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Efficient light absorbers based on thiophene-fused boron dipyrromethene (BODIPY) dyes

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ABSTRACT

We present the development of the thiophene-fused boron dipyrromethene derivatives as efficient light absorbers. The two strategies for the evolution of the optical properties such as the peak positions of absorption wavelengths and molar extinct coefficients were established by the substituent effects: by introducing iodine groups, the bathochromic shifts of the peak positions (+15 nm) and the enhancement of molar extinct coefficients were simultaneously received owing to the heavy atom effect. Next, it was found that the modification with the trifluoromethyl group contributed to the large bathochromic shift (+60 nm) because of the lowering effect on the lowest unoccupied molecular orbital of the dye by the substituent. Finally, we obtained the dyes with large molar extinct coefficients (184,140 M^{-1} cm^{-1} at 592 nm, 72,180 M^{-1} cm^{-1} at 623 nm), sharp absorption bands, and low emissions.

1. Introduction

Efficient light-absorbers are useful for the applications as a wide variety of optical materials in biochemistry and biology. For example, for the construction of artificial photosynthesis systems, the light-absorbing molecules which have a large molar extinct coefficient are a key material as an energy receiver to improve conversion efficiency from light energy to the driving force of chemical reactions.[1] As another instance, the light-absorbing ability with the specific wavelength region is feasible for the regulation of photosynthesis. It is known as the Emerson enhancement effect that the photosynthesis in several types of algae can be enhanced by the light irradiation in the wavelength range around 650 nm.[2,3] In contrast, the light over 690 nm can suppress the efficiency. These phenomena were observed in other plants.[4] This fact suggests the scenario that by loading the efficient light absorbers to the light around 650 nm on the wall of green houses, the sunlight can be transformed to the light which has the suppression effect on weed growths. Thus, the lights with the specific wavelength region around 650 nm or over 690 nm are a valid tool for precisely controlling the plant growth.

Boron dipyrromethene (BODIPY) is well known as a fluorophore for biochemical and biotechnological usages.[5] Because of strong emission intensity, low environmental dependency of optical properties and high stability to photo-degradation, BODIPY can be used as a conventional fluorophore for a marker or a labeling reagent under various situations. Nagano and co-workers reported the bioprobes based on the photochemistry of BODIPY.[6] By regulating energy transfer involving the BODIPYs, they can monitor the bioreactions with the changes of emission intensity from the probe with high sensitivity and specificity. Moreover, hetero ring-fused BODIPYs have been synthesized.[7–9] In particular, thiophene-fused BODIPYs (Fig. 1) were reported as a photosensitizer to generate singlet oxygen.[10] By the modification with sulfur or iodine elements for receiving the heavy atom effect, the intersystem crossing after photo-excitation to these BODIPYs can be readily induced. Accordingly, the triplet-excited states of the BODIPYs efficiently generate the singlet oxygen via a sensitizing reaction. The superior ability of light absorbing contributes to enhancing the sensitizing efficiency. It should be mentioned that these BODIPYs have sharp spectra of light-absorption and emission from the red-light to the near-infrared region. Based on these optical properties of thiophene-fused BODIPYs, we were inspired to develop an efficient light absorber without emission. In particular, we aimed to develop new series of thiophene-fused BODIPYs to improve the light-absorption ability in the red-light region.

Herein, we report the synthesis and the efficient light-absorbing ability of the new series of thiophene-fused BODIPYs. The substituent effects of two distinct groups on the optical properties were examined to improve molar extinct coefficients and the peak position of absorption wavelengths. By employing the heavy atom effect of iodine, the evolution of the optical properties such as the position of absorption bands, the enhancement of absorption ability, and the suppression of the emission can be simultaneously achieved. Next, according to the data of the molecular orbital of the dye calculated by computer simulation, we were inspired the introduction of the trifluoromethyl group into the thiophene-fused

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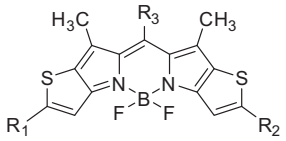


TB: R_1=R_2=R_3=H
TB-I: R_1=I, R_2=R_3=H
TB-I2: R_1=R_2=I, R_3=H
TB-F: R_1=R_2=H, R_3=CF_3

Figure 1. Chemical structures of the thiophene-fused BODIPYs used in this study.

