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Conformationally Restricted Aza-Dipyrromethene Boron Difluorides (Aza-BODIPYs) with High Fluorescent Quantum Yields

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Abstract: A simple approach to the highly fluorescent near-infrared aza-BODIPY dyes with higher fluorescence quantum yields (up to 0.81 in toluene) in comparison with their known analogues is presented. Our approach is based on the restricted rotations of the 1,7-phenyl groups to the mean plane of the aza-BODIPYs, which is achieved through the installation of bulky substituents on the 1,7-phenyl groups of aza-BODIPYs and results in a reduced nonradiative relaxation process in solution. The large torsion angles between the 1,7-phenyl groups and the aza-BODIPY core (ϕ_1 and ϕ_2 in these novel conformationally restricted aza-BODIPYs) were confirmed by X-ray diffraction studies.

Keywords: BODIPY · N ligands · dyes/pigments · fluorescence · heterocycles

Introduction

Highly fluorescent dyes emitting in the far-red or near-infrared (NIR) region are preferred for biological imaging because they offer maximum light penetration through skin and tissue with minimum scattering[1] and have found important applications in materials and medical sciences, for example, as biological sensing and imaging agents. Aza-dipyrromethene boron difluoride (aza-BODIPY), a structural analogue of BODIPY,[2–6] has recently gained increased research attention due to its efficient synthesis and the fine tuning of its photochemical properties through structural modifications.[7–11] For example, aza-BODIPY **A1** (Figure 1) absorbs and emits at $\lambda = 650$ and 682 nm, respectively, whereas the luminophore of aza-BODIPY with the longest wavelength (emitting at $\lambda = 850$ nm) reported to date has been achieved through pyrrolidyl substitution combined with full chelation of the boron atom of aza-BODIPY.[11c] In contrast, the simple installation of two methoxyl groups on the *para*-position of the 3,5-phenyl groups (aza-BODIPY **A2**, Figure 1) can also redshift the absorption and emission to $\lambda = 688$ and 723 nm, respectively. Aza-BODIPY **A2**, developed by O'Shea et al., has a good fluorescence quantum yield (0.36 in $CHCl_3$) and is now widely used in bioprobes for imaging and sensing.[12]

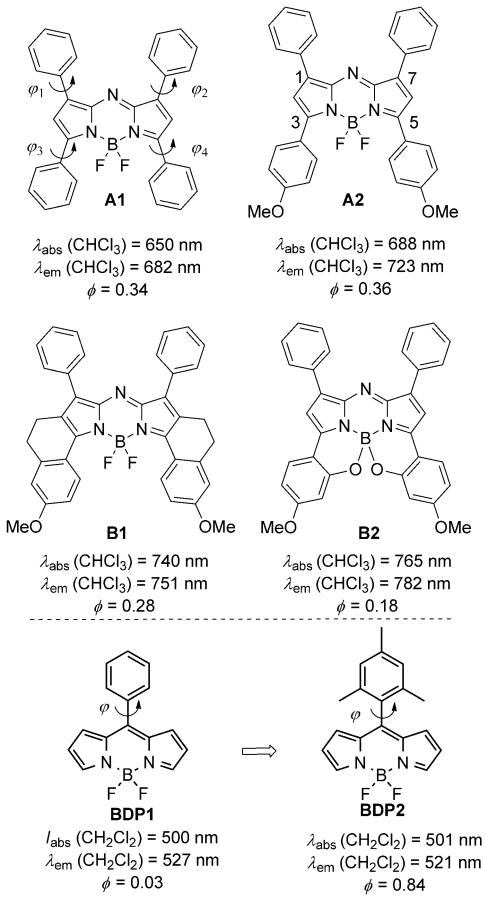

Figure 1. Chemical structure and photophysical properties of representative BODIPYs and aza-BODIPYs. ϕ and ϕ_1–ϕ_4 are the torsion angles between the aromatic rings and the plane of the central chromophores.

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In comparison with BODIPYs, which generally show high fluorescent quantum yields, aza-BODIPYs generally give a much lower fluorescent quantum yield (less than 0.5) in common solvents, despite the approximately 90 nm redshifts in their main absorption band with respect to the BODIPY analogues. Lindsey et al. have reported that the relative rotation of the *meso*-aryl group to the mean plane of the dipyrrin (defined as the dihedral angle ϕ in *meso*-aryl BODIPYs) can greatly affect the excited-state dynamics of the dyes (Figure 1).[13] For example, the fluorescence quantum yield of **BDP1** is much lower than that of its more substituted analogue **BDP2**.[14] These differences are attributed to two methyl groups on the *meso*-phenyl that prevent free rotation of the phenyl group and thus reduce the loss of energy from excited states through nonradiative molecular relaxation.

With this consideration in mind, we decided to study the influence of the torsion angles (ϕ_1–ϕ_4, Figure 1) on the fluorescent quantum yields of aza-BODIPYs. In contrast to BODIPYs, there are four torsion angles to be considered in aza-BODIPY. Of these four angles, ϕ_1 and ϕ_2 in the solid-state conformation of the reported aza-BODIPYs are very small (e.g., ϕ_1 and ϕ_2 of aza-BODIPY **A2** are 14.4 and 7.3°, respectively; Table 1), whereas ϕ_3 and ϕ_4 are very large due

Table 1. Torsion angles in reference compound **A2**[4a] and **C1**–**C3** obtained from x-ray crystallography.

