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A Suzuki Approach to Quinone-Based Diarylethene Photochromes

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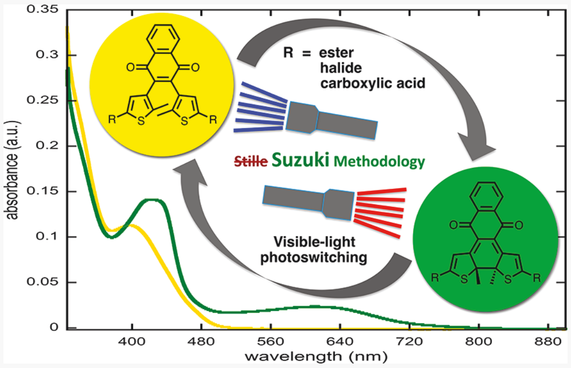
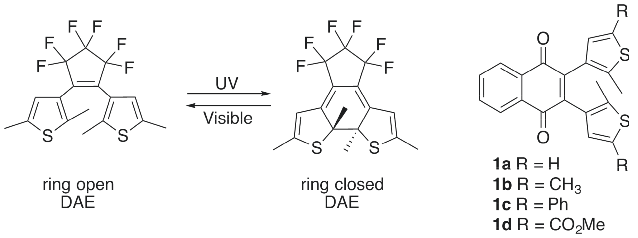
ABSTRACT: Diarylethene photochromes show promise for use in advanced organic electronic and photonic materials with burgeoning considerations for biological applications; however, these compounds typically require UV light for photoswitching in at least one direction, thus limiting their appeal. We here introduce a naphthoquinone-based diarylethene that switches between open and closed forms with visible light. The synthesis of this quinone diarylethene relies on Suzuki methodology, allowing for the inclusion of functional groups not otherwise accessible with current synthetic routes.



Diarylethenes (DAEs, Scheme 1) have enjoyed sustained investigation as p-type[1,2] photochromes with applications in optical data storage devices,[3] photoresponsive quantum dots,[4,5] photomechanical constructs,[6,7] charge transport systems,[8−10] vehicles for drug delivery,[11] photodynamic therapy agents,[12,13] and as linkers in metal−organic frameworks.[14−17] Many of these systems are the result of work focusing on hexafluorocyclopentene scaffolds[18−21] and require ultraviolet light (UV) to achieve ring closure (Scheme 1). Given the limitations inherent to the use of UV for photoswitching, research has moved toward developing DAEs that photoisomerize exclusively with visible light.[22−24]

Scheme 1. (Left) Photoisomerization of a Quintessential Diarylethene; (Right) the Structure of Various qDAEs Shown in the Ring Open Form



Quinone-based diarylethenes (qDAEs, compound **1a** as an example), in contrast to their hexafluorocyclopentene analogues, have received minuscule attention. The limited contributions to the literature, however, have suggested that quinone-based DAEs could exhibit near-ideal visible light facilitated switching.[25,26] When one considers that quinones have great biological importance[27,28] and rich redox chemistry, appropriately functionalized qDAEs could open the door to photochromes that are biologically[29,30] and electrochemically relavent.[31,32]

Katsumura[33] synthesized a series of qDAEs but did not examine their optical properties. Subsequently, Deng and Liebeskind[25] demonstrated that complete photoconversion from ring-open to ring-closed isomers was not possible with a similar set of qDAEs (for example, **1a**−**1c**). Near-complete ring closure was, however, realized in the presence of strong Lewis acids. Most recently, both the groups of Tsuda[26] and König[29] showed that the ring-open and ring-closed forms of qDAEs exhibited stark differences in redox behavior, while the work of König[29] further showed that qDAEs are capable of influencing biological systems.

Thus far, all reported synthetic approaches toward qDAEs involve Stille coupling conditions. These Stille routes require the use of lithiation and stannylation steps, thus limiting the scope of functional groups that can survive to the final photochrome product. As examples, these functional groups include esters (**1d**), carboxylic acids, phosphonates, and phosphonic acids,[10] which are easily accessible in non-qDAE systems. The limitations on functional groups, in turn, limit the possible applications of qDAEs. We seek to enter into the literature qDAEs that can switch in both directions with visible light and that contain otherwise synthetically inaccessible functional groups using current methods. These functional groups (our targets were thienyl esters, carboxylic acids, and halides),

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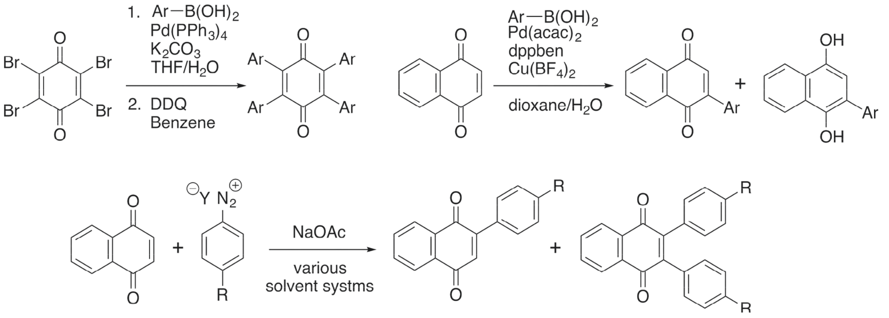
Scheme 2. Selected Arylated Quinones Obtained by Suzuki, Direct Arylation, and Meerwein Coupling Reactions



additionally, are capable of further modification to allow for their potential use in biological systems[34,35] and main chain photochromic polymers,[36−38] both of which have received much attention.

