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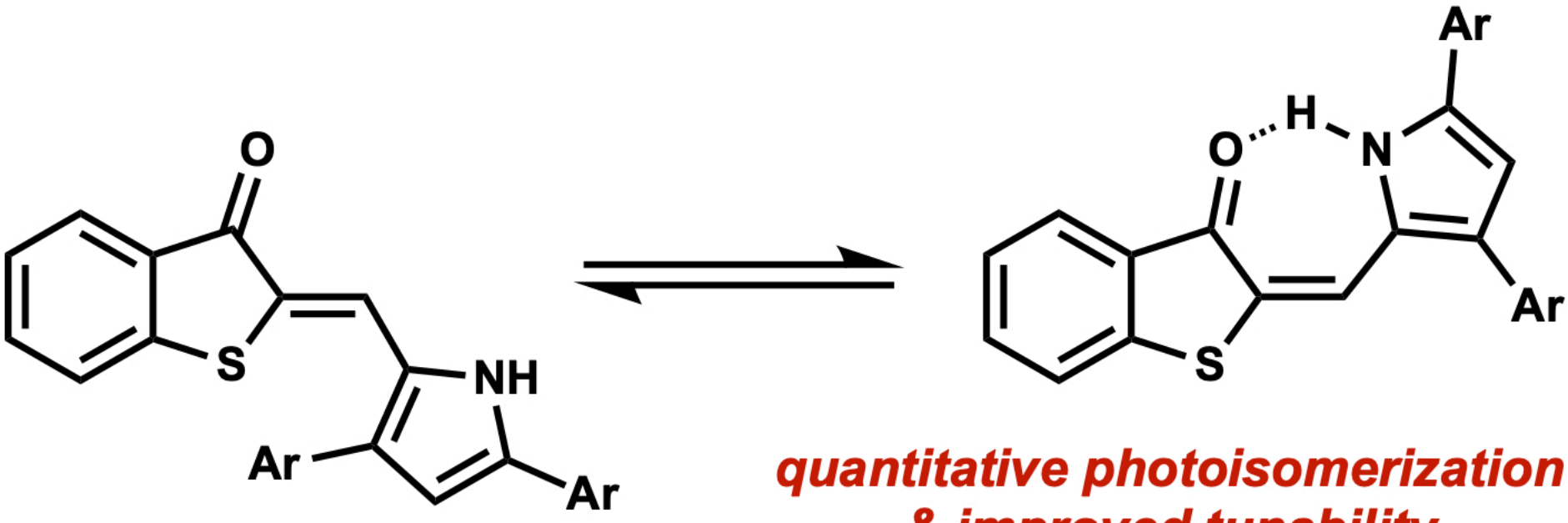

quantitative photoisomerization & improved tunability

Effects of π-Extension on Pyrrole Hemithioindigo Photoswitches

Joshua E. Zweig, Tongil A. Ko, Junrou Huang, and Timothy R. Newhouse*

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Abstract: The most red-shifted hemithioindigo photoswitches have been identified through systematic introduction of aryl units to a parent pyrrole hemithioindigo photoswitch. Increasing the size of the 5'-aryl substituent is ineffective at producing further redshifted chromophores. A second generation of 3',5'-diarylated photoswitches which possess increased tunability is reported. Experimental and computational evidence indicates the 4' position is electronically isolated from the bulk of the conjugated system.

1. Introduction: Visible-light activated small molecule photoswitches comprise a class of molecular machines that are the subject of a great deal of interest in fields such as drug delivery, data storage, and photomechanical polymers.[1] Seminal advances in this field were accordingly recognized with the Nobel Prize in Chemistry in 2016.[2] A particular subclass of these compounds, E/Z-type photoswitches, are of particular interest for controlling biological systems due to the large geometric change conferred by double-bond isomerization.[3] Although the history of hemithioindigo photoswitches, such as **1**, dates to the early 20th century, they have recently received considerable attention in the last five years by Dube[4] and our group[5] in part due to their longer wavelength absorption relative to the more well explored azobenzenes. Our laboratory has recently reported a new class of E/Z-type photoswitches typified by structure **2**, which are designed to possess a key intramolecular hydrogen-bonding interaction in only one of the two isomeric states (Figure 1).[5] As a result of this interaction, these pyrrole hemithioindigo (PHTI) photoswitches can undergo quantitative photoisomerizations using visible light for both isomerization reactions.

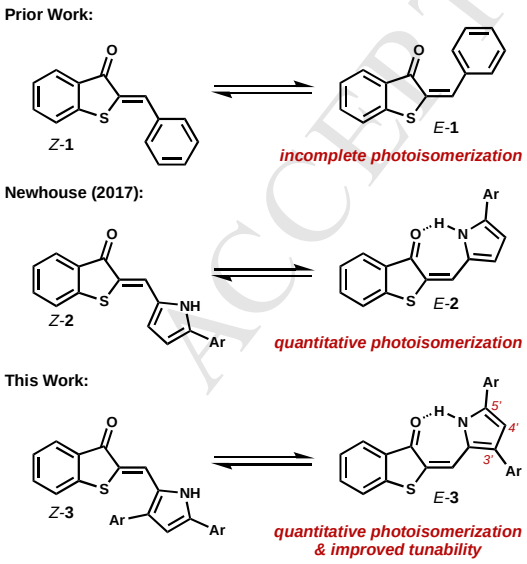
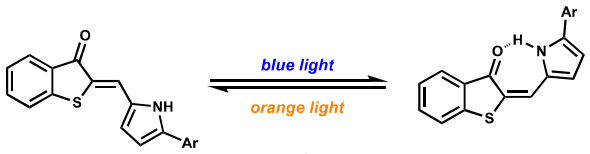
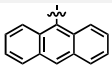
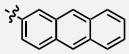
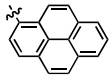
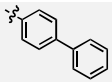
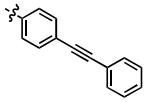


Figure 1. Generations of hemithioindigo and pyrrole hemithioindigo photoswitches.

While the photoswitches we reported undergo quantitative isomerization using blue light for Z→E photoisomerization and red light for E→Z photoisomerization, it would be ideal to induce both isomerizations using light in the infrared window for subsurface drug delivery applications.[6] The amino-substituted photoswitches described in our previous report undergo isomerization at longer wavelengths than their oxygen-substituted analogs, however, they also undergo photobleaching upon repeated irradiation. Therefore, we decided not to test even more electron rich substrates due to photobleaching concerns. Rather, we chose to explore the effects of creating more conjugated π-systems as a strategy towards longer-wavelength photoswitches.[7]



Cmpd	Ar	λ_{max}	PSS [light source]
2a[1]		491 nm (Z) 550 nm (E)	>99% E [460 nm] >97% Z [590 nm]
2b		482 nm (Z) 537 nm (E)	>99% E [460 nm] >99% Z [590 nm]
2c		495 nm (Z) 555 nm (E)	>99% E [460 nm] >99% Z [590 nm]
2d		474 nm (Z) 525 nm (E)	>99% E [490 nm] 99% Z [590 nm]
2e		507 nm (Z) 556 nm (E)	88% E [460 nm] >99% Z [590 nm]
2f		493 nm (Z) 552 nm (E)	>99% E [460 nm] 97% Z [590 nm]
2g		495 nm (Z) 556 nm (E)	96% E [460 nm] >99% Z [590 nm]
2h		498 nm (Z) 558 nm (E)	98% E [460 nm] >99% Z [590 nm]

2. Results and Discussion

Figure 2. A library π-extended pyrrole hemithioindigo photoswitches. (λ_{max} values in CH_2Cl_2, photostationary states determined by HPLC. [1] Ref. 4.)

