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Synthesis of *N,N*-difluoroboryl complexes of 3,3′-diarylazadiisoindolylmethenes

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ABSTRACT

N,N-Difluoroboryl complexes of 3,3′-diarylazadiisoindolylmethenes were synthesized by the reaction of $BF_3{\cdot}OEt_2$ and 3,3′-diarylazadiisoindolylmethenes, which were easily prepared from a reaction between phthalonitrile and aryl Grignard reagents. These novel dyes exhibit strong absorption in the visible region and intense fluorescence in the vis/NIR region. Their synthesis, characterization, and optical properties are reported in this Letter.

In recent years, vis/NIR (visible/near infrared) absorbing dyes with intense fluorescence have been the focus of considerable research interest because their optical properties make them suitable for a variety of applications such as use as dyes in recording devices and in molecular labeling in biological research.[1] Among them, BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, Fig. 1)[2] dyes have been the subject of intense investigation due to their high extinction coefficients, intense fluorescence, high stability, and insensitivity to the polarity of solvents as well as to pH.[3] Currently, one of the key goals in this field of research is to develop methods for shifting the major absorption to the vis/NIR region by modifying the BODIPY core, which includes attachment of electron-donating groups at the periphery, creation of a rigid structure, and extension of the π-conjugation system.[4] Recently, O'Shea and co-workers reported that the replacement of the methine carbon atom at the *meso*-position with a nitrogen atom can also cause a sizable red-shift of the absorption without lowering the extinction coefficients and fluorescence intensity. The resulting aza-BODIPY dyes can be utilized as an efficient sensitizer for photodynamic therapy (PDT).[5,6] During the course of our research on the synthesis of phthalocyanine analogs, we have noticed that the π-extended 3,3′-diarylazadiisoindolylmethenes were obtained in moderate yields from the reaction of phthalonitrile with arylmagnesium bromide, which turned out to be a revisit of an old literature.[7] Their difluoroboryl complexes are of considerable interest as novel vis/NIR dyes, since a significant red-shift can be expected due to the combined effects of introducing a nitrogen atom at the *meso*-position and extension of the π-conjugation system. In this Letter, their synthesis and optical properties are reported in detail.

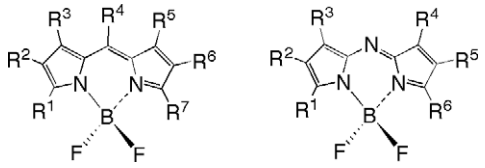

Figure 1. BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, left) and aza-BODIPY (right).

Reaction of phthalonitrile with arylmagnesium bromides in dry benzene at room temperature for 1 h provided 3,3′-diarylazadiisoindolylmethenes (*N*-(3-phenyl-2*H*-isoindol-1-yl)-*N*-(3-phenyl-1*H*-isoindol-1-ylidene)amine (**1**) and *N*-[3-(4-*tert*-butylphenyl)-2*H*-isoindol-1-yl]-*N*-[3-(4-*tert*-butylphenyl)-1*H*-isoindol-1-ylidene]amine (**2**)) in moderate yields (28% for **1** and 27% for **2**, Scheme 1). Compounds **1** and **2** were fully characterized by high resolution electrospray FT-ICR (HR-ESI-FT-ICR) mass and ^1H and ^{13}C NMR spectroscopy.[8,9] Treatment of **1** and **2** with $BF_3{\cdot}OEt_2$ in the presence of diisopropylamine in refluxing benzene resulted in the formation of **3** and **4** in 70% and 73% yields, respectively.[10,11] The HR-ESI-FT-ICR mass spectra of **3** and **4** firstly characterized them as difluoroboryl complexes of 3,3′-diarylazadiisoindolylmethenes (**3**: *m/z*: 468.1452 [M^++Na], calcd for $C_{28}H_{18}BF_2N_3Na$, 468.1454 and **4**: 580.2704 [M^++Na], calcd for $C_{36}H_{34}BF_2N_3Na$, 580.2706).