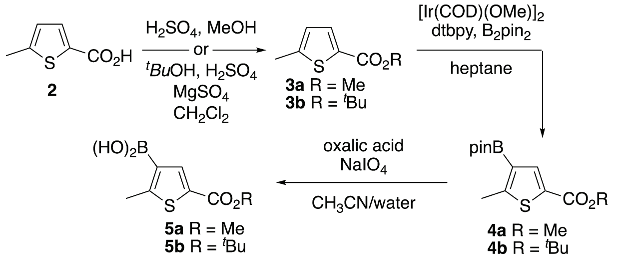
Given that borylation, unlike stannylation, can be accomplished without the need for a lithiation step, we supposed that Suzuki methodology would allow access to qDAEs with increasingly diverse functional groups.[39] To date, Suzuki reactions have been employed for the synthesis of DAEs containing hexafluoro- and perhydro-cyclopentene components in addition to some benzothiophene examples.[40−44] Suzuki methodology, curiously, has seen negligible use in the synthesis of qDAEs. Previous reports have suggested that decomposition of the halogenated quinone coupling partner prevents the reaction.[39,45]

According to the literature, several nonphotochromic monoaryl[39] and tetraaryl quinone compounds have been synthesized by a Suzuki approach, but 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was needed as a final step before the desired products were obtained.[46,47] When not employed, it is assumed that oxidation by atmospheric oxygen during the work up and purification helped achieve the same results as DDQ.[48] Direct arylation using boronic acids has also been explored, but the resulting quinones were only monosubstituted, and $FeCl_3$ was required to reoxidize the product mixture, which contained a reduced side product[49] just as in the reports by Langer and co-workers.[46,47] The Meerwein arylation[50] has also been explored but afforded products in low yield. In all of these reports (Scheme 2), only benzene-derived boronic acids or azides were used and thus gave nonphotochromic qDAEs. We have found no instances of thiophene boronic acids or thiophene boronic acid esters[51] participating in coupling reactions, thus affording photochromic qDAEs.

We sought conditions that would obviate the need for DDQ or other oxidants. Anhydrous Suzuki conditions, we hypothesized, would give products without any needed postsynthetic oxidation and would avoid decomposition of the halogenated quinone precursors. Experiments using thallium carbonate[52] in the absence of water have been examined previously; however, we turned to fluoride as the activating base.[53]

Ester containing compound **1d** served as our initial target, owing to the ease with which the necessary 5-methyl-2-thiophene carboxylic acid (**2**) can be protected as the methyl ester (**3a**, Scheme 3).[54] We proceeded with the assumption that protection would prevent side reactions and that deprotection would give the desired carboxylic acid functional group. Unfortunately, attempts at deprotection of **1d** using standard methods[55] either led to decomposition or returned only the starting material.

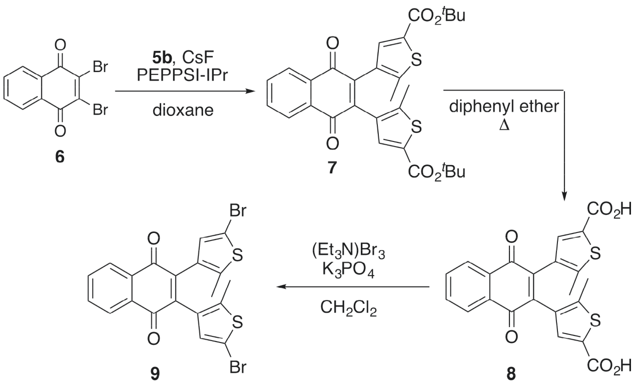
Scheme 3. Synthesis of Required Boronic Acid 5



With consideration to the difficulty encountered in hydrolyzing the methyl ester, we turned our attention to the synthesis of the more labile *t*-butyl analogue (Scheme 3). Starting with compound **2**, we employed the method of Wright[56] to protect the acid functionality to give *t*-butyl ester **3b**. Using the methods of Hartwig[57] and Tatsuo,[58] the 4-position was borylated to give compound **4b**. While Hartwig has shown that boronic acids can be obtained by treating pinacol esters with sodium periodate and aqueous hydrochloric acid, we were concerned that these conditions would lead to unwanted deprotection of the *t*-butyl ester. To our delight, the use of a weaker acid, oxalic acid, in place of hydrochloric acid gave desired compound **5b** with the *t*-butyl protecting group intact. The corresponding methyl ester compounds **4a** and **5a** are obtained using the same procedures as their *t*-butyl analogues.