	ϕ_1 [°]	ϕ_2 [°]	ϕ_3 [°]	ϕ_4 [°]
A2	14.4	7.3	38.8	33.9
C1	62.9	86.1	45.5	34.8
C2	71.0	71.0	19.5	19.5
C3	66.0	67.0	35.5	30.9

to the C–H···F hydrogen bonding.[10b] In addition, the coplanarity of the 3,5-phenyl groups with the core of aza-BODIPY is essential to retain the long wavelength absorption and emission properties of these dyes, as demonstrated in aza-BODIPY **B1** by Carreira and Zhao[15], in aza-BODIPY **B2** by Burgess and O'Shea[16] and Kovtun et al.[11c], and in 3,5-di-, 1,7-di-, and 1,3,5,7-tetrathiophene aza-BODIPYs by Xiao et al.[17]. However, 3,5-phenyl-restricted aza-BODIPYs **B1** and **B2** exhibit reduced fluorescent quantum yields in comparison with analogue **A2**. Therefore, to achieve highly fluorescent NIR aza-BODIPY dyes, we investigated aza-BODIPYs **C1**–**C3**, in which bulky groups were only installed on the 1,7-phenyl groups with the 3,5-phenyl groups left unmodified; aza-BODIPYs **A1** and **A2** were used as reference compounds.

Results and Discussion

Initially, we investigated the sensitivity of the fluorescence of reference compound **A1** to the solvent viscosity of the system, given that **BDP1** and its derivatives have been used as excellent fluorescent probes for solvent viscosity through the tuning of the relative rotation of phenyl groups to the BODIPY core.[18] Fluorescence changes in **A1** were recorded in relation to the variation of the ratio of methanol to glycerol. A fluorescence enhancement was observed as the ratio of glycerol to methanol was increased (Figure 2). This

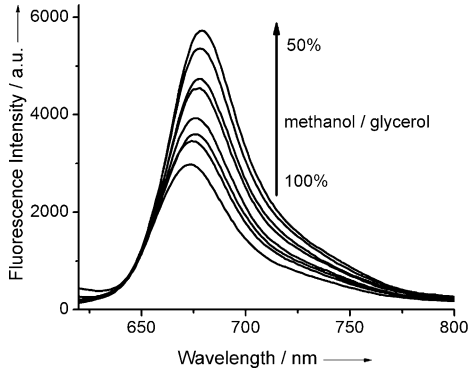
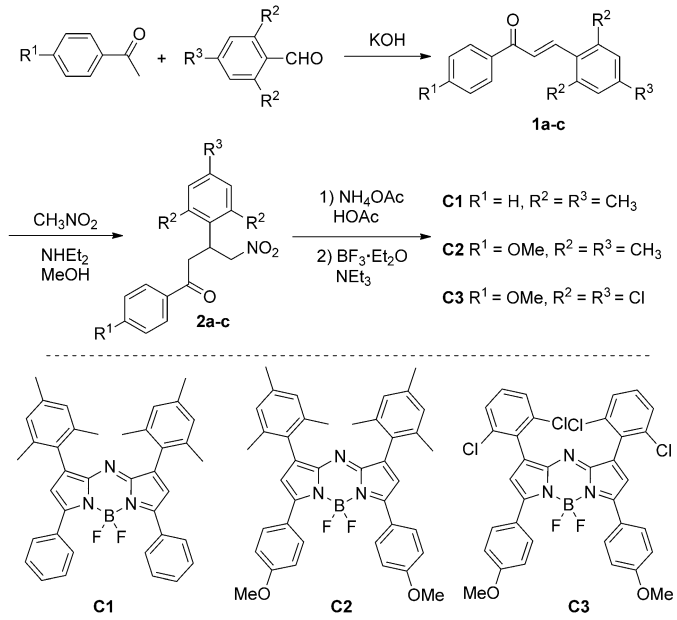


Figure 2. Fluorescence changes in the spectrum of aza-BODIPY **A1** as the ratio between methanol and glycerol was varied. Excitation at $\lambda =$ 610 nm.

indicates that the restricted conformation of aza-BODIPY could indeed lead to fluorescence enhancement.

Encouraged by this positive result, we synthesized conformationally restricted 1,7-phenyl aza-BODIPYs **C1**–**C3**, which were achieved in three steps from an aldol condensation between aldehydes and ketones, a subsequent Michael addition of nitromethane, and a final condensation with ammonium acetate and BF_3 complexation reactions (Scheme 1). Most of these reactions gave high yields, except for the final condensation of ammonium acetate, which only gave yields of around 10% when performed in alcohol or in



Scheme 1. Syntheses of aza-BODIPYs **C1**–**C3**.

solvent-free conditions. By changing the solvent to acetic acid, the yields were improved to 20 to 30%. All new compounds were characterized by using NMR spectroscopy and HRMS.

