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Synthesis and spectroscopic properties of 2-ketopyrrole–BF_2 complexes: a new class of fluorescent dye

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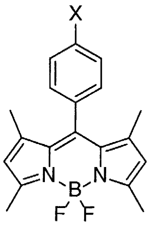
Abstract

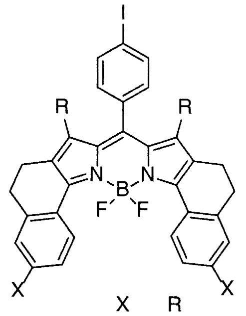
The 2-ketopyrrole complexes **3** and **4** were isolated as minor products in syntheses of the corresponding 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY®) dyes **1** and **2**. Compounds **4** were shown to be highly fluorescent having emissions between 504 and 544 nm with quantum yields between 0.52 and 0.89. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: pyrrole; fluorescence; dye; BODIPY®; labelling.

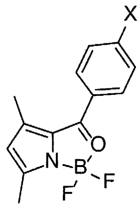
4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY®) dyes[1] are valuable molecular labels because of their intensely fluorescent properties. A long-term project in our laboratories is to incorporate these fragments (and other fluorescent entities) into larger molecular structures with unique spectroscopic properties.[2] Experiments to prepare the new dyes **1a**, **1b**, and **2c**–**2e**, as reported elsewhere,[3] also gave by-products that were uncharacterized until the work described here. This letter discusses the composition of these by-products, structures **3** and **4**, and their fundamental spectroscopic properties.



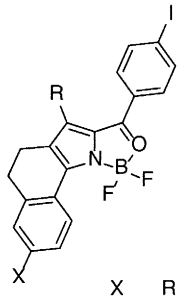
1a; X = Br
1b; X = I



	X	R
2c	H	H
2d	OMe	H
2e	H	Me



3a; X = Br
3b; X = I



	X	R
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4d	OMe	H
4e	H	Me

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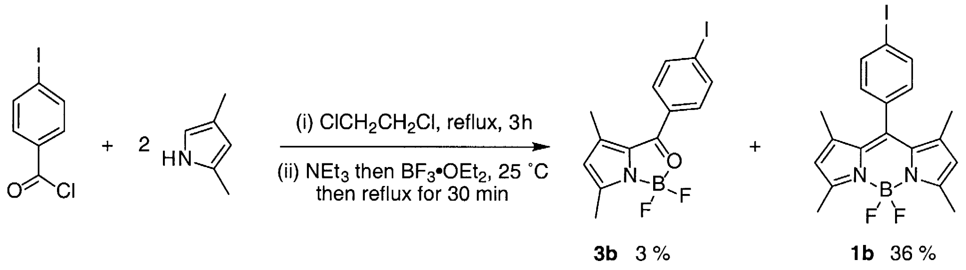
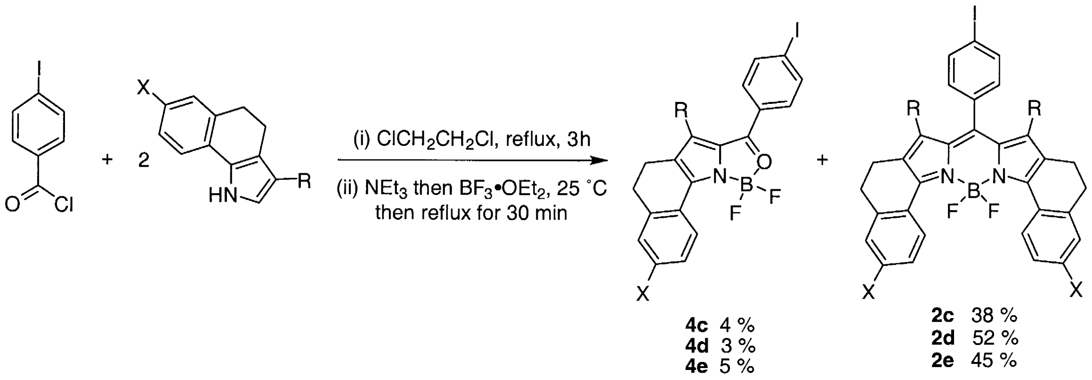
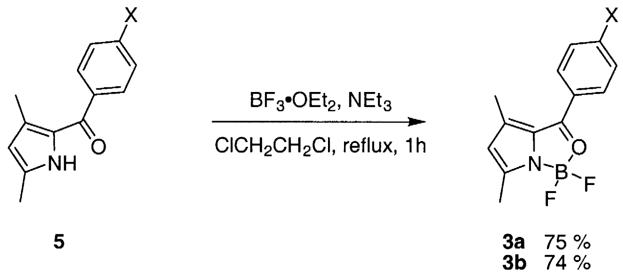
Schemes 1 and 2 depict BODIPY® syntheses and the amounts of by-products **3** and **4** formed under these conditions. These compounds were typically observed as fluorescent yellow spots that have lower RF values than the parent BODIPY® dyes on silica TLC. Yields of **3** and **4** under the conditions used for syntheses of BODIPY® dyes were less than 5%, but they become more prominent as the proportion of acid chloride is increased. For instance, when a 1:1 ratio of acid chloride to pyrrole-derivative was used, then compound **4d** was formed in 18% yield, and the corresponding BODIPY® **2d** was formed in only 13% yield. We were unable to find conditions for exclusive formation of the dyes **3** and **4** from the pyrrole precursors. However, it was shown that the 2-ketopyrroles **5**[4] react to give the corresponding boron complexes **3** in high yield (Scheme 3). The only disadvantage of this route is the extra effort necessary to prepare the 2-ketopyrrole precursors. Curiously, reactions of 2-ketopyrroles with boron trifluoride have been studied previously, but cyclic materials like **3** and **4** were not isolated.[5] The critical difference between that prior work and these studies is that a base was not used in the literature case.