BODIPY. Finally, the selective light absorption in the red-light region was accomplished.

2. Experimental section

^{1}H (400 MHz), ^{13}C (100 MHz), and ^{11}B (128 MHz) NMR spectra were recorded on JEOL JNM-EX400 spectrometers. In the ^{1}H NMR and ^{13}C NMR spectra was used tetramethylsilane (TMS) as an internal standard in $CDCl_3$, and ^{11}B NMR spectra were referenced externally to $BF_3{\cdot}OEt_2$ (sealed capillary). UV–vis absorption spectra were recorded on a SHIMADZU UV-3600 spectrophotometer. Fluorescence emission spectra and absolute quantum yields were recorded on a HORIBA JOBIN YVON Fluoromax-4P spectrofluorometer equipped with the integrating sphere. 2-Acetyl-3-bromothiophene (**1**) was purchased from Aldrich and used without further purification. Computations were performed using the GAUSSIAN 03 suite of programs.[11]

2.1. Ethyl 6-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (2)

The synthesis was performed according to the previous report:[12] to the mixture containing **1** (8.62 g, 42.0 mmol), CuI (0.80 g, 4.20 mmol), and $CsCO_3$ (34.2 g, 105 mmol) in DMSO (42 mL), ethyl isocyanoacetate (5.23 g, 46.2 mmol) was added dropwise at room temperature. After stirring at 50 °C for 4 h, the products were extracted with dichloromethane. The organic layer was washed with brine twice, dried over $MgSO_4$ and filtrated. The filtrate was condensed with evaporation, and the silica gel column chromatography with hexane as a mixture eluent (hexane:ethyl acetate = 7:1) gave **2** as a pale yellow solid (5.35 g, 25.6 mmol, 61%). ^{1}H NMR ($CDCl_3$) δ: 8.88 (1H, s), 7.30 (1H, d, J = 10.51 Hz), 6.91 (1H, d, J = 10.02 Hz), 4.37 (2H, q, J = 28.10 Hz), 2.53 (3H, s), 1.40 (3H, t, J = 24.19 Hz). ^{13}C NMR ($CDCl_3$) δ: 162.3, 139.6, 129.1, 126.6, 123.2, 120.3, 111.42, 60.5, 14.7, 12.3. HRMS (ESI) m/z calcd $[M+H]^+$: 210.0583, found: 210.0582.

2.2. 6-Methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid (3)

The mixture containing **2** (6.00 g, 28.7 mmol) and NaOH aq (17.2 g, 430 mmol in 120 mL) in 225 mL of ethanol was refluxed for 1 h. After cooling to room temperature, concd HCl (10%) was added dropwise to acidify. The products were extracted with dichloromethane, and the organic layer was washed with brine, dried over $MgSO_4$ and filtrated. Evaporation of the filtrate yielded **3** as a dark purple solid (4.96 g, 27.3 mmol, 95%). ^{1}H NMR (DMSO-d_6) δ: 12.44 (1H, s), 11.51 (1H, s), 7.46 (1H, d, J = 10.72 Hz), 6.92 (1H, d, J = 11.21 Hz), 2.40 (3H, s). ^{13}C NMR (DMSO-d_3) δ: 162.8, 139.8, 128.5, 124.6, 123.1, 118.0, 112.0, 11.8. HRMS (ESI) m/z calcd $[M-H]^-$: 180.0125, found: 180.0118.

