

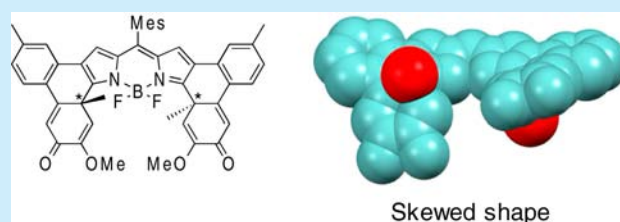
Synthesis and Chiroptical Properties of a Ring-Fused BODIPY with a Skewed Chiral π Skeleton

Yuki Gobo, Masaki Yamamura, Takashi Nakamura, and Tatsuya Nabeshima*

Graduated School of Pure and Applied Science and Tsukuba Research Center for Interdisciplinary Materials Science (TIMS), University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8571, Japan

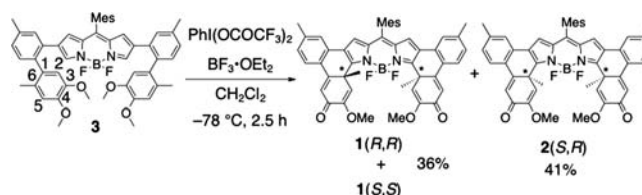
S Supporting Information

ABSTRACT: A twisted chiral boron–dipyrin complex (BODIPY) was synthesized by oxidative annulation of the biphenyl units at the β positions. The chiral BODIPY has two asymmetric carbons in the large planar skeleton, which were generated upon the ring-fused reaction. Its π -elongated and twisted structure resulted in the Cotton effect in the red region ($\lambda_{\text{max}} = 614 \text{ nm}$, $\Delta\epsilon = 60 \text{ M}^{-1}\text{cm}^{-1}$) as well as the strong fluorescence ($\Phi_{\text{F}} = 0.73$) and circularly polarized luminescence (CPL).



Boron-dipyrromethene, BODIPY, is one of the most important fluorophores because of its strong absorption and fluorescence in the visible region and its chemical stability.¹ BODIPY and its derivatives have been investigated for various applications such as the emission moieties of chemical sensors,² bioimaging,³ and dye sensitized solar cells.⁴ In particular, chiral BODIPYs are expected to exhibit significant chiroptical responses, such as circular dichroism (CD) and circularly polarized luminescence (CPL); thus, they can be applied to CD/CPL sensors⁵ and asymmetric synthesis.⁶ Interest in CPL has especially grown in recent years because of its utilization as a source of information about the chiral structures of emitting excited states, as well as its potential for smart photonic applications such as 3D displays and information storage.⁷ Furthermore, the fluorophores possessing a strong Cotton effect in the red region have an advantage in the application of protein and peptide analyses.⁸ Despite their significant potentials, most of the reported chiral BODIPYs have been synthesized by simply introducing chiral auxiliaries into the BODIPY skeleton, but did not exhibit a strong CD or CPL.^{9,10} However, one example of the chiral BODIPYs that exhibits a strong circular dichroism is the bis(BODIPYs) in which each BODIPY is connected in a helical manner with the chiral (*R,R*)- or (*S,S*)-1,2-diphenyl-1,2-ethanodiamine.¹¹ Recently, it has been reported that the aromatic molecules with twisted π skeletons show a strong CD and CPL.¹² Thus, we hypothesized that the twisting of the strongly fluorescent BODIPY skeletons would also produce a functional fluorophore that shows significant chiroptical properties. We now report the synthesis of the novel skewed chiral BODIPY **1** which has two asymmetric carbons in the large planar skeleton (Scheme 1). Interestingly, the chiral BODIPY **1** shows a Cotton effect and circularly polarized luminescence in the red region, because of its elongated π -conjugation and twisted structure.

We have already reported a biphenyl appended BODIPY **3** that shows an interesting fluorescence behavior depending on solvent polarity (Scheme 1).¹³ Upon the oxidation of **3** with

Scheme 1. Synthesis of Chiral BODIPY **1** and Meso BODIPY **2**

PIFA,¹⁴ the annulation reaction at the biphenyl carbons at the 6-position selectively proceeded with a concurrent demethylation, and a unique chiral BODIPY **1** was obtained in 36% yield as the racemic form. The biphenyl carbons linked by the annulation reaction became sp^3 asymmetric centers. As a result, the chiral BODIPY **1** has two asymmetric carbons with the same absolute configuration. The corresponding *meso*-compound **2**, which has two asymmetric carbons with the opposite configuration, was also produced in 41% yield.