To access our desired qDAEs (compounds **7−9**; Scheme 4), we started by treating 2,3-dibromo-1,4-naphthoquinone (**6**)[59] with compound **5b**, cesium fluoride, and catalytic PEPPSI-IPr[60] in anhydrous dioxane. Compound **1d** is obtained in a similar fashion. While several traditional methods for deprotection of the *t*-butyl group exist, we found that heating **7** in diphenyl ether

Scheme 4. Synthetic Route to the Ester, Carboxylic Acid, and Halogen Functionalized Photochromic qDAEs in This Study



(bp = 259 °C) for 2 h afforded dicarboxylic acid **8**. Treatment of **8** with tetrabutylammonium tribromide[61] affords dibromide **9**. Both **8** and **9** can undergo further synthetic manipulation at either the carboxylate or aryl-bromide positions. It is worth noting that compound **9** has previously been obtained by brominating **1a**, which is available through a Stille coupling.[25]

We first examined **1d**, **7**, **8**, and **9** by ^{1}H NMR spectroscopy. All show the expected number of and multiplicity for peaks in the open forms. Using **1d** as a model compound, irradiation of an NMR sample with short-wavelength visible light (405−410 nm) gave ∼22% of the ring-closed form (Supporting Information). This result is similar to the work of Deng and Liebeskind,[25] and no attempt was made to force ring closure using strong Lewis acids. Interestingly, the thienyl proton on **1d**, which appears as a broad singlet centered at 7.42 ppm in the open form, shifts to 8.29 ppm, now as a sharp singlet, in the closed form. The downfield shift is expected as the conjugation imparted by cyclization allows for effective electron withdrawal by the quinone ring. Similarly, both the ester methyl group and thienyl methyl group experience downfield shifts, though much less pronounced. Compounds **1d** and **7** have nearly identical spectra; only the ester alkyl groups have different chemical shifts.

UV−vis spectroscopy of compounds **7** and **8** showed distinct spectra between ring-open and ring-closed forms. The open form of **7** (Figure 1) has a peak absorption at 412 nm and an onset of absorption at ∼500 nm, longer than most previously reported qDAEs. Upon irradiation, a new absorption band appears. The closed form of compound **7** exhibits a long-wavelength absorption band centered at 612 nm; a second absorption band at 441 nm is due to the presence of both the ring-open and ring-closed forms given that complete ring closure was not observed by ^{1}H NMR. The onset of absorption for the closed form of **7** occurs at ∼762 nm. Compound **8**, upon ring closure, exhibits significant broadening of the long-wavelength absorption band (Supporting Information), presumably due to hydrogen bonding in solution as this broadening is not observed in the spectrum of **7** in the closed form.

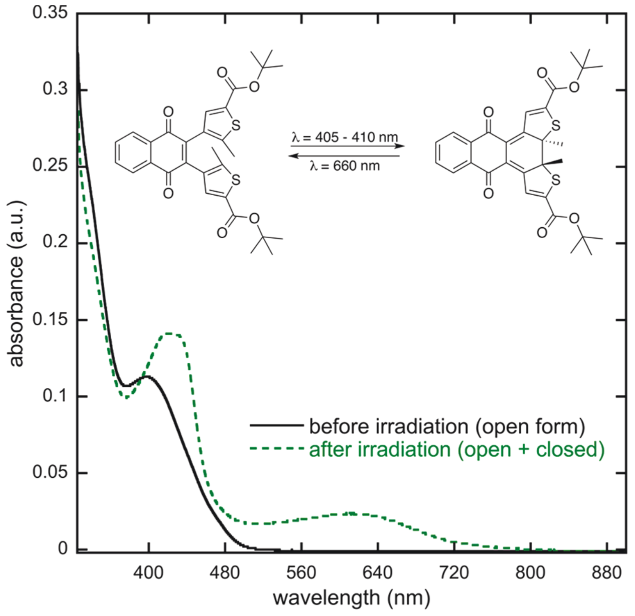


Figure 1. Absorption spectrum of **7** in acetone (5.7×10^{-5} M) before and after irradiation with 405−410 nm light.

The absorption spectrum for brominated compound **9**, in contrast to that of **7** and **8**, shows only minor changes upon irradiation (see Supporting Information); the reason for this diminished response is not immediately apparent though it may be due to some deactivation pathway available to the excited state as a consequence of the heavy atom effect. The long-wavelength absorption due to the closed form has a maximum near 560 nm, much shorter than that for compounds **7** and **8**. This hypsochromic shift informs that the electron-withdrawing nature of the thienyl substituents greatly impacts the absorption spectrum and electronics of the closed form qDAE. Bromine is not as strong an electron-withdrawing group when compared to ester or carboxylic acid functionalities. Given this structure−property relationship, we theorize that even stronger electron-withdrawing groups would lead to more prominent changes in absorption spectra between open and closed forms, while also shifting the long-wavelength closed form absorption band further into the near IR.

