Electronic Supplementary Material (ESI) for Chemical Science.
This journal is © The Royal Society of Chemistry 2023

Supporting information for: Tethered together: DASA design towards aqueous compatibility

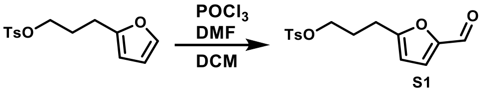
Julie A. Peterson, Natalia M. Neris, Javier Read de Alaniz*

Table of Contents

Synthesis 2
Time dependent UV-Vis Studies: 6
Equilibrium of **3** in toluene, chloroform, methanol, and DMSO measured by ^{1}H NMR 7
Additional photoswitching studies of **3** 9
Solvatochromism of **3-5** 11
Impact of solvent on the equilibrium of **4** and **5** by UV-Vis 13
Photoswitching of **4** and **5** in toluene 16
Behavior of **1** in 75:25 THF:Water 17
Switching of **5** in protic solvents and aqueous solutions 18
Characterization of new compounds 19
DFT Calculations of **3** and **4** 27
- Calculations of **3** 27
    - A 27
    - A-B 28
    - B 29
    - B-B’ 30
    - B’ 31
    - B’-C 33
    - C 34
- Calculations of **4** 35
    - A 35
    - A-B 36
    - B 37
    - B-B’ 39
    - B’ 40
    - B’-C 41
    - C 42
- References 45

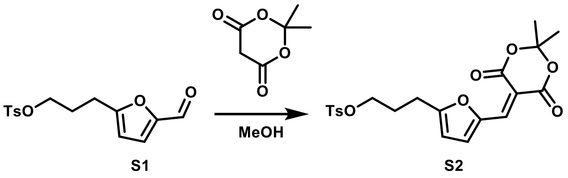
Synthesis

Reagents were purchased and used as arrived unless otherwise stated. 3-(Furan-2-yl)propyl 4-methylbenzenesulfonate[1] and 3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-5(4H)-one[2] were synthesized as previously reported. Normal phase (60 Å, 0.04-0.063 mm, Geduran) silica gel was used for flash column chromatography. ^{13}C and ^{1}H NMR spectra were obtained using Bruker spectrometers (500 MHz with CryProbe Prodigy BBO, or 400 MHz with SmartProbe). FTIR were taken on a Perklin Elmer FT-IR spectrometer (ATR, diamond). High resolution mass spectrometry (HRMS) ESI data was taken on Waters Xevo G2-Xs Time-of-Flight Mass Spectrometer with and electron ionization (ESI) source. Purification via silica plug was done as described previously.[3]



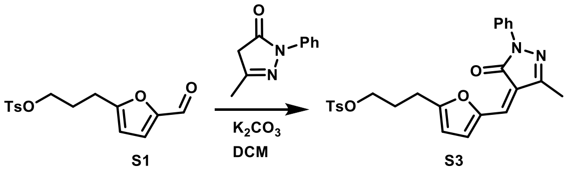
3-(5-Formylfuran-2-yl)propyl 4-methylbenzenesulfonate (S1):

50 mL dichloromethane (DCM) and 2 mL dimethyl formamide (DMF) (26 mmol, 7.6 eq) were added into a 250 mL round bottom flask and stirred at 0 °C. Phosphorus oxychloride (2 mL, 8 mmol, 2.2 eq) was added dropwise over 30 minutes. After addition was complete, the solution was brought to room temperature and stirred for 1 h. The flask was placed back in an ice bath and 3-(furan-2-yl)propyl 4-methylbenzenesulfonate (1 g, 3.6 mmol, 1 eq) dissolved in 1 mL DCM was added slowly. The reaction was then stirred at room temperature for 3 h upon which the reaction turned a bright orange color. The reaction mixture was slowly added to 100 mL of saturated aqueous sodium carbonate stirring in an ice bath. Additional sodium carbonate was added until bubbles no longer formed. The solution was then stirred for 1 h at room temperature after which the color changed from orange to yellow. The aqueous layer was extracted with 100 mL of DCM. The organic layer was collected and washed with saturated sodium carbonate, brine, and dried over magnesium sulfate. The solvent was removed and the resulting crude liquid was purified further via silica gel column chromatography using a 1:1 DCM:Hexanes to DCM gradient to give 380 mg pure **S1** as a pale yellow oil (33% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 3.5 Hz, 1H), 6.21 (d, *J* = 3.5 Hz, 1H), 4.05 (t, *J* = 6.0 Hz, 2H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.44 (s, 3H), 2.05 (p, *J* = 7.3, 5.9 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 152.2, 145.1, 132.9, 130.0, 128.0, 109.6, 69.0, 27.0, 24.5, 21.8 ppm; FTIR (ATR) 3031, 1738, 1675, 1365, 1177, 906, 726, 664, 554 cm^{-1}; HRMS (ESI+) calculated ($C_{15}H_{16}o_5SNa^+$): 331.061617, found: 331.0635.



