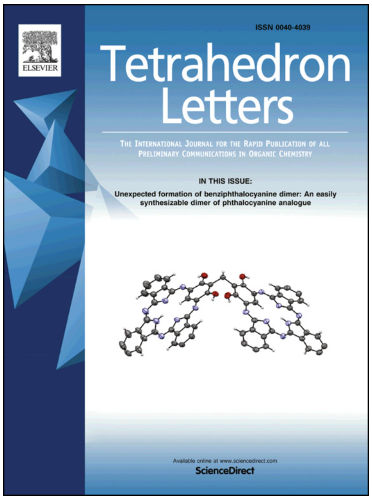
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Synthesis of Furan-Substituted Aza-BODIPYs Having Near-Infrared Emission

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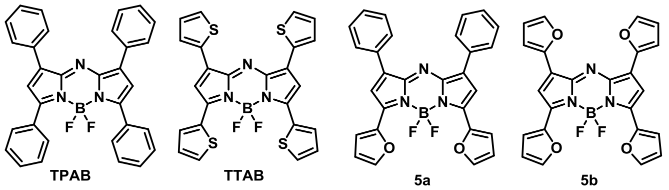
ABSTRACT

Development of near-infrared-emissive aza-boron dipyrromethene (aza-BODIPY) derivatives having furanyl groups is reported. From the optical measurements, it was clearly indicated that the emission bands were presented in the longer wavelength region than those of the conventional aza-BODIPYs. The emission bands with the peaks at 730 nm and 758 nm were observed from the bis- and tetra-substituted furanyl aza-BODIPYs with similar extents of emission efficiencies, respectively. According to the computer calculations, it was proposed that molecular planarity could be enhanced in the case of the furan groups. As a result, band-gap energy could be lowered comparing to those of the conventional benzene and thiophene-substituted aza-BODIPYs.

Because of high permeability on the NIR light through biological samples and even vital bodies, NIR-emissive dyes can be used as a versatile signal transducer in a luminescent probe for bioimaging.[1] By the combination of the NIR-emissive dyes with the stimuli-responsive units toward target reactions or environmental changes, smart bioprobes for surveying biological functions at the deep spot inside vital organs can be constructed.[2,3] Moreover, since the NIR light can efficiently penetrate quartz and aqueous media, NIR-emissive dyes are a building block for fabricating advanced optical devices such as telecommunication devices, laser amplifiers and organic light-emitting diodes.[4,5] In these applications in material science and biotechnology, the NIR-emissive dye presenting a sharp luminescent spectrum is especially advantageous. The intense emission within small wavelength width is valid for improving the signal to noise ratios in the detection as well as for fabricating multi-channel telecommunication system. To meet this demand, conjugated organic molecules are regarded as a suitable platform, and indeed several NIR-emissive dyes have been reported so far.[6,7]

Boron-containing "element-blocks", which are defined as a minimum functional unit composed of heteroatoms, are a promising building block for developing luminescent materials.[8] Particularly, in the boron-containing luminescent "element-blocks", boron dipyromethenes (BODIPYs) are well known to be one of beneficial light-emitting dyes because they have various advantages such as large absorption and luminescent abilities in the narrow wavelength regions, high photo-stability, and environment-resistant emissive properties.[9–17] In addition, optical properties of BODIPYs can be easily tuned. By the introduction of substituents to its core structure, various photochemical properties such as emission color, stimuli-responsive intensity changes, phosphorescence characteristics and energy-transfer efficiencies were drastically varied.[18–32] The NIR emissive materials were also prepared with the BODIPY derivatives.[33–40] It was reported that the class of aza-BODIPYs having the nitrogen atom on the *meso*-position instead of the methylene bridge in BODIPYs showed emission in the longer wavelength region than common BODIPYs because of lower-lying LUMO energy levels.[41–43] As a typical example, it was reported that tetraphenyl aza-BODIPY (TPAB) exhibited emission in the red region with a high quantum yield (Scheme 1).[44] Based on TPAB, the NIR-emissive polymeric materials with large electron-carrier ability were also obtained.[45,46] More recently, it was reported that thiophene-substituted aza-BODIPYs including the tetra-substituted derivative (TTAB) presented emission in far longer wavelength regions than TPAB.[47,48] These results could be derived from less steric hindrance and electron-donating properties of the substituted thiophenes. However, as is often the case with the development of NIR-emissive dyes, thiophene-substituted aza-BODIPYs also suffered from decreases in emission efficiencies. Therefore, it is still required to demonstrate the design strategy for providing red-shifted emission in the NIR region without critical losses of emission efficiencies.

