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Novel intramolecular π-π-interaction in a BODIPY system by oxidation of a single selenium center: geometrical stamping and spectroscopic and spectrometric distinctions

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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A new BODIPY system displaying an intramolecular π-π-interaction was synthesized and studied. When the selenium center was oxidized, the substituted phenyl group undergoes π-π stacking with one side of the BODIPY core. The oxidized form showed, not only a down-field shift in the NMR peak, but also splitting due to geometrical changes that arise when going from C_s to C_1. The compound was characterized by X-ray diffraction; DFT methods helped elucidate the influence of the unexpected π-π stack and its connection to the photophysical properties imparted by the Se oxidation.

Introduction

Organoselenium chemistry has developed rapidly since the 1970s, even though the first organoselenium compound was synthesized in the middle of the 18th century. This lag may be due in part to the malodorous nature, instability, and difficult purification of the compounds involved.[1] Organoselenium chemistry has been rapidly receiving increased attention due to its various roles and redox properties and the relatively low state of toxicity compared to inorganic selenium compounds. Recently, a number of reports have increased in the fields of electroconducting materials and catalysis.[2] The biochemical importance of organoselenium compounds has been investigated after the enzymatic and biological roles such as glutathione peroxidase (GPx) were discovered and clarified.[3] Accordingly, organoselenium compounds have progressed to various fields such as the pharmaceutical scene, medicinal chemistry, bacterial enzymology due to its properties, e.g. antioxidant,[3a, 4] antitumor,[5] and antimicrobial activity.[6] More recently, organoselenium compounds have been exploited in chemodosimeter and chemosensor research for the detection of important biology-based analytes, as well as for reactive oxygen species (ROS)/reactive nitrogen species (RNS), biothiols etc. In the field of molecular chemosening, organoselenium compounds are useful for dynamic measurements of biologically important analytes. In particular, chemical redox properties enable the attribute of reversible detection: oxidation with ROS and reduction with e.g. biothiols.[7]

In the past two decades, the field of and use of emissive organic dyes has been widely extended for diagnostics, electroluminescent devices, labelling DNA/proteins, analyte sensing and so on; these techniques offer advantages such as high sensitivity, rapid response, non-invasive detection, and *in-vivo* biological cellular imaging.[8] As one class of important fluorophore, the usage of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)-based systems has consistently increased due to the available benefit which include sharp excitation peaks and emission wavelengths, high quantum yields, photostability in physiological conditions, and a relative insensitivity to the solution environment.[9] Therefore, continued modification of BODIPY dyes has become one of the potentially workable and usable frameworks of importance in the chemosensing literature.

In terms of photophysical properties, intermolecular interactions are noteworthy for their ability to ease and effectively help change the photomechanism. In different solvents, molecular interactions would affect the photophysical properties with several specific molecular features impacted by the environment including *e.g.* polarity and viscosity.[10] The BODIPY system, in general, shows fairly different photochemical and electrochemical properties depending on whether inter- or intramolecular interactions are available and whether they are engaged or disengaged.[11] For these reasons, intermolecular forces and interactions have been more of a constant focus. While there are many examples of inter/intramolecular interactions in polymer derivatives[12] and fluorophore systems,[13] *intramolecular π-π*-interactions between a substituted group and a fluorophore

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† Electronic Supplementary Information (ESI) available: [^{1}H, ^{11}B, ^{13}C, ^{19}F, ^{77}Se, HMBC, HSQC NMR spectroscopic data, HRMS spectrometric data, fluorescence spectra, DFT calculation data, crystallographic data]. See DOI: 10.1039/x0xx00000x

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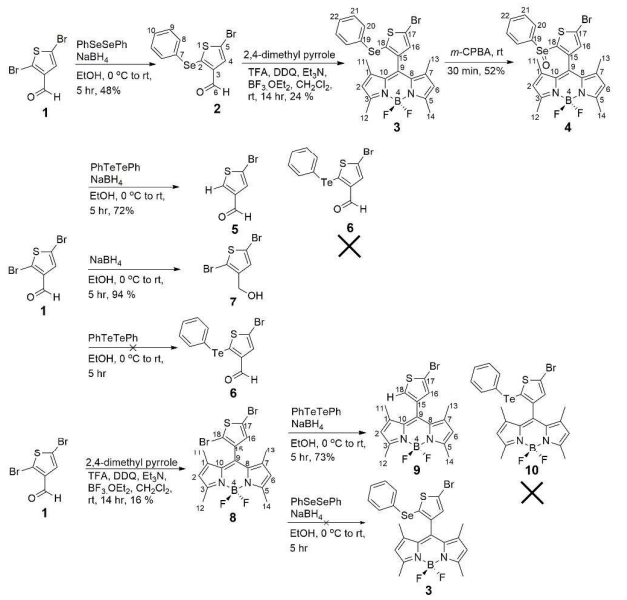
core are rare. Herein, they are discussed as being on important focal point, accompanied by clear and abundant spectroscopic evidence.