Single crystals of aza-BODIPYs **C1**–**C3** suitable for X-ray analysis were obtained by slow evaporation of solutions of these compounds in dichloromethane. As shown in Figure 3

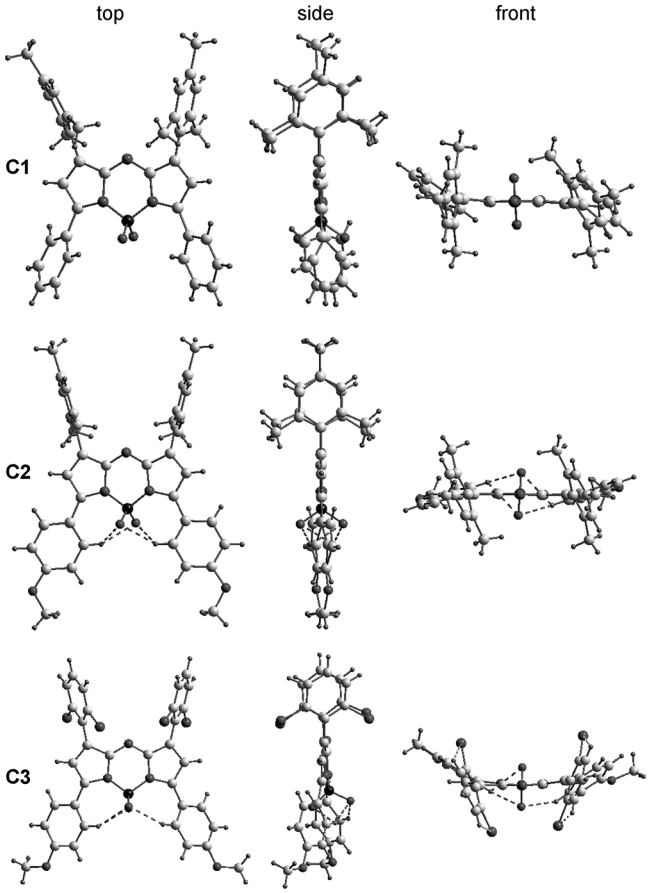


Figure 3. X-ray crystal structures of aza-BODIPYs **C1**–**C3**.

and Table 1, the aza-BODIPY cores in the three compounds remain essentially unperturbed and planar. As expected, target molecules **C1**–**C3** have larger torsion angles in the solid state ($\phi_1=\phi_2=71°$ in 1,7-(2,4,6-trimethylphenyl)aza-BODIPY **C2**; $\phi_1=66$ and $\phi_2=67°$ in 1,7-(2,6-dichlorophenyl)aza-BODIPY **C3**) than those of aza-BODIPY **A2** (14.4 and 7.3° for ϕ_1 and ϕ_2, respectively). This indicates that the installation of methyl or chloro groups on the 1,7-phenyl groups can restrict the rotation of the 1,7-phenyl groups relative to the aza-BODIPY core.

A strong intramolecular interaction between the two fluorine atoms of the BF_2 moiety and the 2,6-protons of the 3,5-phenyl groups were observed in aza-BODIPYs **C1**–**C3**, with contacts ranging from 2.15 to 2.62 Å. These hydrogen bonds affect the ϕ_3 and ϕ_4 angles of aza-BODIPYs **C1**–**C3** in the solid state, which may restrict the free rotation of phenyl groups at the 3- and 5-positions.[10b,19] Multiple C–H···F intermolecular hydrogen bonds were also observed, which facilitate the crystal packing in a head-to-tail fashion for aza-BODIPY **C2** as shown in Figure 4.

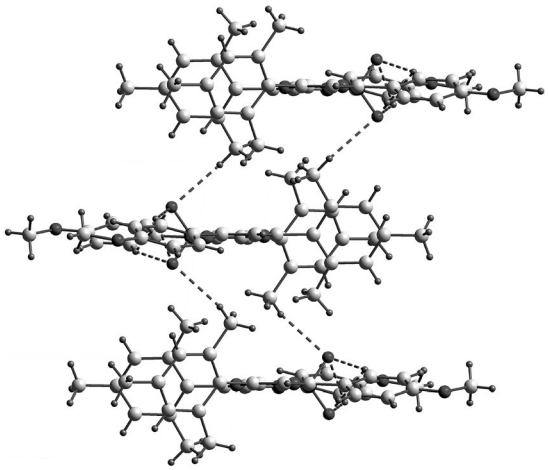


Figure 4. Intermolecular packing of aza-BODIPY **C2**.

Table 2. Photophysical properties of aza-BODIPYs in different solvents.

	Solvent	λ_{abs} [nm] (logε)	λ_{em}[a] [nm]	Stokes shift [cm^{-1}]	ϕ_f[a,b]
C1	toluene	638 (4.86)	665	636	0.76±0.02
	chloroform	635 (4.89)	666	733	0.71±0.02
	methanol	631 (4.88)	660	696	0.33±0.01
C2	toluene	676 (4.99)	705	609	0.81±0.01
	chloroform	671 (4.96)	704	698	0.73±0.02
	methanol	669 (4.97)	704	743	0.51±0.02
C3	toluene	691 (4.98)	723	641	0.67±0.02
	chloroform	687 (4.94)	724	744	0.71±0.03
	methanol	685 (4.95)	721	729	0.48±0.02
A1	toluene	654	684	672	0.44±0.02
	chloroform	650	682	722	0.34±0.01
	methanol	645	673	645	0.17±0.02
A2	toluene	693	723	599	0.39±0.02
	chloroform	688	723	704	0.36±0.01
	methanol	685	720	710	0.26±0.02

[a] Aza-BODIPYs **C1** and **A1** were excited at $\lambda=610$ nm, aza-BODIPYs **C2**, **C3**, and **A2** were excited at $\lambda=620$ nm. [b] The fluorescence quantum yields were calculated by using aza-BODIPY **A1** in $CHCl_3$ ($\phi=0.34$) as the standard.

Photophysical properties of aza-BODIPYs **C1**–**C3** and reference compounds **A1** and **A2** were measured in toluene, chloroform, and methanol as listed in Table 2. The fluorescence quantum yields of conformationally restricted dyes **C1**–**C3** are nearly double those of aza-BODIPYs **A1** and **A2** in the three different solvents. For example, in toluene, the fluorescence quantum yields of aza-BODIPYs **C1**–**C3** are 0.76, 0.81, and 0.67, respectively, which are the highest reported fluorescence quantum yields for aza-BODIPYs so far.

