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Near-infrared BODIPY dyes modulated with spirofluorene moieties

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ABSTRACT

New structurally constrained BODIPY dyes having electron-donating substituents were synthesized. As the key compounds for the construction of the BODIPY dyes, 1′*H*-spiro-[fluorene-9,4′-indeno[1,2-*b*]pyrrole] (**sp-FIP**) derivatives with electron-donating groups, such as OMe and NMe_2 at its 6′-position, were prepared using palladium-catalyzed intramolecular direct C–H arylation of a pyrrole moiety. The resulting BODIPY dyes showed bathochromic shift in absorption and fluorescence spectra in comparison to the unsubstituted analogs. Furthermore, pH-dependent reversible spectrum changes of the BODIPY dye were observed with the addition of trifluoroacetic acid (TFA) and subsequent addition of *i*-Pr_2NEt.

1. Introduction

4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacenes (BODIPY) are attractive fluorescent dyes because of their remarkable physical properties, such as high photoluminescent quantum yields, large molar absorption coefficients, narrow emission bands, and high environmental stability.[1] Therefore, they have been widely used in a variety of organic functional materials where biological applications require light-emitting properties in the near-IR or visible red region.[2] To modulate the optical properties of BODIPY dyes, in particular, the following strategies are elaborated: (1) extension of π-conjugation by introducing aryl[3] or styryl[4] substituents at the 3,5-positions; (2) rigidifying the molecular structure to suppress the free rotation of extended substituents and enhance the coplanarity;[5] and (3) introducing electron-donating groups at the 3,5-positions.[5–8] In particular, the third approach is the most effective for the red shift of both the absorption and the emission spectra. Burgess et al. investigated the phenyl- or *p*-anisyl-substituted BODIPY dyes (**A** and **B**) and found that the introduction of the electron-donating methoxy groups led to the red shift of the spectra by about 30 nm (Fig. 1, **A**: λ_{em} 588 nm, **B**: λ_{em} 626 nm).[6a] Similar phenomena have been observed in styryl-substituted BODIPY dyes **D**[4a] (λ_{em} 639 nm) and **E**[6b] (λ_{em} 653 nm). Ziessel et al. reported that strong electron-donating *p*-aminostyryl groups have great potential to give a bathochromic shift of about 80 nm (Fig. 1, **F**: λ_{em} 767 nm).[6c] In addition, applications in fluorescent sensors of pH[7] and/or metal ions[8,9] take advantage of the basicity or coordination of amino groups. However,

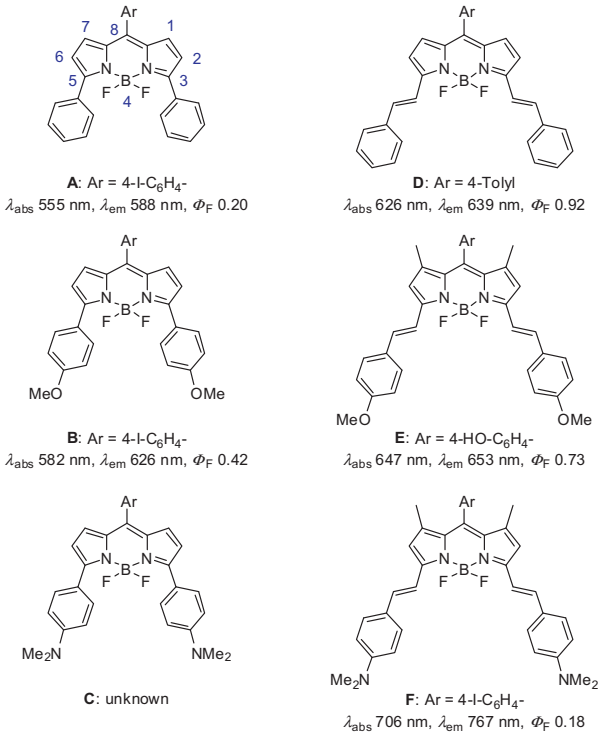

Fig. 1. The photophysical properties of 3,5-diaryl or distyryl-substituted BODIPY dyes.

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p-aminophenyl-substituted BODIPY dyes (type **C**) have not so far been explored.

We recently reported that structurally constrained BODIPY dyes that were synthesized using the strategies 1 and 2 shown above exhibited intense fluorescence with the emission maxima around 670 nm (Fig. 2).[10] We also described solvent-dependent fluorescence of the BODIPY dye with *p*-aminophenyl substituents at the 8-positions, which was caused by photoinduced electron transfer (PeT).[10,11] We now report the synthesis of structurally constrained BODIPY dyes with *p*-anisyl or *p*-aminophenyl substituents at the 3,5-positions (types **B** and **C**).

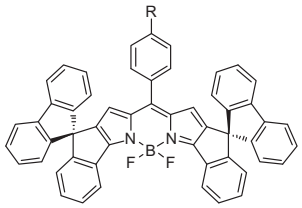
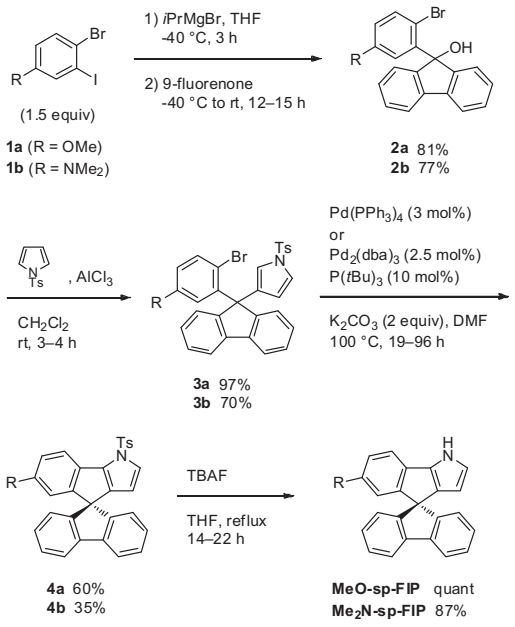


Fig. 2. Structurally constrained BODIPY dyes.