Scheme 1. Chemical structures of aza-BODIPYs

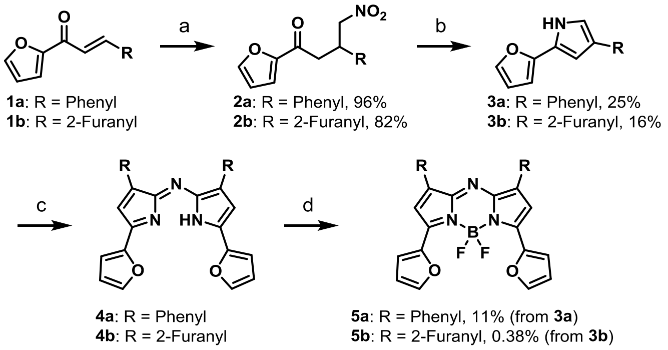


Herein, the new aza-BODIPYs were designed to receive the NIR emission with high quantum yields (Scheme 1). To improve molecular planarity, furan was chosen as the substituents instead of the thiophene groups.[49,50] Furan also works as a donor unit and is a smaller five-membered ring compound than thiophene. Therefore, it was expected that introducing of furan should be the effective tactic to realize strong NIR emission without loss of emission quantum yields. To evaluate validity of this idea, two kinds of furanyl aza-BODIPYs with various numbers of furan substituents were synthesized, and the emission bands were found in the longer wavelength regions than those of the conventional aza-BODIPYs.

The synthetic routes of furan-substituted aza-BODIPYs are outlined in Scheme 2.[51] In the previous reports on the syntheses of TPAB and TTAB, the ligands were directly transformed from the nitro compounds via coupling reactions.[44,47] In the case of furanyl-aza-BODIPYs, these synthetic methods were not applicable. Instead, **3a** and **3b** which were proposed as an intermediate in the conventional methods were once isolated, followed by preparing each ligand in the coupling reaction in the presence of sodium nitrite which was a nitrogen source at the *meso* position in the aza-BODIPY skeleton. The products **5a** and **5b** had good solubility enough for obtaining ^{1}H NMR in the common organic solvents such as chloroform, THF, and ethanol (ca. 1 mg/mL in chloroform). The structures of all compounds were confirmed by NMR spectroscopies and ionization mass measurements (Charts S1−S6). **5a** and **5b** hardly showed critical degradation in the air and during optical measurements. From these results, we concluded that the desired boron complexes were obtained. TPAB and TTAB were also prepared according to the previous studies for comparing optical properties under the same conditions.[44,47]

The optical properties of aza-BODIPYs were evaluated, and the results are presented in Table 1. Figure 1a shows the absorption spectra of aza-BODIPYs in the dichloromethane solution. **5a** and **5b** showed sharp absorption bands with the peaks at 721 nm and 751 nm with larger molar extinction coefficients than those of TPAB and TTAB, respectively. The absorption maxima of **5** and TTAB were obtained in the NIR region, while the absorption band of TPAB was observed in the shorter wavelength region. In particular, **5b** and TTAB with tetra-heterole substitutions had the peak in the longer wavelength region. These data indicate that more effective expansion of conjugation can occur in these heteroles-substituted aza-BODIPYs. It is implied that 5-memebered rings could have less steric hindrance compared with the phenyl ring. Therefore, the bandgap energy of **5** and TTAB decreased, resulting in red-shifted absorption bands. In particular, **5b** presented the emission band in the longer wavelength region than TTAB having thiophene rings, indicating that furan should be favorable for expansion of π-conjugation though the ligand moiety. From electrochemical measurements, the reversible processes in the reduced scan were detected (Figure S1 and Table 2). From the onsets of the first reduction waves, the energy levels of lowest-unoccupied molecular orbital (LUMO) were determined, and similar values were obtained. The band gap energy should be determined by the energy levels of highest-occupied molecular orbital (HOMO) of aza-BODIPYs.