In comparison with aza-BODIPY **A1**, aza-BODIPY **C1** shows blueshifts of 14 to 16 nm and 13 to 9 nm in the absorption and emission, respectively. Similarly, blueshifts of 16 to 17 nm and 16 to 19 nm in the absorption and emission were observed for aza-BODIPY **C2** in comparison with aza-

BODIPY **A2**. These results, in agreement with the X-ray analysis, indicate that the installation of 2,6-dimethyl substituents on the 1,7-phenyl groups indeed leads to an increase in the dihedral angles ϕ_1 and ϕ_2 for aza-BODIPYs **C1** and **C2** compared with aza-BODIPYs **A1** and **A2**, which results in a blueshift in the absorption and the emission spectra in solution.

However, aza-BODIPY **C3**, which has electron-withdrawing chloro substituents attached to the 2,6-positions of the 1,7-phenyl groups, shows redshifted spectra in comparison with aza-BODIPY **C2**, which in turn gives a very similar absorption and emission spectra to those of widely used aza-BODIPY **A2**, as shown in Figure 5. Therefore, aza-BODIPY **C3** with a higher fluorescence quantum yield

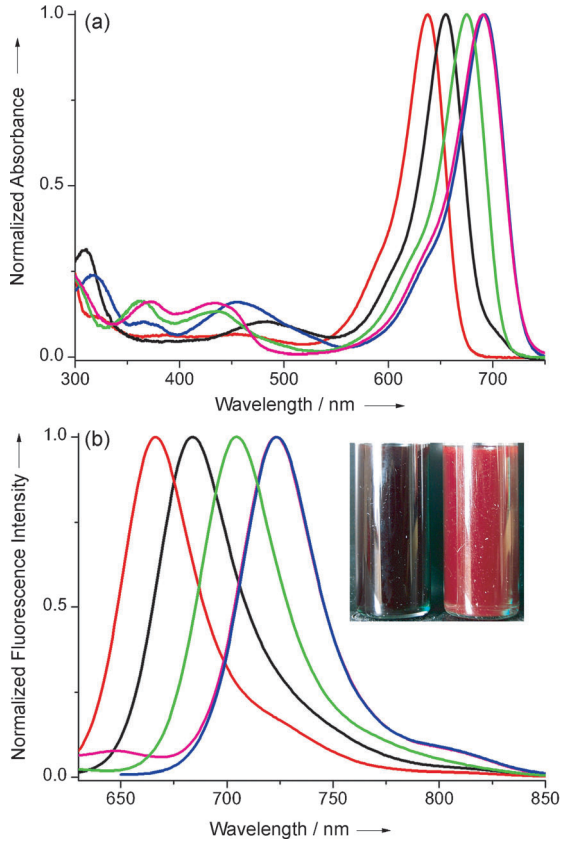


Figure 5. Normalized absorption (a) and emission spectra (b) of aza-BODIPYs **A1** (black), **A2** (blue), **C1** (red), **C2** (green), and **C3** (magenta) in toluene. Inset: Image of **A1** and **C1** in $CHCl_3$ under daylight irradiation conditions.

would be a good substituent for aza-BODIPY **A2** in various applications.

DFT calculations were performed for **A1** and **C1** (Figure 6; Figures S1–S3 and Table S1 in the Supporting Information). A small out-of-plane distortion of the aza-dipyrrin frame (ω within 6–10° for **A1** and **C1**) was observed (Figure S3 in the Supporting Information). In the optimized ground-state conformation, the separation between protons

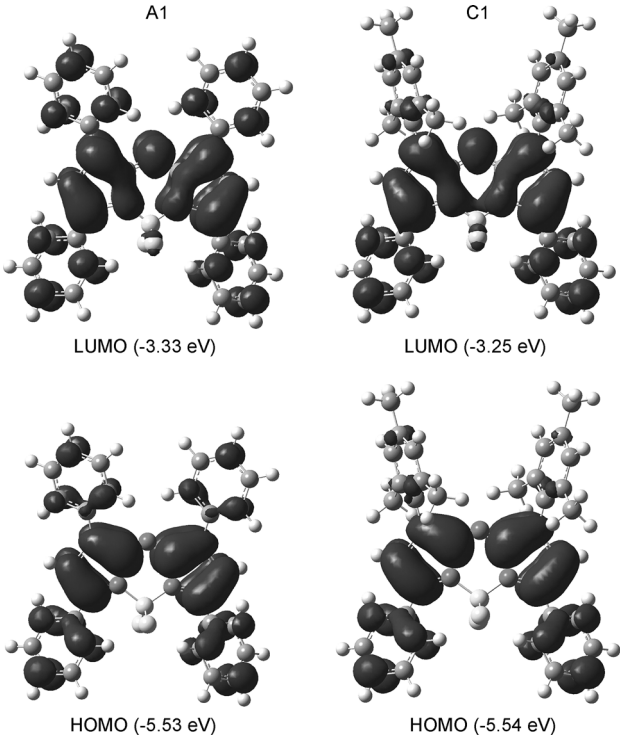


Figure 6. Ground state frontier orbitals for **A1** and **C1**.