Scheme 1. Synthesis of compounds (**1** to **5** and **7** to **9**).

Experimental section

Materials All chemicals and materials used herein were used as received from commercial suppliers (Aldrich, Tokyo chemical Industry and Junsei chemical companies) and used without further purification. Thin layer chromatography (TLC) was performed on DC Kieselgel 60 F254 silica gel plates.

DFT calculations The molecular structures and HOMO-LUMO levels of the probe and oxidized version of the compound were estimated using density functional theory (DFT) calculations [by Gaussian 09 program (B3LYP method with 6-311g* basis set for Se and Br only and 6-31g* basis set for all other atoms).] All calculations were performed with the gas phase.

Spectroscopic data ^{1}H, ^{13}C, ^{11}B, ^{19}F, ^{77}Se and 2D (HMBC and HSQC) NMR spectra were acquired using a Bruker Avance 400 and Agilent-NMR-vnmrs 600 MHz spectrometer. TMS and dimethylselenide were used as external standards. Absorption spectra were measured using a JASCO V–530 spectrophotometer. Fluorescence measurements were carried out with a Shimadzu RF–5301 pc spectrofluorophotometer.

Spectrometric data ESI-mass spectrometry was performed on a BRUKER micrOTOF-QII by the research support staff at KAIST. A Time-of-Flight mass spectrometer was operated at a resolution of 20,000.

X-ray Crystallography The diffraction data of compound **4** was collected on a Bruker D8 QUEST. A suitable size and quality of crystal was coated with Paratone-*N* oil and mounted on a DualThickness MicroLoops LD purchased from MiTeGen. The data were collected with graphite monochromated Mo (Kα) radiation (λ = 0.71073 Å) at 120 K. Cell parameters were determined and refined as done routinely by the SMART software program. Data reduction was performed using SAINT software. An empirical absorption correction was applied using the SADABS program.

Synthesis of 2,5-dibromothiophene-3-carboxaldehyde (1). Compound 1 was synthesized by a known literature procedure.[14]

Synthesis of 5-bromo-2-(phenylselanyl)-thiophene-3-carboxaldehyde (2). To a stirred solution of diphenyl diselenide (1.25 g, 4.0 mmol) in anhydrous ethanol (30 mL) was added $NaBH_4$ (0.3 g, 8.0 mmol) at 0°C under N_2 atmosphere. Then, the reaction mixture was warmed to room temperature and stirred for an additional 30 min. The reaction mixture then changed from yellow to colorless; then, 2,5-dibromothiophene-3-carboxaldehyde (1.08 g, 4.0 mmol) was added to the reaction mixture. The reaction mixture was stirred for 3 hr at room temperature. The reaction was monitored by TLC. After complete consumption of starting material, the solvent was evaporated under reduced pressure. Water (20 mL) was then added to the residue, and the residue mixture was extracted with CH_2Cl_2 (3 × 25 mL). Combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc / hexane (5:95) as the eluent. Yield: 0.8 g, 58%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.93 (s, $1H_6$), 7.61 (dd, $^{3}J_{H\text{-}H}$ = 8.0 Hz, $^{4}J_{H\text{-}H}$ = 1.4 Hz, $2H_8$), 7.41-7.39 (m, $1H_{10}$), 7.38-7.35 (m, $2H_9$), 7.36 (s, $1H_4$); ^{13}C NMR (150.87 MHz, $CDCl_3$): δ 184.2 (C_6), 144.5 (C_2), 139.5 (C_3), 134.7 (C_8), 130.6 (C_4), 130.1 (C_9), 129.6 (C_{10}), 128.6 (C_7), 113.8 (C_5); ^{77}Se NMR (76.3 MHz, $CDCl_3$): δ 418.2.

