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Synthesis of Directly Connected BODIPY Oligomers through Suzuki–Miyaura Coupling

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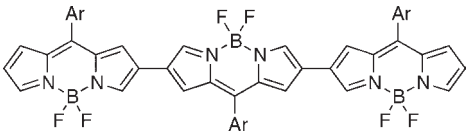
ABSTRACT



Treatment of a *meso*-arylboron dipyrrin (BODIPY) with NBS provides mono- and dibrominated BODIPYs at the 2- and 6-positions in excellent yields with high regioselectivity. Brominated products can be employed as a nice building block for the synthesis of a variety of BODIPY derivatives through Suzuki–Miyaura coupling. Because of a lack of substituents at the 1,3,5,7-positions, a directly β–β-linked BODIPY dimer exhibits a completely coplanar conformation of BODIPY units, offering effective π-conjugation.

Boron dipyrrins (BODIPY) are currently attracting much interest in a wide variety of research areas such as labeling reagents, fluorescent switches, chemosensors, near-IR absorbing/emitting dyes, nonlinear optical materials, light-harvester dye-sensitized solar cells, and bulk heterojunction solar cells owing to their advantageous photophysical properties such as photostability, large extinction coefficients, and high luminescence efficiency.[1] In addition, functionalization of BODIPY dyes allows manipulation of the spectroscopic and electronic properties by introduction of suitable substituents to the BODIPY peripherals. Among synthetic precursors for functionalized BODIPYs, halogenated BODIPYs are one of the most useful building blocks on the basis of a transition-metal-catalyzed cross-coupling strategy.[2,3] However, regioselective halogenation of α-unsubstituted BODIPYs has not been reported. Here we wish to disclose selective and efficient bromination of 1,3,5,7-unsubstituted BODIPY **1** with *N*-bromosuccinimide (NBS) and the use of brominated BODIPYs in a Suzuki–Miyaura coupling reaction for the synthesis of novel BODIPY derivatives including BODIPY oligomers.

We investigated bromination of 1,3,5,7-unsubstituted BODIPY and found that treatment of **1** with 1.2 equiv of NBS at room temperature furnished **2** and **3** in 82% and 12% yields, respectively (Scheme 1).[4] In addition, the use of 2.4 equiv of NBS provided dibromo-BODIPY **3** in excellent yield along with a minor amount of **2**. Even with an excess amount of the brominating agent, none of regioisomeric products such as α-bromo-BODIPYs were detected in the reaction mixture.

(1) (a) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891. (b) Ulrich, G.; Ziessel, R.; Harriman, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1184. (c) Loudet, A.; Burgess, K. In *Handbook of Porphyrin Science*; Kadish, K. M., Smith, K. M., Guilard, K. R., Eds.; World Scientific: Hackensack, 2010; Vol. 8 p 1. (d) Ziessel, R.; Ulrich, G.; Harriman *New J. Chem.* **2007**, *31*, 496. (e) Buyukcakir, O.; Bozdemir, O. A.; Kolemen, S.; Erbas, S.; Akkaya, E. U. *Org. Lett.* **2009**, *11*, 4644.

(2) For α-halogenated BODIPYs, see: (a) Rohand, T.; Baruah, M.; Qin, W.; Boens, N.; Dehaen, W. *Chem. Commun.* **2006**, 266. (b) Rohand, T.; Qin, W.; Boens, N.; Dehaen, W. *Eur. J. Org. Chem.* **2006**, 4658. (c) Baruah, M.; Qin, W.; Basaric, N.; De Borggraeve, W. M.; Boens, N. *J. Org. Chem.* **2005**, *70*, 4152.

(3) For β-halogenated BODIPYs, see: (a) Shah, M.; Thangaraj, K.; Soong, M. L.; Wolford, L. T.; Boyer, J. H.; Politzer, I. R.; Pavlopoulos, T. G. *Heteroatom Chem.* **1990**, *1*, 389. (b) Leen, V.; Braeken, E.; Luckermans, K.; Jackers, C.; Van der Auweraer, M.; Boens, N.; Dehaen, W. *Chem. Commun.* **2009**, 4515.

(4) We also found that treatment of BODIPY **1** with a phenyliodine bis(trifluoroacetate) (PIFA)–Me_3SiBr combination at −78 °C afforded 2-monobromo-BODIPY **2** in 87% yield along with a minor amount of 2,6-dibromo-BODIPY **3** in 5%. For bromination with PIFA–Me_3SiBr, see: Dohi, T.; Ito, M.; Yamaoka, N.; Morimoto, K.; Fujioka, H.; Kita, Y. *Tetrahedron* **2009**, *65*, 10797. Bromination with NBS at −78 °C resulted in much lower conversion.