2.3. 6-Methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carbaldehyde (4)

The solution of **3** (11.1 g, 61.2 mmol) dissolved in trifluoroacetic acid (200 mL) was stirred at 50 °C for 20 min, and then triethyl orthoformate (36.3 g, 245 mmol) was added. After stirring at 50 °C for 30 min, excess amounts of cyclopentyl methyl ether (CPME) and satd $NaHCO_3$ aq were poured into the reaction solution. The organic layer was washed with brine and water, dried over $MgSO_4$, filtrated and condensed by evaporation. The silica gel column chromatography with the mixture eluent (hexane:ethyl acetate = 2:1) afforded **4** as a brown solid (7.11 g, 43.0 mmol, 70%). Because of low stability, the compound **4** was used for the next step immediately after checking the spectrum of ^{1}H NMR. ^{1}H NMR ($CDCl_3$) δ: 9.75 (1H, s), 9.10 (1H, s), 7.44 (1H, d, J = 12.43 Hz), 6.94 (1H, d, J = 11.70 Hz), 2.54 (3H, s). HRMS (EI+) m/z calcd $[M]^+$: 165.0248, found: 165.0244.

2.4. TB (5)

To the solution of **4** (7.11 g, 43.0 mmol) in dichloromethane (215 mL), $POCl_3$ (7.92 g, 51.7 mmol) was added dropwise at 0 °C. After stirring at room temperature for 3 days in the dark, triethylamine (30.0 mL, 215 mmol) was added dropwise at 0 °C. After stirring at 0 °C for 15 min, $BF_3{\cdot}Et_2O$ (38 mL, 308 mmol) was added dropwise, and then the mixture was stirred at room temperature for 2 days. The reaction was quenched by adding 100 mL of water, and the products were extracted with dichloromethane. The organic layer was washed with water twice and brine, dried over $MgSO_4$, filtrated, and condensed by evaporation. The residue was passed through the silica gel column with the mixture eluent (hexane:ethyl acetate = 3:1). The resulting product was dissolved in THF, and **5** was obtained as a red purple solid (0.684 g, 2.07 mmol, 10%) from the reprecipitation in methanol. ^{1}H NMR ($CDCl_3$) δ: 7.64 (2H, d, J = 10.26 Hz), 7.40 (1H, s), 7.11 (2H, d, J = 9.53 Hz), 2.47 (6H, s). ^{13}C NMR ($CDCl_3$) δ: 158.5, 140.9, 139.9, 132.1, 131.8, 123.6, 114.0, 11.0. ^{11}B NMR ($CDCl_3$) δ: 0.39. HRMS (EI+) m/z calcd $[M]^+$: 332.0425, found: 332.0425.

2.5. TB-I (6) and TB-I2 (7)

The mixture containing **5** (0.312 g, 0.934 mmol) and *N*-iodosuccinimide (0.210 g, 0.934 mmol) in chloroform (140 mL) and acetic acid (14 mL) was stirred at room temperature for 24 h in the dark under Ar atomosphere. Then, the reaction solution was washed with NaOH aq (2.5 M, 200 mL) twice, water, and brine, dried over $MgSO_4$, and filtrated. After evaporation, the products were suspended onto silica gel. **TB-I** (0.137 g, 32%) and **TB-I2** (0.129 g, 23%) were purified with the silica gel colum chromatography with toluene as an eluent as a green silver and a black powder, respectively. Because of poor solubility of **TB-I** in conventional organic solvents, the clear spectrum of ^{13}C NMR was not obtained. **TB-I**: ^{1}H NMR ($CDCl_3$) δ: 7.68 (1H, d, J = 12.70 Hz), 7.42 (1H, s), 7.40 (1H, s), 7.09 (1H, d, J = 14.16 Hz), 2.43 (3H, s), 2.41 (3H, s). ^{11}B NMR ($CDCl_3$) δ: 0.293. HRMS (EI+) m/z calcd $[M]^+$: 457.9391, found: 457.9404. **TB-I2**: ^{1}H NMR (THF-d_8) δ: 7.85 (1H, s), 7.39 (2H, s), 2.42 (6H, s). ^{13}C NMR ($CDCl_3$) δ: 157.3, 139.7, 135.6, 130.7, 125.6, 123.6, 95.4, 9.7. ^{11}B NMR ($CDCl_3$) δ: 0.195. HRMS (ESI) m/z calcd $[M-H]^-$: 582.8285, found: 582.8292.