Synthesis of 5-bromo-2-(phenylselanyl)-thiophene-substituted BODIPY (3). 2,4–Dimethylpyrrole (476 mg, 5.0 mmol) and 5-bromo-2-(phenylselanyl)thiophene-3-carboxaldehyde (692 mg, 2 mmol) were mixed into dichloromethane. Then, TFA (trifluoroacetic acid) was added to the reaction mixture and stirred at room temperature. After 1 hr, DDQ (2,3–dichloro–5,6–dicyano–1,4–benzoquinone, 545 mg, 2.4 mmol) was added to the reaction mixture. While stirring for 1 hr at room temperature, $BF_3{\cdot}OEt_2$ (2.5 ml, 20 mmol) and triethylamine were added to achieve basic solution conditions. This reaction mixture was stirred at room temperature for 12 hrs. After this time, the volatiles were then removed by rotary evaporation. The residue was re-dissolved into ethyl acetate and washed with an aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using

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dichloromethane / hexane (1:1) as the eluent. Yield: 276 mg, 24%; ^{1}H NMR (600 MHz, CD_2Cl_2): δ 7.51 (d, $^3J_{H-H}$ = 7.0 Hz, $2H_{20}$), 7.30 (t, $^3J_{H-H}$ = 7.4 Hz, $1H_{22}$), 7.20 (t, $^3J_{H-H}$ = 7.7 Hz, $2H_{21}$), 6.90 (s, $1H_{16}$), 5.98 (s, $2H_{2,6}$), 2.53 (s, $6H_{12,14}$), 1.48 (s, $6H_{11,13}$); ^{13}C NMR (150.87 MHz, CD_2Cl_2): δ 156.5 ($C_{3,5}$), 143.3 ($C_{8,10}$), 139.6 (C_9), 135.9 (C_{20}), 134.8 (C_{18}), 131.7 ($C_{1,7}$), 131.4 (C_{16}), 129.7 (C_{21}), 129.5 (C_{22}), 128.2 (C_{19}), 126.0 (C_{15}), 121.7 ($C_{2,6}$), 116.8 (C_{17}), 14.8 ($C_{12,14}$), 13.9 ($C_{11,13}$); ^{11}B NMR (128.34 MHz, CD_2Cl_2): δ 0.56 (t, J_{B-F} = 32.8 Hz); ^{19}F NMR (376.38 MHz, CD_2Cl_2): δ –146.1 (q, J_{B-F} = 32.8 Hz); ^{77}Se NMR (CD_2Cl_2): δ 344.4; HRMS (ESI) (m/z): $[M + Na]^+$ calc. for $C_{23}H_{20}BBrF_2N_2SSe$ + Na: 586.9655, found: 586.9694.

Synthesis of (4). To a stirred solution of compound 3 (56 mg, 0.10 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (17 mg, 0.10 mmol) at room temperature. After stirring for 30 min at this temperature, the solvent was removed by rotary evaporation. The crude residue was purified by silica gel column chromatography using EtOAc / hexane (1:1) as the eluent. Yield: 30 mg, 52 %; ^{1}H NMR (600 MHz, CD_2Cl_2): δ 7.55 (d, $^3J_{H-H}$ = 6.2 Hz, $2H_{21}$), 7.45 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 2.5 Hz, $1H_{22}$), 7.38 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 2.6 Hz, $2H_{20}$), 7.00 (d, J = 2.6 Hz, $1H_{16}$), 6.14 (s, $1H_6$), 5.84 (s, $1H_2$), 2.56 (s, $3H_{14}$), 2.53 (s, $3H_{12}$), 1.78 (s, $3H_{13}$), 1.11 (s, $3H_{11}$); ^{13}C NMR (150.87 MHz, CD_2Cl_2): δ 158.2 (C_5), 157.5 (C_3), 144.6 (C_{15}), 143.7 (C_8), 143.4 (C_{10}), 141.5 (C_{19}), 137.7 (C_{18}), 132.5 (C_{22}), 132.2 (C_{16}), 131.5 (C_9), 131.4 (C_1), 131.3 (C_7), 130.2 (C_{20}), 126.3 (C_{21}), 122.7 (C_6), 122.2(C_2), 120.0 (C_{17}), 15.1 (C_{14}), 15.0 (C_{12}) 14.3 (C_{13}), 13.9 (C_{11}); ^{11}B NMR (128.34 MHz, CD_2Cl_2): δ 0.51 (t, J_{B-F} = 32.2 Hz); ^{19}F NMR (376.38 MHz, CD_2Cl_2): δ –145.6 (dq, $^2J_{F-F}$ = 107.9 Hz, $^1J_{B-F}$ = 32.8 Hz), –146.3 (dq, $^2J_{F-F}$ = 107.9 Hz, $^1J_{B-F}$ = 32.7 Hz); ^{77}Se NMR (76.3 MHz, CD_2Cl_2): δ 865.9; HRMS (ESI) (m/z): $[M + Na]^+$ calc. for $C_{23}H_{20}BBrF_2N_2OSSe$ + Na: 602.9604, found: 602.9643.

