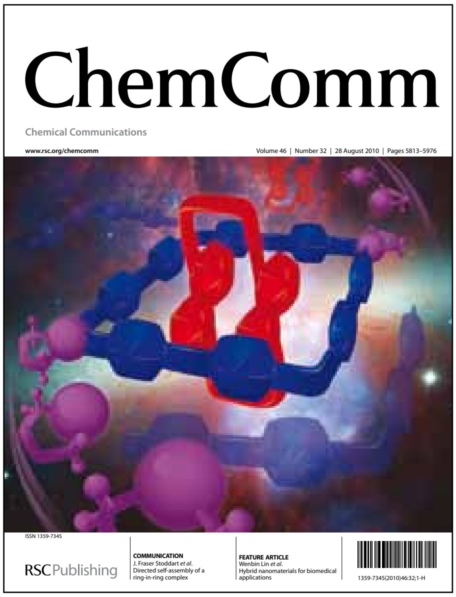
ChemComm

Accepted Manuscript



ChemComm

Chemical Communications

www.rsc.org/chemcomm

Volume 46 | Number 32 | 28 August 2010 | Pages 5813–5976

ISSN 1359-7345

RSC Publishing

COMMUNICATION
J. Fraser Stoddart *et al.*
Directed self-assembly of a ring-in-ring complex

FEATURE ARTICLE
Wenbin Lin *et al.*
Hybrid nanomaterials for biomedical applications

1359-7345(2010)46:32;1-H

This is an *Accepted Manuscript*, which has been through the RSC Publishing peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, which is prior to technical editing, formatting and proof reading. This free service from RSC Publishing allows authors to make their results available to the community, in citable form, before publication of the edited article. This *Accepted Manuscript* will be replaced by the edited and formatted *Advance Article* as soon as this is available.

To cite this manuscript please use its permanent Digital Object Identifier (DOI®), which is identical for all formats of publication.

More information about *Accepted Manuscripts* can be found in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics contained in the manuscript submitted by the author(s) which may alter content, and that the standard **Terms & Conditions** and the **ethical guidelines** that apply to the journal are still applicable. In no event shall the RSC be held responsible for any errors or omissions in these *Accepted Manuscript* manuscripts or any consequences arising from the use of any information contained in them.

RSC Publishing

www.rsc.org/chemcomm

Registered Charity Number 207890

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Oxidation of 2-amino-substituted BODIPYs providing pyrazine-fused BODIPY trimers

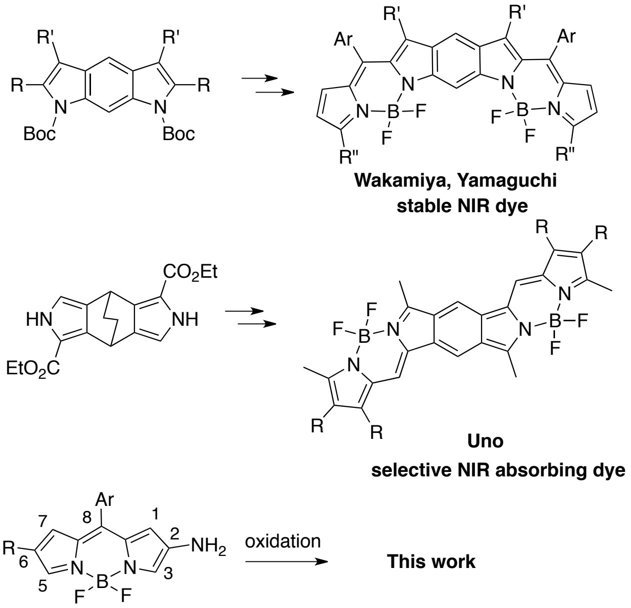
Hiroki Yokoi, Naruhiko Wachi, Satoru Hiroto* and Hiroshi Shinokubo*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