The ^1H NMR spectrum of **3** shows signals at 8.07 (α-*benzo*), 7.82 (*ortho*), 7.61 (α-*benzo*), 7.53–7.50 (*meta*, *para*, and β-*benzo*), and 7.32 (β-*benzo*) ppm, while that of **4** exhibits signals at 8.10 (α-*benzo*), 7.85 (*ortho*), 7.67 (α-*benzo*), 7.53 (*meta*), 7.49 (β-*benzo*), and 7.29 (β-*benzo*) ppm, and a peak due to the *t*-butyl groups is observed at 1.37 ppm. These results are consistent with C_{2v} symmetry and free rotation of aryl groups at 3 and 3′ positions.

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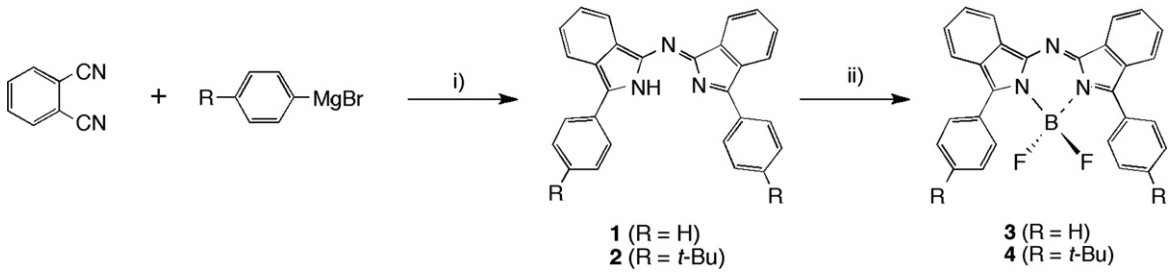

Scheme 1. Synthesis of difluoroboryl complexes of 3,3′-diarylazadiisoindolylmethenes. Reagents and conditions: (i) dry benzene, rt, 1 h; (ii) $BF_3{\cdot}OEt_2$, diisopropylamine, benzene, reflux.

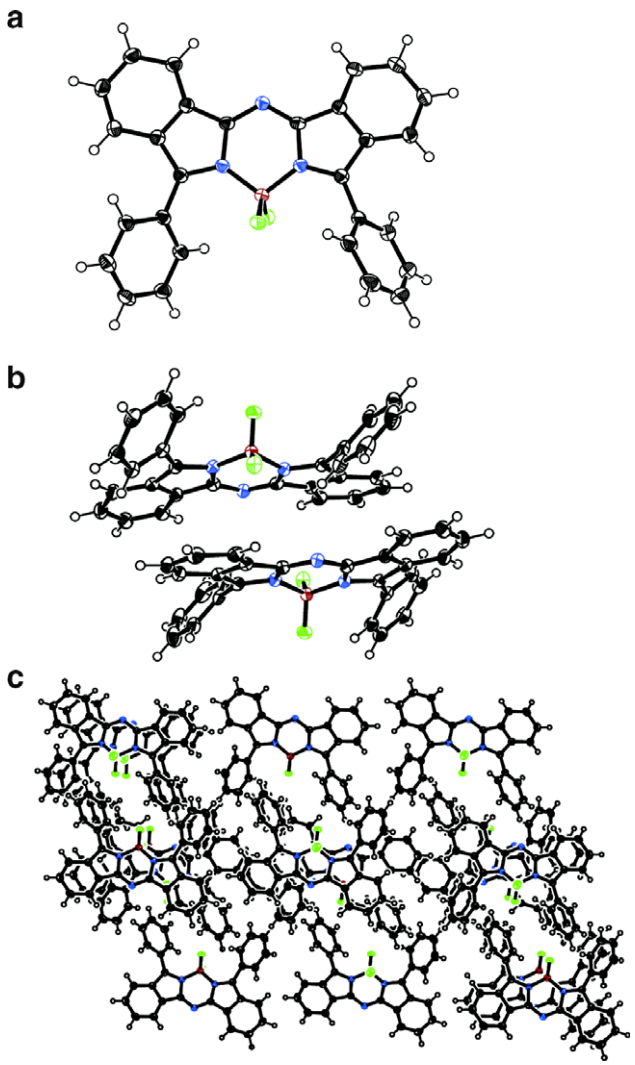

Figure 2. Crystal structure of **3**; (a) top view, (b) side view, and (c) packing diagram. Thermal ellipsoids were scaled to 50% probability level.

Further evidence for this is provided, in the case of **3**, by the NOE correlation between the peaks at 7.82 and 7.61 ppm.