2.6. TB-F (8)

The mixture of **3** (1.0 g, 5.52 mmol) in trifluoroacetic acid (50 mL) was stirred at 40 °C for 40 min under Ar atomosphere, and then trifluoroacetic anhydride (2.29 mL, 16.6 mmol) was added dropwise to the reaction solution. After stirring at 80 °C for 1 h and cooling to room temperature, the deep blue solution was poured into the mixture with water (100 mL) and toluene (100 mL). After neutralization by adding $NaHCO_3$, the products were extracted with toluene. The organic layer was washed with satd $NaHCO_3$ aq, water, and brine, dried over $MgSO_4$, and filtrated.

After evaporartion, the crude products containing the aldehyde were used for the next step without further purification because of low stability. The residue was dissolved in 50 mL of toluene, and triethylamine (1.54 mL, 22.07 mmol) was added dropwise to the solution. After stirring at room temperature for 15 min, $BF_3{\cdot}Et_2O$ (2.72 mL, 22.1 mmol) was added dropwise. After stirring at room temperature for 10 min, the mixture was heated at 80 °C and stirred for 2 h. After quenching the reaction by adding water, the product was extracted with toluene. The organic layer was washed with brine twice, dried over $MgSO_4$, and filtrated. After evaporation, the silica gel column chromatography with the mixture eluent (toluene:ethyl acetate = 9:1) was performed. The resulting solid was dissolved in THF, and **TB-F** was obtained from the precipitation in methanol as a glossy green solid (7.2 mg, 0.7%). ^{1}H NMR ($CDCl_3$) δ: 7.67 (2H, d, J = 16.57 Hz), 7.05 (2H, d, J = 16.32 Hz). ^{13}C NMR ($CDCl_3$) δ: 159.1, 143.8, 138.1, 136.5, 133.4, 128.6, 122.3 (q, J = 275 Hz), 114.5, 15.4. ^{11}B NMR ($CDCl_3$) δ: 0.195. HRMS (EI+) m/z calcd $[M]^+$: 400.0299, found: 400.0282.

3. Results and discussion

We designed the thiophene-fused BODIPYs as shown in Figure 1. The synthesis of **TB** derivatives is outlined in Scheme 1. Until the preparation of the precursors before the ligand formation, all reactions proceeded in good yields. Because of the instability of the aldehyde **4** and the ligand moiety before the introduction of boron, the reaction yields in the formation of boron complexes were relatively low. From the characterization with ^{1}H and ^{11}B NMR spectroscopies and mass measurements, the products have the expected structures. The dyes were obtained as colored solids with the solubility in conventional organic solvents such as chloroform and THF. During the measurements, the decomposition and photo-degradation were subtly observed.

The optical properties of **TB** were investigated. The absorption band was observed with the peak at 562 nm from UV–vis absorption measurement (Fig. 2). The molar extinct coefficient exceeded 10^5 M^{-1} cm^{-1} (Table 1). These data mean that **TB** possesses the sharp and large absorption in the visible region. From the photoluminescence spectrum, although the emission band was obtained with the peak at 571 nm, the quantum yield of **TB** can be efficiently suppressed (Φ_F = 0.04). The low emission intensity of **TB** should be originated from the fact that the decay of the excited state of **TB** should proceed via the triplet-excited state. Indeed, new emission bands with long lifetimes at the similar peak position and in the longer wavelength region than that of the emission at room temperature at 77 K assigned as a delayed fluorescence and phosphorescence, respectively. These data clearly indicate that **TB** is a promising seed compound for realizing expected optical properties such as sharp spectra, large molar extinct coefficients and low emissions.