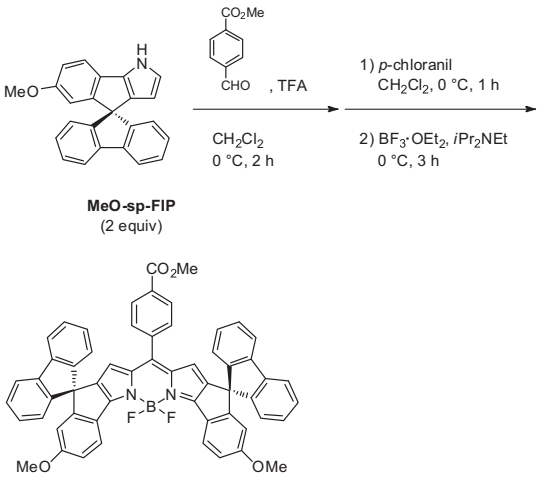
2. Results and discussion

The preparations of 6′-methoxy-1′*H*-spiro[fluorene-9,4′-indeno-[1,2-*b*]pyrrole] (**MeO-sp-FIP**) and 6′-(*N*,*N*-dimethylamino)-1′*H*-spiro [fluorene-9,4′-indeno[1,2-*b*]pyrrole] (**Me$_2$N-sp-FIP**) as key compounds for the synthesis of structurally constrained BODIPY dyes are summarized in Scheme 1. The reaction of 1-bromo-2-iodo-4-methoxybenzene (**1a**) and 4-bromo-3-iodo-*N*,*N*-dimethylaniline (**1b**) with isopropyl Grignard reagent followed by quenching with 9-fluorenone gave **2a** and **2b** in 81% and 77% yield, respectively. Friedel–Crafts alkylation of *N*-tosylpyrrole with **2a** and **2b** using $AlCl_3$ afforded **3a** and **3b** in 97% and 70% yield, respectively. The catalytic intramolecular direct C–H arylation[10,12] of **3a** using Pd-$(PPh_3)_4$ proceeded smoothly to afford **4a** in 60% yield. From **3b**, **4b** was obtained in 35% yield using $Pd_2(dba)_3$ and P(*t*-Bu)$_3$ instead of $Pd(PPh_3)_4$. Detosylation of **4** using tetrabutylammonium fluoride (TBAF) gave **sp-FIP** derivatives, **MeO-sp-FIP** and **Me$_2$N-sp-FIP**, in excellent yields (quantitative yield and 87%, respectively).[13]

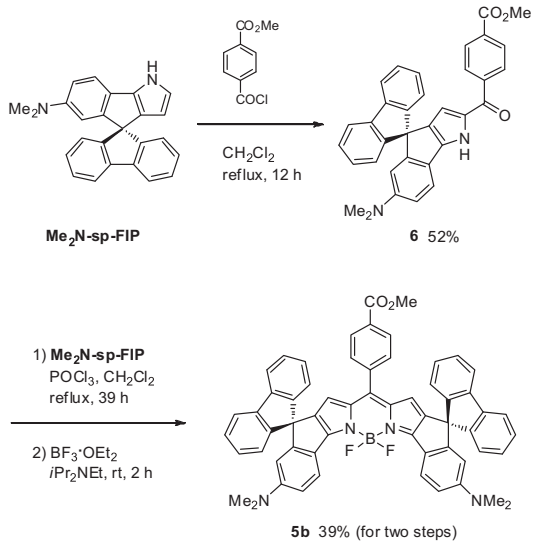


Scheme 1.

We next examined the transformation of **sp-FIP** derivatives to BODIPY dyes (Schemes 2 and 3). **MeO-sp-FIP** was reacted with methyl 4-formylbenzoate to give dipyrromethane, which was subsequently oxidized and complexed with $BF_3 \cdot OEt_2$, leading to the formation of BODIPY dye **5a**. Although we attempted to prepare **5b** using **Me$_2$N-sp-FIP** in a similar manner, the oxidation using DDQ or *p*-chloranil resulted in decomposition or recovery of the corresponding dipyrromethane. Thus, we changed the synthetic route to **5b** (Scheme 3). Acylpyrrole **6** was prepared by the reaction of **Me$_2$N-sp-FIP** with methyl 4-(chlorocarbonyl)benzoate in 52% yield, and then the condensation of **6** with 1 equiv of **Me$_2$N-sp-FIP**, followed by complexation with $BF_3 \cdot OEt_2$ led to the desired BODIPY dye **5b**.



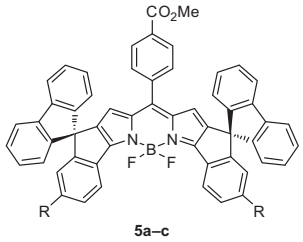
Scheme 2.



Scheme 3.

The absorption and emission spectra of **5a** and **5b** were measured in THF (Table 1). The absorption maximum and the emission maximum of **5a** were red-shifted by about 30 nm compared with those of **5c** without electron-donating groups. Furthermore, **5a** showed intense fluorescence (Φ_F=0.61) with a small Stokes shift (15 nm) because of its rigid structure. Because of the strong electron-donating ability of *N*,*N*-dimethylamino groups, **5b** exhibited bathochromic shifts of about 80 nm in both absorption and emission maxima compared with **5c**. However, **5b** showed lower

Table 1
Photophysical properties of BODIPY dyes **5a–c** in THF (c=1.00×10^{-6} M)



5a–c

	R	λ_{abs} [nm]	ε [M^{-1} cm^{-1}]	λ_{ex} [nm]	λ_{em} [nm]	Φ_F[a]
5a	OMe	666	159,000	666	681	0.61
5b	NMe_2	738	133,000	733	769	0.24
5c[b]	H	641	161,100	640	652	0.67

[a] Determined by the calibrated integrating sphere system.
[b] Ref. 10.

quantum yield (Φ_F=0.30) with larger Stokes shift (31 nm) than **5a** and **5c**. This indicates the occurrence of intramolecular charge transfer (ICT)[7,8,14] in **5b**.