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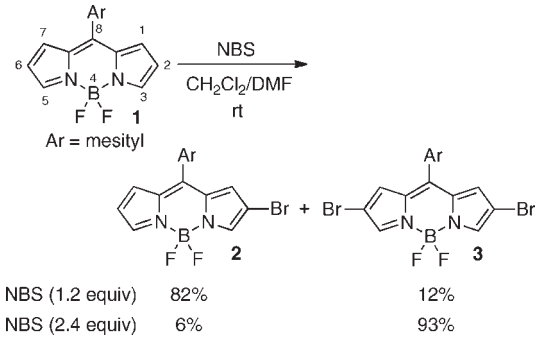
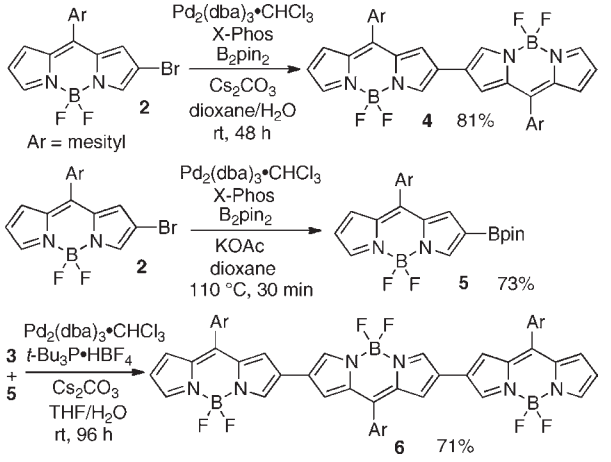
Scheme 1. Selective Bromination of BODIPY **1**



With the efficient protocol to selectively brominated BODIPYs **2** and **3** in hand, we then attempted synthesis of a directly linked BODIPY dimer and trimer (Scheme 2). Although directly α−α-linked BODIPY dimers were recently synthesized and investigated,[5] directly *β*−*β*-linked BODIPY dimers remained unexplored until the very recent report by Ziessel and De Nicola.[6,7] BODIPY **2** was homocoupled to the dimer **4** in 81% yield through Pd-catalyzed borylation[8] with bis(pinacolato)diboron (pin_2B_2) and an in situ cross-coupling sequence by the use of Cs_2CO_3 as the base. The use of potassium acetate instead of cesium carbonate afforded monoboryl BODIPY **5**[9] in 73% yield, which was then converted to trimer **6** in 71% yield via Suzuki−Miyaura cross-coupling with 2.4 equiv of **2**. Unfortunately, the solubility of the trimer was considerably low and hampered the synthesis of further extended BODIPY oligomers.

Scheme 2. Synthesis of BODIPY Dimer and Trimer via Homo- and Cross-Coupling Strategy



Single crystals of BODIPY dimer **4** were obtained by slow vapor diffusion of methanol into a chloroform solution of **4**. X-ray crystallographic analysis of **4** unambiguously elucidated its tapelike structure with a completely flat conformation (Figure 1). The dihedral angle between two adjacent pyrrole moiety is only 0.57°. This orientation of the chromophores is clearly due to the lack of steric interaction

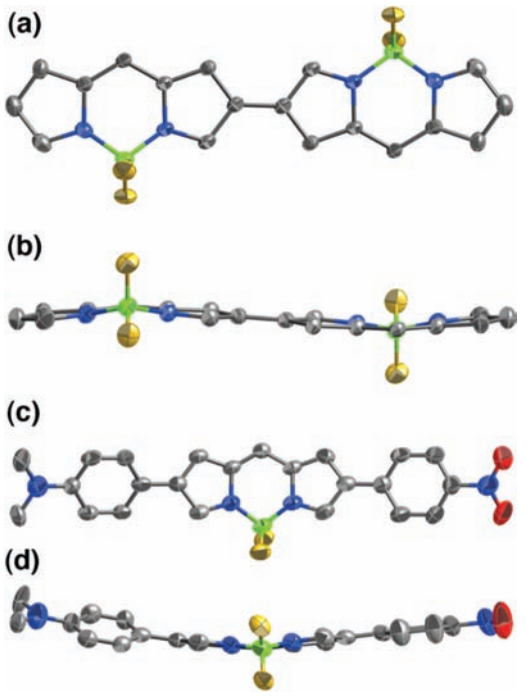


Figure 1. X-ray crystal structures of **4** and **11**. (a) Top view of **4**, (b) side view of **4**, (c) top view of **11**, and (d) side view of **11**. The thermal ellipsoids were scaled to the 50% probability level. Hydrogen atoms and aryl substituents were omitted for clarity.