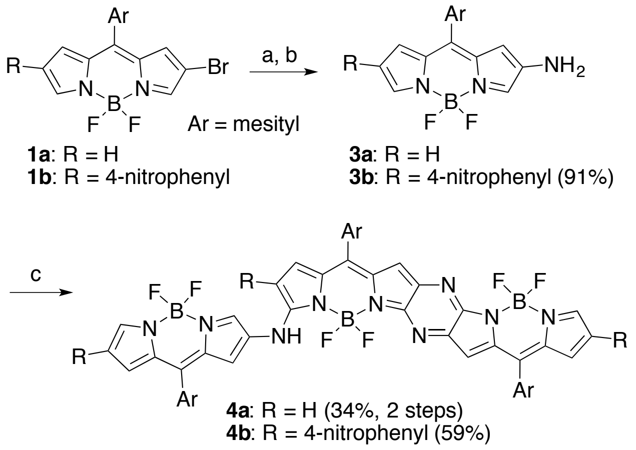
Oxidation of 2-amino-substituted BODIPYs afforded BODIPY trimers in a one-step operation. The trimer consists of a pyrazine-fused BODIPY dimer to which one BODIPY unit is connected through an NH linkage. Effective expansion of π-conjugation over the fused dimer was observed in optical and electrochemical measurements.

BODIPYs, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes, have been one of the most attractive functional dyes for material science.[1] They exhibit high thermal and photochemical stability as well as strong absorption and emission in the visible region due to their rigid frameworks and betain-like electronic structures. These characteristics are now applied to fluorescent probes for bio-imaging[2], photodynamic therapy[3] and organic emissive materials such as OLEDs[4]. Many chemists have recently focused on the synthesis of BODIPY oligomers to achieve near-IR absorption and emission properties through expansion of π-conjugation.[5] In particular, BODIPY oligomers with fused structures have attained fascinating features. Yamaguchi and Wakamiya have demonstrated potential application of an α,β-benzene-fused BODIPY dimer to stable NIR dyes owing to the lowered HOMO energy by the fused structure.[6a] Uno and co-workers have also reported β,β'-benzene-fused BODIPY oligomers as NIR-selective light-absorbing materials.[6b]

Oxidation of amino-substituted π-conjugated molecules has been a useful tool for construction of fused systems. For example, aniline is oxidized into well-known black pigments, which are a mixture of oligomeric materials containing C–N double bonds and fused structures. We have recently developed oxidative coupling of amino-substituted functional π-systems such as porphyrins and anthracenes, providing pyrazine and pyrrole-fused dimers in high yields with excellent regioselectivity.[7] We then investigated the reactivity of amino BODIPYs under oxidative conditions. Herein we report that one-step oxidation of β-amino BODIPYs provides BODIPY trimers with a pyrazine-fused BODIPY dimer structure, which have strong NIR absorption bands.



Scheme 1. Examples of fused BODIPY dimers.



Scheme 2. Synthesis of BODIPY trimers. Conditions; a: benzophenone imine (1.5 equiv), Cs_2CO_3 (2.0 equiv), Xantphos (10 mol%), Pd_2dba_3•$CHCl_3$ (5 mol%), dioxane, 100 °C, 3 h, for **3a**; benzophenone imine (1.5 equiv), Cs_2CO_3 (2.0 equiv), Xantphos (40 mol%), Pd_2dba_3•$CHCl_3$ (20 mol%), dioxane, 100 °C, 2 h, for **3b**, b: HCl (1 M, equiv), THF, 60 °C, 1 h, c: DDQ (2.1 equiv), $CHCl_3$, RT, 0.5 h, for **4a**; DDQ (2.1 equiv), $CHCl_3$, RT, 4 h, for **4b**.

2-Amino-8-mesityl BODIPY **3a** was prepared from 2-bromo BODIPY **1a**. Palladium-catalysed imination of **1a** with benzophenone imine provided imino BODIPY **2a** in 69% yield, which afforded a purple-coloured solution containing **3a** and benzophenone after hydrolysis of **2a** with aqueous HCl. Because decomposition of amino BODIPY **3a** occurred during concentration of its solution, we subjected the crude product **3a** to the oxidation reaction without complete evaporation of solvents. Oxidation of **3a** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded a blue compound **4a** in 34% yield in two steps, which was stable under air. Its parent mass ion peaks were observed at $m/z = 968.4118$, suggesting its trimeric structure.

The structure of **4a** was unambiguously elucidated by X-ray diffraction analysis. Fig. 1 shows the crystal structure of **4a**, which contains three BODIPY skeletons. Two of BODIPY units constitute a pyrazine-fused BODIPY dimer, to which one BODIPY unit is connected through an NH linkage. The BODIPY dimer part is completely planar and the mean plane deviation from the plane consisted of 18 carbon and six nitrogen atoms in the dimer is 0.107 Å. The planar geometry suggests effective π-extension among the dimer unit. On the other hand, the flanking BODIPY moiety is tilted at 44.5° from the dimer plane, indicating a small π-conjugation with the dimer moiety. The bond length between C(1)–N(9) is 1.33 Å which is shorter than that of a standard C_{sp3}–N bond (1.47 Å), while C(20)–N(9) is standard (1.42 Å). These data indicate that the lone pair on the N(9) atom mainly participates in π-conjugation with the fused BODIPY dimer.