When the absorption spectra of **5b** were measured in various solvents, the positions of the absorption maxima were slightly affected by the solvent polarity (Fig. 3, Table 2). In contrast, the features of solvent-dependent fluorescence of **5b** were found in the emission spectra. The emission maximum obviously shifts to a longer wavelength, and the emission spectra were broadened and weakened by going from nonpolar to polar solvents (cyclohexane: 741 nm; DMF: 792 nm). Furthermore, in cyclohexane, **5b** showed sharp and narrow emission spectrum with the highest fluorescence quantum yield (Φ_F=0.51).

solution of **5b** (Fig. 4). In the absorption spectra, the initial absorption band at 741 nm decreased and a distinctive sharp absorption band of a BODIPY dye appeared at 636 nm, which can correspond to **5b**-**2H**$^+$ ([TFA]=1 M, Fig. 4). The emission spectra showed a parallel change with the absorption spectra. The original broad fluorescence band of **5b** changed with blue shift as TFA was added, and a sharp and strong emission peak arose at 647 nm when the TFA concentration reached 1 M. This indicates that the protonated amino groups no longer act as electron-donors. Then, to prove that the phenomenon is caused by the protonation on amino groups rather than such structural changes as hydrolysis of the ester group or deboronation, *i*-Pr_2NEt was added to the acidic solution (**5b** with [TFA]=1 M). As expected, the identical spectra of the original **5b** were restored (Fig. 4). Thus, it is obvious that ICT between amino groups and boron atom is inhibited by the protonation on amino groups.

In conclusion, we have developed structurally constrained BODIPY dyes with electron-donating groups, such as MeO or Me_2N at the *para* position of phenyl groups substituted at 3,5-positions on the BODIPY core. Palladium-catalyzed intramolecular direct C–H arylation of a pyrrole moiety allowed us to synthesize **sp-FIP** derivatives as the key compounds for the construction of the BODIPY dyes. The emission bands of the resulting BODIPY dyes were shifted bathochromically in comparison to unsubstituted analogs because of the electron donation from the MeO and Me_2N groups. In addition, amino-substituted BODIPY dye **5b** showed ICT character. The ICT process could be modulated by protonation on amino groups and recovery of original absorption and fluorescence upon deprotonation with an additional base was demonstrated. We envision the application of **5b** in pH and/or metal ion sensors and further investigations will be reported in due course.

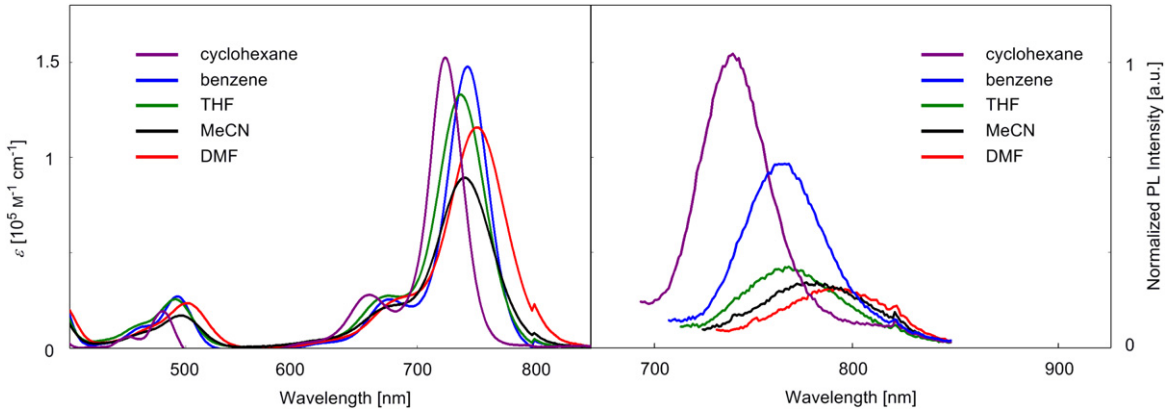


Fig. 3. The absorption (left) and emission spectra (right) of **5b** in various solvents.

Table 2
Photophysical properties of BODIPY dyes **5b** in various solvents (c=1.00×10^{-6} M)

Solvent	λ_{abs} [nm]	ε [M^{-1} cm^{-1}]	λ_{ex} [nm]	λ_{em} [nm]	Φ_F[a]
Cyclohexane	724	152,500	714	741	0.44
Benzene	743	147,800	732	769	0.37
THF	738	133,000	733	769	0.24
MeCN	741	89,340	741	783	0.23
DMF	752	115,800	741	792	0.11

[a] Determined by the calibrated integrating sphere system. Corrected for background noise at around 820 nm.

In general, the emission properties of the ICT fluorophores having amino groups can be modulated by cation binding, which reduces the electron-donating ability of the nitrogen atom. As a result, ICT process is prohibited and the inherent sharp emission of the BODIPY dye is restored. We next added TFA to the acetonitrile

3. Experimental section

3.1. General

Unless otherwise specified, all reagents were purchased from a chemical supplier and used without further purification. Tetrahydrofuran (THF) was distilled over benzophenone ketyl under nitrogen atmosphere. *N*,*N*-Dimethylformamide (DMF) was distilled over CaH_2 under nitrogen atmosphere. CH_2Cl_2 was dried and collected using a Grubbs-type solvent purification system manufactured by Glass Contour. Melting points are uncorrected. ^{1}H and ^{13}C spectra were recorded on a JEOL AL-300 (300 MHz for ^{1}H and 75.5 MHz for ^{13}C) instrument or a JEOL EX-400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) instrument. IR spectra were obtained on a JASCO 460 plus FT/IR spectrometer. Mass spectra were measured with a JEOL JMS-SX102A. Analytical thin-layer chromatography (TLC)

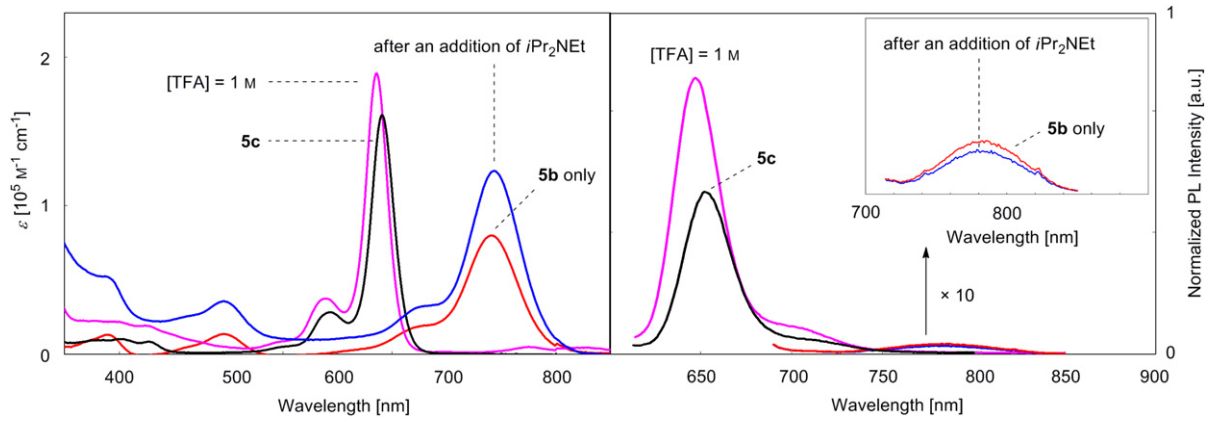


Fig. 4. The absorption spectra (left) and the emission spectra (right) of **5b** after an addition of i-Pr$_2$NEt.