Upon reinvestigation of our previously described synthesis of arylpyrrole HTIs,[5] it was found that the condensation of appropriate pyrrole-2-carboxaldehydes with benzothiophen-3-one was adequately catalyzed by piperidine, rather than using stoichiometric DBU. This eliminated the need for removal of the DBU-water adduct and provided improved yields and purity (Figure 2). For example, while **2a** was previously obtained in 44% using DBU as base, **2b-h** were each obtained in yields not lower than 76%. If was found that replacement of the 5'-phenyl group (**2a**) with a 5'-(1-naphthyl) moiety (**2b**) provided a photoswitch with shorter wavelength absorption

maxima.[4] The 2-naphthyl isomer **2c**, proved superior, affording longer absorption maxima than **2a** or **2b**. Anthracenyl derivatives **2d** and **2e** were prepared, and a similar trend was observed, with the longer end-to-end 2-anthracenyl PHTI **2e** absorbing at longer wavelength than the 9-anthracenyl analog **2d (***Z*: 474 nm → 507 nm; *E*: 525 nm → 556 nm). This came at the cost of a reduced bathochromic shift and poor photostationary state selectivity. Further extension of the π-system with a pendant 1-pyrenyl moiety (**2f**) provided only a minimal redshift compared to the 5'-phenyl PHTI. Considering the drawbacks of such polycyclic arenes, namely poor solubility and step-intensive routes for tuning polycyclic aromatic hydrocarbons via substituent effects, we decided against further exploration of these avenues of π-extension.

At this point instead of employing larger fused aromatics, we turned our attention to exploring biphenyl type moieties. In our previous report, we had previously observed that the introduction of an aromatic group at the 5'-position not only resulted in a redshift, but also an augmented bathochromic shift relative to a photoswitch without substitution on the pyrrole. It had been hypothesized that this increased bathochromic shift was the result of the increased change in geometry of the longer π-system. Therefore, **2g** was synthesized to see if this effect would manifest itself further. However, **2g** was found to possess a redshift of only 4-6 nm of either isomer was observed relative to the 5'-phenyl PHTI **(2a**). Introduction of an alkynyl linker (**2h**) led to a further small redshift, potentially due to diminished out-of-plane distortion of the two arenes. Unfortunately, these substantial increases in end-to-end distance change upon isomerization did not translate to a substantial increase in the bathochromic shift of the two isomers. Although some redshifting was observed with these compounds, the solubility and synthetic challenges associated with the fused arenes are still present, albeit to a somewhat lesser degree.

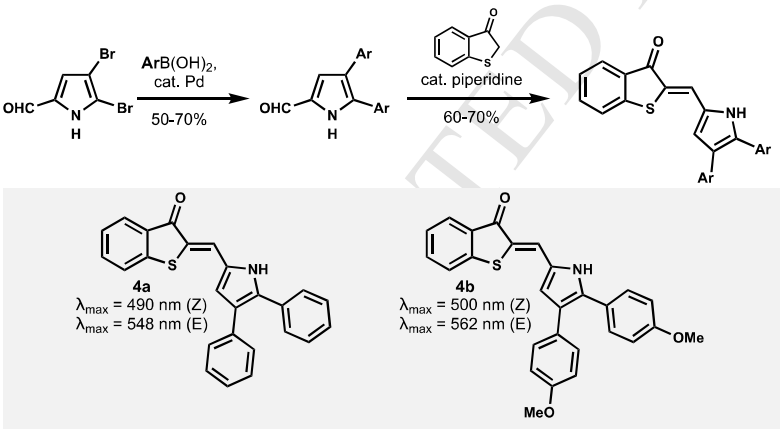


Figure 3. 4',5'-bisarylated pyrrole hemithioindigo photoswitches.

Therefore, we hypothesized that instead of extending the 5'-substituent, installation of an additional arene moiety on the pyrrole could induce the desired redshift. Synthesis of the 4,5-diaryl photoswitches **4a-b** was accomplished by double Suzuki-Miyaura coupling of 4,5-dibromopyrrole-2-carboxaldehyde and then aldol condensation with benzothiophen-3-one. Diphenyl photoswitch **4a** (Figure 3), however, showed no discernible redshifting over its monoarylated congener **2a**. Installation of electron-donating methoxy substituents at the *para* position of both arenes also proved inferior to the single 5'-*p*-methoxy photoswitch.

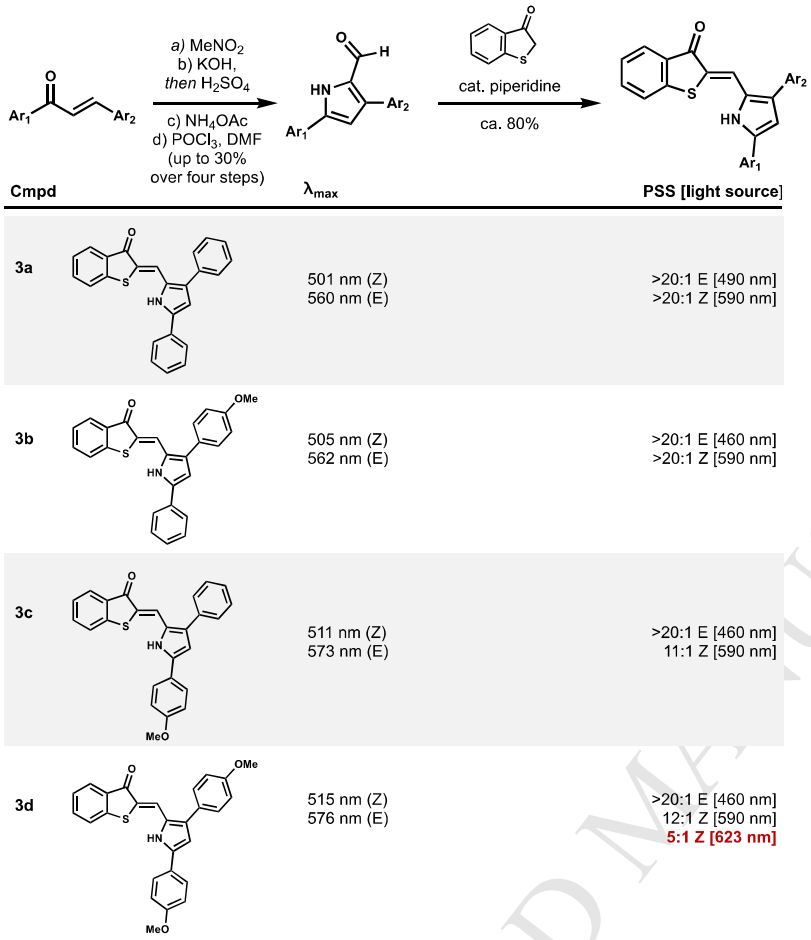


Figure 4. 3',5'-bisarylated pyrrole hemithioindigo photoswitches. (λ_{max} values in CH_2Cl_2, photostationary states determined by ^1H NMR in CD_2Cl_2.)

Steric distortion between the 4',5'-diaryl groups may lead to these poor properties, thus, a library of 3',5'-diaryl photoswitches was synthesized. The precursor diarylpyrrole-2-carboxaldehydes are conveniently synthesized from a chalcone starting material, enabling the synthesis of differentially substituted diarylpyrrole photoswitches with complete regioselectivity.[8] Fortuitously, as shown in Figure 4, it was found that introduction of a 3'-aryl group (**3a**) provided a 10 nm redshift when compared to **2a** (*Z*: 491 nm → 501 nm; *E*: 550 nm → 560 nm). In addition to this redshift, introduction of a methoxy group to the 3'-arene (**3b**) substituent provides a 4 nm redshift, roughly half as large of the 10 nm shift induced by addition of a methoxy group to the 5'-arene (**3c**). Remarkably, these substituent effects appear to be additive, with bis-*p*-methoxy photoswitch **3d** displaying a redshift of approximately 15 nm relative to the unsubstituted **3a**. Like the previously disclosed first-generation 5'-aryl photoswitches, these compounds undergo highly selective photoisomerization in both directions using visible light. These photoswitches are also considerably more soluble in organic solvents. This increase in solubility is sufficient for convenient observation and quantitation of the photoisomerization via ^1H NMR (Figure 5).