Single crystals of compound **8** were obtained by slow evaporation of chromatographic fractions leading to the formation of two different morphologies: the photoinactive form as orange prisms (**8a**, Figure 2) and the photoactive form as yellow plates (**8b**, Figure 3). A suitable crystal from each morphology was analyzed by X-ray diffraction.

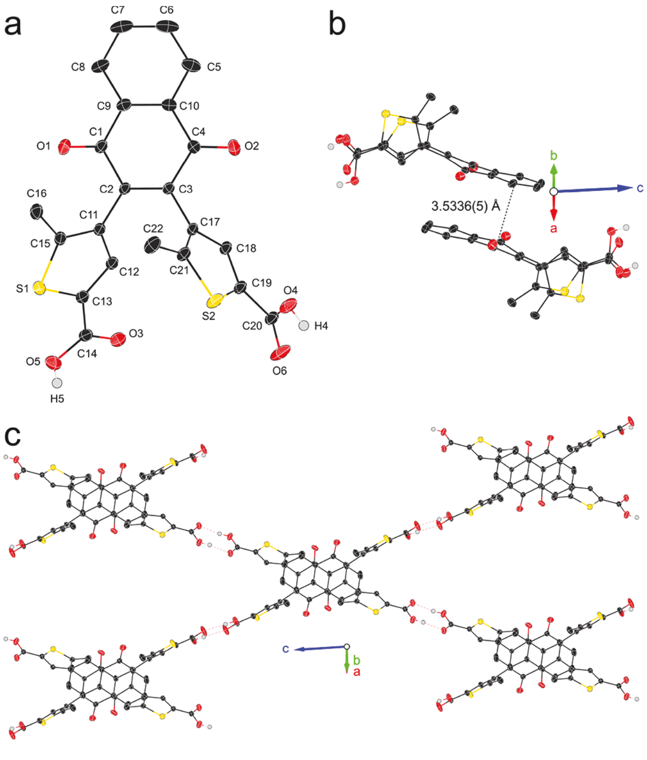


Figure 2. (a) Molecular structure of qDAE **8a**. Aromatic and alkyl hydrogen atoms are omitted for clarity. (b) Face-to-face π···π stacking viewed down [1 1 0]. (c) Hydrogen bonding between π···π stacked dimers viewed down [1 $\bar{1}$ 0].

The orange prisms of **8a** crystallize in the centrosymmetric space group $P\bar{1}$ with one qDAE molecule in the asymmetric unit. The crystal structure of **8a** assumes the parallel conformation leading to photoinactivity in the solid state.[62,63] Dimers of this qDAE form parallel to the [1 $\bar{1}$ 0] through face-to-face π···π stacking between the quinoid and benzenoid rings separated by a distance of 3.5336(5) Å (Figure 2b). Each dimer hydrogen

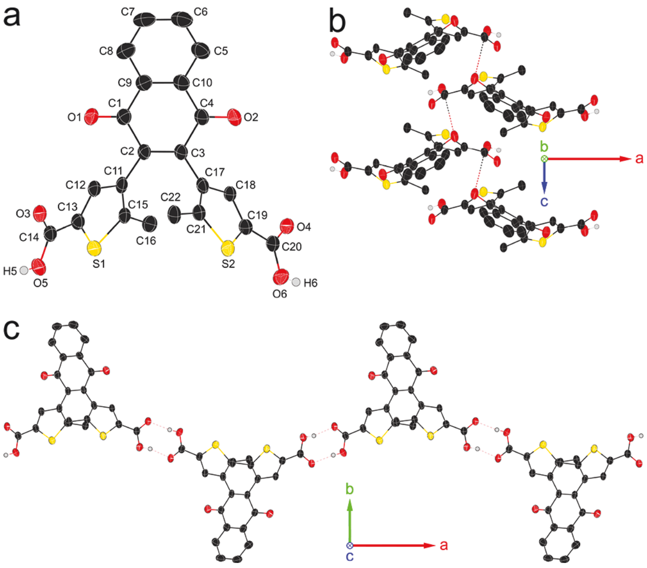


Figure 3. (a) Molecular structure of qDAE **8b**. Aromatic and alkyl hydrogen atoms are omitted for clarity. (b) Electrostatic interaction between quinoidal oxygen and carboxyl carbon. (c) Infinite chain imposed by hydrogen bonds between carboxylic acids on adjacent qDAE molecules.

bonds to four neighboring dimers through the carboxylic acid groups forming 2D sheets (Figure 2c, Table S1) that possess solvent-accessible pores parallel to $[1\ \bar{1}\ 0]$. Attempts to model the electron density within the pores, presumably arising from highly disordered solvent molecules, were unsuccessful. The electron density was subsequently removed using the SQUEEZE routine in PLATON.[64]