3-(5-((2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)methyl)furan-2-yl)propyl 4-methylbenzenesulfonate (S2):

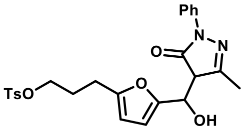
Meldrum's acid (70 mg, 0.48 mmol, 1.5 eq) was added to a scintillation vial with **S1** (100 mg, 0.32 mmol, 1 eq). Methanol (0.5 mL) was then added and the reaction was stirred at room temperature overnight after which the product precipitated out. Methanol (1 mL) was added and the resulting slurry was filtered via vacuum filtration, rinsed twice with 5 mL methanol, and dried under vacuum to give 98 mg pure **S2** as a yellow solid (70% yield). When necessary, additional purification was done using flash column chromatography with DCM as the eluent. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 3.4 Hz, 1H), 8.22 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 6.37 (d, *J* = 3.8 Hz, 1H), 4.08 (t, *J* = 6.0 Hz, 2H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.46 (s, 3H), 2.08 (p, *J* = 6.4 Hz, 2H), 1.76 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 163.7, 160.6, 149.7, 145.2, 140.7, 132.9, 130.4, 130.1, 128.1, 112.9, 105.9, 104.5, 68.9, 27.7, 26.9, 24.9, 21.8; FTIR(APR) 3020, 2939, 1738, 1425, 1366, 1228, 1217, 905, 727, 528 cm^{-1}; HRMS (ESI+) calculated ($C_{21}H_{22}O_8SNa^+$): 457.093311, found: 457.0913.



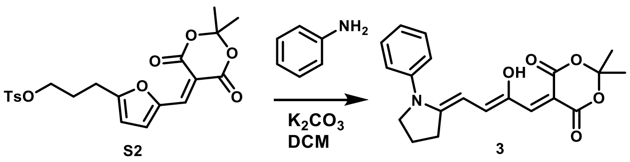
3-(5-((3-Methyl-5-oxo-1-phenyl-1,5-dihydro-4H-pyrazol-4-ylidene)methyl)furan-2-yl)propyl 4-methylbenzenesulfonate (S3):

3-methyl-1-phenyl-2-pyrazoline-5-one (500 mg, 2.3 mmol, 1.75 eq) was added to a scintillation vial containing a solution of **S1** (400 mg, 1.3 mmol, 1.00 eq) stirring in 1 mL DCM. Methanol (1 mL) was added and the reaction mixture was stirred overnight after which the solvent was removed under vacuum. The crude mixture was purified through a silica plug using DCM to elute off the orange product to give 87 mg **S3** in a mixture of *E/Z* isomers (14% yield).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 3.7 Hz, 3H), 8.00 – 7.92 (m, 8H), 7.78 (d, *J* = 8.4 Hz, 8H), 7.44 – 7.37 (m, 8H), 7.37 – 7.31 (m, 9H), 7.20 – 7.13 (m, 4H), 6.29 (d, *J* = 3.7 Hz, 4H), 4.09 (td, *J* = 6.3, 3.7 Hz, 8H), 2.84 (dt, *J* = 14.9, 7.5 Hz, 8H), 2.54 (s, 3H), 2.44 (s, 12H), 2.13 – 2.05 (m, 8H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 162.3, 161.9, 150.0, 149.9, 149.5, 147.9, 145.2, 145.1, 138.7, 138.5, 132.9, 130.1, 130.0, 129.0, 128.9, 128.9, 128.0, 127.0, 126.9, 126.6, 124.8, 124.7, 121.4, 120.8, 119.1, 118.8, 112.0, 111.2, 77.5, 77.4, 77.2, 76.8, 69.0, 68.8, 27.0, 25.0, 24.8, 21.8, 18.1, 13.1 ppm; FTIR(APR) 3036, 2939, 1738, 1441, 1366, 1217, 903, 725, 527 cm^{-1}. HRMS(ESI+) calculated ($C_{25}H_{24}N_2O_5SNa^+$): 487.1304, found: 487.1290.