was performed on Merck 60 F_{254} silica plates and visualized by UV light. Column chromatography was carried out on Silicycle SiliaFlash F60 60–63 μm (230–400 mesh) silica gel. UV–vis absorption spectra were recorded on a JASCO V-570 UV–vis–NIR spectrometer. Emission spectra were measured with a Jobin Yvon-Horiba FluoroMax-3. Degassed spectral grade solvents were used for the measurements. Absolute fluorescence quantum yields were determined by the calibrated integrating sphere system.

3.2. Syntheses

*3.2.1. 4-Bromo-3-iodo-N,N-dimethylaniline (**1b**).* To a solution of 4-bromo-3-iodoaniline[15] (12.8 g, 42.9 mmol) in DMF (120 mL) was added K_2CO_3 (23.7 g, 172 mmol) and MeI (6.42 mL, 103 mmol), and the solution was stirred at 70 °C for 13 h. After cooling to ambient temperature, water (180 mL) was added and the solution was extracted with Et_2O (5×40 mL). The organic layers were combined, washed with brine (3×100 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure to give brown solid. The crude product was purified by recrystallization from EtOAc/hexane (v/v=1/4) to give **1b** (10.5 g, 75%) as a pale brown solid; mp 93.8–94.8 °C. IR (KBr) 580, 797, 827, 955, 1231, 1362, 1496, 1582, 2810, 2889 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.90 (s, 6H), 6.54 (dd, J=2.9, 8.8 Hz, 1H), 7.15 (d, J=3.3 Hz, 1H), 7.35 (d, J=8.8 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=40.3, 101.7, 113.8, 115.1, 123.5, 132.2, 150.0. Anal. Calcd for C_8H_9NBrI: C, 29.48; H, 2.78. Found: C, 29.39; H, 2.51.

*3.2.2. 9-(2-Bromo-5-methoxyphenyl)-9H-fluoren-9-ol (**2a**).* The solution of 1-bromo-2-iodo-4-methoxybenzene (**1a**)[16] (14.1 g, 45.0 mmol) in dry THF (45 mL) was cooled to −40 °C. To the solution was added dropwise 1.0 M THF solution of isopropyl magnesium bromide (45 mL), prepared from isopropyl bromide and magnesium turnings. After stirring for 4 h, 9-fluorenone (6.34 g, 35.2 mmol) in dry THF (35 mL) was added over 15 min and stirred at room temperature for 18 h. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (100 mL) and extracted with EtOAc (3×30 mL). The organic layers were combined, washed with brine (2×50 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure to give a pale yellow solid. The crude product was purified by washing with $CHCl_3$/hexane (v/v=1/3) to give **1a** (10.5 g, 81%) as a white solid; mp 217.8–218.5 °C. IR (KBr) 734, 771, 1009, 1029, 1288, 1462, 1572, 1598, 2939, 3066, 3437 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.40 (br s, 1H), 3.91 (s, 3H), 6.72 (dd, J=3.3, 8.8 Hz, 1H), 7.15–7.30 (m, 5H), 7.39 (dd, J=7.3, 7.3 Hz, 2H), 7.67 (d, J=7.7 Hz, 2H), 8.06 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=55.5, 111.1, 114.6, 115.1, 120.2, 124.0, 128.4, 129.3, 135.0, 141.4, 141.9, 148.6, 158.8 (two peaks are overlapped). Anal. Calcd for $C_{20}H_{15}O_2Br$: C, 65.41; H, 4.12. Found: C, 65.18; H, 3.92.

*3.2.3. 9-(2-Bromo-5-(dimethylamino)phenyl)-9H-fluoren-9-ol (**2b**).* The solution of **1b** (3.42 g, 10.5 mmol) in dry THF (10 mL) was cooled to −40 °C. To the solution was added dropwise 1.0 M THF solution of isopropyl magnesium bromide (15 mL), prepared from isopropyl bromide and magnesium turnings. After stirring for 4 h, 9-fluorenone (1.26 g, 7.00 mmol) in dry THF (10 mL) was added and stirred at room temperature for 17 h. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (20 mL) and extracted with EtOAc (3×10 mL). The organic layers were combined, washed with brine (2×30 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, the residue was purified with column chromatography on SiO_2 with EtOAc/hexane (v/v=1/10) as an eluent to give **2b** (1.91 g, 72%) as a white solid; mp 161.9–162.8 °C. IR (KBr) 733, 746, 770, 1149, 1361, 1446, 1491, 1591, 2808, 2879, 3457 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.40 (br s, 1H), 3.03 (s, 6H), 6.51 (dd, J=3.4, 8.8 Hz, 1H), 7.19–7.25 (m, 5H), 7.37 (dd, J=7.3, 8.3 Hz, 2H), 7.66 (d, J=7.3 Hz, 2H), 7.87 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ=40.7, 106.9, 113.1, 113.3, 120.1, 124.0, 128.3, 129.1, 134.6, 140.6, 141.3, 149.0, 149.6 (two peaks are overlapped). HRMS (FAB): calcd for $C_{21}H_{18}{}^{79}BrNO$ (M^+), 379.0572. Found 379.0564.