H^a and H^b on the 1,7-phenyl groups of **A1** is 3.7 Å, which would have no effect on the free rotation of these 1,7-phenyl groups. In contrast, the separation between protons H^a and H^b on 1,7-phenyl groups on **C1** is only 0.7 Å, which would greatly restrict the rotation of the 1,7-phenyl groups (Figure S2 in the Supporting Information). There is an obvious electron delocalization from the aza-BODIPY core to the 1,7-phenyl groups for **A1**, whereas only negligible distribution of electron density from the aza-BODIPY core to the 1,7-phenyl groups was observed for **C1** in both the ground and excited state (Figure 6 and Figure S1 in the Supporting Information). This is in good agreement with the blueshift observed in the spectra of **C1** in solution.

Conclusion

In summary, by introducing methyl and chloro substituents on the 1,7-phenyl groups of aza-BODIPYs, three novel conformationally restricted aza-BODIPYs were synthesized and characterized by using X-ray analysis and DFT calculations. These conformationally restricted aza-BODIPYs all give large torsion angles between the 1,7-phenyl groups and the aza-BODIPY core, with the planarity of the core structure remaining unaffected. These bulky groups prevent the free rotation of the 1,7-phenyl groups of aza-BODIPYs, reduce the nonradiative relaxation process, and result in a significantly high fluorescence quantum yield (up to 0.81 in toluene) in three different solvents studied.

Experimental Section

The NMR spectroscopic experiments were performed by using a 300 MHz NMR spectrometer at RT. Chemical shifts (δ) are given in ppm relative to TMS. High-resolution mass spectra (HRMS) were obtained by using an APCI-TOF spectrometer in positive mode. UV/Vis absorption spectra and fluorescence emission spectra were recorded by using commercial spectrophotometers (Shimadzu UV 2450 and Hitachi F4500, 190–900 nm scan range). The slit width was set at 2.5 nm for excitation and 5.0 nm for emission. Relative fluorescence quantum yields were calculated by using **A1** in $CHCl_3$ ($\phi = 0.34$) as the standard. All ϕ values are corrected for changes in refractive index by using a previously reported method.[20] Crystals of aza-BODIPYs **C1–C3** suitable for X-ray analysis were obtained by slow evaporation of their solutions in dichloromethane. X-ray intensity data measurements were carried out by using a SMART APEX II CCD diffractometer with graphite-monochromated radiation ($Mo_{K\alpha} = 0.71073$ Å) at 297 K.[21,22] CCDC 958519 (**C1**), CCDC 958520 (**C2**), and CCDC 958521 (**C3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*General synthetic procedure for **1a–c***

The synthesis of **1a** is given as an example. KOH (3 g) was added to 2,4,6-trimethylbenzaldehyde (10.0 mL, 0.067 mol) and acetophenone (7.8 mL, 0.067 mol) in anhydrous methanol (50 mL). The mixture was stirred at RT for 1 h. The precipitate was filtered, washed with methanol, and dried under vacuum to give **1a** as a light yellow solid (89% yield, 15.0 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.02$–7.97 (m, 3H), 7.60–7.51 (m, 3H), 7.16 (d, $J = 15.6$ Hz, 1H), 6.94 (s, 2H), 2.41 (s, 6H), 2.32 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 190.5$, 143.3, 138.6, 138.2, 137.2, 132.8, 131.6, 129.4, 128.7, 128.6, 127.2, 21.3, 21.2 ppm; HRMS (APCI): *m/z* calcd for $C_{18}H_{18}O$: 251.1430; found: 251.1428 $[M+H]^+$.

Compound **1b** was obtained from 2,4,6-trimethylbenzaldehyde (10.0 mL, 0.067 mol) and 4-methoxyacetophenone (10.1 g, 0.067 mol) as a light yellow solid (91% yield, 17.1 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 8.4$ Hz, 2H), 7.92 (s, 1H), 7.16 (d, $J = 15.9$ Hz, 1H), 6.97 (d, $J = 8.3$ Hz, 2H), 6.92 (s, 2H), 3.88 (s, 3H), 2.39 (s, 6H), 2.31 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 188.8$, 163.4, 142.5, 138.4, 137.1, 131.8, 131.1, 130.9, 129.3, 127.2, 113.9, 55.5, 21.3, 21.1 ppm; HRMS (APCI): *m/z* calcd for $C_{19}H_{20}O_2$: 281.1536; found: 281.1536 $[M+H]^+$.

Compound **1c** was obtained from 2,6-dichlorobenzaldehyde (8.7 g, 0.05 mol) and 4-methoxyacetophenone (7.5 g, 0.05 mol) as a light yellow solid (95% yield, 14.5 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.05$ (d, $J = 9.0$ Hz, 2H), 7.85 (d, $J = 18.1$ Hz, 1H), 7.68 (d, $J = 15.2$ Hz, 1H), 7.40 (d, $J = 9.0$ Hz, 2H), 7.24–7.18 (m, 1H), 6.99 (d, $J = 9.1$ Hz, 2H), 3.90 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 188.4$, 163.7, 137.0, 135.2, 132.8, 131.1, 130.6, 130.4, 129.7, 128.8, 113.9, 55.5 ppm; HRMS (APCI): *m/z* calcd for $C_{16}H_{12}Cl_2O_2$: 307.0287; found: 307.0285 $[M+H]^+$.

