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Highly Fluorescent BODIPY Dyes Modulated with Spirofluorene Moieties

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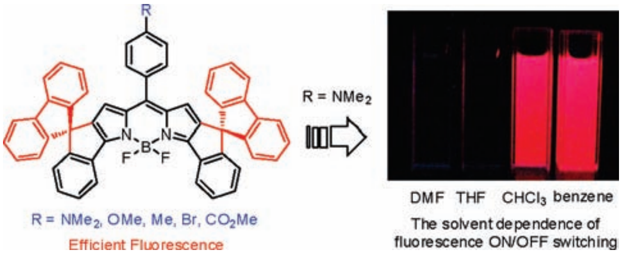
ABSTRACT



A new type of structurally rigid BODIPY dye having spirofluorene moieties has been synthesized. These structurally constrained BODIPY dyes with spirofluorene moieties exhibit an intense bathochromic fluorescence. The solvent dependence of fluorescence ON/OFF switching of a BODIPY dye having an amino moiety was observed.

The technique of visualizing living cells by labeling proteins or DNA with fluorescent dyes is widely applicable to early detection of focus and elucidation of cellular mechanisms.[1] 4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) derivatives are regarded as among the most promising candidates for fluorescent labels and probes.[2] In general, BODIPY dyes are relatively insensitive to the surrounding environment such as polarity and pH and have large molar absorption coefficients and high fluorescence quantum yields. Furthermore, their absorption and emission bands are narrow and sharp, and their photophysical properties are readily tunable by modification of the BODIPY core.

Extension of π-conjugated systems in general brings about a bathochromic shift of the emission maxima of fluorophores. However, free rotation between the BODIPY core and π-conjugated groups results in a decrease in quantum yields. Thus, constrained linkage of the BODIPY core with the π-conjugated moieties is essential to obtain efficient bathochromic fluorescence.[3] Although structurally constrained BODIPY dyes with moderate quantum yields have been reported so far, only a limited number of studies have appeared.[4]

Herein, we report the synthesis and photophysical properties of novel BODIPY dyes (**sp-BODIPY**) derived from spiro[fluorene-9,4′(1′*H*)-indeno[1,2-*b*]pyrrole] (**sp-FIP**)[5] (Figure 1). To prepare **sp-FIP** as a key structure, we have explored the palladium-catalyzed intramolecular direct C−H arylation of a pyrrole moiety.[6−8] This approach enabled us to obtain a new type of BODIPY dye. Furthermore, their highly rigid structures reduced nonradiative decay of excited states, resulting in a high photoluminescence quantum yield.

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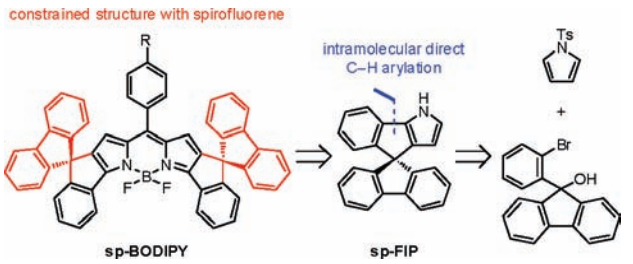
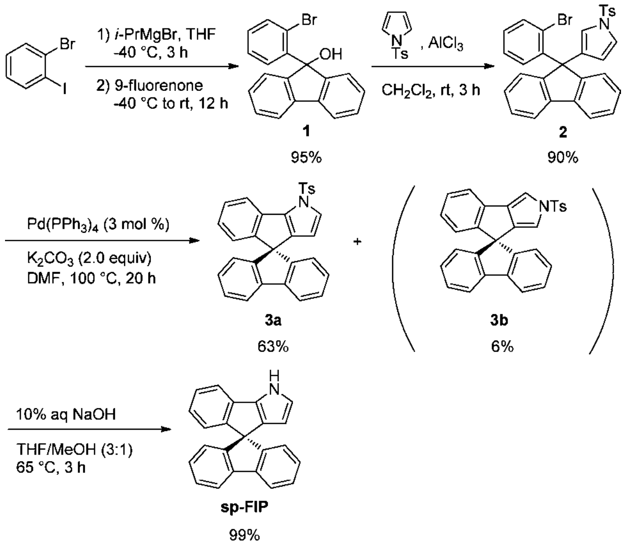
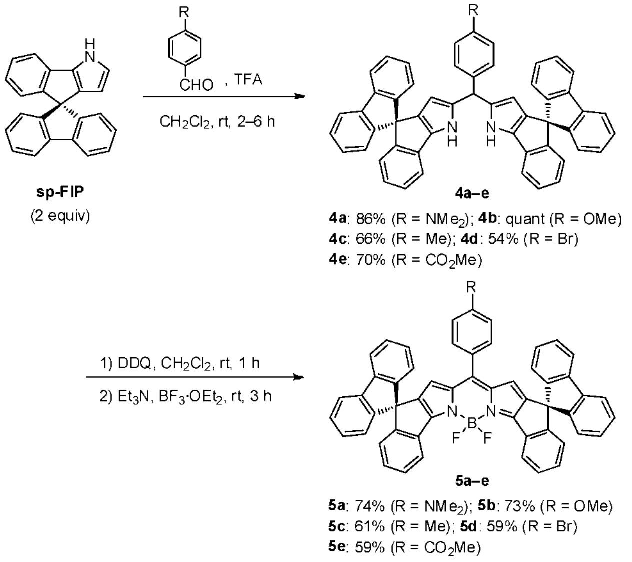