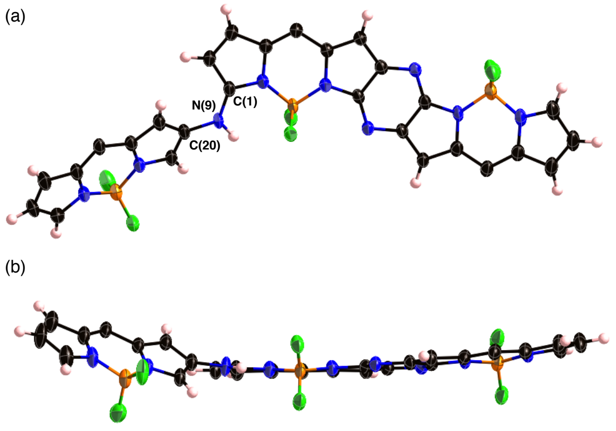


Fig. 1 X-Ray crystal structure of **4a**. (a) Top view and (b) side view. The thermal ellipsoids are scaled at 50% probability level. *meso*-Mesityl groups are omitted for clarity.

To stabilize amino-substituted BODIPY **3a**, we introduced electron-withdrawing groups. As we expected, nitrophenyl-substituted BODIPY **3b** could be purified as a stable compound. Oxidation of **3b** with DDQ in chloroform exclusively afforded the pyrazine-fused trimer **4b** in 59%. In this reaction, no other oligomers were observed. The structure of **4b** was also confirmed by X-ray diffraction analysis (Fig. S11). Two nitrophenyl groups at the terminal positions are placed almost in the same plane with the adjacent BODIPY core, indicating effective π-conjugation. The hanging BODIPY monomer unit is displaced from the plane of the dimeric unit with the angle of 21.5°. The dihedral angle between the dimer plane and the flanking BODIPY unit is 54.8°, which is larger than that of **4a**. These displacements are caused by steric repulsion between the nitrophenyl substituent and the BODIPY monomer unit.

Fig. 2a shows the UV/vis/NIR absorption spectra of **4a** and **4b** in dichloromethane along with the spectra of the corresponding monomers, 8-mesityl BODIPY **5a** and 2-(4-nitrophenyl)-8-mesityl BODIPY **5b**. As compared to the monomers **5a** and **5b**, the absorption spectra of trimers **4a** and **4b** are significantly intensified. The lowest energy absorption bands of **4a** and **4b** are red-shifted to 701 and 761 nm, respectively. The absorption maximum of trimer **4b** is longer than that of **4a** because of extended π-conjugation by the nitrophenyl groups. Interestingly, a new absorption band of **4a** appeared around 850 nm in polar solvents such as acetone and acetonitrile (Fig. 2b). Further investigation was conducted by theoretical calculations. The frontier orbitals of **4a** were calculated by the DFT method at the B3LYP/6-31G(d) level (Fig. S13). While the HOMO is delocalized over the fused BODIPY dimer unit, the LUMO+1 is located at the monomeric BODIPY moiety. Time-dependent (TD) DFT calculations revealed that the lowest energy absorption band consists of three transitions. All of the transitions contain the transition from HOMO to LUMO+1. These results indicate that intramolecular charge transfer interactions between the pyrazine-fused BODIPY dimer and amino BODIPY unit resulted in the broad and red-shifted absorption band. In the fluorescence spectra, **4a** and **4b** show weak emissions in the near infrared region ($\Phi_F < 0.01$, Figure S15). The low fluorescence quantum yields are probably due to the non-radiative decay by rotation of the amino BODIPY substituent.[8]