*General synthetic procedure for **2a–c***

The synthesis of compound **2a** is used as an example. Diethylamine (15 mL) and nitromethane (15 mL) were added to **1a** (5.0 g, 20 mmol) in anhydrous methanol (50 mL). The resulting solution was heated at reflux for 24 h, then concentrated under vacuum to afford **2a** (93% yield, 5.8 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.93$ (d, $J = 7.6$ Hz, 2H), 7.56–7.53 (m, 1H), 7.46–7.43 (m, 2H), 6.85 (d, $J = 9.0$ Hz, 2H), 4.93–4.75 (m, 3H), 3.53 (d, $J = 1.9$ Hz, 2H), 2.44 (s, 6H), 2.24 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 197.2$, 137.6, 137.0, 136.2, 135.5, 133.5, 132.7, 131.3, 129.9, 128.8, 128.0, 78.2, 40.5, 33.9, 21.5, 21.2, 20.7 ppm; HRMS (APCI): *m/z* calcd for $C_{19}H_{21}NO_3$: 312.1594; found: 312.1593 $[M+H]^+$.

Compound **2b** was synthesized from **1b** (5.6 g, 20 mmol) and obtained as a yellow oil (84% yield, 5.7 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.89$ (d, $J = 6.0$ Hz, 2H), 6.92 (d, $J = 9.0$ Hz, 2H), 6.83 (s, 2H), 4.89–4.75 (m, 3H), 3.85 (s, 3H), 3.44 (br s, 2H), 2.43 (s, 6H), 2.22 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 195.7$, 163.8, 137.6, 136.9, 135.6, 132.9, 131.3, 130.4, 129.9, 129.4, 113.9, 78.3, 55.5, 40.1, 34.1, 21.5, 21.2, 20.7 ppm; HRMS (APCI): *m/z* calcd for $C_{20}H_{23}NO_4$: 342.1700; found: 342.1699 $[M+H]^+$.

Compound **2c** was synthesized from **1c** (6.1 g, 20 mmol) and obtained as a yellow oil (89% yield, 6.5 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.94$ (d, $J = 8.5$ Hz, 2H), 7.38–7.12 (m, 3H), 6.92 (d, $J = 8.5$ Hz, 2H), 5.31–5.27 (m, 1H), 5.11–4.94 (m, 2H), 3.86 (s, 3H), 3.73–3.62 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 195.0$, 163.9, 134.6, 130.4, 130.1, 129.4, 129.3, 129.2, 113.9, 76.3, 55.5, 38.5, 35.5 ppm; HRMS (APCI): *m/z* calcd for $C_{17}H_{15}Cl_2NO_4$: 368.0451; found: 368.0450 $[M+H]^+$.

*General synthetic procedure for **C1–C3***

The synthesis of **C1** is used as an example. Ammonium acetate (7.5 g, 100 mmol) was added to **2a** (2.2 g, 6.6 mmol) in acetic acid (20 mL). The resulting mixture was heated at reflux for 4 h, then the solvent was removed under vacuum. The residue was purified by using column chromatography on silica (eluent dichloromethane/hexane (1:1 v/v)) to give the aza-dipyrromethene as a metallic blue-black powder (33% yield, 0.61 g) that was directly used for the subsequent BF_2 complexation reaction. The aza-dipyrromethene (0.54 g, 1 mmol) in dichloromethane (100 mL) was treated with triethylamine (2 mL) and borontrifluoride diethyletherate (3 mL). The resulting mixture was stirred at RT for 6 h, then quenched by addition of distilled water (100 mL). The organic layers were combined, washed with water (2×100 mL), dried over anhydrous sodium sulfate, and evaporated to dryness under vacuum. Purification was performed by using column chromatography on silica (eluent dichloromethane/hexane (1:2 v/v)) to give **C1** as a green solid (91% yield, 0.53 g). ^{1}HNMR (300 MHz, $CDCl_3$): $\delta = 8.07$–8.04 (m, 4H), 7.51–7.48 (m, 6H), 6.87 (s, 4H), 6.67 (s, 2H), 2.28 (s, 6H), 2.14 ppm (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.6$, 146.8, 146.0, 137.7, 136.8, 131.6, 129.7, 129.4, 128.7, 128.2, 123.9, 110.0, 21.1 ppm; HRMS (APCI): *m/z* calcd for $C_{38}H_{34}BF_2N_3$: 581.2814; found: 581.2821 $[M+H]^+$.

Compound **C2** was synthesized from **2b** (0.8 g, 2.4 mmol) and ammonium acetate (3.8 g, 100 mmol) and obtained as a greenish solid (22% overall yield, 0.34 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.08$ (d, $J = 8.4$ Hz, 4H), 7.01 (d, $J = 8.4$ Hz, 4H), 6.85 (s, 4H), 6.65 (s, 2H), 3.89 (s, 6H), 2.27 (s, 6H), 2.13 ppm (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.2$, 153.1, 148.6, 143.1, 136.0, 135.5, 127.1, 126.8, 124.3, 117.3, 113.8, 54.6, 20.2, 20.1 ppm; HRMS (APCI): *m/z* calcd for $C_{40}H_{38}BF_2N_3O_2$: 642.3098; found: 642.3095 $[M+H]^+$.

Compound **C3** was synthesized from **2c** (0.9 g, 2.5 mmol) and ammonium acetate (3.8 g, 100 mmol) and obtained as a greenish solid (16% over two steps, 0.28 g). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.12$ (d, $J = 8.0$ Hz, 4H), 7.31 (d, $J = 7.8$ Hz, 4H), 7.17 (m, 2H), 7.03 (d, $J = 8.0$ Hz, 4H), 6.87 (s, 2H), 3.90 ppm (s, 6H); ^{13}C NMR was not available due to poor solubility; HRMS (APCI): *m/z* calcd for $C_{34}H_{22}BF_2Cl_4N_3O_2$: 694.0600; found: 694.0602 $[M+H]^+$.