Scheme 2. Synthesis of **5**^{a}



^{a}Reagents and conditions: (a) CH_3NO_2, K_2CO_3, EtOH, reflux, 12 h; (b) i) NaOMe, MeOH, THF, r.t., 1.5 h; ii) H_2SO_4, MeOH, 0 °C to r.t., then stirred for 1.5 h; iii) NH_4OAc, AcOH, 100 °C, 1 h; (c) AcOH, Ac_2O, $NaNO_2$, r.t., 1 h; (d) $BF_3{\cdot}Et_2O$, Et_3N, CH_2Cl_2, r.t., 12 h for **5a**, 1 d for **5b**.

Table 1. Optical properties of aza-BODIPYs^a

	λ_{abs} (nm)^a	ε (10^4 $M^{-1}cm^{-1}$)	λ_{em} (nm)^b	Φ_{PL}^{c}	FWHM (cm^{-1})^d
TPAB	648	82,400	669	0.12	802
TTAB	741	99,500	750	0.14	584
5a	721	133,900	730	0.22	543
5b	751	130,700	758	0.08	644

^{a}1.0×10^{-5} M. ^{b}1.0×10^{-6} M. ^{c}Determined as an absolute value with the integration sphere method. ^{d}Calculated from the data in Figure 1b.

Table 2. Results of the absorption spectroscopy and the cyclic voltammetry

	λ_{onset} (nm)^a	E_g^{opt} (eV)^b	E_{red}^{CV} (V)^{c,d}	E_{HOMO} (eV)^e	E_{LUMO} (eV)^f
TPAB	691	1.79	−0.78	−2.23	−4.02
TTAB	783	1.58	−0.74	−2.48	−4.06
5a	759	1.63	−0.78	−2.39	−4.02
5b	794	1.56	−0.76	−2.48	−4.04

^{a}Onset value of the UV–vis spectra measured in dichloromethane (1.0×10^{-5} M). ^{b}Optical band gap estimated from the onset wavelength of the UV–vis spectra in dichloromethane. ^{c}Cyclic voltammetry was carried out in dichloromethane with 0.1 M tetrabutylammonium hexafluorophosphate as a supporting electrolyte and the Fc/Fc+ redox couple as an external standard. ^{d}E_{red} is the onset potential of first reduction wave. ^{e}Calculated from LUMO and optical band gap (E_g^{opt}) of the synthesized compounds, E_{HOMO} / eV = E_{LUMO} / eV – E_g^{opt} / eV. ^{f}Calculated from the empirical formula, E_{LUMO} / eV = – E_{red} / eV – 4.80.

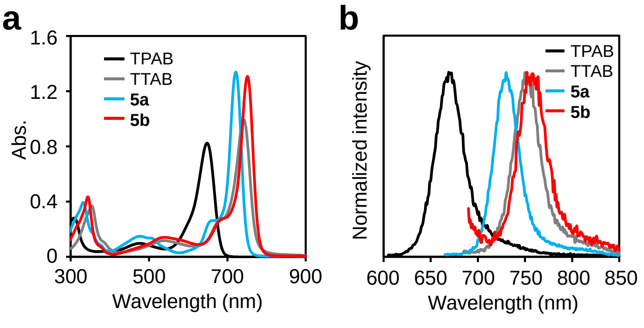


Figure 1. UV–vis–NIR absorption (1×10^{-5} M) and PL (1×10^{-6} M) spectra of aza-BODIPYs in dichloromethane.