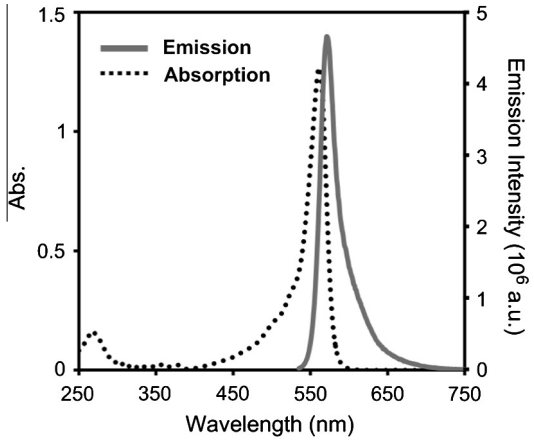
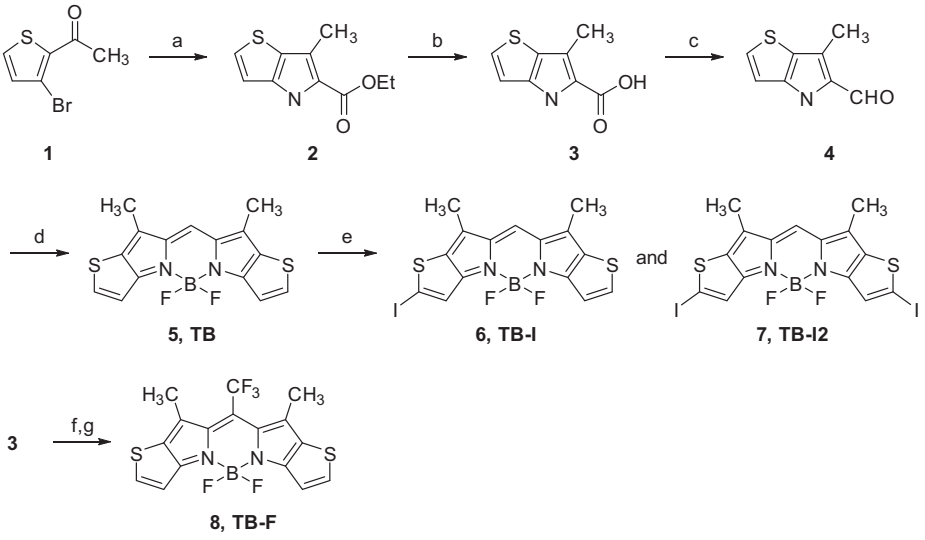


Figure 2. UV–vis absorption (10 μM) and photoluminescence spectra (1 μM) of **TB** in THF. The wavelength of the excitation light was at 530 nm.

Table 1
Optical properties of thiophene-fused BODIPYs

	$\lambda_{max,abs}$ (nm)	ε (M^{-1} cm^{-1})	Φ_F[a]
TB	562	127,000	0.04
TB-I	577	170,000	<0.01
TB-I2	592	184,000	<0.01
TB-F	623	72,200	<0.01

[a] Determined as an absolute value.



Scheme 1. Synthetic outlines for thiophene-fused BODIPYs. Reagents and conditions: (a) ethyl cyanoacetate, CuI, Cs_2CO_3, DMSO, 50 °C, 4 h, 61%; (b) NaOH, H_2O, ethanol, reflux, 1 h, 95%; (c) (i) trifluoroacetic acid, 50 °C, 20 min, (ii) $CH(OEt)_3$ 50 °C, 30 min, 70%; (d) (i) $POCl_3$, dichloromethane, rt, 3 days, (ii) triethylamine, $BF_3{\cdot}Et_2O$, rt, 2 days, 10%; (e) *N*-iodosuccinimide, acetic acid, chloroform, rt, 24 h, 32% for **TB-I**, 23% for **TB-I2**; (f) (i) trifluoroacetic acid, 40 °C, 40 min, (ii) trifluoroacetic anhydride, 80 °C, 1 h; (g) $BF_3{\cdot}Et_2O$, triethylamine, toluene, 80 °C, 2 h, 0.7% (in two steps).