Compounds **1** and **2** were characterized by ^1H , ^{13}C , ^{11}B , ^{19}F NMR, HRMS, and elemental analysis (see the Supporting Information). The crystal structures of **1** and **2** were unambiguously determined by an X-ray diffraction analysis (Figure 1). The crystal of **1** was a racemate, and it was revealed that **1** has two asymmetric carbons and a unique skewed structure in the solid state. The two six-membered rings of **1** were pushed in the opposite direction with regard to the plane of the BODIPY core due to the sp^3 asymmetric carbons with the same absolute configurations, which resulted in the twisted chiral π -skeleton. Meso BODIPY **2** also had two asymmetric carbons and a bent structure in the solid state, but the carbons had the opposite (*R,S*) absolute configurations. As a result, the two ends of the skeleton of **2** bent to the same side. The

Received: April 27, 2016

Published: May 23, 2016

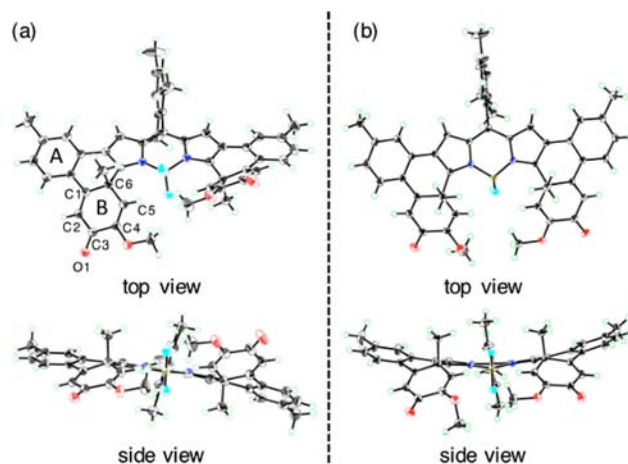


Figure 1. X-ray crystal structures of chiral BODIPY **1** and meso-BODIPY **2**. ORTEP drawing (50% probability). C, black; H, light green; N, blue; O, red; B, yellow; F, light blue. (a) **1**(*R,R*) (one of the enantiomers is shown), top and side views. (b) **2**, top and side views.

representative bond lengths of ring B (see Figure 1) of **1** were 1.341(3) (C1–C2), 1.329(3) (C4–C5), and 1.229(2) (C3–O1), and those of **2** were 1.3414(19) (C1–C2), 1.3331(19) (C4–C5), and 1.2301(17) (C3–O1) Å. These results confirmed that ring B of **1** and **2** had a cyclohexadienone structure. The distortion of the BODIPY cores was evaluated from the dihedral angles between the two pyrrole rings to be 7.3° and 15.3° for **1** and **2**, respectively. The degree of twisting in the periphery of the scaffold was also evaluated from the dihedral angles between the phenyl moiety and the terminal cyclohexadienone ring (rings A and B) to be 14.4° and 34.5° for **1** and **2**, respectively. Thus, the skewed π skeletons of the compounds were confirmed.

The X-ray analysis revealed the large planar molecular skeletons of **1** and **2**. To confirm the extension of the π -conjugation, the optical properties of **1** and **2** were investigated by UV–vis absorption and fluorescence spectroscopies (Figure 2). The absorption maxima of **1** and **2** were 614 and 598 nm,

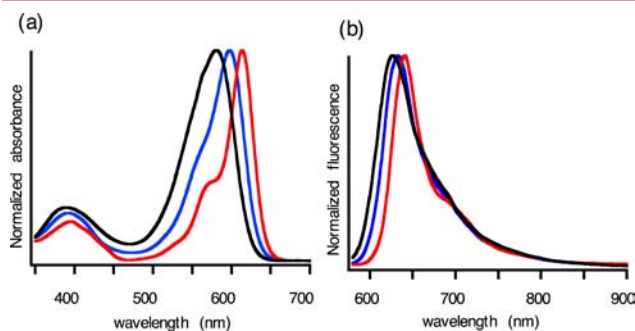


Figure 2. (a) UV–vis and (b) fluorescence ($\lambda_{\text{ex}} = 550$ nm) spectra of **1** (red), **2** (blue), and **3** (black) in CHCl_3 solution ($[\mathbf{1}, \mathbf{2}, \mathbf{3}] = 5.0 \times 10^{-6}$ M).

respectively, which were shifted to longer wavelengths than that of the biphenyl appended BODIPY **3** (580 nm).¹³ The fluorescence maxima of **1** and **2** were 641 and 633 nm, respectively, which were also shifted to longer wavelengths than that of **3** (627 nm). These facts suggested the more effective delocalization of the π -electrons over the molecules of **1** and **2**. From the X-ray analysis, it was shown that the structure of **1** is

more planar than that of **2**. The higher planarity of **1** is considered to be the reason for the more red-shifted absorption/fluorescence and larger absorption coefficient. The fluorescence quantum yields (Φ_F) of **1** and **2** were also investigated, and they were 0.73 and 0.61 for **1** and **2**, respectively (Table 1). The notably high fluorescence quantum yields were probably due to their rigid skeletons.