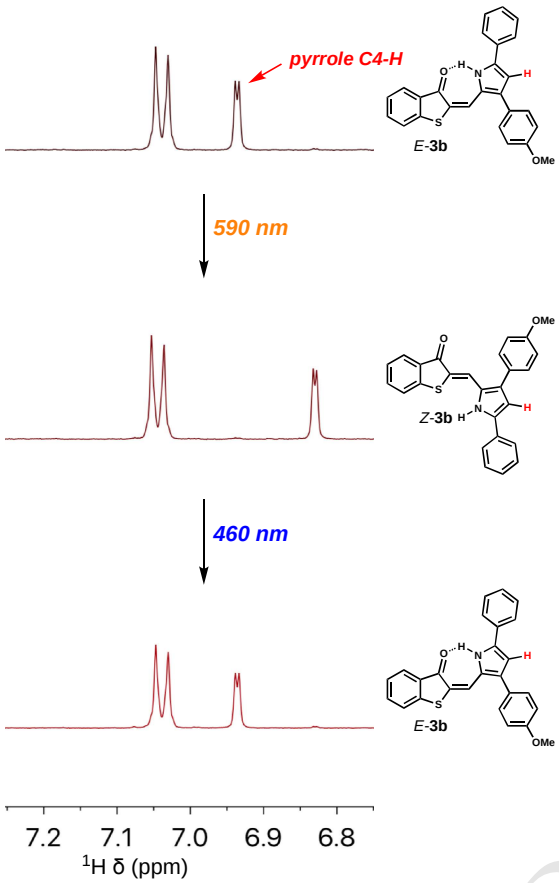


Figure 5. NMR isomerization of 3b. Top to bottom: Prior to irradiation; after irradiation with 460 nm light; after irradiation again with 590 nm light (in CD_2Cl_2).

As described above, our initial hypothesis was that out-of-plane distortions between the pendant aryl groups in **4a** and **4b** lead to diminished conjugation such that two non-planar aryl groups provided similar redshifting to a single, more co-planar π-extension. Separating these groups as in the series **3a-d** allowed their effects to be additive. However, when monoarylated photoswitches **5** and **6** were synthesized (by condensation of the appropriate pyrrole carboxaldehydes with benzo[*b*]thiophen-3(2*H*)-one), we were surprised to observe that even in the absence of an out-of-plane distortion, 4'-phenyl switch **5** was markedly less redshifted than its 5'-phenyl isomer **2a** (Figure 6). Photoswitch **6** was slightly redshifted relative to **5**, although still substantially blueshifted relative to **2a**.

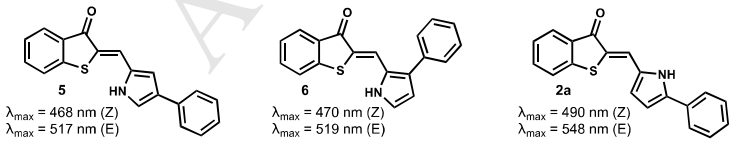


Figure 6. Monoarylated pyrrole hemithioindigos. (λ_{max} values in CH_2Cl_2.)

After these observations were made, we turned to DFT calculations to understand the physical basis of these disparate electronic effects between the arylpyrrole hemithioindigos

analogs[9]. Structures for photoswitches **5**, **6**, **2a**, **4a**, and **3a**, were optimized at the B3LYP/6-31G* level of theory. While the out-of-plane distortions in **4a** were apparent, another striking trend was observed. Regardless of the presence of other arenes, the coefficients of the LUMO on the 4' aryl groups were minimal. This indicates that electronic insulation of the 4' position is responsible for the poor performance of photoswitches possessing aryl groups at this position. The extent of the LUMO on 3' phenyl groups was diminished but non-zero, in line with the reduced redshifts observed by introduction of electron-donating substituents at this position (**3b, 3d**). These results suggest that the minimal redshifting of 4' aryl pyrrole HTIS is primarily a consequence of electronics, rather than steric out-of-plane distortions.

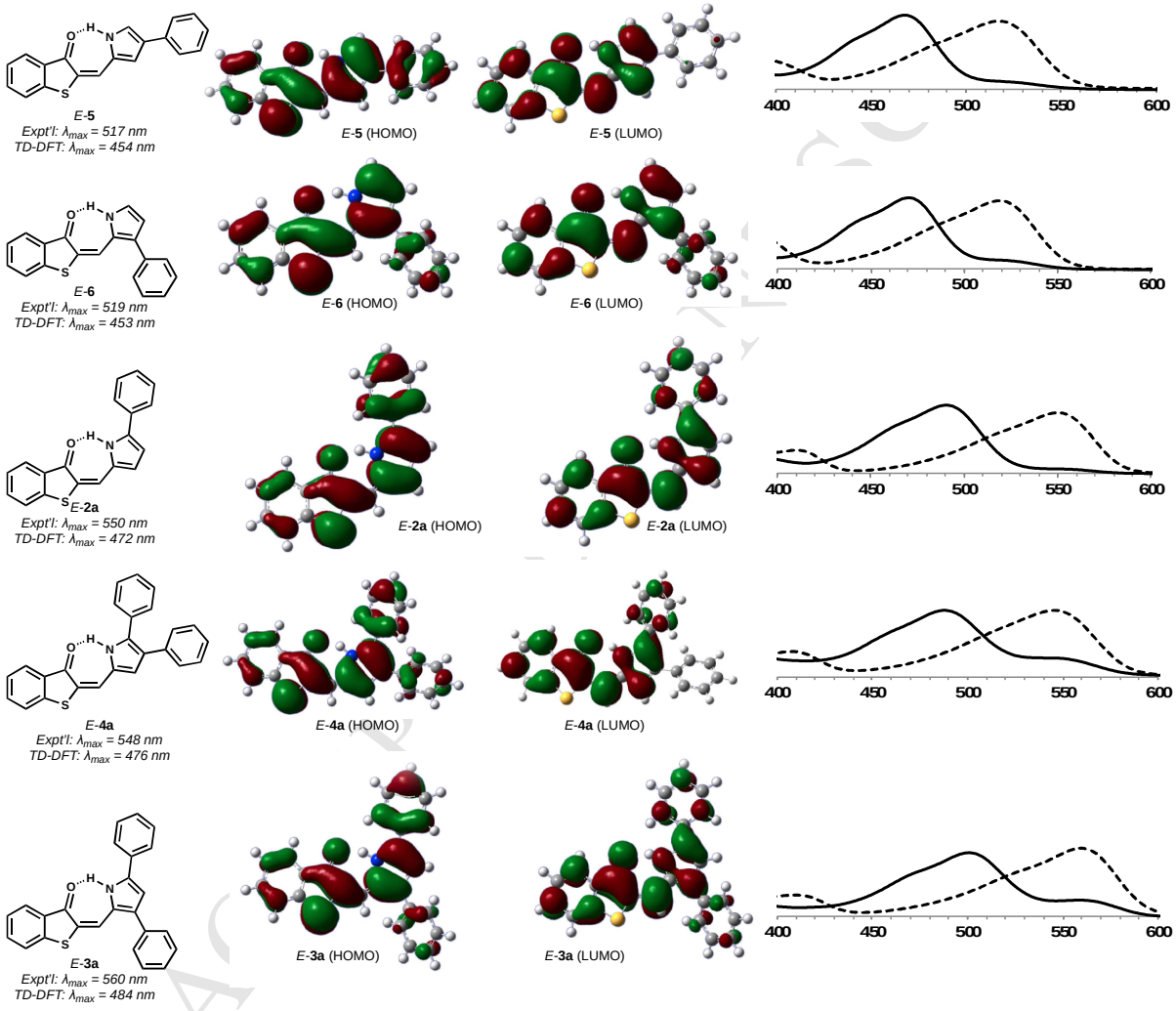


Figure 7. Molecular orbitals of arylated pyrrole hemithioindigos. *Left:* Molecular orbitals of pyrrole HTI photoswitches. Calculations at the B3LYP/6-31G* level of theory. *Right:* Experimental UV/Vis spectra (CH_2Cl_2, 0.01 mg/mL) Solid lines = Z-isomers, dashed lines = E-isomers.

3. Conclusion

In conclusion, we have mapped the effects of π-extension on the pyrrole moiety of pyrrole hemithioindigos. Previously reported 5'-arylated pyrrole hemithioindigos are a uniquely selective class of visible-light photoswitches. Substitution of the pyrrole unit with an aryl group leads to increasing conjugation in the following order: 4' < 3' < 5'. Experimental and computational evidence suggests the 4' position is mostly electronically isolated from the system. Combining 3'-and 5'-aryl substitution results in a system with improved solubility that maintains the high selectivity of the first generation while providing more opportunities for tuning and derivatization. Importantly, the computational results described herein demonstrate that this system is amenable to redshift predictions based on DFT calculations.