*3.2.4. 3-(9-(2-Bromo-5-methoxyphenyl)-9H-fluoren-9-yl)-N-tosylpyrrole (**3a**).* To a solution of **2a** (372 mg, 1.01 mmol) and *N*-tosylpyrrole (248 g, 1.12 mmol) in CH_2Cl_2 (30 mL) was added $AlCl_3$ (171 mg, 1.28 mmol) portionwise, and the solution was stirred at room temperature for 3 h. The reaction mixture was quenched with water (20 mL) and extracted with CH_2Cl_2 (3×10 mL). The organic layers were combined, washed with saturated aqueous solution of $NaHCO_3$ (2×20 mL) and brine (2×20 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified with column chromatography on SiO_2 with EtOAc/hexane (v/v=1/6) as an eluent to give **3a** (559 g, 97%) as a white solid; mp 205.8–206.6 °C. IR (KBr) 592, 675, 745, 796, 1067, 1173, 1367, 1465, 1595, 3119, 3134 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.37 (s, 3H), 3.60 (s, 3H), 6.42 (dd, J=1.8, 3.3 Hz, 1H), 6.60–6.63 (m, 2H), 6.85 (br s, 1H), 7.08 (dd, J=2.2, 3.3 Hz, 1H), 7.20–7.40 (m, 9H), 7.61 (d, J=8.4 Hz, 2H), 7.72 (d, J=7.3 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.6, 55.1, 60.4, 113.3, 113.4, 115.6, 118.8, 119.3, 120.4, 121.5, 124.6, 126.8, 127.4, 127.6, 129.9, 131.8, 135.9, 136.0, 141.1, 143.1, 144.8, 149.6, 158.3. HRMS (FAB): calcd for $C_{31}H_{25}{}^{81}BrNO_3S$ ($M+H^+$), 572.0722. Found 572.0733.

*3.2.5. 3-(9-(2-Bromo-5-(dimethylamino)phenyl)-9H-fluoren-9-yl)-N-tosylpyrrole (**3b**).* To a solution of **2b** (188 mg, 0.494 mmol) and *N*-

tosylpyrrole (116 mg, 0.525 mmol) in CH_2Cl_2 (5 mL) was added $AlCl_3$ (90.3 mg, 0.677 mmol) portionwise, and the solution was stirred at room temperature for 4 h. The reaction mixture was quenched with water (20 mL) and extracted with CH_2Cl_2 (3×5 mL). The organic layers were combined, washed with saturated aqueous solution of $NaHCO_3$ (2×20 mL) and brine (2×20 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified with column chromatography on SiO_2 with EtOAc/hexane (v/v=1/2) as an eluent to give **3b** (199 mg, 70%) as a white solid; mp 216.0–216.8 °C. IR (KBr) 676, 743, 1063, 1173, 1371, 1593 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.38 (s, 3H), 2.68 (s, 6H), 6.41 (dd, J=3.3, 8.8 Hz, 1H), 6.45 (br s, 1H), 6.60 (br s, 1H), 7.08 (dd, J=2.6, 2.9 Hz, 1H), 7.16–7.39 (m, 9H), 7.62 (d, J=8.1 Hz, 2H), 7.72 (d, J=7.3 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.6, 40.1, 60.6, 109.0, 112.6, 116.0, 116.9, 119.3, 120.3, 121.3, 124.7, 126.7, 127.3, 127.5, 129.8, 132.4, 135.4, 136.2, 141.1, 141.9, 144.7, 149.1, 150.0. HRMS (FAB): calcd for $C_{32}H_{28}{}^{79}BrN_2O_2S$ ($M+H^+$), 583.1055. Found 583.1057.

*3.2.6. 6′-Methoxy-1′-tosyl-1′H-spiro[fluorene-9,4′-indeno[1,2-b]pyrrole] (**4a**).* A flame dried flask was charged with **3a** (6.85 g, 12.0 mmol), K_2CO_3 (3.32 g, 24.0 mmol), $Pd(PPh_3)_4$ (417 mg, 0.361 mmol), and dry DMF (100 mL) under nitrogen atmosphere. The solution was stirred at 100 °C for 13 h. The reaction mixture was cooled down to room temperature and filtered through a short silica gel pad. After an addition of CH_2Cl_2 (100 mL), the filtrate was washed with brine (6×150 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure to give a brown solid. The crude product was purified by washing with $CHCl_3$/hexane (v/v=1/3) to give **4a** (3.93 g, 67%) as a pale green solid; mp 211.3–212.0 °C. IR (KBr) 539, 583, 679, 750, 1125, 1171, 1276, 1368, 1586, 3139 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.42 (s, 3H), 3.60 (s, 3H), 5.83 (d, J=3.3 Hz, 1H), 6.09 (d, J=2.6 Hz, 1H), 6.64 (d, J=7.7 Hz, 2H), 6.80 (dd, J=2.6, 8.4 Hz, 1H), 7.08 (dd, J=6.6, 7.3 Hz, 2H), 7.14 (d, J=2.9 Hz, 1H), 7.29–7.35 (m, 4H), 7.78 (d, J=7.7 Hz, 2H), 7.81 (d, J=8.4 Hz, 2H), 8.05 (d, J=8.4 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.6, 55.3, 60.2, 108.8, 110.7, 112.2, 120.0, 120.1, 123.6, 125.7, 126.7, 127.2, 127.7, 127.8, 130.0, 136.0, 138.2, 138.3, 141.7, 145.0, 146.7, 154.6, 158.2. HRMS (FAB): calcd for $C_{31}H_{24}NO_3S$ ($M+H^+$), 490.1477. Found 490.1494.

*3.2.7. 6′-(N,N-Dimethylamino)-1′-tosyl-1′H-spiro[fluorene-9,4′-indeno[1,2-b]pyrrole] (**4b**).* A flame dried flask was charged with **3b** (2.93 g, 5.02 mmol), K_2CO_3 (1.38 g, 10.0 mmol), $Pd_2(dba)_3$ (115 mg, 0.126 mmol), P(*t*-Bu)$_3$ (103 mg, 0.510 mmol), and dry DMF (50 mL) under nitrogen atmosphere. The solution was stirred at 100 °C for 96 h. The reaction mixture was cooled down to room temperature and filtered through a short silica gel pad. After an addition of CH_2Cl_2 (50 mL), the filtrate was washed with brine (6×100 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, the residue was purified with column chromatography on SiO_2 with EtOAc/hexane (v/v=1/6) as an eluent to give **4b** (897 mg, 35%) as a greenish brown solid; mp 199.6 °C (dec). IR (KBr) 576, 679, 743, 1122, 1174, 1371, 1432, 1606, 3130 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.41 (s, 3H), 2.73 (s, 6H), 5.78 (d, J=2.9 Hz, 1H), 5.91 (d, J=2.6 Hz, 1H), 6.60–6.67 (m, 3H), 7.04–7.09 (m, 3H), 7.25–7.34 (m, 4H), 7.77 (d, J=7.3 Hz, 2H), 7.81 (d, J=8.4 Hz, 2H), 8.00 (d, J=8.4 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.6, 40.6, 60.4, 108.5, 108.8, 111.0, 119.9, 120.0, 123.4, 123.7, 124.7, 126.8, 127.56, 127.61, 129.9, 136.1, 136.9, 138.9, 141.6, 144.7, 147.5, 149.0, 154.3. HRMS (FAB): calcd for $C_{32}H_{26}N_2O_2S$ (M^+), 502.1715. Found 502.1705.