Finally, the structure of **3** was revealed by single crystal X-ray analysis as shown in Figure 2.[12] **3** takes a near C_{2v} symmetric conformation, in which the isoindole moieties are arranged in a coplanar manner, and the boron atom is coordinated in a tetrahedral fashion by two nitrogen atoms with B–N distances of 1.573(2) and 1.579(2) Å and by two fluorine atoms with B–F distances of 1.372(2) and 1.380(2) Å. The coordination geometry around the boron atom is quite similar to those of the other aza-BODIPY dyes reported previously. In the crystal structure, columnar π–π stacking with intermolecular distance of 3.27–3.65 Å is observed with neighboring molecules aligned in opposite directions.

The absorption spectra of **1** and **2** contain intense bands at 653 nm and 658 nm, respectively, which exhibit a red-shift similar to that observed previously in the spectra of azadipyrromethenes with extended π-conjugation systems.[4,5] The fluorescence spectra of **1** and **2** exhibit emission at 701 and 705 nm with $\Phi_F = 9.6 \times 10^{-3}$ and 9.7×10^{-3}, respectively, upon excitation at 630 nm (Table 1).[13] Complexation of a difluoroboryl unit further caused a red-shift of absorption (715 nm for **3** and 724 nm for **4**, Fig. 3 and Table 1). **3** and **4** exhibit intense emission at 736 nm ($\Phi_F = 0.15$) and 749 nm ($\Phi_F = 0.11$), respectively, whose decays are found to obey a single exponential function with $\tau_F = 2.1$ ns for **3** and 2.0 ns for **4**.

The transition energies and oscillator strength were calculated using TDDFT methods to derive a further insight into the electronic structure of difluoroboryl complex of 3,3′-diarylazadiisoindolylmethene. A geometry optimization was carried out for **3** using the B3LYP hybrid functional with 6-31G(d) basis sets. TDDFT calculations were also carried out for a model compound consisting of the carbon counterpart of **3** (**5**). In both the calculations, the red-shifted absorption band mainly arises from a transition from HOMO to LUMO. The energies of the HOMO and LUMO of **3** are both stabilized relative to those of **5**, but the stabilization of the LUMO of **3** is greater than that of HOMO (Fig. 4). Since the LUMO is delocalized over the *meso*-position, this can readily be accounted for in terms of the comparatively stronger electron-withdrawing nature of a nitrogen atom. The HOMO–LUMO gap of **3** is, therefore, smaller than that of **5**, resulting in the observed red-shift of the absorption of **3**.[4d]

Table 1
Absorption and fluorescence properties of **1**–**4**

Compound	λ_{max} (nm)	ε (M^{-1} cm^{-1})	fwhm (nm)	λ_{em} (nm)	Φ_F	τ_F (ns)	Stokes shift (nm)
1	653	47,900	82.3	701	9.6×10^{-3}	0.1	48
2	658	46,800	83.0	705	9.7×10^{-3}	0.1	47
3	715	87,100	46.7	736	0.15	2.1	21
4	724	85,100	49.7	749	0.11	2.0	25

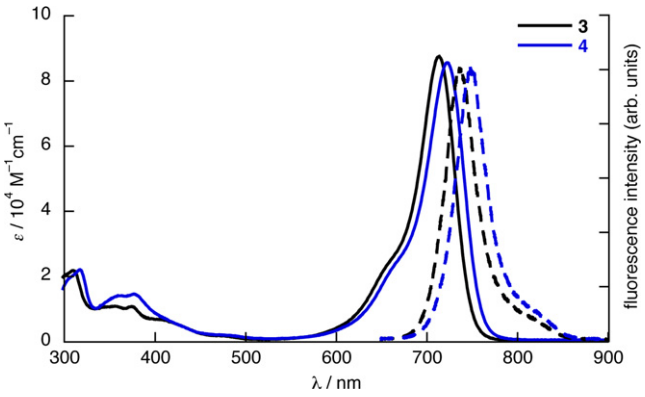

Figure 3. UV–vis absorption spectra of **3** and **4** in $CHCl_3$. Dotted lines indicate their fluorescence spectra in $CHCl_3$.

