. A. Gõmez-Durán, A. Urías-Benavides, M. L. Betancourt-Mendiola, I. Lõpez-Arbeloa, J. Bañuelos, I. García-Moreno, A. Costela and E. Peña-Cabrera, *ChemPhysChem*, 2013, **14**, 4134; (d) R. I. Roacho, A. Metta-Magaña, M. M. Portillo, E. Peña-Cabrera and K. H. Pannell, *J. Org. Chem.*, 2013, **78**, 4245; (e) C. A. Osorio-Martínez, A. Urías-Benavides, C. F. A. Gómez-Durán, J. Bañuelos, I. Esnal, I. López Arbeloa and E. Peña-Cabrera, *J. Org. Chem.*, 2012, **77**, 5434; (f) W. Qin, V. Leen, T. Rohand, W. Dehaen, P. Dedecker, M. Van Der Auweraer, K. Robeyns, L. Van Meervelt, D. Beljonne, B. Van Averbeke, J. N. Clifford, K. Driesen, K. Binnemans and N. Boens, *J. Phys. Chem. A*, 2009, **113**, 439; (g) X. Shao, R. Kang, Y. Zhang, Z. Huang, F. Peng, J. Zhang, Y. Wang, F. Pan, W. Zhang, and W. Zhao, *Anal. Chem.*, 2015, **87**, 399; (h) M. Gupta, S. Mula, M. Tyagi, T. K. Ghanty, S. Murudkar, A. K. Ray and S. Chattopadhyay, *Chem. Eur. J.*, 2013, **19**, 17766; (i) H. Yokoi, N. Wachi, S. Hiroto and H. Shinokubo, *Chem. Commun.*, 2014, **50**, 2715; (j) H. Yokoi, S. Hiroto and H. Shinokubo, *Org. Lett.*, 2014, **16**, 3004..
10. (a) X. He, J. Zhang, X. Liu, L. Dong, D. Li, H. Qiu and S. Yin, *Sensors and Actuators, B: Chemical*, 2014, **192**, 29; (b) E. Ganapathi, S. Madhu, T. Chatterjee, R. Gonnade and M. Ravikanth, *Dyes and Pigments*, 2014, **102**, 218; (c) M. De Lourdes Betancourt-Mendiola, E. Peña-Cabrera, S. Gil, K. Chulvi, L. E. Ochando and A. M. Costero, *Tetrahedron*, 2014, **70**, 3735; (d) Y. A. Volkova, B. Brizet, P. D. Harvey, A. D. Averin, C. Goze and F. Denat, *Eur. J. Org. Chem.*, 2013, 4270; (e) L. Y. Niu, H. Li, L. Feng, Y. S. Guan, Y. Z. Chen, C. F. Duan, L. Z. Wu, Y. F. Guan, C. H. Tung and Q. Z. Yang, *Anal. Chim. Acta*, 2013, **775**, 93; (f) X. Jia, X. Yu, X. Yang, J. Cui, X. Tang, W. Liu and W. Qin, *Dyes and Pigments*, 2013, **98**, 195; (g) M. J. Ortiz, A. R. Agarrabeitia, G. Duran-Sampedro, J. Bañuelos Prieto, T. A. Lopez, W. A. Massad, H. A. Montejano, N. A. García and I. Lopez Arbeloa, *Tetrahedron*, 2012, **68**, 1153; (h) L. Jiao, W. Pang, J. Zhou, Y. Wei, X. Mu, G. Bai and E. Hao, *J. Org. Chem.*, 2011, **76**, 9988; (i) S. C. Dodani, S. C. Leary, P. A. Cobine, D. R. Winge and C. J. Chang, *J. Am. Chem. Soc.*, 2011, **133**, 8606; (j) J. Bañuelos, V. Martín, C. F. A. Gómez-Durán, I. J. A. Córdoba, E. Peña-Cabrera, I. García-Moreno, A. Costela, M. E. Pérez-Ojeda, T. Arbeloa and I. L. Arbeloa, *Chem. Eur. J.*, 2011, **17**, 7261; (k) C. F. A. Gómez-Durán, I. García-Moreno, A. Costela, V. Martin, R. Sastre, J. Bañuelos, F. López Arbeloa, I. López Arbeloa and E. Peña-Cabrera, *Chem. Commun.*, 2010, **46**, 5103; (l) D. W. Domaille, L. Zeng and C. J. Chang, *J. Am. Chem. Soc.*, 2010, **132**, 1194; (m) L. Li, B. Nguyen and K. Burgess, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 3112; (n) O. Dilek and S. L. Bane, *Tetrahedron Lett.*, 2008, **49**, 1413; (o) T. Rohand, M. Baruah, W. Qin, N. Boens and W. Dehaen, *Chem. Commun.*, 2006, 266; . (p) V. Goud, A. Tutar and J. F. Biellmann, *Tetrahedron*, 2006, **62**, 5084; (q) M. Baruah, W. Qin, R. A. L. Vallée, D. Beljonne, T. Rohand, W. Dehaen and N. Boens, *Org. Lett.*, 2005, **7**, 4377.