Figure 1. New approach to structurally constrained BODIPY dyes.

Scheme 1. Synthesis of **sp-FIP**



Scheme 2. Synthesis of BODIPY Dyes **5a**−**e**



The preparation of **sp-FIP** is summarized in Scheme 1. The reaction of 1-bromo-2-iodobenzene with isopropyl Grignard reagent[9] followed by quenching with 9-fluorenone gave **1** in excellent yield (95%). Friedel−Crafts alkylation of *N*-tosylpyrrole with **1** using $AlCl_3$ afforded **2** in 90% yield. When we carried out the palladium-catalyzed intramolecular direct C−H arylation of **2**, **3a** and **3b** were isolated in 63% and 6% yields, respectively. We determined the structures of both isomers by X-ray crystallography (see the Supporting Information). Hydrolysis of the tosyl group of **3a** proceeded smoothly to give **sp-FIP** in quantitative yield (99%).

We next examined the transformation of **sp-FIP** to BODIPY dyes having various aryl substituents at the meso position (Scheme 2). Several para-substituted aryl aldehydes were reacted with 2 equiv of **sp-FIP** in the presence of catalytic amounts of trifluoroacetic acid to afford the corresponding dipyrromethanes **4a**−**e** in good to excellent yields. Subsequent DDQ oxidation and complexation with $BF_3{\cdot}OEt_2$ led to the formation of BODIPY dyes **5a**−**e** in good yields. The structure of **5d** was unambiguously determined by X-ray crystallography (see the Supporting Information).

The absorption and emission spectra of **5a**−**e** were measured in THF (Table 1). All BODIPY dyes show an intense, narrow, and sharp absorption band at $\lambda_{abs} = 627-641$ nm with $\varepsilon = 161060-180700\ M^{-1}cm^{-1}$. The absorption maxima of **5a**−**e** were scarcely affected by the electronic nature of substituents R. Their Stokes shifts are less than 10 nm, while the emission maxima of **5a**−**e** were observed at 636−652 nm. Furthermore, the emission maxima were also scarcely affected by substituents R. As shown later, it is noteworthy that all BODIPY dyes except for **5a** show higher quantum yields in comparison with those reported by Burgess's group.[4a] This suggests that the constraint of the spirofluorene moieties increases the rigidity of the BODIPY core, thereby reducing the nonradiative decay.

It is noted that the fluorescence quantum yield of **5a** having an *N*,*N*-dimethylamino group was exceptionally low relative to the BODIPY dyes **5b**−**e**. We measured absorption and emission spectra of **5a** in various solvents with different dielectric constants (Figure 2) because we suspected photoinduced electron transfer (PeT)[10] leading to fluorescence quenching.[11] The positions of the absorption maxima and the emission maxima in all solvents were scarcely affected

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Table 1. Optical Properties of **5a**−**e** in THF ($c = 1.00 \times 10^{-6}$ M)

compd	λ_{abs} (nm)	ε (M^{-1} cm^{-1})	λ_{ex} (nm)	λ_{em} (nm)	Φ_F[a]
5a	627	180700	580	636	0.16
5b	632	178570	585	640	0.76
5c	634	167210	585	642	0.67
5d	638	163890	587	648	0.73
5e	641	161060	592	652	0.61