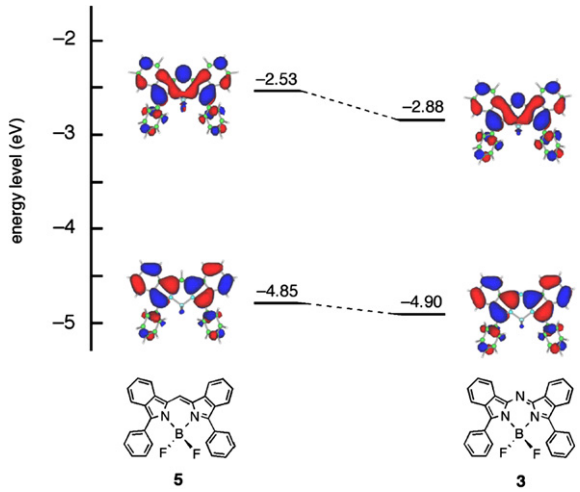

Figure 4. Calcualted MO diagrams of 3 (right) and 5 (left).

Difluoroboryl complexes of 3,3′-diarylazadiisoindolylmethenes were synthesized for the first time, and were characterized based on the analysis of the NMR spectral data and the single crystal structure. These dyes exhibit sizable red-shifts in both the absorption and emission spectra relative to what is observed for normal BODIPY dyes. Since other arylmagnesium bromides can also potentially be utilized, further modification of the properties should be relatively straightforward. It should be noted that 3,3′-diarylazadiisoindolylmethene can also be used as a planar bidentate ligand.[14] We are currently carrying out additional experiments to explore these possibilities.