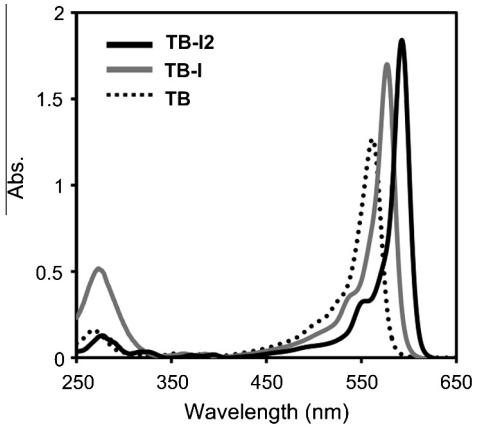


Figure 3. Absorption changes of **TB** by introducing iodine groups. The spectra were obtained from the solutions containing the dyes (10 μM) in THF.

Next, for tuning the optical properties of **TB**, an iodide group was introduced via the heavy atom effect. To maximize the expression of the heavy atom effect, iodide groups were directly attached to the thiophene rings.[13] Figure 3 clearly represents that the absorption bands of **TB-I**s showed the bathochromic shifts than that of **TB**. By introducing a single iodide group, the peak positions were moved by 15 nm to the red-light region. These data can be supported by the results from computer calculations. The gap widths of the energy levels between the frontier orbitals were narrowed by increasing the number of the iodine substituents (Fig. 4). Moreover, the molar extinct coefficients were enhanced by increasing the number of iodide groups. According to the previous report on the photophysical properties of iodinated BODIPY derivatives, these changes could be owing to the heavy atom effect.[14] Indeed, the iodinated **TB** derivatives hardly showed emissions (Φ_F <0.01). The heavy atom effect of iodine could contribute to inhibiting the fluorescence emission. In summary, the introduction of iodine into BODIPYs is valid for regulating the peak positions of absorption.

To explore another method for the modulation of the peak position of absorption wavelength, initially we carried out the density functional theory (DFT) calculation of **TB** with a B3LYP/SVP method. According to the computer modeling on the shape of the lowest unoccupied molecular orbital (LUMO) of **TB**, the localization of the orbital was found at the *meso* position (Fig. 4). Based on this result, we designed the new dye, **TB-F**, having a trifluoromethyl group. The strong ability of electron withdrawing can lower the energy level of LUMO and decrease the gap width of the energy level between the frontier orbitals. Thus, it can be expected that drastic bathochromic shift of the absorption band should be received. The synthesis of **TB-F** was executed with similar procedures as other **TB** derivatives. Because of low stability of the intermediate before boron complexation, the reaction yield in the formation of the BODIPY ring was low. The desired compound was obtained as a solid, and it was confirmed that **TB-F** has enough solubility in conventional organic solvents such as chloroform and THF for the optical measurements. During the measurements, less decomposition and photo-degradation were also observed with **TB-F**.

Figure 5 presents the absorption spectrum of **TB-F**. As we expected, **TB-F** showed the large absorption band at longer wavelength region by +60 nm than that of **TB** (λ_{max} = 623 nm). Similarly as **TB**, the emission band was mainly obtained between 550 nm and 650 nm. This absorption wavelength is adequate for generating the light which can inhibit the photosynthesis.[3] Furthermore, the emission was subtly obtained from **TB-F** (Φ_F <0.01). These data suggest that the efficient light absorbers for the red light can be prepared based on the thiophene-fused BODIPYs. In addition, these optical properties suggest another possibility for using the thiophene-fused BODIPYs as a quencher. Comparing to the conventional efficient absorbers called as QSY (ε_{max} = 90,000 cm^{-1} M^{-1})[15] and BHQ (ε_{max} = 35,600 cm^{-1} M^{-1}),[16] the thiophene-fused BODIPYs have several advantages as a quencher besides of the intrinsic merits of BODIPY dyes. It should