caused by substituents on 1,3,5,7-positions and is beneficial for the effective elongation of conjugation. In contrast to this BODIPY dimer, directly α−α-linked dimer exhibits substantially twisted conformation because of steric demands of the proximal positions.[5]

The UV/vis absorption spectra of **4** and **6** are substantially red-shifted in comparison to monomer **1** due to effective extension of conjugation caused by highly coplanar conformation (Figure 2 and Table 1). Dimer **4** and trimer **6** also show significant red-shifts in their fluorescence

(5) (a) Broring, M.; Kruger, R.; Link, S.; Kleeberg, C.; Kohler, S.; Xie, X.; Ventura, B.; Flamigni, L. *Chem.—Eur. J.* **2008**, *14*, 2976. (b) Ventura, B.; Marconi, G.; Broring, M.; Kruger, R.; Flamigni, L. *New J. Chem.* **2009**, *33*, 428.

(6) (a) For *β*−*β* phenylene ethynylene-bridged BODIPY oligomers, see: Cakmak, Y.; Akkaya, E. U. *Org. Lett.* **2009**, *11*, 85. (b) Zhu, M.; Jiang, L.; Yuan, M.; Liu, X.; Ouyang, C.; Zheng, H.; Yin, X.; Zuo, Z.; Liu, H.; Li, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 7401.

(7) During preparation this manuscript, Ziessel and De Nicola have reported the synthesis of directly *β*−*β*-linked oligomers of 1,3,5,7-tetramethyl-BODIPY by oxidative homocoupling with PIFA−BF_3•OEt_2. Because of steric hindrance around the *β*−*β* lingkage, these oligomers take a rather twisted conformation with a large dihedral angle (64.1°), resulting in smaller electronic interaction between BODIPY units than our coplanar analogues. See: Rihn, S.; Erdem, M.; De Nicola, A.; Retailleau, P.; Ziessel, R. *Org. Lett.* **2011**, *13*, 1916. We have presented preparation of **4** and **6** at the 90th Annual Meeting of the Chemical Society of Japan, Osaka, March 26−29, 2010; 2PA096.

(8) (a) Billingsley, K. L.; Barder, T. E.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5359. (b) Ishiyama, T.; Itoh, Y.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1997**, *38*, 3447. (c) Ishiyama, T.; Ishida, K.; Miyaura, N. *Tetrahedron* **2001**, *57*, 9813.

(9) *β*-Borylated BODIPYs have been pareared in low yields via iridium-catalyzed direct borylation; see: Chen, J.; Mizumura, M.; Shinokubo, H.; Osuka, A. *Chem.—Eur. J.* **2009**, *15*, 5942.

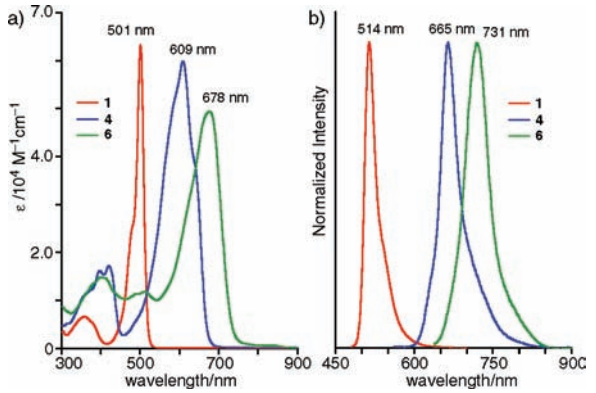


Figure 2. (a) UV/vis absorption spectra of **1**, **4**, and **6** and (b) fluorescence spectra of **1**, **4**, and **6** measured in CH_2Cl_2.