Acknowledgments

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8. *Experimental procedure for the synthesis of N-(3-phenyl-2H-isoindol-1-yl)-N-(3-phenyl-1H-isoindol-1-ylidene)amine* (**1**): To a vigorously stirred dry benzene solution (60 ml) of phthalonitrile (12.8 g, 0.1 mol), a diethyl ether solution (60 ml) of phenylmagnesium bromide prepared from 6.1 g of magnesium and 26 ml of bromobenzene was added at room temperature, and the resultant mixture was stirred for a further 1 h. The flask was then cooled to 0–5 °C, and the excess of Grignard reagent was decomposed carefully with 20% ammonium chloride. The solvents were removed by evaporator, and the residue was distilled with water steam. The residue was ground into a fine powder, and was recrystallized from a mixture of pyridine and methanol to give **1** as violet powder (5.5 g, 0.014 mol, 28%). ^{1}H NMR (594.17 MHz, $CDCl_3$, 297 K): δ = 8.15 (d, J = 4.10 Hz, 2H; α-*benzo*), 8.04 (m, 4H; *ortho*), 7.97 (d, J = 4.01 Hz, 2H; α-*benzo*), 7.58 (m, 4H; *meta*), 7.49 (m, 2H; *para*), 7.43 (dd, J_1 = 7.31 Hz, J_2 = 7.22 Hz, 2H; β-*benzo*), and 7.34 (dd, J_1 = 7.13 Hz, J_2 = 7.13 Hz, 2H; β-*benzo*) ppm; ^{13}C NMR (149.40 MHz, $CDCl_3$, 297 K): δ = 148.6 (α-*pyrrole*), 143.9 (α-*pyrrole*), 135.4 (β-*pyrrole*), 133.2 (*ipso*), 129.9 (β-*pyrrole*), 129.4 (*para*), 129.2 (*meta*), 127.7 (*ortho*), 127.6 (β-*benzo*), 126.3 (β-*benzo*), 122.1 (α-*benzo*), and 121.3 (α-*benzo*) ppm; UV–vis ($CHCl_3$): λ_{max} [nm] (ε) = 653 (47,900); HR-ESI-MS: *m/z* (% intensity): 398.1651 (100) [M$^+$+H]; calcd for $C_{28}H_{20}N_3$, 398.1652.
9. *Experimental procedure for the synthesis of N-[3-(4-tert-butylphenyl)-2H-isoindol-1-yl]-N-[3-(4-tert-butylphenyl)-1H-isoindol-1-ylidene]amine* (**2**): **2** was prepared under similar reaction conditions in 27% yield from phthalonitrile and *tert*-butylphenylmagnesium bromide. ^{1}H NMR (500.16 MHz, $CDCl_3$, 297 K): δ = 8.13 (d, J = 4.05 Hz, 2H; α-*benzo*), 7.99–7.95 (m, *ortho* (4H), α-*benzo* (2H)), 7.60 (m, 4H; *meta*), 7.40 (dd, J_1 = 7.70 Hz, J_2 = 7.48 Hz, 2H; β-*benzo*), 7.31 (dd, J_1 = 8.10 Hz, J_2 = 7.48 Hz, 2H; β-*benzo*), and 1.42 (s, 18 H; *t-butyl*) ppm; UV–vis ($CHCl_3$): λ_{max} [nm] (ε) = 658 (46,800); HR-ESI-MS: *m/z* (% intensity): 510.2903 (100) [M$^+$+H]; calcd for $C_{36}H_{36}N_3$, 510.2904.
10. *Experimental procedure for the synthesis of N,N-difluoroboryl-[N-(3-phenyl-2H-isoindol-1-yl)-N-(3-phenyl-1H-isoindol-1-ylidene)amine]* (**3**): **1** was reacted with $BF_3{\cdot}OEt_2$ in the presence of diisopropylamine in a refluxing benzene to give difluoroboryl complex of **1** (**3**) in 70% yield. ^{1}H NMR (594.17 MHz, $CDCl_3$, 297 K): δ = 8.07 (d, J = 3.98 Hz, 2 H; α-*benzo*), 7.82 (m, 4H; *ortho*), 7.61 (d, J = 4.07 Hz, 2H; α-*benzo*), 7.53–7.50 (m, *meta* (4H), para (2H), β-*benzo* (2H)), and 7.32 (dd, J_1 = 7.45 Hz, J_2 = 7.53 Hz, 2H; β-*benzo*) ppm; ^{13}C NMR (149.40 MHz, $CDCl_3$, 297 K): δ = 153.7 (α-*pyrrole*), 139.7 (α-*pyrrole*), 134.0 (β-*pyrrole*), 131.6 (β-*pyrrole*), 131.1 (β-*benzo*), 130.7 (*para*), 130.6 (*ortho*), 128.8 (*meta*), 127.6 (β-*benzo*), 124.5 (α-*benzo*), and 121.3 (α-*benzo*) ppm; UV–vis ($CHCl_3$): λ_{max} [nm] (ε) = 715 (87,100); HR-ESI-MS: *m/z* (% intensity): 468.1452 (100) [M$^+$+Na]; calcd for $C_{28}H_{18}BF_2N_3Na$, 468.1454.
11. *Experimental procedure for the synthesis of N,N-difluoroboryl-{N-[3-(4-tert-butylphenyl)-2H-isoindol-1-yl]-N-[3-(4-tert-butylphenyl)-1H-isoindol-1-ylidene]amine}* (**4**): **4** was similarly obtained in 73% yield from the reaction of **2** and $BF_3{\cdot}OEt_2$. ^{1}H NMR (500.16 MHz, $CDCl_3$, 297 K): δ = 8.10 (d, J = 4.05 Hz, 2H; α-*benzo*), 7.85 (m, 4H; *ortho*), 7.67 (d, J = 4.05 Hz, 2H; α-*benzo*), 7.53 (m, 4H; *meta*), 7.49 (dd, J_1 = 7.30 Hz, J_2 = 7.48 Hz, 2H; β-*benzo*), 7.29 (dd, J_1 = 7.70 Hz, J_2 = 7.48 Hz, 2H; β-*benzo*), and 1.37 (s, 18H; *t-butyl*); UV–vis ($CHCl_3$): λ_{max} [nm] (ε) = 724 (85,100); HR-ESI-MS: *m/z* (% intensity): 580.2704 (100) [M$^+$+Na]; calcd for $C_{36}H_{34}BF_2N_3Na$, 580.2706.
12. *Crystallographic data of* **3**: $C_{28}H_{18}B_1N_3F_2$, M_W = 445.26, monoclinic, space group $P2_1/c$ (no. 14), a = 10.221(4), b = 8.486(3) c = 25.565(8) Å, β = 112.185(12)°, V = 2053.2(13) Å^3, Z = 4, ρ_{calcd} = 1.440 g/cm^3, T = −100 °C, 28,680 measured reflections, 4688 unique reflections (R_{int} = 0.0513), R = 0.0528, R_w = 0.1260 (all data), GOF = 1.160. CCDC 691385 contains the supplementary crystallographic data for **3**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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