Figure 1b shows the photoluminescence (PL) spectra of aza-BODIPYs in dichloromethane solution. **5a** presented the NIR emission with the largest emission efficiency of the aza-BODIPYs used in this study. **5b** showed red-shifted emission bands compared with those of TTAB as well as TPAB with the similar extent of emission efficiency to these aza-BODIPYs. Similarly to the absorption spectra, less steric hindrances of 5-membered rings should play a significant role in extension of π-conjugation though the ligand moiety. Typical sharp emission bands were observed from **5**. Even in the spectrum of **5b**, the smaller full width at half maximum (FWHM) of the emission band was obtained than that of TPAB (Table 1). Because of intrinsic rigidity of the aza-BODIPY ligand, sharp shapes of emission bands should be obtained. From the emission decay measurements, it was shown that all components were within ns orders, indicating aza-BODIPYs showed fluorescence (Table S1). Solvent dependencies on optical properties were investigated in various solvents, and significant changes were hardly obtained (Tables S2−S5). This fact means that emission should be derived not from intramolecular charge transfer states but from locally-excited states in the ligand moiety. Therefore, optical properties were sensitive in the degree of π-conjugation.

To elucidate optical properties originated from electronic structures of aza-BODIPYs, computer calculations were performed. By the density functional theory (DFT), the optimized geometries of aza-BODIPYs in the ground state were estimated (Figure 2). Obviously, the 5-membered rings had higher planar

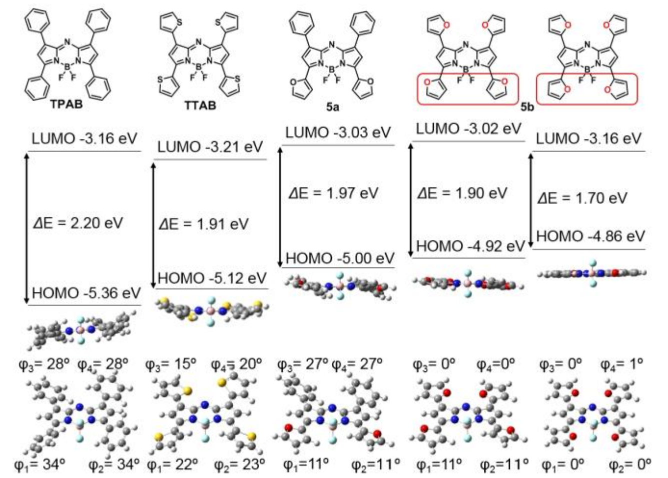


Figure 2. Optimized structures and estimated energy diagrams of aza-BODIPYs from DFT calculations.

conformations than that of TPAB. Thereby, π-conjugated systems can be developed through the whole molecules (Figure S2). Another impressive point was concerned to the type of heteroatoms in the 5-membered ring. According to the dihedral angles (*φ*), it was clearly indicated that the furan rings (*φ* = 10°) contributed to enhancing molecular planarity than the thiophene ones (*φ* = 20°). Correspondingly, the HOMO−LUMO band gap was narrowed by replacing from thiophenes to furans. These data indicate that the red-shifted absorption and emission bands of **5** should be derived from improvement of planarity of the molecular skeletons. Furthermore, the calculation with **5b** proposed the far more stable conformation where all oxygen atoms in each furan ring were directed to the boron difluoride side. According to the previous report, the ring direction can be evaluated from the coupling with difluoride in ^{13}C NMR spectra.[52] From the ^{13}C NMR spectra (Figure S3), the ^{19}F−^{13}C couplings were detected from both **5a** and **5b**. These data mean that heteroatoms of the 5-membered rings at the boron difluoride side in **5** as well as TTAB should be mainly located outside. Meanwhile, from the calculation of total energies, similar values were obtained from both conformations (Table S6), suggesting that rotation at the furan rings could be acceptable. This highly-planar conformation might also contribute to presenting red-shifted emission from **5b**. These results suggest that introduction of furan rings into BODIPY could induce various beneficial changes to optical properties of aza-BODIPY such as bathochromic shifts in absorption and PL spectra without critical loss of emission efficiency. Finally, the NIR-emissive ability can be enhanced.