4. Experimental

4.1 General Experimental Procedure

All reactions were carried out under an inert nitrogen atmosphere with dry solvents under anhydrous conditions unless otherwise stated. All reactions were capped with a rubber septum, or Teflon-coated silicon microwave cap unless otherwise stated. Stainless steel cannula or syringe were used to transfer solvent, and air- and moisture sensitive liquid reagents. Reactions were monitored by thin-layer chromatography (TLC) and carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as the visualizing agent and potassium permanganate, an acidic solution of p-anisaldehyde, a solution of 2,4-dinitrophenylhydrazine, or vanillin as developing agents. Flash column chromatography employed SiliaFlash® P60 (40-60 µm, 230-400 mesh) silica gel purchased from SiliCycle Inc.

4.2 Materials

All reaction solvents were purified using a Seca solvent purification system by Glass Contour, except for *n*-butanol. Anhydrous n-butanol was purchased from Sigma-Aldrich and degassed by bubbling N_2 through the solvent while sonicating for 30 minutes. $Pd(OAc)_2$ was purchased from Strem Chemical Inc. XPhos (CAS: 564483-18-7) was purchased from Oakwood Chemical. All other reagents were used as received without further purification, unless otherwise stated.

4.3 Instrumentation

All new compounds were characterized by means of ^{1}H-NMR, ^{13}C-NMR, FTIR (thin film), and HR-MS. Copies of the ^{1}H- and ^{13}C-NMR spectra can be found at the end of each experimental procedure. NMR spectra were recorded using a Varian 400 MHz NMR spectrometer, Varian 500 MHz NMR spectrometer, or a Varian 600 MHz NMR spectrometer. All ^{1}H-NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual dichloromethane in CD_2Cl_2 (5.32 ppm), residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$), or residual DMSO (2.50 ppm) in DMSO-d_6. All ^{13}C-NMR data are reported in ppm relative to CD_2Cl_2 (54.0 ppm), $CDCl_3$ (77.16 ppm), or DMSO-d_6 (39.52) and were obtained with ^{1}H decoupling unless otherwise stated. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, and a = apparent. All IR spectra were taken on an FT-IR/Raman Thermo Nicolet 6700. High resolution mass spectra (HR-MS) were recorded on a

Bruker microTOF mass spectrometer using ESI-TOF (electrospray ionization-time of flight). All UV/Vis spectra were taken on a Cary 3E Spectrophotometer using quartz cuvettes purchased from Starna Cells (P/N: 29-Q-10) and spectrometric or HPLC grade solvents. Photoirradiation was carried out with LEDs purchased from Mouser Electronics (405, 460, 523, 567, 590, 623, 660, and 740 nm) or Roithner-LaserTechnik GmbH (420, 490, 505, 690, and 720 nm). For photostationary state determination, samples were irradiated in borosilicate glass HPLC vials purchased from Thermo Scientific (C4000-1). For part numbers of individual LEDs and detailed description of the irradiation setup, see the accompanying Supplementary Information**.** HPLC quantitation of photostationary state composition was performed using an Agilent 1260 HPLC with a Chiralpak IA column ((250 x 4.6mm, 5µM particle size).

4.4 General Procedures

4.4.1 General Procedure for Suzuki coupling with solid aryl bromides

To a flame-dried 5 mL microwave vial flask equipped with a magnetic stir bar was added N-Boc-pyrrole-2-boronic acid (316 mg, 1.5 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5mg, 0.02 mmol, 0.02 equiv), XPhos (19.0 mg, 0.04 mmol, 0.04 equiv), K_3PO_4 (424 g, 2.0 mmol, 2.0 equiv), and aryl bromide (1.0 mmol, 1.0 equiv). The flask was evacuated and backfilled with nitrogen three times, and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To the flask was added degassed (by sonication for 30 minutes with N_2 sparging), anhydrous *n*-butanol [2 mL (0.5 M in ArBr)]. The heterogeneous reaction mixture was stirred vigorously for 2 hours and then poured into ethyl acetate (~20 mL). This mixture was filtered through a pad of silica and concentrated under reduced pressure by rotary evaporation. This product was used without further purification.

To the flask containing the crude product of the crude Suzuki coupling product was added an oven-dried magnetic stir bar. The flask was evacuated and backfilled with nitrogen three times, and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To the flask was added anhydrous THF (10 mL) and then NaOMe (5 wt. % in MeOH; 342 µL, 1.5 mmol, 1.5 equiv). The reaction mixture was stirred until no more starting material was observed by TLC (30 – 60 minutes). The reaction was quenched by the addition of sat. aq. NH_4Cl (10 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were then washed water (1 x 10 mL), brine (1 x 10 mL) and dried over anhydrous Na_2SO_4. . The combined organic layers were then filtered and concentrated under reduced pressure by rotary evaporation. This product was used without further purification.

The crude product from the deprotection was dried by azeotropic distillation with benzene under reduced pressure by rotary evaporation three times. This flask was then evacuated and backfilled with nitrogen, and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To this flask was added anhydrous CH_2Cl_2 (3 mL) and the flask was sonicated to dissolve the solid.

To a flame-dried 25mL round bottomed flask equipped with a magnetic stir bar was added anhydrous CH_2Cl_2 (1 mL), $POCl_3$ (98 µL, 1.05 mmol, 1.05 equiv), and anhydrous DMF (92µL, 1.2 mmol, 1.2 equiv). After stirring for 5 minutes, the solution of 2-arylpyrrole in CH_2Cl_2 was

transferred by syringe to this flask. Upon addition of the arylpyrrole, the solution immediately became brightly colored (color depending on substrate).

After stirring for 8-16 hours, the reaction was concentrated first under a stream of N_2 and then under reduced pressure. When no solvent remained, the flask was backfilled with N_2 and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To this flask was added THF (2 mL) and 3M NaOH (aq) (2 mL). This biphasic mixture was stirred vigorously for 30–60 minutes. To the flask was added H_2O (5 mL) and Et_2O (5 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with water (1 × 20 mL) and brine (1 × 20 mL). The combined organic layers were then dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure by rotary evaporation. Purification by flash column chromatography on silica gel afforded the corresponding aldehydes.

4.4.2 General Procedure for Suzuki coupling with liquid aryl bromides

To a flame-dried 5 mL microwave vial equipped with a magnetic stir bar was added N-Boc-pyrrole-2-boronic acid (316 mg, 1.5 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5mg, 0.02 mmol, 0.02 equiv), XPhos (19.0 mg, 0.04 mmol, 0.04 equiv), and K_3PO_4 (424 g, 2.0 mmol, 2.0 equiv),. The flask was evacuated and backfilled with nitrogen three times, and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To the flask was added degassed (by sonication for 30 minutes with N_2 sparging), anhydrous *n*-butanol [2 mL (0.5 M in ArBr)] and aryl bromide (1.0 mmol, 1.0 equiv). The heterogeneous reaction mixture was stirred vigorously for 2 hours at room temperature and then poured into ethyl acetate (~20 mL). This mixture was filtered through a pad of silica and concentrated under reduced pressure by rotary evaporation. This product was used without further purification as described in the general procedure above.

4.4.3 General Procedure for synthesis of ArylPyrrole–HTI photoswitiches

To a 5 mL flame-dried microwave flask was added benzo[*b*]thiophen-3(2*H*)-one (0.24 mmol, 0.12 equiv) and 5-aryl-2-formylpyrrole (0.2 mmol, 0.1 equiv). The flask was capped with an aluminum–PTFE crimp cap, sealed, and evacuated and backfilled with nitrogen three times. To the flask was then added anhydrous toluene (2 mL, 0.1 M in aldehyde) and piperidine (10 µL, 0.1 mmol, 0.5 equiv). The flask was transferred to a pre-warmed oil bath set to 111 ˚C and stirred for two hours. After two hours the flask was removed from the oil bath and cooled to room temperature and then to 0 ˚C in a water-ice bath. To the flask was added hexanes (5 mL) and the flask was allowed to sit for an addition 10–30 minutes. The mixture was the filtered, and the precipitate was then triturated with hexanes to until the filtrate ran clear to provide the pure product as a red, blue, or purple solid depending on the substrate.