The yellow plates of **8b** crystallize in the noncentrosymmetric space group $Pna2_1$ with one qDAE molecule in the asymmetric unit. The crystal structure of **8b** assumes the antiparallel conformation with a C−C separation distance of 3.284(6) Å for the carbon atoms involved in photocyclization; this value is characteristic of photoactive DAEs in the solid state.[65] The solid-state photochromism of **8b** will be examined in future work. Each qDAE molecule parallel to the *n*-glide plane (or molecule parallel to [0 1/2 1/2]) undergoes an electrostatic interaction between the carbonyl carbon adjacent to the thiophene ring of one molecule and the quinoidal oxygen on the backbone of a neighboring molecule (Figure 3b, C14 ··· O1^{i} = 3.048(6) Å, (i) = 1/2−x, −1/2−y, 1/2+z).[66] In addition, each **8b** qDAE molecule hydrogen bonds with adjacent qDAE molecules through the carboxylic acid groups forming infinite chains with 2-fold helical symmetry along the crystallographic *a*-axis (Figure 3c, Table S2).[67]

In conclusion, we have demonstrated the use of the Suzuki coupling methodology to obtain photochromic quinone-based diarylethenes with previously inaccessible functional groups. These compounds show ideal visible-light absorption characteristics and photoswitchability and are amenable to further synthetic modification. Crystal structure data on a carboxylic acid-terminated qDAE show extensive hydrogen bonding and that potentially photoactive crystals can be obtained. Future work will focus on computations, photocrystallography, and the realization of qDAE based polymers and metal−organic frameworks.

■ EXPERIMENTAL SECTION

All reagents were obtained from commercial sources and used as received unless otherwise noted in the text. Flash column chromatography was accomplished using silica gel purchased from Fisher Scientific (230−400 mesh, grade 60, catalog number S825-212). Polyester-backed TLC silica plates (grade 60 with UV indicator) were obtained from EMD Millipore (catalog number 1.05735.0001). NMR spectra were obtained on a Bruker AVIII-500 spectrometer operating at 500 MHz for ^{1}H NMR spectra and 125 MHz for ^{13}C NMR spectra or on a Bruker DRX-400 spectrometer operating at 400 MHz for ^{1}H NMR spectra and 100 MHz for ^{13}C NMR spectra; the ^{1}H NMR spectrum for **1d** after irradiation (Supporting Information) was acquired on a Varian Inova spectrometer operating at 500 MHz. NMR peaks are referenced to residual solvent signals[68] in either $CDCl_3$ (7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C) or acetone-d_6 (2.05 ppm for ^{1}H, 29.84 for ^{13}C). Solution UV−vis experiments were preformed in methylene chloride or acetone using a Shimadzu UV-1800 spectrometer. Solvents for these experiments were used as received and not degassed prior to use. Mass spectrometric analyses were performed at the Pennsylvania State University Proteomics and Mass Spectrometry Core Facility, University Park, PA, with high-resolution mass spectra (HRMS) obtained on a Waters Q-TOF quadrupole time-of-flight mass spectrometer. Data were obtained in either positive or negative mode, as denoted in each compound's characterization. X-ray diffraction data were collected on either a home source or a synchrotron source, as described in the Supporting Information.

5-Methyl-2-thiophene Carboxylic Acid Methyl Ester (3a). The procedure by Rückle[54] was followed; to a 500 mL round-bottom flask was added methanol (250 mL). Concentrated sulfuric acid (11 mL, 18 M) was added slowly and with vigorous stirring. The heat was evolved during the addition; without cooling, 5-methyl-2-thiophene carboxylic acid (9.300 g, 65.42 mmol) was added in a single portion followed by reflux for 24 h. Upon cooling to room temperature, neutralization was achieved by the addition of small portions of sodium carbonate. Some solids were present after complete neutralization and were removed by suction filtration. The filtrate was concentrated to approximately 30 mL and then diluted with water (200 mL), and the product was extracted with hexanes (3 × 100 mL). The combined hexane phases were dried over magnesium sulfate and filtered, and the solvent was removed under reduced pressure to afford a faint yellow oil (8.910 g, 87%): ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.59 (d, 1H, J = 3.8 Hz), 6.74 (d, 1H, J = 3.3 Hz), 3.83 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, chloroform-*d*) δ 162.6, 147.8, 133.8, 130.8, 126.3, 51.8, 15.6; HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_7H_9O_2S$ 157.0323, found 157.0318.