In conclusion, this manuscript demonstrates that introduction of furan should be an effective strategy to obtain strong emission in the NIR region by employing aza-BODIPY. Molecular planarity can be significantly improved by introducing furan, leading to bathochromic shifts not only in the absorption band with a larger extinct coefficient but also in the emission without critical losses of sharp spectrum shapes and emission efficiencies. Taking versatility of BODIPY dyes into account, our findings could be widely applicable in the design of NIR-emissive materials in a variety of fields.

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References

1. Fabian J, Nakazumi H, Matsuoka M. *Chem. Rev.* 1992; 92: 1197–1226.
2. Yang G, Liu J, Wu Y, Feng L, Liu Z. *Coord. Chem. Rev*. 2016; 320–321: 100−117.
3. Kiyose K, Kojima H, Nagano T. *Chem. Asian J.* 2008; 3: 506–515.
4. Qian G, Wang ZY. *Chem. Asian J.* 2010; 5: 1006–1029.
5. Bünzli J-C G, Eliseeva SV. *J. Rare Earths*. 2010; 28: 824–842.
6. Yoshii R, Nagai A, Tanaka K, Chujo Y. *J. Polym. Sci. Part A: Polym. Chem.* 2013; 51: 1726−1733.
7. Kajiwara Y, Nagai A, Tanaka K, Chujo Y. *J. Mater. Chem. C*. 2013; 1: 4437−4444.
8. Chujo Y, Tanaka K. *Bull. Chem. Soc. Jpn*. 2015; 88: 633−643.
9. Loudet A, Burgess K. *Chem. Rev.* 2007; 107: 4891–4932.
10. Ulrich G, Ziessel R, Harriman A. *Angew. Chem. Int. Ed.* 2008; 47: 1184–1201.
11. Ziessel R, Ulrich G, Harriman A. *New J. Chem.* 2007; 31: 496–501.
12. Bones N, Leen V, Dehaen W. *Chem. Soc. Rev*. 2012; 41: 1130–1172.
13. Yamazawa S, Nakashima M, Suda Y, Nishiyabu R, Kubo Y. *J. Org. Chem*. 2016; 81: 1310−1315.
14. Lu H, Mack J, Yang Y, Shen Z. *Chem. Soc. Rev*. 2014; 43: 4778−4823.
15. Hu W, Ma H, Hou B, Zhao H, Ji Y, Jiang R, Hu X, Lu X, Zhang L, Tang Y, Fan Q, Huang W. *ACS Appl. Mater. Interfaces.* 2016; 8: 12039−12047.
16. Jiao L, Wu Y, Wang S, Hu X, Zhang P, Yu C, Cong K, Meng Q, Hao E, Vicente MGH. *J. Org. Chem*. 2014; 79: 1830−1835.
17. Wu Y, Cheng C, Jiao L, Yu C, Wang S, Wei Y, Mu X, Hao E. *Org. Lett*. 2014; 16: 748−751.
18. Tanaka K, Yamane H, Yoshii R, Chujo Y. *Bioorg. Med. Chem*. 2013; 21: 2715−2719.
19. Yeo H, Tanaka K, Chujo Y. *Macromolecules*. 2013; 46: 2599−2605.
20. Yoshii, R, Yamane H, Tanaka K, Chujo Y. *Macromolecules*. 2014; 47: 3755−3760.
21. Yamane H, Tanaka K, Chujo Y. *Tetrahedron Lett*. 2015; 56: 6786−6790.
22. Yamane H, Ito S, Tanaka K, Chujo Y. *Polym. Chem*. 2016; 7: 2799−2807.
23. Yeo H, Tanaka K, Chujo Y. *Macromolecules*. 2016; 49: 8899−8904.
24. Yeo H, Tanaka K, Chujo Y. *Polymer*. 2015; 60: 228−233.
25. Yeo H, Tanaka K, Chujo Y. *J. Polym. Sci. A: Polym. Chem.* 2015; 53: 2026−2035.
