Synthesis and spectroscopic properties of a new 4-bora-3a,4a-diaza-*s*-indacene (BODIPY®) dye

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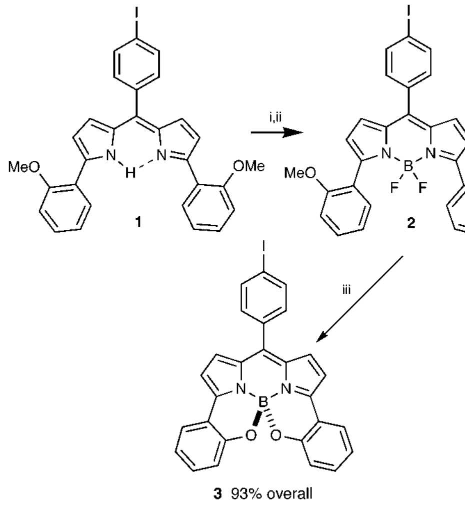
The constrained dye 3 was prepared and shown to have a sharper, red-shifted, and more intense fluorescence emission than the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY®) dye 2 in which the aryl groups can rotate freely.

4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY®) dyes[1] are highly fluorescent materials that have been used for several different applications.[2–5] Relatively recent efforts in our laboratories have focussed on syntheses of the new 3,5-diaryl-substituted BODIPYs of which compound **2** is typical.[6] The goal of this research was to increase the diversity of emission maxima available in the BODIPY series by introducing different substituents on the 3,5-diaryl rings. These studies were largely successful, but the 3,5-diaryl-substituted BODIPY dyes had diminished fluorescence intensities relative to similar alkyl-substituted systems. We hypothesized that this was due to dissipation of energy from an electronic excited state *via* a non-radiative process involving rotation of the aryl rings relative to the dipyrromethene core. Here we report the synthesis and investigation of the new structure **3**, work that was motivated by several considerations. First, the aryl rings in this system would not be able to spin about the aryl–pyrrole bond and this constraint could lead to enhanced fluorescence. Secondly, the ring system was completely new and might have interesting fluorescence properties. Moreover the structure should be accessible *via* demethylation of compound **1**.

A one-pot, two-step process, beginning with the dipyrromethene **1** proved to be the most convenient way to prepare compound **3** (Scheme 1).† It was isolated in high yield as a dark green solid that was stable at room temperature and to chromatography on basic alumina. The ^{11}B NMR spectrum of **2** gave a distinct triplet due to B–F coupling [δ −1.26, (t, J_{BF} = 30.6 Hz in $CDCl_3$ relative to $BF_3 \cdot OEt_2$ external reference)], whereas the corresponding spectrum of **3** consisted of one singlet (δ −0.89).



3 93% overall

Scheme 1 *Reagents and conditions*: i, Et_3N, PhMe; ii, $BF_3 \cdot OEt_2$, 80 °C; iii, BBr_3, O to 25 °C.

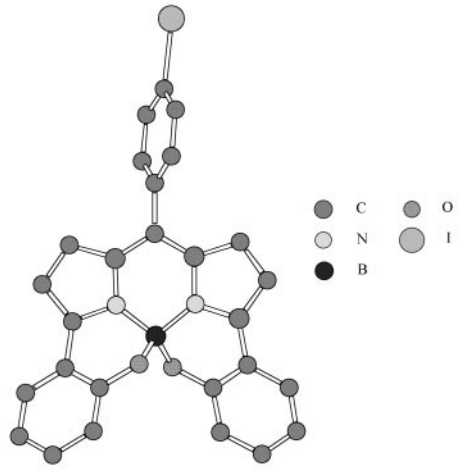


Fig. 1 Chem3D representation of **3** based on coordinates from the single crystal structure analysis.

It occurred to us that **3** is chiral, and the enantiomers of this compound might be separable at room temperature. No preparative resolution of this material has been accomplished, but HPLC analysis of pure racemic material on a Pirkle column [covalent (*S*,*S*) whelk-01 from Aldrich; Pr^{i}OH–hexanes eluant] gave two peaks. These were not baseline resolved, but they were distinct enough to indicate separation is possible.

X-Ray single crystal analysis of **3** revealed some interesting features (Fig. 1).‡ As expected, the 4-iodophenyl substituent is twisted with respect to the heterocyclic core. The tetrahedral structure of the boron in this molecule is slightly distorted. For instance, the O–B–O, N–B–N and O–B–N bond angles are 107.5, 105.5 and 115.4, respectively, showing progressively larger deviations from the perfect tetrahedral angle of 109.5°. Moreover, the torsional angles between the heterocyclic core and the 3- and 5-aryl substituents (25°) are considerably less than in the 4,4-difluoro-3,5-bis(1′-naphthyl)-BODIPY derivative (55°), whose structure was investigated recently.[7] The B–O and B–N distances are 1.47 and 1.52 Å, respectively.