5-Methyl-2-thiophene Carboxylic Acid *t*-Butyl Ester (3b). This compound has been previously reported,[69] obtained by a different route than presented here, and has not been fully characterized; based on the procedure by Wright and co-workers,[56] a 500 mL round-bottom flask was charged with magnesium sulfate (42.33 g, 351.7 mmol), methylene chloride (200 mL), and concentrated sulfuric acid (6.90 g, 3.75 mL, 70.3 mmol). After stirring the suspension for 5 min, 5-methyl-2-thiophene carboxylic acid (**2**, 10.000 g, 70.33 mmol) was added in a single portion and immediately followed by the addition of *t*-butanol (20.85 g, 28 mL, 281.3 mmol). The reaction was allowed to stir, tightly capped (a rubber septum was used), for 48 h. At this point, the magnesium sulfate was removed by suction filtration, and the filter cake was washed with hexanes (150 mL). Owing to the small particulate size of the magnesium sulfate resulting from stirring for 48 h, the filtration process took several hours. The washings and filtrate were combined and then washed with aqueous sodium hydroxide (1 M, 2 × 40 mL). Upon drying the remaining organic phase over magnesium sulfate and filtration, the solvent was removed under reduced pressure. The resulting oil was chromatographed on silica eluting with 100% hexanes to 10% ethyl acetate (EtOAc) in hexanes. Removal of the solvent afforded a clear, faint yellow oil (9.348 g, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, 1H, J = 3.7 Hz), 6.72 (d, 1H, J = 3.7 Hz), 2.49 (s, 3H), 1.55 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.5, 147.0, 133.1, 133.0, 126.0, 81.2, 28.1, 15.6; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{10}H_{14}O_2SNa$ 221.0612, found 221.0602.

Methyl 5-Methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylate (4a). As in the procedure by Sawamura and co-workers,[70] a 250 mL Schlenk tube was charged with compound **3a** (7.000 g, 44.81 mmol), bis(pinacolato)diboron (B_2pin_2, 6.828 g, 26.89 mmol), and 4,4′-di-*tert*-butylbipyridine (dtbpy, 0.024 g, 0.09 mmol). Heptane (40 mL) was added, and the solution was subjected to three freeze−pump−thaw cycles followed by a nitrogen backfill. Upon warming to room temperature, (1,5-cyclooctadiene)(methoxy)iridium(I) dimer ($[Ir(COD)(OMe)]_2$, 0.030 g, 0.04 mmol) was added under a stream of nitrogen. After approximately 1−2 min, the initially yellow solution turned dark brown; heating at 100 °C was carried out for 24 h. Upon cooling, a white precipitate was visible. The reaction was transferred to a separatory funnel, and a 1:1 solution of hexanes/methylene chloride was added. This organic phase was washed with potassium acetate (0.10 M aqueous, 2 × 50 mL) and brine (50 mL). The remaining organic phase was passed through a short plug of silica eluting with 1:1 hexanes/methylene chloride. A white solid was obtained upon removal of the solvent (12.356 g, 98%); spectral data matched that in the literature:[70] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 3.86 (s, 3H), 2.72 (s, 3H), 1.34 (s, 12H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 159.7, 140.4, 130.1, 129.1, 83.6, 51.9, 24.9, 16.3; HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{13}H_{20}BO_4S$ 283.1178, found 283.1167.

***tert*-Butyl 5-Methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylate (4b).** Following a previously reported procedure,[57,58] in a 250 mL Schlenk flask was combined compound **3b** (5.000 g, 25.21 mmol), B_2pin_2 (3.665 g, 0.57 mmol), dtbpy (0.010 g, 0.04 mmol), and heptane (50 mL). The solution was degassed by three freeze−pump−thaw cycles and then backfilled with nitrogen. Under a stream of nitrogen, $[Ir(COD)OMe]_2$ (0.012 g, 0.02 mmol) was added quickly and the reaction heated to 100 °C and followed until TLC (silica, 5% EtOAc in hexanes) showed that no starting material remained. The reaction solution was passed through a short silica column followed by elution with 100% hexanes to 5% EtOAc in hexanes. The fractions containing the product were collected, affording a white solid upon removal of the solvent (6.743 g, 82%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 2.67 (s, 3H), 1.55 (s, 9H), 1.32 (s, 12 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.6, 159.1, 139.1, 132.7, 128.7, 83.4, 81.2, 28.2, 24.8, 16.3; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{16}H_{25}BO_4SNa$ 347.1464, found 347.1437.

(5-(Methoxycarbonyl)-2-methylthiophen-3-yl)boronic Acid (5a). A modification of the procedure by Hartwig and co-workers was followed.[57] A 250 mL flask was charged with compound **4b** (7.000 g, 24.81 mmol), oxalic acid dihydrate (6.253 g, 49.62 mmol), water (30 mL), and acetonitrile (150 mL). After stirring for 1 min, $NaIO_4$ (7.960, 37.21 mmol) was added in a single portion and the resulting mixture stirred for 2 h. During this time, the reaction increased in cloudiness; a solid mass was apparent when pouring the reaction into a separatory funnel. The material in the separatory funnel was diluted with water (150 mL) and extracted with diethyl ether (5 × 100 mL). A white precipitate remained at the aqueous/organic interface during the extraction process. The combined organic phases were washed with brine (100 mL), dried over magnesium sulfate, filtered, and the solvent removed under reduced pressure. The obtained solid was suspended inhexanes, and then collected by suction filtration as a white solid (4.280 g, 86%): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.97 (s, 1H), 7.22 (br s, 2H), 3.80 (s, 3H), 2.71 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, acetone-d_6) δ 163.0, 159.9, 158.6, 141.1, 130.0, 52.1, 16.4; HRMS (ESI-TOF) *m/z* [M − H]$^-$ calcd for $C_7H_8BO_4S$ 199.0238, found 199.0229.