*It should be noted that the two *E/Z* isomers elute close to each other and appear to interconvert at room temperature. In addition to the *E/Z* isomers, there is a colorless side product that forms, corresponding to **S3a** (to the right). **S3a** appears to be the major product due to slow elimination after the addition of the carbon acid to the furfural. **S3a** is colorless and more polar than **S3**. It slowly converts to **S3** on silica gel; therefore, after eluting off **S3**, the remaining silica gradually turns orange. **S3a** can be eluted off the silica with 9:1 DCM:EtOAc and directly reacted with amine in the presence of potassium carbonate to form DASA; however, purification of DASA becomes more difficult due to the similar polarity between DASA and **S3a**.

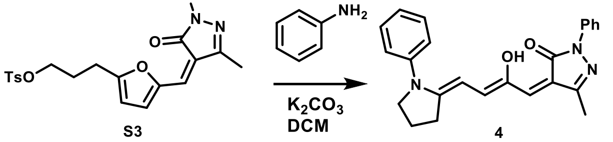


S3a



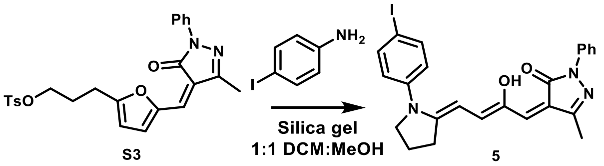
5-((2Z,4E)-2-hydroxy-4-(1-phenylpyrrolidin-2-ylidene)but-2-en-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3):

To a solution of **S2** (400 mg, 0.92 mmol, 1.0 eq) stirring in 10 mL DCM in a scintillation vial, 100 µL aniline (1.1 mmol, 1.2 eq) was added. An excess (250 mg) of potassium carbonate was added, the vial was capped with an outlet needle and allowed to stir overnight after which the solution was dark pink. The potassium carbonate was filtered off and the reaction mixture was run through a silica plug. The plug was washed with DCM until the yellow starting material was washed off and the DASA was subsequently eluted off with 1:1 ethyl acetate:DCM. The pink fractions were collected and the solvent was removed under vacuum to give 35 mg pure **3** (11% yield). ^{1}H NMR (500 MHz, CD_2Cl_2) δ 11.26 (s, 1H), 7.53 (t, *J* = 7.9 Hz, 2H), 7.44 (t, *J* = 6.9 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 2H), 6.97 (s, 1H), 6.89 (d, *J* = 13.1 Hz, 1H), 6.04 (d, *J* = 13.3 Hz, 1H), 4.10 (t, *J* = 7.2 Hz, 2H), 3.25 (t, *J* = 7.9 Hz, 2H), 2.30 (p, *J* = 7.6 Hz, 2H), 1.66 (s, 6H) ppm; ^{13}C NMR (125 MHz, CD_2Cl_2) δ 169.5, 167.4, 165.1, 148.7, 145.1, 139.1, 138.2, 130.5, 129.2, 125.3, 103.5, 99.6, 90.5, 59.2, 32.7, 30.1, 26.8, 20.9 ppm; FTIR (APR) 2993, 2923, 1687, 1602, 1494, 1446, 1388, 1357, 1304, 1260, 1235, 1197, 1142, 929, 833, 773, 694, 654 cm^{-1}; HRMS(ESI+) calculated ($C_{20}H_{21}NO_5Na^+$): 378.1317, found: 378.1314.



(Z)-4-((2Z,4E)-2-hydroxy-4-(1-phenylpyrrolidin-2-ylidene)but-2-en-1-ylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4):