Scheme 1.



Scheme 2.



Scheme 3.

Compounds **3** and **4** are yellow to orange crystalline materials.[6] In IR spectroscopy, their C=O stretches occur between 1594 and 1571 cm^{-1}; this is an even lower wave number range than that observed for the corresponding 2-ketopyrroles (ca. 1620 cm^{-1}).[4] ^{11}B NMR resonances for compounds **3** and **4** occur between 2.61 and 3.50 ppm; these values fall in the range of the corresponding BODIPY® dyes that resonate from -1.0 to +9.0 ppm.[3,7] Curiously, B–F coupling was not observed in these compounds.

We previously noted distinctive long-range couplings of around 11 Hz between the fluorine atoms of compounds **2** and the aromatic carbon atoms closest to them.[8] Such long range C–F coupling (J=4 Hz) was also observed for compounds **4c** and **4e**. No long-range coupling was observed for the corresponding compound **4d**.

A single crystal X-ray structural analysis of **4e** was obtained, thus elucidating the origins of the long-range C–F couplings and other structural effects. Fig. 1 shows a representation of the structure. The C–F distances shown (average 3.46 Å) are longer than the sum of the Van der Waal's radii for carbon and fluorine (3.19 Å). Crystallographic data collected previously for BODIPY® **2d** indicates that the corresponding contact in that compound is shorter (average 3.04 Å).[8] The longer distances obtained for **4e** are apparently short enough to give coupling but with a smaller coupling constant. It is unclear why no coupling was observed for compound **4d**.