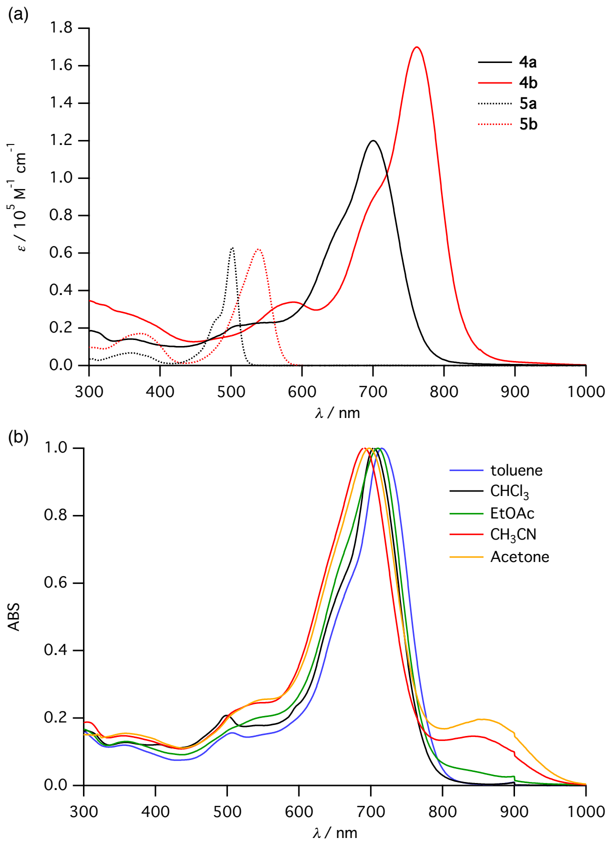


Fig. 2 (a) UV/vis absorption spectra of **4a** (black) and **4b** (red) along with corresponding monomers **5a** and **5b** in CH_2Cl_2. (b) UV/vis absorption spectra of **4a** in various solvents.

Electrochemical properties of **4a**, **4b** and the corresponding monomers **5a** and **5b**[5c] were investigated by the cyclic voltammetry (Fig. S12). The results are summarized in Table 1. Both **4a** and **4b** exhibited clear and reversible reduction waves and irreversible oxidation waves. As compared to the corresponding monomers **5a** and **5b**, the gap between the first oxidation and first reduction potentials (ΔE) becomes narrower in trimers **4a** and **4b**. Because the value of the third reduction potential of **4** is almost identical with the first reduction potential of monomer **5**, the third reduction can be considered to occur on the amino BODIPY unit. Accordingly, both the first and second reductions proceed at the fused dimer unit. The theoretical calculations also support this assignment: the calculated energy levels of HOMO, HOMO–1 and LUMO of the corresponding pyrazine-fused BODIPY dimer unit are almost comparable with those of **4a** (Fig. S13). The split of the reduction waves indicates the strong electronic interaction between two BODIPY moieties in the fused dimer. The remarkable decrease of the first reduction potential in trimers suggests that fusion with the pyrazine ring at 2,3-positions is effective to lower the LUMO level. Such a compound with a low LUMO level is a promising candidate for effective electron-accepting molecules applied for solar cells and n-type conducting materials.

Table 1. Summary of electrochemical data[a]

compound	E_{ox}^2	E_{ox}^1	E_{red}^1	E_{red}^2	E_{red}^3	E_{red}^4	ΔE^b
5a	—	1.12^c	–1.35	—	—	—	2.47
4a	1.04^c	0.716^c	–0.735	–0.950	–1.39	–1.92	1.45
5b	—	1.15^c	–1.21	–1.67	—	—	2.36
4b	1.08^c	0.796^c	–0.556	–0.817	–1.33	–1.73	1.35

[a] The values are described versus the potential of ferrocene/ferrocenium cation. [b] $\Delta E = (E_{ox}^1 - E_{red}^1)$ [c] irreversible waves. The values were obtained by DPV measurement.

In conclusion, we have achieved one-pot synthesis of pyrazine-fused BODIPY trimers through oxidation of 2-amino-substituted BODIPYs. The reaction proceeded with excellent regioselectivity due to high electrophilicity at 3,5-positions. BODIPY trimers **4** exhibit bathochromic shifted strong absorption bands, indicating effective expansion of π-conjugation. Theoretical calculations revealed the presence of intramolecular charge transfer interactions between the BODIPY dimer and monomer units. This protocol would be applicable to efficient access to NIR dyes not only with BODIPYs but also with other functional π-systems.

This work was supported by a Grant-in-Aid for Scientific Research on Innovative Areas "New Polymeric Materials Based on Element-Blocks (No. 2401)" (25102514). H.S. acknowledges Yamada Science Foundation for financial support.