4.5 Precursor Synthesis

Benzo[b]thiophen-3(2H)-one, 4,5-bis(4-methoxyphenyl)-pyrrole-2-carboxalehyde, and 4-phenyl-pyrrole-2-carboxaldehyde, and 3-phenyl-pyrrole-2-carboxaldehyde were synthesized according to published procedures.

*4.5.1 5-(naphthalen-1-yl)-1H-pyrrole-2-carbaldehyde (**SI-1**):*

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 80:20) afforded the title compound (158 mg, 71%) as a pink solid. **Rf**: 0.32 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.59 (s, 1H), 9.44 (br s, 1H), 8.20 – 8.15 (m, 1H), 7.95 – 7.89 (m, 2H), 7.60 – 7.49 (m, 4H), 7.13 (dd, *J* = 3.9, 2.5 Hz, 1H), 6.64 (dd, *J* = 3.9, 2.5 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.1, 138.9, 134.1, 133.3, 131.2, 129.5, 129.5, 128.8, 127.2, 127.1, 126.5, 125.5, 125.2, 121.9, 112.8. **IR (cm^{-1}):** 3273, 1658, 1628, 1510, 1491, 1423, 1388, 1267, 1228, 1055, 810, 786, 771, 691, 566. **ESI-MS (m/z):** $[M+H]^+$ calc'd for $C_{15}H_{12}NO^+$: 222.1; found: 222.1

4.5.2 *5-(naphthalen-2-yl)-1H-pyrrole-2-carbaldehyde* (**SI-2**):

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 80:20) afforded the title compound (201 mg, 91%) as a lavender solid. **Rf**: 0.30 (hexanes:Et_2O = 1:1) **^{1}H NMR (**600 MHz, $CDCl_3$): δ 9.69 (br s, 1H), 9.56 (s, 1H), 8.07 (s, 1H), δ 7.91 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 7.2 Hz, 1H), 7.72 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.55–7.49 (m, 2H), 7.07 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.77 (dd, *J* = 3.9, 2.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 178.9, 139.9, 133.6, 133.3, 129.2, 129.2, 128.3, 128.0, 127.9, 127.1, 126.8, 124.1, 123.2, 122.7, 109.6. **IR (cm^{-1}):** 3280, 1645, 1488, 1425, 1288, 1261, 1049, 1006, 787, 766, 718, 473. **ESI-MS (m/z):** $[M+H]^+$ calc'd for $C_{15}H_{12}NO^+$: 222.1; found: 222.1

4.5.3 *5-(anthracen-9-yl)-1H-pyrrole-2-carbaldehyde* (**SI-3**):

Prepared on 2.0 mmol scale according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 90:10) afforded the title compound (321 mg, 59%) as a yewllow solid. **Rf**: 0.50 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.66 (s, 1H), 9.37 (br s, 1H), 8.56 (s, 1H), 8.05 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.51 – 7.47 (m, 2H), 7.47 –7.43 (m, 2H), 7.26 – 7.24 (m, 1H), 6.62 (dd, *J* = 3.8, 2.5 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.1, 136.4, 133.4, 131.4, 131.3, 128.9, 128.7, 126.8, 125.9, 125.8, 125.6, 121.6, 114.8. **IR (cm^{-1}):** 3250, 1634, 1498, 1411, 1329, 1309, 1282, 1240, 1043, 908, 789, 762, 730, 621. **ESI-MS (m/z):** $[M+H]^+$ calc'd for $C_{19}H_{14}NO^+$: 272.1; found: 272.1

4.5.4 5-(anthracen-2-yl)-1*H*-pyrrole-2-carbaldehyde (**SI-4**):

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 80:20) afforded the title compound (101 mg, 37%) as a yellow solid. **Rf**: 0.27 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.66 (br s, 1H), 9.57 (s, 1H), 8.44 (d, *J* = 19.6 Hz, 2H), 8.22 (s, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 8.04 – 7.98 (m, 2H), 7.69 (d, *J* = 8.9, 1H), 7.50 (td, *J* = 6.3, 5.7, 3.0 Hz, 2H), 7.09 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.82 (at, *J* = 3.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 178.8, 139.7, 133.5, 132.3, 132.2, 131.3, 131.0, 129.4, 128.2, 128.2, 127.2, 126.8 126.4, 125.9, 125.9, 123.9, 122.7, 122.7, 109.6. **IR** (cm^{-1}): 3269, 1644, 1628, 1502, 1474, 1425, 11259, 1217, 1042, 896, 810, 775, 750, 476. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{19}H_{14}NO^+$: 272.1; found: 272.1

4.5.5 5-(pyren-1-yl)-1*H*-pyrrole-2-carbaldehyde (**SI-5**):

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 0:100) afforded the title compound (156 mg, 52%) as a green solid. **Rf**: 0.27 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.64 (s, 1H), 9.62 (br

s, 1 H), 8.45 (d, *J* = 9.3 Hz, 1H), 8.23 (at, *J* = 7.9 Hz, 3H), 8.16 – 8.12 (m, 2H), 8.11 – 8.03 (m, 3H), 7.20 (dd, *J* = 3.8, 2.5 Hz, 1H), 6.79 (dd, *J* = 3.8, 2.5 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.1, 139.5, 133.7, 131.8, 131.6, 131.0, 128.9, 128.9, 128.5, 127.4, 126.8, 126.6, 126.5, 126.0, 125.62, 125.3, 125.1, 124.8, 124.3, 122.2, 113.3. **IR** (cm^{-1}): 3285, 2805, 1651, 1481, 1418, 1251, 1223, 1045, 1044, 1005, 847, 773, 712, 517. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{21}H_{14}NO^+$: 296.1; found: 296.1

4.5.6 5-([1,1'-biphenyl]-4-yl)-1*H*-pyrrole-2-carbaldehyde (**SI-6**):

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 80:20) afforded the title compound (153 mg, 62%) as a grey solid. **Rf**: 0.24 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.53 (s, 1H), δ 9.53 (br s, 1H), 7.68 (s, 4H), 7.65 – 7.60 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.38 (td, *J* = 7.3, 1.2 Hz, 1H), 7.05 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.69 (dd, *J* = 4.0, 2.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 178.7, 141.4, 140.1, 139.3, 133.3, 129.4, 128.9, 127.8, 127.7, 126.9, 125.5, 122.5, 109.1. **IR** (cm^{-1}): 3279, 1644, 1549, 1464, 1389, 1310, 1282, 1211, 1083, 1067, 835, 782, 759, 729, 706. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{17}H_{14}NO^+$: 248.1; found: 248.1

4.5.7 5-(4-(phenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (**SI-7**):

Prepared according to general procedure. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 80:20) afforded the title compound (135 mg, 50%) as a grey solid. **Rf**: 0.30 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.60 (br s, 1H), 9.53 (s, 1H), 7.59 (s, 4H), 7.56 – 7.52 (m, 2H), 7.38 – 7.34 (m, 3H), 7.03 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.68 (dd, *J* = 3.9, 2.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.0, 139.0, 133.6, 132.5, 131.8, 130.3, 128.7, 128.6, 126.0, 125.1, 123.6, 123.1, 122.6, 109.6, 91.3, 89.0. **IR** (cm^{-1}): 3172, 1639, 1489, 1426, 1286, 1261, 1225, 1070, 1052, 1028, 1000, 783, 766, 689, 542. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{19}H_{14}NO^+$: 272.1; found: 272.1

4.5.8 4,5-diphenyl-1*H*-pyrrole-2-carbaldehyde (**SI-8**):