*3.2.8. 6′-Methoxy-1′H-spiro[fluorene-9,4′-indeno[1,2-b]pyrrole] (**MeO-sp-FIP**).* To a solution of **4a** (1.96 g, 4.00 mmol) in THF (300 mL) was added 1.0 M THF solution of TBAF (40 mL), and the solution was stirred at 65 °C for 14 h under nitrogen atmosphere. After cooling to ambient temperature, water (40 mL) was added and THF was removed under reduced pressure. The residue was extracted with CH_2Cl_2 (3×15 mL). The organic layers were combined, washed with brine (2×50 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, the residue was purified with column chromatography on SiO_2 with CH_2Cl_2/hexane (v/v=1/1) as an eluent to give **MeO-sp-FIP** (1.34 g, quantitative yield) as a pale pink solid; mp 156.9–157.8 °C. IR (KBr) 742, 1274, 1444, 1461, 1587, 3063, 3418 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.58 (s, 3H), 5.77 (br s, 1H), 6.13 (d, J=2.2 Hz, 1H), 6.71–6.76 (m, 2H), 6.85 (d, J=7.7 Hz, 2H), 7.11 (dd, J=7.3, 7.7 Hz, 2H), 7.23 (d, J=8.4 Hz, 1H), 7.33 (dd, J=7.3, 7.7 Hz, 2H), 7.80 (d, J=7.7 Hz, 2H), 8.33 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=55.4, 60.8, 103.9, 111.1, 111.6, 116.1, 119.8, 120.9, 123.8, 127.4, 127.6, 128.7, 132.4, 137.6, 141.6, 148.7, 155.1, 157.3. HRMS (FAB): calcd for $C_{24}H_{18}NO$ ($M+H^+$), 336.1388. Found 336.1371.

*3.2.9. 6′-(N,N-Dimethylamino)-1′H-spiro[fluorene-9,4′-indeno-[1,2-b]pyrrole] (**Me$_2$N-sp-FIP**).* To a solution of **4b** (736 mg, 1.46 mmol) in THF (2 mL) was added 1.0 M THF solution of TBAF (14.6 mL), and the solution was stirred at 65 °C for 22 h under nitrogen atmosphere. After cooling to ambient temperature, water (40 mL) was added and THF was removed under reduced pressure. The residue was extracted with CH_2Cl_2 (3×10 mL). The organic layers were combined, washed with brine (2×40 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, the residue was purified with column chromatography on SiO_2 with CH_2Cl_2/hexane (v/v=1/1) as an eluent to give **Me$_2$N-sp-FIP** (441 mg, 87%) as a pale green solid; mp 178.2 °C (dec). IR (KBr) 737, 797, 1440, 1488, 1582, 3396 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.71 (s, 3H), 5.73 (dd, J=1.8, 2.6 Hz, 1H), 6.00 (d, J=2.2 Hz, 1H), 6.56 (dd, J=2.2, 8.1 Hz, 1H), 6.70 (dd, J=2.2, 2.6 Hz, 1H), 6.87 (d, J=7.7 Hz, 2H), 7.11 (dd, J=7.3, 7.3 Hz, 2H), 7.20 (d, J=8.4 Hz, 1H), 7.32 (dd, J=7.3, 7.7 Hz, 2H), 7.80 (d, J=7.7 Hz, 2H), 8.28 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=41.0, 60.9, 103.7, 109.7, 110.8, 116.2, 119.7, 120.1, 123.9, 125.4, 127.2, 127.5, 131.4, 138.2, 141.5, 148.4, 149.5, 154.6. HRMS (FAB): calcd for $C_{25}H_{20}N_2$ (M^+), 348.1626. Found 348.1631.

*3.2.10. BODIPY dye **5a**.* To a solution of **MeO-sp-FIP** (336 mg, 1.00 mmol) and methyl 4-formylbenzoate (81.8 mg, 0.50 mmol) in dry CH_2Cl_2 (20 mL) was added two drops of TFA, and the solution was stirred at 0 °C for 2 h under nitrogen atmosphere. The reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3×10 mL). The organic layers were combined, washed with brine (2×25 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was partially purified with column chromatography on SiO_2 with CH_2Cl_2 as an eluent to afford a crude product (220 mg) as a purple solid. The crude product was then dissolved in dry CH_2Cl_2 (10 mL). After an addition of *p*-chloranil (66.5 mg, 0.270 mmol) in dry CH_2Cl_2 (10 mL), the solution was stirred at 0 °C for 90 min under nitrogen atmosphere. *i*-Pr_2NEt (0.231 mL, 1.33 mmol) and $BF_3{\cdot}OEt_2$ (0.360 mL, 1.32 mmol) were successively added and after 2 h, the reaction mixture was washed with 10% aqueous solution of NaCl (3×30 mL), and dried over Na_2SO_4. The solvents were removed under reduced pressure, and the residue was purified with column chromatography on SiO_2 with CH_2Cl_2 as an eluent to afford **5a** (152 mg, 36% yield based on **MeO-sp-FIP**) as a dark brown solid; mp>300 °C. IR (KBr) 745, 1060, 1176, 1260, 1323, 1548, 1606, 1723, 3062 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ=3.67 (s, 6H), 3.82 (s, 3H), 6.03 (s, 2H), 6.14 (d, J=2.2 Hz, 2H), 6.96 (d, J=7.3 Hz, 4H), 7.04 (dd, J=2.6, 8.8 Hz, 2H), 7.16 (dd, J=7.3, 7.7 Hz, 4H), 7.33–7.41 (m, 6H), 7.77 (d, J=7.3 Hz, 4H), 7.87 (d, J=8.1 Hz, 2H), 8.40 (d, J=8.8 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ=52.2, 55.6, 59.8, 109.9, 115.0, 119.3, 120.0, 124.2, 125.47, 125.53, 127.9, 128.0, 129.2, 130.3, 130.8, 138.1, 138.9, 140.2, 141.2, 142.9, 148.2,

159.3, 161.1, 162.2, 166.2. HRMS (FAB): calcd for $C_{57}H_{38}O_4N_2F_2B$ ($M+H^+$), 863.2902. Found 863.2916.