Notes and references

[a] *Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-8603, Japan. Fax: +81-52-789-3188; E-mail: hitoro@apchem.nagoya-u.ac.jp; hshino@apchem.nagoya-u.ac.jp*

† Electronic Supplementary Information (ESI) available: Experimental details for **4a** and **4b**, summary of the electrochemical investigation and X-ray crystallographic data for **4a** and **4b** are included in the supplementary information. See DOI: 10.1039/b000000x/

‡ X-ray crystallographic data for **4a**: Formula: $C_{58}H_{50}B_3Cl_{12}F_6N_9$, M_w = 1444.90; monoclinic, $P2_1/n$; a = 15.068(5) Å, b = 14.208(5) Å, c = 20.518(10) Å, β = 99.173(4)°; V = 6450(4) Å^3, Z = 4; D_c = 1.488 g/cm^3; R_1 =0.0938 ($I > 2\sigma(I)$), wR_2 = 0.2931 (all data), GOF = 1.050.

X-ray crystallographic data for **4b**: Formula: $C_{80}H_{68}B_3Cl_1F_6N_{16}O_6$, M_w = 1533.00; triclinic, P-1; a = 14.6707(6) Å, b = 17.1450(7) Å, c = 18.0545(10) Å, a = 118.3350(17), β = 96.657(3)°, g = 90.695(2)°; V = 3958.5(3) Å^3, Z = 2; D_c = 1.286 g/cm^3; R_1 =0.0871 ($I > 2\sigma(I)$), wR_2 = 0.2809 (all data), GOF = 1.026.

1 (a) S. Chibani, B. L. Guennic, A. Charaf-Eddin, A. D. Laurent and D. Jacquemin, *Chemical Science*, 2013, **4**, 1950; (b) G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem. Int. Ed.*, 2008, **47**, 1184; (c) A. Laudet and K. Burgess, *Chem. Rev.* 2007, **107**, 4891.

2 (a) Y. Urano, D. Asanuma, Y. Hama, Y. Koyama, T. Barrett, M. Kamiya, T. Nagano, T. Watanabe, A. Hasegawa, P. L. Choyke and H. Kobayashi, *Nat. Med.*, 2009, **15**, 104; (b) J. Han, A. Loudet, R. Barhoumi, R. C. Burghardt and K. Burgess, *J. Am. Chem. Soc.*, 2009, **131**, 1642.

3 (a) T. Myochin, K. Hanaoka, T. Komatsu, T. Terai and T. Nagano, *J. Am. Chem. Soc.*, 2012, **134**, 13730; (b) T. Yogo, Y. Urano, Y. Ishitsuka, F. Maniwa and T. Nagano, *J. Am. Chem. Soc.* 2005, **127**, 12162.

4 L. Bonardi, H. Kanaan, F. Camerel, P. Jolinat, P. Retailleau and R. Ziessel, *Adv. Funct. Mater.* 2008, **18**, 401.

5 (a) M. Bröring, R. Krüger, S. Link, C. Kleeberg, S. Köhler, X. Xie, B. Ventura and L. Flamigni, *Chem. Eur. J.*, 2008, **14**, 2976; (b) S. Rihn, M. Erdem, A. D. Nicola, P. Retailleau and R. Ziessel, *Org. Lett.*, 2011, **13**, 1916; (c) Y. Hayashi, S. Yamaguchi, W. Y. Cha, D. Kim and H. Shinokubo, *Org. Lett.*, 2011, **13**, 2992; (d) A. Poirel, A. De Nicola, P. Retailleau and Z. Ziessel, *J. Org. Chem.*, 2012, **77**, 7512.

6 (a) A. Wakamiya, T. Murakami and S. Yamaguchi, *Chem. Sci.*, 2013, **4**, 1002. (b) M. Nakamura, T. Tahara, K. Yakahashi, T. Nagata, H. Uoyama, D. Kuzuhara, S. Mori, T. Okujima, H. Yamada and H. Uno, *Org. Biomol. Chem.*, 2012, **10**, 6840.

7 (a) K. Goto, R. Yamaguchi, S. Hiroto, H. Ueno, T. Kawai and H. Shinokubo, *Angew. Chem. Int. Ed.*, 2012, **51**, 10333; (b) M. Akita, S. Hiroto and H. Shinokubo, *Angew. Chem. Int. Ed.*, 2012, **51**, 2894.

8 The addition of various acids in the solution of **4a** to prevent CT interactions did not enhance its fluorescence intensity.