[a] Determined by using a calibrated integrating sphere system.

by the dielectric constants of the solvents, whereas the fluorescence quantum yields varied in each solvent. When we used DMF with a high dielectric constant, the quantum yield of **5a** was very low ($\Phi_F = 0.06$). On the other hand, $CHCl_3$ and benzene with relatively low dielectric constant showed high quantum yields ($\Phi_F = 0.73$ and 0.78, respectively). Because the absorption maxima and the emission maxima of **5a** are not changed by varying the solvent, we deduced that in a more polar solvent, such as DMF, PeT from the *N*,*N*-dimethylaminophenyl group to the BODIPY core (a-PeT) readily occurred.

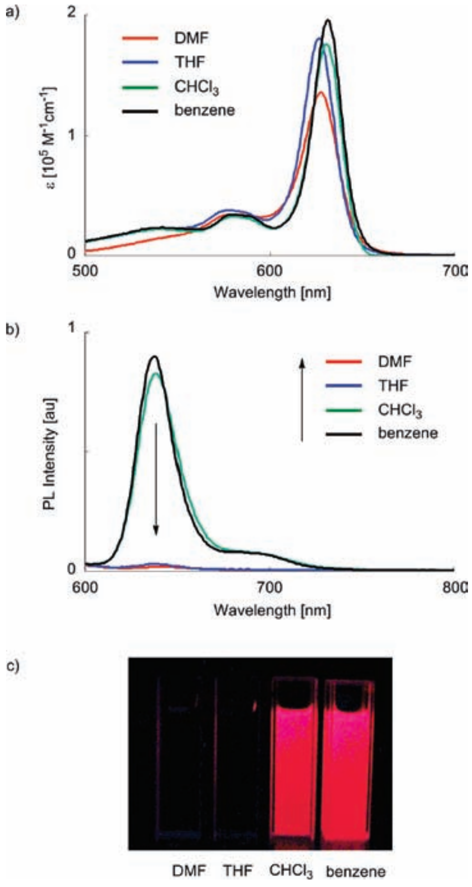

Figure 2. (a) UV−vis absorption and (b) photoluminescence spectra of **5a** in various solvents. (c) Solvent dependence of fluorescence.

The feasibility of electron transfer from the electron donor (*N*,*N*-dimethylaminophenyl group) to the electron acceptor (BODIPY core) was estimated by the Rehm−Weller equation (eq 1)[10,12]

$$\Delta G_{ET} = E_{1/2}(D^+/D) - E_{1/2}(A/A^-) - \Delta E_{00} - w_P \qquad (1)$$

where $E_{1/2}(D^+/D)$ and $E_{1/2}(A/A^-)$ are the ground-state redox potentials of the donor and acceptor moiety, respectively, ΔE_{00} is the singlet excited energy of the fluorophore, and w_P is the work term for the charge separation.[13] The relative free energies ($\Delta\Delta G_{ET}$) of **5a** in various solvents according to Rehm−Weller equation are summarized in Table 2. The *N*,*N*-dimethylaminophenyl group and BODIPY core are twisted by 79° and conjugately uncoupled according to the result of X-ray analysis.[14] As shown in Table 2, $\Delta\Delta G_{ET}$ in various solvents indicates that the electron transfer can take place more easily in following order: in DMF > in THF > in $CHCl_3$. The emission apparently disappear in THF (Φ_F = 0.16) because fluorescence ON/OFF threshold seems to exist between $CHCl_3$ and THF (Figure 2c).[10]

Table 2. Relative Free Energies ($\Delta\Delta G_{ET}$) of **5a** Calculated by Fitting the Data to the Rehm−Weller Equation

solvent	$E_{1/2}(D^+/D)$[a,b] (V)	$E_{1/2}(A/A^-)$[a,c] (V)	ΔE_{00}[d] (eV)	$\Delta\Delta G_{ET}$[e] (eV)
DMF	0.34	−1.19	1.79	−0.29
THF	0.32	−1.44	1.81	−0.08
$CHCl_3$	0.34	−1.58	1.89	0

[a] Measured by CV with 0.1 M *n*-Bu_4NPF_6 vs Fc/Fc$^+$ 0.1 V s^{-1}. [b] Oxidation potential of *N*,*N*-dimethylaniline. [c] Reduction potential of **5a**. [d] Estimated by the absorption edge of the UV−vis spectrum. [e] Relative ΔG_{ET} values were calculated with respect to the value in $CHCl_3$ as a standard.