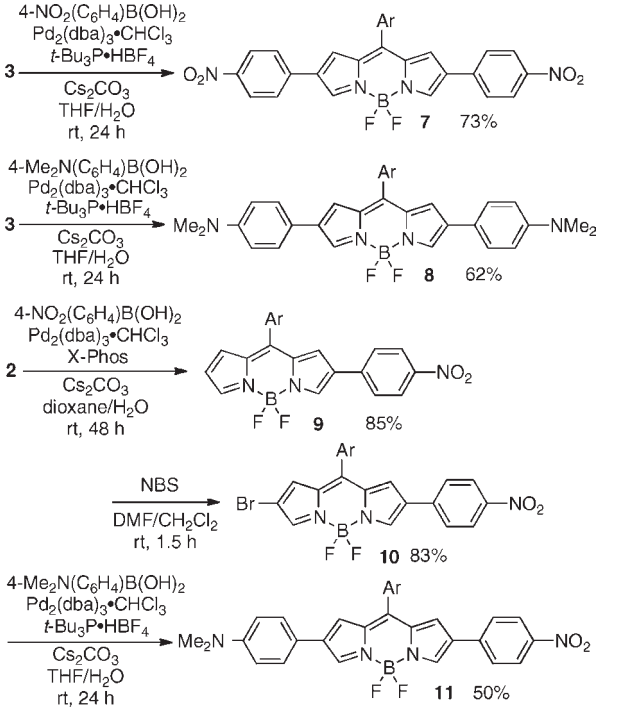
spectra with attenuated quantum efficiency ($\Phi_F = 0.15$ and 0.25, respectively). To obtain further insight into their photophysical properties, we have measured the fluorescence lifetimes, fluorescence anisotropy decay and spectra (Supporting Information). Compared with the fluorescence lifetime of 6.7 ns for BODIPY monomer **1**, dimer **4** and trimer **6** exhibit much reduced fluorescence lifetimes of 1.8 ns. This feature is mainly due to the enhancement of nonradiative decay processes contributed by the decreased HOMO−LUMO gap as well as increased vibrational relaxation channels including the torsional motions around the $\beta-\beta$ linkage in **4** and **6**. While both **4** and **6** exhibit the similar fluorescence lifetime of 1.8 ns, the radiative decay rate for **6** is larger, but the nonradiative decay rate is larger for **4**, which leads to a larger fluorescence quantum yield for **6** compared with **4**. This feature is attributable to an increase in radiative decay coupling in **6** compared with **4** probably because the molecular rotation around the $\beta-\beta$ linkage should experience more restriction from the surrounding solvent molecules. The fluorescence excitation anisotropy spectra reflect the overall molecular geometry (Supporting Information). For **1**, the anisotropy values are nearly zero in the entire spectral region, indicating that the dipole orientation along the long and short molecular axes is completely mixed in the excited state. On the other hand, the anisotropy values for **4** and **6** become positive and those for **6** is larger than **4** in the entire spectral region. This feature indicates that the dipole orientation in the excited state is predominantly aligned along the long molecular axis and the difference in the orientation between absorption and fluorescence dipoles becomes smaller as the molecule becomes elongated in the long molecular axis like trimer **3**. In addition, as the overall molecular size increases in going from monomer to dimer **4** and trimer **6**, the rotational diffusion motion becomes slower as demonstrated by the fluorescence anisotropy decay times (40, 124, and 303 ps for **1**, **4**, and **6**, respectively, Supporting Information). Nevertheless, the relatively high emission efficiency of $\beta-\beta$-linked BODIPY oligomers promises their use as near-infrared (NIR) fluorescence dyes.

Table 1. Summary of Optical Properties of BODIPYs

compd	λ_{max} (nm)	ε (M^{-1} cm^{-1})	λ_{em} (nm)	Φ_f
1	501	6.3×10^4	514	0.92
2	518	5.8×10^4	537	0.16
3	538	5.8×10^4	577	0.14
4	609	6.0×10^4	655	0.15
5	502	8.0×10^4	515	0.89
6	678	4.9×10^4	731	0.25
7	577	6.7×10^4	606	0.78
8	686	2.7×10^4		
9	537	6.2×10^4	565	0.81
10	558	6.8×10^4	583	0.35
11	644	2.7×10^4		

Brominated BODIPYs **2** and **3** are also useful precursors for the synthesis of unsymmetrically and symmetrically substituted BODIPY derivatives. Suzuki−Miyaura cross-coupling of dibromo BODIPY **3** with 4-nitrophenyl- and 4-*N*,*N*-dimethylaminophenylboronic acids furnished acceptor−acceptor- and donor−donor-substituted BODIPYs **7** and **8** in good yields (Scheme 3). Monobromo BODIPY **2** is particularly useful for the synthesis of unsymmetrically BODIPY derivatives. First, **2** was coupled with 4-nitrophenylboronic acid followed by bromination with NBS provided BODIPY **7** in 83% yield, which was eventually cross-coupled with 4-*N*,*N*-dimethylaminophenylboronic acid to furnish donor−acceptor-substituted BODIPY. X-ray diffraction analysis of these 2,6-diaryl-substituted BODIPY revealed almost coplanar orientation between the aromatic groups and the BODIPY core, allowing effective electronic communication. This is again owing to the lack of steric hindrance of substituents on 1,3,5,7-positions.