26. Peng X, Du J, Fan J, Wang J, Wu Y, Zhao J, Sun S, Xu T. *J. Am. Chem. Soc.* 2007; 129: 1500−1501.
27. Yamamura M, Yazaki S, Seki M, Matsui Y, Ikeda H, Nabeshima T. *Org. Biomol. Chem*. 2015; 13: 2574−2581.
28. Kubota Y, Uehara J, Funabiki K, Ebihara M, Matsui M. *Tetrahedron Lett.* 2010; 51: 6195−6198.
29. Ni Y, Lee S, Son M, Aratani N, Ishida M, Yamada H, Furuta H, Kim D, Wu J. *Angew. Chem. Int. Ed*. 2016; 18: 2815−2819.
30. Shimizu S, Murayama A, Haruyama T, Iino T, Mori S, Furuta H, Kobayashi N. *Chem. Eur. J.* 2015; 21: 12996−13003.
31. Saikawa M, Daicho M, Nakamura T, Uchida J, Yamamura M, Nabeshima T. *Chem. Commun*. 2016; 52: 4014−4017.
32. Ooyama Y, Hagiwara Y, Oda Y, Fukuoka H, Ohshita J. *RSC Adv*. 2014; 4: 1163−1167.
33. Kubo Y, Watanabe K, Nishiyabu R, Hata R, Murakami A, Shoda T, Ota H. *Org. Lett.* 2011; 13: 4574−4577.
34. Gao L, Senevirathna W, Sauvé G. *Org. Lett.* 2011; 13: 5354–535.
35. Gao L, Tang S, Zhu L, Sauvé G. *Macromolecules.* 2012; 45: 7404−7412.
36. Wu L, Burgess K. *Chem. Commun*. 2008; 4933−4935.
37. Wu D, O’Shea DF. *Org. Lett.* 2013; 15: 3392−3395.
38. Ni Y, Wu J. *Org. Biomol. Chem.* 2014; 12: 3774−3791.
39. Poirel A, Nicola AD, Retailleau P, Ziessel R. *J. Org. Chem*. 2012; 77: 7512−7525.
40. Saino S, Saikawa M, Nakamura T, Yamamura M, Nabeshima T. *Tetrahedron Lett*. 2016; 57: 1629−1634.
41. Gorman A, Killoran J, O'Shea C, Kenna T, Gallagher WM, O'Shea DF. *J. Am. Chem. Soc.* 2004; 126: 10619–10631.
42. Loudet A, Bandichhor R, Wu L, Burgess K. *Tetrahedron.* 2008; 64: 3642–3654.
43. Ge Y, O'Shea DF. *Chem. Soc. Rev.* 2016; 45: 3846–3864.
44. Yoshii R, Nagai A, Chujo Y. *J. Polym. Sci. Part A: Polym. Chem.* 2010; 48: 5348–5356.
45. Tanaka K, Yanagida T, Yamane H, Hirose A, Yoshii R, Chujo Y. *Bioorg. Med. Chem. Lett*. 2015; 25: 5331−5334.
46. Yoshii R, Yamane H, Nagai A, Tanaka K, Taka H, Kita H, Chujo Y. *Macromolecules.* 2014; 47: 2316−2323.
47. Gresser R, Hartmann H, Wrackmeyer M, Leo K, Riede M. *Tetrahedron.* 2011; 67: 7148–7155.
48. Zhang X, Yu H, Xiao Y. *J. Org. Chem.* 2012; 77: 669–673.

49. Liao J, Wang Y, Xu Y, Zhao H, Xiao X, Yang X. *Tetrahedron* 2015; 71: 5078−5084.
50. Feng, Z, Jiao L, Feng Y, Yu C, Chen N, Wei Y, Mu X, Hao E. *J. Org. Chem*. 2016; 81: 6281−6291.
51. Budhiraja A, Kadian K, Kaur M, Aggarwal V, Garg A, Sapra S, Nepali K, Suri OP, Dhar KL. *Med. Chem. Res.* 2011; 21: 2133–2138.
52. Bellier Q, Dalier F, Jeanneau E, Maury O, Andraud C. *New J. Chem*. 2012; 36: 768−773.

Highlights

-Novel BODIPY derivatives having furan rings were synthesized.
-The synthesized BODIPYs showed bright emission in the NIR region.
-We clarified that introduction of furan rings should enhance molecular planarity.

Graphical Abstract