*3.2.11. 1′-(4-(Methoxycarbonyl)benzoyl)-6′-(N,N-dimethyl-amino)-1′H-spiro[fluorene-9,4′-indeno[1,2-b]pyrrole] (**6**).* To a solution of **Me$_2$N-sp-FIP** (108 mg, 0.310 mmol) in dry CH_2Cl_2 (8 mL) was added methyl 4-(chlorocarbonyl)benzoate in dry CH_2Cl_2 (7 mL), and the solution was stirred at 40 °C for 12 h under nitrogen atmosphere. After an addition of water (20 mL), the reaction mixture was extracted with CH_2Cl_2 (3×5 mL). The organic layers were combined, washed with brine (2×20 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified with column chromatography on SiO_2 with EtOAc/CH_2Cl_2 (v/v=1/20) as an eluent to afford **6** (82.6 mg, 52%) as a orange solid; mp 163.5 °C (dec). IR (KBr) 740, 1279, 1352, 1583, 1725, 3223 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ=2.78 (s, 6H), 3.91 (s, 3H), 5.92 (d, *J*=2.2 Hz, 1H), 6.37 (s, 1H), 6.60 (dd, *J*=2.2, 8.4 Hz, 1H), 6.91 (d, *J*=7.3 Hz, 2H), 7.15 (dd, *J*=7.3, 7.7 Hz, 2H), 7.36 (dd, *J*=7.3, 7.7 Hz, 2H), 7.62 (d, *J*=8.4 Hz, 1H), 7.80 (d, *J*=7.7 Hz, 2H), 7.86 (d, *J*=8.1 Hz, 2H), 8.04 (d, *J*=8.1 Hz, 2H), 11.02 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ=40.4, 52.3, 60.6, 107.9, 111.4, 115.9, 119.9, 120.7, 121.2, 124.0, 127.6, 127.8, 128.7, 129.4, 132.0, 134.1, 134.9, 141.4, 143.2, 148.4, 148.8, 150.7, 157.0, 166.5, 182.2. HRMS (FAB): calcd for $C_{34}H_{27}O_3N_2$ ($M+H^+$), 511.2022. Found 511.2018.

*3.2.12. BODIPY dye **5b**.* To a solution of **6** (77.2 mg, 0.151 mmol) and **Me$_2$N-sp-FIP** (53.1 mg, 0.152 mmol) in CH_2Cl_2 (4 mL) was added $POCl_3$ (18 μl, 0.197 mmol), and the solution was stirred at 40 °C for 39 h under nitrogen atmosphere. After cooling to ambient temperature, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3×5 mL). The organic layers were combined, washed with brine (2×25 mL), and dried over Na_2SO_4. The solvents were removed under reduced pressure, and the residue was partially purified with column chromatography on SiO_2 with CH_2Cl_2/EtOAc (v/v=10/1) as an eluent to afford a crude product (53.8 mg) as a dark green solid. The crude product was then dissolved in CH_2Cl_2 (8 mL). *i*-Pr_2NEt (0.056 mL, 0.321 mmol) and $BF_3\cdot OEt_2$ (0.087 mL, 0.320 mmol) were added and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was washed with 10% aqueous solution of NaCl (3×20 mL), and dried over Na_2SO_4. The solvents were removed under reduced pressure, and the residue was partially purified with column chromatography on SiO_2 with CH_2Cl_2/EtOAc (v/v=40/1) as an eluent to afford **5b** (55.5 mg, 39% yield based on **6**) as a dark brown solid; mp>300 °C. IR (KBr) 1019, 1057, 1276, 1313, 1541, 1602, 1727 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ=2.87 (s, 12H), 3.82 (s, 3H), 5.86 (s, 2H), 5.90 (s, 2H), 6.81 (d, *J*=8.8 Hz, 2H), 6.99 (d, *J*=7.7 Hz, 4H), 7.16 (dd, *J*=7.3, 7.7 Hz, 4H), 7.31–7.40 (m, 6H), 7.76 (d, *J*=7.7 Hz, 4H), 7.85 (d, *J*=8.4 Hz, 2H), 8.32 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ=40.4, 52.1, 59.9, 106.7, 112.6, 117.7, 119.8, 121.3, 124.3, 125.2, 127.7, 127.8, 129.1, 130.2, 130.4, 134.4, 139.7, 139.9, 141.2, 142.3, 149.2, 152.0, 159.0, 160.6, 166.4. HRMS (FAB): calcd for $C_{59}H_{43}O_2N_4F_2B$ (M^+), 888.3457. Found 888.3448.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.02.073.