Fig. 2 shows the UV absorption and fluorescence emission spectra of **2** and **3**, and some important data are presented in

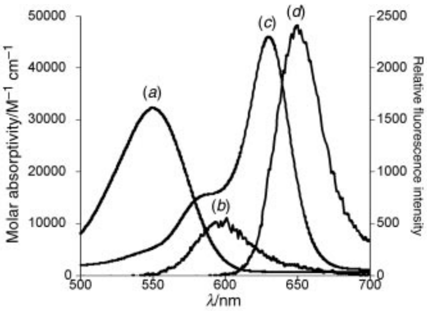


Fig. 2 Absorption (4 μM in $CHCl_3$) and fluorescence (1 μM in $CHCl_3$) spectra of **2** and **3**; (*a*) and (*b*) are absorption and fluorescence spectra of **2**; (*c*) and (*d*) are the corresponding spectra of **3**.

Table 1 Important UV and fluorescence data for **2** and **3**

	$\lambda_{\max}$/nm (abs)[a]	ε/M^{-1} cm^{-1}	$\lambda_{\max}$/nm (em)[a]
2	550	34 500	597
3	630	46 000	654

[a] In $CHCl_3$.

Table 1. The most striking difference between the emission spectra of **2** and **3** is that the $\lambda_{\max}$(em) for the new ring system **3** is red-shifted by approximately 57 nm relative to the parent system **2**. This is probably due to extended conjugation in **3** as a result of the aryl substituents being constrained closer to planarity with the dipyrromethene nucleus. Fluorescence emission for **3** was also sharper than that of the parent BODIPY **2**; peak widths at half peak height for the emission spectra shown in Fig. 2 were 36 and 44 nm, respectively. Quantum yields for fluorescence of **2** and **3** were determined[8] in $CHCl_3$ relative to Cresyl Violet.[9] The quantum yield measured for **3** (ϕ = 0.41) is much higher than that obtained for **2** (ϕ = 0.07), validating the original premise of this work, *i.e.* that the constrained system **3** would be more fluorescent than the BODIPY system **2**.

Finally, cyclic voltammetry showed that **3** was irreversibly oxidized at a peak potential E_{pa} = +0.70 V (*vs.* ferrocene/ferrocenium at 100 mV s^{-1} in MeCN throughout), which is significantly lower than the oxidation potential of **2** (E_{pa} = +0.84 V). This implies that the rigidity of **3** allows for a more extended conjugation as compared to **2**. Both compounds are reversibly reduced at about the same potential (**3**: $E_{1/2} = -1.18$ V, **2**: $E_{1/2} = -1.19$ V).

In summary, the new fluorescent dye **3** gives a red-shifted, sharper fluorescence emission than the parent system **2**, and the quantum yield for its fluorescence was determined to be 5.5–6.0 times larger. It contains a unique chiral, heptacyclic core with a distorted N_2BO_2 unit. Possible applications for this new dye include studies of chiral molecular environments *via* fluorescence.

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Notes and references

† *Synthesis* of **3**: Compound **2** was formed *in situ* from the corresponding dipyrromethene **1** (ref. 10) (100 mg, 0.179 mmol) in PhMe (5 ml) by addition of Et_3N (0.075 ml, 0.537 mmol), then $BF_3{\bullet}OEt_2$ (0.113 ml, 0.896 mmol). This mixture was heated to 80 °C for 20 min to give the intermediate **2** *in situ*. The solution was cooled to 0 °C, BBr_3 (0.17 ml, 1.79 mmol) was added dropwise over 1 min, then the solution was allowed to warm to 25 °C and stirred for 5 h. The reaction mixture was filtered through Celite, concentrated and purified by column chromatography on basic alumina using 20% EtOAc–hexanes as eluant. Compound **3** was isolated as a dark green solid (90 mg, 93% yield): mp 295–296 °C; δ_{H}($CDCl_3$, 300 MHz) 7.89 (d, *J* 8.4, 2H), 7.77 (dd, *J* 7.8, 1.5, 2H), 7.46 (d, *J* 8.4, 2H), 7.31–7.36 (m, 2H), 7.03–7.07 (m, 2H), 7.04 (d, *J* 4.5, 2H), 6.95 (d, *J* 8.2, 2H), 6.91 (d, *J* 4.5, 2H); δ_{B}($CDCl_3$, 64 MHz) -0.89 (s); *m/z* (FAB) 538 (M$^+$); (HRMS: calc. [M$^+$] 538.0374, found [M$^+$] 538.0354).

‡ *Crystal data* for **3**: $C_{27}H_{16}BIN_2O_2$, M = 538.13, dark green crystal, triclinic, a = 8.1736(11), b = 9.2522(9), c = 15.222(2) Å, α = 97.112(10), β = 100.579(11), γ = 104.200(10)°, V = 1079.7(2) Å^3, space group $P\bar{1}$, Z = 2, D = 1.655 g cm^{-3}, μ = 1.512 mm^{-1}, F(000) = 532, λ (Mo-Kα) = 0.71073 Å. The data were collected by omega scanning techniques, at 298 K on a Siemens P4 X-ray diffractometer in the range $2.31 < \Theta < 25.00°$. 4078 reflections were collected, corrected for Lorentzian and polarization effects, of which 3786 were independent reflections [R(int) = 0.0371]. Structure solution by direct methods (ref. 11) and least-squares refinement of 299 parameters (ref. 12) on F^2 yielded final R indices [$I > 2\sigma(I)$]: $R(F)$ = 0.0379 $wR(F^2)$ = 0.0946; R indices (all data): $R(F)$ = 0.0406; $wR(F^2)$ = 0.0974. CCDC 182/1380.

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