To a flame-dried 20 mL microwave vial equipped with a magnetic stir bar was added N-4,5-dibromopyrrole-2-carboxaldehyde (121 mg, 0.48 mmol, 1.0 equiv), phenylboronic acid (292 mg, 2.4 mmol, 5.0 equiv), $Pd(PPh_3)_4$ (56 mg, 0.048 mmol, 0.10 equiv), and Na_2CO_3 (305 mg, 2.88 mmol, 6.0 equiv). The flask was evacuated and backfilled with nitrogen three times, and sealed with an aluminum crimp cap. To the flask was added water (4.2 mL) and dioxane (4.2 mL, final concentration ~0.6M in pyrrole). The reaction apparatus was then transferred into a pre-heated oil bath and stirred at 80˚C for two hours. After two hours the reaction was cooled to room temperature, poured into H_2O (20 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude brown solid. Purification by flash column chromatography on silica gel (Et_2O/hexanes = 0/10 to 2/8) afforded **SI-8** (107.2 mg, 73%) as a tan solid. **Rf**: 0.37 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.44 (br s, 1H), 9.56 (s, 1H), 7.42 – 7.38 (m, 2H), 7.38 – 7.33 (m, 3H), 7.32 – 7.28 (m, 2H), 7.25 – 7.21 (m, 3H), 7.19 (d, *J* = 2.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.6, 136.6, 135.6, 133.0, 131.6, 129.0, 128.9, 128.87, 128.8, 128.7, 128.6, 126.8, 124.6. **IR** (cm^{-1}): 3252, 3225, 1634, 1608, 1508, 1457, 1381, 1249, 1180, 1032, 805, 745, 526.**ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{19}H_{18}NO_3^+$: 308.1; found: 308.1

4.5.9 3,5-diphenyl-1*H*-pyrrole-2-carbaldehyde (**SI-9**):

To a flame-dried 5 mL microwave vial equipped with a magnetic stir bar was added anhydrous CH_2Cl_2 (1 mL), $POCl_3$ (98 μL, 1.05 mmol, 1.05 equiv), and anhydrous DMF (92μL, 1.2 mmol, 1.2 equiv). After stirring for 5 minutes, a solution of 2,4-diphenylpyrrole (219 mg, 1.0 mmol 1.0 equiv) in CH_2Cl_2 (3 mL) was transferred by syringe to this flask. After stirring for 16 hours, the reaction was concentrated first under a stream of nitrogen and then under reduced pressure. When no solvent remained, the flask was backfilled with nitrogen and then the gas line adapter was quickly replaced with a rubber septum and a balloon of nitrogen. To this flask was added THF (2 mL) and 3M NaOH (aq) (2 ml). This biphasic mixture was stirred vigorously for 30–60 minutes. To the flask was added H_2O (5 mL) and Et_2O (5 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with water (1 × 100 mL) and brine (1 × 100 mL). The combined organic layers were then dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure by rotary evaporation. Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 70:30) afforded the title compound (132 mg, 53%) as a pink solid. **Rf**: 0.39 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.65 (s, 1H), 9.49 (br s, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.47 (at, *J* = 7.6 Hz, 4H), 7.43 – 7.35 (m, 2H), 6.74 (dd, *J* = 2.9, 1.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.3, 138.7, 138.1, 133.4, 130.4, 129.2, 129.2, 129.1, 128.8, 128.8, 123.0, 125.2, 109.0. **IR** (cm^{-1}): 3282, 1640, 1467, 1449, 1260, 1078, 1008, 813, 758, 699, 685, 667, 486. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{17}H_{14}NO^+$: 248.1; found: 248.1

4.5.10 3-(4-methoxyphenyl)-5-phenyl-1*H*-pyrrole-2-carbaldehyde (**SI-10**):

Aldehyde **SI-10** was prepared from 2.0 mmol 3-(4-methoxyphenyl)-4-nitro-1-phenylbutan-1-one according to O'Shea's procedure. [8] Without purification, this crude diarrylpyrrole was then formylated as per the procedure for compounds **SI-1–SI-7.** Purification by flash column chromatography on silica gel (hexanes/Et_2O = 100:0 to 70:30) afforded the title compound (164 mg, 29.5% over three steps) as a pink solid. **Rf**: 0.25 (hexanes:Et2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.62 (d, *J* = 1.1 Hz, 1H), 9.39 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.52 – 7.43 (m, 4H), 7.43 – 7.34 (m, 1H), 7.04 – 6.92 (m, 2H), 6.69 (dd, *J* = 2.8, 1.1 Hz, 1H), 3.87 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.2, 159.6, 138.7, 138.0, 130.4, 130.2, 129.2, 129.02, 128.8, 125.9, 125.2, 114.3, 108.8, 55.4. **IR** (cm^{-1}): 3296, 3276, 1634, 1610, 1467, 1452, 1292, 1251, 1177, 1034, 805, 764, 685. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{18}H_{16}NO_2^+$: 278.1; found: 278.1

4.5.11 5-(4-methoxyphenyl)-3-phenyl-1*H*-pyrrole-2-carbaldehyde (**SI-11**):

Aldehyde **SI-11** was prepared from 1.0 mmol 1-(4-methoxyphenyl)-4-nitro-3-phenylbutan-1-one according to O'Shea's procedure. [8] Without purification, this crude diarrylpyrrole was then formylated as per the procedure for compound **SI-1–SI-7**. Purification by flash column chromatography on silica gel (hexanes/Et^2O = 100:0 to 70:30) afforded the title compound (68 mg, 24.5% over three steps) as a pink solid. **Rf**: 0.25 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.61 (s, 1H), 9.43 (br s, 1H), 7.65 – 7.57 (m, 2H), 7.55 (dd, *J* = 6.9, 1.5 Hz, 2H), 7.46 (td, *J* = 7.4, 1.3 Hz, 2H), 7.43 – 7.34 (m, 1H), 7.06 – 6.88 (m, 2H), 6.64 (dd, *J* = 2.8, 1.2 Hz, 1H), 3.87 (d, *J* = 1.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.1, 160.4, 139.1, 138.5, 133.7, 129.2, 129.0, 128.9, 128.1, 126.8, 123.2, 114.8, 114.8, 108.4, 55.6. **IR** (cm^-

[1]): 3274, 1623, 1601, 1472, 1436, 1381, 1267, 1244, 1189, 1030, 836, 762, 699. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{18}H_{16}NO_2^+$: 278.1; found: 278.1

4.5.12 3,5-bis(4-methoxyphenyl)-1*H*-pyrrole-2-carbaldehyde (**SI-12**):

Aldehyde **SI-12** was prepared from 2.0 mmol 3-(4-methoxyphenyl)-4-nitro-1-phenylbutan-1-one according to O'Shea's procedure.[8,*] Without purification, this crude diarrylpyrrole was then formylated as per the procedure for compound **SI-1–SI-7.** Purification by flash column chromatography on silica gel (hexanes/Et2O = 100:0 to 50:50) afforded the title compound (269.6 mg, 17% over four steps) as a purple solid. **Note*: In a variation from the reported procdure procedure,[8] the Paal-Knorr cyclization step was conducted at 50˚C for 30 minutes to minimize degradation, and then *immediately* formylated. **Rf**: 0.11 (hexanes:Et_2O = 1:1) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.58 (s, 1H), 9.35 (s, 1H), 7.57 (d, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.07 – 6.94 (m, 4H), 6.59 (d, *J* = 2.8 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 179.0, 160.3, 159.8, 139.1, 138.4, 130.3, 128.8, 126.8, 126.2, 123.3, 114.8, 114.4, 108.2, 55.57, 55.54. **IR** (cm^{-1}): 3252, 3225, 1634, 1608, 1508, 1457, 1381, 1249, 1180, 1032, 805, 745, 526. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{19}H_{18}NO_3^+$: 308.1; found: 308.1