Synthesis of 5-bromothiophene-3-carbaldehyde (5).[15] To a stirred solution of diphenyl ditelluride (303 mg, 0.740 mmol) in anhydrous ethanol (6 mL) was added $NaBH_4$ (30.4 mg, 0.800 mmol) at 0°C under N_2 atmosphere. Then, the reaction mixture was warmed to room temperature and stirred for an additional 30 min. The reaction mixture was changed from reddish-yellow to colorless and then 2,5-dibromothiophene-3-carboxaldehyde (201 mg, 0.740 mmol) was added to the reaction mixture. The reaction mixture was stirred for 3 hr at the same temperature. The reaction was monitored by TLC. After complete consumption of the starting material, the solvent was evaporated under reduced pressure. Water was then added to the residue, and subsequently extracted with CH_2Cl_2. Combined organic layers were washed with brine, dried over Na_2SO_4 and was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc / hexane (5:95) as the eluent. Yield: 102.1 mg, 72 %; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.74 (s, 1H), 7.98 (s, 1H), 7.46 (s, 1H); ^{13}C NMR (150.87 MHz, $CDCl_3$): δ 183.6, 143.1, 137.9, 127.8, 115.1.

Synthesis of (2,5-dibromothiophen-3-yl)methanol (7).[16] To a stirred solution of 2,5-dibromothiophene-3-carboxaldehyde (101 mg, 0.370 mmol) in anhydrous ethanol (3.0 mL) was added $NaBH_4$ (14.2 mg, 0.370 mmol) at 0°C under N_2 atmosphere. Then, the reaction mixture was warmed to room temperature and stirred for an additional 5 hr. The reaction was monitored by TLC. After complete consumption of the starting material, solvent was then evaporated under reduced pressure. Water was added to the residue, and the mixture was summarily extracted with CH_2Cl_2. Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc / hexane (1:9) as the eluent. Yield: 94.5 mg, 94 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (s, 1H), 4.45 (s, 2H), 3.39 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.3, 130.5, 111.5, 109.2, 59.0.

Synthesis of 2,5-dibromothiophene-substituted BODIPY (8). 2,4–Dimethylpyrrole (233 mg, 2.5 mmol) and 2,5-dibromothiophene-3-carboxaldehyde (300 mg, 1.1 mmol) were mixed in dichloromethane. Then, TFA (trifluoroacetic acid) was added to the reaction mixture and stirred at room temperature. After 1 hr, DDQ (2,3–dichloro–5,6–dicyano–1,4–benzoquinone, 272.4 mg, 1.2 mmol) was added to the reaction mixture. While stirring for 1 hr at room temperature, $BF_3{\cdot}OEt_2$ (0.822 ml, 6.00 mmol) and triethylamine were added to achieve basic solution conditions. The reaction mixture was then stirred for 12 hrs at room temperature. After this time, the volatiles were removed by rotary evaporation. The residue was re-dissolved in ethyl acetate and washed with aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$ and was then concentrated under reduced pressure. The residue was purified by silica gel column chromatography using EtOAc / hexane (5:95) as the eluent. Yield: 88 mg, 16%; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.85 (s, $1H_{16}$), 6.02 (s, $2H_{2,6}$), 2.55 (s, $6H_{12,14}$), 1.69 (s, $6H_{11,13}$); ^{13}C NMR (150.87 MHz, $CDCl_3$): δ 156.8 ($C_{3,5}$), 142.6 ($C_{8,10}$), 136.2 (C_{15}), 132.6 (C_9) 131.2 ($C_{1,7}$), 130.4 (C_{16}), 121.7 ($C_{2,6}$), 113.5 (C_{18}), 111.8 (C_{17}), 14.9 ($C_{12,14}$), 13.6 ($C_{11,13}$); ^{11}B NMR (128.34 MHz, $CDCl_3$): δ 0.55 (t, J_{B-F} = 32.9 Hz); ^{19}F NMR (376.38 MHz, $CDCl_3$): δ –145.8 (dq, $^2J_{F-F}$ = 109.5 Hz, $^1J_{B-F}$ = 33.1 Hz), –146.6 (dq, $^2J_{F-F}$ = 109.5 Hz, $^1J_{B-F}$ = 32.3 Hz); HRMS (ESI) (m/z): $[M + Na]^+$ calc. for $C_{17}H_{15}BBr_2F_2N_2S$ + Na: 510.9261, found: 510.9442.