(5-(*tert*-Butoxycarbonyl)-2-methylthiophen-3-yl)boronic Acid (5b). A modification of the procedure by Hartwig and co-workers was followed.[57] To a 100 mL round-bottom flask was added compound **4b** (3.00 g, 9.25 mmol), oxalic acid dihydrate (2.332 g, 18.50 mmol), acetonitrile (50 mL), and water (10 mL). After stirring for 1 min, $NaIO_4$ (2.968 g, 13.88 mmol) was added in a single portion. After stirring at room temperature for 7 h, TLC (silica, 1:1 hexanes/EtOAc) showed a new spot of low R_f (∼0.1−0.2) and some starting material; stirring was continued for an additional 9 h, at which point TLC showed no starting material. Upon dilution with water (50 mL), the product was extracted with diethyl ether (3 × 50 mL). The ether phases were washed with brine (50 mL) and dried over $MgSO_4$; upon removal of the solvent, a white solid was obtained. This solid was washed with hexanes and water and dried under a vacuum (1.880 g, 84%): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.90 (s, 1H), 7.19 (s, 2H), 2.69 (s, 3H), 1.53 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.0, 158.0, 140.4, 132.3, 81.4, 28.4, 16.4; HRMS (ESI-TOF) *m/z* [M − H]$^-$ calcd for $C_{10}H_{14}BO_4S$ [M − H]$^-$ 241.0708, found 241.0698.

2,3-Dibromonaphthalene-1,4-dione (6). According to the slightly modified procedure by Anuratha and co-workers,[71] a 250 mL round-bottom flask was charged with 1,4-naphthoquinone (5.000 g, 31.62 mmol) and sodium acetate (26.934 g, 316.15 mmol). After holding under a high vacuum for 30 min and then backfilling with nitrogen, acetic acid (AcOH, 125 mL) was added. With vigorous stirring, bromine (15.157 g, 4.88 mL, 94.85 mmol) was introduced in portions over 2−3 min. After the complete addition of bromine, the reaction was refluxed for 2 h, followed by cooling to room temperature overnight. The resulting orange suspension was poured into water (300 mL), and the solids were collected by suction filtration. The resulting filter cake was collected and suspended in a 5 wt % sodium thiosulfate solution with gentle swirling; the solids were again collected and suspended, with stirring, in hot ethanol. Upon cooling to room temperature, a bright yellow solid was collected by suction filtration and dried under a vacuum (6.656 g, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, 2H, *J* = 5.7 Hz, 3.3 Hz), 7.79 (dd, 2H, 5.8 Hz, 3.3 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 175.8, 142.6, 134.5, 130.8, 128.2; HRMS (ESI-TOF) *m/z* [M]$^-$ calcd for $C_{10}H_4Br_2O_2$ 313.8578, found 313.8615.

4,4′-(1,4-Dioxo-naphthalene-2,3-diyl)bis(5-methylthiophene-2-carboxylic acid *tert*-butyl ester) (7). To a 50 mL Schlenk tube was added compound **6** (0.746 g, 2.36 mmol), compound **5b** (1.200 g, 4.96 mmol), cesium fluoride (1.510 g, 9.91 mmol), and 1,4-dioxane (10 mL). The yellow mixture was subjected to three freeze−pump−thaw cycles and then backfilled with nitrogen. PEPPSI-IPr (0.064 g, 0.09 mmol) was quickly added under a stream of nitrogen, and the reaction was refluxed for 15 h and then cooled to room temperature. After dilution with EtOAc (200 mL), the organic phase was washed with water (3 × 50 mL), followed by brine (50 mL). The remaining organic phase was dried over $MgSO_4$ and then adsorbed onto silica followed by chromatography on silica eluting with 100% hexanes to 25% EtOAc in hexanes. The pure fractions were collected; upon removal of the solvent under reduced pressure, a dark green solid was obtained (0.954 g, 72%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, 2H, *J* = 5.7 Hz, 3.3 Hz), 7.81 (dd, 2H, *J* = 5.7 Hz, 3.3 Hz), 7.30 (br s, 2H), 2.08 (s, 6H), 1.53 (s, 18H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 183.6, 161.0, 145.9, 141.8, 134.9, 134.1, 132.1, 132.0, 130.6, 126.8, 81.7, 28.2, 15.2; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{30}H_{30}O_6S_2Na$ 573.1376, found 573.1355.