4.6 Product Characterization

*4.6.1 Photoswitch **2b**:*

Prepared according to general procedure. Obtained as a red solid (62.9 mg, 89%).**^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.30 (s, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.06 – 8.01 (m, 1H), 7.99 (d, *J* = 7.7 Hz, 1H), 7.98 (s, 1H), 7.86 – 7.79 (m, 2H), 7.76 – 7.69 (m, 1H), 7.67 (d, *J* = 7.3 Hz, 1H), 7.62 (ddd, *J* = 13.4, 7.4, 2.5 Hz, 3H), 7.40 (td, *J* = 8.0, 7.5, 1.9 Hz, 1H), 7.04 – 6.91 (m, 1H), 6.81 (t, *J* = 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 186.5, 144.2, 136. 7, 135.1, 133.6, 131.0, 130.3, 129.5, 129.3, 128.6, 128.5, 126.9, 126.8, 126.3, 126.0, 125.8, 125.6, 125.1, 124.5, 123.4, 123.1, 116.1, 114.3. **IR** (cm^{-1}): 3264, 1649, 1582, 1555, 1484, 1332, 1286, 1215, 1093, 1059, 803, 782, 734, 718. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{23}H_{16}NOS^+$: 354.1; found: 354.1. **UV-Vis:** λ_{max}(Z) = 482 nm, λ_{max}(E) = 537 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.2 Photoswitch **2c**:*

Prepared according to general procedure. Obtained as a red solid (59.7 mg, 84%).**^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.40 (s, 1H), 8.31 (s, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.99 (s, 1H), 7.93 (td, *J* = 8.6, 3.1 Hz, 3H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.13 (s, 1H), 6.92 (s, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 186.9, 144.5, 138.1, 135.5, 133.7, 132.7, 131.4, 130.4, 129.1, 128.8, 128.3, 128.2, 127.3, 126.7, 126.4, 126.3, 125.0, 124.0, 123.5, 123.1, 123.0, 117.3, 112.1. **IR** (cm^{-1}): 3289, 1649, 1581, 1543, 1441, 1281, 1209, 1071, 1065, 1051, 889, 783, 732, 678, 473. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{23}H_{16}NOS^+$: 354.1; found: 354.1. **UV-Vis:** λ_{max}(Z) = 495 nm, λ_{max}(E) = 555 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.3 Photoswitch **2d**:*

Prepared according to general procedure. Obtained as a red solid (63.8 mg, 79 %).**^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.42 (s, 1H), 8.77 (s, 1H), 8.19 (d, *J* = 8.2 Hz, 2H), 7.92 (s, 1H), 7.86 – 7.76 (m, 4H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.60 – 7.49 (m, 4H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 2.9 Hz, 1H), 6.75 (t, *J* = 3.0 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 186.6, 144.2, 135.1, 134.1, 131.0, 130.8, 130.6, 129.1, 128.5, 128.0, 126.6, 126.0, 125.8, 125.6, 124.6, 123.3, 123.0, 116.0, 115.8. **IR** (cm^{-1}): 3223, 1654, 1595, 1581, 1562, 1330, 1288, 1219, 1088, 1043, 880, 782, 614. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{27}H_{18}NOS^+$: 404.1104; found: 404.1. **UV-Vis:** λ_{max}(Z) = 474 nm, λ_{max}(E) = 525 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.4 Photoswitch **2e**:*

Prepared according to general procedure. Obtained as a red solid (62.0 mg, 77%). **^{1}H NMR** ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.46 (br s, 1H), 8.57 (s, 2H), 8.47 (s, 1H), 8.17 (d, *J* = 8.9 Hz, 1H), 8.13 (d, *J* = 7.3 Hz, 1H), 8.10 – 8.07 (m, 1H), 8.01 (s, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.20 – 7.18 (m, 1H), 7.00 – 6.87 (m, 1H). **^{13}C NMR** (126 MHz, DMSO-d_6 @ 120˚C): 186.9, 144.8, 138.3, 135.2, 132.6, 132.1, 132.0, 131.8, 131.1, 130.9, 129.3, 128.5, 128.4, 126.5, 126.5, 126.3, 126.2, 126.1, 126.0, 124.7, 124.7, 124.5, 123.7, 123.2, 123.0, 117.3, 112.1 **IR** (cm^{-1}): 3287, 1642, 1578, 1544, 1441, 1306, 1279, 1205, 1084, 1069, 894, 776, 728, 476. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{27}H_{18}NOS^+$: 404.1; found: 404.1. **UV-Vis:** λ_{max}(Z) = 507 nm, λ_{max}(E) = 556 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.5 Photoswitch **2f**:*

Prepared according to general procedure. Obtained as a brown/red solid (64.2 mg, 76%). **^{1}H NMR** (600 MHz, DMSO-d_6): δ 8.52 (d, *J* = 9.2 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.34 – 8.29 (m, 2H), 8.29 – 8.18 (m, 5H), 8.16 – 8.04 (m, 2H), 7.86 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.69 (td, *J* = 7.5, 1.3 Hz, 1H), 7.40 (td, *J* = 7.5, 1.1 Hz, 1H), 7.08 (d, *J* = 3.9 Hz, 1H), 6.93 (d, *J* = 3.9 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6, 120˚C): δ ^{13}C NMR (126 MHz, dmso) δ 185.9, 143.8, 136.5, 134.1, 130.7, 130.6, 130.01, 130.00, 129.5, 127.4, 127.3, 127.1, 126.6, 126.6, 126.3, 125.8, 125.3, 125.0, 124.8, 124.5, 124.2, 124.0, 123.9, 123.7, 123.6, 123.4, 122.5, 115.8, 114.1. **IR** (cm^{-1}): 32576, 3037, 1649, 1597, 1553, 1421, 1310, 1211, 1093, 1062, 1019, 839, 733. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{29}H_{18}NOS^+$: 428.1; found: 428.1. **UV-Vis:** λ_{max}(Z) = 493 nm, λ_{max}(E) = 552 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.6 Photoswitch **2g**:*

Prepared according to general procedure. Obtained as a bright red solid (62.8 mg,79 %). **^{1}H NMR** (500 MHz, DMSO-d_6 @ 120˚C): δ ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 8.01 (s, 1H), 7.84 (t, *J* = 7.8 Hz, 3H), 7.77 – 7.69 (m, 5H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 2H), 6.93 (t, *J* = 3.3 Hz, 1H), 6.91 (t, *J* = 2.4 Hz, 1H) **^{13}C NMR** (125 MHz, DMSO-d_6 @ 120˚C): δ 185.8, 143.7, 139.1, 138.7, 136.9, 134.0, 130.7, 129.6, 129.4, 128.2, 126.7, 126.5, 125.8, 125.2, 124. 9, 124.5, 123.6, 123.2, 122.1, 116.1, 110.2. **IR** (cm^{-1}): 3279, 1644, 1549, 1464, 1389, 1310, 1282, 1211, 1083, 1067, 835, 782, 759, 729, 706. **ESI-MS** (m/z): $[M+H]^+$ calc'd for $C_{25}H_{18}NOS^+$: 380.1; found: 380.1. **UV-Vis:** λ_{max}(Z) = 495 nm, λ_{max}(E) = 556 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.7 Photoswitch **2h**:*

Prepared according to general procedure. Obtained as a red/brown solid (62.8mg, 77%). **^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.31 (br s, 1H), 7.94 (s, 1H), 7.83 (ad, *J* = 7.8 Hz, 3H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.73 – 7.67 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.58 – 7.52 (m, 2H), 7.50 – 7.42 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 4.0 Hz, 1H), 6.88 (d, *J* = 4.0 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 186.5, 144.1, 136.7, 135.1, 132.1, 131.4, 130.9, 130.9, 130.2, 128.9, 128.8, 126.0, 125.9, 124.6, 124.5, 124.0, 122.5, 122.3, 120.9, 116.7, 111.8, 90.5, 89.4. **IR** (cm^{-1}): 3279, 1646, 1578, 1556, 1318, 1091, 831, 780, 731, 679, 657. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{27}H_{18}NOS^+$: 404.1; found 404.1. **UV-Vis:** λ_{max}(Z) = 498 nm, λ_{max}(E) = 558 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.8 Photoswitch **3a**:*