Synthesis of 5-bromothiophene-substituted BODIPY (9). To a stirred solution of diphenyl ditelluride (25.2 mg, 0.062 mmol) in anhydrous and degassed ethanol (3.0 mL) was added $NaBH_4$ (4.7 mg, 0.12 mmol) at 0°C under N_2 atmosphere. Then reaction mixture was warmed to room temperature and stirred for an additional 30 min. The reaction mixture changed from reddish-yellow to colorless; after this time compound **8** (30.0 mg, 0.062 mmol) was added to the reaction mixture. The reaction mixture was stirred for 3 hr at room temperature. The

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reaction was monitored by TLC. After complete consumption of the starting material, the solvent was evaporated under reduced pressure. Water was then added to the residue, and this layer was then extracted with CH_2Cl_2. Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc / hexane (1:50) as the eluent. Yield: 18.3 mg, 75 %; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.44 (d, $^4J_{H-H}$ = 5.6 Hz, $1H_{18}$), 6.83 (d, $^4J_{H-H}$ = 5.6 Hz, $1H_{16}$), 6.01 (s, $2H_{2,6}$), 2.56 (s, $6H_{12,14}$), 1.59 (s, $6H_{11,13}$); ^{13}C NMR (150.87 MHz, $CDCl_3$): δ 156.4 ($C_{3,5}$), 142.8 ($C_{8,10}$), 135.5 (C_{15}), 134.4 (C_9), 131.4 ($C_{1,7}$), 128.4 (C_{18}), 128.0 (C_{16}), 121.4 ($C_{2,6}$), 112.4 (C_{17}), 14.8 (C_{12}), 13.3 (C_{11}); ^{11}B NMR (128.34 MHz, $CDCl_3$): δ 0.62 (t, J_{B-F} = 32.9 Hz); ^{19}F NMR (376.38 MHz, $CDCl_3$): δ –146.3 (dq, $^2J_{F-F}$ = 106.7 Hz, $^1J_{B-F}$ = 33.4 Hz); HRMS (ESI) (m/z): $[M + Na]^+$ calc. for $C_{17}H_{16}BBrF_2N_2S$ + Na: 431.0176, 433.0156, found: 431.0263, 433.0243.