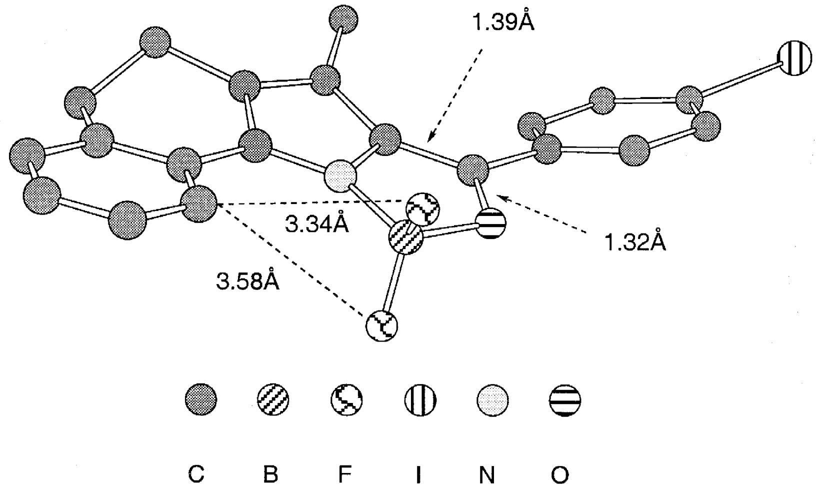


Fig. 1. Chem3D diagram of compound **4e** generated from X-ray coordinates

Other observations regarding the structure of **4e** are as follows. The 4-iodophenyl ring is twisted at an angle of 30° relative to the fluorophore, probably due to the repulsion between the methyl group and the phenyl H-atoms (Fig. 1). The B–F and B–N bond lengths are very similar to those of the BODIPYs®,[8] and the B–O bond length is a little shorter than the B–N bond. However, the C=O double bond (1.32 Å) is significantly longer than a typical carbonyl bond (ca. 1.20 Å), and its length is in fact closer to most C–O single bonds (ca. 1.34 Å). The C–C bond between the carbonyl carbon and the α-carbon of the pyrrole is significantly shorter (1.39 Å) than normal C–C bonds (ca. 1.48 Å) suggesting significant delocalized multiple bond character. This conclusion is supported by the IR data (vide supra).

Table 1 summarizes data collected to assess the optical properties of compounds **3** and **4**. All the compounds fluoresce, particularly compounds **4**. Absorption and emission wavelengths and extinction coefficients for these materials are less than the corresponding BODIPY® dyes, as expected since they are less conjugated systems. However, their Stokes shifts are greater (cf. representative $\lambda_{\mathrm{max.\ emis}}$, Stokes shifts, extinction coefficients, and quantum yields: **1b**, 510 nm, 10 nm, 47,100 M^{-1} cm^{-1}, 0.64; **2c**, 647 nm, 13 nm, 126,250 M^{-1} cm^{-1}, 0.38). Emission bands for compounds **3** and **4** are considerably broader than the corresponding BODIPYs®.

Table 1
Optical properties of compounds **3** and **4** in chloroform

	$\lambda_{max.abs}$ (nm)	ε ($M^{-1}cm^{-1}$)	$\lambda_{max.emis}$ (nm)	Stokes shift (nm)	Φ^a
3a	321	19,000	475	154	[b]
3b	322	16,000	475	153	[b]
4c	468	48,000	516	48	0.89
4d	488	43,000	544	56	0.52
4e	445	46,000	504	59	0.58

[a] Fluorescein in 0.1 M $NaOH_{(aq)}$ as reference ($\Phi = 0.925$).[9,10] [b] Too low to be measured accurately.

In conclusion, the aryl substituted compounds **4** are quite fluorescent materials that tend to emit at lower wavelengths than the corresponding BODIPY® dyes. However, their broader fluorescence means that these materials are less likely to be useful in multi-dye experiments. Compounds **3** are much less fluorescent thereby demonstrating the importance of the added, constrained, aromatic ring in these systems.

Acknowledgements

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6. Representative spectral data: **4e** ^1H NMR (300 MHz, $CDCl_3$): δ 8.22 (m, 1H), 7.97 (d, *J*=8.7 Hz, 2H), 7.73 (d, *J*=8.4 Hz, 2H), 7.42 (m, 2H), 7.32 (m, 1H), 3.04 (t, *J*=7.2 Hz, 2H), 2.78 (t, *J*=7.2 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.0, 138.1, 133.5, 132.9, 131.7, 131.4, 131.2, 129.3, 128.6, 127.9, 126.5, 126.3 (t, *J*=4.1 Hz), 101.7, 29.3, 20.4, 12.7. ^{19}F NMR (282 MHz, $CDCl_3$, $CFCl_3$ as external reference): δ −156.98, −157.06. ^{11}B NMR (64 MHz, $CDCl_3$, BF_3 etherate as external reference): δ 3.15 (s). IR ($CHCl_3$): 1590 (shoulder 1572) cm^{-1}. Anal. calcd for $C_{20}H_{15}BF_2INO$: C, 52.10; H, 3.28; N, 3.04. Found: C, 51.97; H, 3.32; N, 2.94. Compound **3b** ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (d, *J*=8.7 Hz, 2H), 7.65 (d, *J*=8.4 Hz, 2H), 6.23 (s, 1H), 2.42 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.0, 155.1, 138.3, 138.2, 132.8, 131.2, 128.9, 124.1, 102.2, 15.0, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$, $CFCl_3$ as external reference): δ −158.35, −158.43. ^{11}B NMR (64 MHz, $CDCl_3$, BF_3 etherate as external reference): δ 2.61 (s). IR ($CHCl_3$): 1588, 1571 cm^{-1}. Anal. calcd for $C_{13}H_{11}BF_2INO$: C, 41.87; H, 2.97; N, 3.76. Found: C, 41.93; H, 3.04; N, 3.68.

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