Table 1. Summary of UV–vis Absorption Maxima (λ_{max}), Fluorescence Emission Maxima (λ_{flu}), and Fluorescence Quantum Yields (Φ_F) Excited at 550 nm in CHCl_3 of BODIPY **1**–**3**

	λ_{max} (nm)	ϵ ($\text{M}^{-1} \text{cm}^{-1}$)	λ_{flu} (nm)	Φ_F
1	614	10×10^4	641	0.73
2	598	6.8×10^4	633	0.61
3 ¹³	580	4.3×10^4	627	0.58

To evaluate the chiroptical properties of the skewed BODIPY **1**, we attempted its optical resolution. We succeeded in the separation of each enantiomer of **1** by chiral HPLC (column: CHIRALPAK IA) with CHCl_3 /hexane = 1:1 as the eluent. The CD spectra of **1**(*R,R*) and **1**(*S,S*) were investigated. The enantiopure **1**(*R,R*) and **1**(*S,S*) show opposite Cotton effects at 614 nm ($\Delta\epsilon = 60 \text{ M}^{-1} \text{cm}^{-1}$) in the red region. The $\Delta\epsilon$ value is higher than those of the reported BODIPYs to which the chiral auxiliaries were attached.^{9,10} The entire CD spectra of **1**(*R,R*) and **1**(*S,S*) gave clear mirror images (Figure 3a). The spectrum that showed a negative Cotton effect was

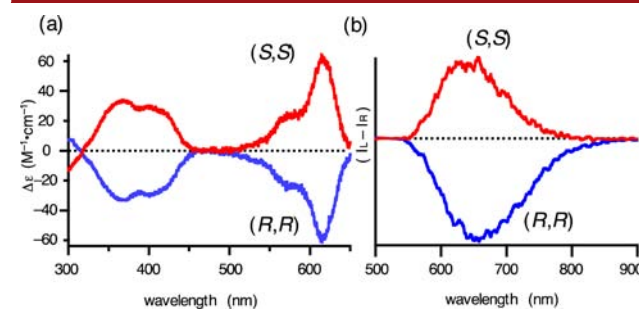


Figure 3. (a) CD spectra of **1**(*R,R*) (blue) and **1**(*S,S*) (red) in CHCl_3 solution (5.0×10^{-6} M). (b) CPL spectra for **1**(*R,R*) (blue) and for **1**(*S,S*) (red) in CHCl_3 solution (10×10^{-6} M).

attributed to that of **1**(*R,R*) by time-dependent density functional theory (TD-DFT) calculations at the M062X/6-31G(d,p) level of theory (see the Supporting Information).

Finally, we measured the CPL properties of the enantiopure **1** in chloroform. **1**(*S,S*) and **1**(*R,R*) exhibited CPL activities, and their CPL spectra are almost mirror images of each other (Figure 3b). The dissymmetric factor for luminescence, $|g_{\text{lum}}|$, was estimated to be $(6 \pm 2) \times 10^{-4}$. Although this value of $|g_{\text{lum}}|$ is comparable to those of the previously reported chiral BODIPY derivatives,¹⁰ these results proved the effectiveness of the structural design to skew the aromatic skeleton in achieving CPL in the red region.

In summary, we synthesized the chiral BODIPY **1** bearing a twisted skeleton by oxidative annulation. **1** exhibited a high fluorescence quantum yield ($\Phi_F = 0.73$) and a Cotton effect ($\lambda_{\text{max}} = 614$ nm, $\Delta\epsilon = 60 \text{ M}^{-1} \text{cm}^{-1}$) and CPL activities ($|g_{\text{lum}}| = (6 \pm 2) \times 10^{-4}$) in the red region, demonstrating the importance of the molecular design to twist the BODIPY

fluorophore. This study contributes to the future development of novel chiral BODIPYs bearing a chiral skeleton toward applications such as bioimaging and chiral sensing.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01237.

Experimental details, spectral data, and crystallographic information (PDF)

Crystallographic data for 1 (CIF)

Crystallographic data for 2 (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: nabesima@chem.tsukuba.ac.jp.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We would like to thank Prof. Yoshiki Chujo, Assoc. Prof. Kazuo Tanaka, Assist. Prof. Masayuki Gon, Ms. Risa Sawada of Kyoto University, and Mr. Makoto Saikawa of University of Tsukuba for the CPL measurements. We would also like to thank Assist. Prof. Yosuke Uchiyama of Kitasato University for the chiral HPLC. This research was financially supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (Nos. 15H00723 and 15H00914).

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