Prepared according to general procedure (0.25 mmol scale of aldehyde). Obtained as a red/purple solid (77.0 mg, 73 %). **^{1}H NMR** (500 MHz, CD_2Cl_2): δ 8.03 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 2H), 7.54 (ddt, *J* = 20.5, 14.7, 7.3 Hz, 8H), 7.42 (q, *J* = 7.1 Hz, 2H), 7.35 (d, *J* = 3.4 Hz, 2H), 6.98 (d, *J* = 2.6 Hz, 1H). **^{13}C NMR** (126 MHz, CD_2Cl_2): δ 185.1, 145.9, 138.2, 137.9, 135.4, 134.3, 134.2, 131.3, 130.0, 129.9, 129.8, 129.34, 129.1, 128.6, 128.2, 127.1, 125.5, 125.1, 124.0, 123.4, 111.3. **IR** (cm^{-1}): 3057, 1630, 1588, 1521, 1480, 1448, 1290, 1263, 1213, 1074, 1039, 1028. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd $C_{25}H_{18}NOS^+$: 380.1; found 380.1. **UV-Vis:** λ_{max}(Z) = 501 nm, λ_{max}(E) = 560 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.9 Photoswitch **3b**:*

Prepared according to general procedure. Obtained as a red solid (65.4 mg, 80%). **^{1}H NMR** (600 MHz, CD_2Cl_2): δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.60 – 7.51 (m, 4H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.42 – 7.38 (m, 1H), 7.35 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H), 7.33 (s, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 2.6 Hz, 1H), 3.88 (s, 3H). **^{13}C NMR** (151 MHz, CD_2Cl_2): δ 184.8, 160.1, 145.9, 138.3, 138.0, 134.3, 134.0, 131.30, 131.0, 130.1, 129.8, 129.1, 128.8, 127.7, 127.0, 125.5, 125.1, 124.0, 122.9, 114.8, 111.0, 55.9. **IR** (cm^{-1}): 1630, 1605, 1588, 1503, 1443, 1368, 1272, 1246, 1211, 1169m 1071, 921, 759, 596. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for: $C_{26}H_{20}NO_2S^+$:410.1; found 410.1. **UV-Vis:** λ_{max}(Z) = 505 nm, λ_{max}(E) = nm; 0.01mg/mL in CH_2Cl_2.

*4.6.10 Photoswitch **3c**:*

Prepared according to general procedure. Obtained as a red solid (65.3 mg, 80%).**^{1}H NMR** (600 MHz, CD_2Cl): δ 8.02 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.61 – 7.46 (m, 6H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 2.5 Hz, 1H), 3.89 (s, 3H). **^{13}C NMR** (151 MHz, CD_2Cl_2): δ 184.5, 160.9, 145.8, 138.8, 138.4, 135.4, 134.4, 133.84, 129.9, 129.9, 129.4, 128.6, 128.2, 127.1, 126.9, 125.0, 124.0, 123.9, 122.4, 115.3, 110.8, 56.0. **IR** (cm^{-1}): 1631, 1607, 1586, 1504, 1489, 1445, 1366, 1274, 1264, 1179, 1024, 921, 744, 662. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for: $C_{26}H_{20}NO_2S^+$: 410.1; found: 410.1. **UV-Vis:** λ_{max}(Z) = 511 nm, λ_{max}(E) = 573 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.11 Photoswitch **3d**:*

Prepared according to general procedure. Obtained as a purple solid (67.5 mg, 77%). **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 8.02 (d, *J* = 7.9 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.60 – 7.53 (m, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.34 (td, *J* = 6.0, 5.4, 3.4 Hz, 1H), 7.30 (s, 1H), 7.07 (d, *J* = 8.6 Hz,

2H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 2.6 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 184.2, 160.9, 160.1, 145.7, 138.9, 138.5, 134.6, 133.7, 131.0, 130.1, 128.7, 127.7, 127.1, 126.9, 125.0, 123.97, 123.9, 121.9, 115.3, 114.8, 110.6, 56.0, 55.9. **IR** (cm^{-1}): 1608, 1588, 1499, 1276, 1250, 1178, 1032, 922, 832, 797, 735, 529. **ESI-MS** (m/z): $[M+H]^+$ calc'd for: $C_{27}H_{22}NO_3S^+$:440.1; found: 440.1. **UV-Vis:** λ_{max}(Z) = 515 nm, λ_{max}(E) = 576 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.12 Photoswitch **4a**:*

Prepared according to general procedure (0.16 mmol of aldehyde scale). Obtained as a red solid (43.4 mg, 72%). **^{1}H NMR** (600 MHz, DMSO-d_6): δ 12.22 (s, 1H), 7.92 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.74 – 7.65 (m, 1H), 7.45 – 7.37 (m, 5H), 7.37 – 7.30 (m, 5H), 7.31 – 7.25 (m, 1H), 6.90 (d, *J* = 2.4 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 187.0, 144.6, 135.7, 135.6, 134.8, 131.8, 131.3, 129.2, 129.1, 129.0, 128.7, 128.4, 128.1, 127.1, 126.4, 126.3, 125.0, 124.4, 123.0, 116.6. **IR** (cm^{-1}): 3279, 1648, 1577, 1546, 1271, 1188, 1080, 813, 737, 695, 678, 543. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{25}H_{18}NOS^+$: 380.1; found: 380.1. **UV-Vis:** λ_{max}(Z) = 490 nm, λ_{max}(E) = 548 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.13 Photoswitch **4b**:*

Prepared according to general procedure (0.14 mmol of aldehyde scale). Obtained as a red/brown solid (49.2 mg, 82%). **^{1}H NMR** (500 MHz, DMSO-d_6): δ 7.90 (s, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 2.4 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ 182.7, 155.4, 154.4, 140.4, 131.3, 130.8, 127.5, 125.7, 125.3, 124.4, 124.0, 122.3, 122.1, 121.8, 120.9, 120.2, 119.5, 119.0, 112.7, 110.6, 110.5, 51.6, 51.5. **IR** (cm^{-1}): 3285, 2951, 2833, 1640, 1576, 1543, 1453, 1277, 1211, 1179, 1081, 954, 827, 733, 676. **ESI-MS** *(m/z)*: $[M+H]^+$ calc'd for $C_{27}H_{22}NO_3S^+$: 440.1, found: 440.1. **UV-Vis:** λ_{max}(Z) = 500 nm, λ_{max}(E) = 562 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.14 Photoswitch **5**:*

Prepared according to the general procedure. Obtained as a red solid (39.6 mg, 65%). **^{1}H NMR** (600 MHz, DMSO-d_6): δ 7.84 (s, 1H), 7.84 – 7.78 (m, 3H), 7.72 – 7.68 (m, 1H), 7.67 – 7.64 (m, 2H), 7.43 – 7.33 (m, 3H), 7.27 – 7.17 (m, 1H), 7.08 (s, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 187.1, 144.7, 135.6, 134.6, 131.3, 129.6, 129.3, 128.2, 126.6, 126.5, 126.3, 125.3, 124.9, 124.0, 123.5, 123.4, 111.6. **IR** (cm^{-1}): 3252, 1658 1592, 1568, 1515, 1472, 1344, 1310, 1285, 1222, 1145, 1084, 1061, 751, 623, 511. **ESI-MS** (m/z): $[M+H]^+$ calc'd for: $C_{19}H_{14}NOS^+$: 304.1; found: 304.1. **UV-Vis:** λ_{max}(Z) = 468 nm, λ_{max}(E) = 517 nm; 0.01mg/mL in CH_2Cl_2.

*4.6.15 Photoswitch **6**:*

Prepared according to the general procedure. Obtained as a red solid (42.6 mg, 70%). **^{1}H NMR** (600 MHz, DMSO-d_6): δ 7.87 – 7.75 (m, 3H), 7.70 (ddd, *J* = 8.2, 7.2, 1.4 Hz, 1H), 7.49 (dd, *J* = 8.6, 6.8 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.34 (d, *J* = 2.7 Hz, 1H), 6.53 (d, *J* = 2.6 Hz, 1H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ 186.5, 144.3, 135.1, 135.1, 134.9, 130.6, 128.9, 128.8, 127.6, 127.2, 126.2, 125.8, 124.4, 123.6, 122. 6, 122.5, 111.7. **IR** (cm^{-1}): 1632, 1586, 1496,

1442, 1348, 1296, 1176, 1065, 1035, 738, 663. **ESI-MS** (m/z): $[M+H]^+$ calc'd for $C_{19}H_{14}NOS^+$: 304.1; found: 304.1. **UV-Vis:** $\lambda_{max}(Z)$ = 470 nm, $\lambda_{max}(E)$ = 519 nm; 0.01mg/mL in CH_2Cl_2.

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