Results and discussion

Previously, BODIPY organochalcogen-substituents in meso-positions have been developed and reported.[17] As reported previously, organochalcogen substitutions impact special properties: fluorescent quenchers by PET process,[18] oxidation with ROS/RNS[16] and reversible reactions with biothiols.[17a-d, 20] Based on the synthetic details in these previous reports, compound **3** was synthesized for potential sensing system in the anticipation of allowing for its use as a key component of a reversible detection of ROS, in particular hypochlorite detection (Scheme 1). Compound **3** showed selective detection for hypochlorite over other ROS. While obtaining spectroscopic and spectrometric data of the oxidized version of **3** to confirm the structural changes and photo-mechanism, NMR spectroscopic peak splittings were observed in the ^{1}H NMR spectrum. The splitting of ^{1}H NMR peaks is not observed in *meso*-chalcogen-substituted BODIPY systems. A possibility of by-product formation was ruled out since close integer ratio and symmetry of the splitting patterns existed. To explain these phenomena, the reaction of **3** with a strong oxidizing agent, e.g. *m*-CPBA, and further purification were performed to obtain compound **4** on preparative scale (Scheme 1). High resolution mass spectrometric data (HRMS) was acquired as a first point in analysis. The mass spectrometric results showed calculated (M/Z) values for both compounds matched the experimentally obtained values for compound **3** (M/Z = 586.9694) and compound **4** (M/Z = 602.9643) (Figures S17-S18). After Se oxidation was identified by HRMS, ^{77}Se NMR spectral data of compound **4** was recorded to better confirm the oxidation of the selenium center. As expected, the oxidized selenium center showed a downfield shift of δ 865.9 ppm, compared to the original value of δ 344.4 ppm confirming the formation of a tetravalent center[17b, 17d, 20a, 21] (Figures S7 and S13). Then, a comparison of ^{1}H NMR spectra between compounds **3** and **4** was carefully carried out. The ^{1}H NMR peak of the methine group in BODIPY was split from one (δ 5.98 ppm) to two different signals (δ 6.14 and 5.84 ppm). In the aliphatic region, peaks splitting the 1- and 3-position methyl groups of the BODIPY system (signal for 3-position was centered at δ 2.53 ppm and moved to δ 2.56 and 2.53 ppm, that for the 1-position, moved from δ 1.48 ppm to δ 1.78 and 1.11 ppm), were observed (Figures 2, S5 and S11). Also, there were concomitant shifts in the carbon NMR signals. The ^{13}C NMR signal of methyl groups has become clearly split from two to four peaks (from δ 14.8 ppm to δ 15.1 and 15.0 ppm; from δ 13.9 ppm to 13.9 and 14.3 ppm). The methine group of ^{13}C NMR spectral peaks changed from δ 121.7 ppm to δ 122.7 and 122.2 ppm (Figures S5 and S11). In the case of ^{19}F NMR spectroscopic data, splitting of the fluorine NMR spectroscopic signal was observed. The ^{19}F NMR spectrum of compound **3** showed a quartet at δ –146.1 (q, $^1J_{B-F}$ = 32.8 Hz) corresponding to the BF_2–group signal (Figure S6). The mono-oxidation of the sole selenium center then induced formation of a doublet of doublet of quartets of signals centered at δ –145.6 (dq, $^2J_{F-F}$ = 107.9 Hz, $^1J_{B-F}$ = 32.8 Hz), δ –146.3 (dq, $^2J_{F-F}$ = 107.9 Hz, $^1J_{B-F}$ = 32.7Hz). The splitting and general appearance of the ^{11}B NMR spectrum peaks, however, do not change significantly upon chemical oxidation (Figures S12).

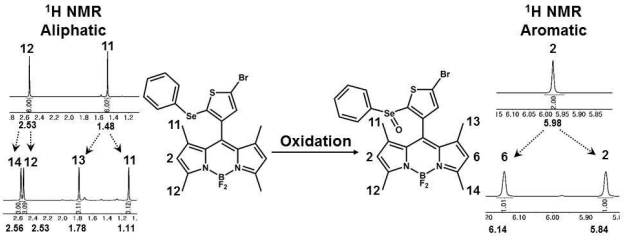

Figure 1. Spectroscopic changes of ^{1}H NMR by oxidation.

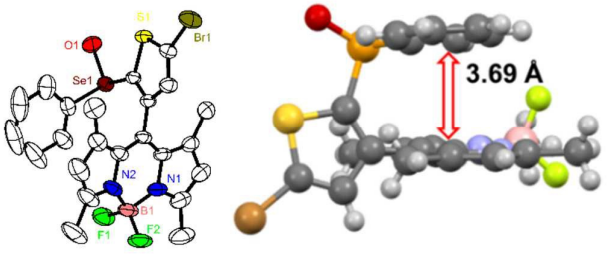

Figure 2. Molecular structure of compound **4**. Crystallographic parameters (CCDC# 1000278): *a* = 8.9526(2) Å, *b* = 10.2532(3) Å, *c* = 14.7976(4) Å, α = 94.4778(14)°, β = 106.8774(12)°, γ = 114.9387(12)°.

As compared with reports of unsymmetrical and annulated BODIPY systems, the NMR spectroscopic data for compound **4** showed unusual splittings. Based on this splitting, the integration of the NMR spectral peaks were not able to be caused by only a rotational hindrance of ring current effects and simple transformations. Therefore, we hypothesized (i) the symmetry of the compound converted to C_s symmetric energetically to a static non-symmetric C_1 form, and (ii) other inter- or intra- interactions must exist.