11. V. Leen, V. Z. Gonzalvo, W. M. Deborggraeve, N. Boens and W. Dehaen, *Chem. Commun.*, 2010, **46**, 4908.
12. For selected reviews of copper catalysed amination see: (a) C. Sambiagio, S. P. Marsden, A. J. Blacker and P. C. McGowan, *Chem. Soc. Rev.*, 2014, **43**, 3525; (b) I. P. Beletskaya and A. V. Cheprakov, *Organometallics*, 2012, **31**, 7753; (c) D. S. Surry and S. L. Buchwald, *Chem. Sci.*, 2010, **1**, 13; (d) E. Sperotto, G. P. M. Van Klink, G. Van Koten and J. G. De Vries, *Dalton Transactions*, 2010, **39**, 10338.
13. E. Kuhn, V. Bulach and M. W. Hosseini, *Chem. Commun.*, 2008, 5104.
14. Z. Lu and R. J. Twieg, *Tetrahedron*, 2005, **61**, 903.
15. A. Shafir and S. L. Buchwald, *J. Am. Chem. Soc.*, 2006, **128**, 8742.
16. D. Wang and K. Ding, *Chem. Commun.*, 2009, 1891.
17. For example, in amination of 3-bromothiophene, see Y. B. Huang, C. T. Yang, J. Yi, X. J. Deng, Y. Fu and L. Liu, *J. Org. Chem.*, 2011, **76**, 800.
18. S. V. Ley and A. W. Thomas, *Angew. Chem. Int. Ed.*, 2003, **42**, 5400; A. Rolfe and P. R. Hanson, *Tetrahedron Lett.*, 2009, **50**, 6935.
19. A consequence of this is that amination can be performed on a mixture of the mono- and di-iodoBODIPYs **2** and **3** to give the 3-

aminoBODIPY **4** and unreacted diiodide **3**, which can be easily separated by column chromatography.

20. Since iodoBODIPY compounds are known to act as initiators for photooxidation,[5] the reaction between the iodide **2** and 4-cyanoaniline was repeated with careful exlusion of light and also with a 5-cycle freeze-pump-thaw sequence to degas the solution prior to reaction. This did not significantly change the yields of the products (**4l** and **5l**) and so the reaction does not appear to be photoinitiated or require the presence of dioxygen.
21. Hartwig has suggested the intermediacy of highly reactive bisamido cuprate species in aminations catalysed by CuI/phenanthroline: R. Giri and J. F. Hartwig, *J. Am. Chem. Soc.*, 2010, **132**, 15860.
22. (a) V. Bocchi and G. Palla, *J. Chem. Soc., Chem. Commun*., 1983, 1074; (b) M. Poirier, S. Goudreau, J. Poulin, J. Savoie and P. L. Beaulieu, *Org. Lett.*, 2010, **12**, 2334; (c) for a review of 'vicarious' hydrogen substitution see: M. Makosza, *Pure Appl. Chem.*, 1997, **69**, 559.
23. Reductive loss of iodine from C-2 might have been linked to oxidation of the copper (I) catalyst[25] [e.g. via a copper (I)/copper (III) cycle or single electron transfers involving copper (II)] (Scheme S2, Electronic Supplementary Information). Such a mechanism would provide the oxidant required for direct nucleophilic hydrogen displacement by the amine[11] and could explain formation of the iodinated byproduct **5**. The unreactivity of the 2,6-diiodide **3,** the formation of a 1:1 ratio of **12**:**13** in the amination of the deuterioBODIPY **11** (Scheme 5) and the success of the amination with aniline nucleophiles all indicate that such a mechanism does not operate.
24. A base-catalysed halogen dance[26] (BCHD) might also be envisaged involving reversible sequential deprotonations to give anionic intermediates which abstract the halogen from another molecule to set up an equilibrium of iodinated BODIPY species. The ultimate outcome of the reaction would be determined by nucleophilic interception of the 3-iodo species to give the product **4** (Scheme S3, Electronic Supplementary Information). The insensitivity of the reaction to the nature of the halogen (Scheme 3) and the failure of an attempted copper catalysed amination of a 1:1 mixture of the unhalogenated BODIPY **1** and the 2,6-diiodide **3** with pyrrolidine strongly suggest that a BCHD is not involved.
25. For a related proposal see: A. John and K. M. Nicholas, *Organometallics*, 2012, **31**, 7914.
26. For a review see: M. Schnürch, M. Spina, A. F. Khan, M. D. Mihovilovic and P. Stanetty, *Chem. Soc. Rev.*, 2007, **36**, 1046.
27. M. Fischer and J. Georges, *Chem. Phys. Lett.*, 1996, **260**, 115.
28. M. Baruah, W. Qin, N. Basarić, W. M. De Borggraeve and N. Boens, *J. Org. Chem.*, 2005, **70**, 4152.
29. V. Leen, T. Leemans, N. Boens and W. Dehaen, *Eur. J. Org. Chem.*, 2011, 4386.
30. C. Yu, L. Jiao, H. Yin, J. Zhou, W. Pang, Y. Wu, Z. Wang, G. Yang and E. Hao, *Eur. J. Org. Chem.*, 2011, 5460.
31. CrysAlisPro version 1.171.35; Agilent Technologies, 2010.
32. R. C. Clark and J. S. Reid, *Acta Crystallogr., Sect. A*, 1995, **51**, 887.
33. G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2008, **64**, 112.
34. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 229.