References and notes

1. (a) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891–4932; (b) Ulrich, G.; Ziessel, R.; Harriman, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1184–1201.
2. Lavis, L. D.; Raines, R. T. *ACS Chem. Biol.* **2008**, *3*, 142–155.
3. Wakamiya, A.; Sugita, N.; Yamaguchi, S. *Chem. Lett.* **2008**, *37*, 1094–1095.
4. (a) Rohand, T.; Qin, W.; Boens, N.; Dehaen, W. *Eur. J. Org. Chem.* **2006**, 4658–4663; (b) Qin, W.; Rohand, T.; Dehaen, W.; Clifford, J. N.; Driesen, K.; Beljonne, D.; Van Averbeke, B.; Van der Auweraer, M.; Boens, N. *J. Phys. Chem. A* **2007**, *111*, 8588–8597; (c) Dost, Z.; Atilgan, S.; Akkaya, E. U. *Tetrahedron* **2006**, *62*, 8484–8488.
5. (a) Chen, J.; Burghart, A.; Derecskei-Kovacs, A.; Burgess, K. *J. Org. Chem.* **2000**, *65*, 2900–2906; (b) Umezawa, K.; Nakamura, Y.; Makino, H.; Citterio, D.; Suzuki, K. *J. Am. Chem. Soc.* **2008**, *130*, 1550–1551; (c) Wu, L.; Burgess, K. *Chem. Commun.* **2008**, 4933–4935; (d) Mei, Y.; Bentley, P. A.; Wang, W. *Tetrahedron Lett.* **2006**, *47*, 2447–2449; (e) For aza-BODIPY derivatives, see: Zhao, W.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1677–1679; (f) Zhao, W.; Carreira, E. M. *Chem.—Eur. J.* **2006**, *12*, 7254–7263; (g) Loudet, A.; Bandichhor, R.; Burgess, K.; Palma, A.; McDonnell, S. O.; Hall, M. J.; O'Shea, D. F. *Org. Lett.* **2008**, *10*, 4771–4774.
6. (a) Burghart, A.; Kim, H.; Weich, M.; Thoresen, L. H.; Reibenspies, J.; Burgess, K.; Bergström, F.; Johansson, L. B.-Å. *J. Org. Chem.* **1999**, *64*, 7813–7819; (b) Liu, J.-Y.; Yeung, H.-S.; Xu, W.; Li, X.; Ng, D. K. P. *Org. Lett.* **2008**, *10*, 5421–5424; (c) Ziessel, R.; Ulrich, G.; Harriman, A.; Alamiry, M. A. H.; Stewart, B.; Retailleau, P. *Chem.—Eur. J.* **2009**, *15*, 1359–1369; (d) Yamada, K.; Toyota, T.; Takakura, K.; Ishimaru, M.; Sugawara, T. *New J. Chem.* **2001**, *25*, 667–669; (e) Buyukcakir, O.; Bozdemir, O. A.; Kolemen, S.; Erbas, S.; Akkaya, E. U. *Org. Lett.* **2009**, *11*, 4644–4647.
7. (a) Rurack, K.; Kollmannsberger, M.; Daub, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 385–387; (b) Coskun, A.; Denis, E.; Akkaya, E. U. *Org. Lett.* **2005**, *7*, 5187–5189; (c) Bonardi, L.; Ulrich, G.; Ziessel, R. *Org. Lett.* **2008**, *10*, 2183–2186; (d) Deniz, E.; Isbasar, G. C.; Bozdemir, ÖA.; Yildirim, L. T.; Siemiarczuk, A.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 3401–3403; (e) Baruah, M.; Qin, W.; Flors, C.; Hofkens, J.; Vallée, R. A. L.; Beljonne, D.; Van der Auweraer, M.; De Borggraeve, W. M.; Boens, N. *J. Phys. Chem. A* **2006**, *110*, 5998–6009; (f) Saki, N.; Dinc, T.; Akkaya, E. U. *Tetrahedron* **2006**, *62*, 2721–2725; (g) 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**, *1–2*, 176–187.
8. (a) Peng, X.; Du, J.; Fan, J.; Wang, J.; Wu, Y.; Zhao, J.; Sun, S.; Xu, T. *J. Am. Chem. Soc.* **2007**, *129*, 1500–1501; (b) Atilgan, S.; Ozdemir, T.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 4065–4067; (c) Yuan, M.; Li, Y.; Li, J.; Li, C.; Liu, X.; Lv, J.; Xu, J.; Liu, H.; Wang, S.; Zhu, D. *Org. Lett.* **2007**, *9*, 2313–2316; (d) Baruah, M.; Qin, W.; Vallée, R. A. L.; Beljonne, D.; Rohand, T.; Dehaen, W.; Boens, N. *Org. Lett.* **2005**, *5*, 4377–4380; (e) Qin, W.; Baruah, M.; Sliwa, M.; Van der Auweraer, M.; De Borggraeve, W. M.; Beljonne, D.; Van Averbeke, B.; Boens, N. *J. Phys. Chem. A* **2008**, *112*, 6104–6114; (f) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2005**, *127*, 10464–10465; (g) Guliyev, R.; Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2009**, *131*, 9007–9013; (h) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2006**, *128*, 14474–14475.
9. (a) Qi, X.; Kim, S. K.; Han, S. J.; Xu, L.; Jee, A. Y.; Kim, H. N.; Lee, C.; Kim, Y.; Lee, M.; Kim, S.-J.; Yoon, J. *Tetrahedron Lett.* **2008**, *49*, 261–264; (b) Qi, X.; Jun, E. J.; Xu, L.; Kim, S.-J.; Hong, J. S. J.; Yoon, Y. J.; Yoon, J. *J. Org. Chem.* **2006**, *71*, 2881–2884.
10. Kowada, T.; Yamaguchi, S.; Ohe, K. *Org. Lett.* **2010**, *12*, 296–299.
11. (a) Sunahara, H.; Urano, Y.; Kojima, H.; Nagano, T. *J. Am. Chem. Soc.* **2007**, *129*, 5597–5604; (b) Gabe, Y.; Urano, Y.; Kikuchi, K.; Kojima, H.; Nagano, T. *J. Am. Chem. Soc.* **2004**, *126*, 3357–3367; (c) Kennedy, D. P.; Kormos, C. M.; Burdette, S. C. *J. Am. Chem. Soc.* **2009**, *131*, 8578–8586; (d) Baruah, M.; Qin, W.; Basarić, N.; De Borggraeve, W. M.; Boens, N. *J. Org. Chem.* **2005**, *70*, 4152–4157.
12. For recent reviews, see: (a) Alberico, D.; Scott, M. K.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238; (b) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200–205; (c) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35–41.
13. In our previous paper (Ref. 10), we used sodium hydroxide for a detosylation of **sp-FIP** precursor and obtained **sp-FIP** in 99% yield. However, in the case of **4a** and **4b**, the reaction systems were so complicated that the yields were 40% and 0%, respectively.
14. Valeur, B. *Molecular Fluorescence*; Wiley-VCH: Weinheim, Germany, 2002.
15. Sugiura, M.; Hirano, K. *Biochem. Med.* **1977**, *17*, 222–228.
16. Jensen, T.; Pedersen, H.; Bang-Andersen, B.; Madsen, R.; Jørgensen, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 888–890.