To confirm our hypothesis and to eliminate other possibilities, **4** was characterized by X-ray crystallography

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(Figure 2, Tables S1 and S2). Compound **4** featured an intramolecular planar π–π stacking interaction between one side of the fluorophore largely involving (i) one entire pyrrolyl group, and (ii) the entire aryl group of the PhSe- group. The planar systems are linked by four atoms with a Ph_{cent}–Pyr_{cent} distance of 3.69 Å. The dihedral angle between the phenylselenium plane and the BODIPY core is 7.9° corresponding to a nearly parallel positioning. Such an intramolecular π–π stack system has neither been reported between any fluorophore / chromophore-type group nor for any phenylchalcogen-substituted group to the best of our knowledge. The desymmetrization (C_s → C_1) and intramolecular π-π-interaction caused the observed spectroscopic changes. Secondarily, selenium was mono-oxidized and bears the expected pyramidal geometry (C–Se–C angle of 96.7(1)°) which assisted in adopting the unique intramolecular effect.

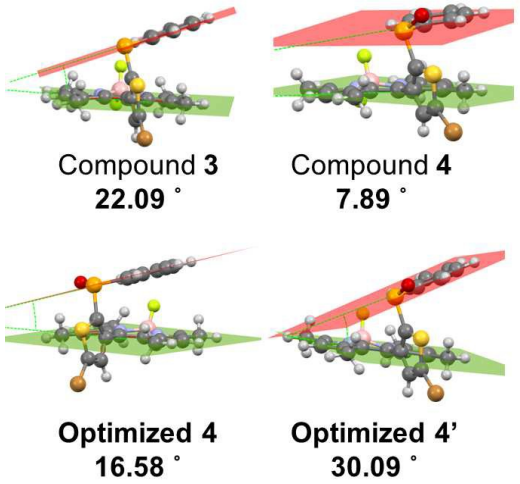

Figure 3. Dihedral angles between PhSe-plane and BODIPY plane of **3, 4** and **optimized 4 / 4'** (C's and Se were picked for the PhSe- plane and C's, N and B were picked to represent the BODIPY plane).

Density functional theory (DFT) calculations were exploited to help elucidate π-π-stacking. Calculations were carried out with the geometry optimized structure of **3** with the use of the B3LYP/6-31g* basis set (6-311g* for Se/Br). Furthermore, the structure of **4** was also calculated by optimization. Compound **4** was calculated twice in two different orientations of the oxidized group corresponding to the geometries labelled **optimized 4/4'**. Dihedral angles between the PhSe and BODIPY were compared among **3**, **4** and **optimized 4/4'**. To build up two planes for analysis, carbon and the selenium atoms were chosen on oxidized PhSe and carbon, nitrogen and boron atoms belonging to the BODIPY core were used. As mentioned above, the dihedral angle of **4** showed a near-parallel orientation of ~7.9 °. Separately, **3** and **optimized 4/4'** showed ~22.1 ° and 16.6 °/30.1 °, not considered as π-π-stacking (Figure 3). In the case of the rotamer **optimized 4'**, having the same orientation as oxidation **4**, the dihedral angle was even greater than the dihedral angle found for that in **optimized 4**. The geometric differences among **3**, **4** and **optimized 4/4'** support π-π-stacking between PhSe- and the BODIPY core for compound **4** and oxidation as a causative factor for the stacking formation.

Upon π-π-stacking between the oxidized PhSe- and BODIPY skeleton in compound **4**, the targeted phenyltelluride analogue (**10**), expected to have similar chemical and photophysical properties, was sought via synthesis by analogous synthetic methods (Scheme 1). The reaction of compound **1** with diphenylditelluride under the same conditions as those for the synthesis of **3** was expected to give **6**; surprisingly, compound **5** was obtained instead in 72% yield (Figures S19-S21). To understand the role of the phenyltelluride for dehalogenation, several control experiments were carried out. Compound **1** was treated with $NaBH_4$; as expected, the aldehyde was reduced to alcohol **7** (Figure S22). Even excess amounts of $NaBH_4$ were insufficient to effect debromination. The other control experiment with diphenylditelluride did not show changes; virtually all starting material was recovered. Accordingly, 2,5-dibromothiophene *meso*-substituted BODIPY (**8**) was synthesized and allowed us to perform the debromination reaction with phenyltelluride in the presence of $NaBH_4$ to give the telluride analogue (**10**) (Figures S23-S27).