S3 (500 mg, 1.1 mmol, 1 eq) and aniline (100 µL, 1.1 mmol, 1 eq) were added to a vial containing 2 mL of DCM with 100 mg potassium carbonate. The solution was allowed to stir for three days after which it was filtered to remove the potassium carbonate. The solution was then diluted with 10 mL DCM and run through a silica plug. The plug was rinsed with DCM to remove the aniline and activated furan after which the DASA was eluted off using 4:1 DCM:ethyl acetate to give 92 mg pure **4** (22% yield). When necessary, further purification was conducted by adding 1 mL of toluene, sonicating, and placing in freezer for one hour to precipitate **4**. ^{1}H NMR (600 MHz, cd_2cl_2) δ 12.79 (s, 1H), 7.93 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 6.9 Hz, 1H), 7.37 – 7.32 (m, 4H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.61 (d, *J* = 12.9 Hz, 1H), 6.32 (s, 1H), 6.06 (d, *J* = 12.9 Hz, 1H), 4.04 (t, *J* = 7.0 Hz, 2H), 3.18 (t, *J* = 7.9 Hz, 2H), 2.24 (p, *J* = 7.7 Hz, 2H) ppm; ^{13}C NMR (125 MHz, CD_2Cl_2) δ 165.7, 164.9, 149.9, 148.5, 142.1, 139.8, 139.4, 133.0, 130.3, 129.2, 128.9, 128.4, 125.1, 124.6, 119.5, 111.3, 98.8, 58.4, 32.3, 21.1, 12.9 ppm; FTIR: 2970, 2923, 2875, 1738, 1595, 1542, 1496, 1461, 1440, 1385, 1341, 1293, 1218, 1184, 1142, 1096, 1062, 1043, 1027, 998, 940, 905, 786, 757, 693, 673, 621, 585, 493, cm^{-1}; HRMS (ESI$^+$) calculated ($C_{24}H_{23}N_3O_2H^+$) 386.1869, found: 386.1867.



(Z)-4-((2Z,4E)-2-hydroxy-4-(1-(4-iodophenyl)pyrrolidin-2-ylidene)but-2-en-1-ylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (5):

S3 (80 mg, 0.18 mmol, 1 eq) and 4-iodoaniline (156 mg, 0.72 mmol, 4 eq) was added to 2 mL of a 1:1 DCM:methanol solution in a scintillation vial to which approximately 0.5 g silica gel was added. Additional solvent was added if necessary to make a slurry after which the solvent was allowed to evaporate. Additional 1:1 DCM:methanol solvent mixture (≈1 mL) was added periodically to allow for mixing and subsequently removed under vacuum. The reaction ran for 3 days after which the mixture was a blue/green color. Residual solvent was removed under vacuum and the silica mixture was dry loaded to the top of a silica plug. Starting materials were eluted off with 9:1 hexanes:acetone after which the DASA (purple/blue on silica) was eluted using acetone. Further purification was done by redissolving in DCM, washing with 1 M sodium hydroxide and water. The organic layer was dried over sodium sulfate, evaporated under reduced pressure, and run through a column with 9:1 DCM:ethyl acetate eluent. The blue spots were collected, and the solvent was removed via rotary evaporation. 0.2 mL of ethyl acetate was added, sonicated, and removed. The remaining solid was dried under vacuum to give pure **5** with typical yields between 11-40 mg (8-45%). ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.92 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.6 Hz, 2H), 7.37 (t, J = 7.9 Hz, 2H), 7.15 (t, J = 8.1 Hz, 1H), 7.11 (d, J = 8.5 Hz, 2H), 6.63 (s, 1H), 6.35 (s, 1H), 6.14 (d, J = 10.5 Hz, 1H), 4.03 (s, 2H), 3.19 (s, 2H), 2.25 (m, 5H). FTIR: 3466, 3016, 2928, 2848, 1738, 1618, 1544, 1502, 1478, 1366, 1230, 1218, 1204, 1062, 1001, 756, 694, 513, 496. HRMS (ESI$^+$) calculated ($C_{24}H_{22}IN_2O_2H^+$): Calc: 512.0835, found: 512.0834.

Note: ^{13}C NMR was not fully obtained due to poor solubility, see **Figures S22-S26** for more details.

Time dependent UV-Vis Studies:

Instrument:

Our time dependent UV-Vis studies were done on an instrument built in house that allows for irradiation perpendicular to UV-Vis setup, as previously published by our group.[4] The irradiation was done with Thorlab LEDs (530, 595, or 617 nm) coupled to a multimode optical fiber terminated with an output collimator. Intensity of the LEDs was controlled using LabVIEW through a digital-to-analog converter (National Instruments USB-6009). The probe beam was produced by High Power MINI Deuterium Tungsten Halogen Source w/shutter 200–2000 nm (Ocean Optics DH-MINI) coupled into a multimode fiber with an output collimator for the light delivery. The probe light was modulated by a shutter (Uniblitz CS25) which could be controlled manually or through a digital output port (National Instruments USB-6009) using LabVIEW. Pump and probe beams were overlapped using steering and focusing optics at a 90° angle inside a sample holder, which allowed for a 10x10 mm rectangular spectrophotometer cells that was connected to a circulating bath for temperature control (not used for the experiments described in this study). The solutions were stirred during the measurements by a miniature stirring plate inserted into the sample holder (Starna Cells SCS 1.11). Both pump and probe beams were nearly collimated inside the cell with a diameter of about 2 mm. The pump beam was blocked after passing through the sample and the probe beam was directed by a system of lenses into the detector (Ocean Optics Flame-S1-XR spectrometer), which acquired spectra of the probe light. The detector was connected to a PC via USB port. The experiment was controlled by a National Instrument LabVIEW program which collected the probe light spectra, determined sample optical absorption spectra, controlled pump and probe light sources, and stored the data on the computer S3 hard drive according to the experimental protocol.