4,4′-(1,4-Dioxonaphthalene-2,3-diyl)bis(5-methylthiophene-2-carboxylic acid) (8). To a 50 mL flask with a reflux condenser were added diphenyl ether (15 mL) and compound **7** (0.800 g, 1.45 mmol). The dark green solution was refluxed (259 °C) for 2 h. After cooling, the product was precipitated by the slow addition of the reaction solution to stirring hexanes. The resulting solid was collected by suction filtration, dissolved in acetone, and then adsorbed onto silica followed by chromatography on silica eluting with 1:1 hexanes/EtOAc to 100% EtOAc to 5% AcOH in EtOAc. The photochromic fractions were collected; upon removal of the solvent under reduced pressure, a dark green solid was obtained (0.362 g, 57%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.15 (dd, 2H, *J* = 5.7 Hz, 3.3 Hz), 7.92 (dd, 2H, *J* = 5.7 Hz, 3.3 Hz), 7.54 (s, 2H), 2.24 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, acetone-d_6) δ 184.3, 162.8, 147.3, 142.8, 137.1, 134.8, 133.2, 132.7, 130.8, 127.1, 15.1; HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{22}H_{15}O_6S_2$ 439.0310, found 439.0281.

2,3-Bis(5-bromo-2-methylthiophen-3-yl)naphthalene-1,4-dione (9). To a 35 mL pressure tube were added **8** (0.100 g, 0.23 mmol), anhydrous K_3PO_4 (0.102 g, 0.48 mmol), and tetrabutylammonium tribromide (0.231 g, 0.48 mmol). Acetonitrile (5 mL) was added, and the capped tube was heated to 100 °C. During the first few minutes, the reaction clarified slightly and went from a white-green mixture to orange. After stirring for 24 h, the reaction was cooled to room temperature and diluted with methylene chloride (50 mL). The cloudy mixture was then washed with water (2 × 30 mL), saturated aqueous $NaHCO_3$ (30 mL), sodium thiosulfate (10%, 30 mL), and finally with brine (30 mL). The remaining organic phase was dried over magnesium sulfate, filtered, and adsorbed onto silica, followed by chromatography on silica eluting with 100% hexanes to 20% EtOAc in hexanes. The yellow band was collected; those fractions deemed pure were combined, and the solvent was removed to give a brown solid with a metallic luster (0.043 g, 37%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, 2H, J = 5.8 Hz, 3.3 Hz), 7.80 (dd, 2H, J = 5.8 Hz, 3.3 Hz,), 6.64 (s, 2H), 2.02 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.6, 141.5, 140.9, 134.1, 132.0, 131.5, 130.4, 126.8, 108.0, 14.8; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{12}Br_2O_2S_2Na$ 528.8543, found 528.8516.

4,4′-(1,4-Dioxo-naphthalene-2,3-diyl)bis(5-methylthiophene-2-carboxylate methyl ester) (1d). Compounds **6** (0.376 g, 1.19 mmol) and **5a** (0.500 g, 2.50 mmol) were combined in a 100 mL Schlenk tube followed by the addition of cesium fluoride (0.759 g, 5.00 mmol) and 1,2-dimethoxyethane (10 mL). The mixture was degassed by three freeze−pump−thaw cycles and then backfilled with nitrogen. Upon warming to room temperature, and under a stream of nitrogen, PEPPSI-IPr (0.016 g, 0.02 mmol) was quickly added. After refluxing for 18 h, TLC (silica, 10% EtOAc in hexanes) showed a photochromic spot of a low R_f. Removal of the solvent led to a brown solid that was adsorbed onto silica and chromatographed on silica eluting with 100% hexanes to 30% EtOAc in hexanes. The photochromic spots were collected, and solvent was removed to afford a yellow powdery solid that was pure by ^1H NMR (0.514 g, 57%). Alternatively, purification can be achieved by passing the crude product (after aqueous workup extracting with chloroform) through a short plug of silica eluting with chloroform. The solid obtained after removal of the solvent is heated in methanol until boiling. After storing cold overnight, the remaining solids can be collected by suction filtration, washed with cold methanol, and dried under a high vacuum. In this case, a greenish solid is obtained in a lower yield (36% yield) than achieved by chromatography but at the same level of purity: ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, 2H, J = 5.7, 3.3 Hz), 7.81 (dd, 2H, J = 5.8, 3.3 Hz), 7.42 (br s, 2H), 3.84 (s, 6H), 2.09 (s, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 183.5, 162.1, 146.6, 141.6, 135.6, 134.2, 131.9, 130.8, 129.8, 126.8, 52.1, 15.3; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{18}O_6S_2Na$ 489.0443, found 489.0436.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.9b02632.

Crystal structure of **8b** (CIF)
Crystal structure of **8a** (CIF)
^1H and ^{13}C NMR data for all compounds, UV−vis data for compounds **8** and **9**, hydrogen bonding tables for **8a** and **8b**, and additional experimental information (PDF)

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Notes

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