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[1] a) R. Weissleder, V. Ntziachristos, *Nat. Med.* **2003**, *9*, 123; b) K. Kiyose, H. Kojima, T. Nagano, *Chem. Asian J.* **2008**, *3*, 506; c) L. Yuan, W. Lin, K. Zheng, L. He, W. Huang, *Chem. Soc. Rev.* **2013**, *42*, 622; d) C. Yu, Y. Xu, L. Jiao, J. Zhou, Z. Wang, E. Hao, *Chem. Eur. J.* **2012**, *18*, 6437; e) Z. Zhang, B. Xu, J. Su, L. Shen, Y. Xie, H. Tian, *Angew. Chem.* **2011**, *123*, 11858; *Angew. Chem. Int. Ed.* **2011**, *50*, 11654.

[2] a) A. Loudet, K. Burgess, *Chem. Rev.* **2007**, *107*, 4891; b) G. Ulrich, R. Ziessel, A. Harriman, *Angew. Chem.* **2008**, *120*, 1202; *Angew. Chem. Int. Ed.* **2008**, *47*, 1184; c) R. Ziessel, G. Ulrich, A. Harriman, *New J. Chem.* **2007**, *31*, 496; d) N. Boens, V. Leen, W. Dehaen, *Chem. Soc. Rev.* **2012**, *41*, 1130.

[3] a) L. Gartzia-Rivero, H. Yu, J. Banuelos, I. Lopez-Arbeloa, A. Costela, I. Garcia-Moreno, Y. Xiao, *Chem. Asian J.* **2013**, *8*, 3133;

b) J. O. Flores-Rizo, I. Esnal, C. A. Osorio-Martı'nez, C. F. A. Gómez-Durán, J. Bañuelos, I. L. Arbeloa, K. H. Pannell, A. J. Metta-Magaña, E. Peña-Cabrera, *J. Org. Chem.* **2013**, *78*, 5867; c) I. Esnal, A. Urias-Benavides, C. F. A. Gomez-Duran, C. A. Osorio-Martinez, I. Garcia-Moreno, A. Costela, J. Banuelos, N. Epelde, I. L. Arbeloa, R. Hu, B. Z. Tang, E. Pena-Cabrera, *Chem. Asian J.* **2013**, *8*, 2691; d) X. Zhang, Y. Xiao, J. Qi, J. Qu, B. Kim, X. Yue, K. D. Belfield, *J. Org. Chem.* **2013**, *78*, 9153.

[4] a) H. He, D. K. P. Ng, *Chem. Asian J.* **2013**, *8*, 1441; b) W. Shi, J. Liu, D. K. P. Ng, *Chem. Asian J.* **2012**, *7*, 196; c) T. Kim, S. Park, Y. Choi, Y. Kim, *Chem. Asian J.* **2011**, *6*, 1358; d) V. Lakshmi, M. Ravikanth, *J. Org. Chem.* **2013**, *78*, 4993.

[5] a) A. Poirel, A. D. Nicola, P. Retailleau, R. Ziessel, *J. Org. Chem.* **2012**, *77*, 7512; b) J. Wang, X. Fang, X. Pan, S. Dai, Q. Song, *Chem. Asian J.* **2012**, *7*, 696; c) S. Kusaka, R. Sakamoto, Y. Kitagawa, M. Okumura, H. Nishihara, *Chem. Asian J.* **2013**, *8*, 723.

[6] a) C. Zhang, J. Zhao, S. Wu, Z. Wang, W. Wu, J. Ma, L. Huang, *J. Am. Chem. Soc.* **2013**, *135*, 10566; b) L. Huang, J. Zhao, S. Guo, C. Zhang, J. Ma, *J. Org. Chem.* **2013**, *78*, 5627.

[7] a) J. Killoran, L. Allen, J. F. Gallagher, W. M. Gallagher, D. F. O'Shea, *Chem. Commun.* **2002**, 1862; b) S. O. McDonnell, M. J. Hall, L. T. Allen, A. Byrne, W. M. Gallagher, D. F. O'Shea, *J. Am. Chem. Soc.* **2005**, *127*, 16360; c) J. Killoran, D. F. O'Shea, *Chem. Commun.* **2006**, 1503; d) S. O. McDonnell, D. F. O'Shea, *Org. Lett.* **2006**, *8*, 3493; e) D. Wu, D. F. O'Shea, *Org. Lett.* **2013**, *15*, 3392.

[8] a) A. Loudet, R. Bandichhor, L. Wu, K. Burgess, *Tetrahedron* **2008**, *64*, 3642; b) M. Yuan, X. Yin, H. Zheng, C. Quyang, Z. Zuo, H. Liu, Y. Li, *Chem. Asian J.* **2009**, *4*, 707.

[9] a) A. Coskun, M. D. Yilmaz, E. U. Akkaya, *Org. Lett.* **2007**, *9*, 607; b) H. Liu, J. Mack, Q. Fuo, H. Lu, N. Kobayashi, Z. Shen, *Chem. Commun.* **2011**, *47*, 12092.

[10] a) N. Adarsh, M. Shanmugasundaram, R. R. Avirah, D. Ramaiah, *Chem. Eur. J.* **2012**, *18*, 12655; b) N. Adarsh, R. R. Avirah, D. Ramaiah, *Org. Lett.* **2010**, *12*, 5720; c) Q. Bellier, S. Pegaz, C. Aronica, B. L. Guennic, C. Andraud, O. Maury, *Org. Lett.* **2011**, *13*, 22; d) X. Ma, X. Jiang, S. Zhang, X. Huang, Y. Cheng, C. Zhu, *Polym. Chem.* **2013**, *4*, 4396.