Sample preparation:

Stock solutions (1 mM) of the compounds were prepared in dry DCM and left to equilibrate overnight at room temperature. These stock solutions were stored for up to one week before use. 10 µM solutions were prepared by injecting 100 µL of the stock solution into separate vials containing 10 mL of the desired solvent. Isopropanol, ethanol, and hexanol were dried over activated 3 angstrom sieves (50 vol%) for 1 week before use. Toluene, DCM, diethyl ether, acetone, and *t*-butanol were used from fresh bottles. Note: *t*-butanol was used from a freshly opened bottle and not further dried because it freezes at room temperature. The 10 µM solutions were prepared the same day of the studies and underwent one cycle of irradiation and recovery before collection of data to ensure they reached equilibrium.

Equilibrium of **3** in toluene, chloroform, methanol, and DMSO measured by ^{1}H NMR

3 is relatively soluble in a variety of solvents from toluene to methanol and so we were able to investigate the equilibrium by ^{1}H NMR. Fresh solutions were prepared in ampules of deuterated solvent and stored in the dark for at least 2 days before measurement. The coupling constants of the protons on the triene (g and h) were used as an indicator of open or closed form, where the open form has coupling constants of around 12 Hz or higher (trans alkene coupling) and the closed form would have coupling constants closer to 5 Hz. In each of the four solvents measured only one species was visible with g-h coupling above 12 Hz indicating that **3** is completely open, though the chemical shifts change dramatically in the different solvents due to the charge separation.

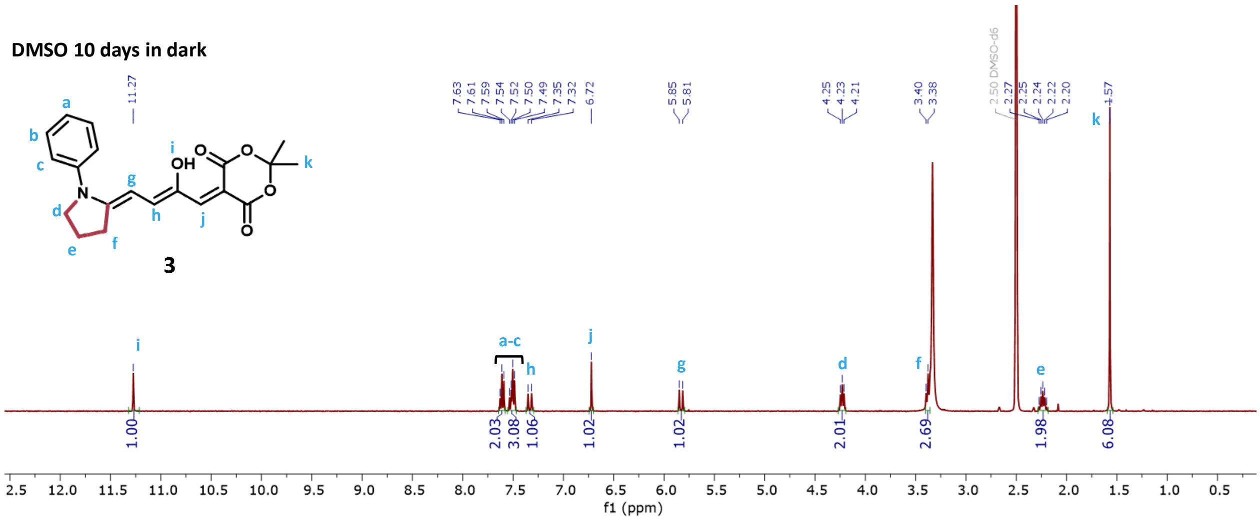


Figure S1. ^{1}H NMR of **3** dissolved in DMSO and kept in the dark for 10 days. Coupling between g-h J = 13.5 Hz, indicating that the present isomer is the open form.