Under the above-mentioned reaction conditions, 5-bromothiophene BODIPY (**9**) was obtained (73 %) (Figures S28-S32). In an analogous reaction of **8** with diphenyldiselenide with $NaBH_4$ under the same conditions, starting materials (**8**) were recovered (Scheme 1). In previous related reports, telluride and selenide derivatives undergo substitution reactions with aryl compounds under similar conditions.[22] While only a few examples showed dehalogenation, however, aryl compounds contain phenol groups that undergo dienone-phenol rearrangements.[23] Based on control experiments, and bolstered by findings from related reports, phenyltelluride undergoes reaction to become substituted with the 2-bromothiophene moiety; however, it seems that the *in situ* generated phenyltelluride analogue is rapidly substituted by hydride. This is driven partly because of bond strength differences: C–Te and H–Te have bond enthalpies approximately 30-40 kJ mol^{-1} greater than those for C–Se and H–Se bonds.[24]

The original aim of preparing **3** was to study the reversible detection of ROS by discrete redox chemistry changes at the selenium center. As with analogous sulfide chemistry, it is well-known that a selenium-centered probe can be oxidized with hypochlorite resulting in 'turn-on' fluorescence by a blocking of the PET process.[7] Compound **3** shows a strong green fluorescent enhancement after addition of hypochlorite. Then, a screening test was performed with various ROS such as KO_2, H_2O_2, ^tBuOOH, NaOCl, $ONOO^-$ in the presence of compound **3** (acetonitrile/water, v/v, 1:1) (Figure S33). The fluorescence of compound **4** was also measured in acetonitrile solvent (Figure S34). Other photophysical studies were carried out: *e.g.* titrations with various concentrations of NaOCl (Figure S35),

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testing of reversibility with glutathione (GSH) (Figure S36), and related time dependent data (Figure S37).

To confirm the photomechanism of the 'turn-on' fluorescence by the blocking of the PET process, time-dependent density functional theory (TD-DFT) was exploited. The largest intense transition in **4** is from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) (CI = 87.6 %) with an oscillator strength of ƒ = 0.6524, defined here as the dominant transition. Corresponding with fluorescence enhancement, electronic distributions of HOMO and LUMO are exhibited on the BODIPY core in both **3** and **4**. However, in the case of **3**, two large intense transitions were shown. The dominant transition is from HOMO to LUMO (CI = 77.7 %) with an oscillator strength of ƒ = 0.2996. The other large intense transition is from HOMO-1 to LUMO (CI = 79.2 %) and involves an oscillator strength of ƒ = 0.1007 (Table S3). Concerning the strength of the oscillator and second largest transition from HOMO-1 to LUMO, these data assist the assignment of the fluorescence enhancement as originating from a photo-induced electron transfer (PET) type mechanism (Figure S38). Moreover, **optimized 4/4'** showed results similar to those for **4**: the HOMO to LUMO transition with largest oscillator strength (CI = 93.7 and 95.3 %, respectively).

Conclusions

We have herein explored novel intramolecular π-π-conjugated systems in *meso*-aryl-substituted BODIPY systems. The oxidation of **3** gives geometrical changes supported by excellent spectroscopic and spectrometric evidence. The molecular changes by oxidation showed, not only down-field shifting, but also splitting of the NMR spectroscopic peaks and fluorescent enhancement. Hindering the rotation of the *meso*-substitution in this study induced intramolecular π-π-conjugation between the substituted phenyl ring and BODIPY fluorophore core giving a geometrical change from C_s to C_1. Geometrical changes were confirmed by X-ray crystallography. A comparison of the geometry of **4** with calculated geometry optimized versions (**optimized 4/4'**) also helped confirm the nature of π-π-stacking between the oxidized PhSe- group and one side of the BODIPY core. As per our knowledge, this is the first example clearly showing intramolecular π-π-conjugated system between a BODIPY fluorophore and its aryl substituent, as well as any fluorophore / chromophore type group and phenylchalcogen-substituted group for that matter. Based on the unexpected optical properties of the selenium compound, the tellurium analogue was attempted for synthesis. However, the analogous tellurium-substituted BODIPY was not able to be synthesized under analogous conditions in our hands. Model reactions helped better define the debromination for the exact analogues when Ph_2Te_2 was used as the reagent.

Acknowledgements

This work was supported by the (i) Mid-Career Researcher Program through the NRF (National Research Foundation) of Korea (NRF-2014R1A2A1A11052980) funded by MEST, (ii) the Institute for Basic Science (IBS) and (iii) the High Risk High Return Program (HRHRP) funded by KAIST. Mr. Youngsam Kim and Dr. Sandip V. Mulay acknowledge IBS research Fellowships. Ph. D candidate J. Kim under supervision of Prof. Dr. W. Y. Kim at KAIST helped with interpretation of the DFT/TDDFT calculations. The research support staff at KAIST facilitated the acquisition of MS data.

Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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