[11] a) H. Lu, S. Shimizu, J. Mack, Z. Shen, N. Kobayashi, *Chem. Asian J.* **2011**, *6*, 1026; b) G. Gresser, M. Hummert, H. Hartmann, K. Leo, M. Riede, *Chem. Eur. J.* **2011**, *17*, 2939; c) V. P. Yakubovskyi, M. P. Shandura, Y. P. Kovtun, *Synth. Commun.* **2010**, *40*, 944.

[12] a) M. Tasior, D. F. O'Shea, *Bioconjugate Chem.* **2010**, *21*, 1130; b) J. Murtagh, D. O. Frimannsson, D. F. O'Shea, *Org. Lett.* **2009**, *11*, 5386; c) M. Tasior, J. Murtagh, D. O. Frimannsson, S. O. McDonnell, D. F. O'Shea, *Org. Biomol. Chem.* **2010**, *8*, 522; d) S. Bhuniya, M. H. Lee, H. M. Jeon, J. H. Han, J. H. Lee, N. Park, S. Maiti, C. Kang, J. S. Kim, *Chem. Commun.* **2013**, *49*, 7141.

[13] a) H. L. Kee, C. Kirmaier, L. Yu, P. Thamyongkit, W. J. Youngblood, M. E. Calder, L. Ramos, B. C. Noll, D. F. Bocian, R. Scheidt, R. R. Birge, J. S. Lindsey, D. Holten, *J. Phys. Chem. B* **2005**, *109*, 20433; b) G. J. Hedley, A. Ruseckas, A. Harriman, D. W. Samuel, *Angew. Chem.* **2011**, *123*, 6764; *Angew. Chem. Int. Ed.* **2011**, *50*, 6634; c) Q. Zheng, G. Xu, P. N. Prasad, *Chem. Eur. J.* **2008**, *14*, 5812; d) W. Pang, X.-F. Zhang, J. Zhou, C. Yu, E. Hao, L. Jiao, *Chem. Commun.* **2012**, *48*, 5437.

[14] C. Yu, L. Jiao, H. Yin, Z. Zhou, W. Pang, Y. Wu, Z. Wang, Y. Gao, E. Hao, *Eur. J. Org. Chem.* **2011**, 5460.

[15] a) W. Zhao, E. M. Carreira, *Angew. Chem.* **2005**, *117*, 1705; *Angew. Chem. Int. Ed.* **2005**, *44*, 1677; b) W. Zhao, E. M. Carreira, *Chem. Eur. J.* **2006**, *12*, 7254.

[16] a) A. Loudet, R. Bandichhor, K. Burgess, A. Palma, S. O. McDonnell, M. J. Hall, D. F. O'Shea, *Org. Lett.* **2008**, *10*, 4771; b) Y. P. Kovtun, V. P. Yakubovskiy, M. P. Shandura, *Chem. Heterocycl. Compd.* **2008**, *44*, 1298.

[17] a) X. Zhang, H. Yu, Y. Xiao, *J. Org. Chem.* **2012**, *77*, 669; b) G. Gresser, H. M. Hartmann, K. L. Wrackmeyer, M. Riede, *Tetrahedron* **2011**, *67*, 7148; c) Q. Bellier, F. Dalier, E. Jeanneau, O. Maury, C. Andraud, *New J. Chem.* **2012**, *36*, 768.

[18] a) M. K. Kuimova, G. Yahioglu, J. A. Levitt, K. Suhling, *J. Am. Chem. Soc.* **2008**, *130*, 6672; b) L. Wang, Y. Xiao, W. Tian, L. Deng, *J. Am. Chem. Soc.* **2013**, *135*, 2903; c) Z. Yang, Y. He, J. Lee, N. Park, M. Suh, W. Chae, J. Cao, X. Peng, H. Jung, C. Kang, J. S. Kim, *J. Am. Chem. Soc.* **2013**, *135*, 9181.

[19] J. Chen, J. Reibenspies, A. Derecskei-Kovacs, K. Burgess, *Chem. Commun.* **1999**, 2501.

[20] L. Jiao, W. Pang, J. Zhou, Y. Wu, X. Mu, G. Bai, E. Hao, *J. Org. Chem.* **2011**, *76*, 9988.

[21] SHELXL-97, *Program for the Refinement of Crystal Structure*, University of Göttingen, Germany, **1997**.

[22] SHELXTL 5.10 (PC/NT-Version), *Program Library for Structure Solution and Molecular Graphics*, Bruker Analytical X-ray Systems, Madison, WI, **1998**.

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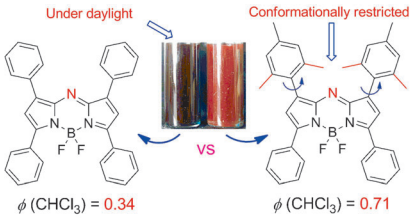

Fluorescent Probes

Lijuan Jiao, Yayang Wu, Yin Ding, Sufan Wang,* Ping Zhang, Changjiang Yu, Yun Wei, Xiaolong Mu, Erhong Hao** ▬ ▮▮▮–▮▮▮

Conformationally Restricted Aza-Dipyrromethene Boron Difluorides (Aza-BODIPYs) with High Fluorescent Quantum Yields