To reveal the effect of spirofluorene moieties on photophysical properties, the absorption and emission spectra of **5b** were compared with those of BODIPY dyes **6**, **7**, and **8a**−**c** (Table 3). The absorption and emission maxima of **5b** showed a bathochromic shift in comparison with those of **6** and **7**. On the other hand, compared with both maxima of **8a**−**c**, a hypsochromic shift of **5b** was observed. However, the photoluminescence quantum yield of **5b** was much higher than those of **6**−**8**. Compared with **6**, it is obvious that spirofluorene

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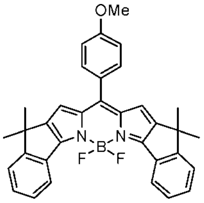
Table 3. Comparison of Optical Properties in THF



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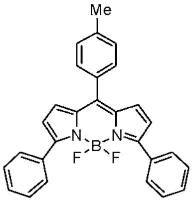

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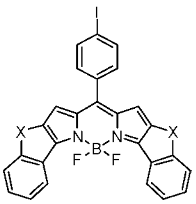

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X = **a**, O; **b**, S; **c**, -CH_2CH_2-

compd	λ_{abs} (nm)	λ_{ex} (nm)	λ_{em} (nm)	Φ_F
5b	632	585	640	0.76
6	623	579	629	0.60
7[a]	553	553	586	0.22
8a[b]	637		647	0.34
8b[b]	658		673	0.05
8c[b]	634		647	0.38

[a] Reference 15. [b] Reference 4a, in $CHCl_3$.

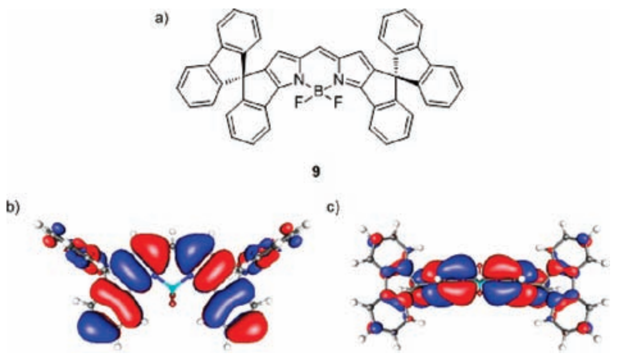

Figure 3. Molecular orbital plots of the HOMO for model compound **9**: (a) structure of **9**; (b) front view; (c) top view.

moieties effectively affect the red shift of absorption and emission spectra and increase the quantum yield.

To gain insight into the red shift of absorption and emission maxima of **5b** relative to those of **6**, theoretical calculations of model compound **9** were carried out at the B3LYP/6-31G(d) level (Figure 3).[16,17] A TD-DFT calculation at the B3LYP/6-31G(d) level indicates that the most allowed transition is from HOMO to LUMO and HOMO-2 to LUMO, the oscillator strength being 1.04 (see the Supporting Information). HOMO-2 was mainly delocalized over the fluorene moieties, whereas the HOMO and LUMO of **9** were mainly delocalized over the indene-fused BODIPY core. This result implies that an intramolecular charge transfer process might exist in this system. Furthermore, it is noteworthy that the HOMO level is slightly delocalized over the fluorene moieties. This phenomenon is well-known as spiro conjugation,[18] leading to through-space elongation of the π-system. As a result, it is considered that absorption and emission maxima of **5b** were bathochromically shifted relative to those of **6**.

In conclusion, we have demonstrated that structurally constrained BODIPY dyes based on spiro[fluorene-9,4′(1′*H*)-indeno[1,2-*b*]pyrrole] exhibit a significant increase in the fluorescence quantum yield as well as a red shift of the absorption and emission maxima. Spirofluorene moieties lead to high rigidity and good planarity of the BODIPY core. Furthermore, the fluorescence ON/OFF phenomenon was observed arising from a PeT process from an *N*,*N*-dimethylaminophenyl unit to the BODIPY core. DFT calculations indicate that the π-system of BODIPY derivatives **5a−d** was delocalized over the fluorene moieties as well as the BODIPY core because of spiro conjugation.

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Supporting Information Available: Experimental procedures, copies of ^1H and ^{13}C NMR spectra for new compounds, X-ray data of **3a**, **3b**, and **5d**, and DFT calculation data of **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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