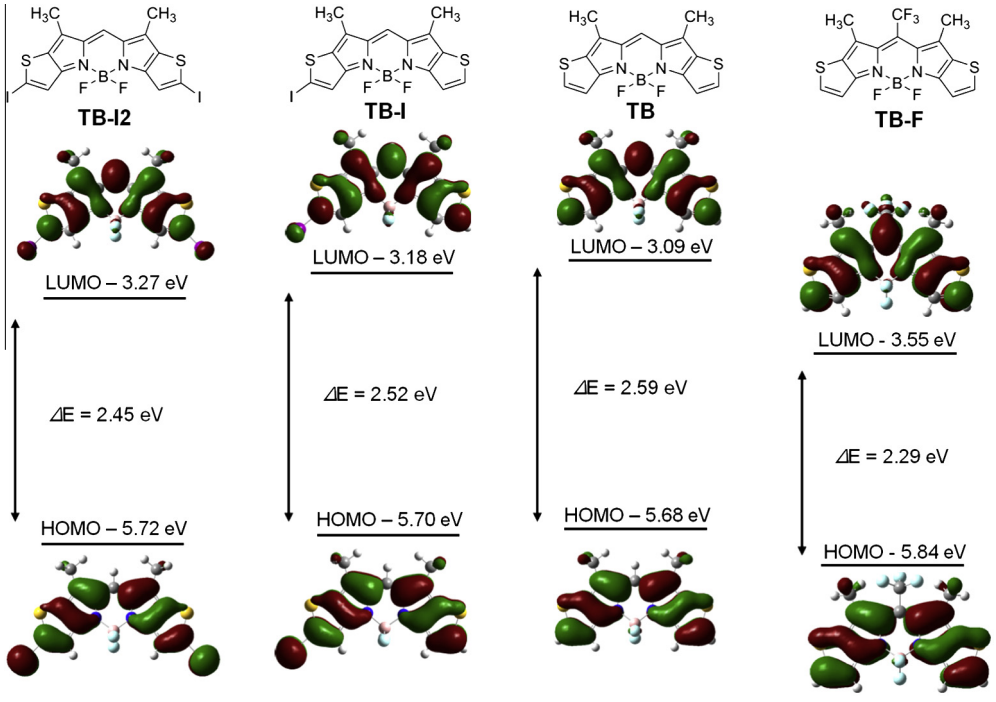


Figure 4. The changes in energy levels and shapes of frontier orbitals by introducing a trifluoromethyl group into the *meso* position in **TB**. The DFT calculations were performed with a B3LYP/SVP method.

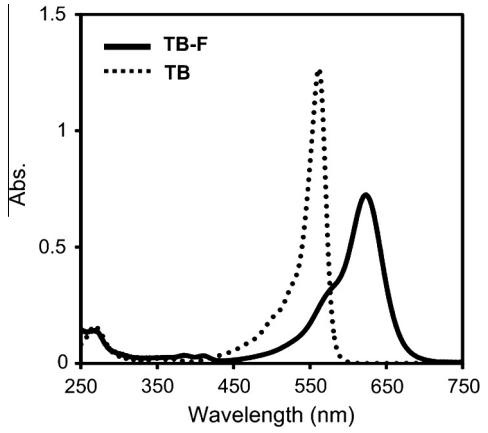


Figure 5. Absorption changes of **TB** by introducing a trifluoromethyl group. The spectra were obtained from the solutions containing the dyes (10 μM) in THF.

be emphasized that the molar extinct coefficients of the thiophene-fused BODIPYs are two or three times larger than those of the conventional absorbers.[15,16] Thus, we can say that the thiophene-fused BODIPYs are promised to be an efficient quencher on the biotechnological assays.[17]

4. Conclusions

We demonstrate the validity of the **TB** skeleton for the design of an efficient light absorber. We established two manners for evolving the optical properties of **TB**: by employing the heavy atom effect, the peak positions can be shifted to the red-light region. The enhancement of molar extinct coefficients was also obtained. It was found that the introduction of the strong electron-withdrawing group at the *meso* position in the BODIPY skeleton was responsible for the drastic bathochromic shift in the absorption spectrum. Finally, we obtained the series of efficient light absorbers for the red light. These compounds have suitable optical properties for generating the light to control photosynthesis and plant growth. Furthermore, thiophene-fused BODIPYs with the efficient light-absorbing ability are promised to be applicable for efficient sensitizers. Our materials and chemical modification methods for modulating the optical properties presented here could be versatile for developing efficient photo-responsive bio-related materials to control the biological activities and efficient quenchers on the biotechnological assays with labelled biomolecules.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bmc.2013.03.050.

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