Scheme 3. Synthesis of Donor- and Acceptor-Substituted BODIPYs



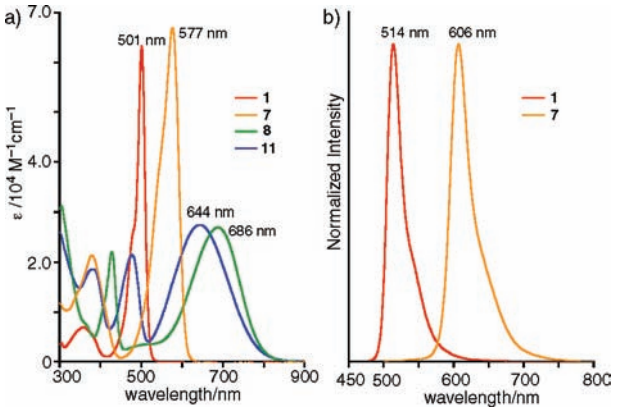


Figure 3. (a) UV/vis absorption spectra of **1**, **7**, **8**, and **11** and (b) fluorescence spectra of **1** and **7** in CH_2Cl_2.

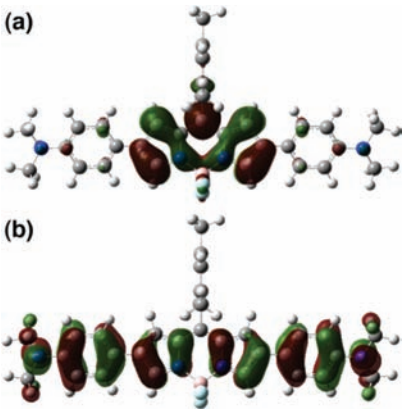


Figure 4. (a) LUMO and (b) HOMO of **8** calculated at the B3LYP/6-31G(d) level.

In the case of **7**, introduction of two 4-nitrophenyl substituents on the BODIPY core resulted in a considerable red-shift and increase of extinction coefficient in the UV/vis absorption spectra due to effective expansion of conjugation along with high fluorescence quantum yield (Φ_F = 0.78) (Figure 3 and Table 1). In contrast, **8** and **11** exhibit considerably different shapes of absorption spectra with much red-shifted and broadened S_1-S_0 transition band. Furthermore, fluorescence of BODIPYs **8** and **11** is completely quenched. These photophysical features clearly indicate intramolecular charge transfer (ICT) owing to the strongly donating nature of 4-*N*,*N*-dimethylaminophenyl moiety. DFT calculations at the B3LYP/6-31G(d) level support charge transfer character in **8** and **11**, of which HOMOs have large contribution from the orbital on aminophenyl substituents (Figure 4). BODIPY-based ICT dyes often utilize α-styryl derivatives because of their favorable coplanar conformation of the styryl groups to the BODIPY core for ICT interaction.[10] However, the present study clearly demonstrates that *β*-aryl BODIPYs without substituents on 1,3-positions are also good candidates to create BODIPY derivatives bearing strong ICT character.[11]

In summary, we have accomplished regioselective bromination of 1,3,5,7-unsubstituted BODIPY with NBS. Brominated BODIPYs can be used as a versatile synthetic intermediate for novel BODIPY derivatives, as demonstrated by expeditious preparation of directly *β*–*β*-linked BODIPY oligomers and donor–acceptor-substituted unsymmetrical BODIPY. Further direct functionalization of BODIPYs is currently underway in our group.

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Supporting Information Available. General procedures, spectral data for compounds, absorption and fluorescence spectra. X-ray analysis of **4**, **7**, **8**, and **11** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

(10) (a) Rurack, K.; Kollmannsberger, M.; Daub, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 385. (b) Deniz, E.; Isbasar, G. C.; Bozdemir, O. A.; Yildirim, L. T.; Siemiarczuk, A.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 3401. (c) Yu, Y.-H.; Descalzo, A. B.; Shen, Z.; Röhr, H.; Liu, Q.; Wang, Y.-W.; Spieles, M.; Li, Y.-Z.; Rurack, K.; You, X.-Z. *Chem. Asian J.* **2006**, *1*, 176. (d) Rurack, K.; Kollmannsberger, M.; Daub, J. *New J. Chem.* **2001**, *25*, 289.

(11) Bonardi, L.; Ulrich, G.; Ziessel, R. *Org. Lett.* **2008**, *10*, 2183.