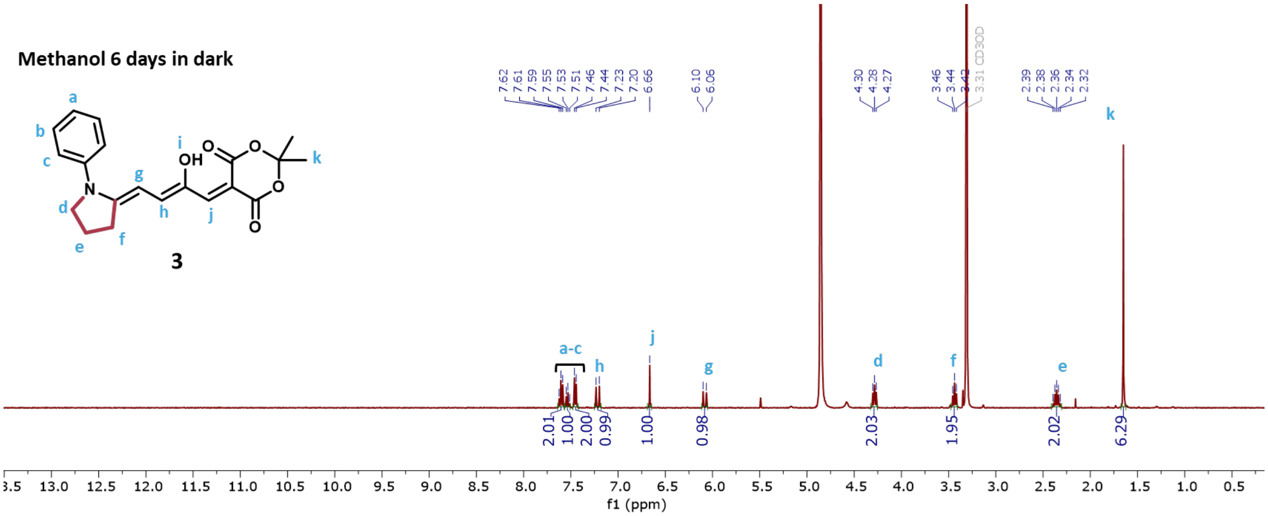


Figure S2. ^{1}H NMR of **3** dissolved in methanol and kept in the dark for 6 days. Hydrogen on the OH does not appear due to deuterium exchange. Coupling between g-h *J* = 13.8 Hz, indicating that the present isomer is the open form.

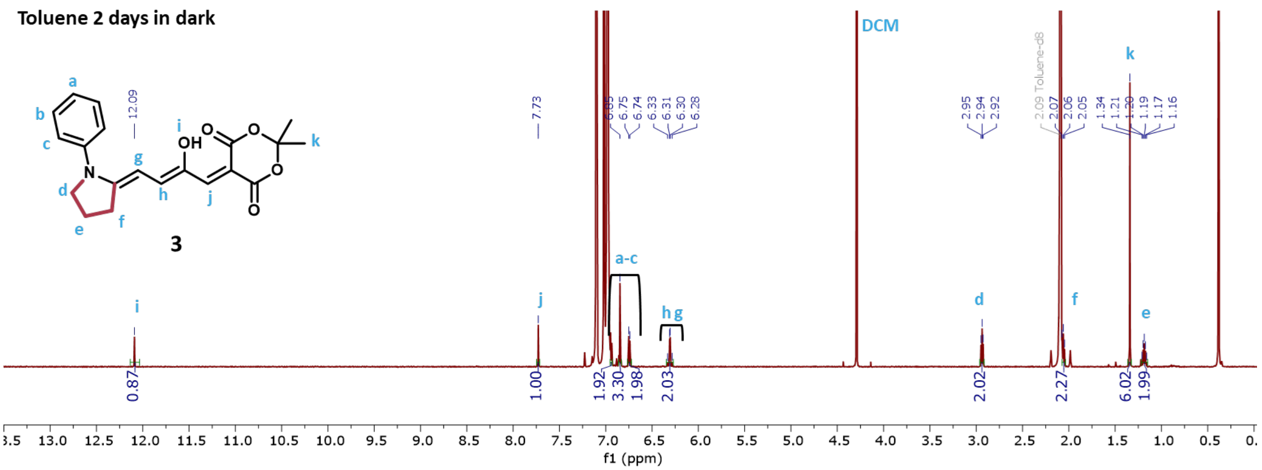


Figure S3. 3 dissolved in toluene and stored in the dark for two days before measurement. The compound is weakly soluble in toluene. Toluene and its satellite peaks interfere with the identification and integration of the aromatic region, however the rest of the NMR is clean. Coupling between h and g is 13 Hz, indicating that the present isomer is open form.

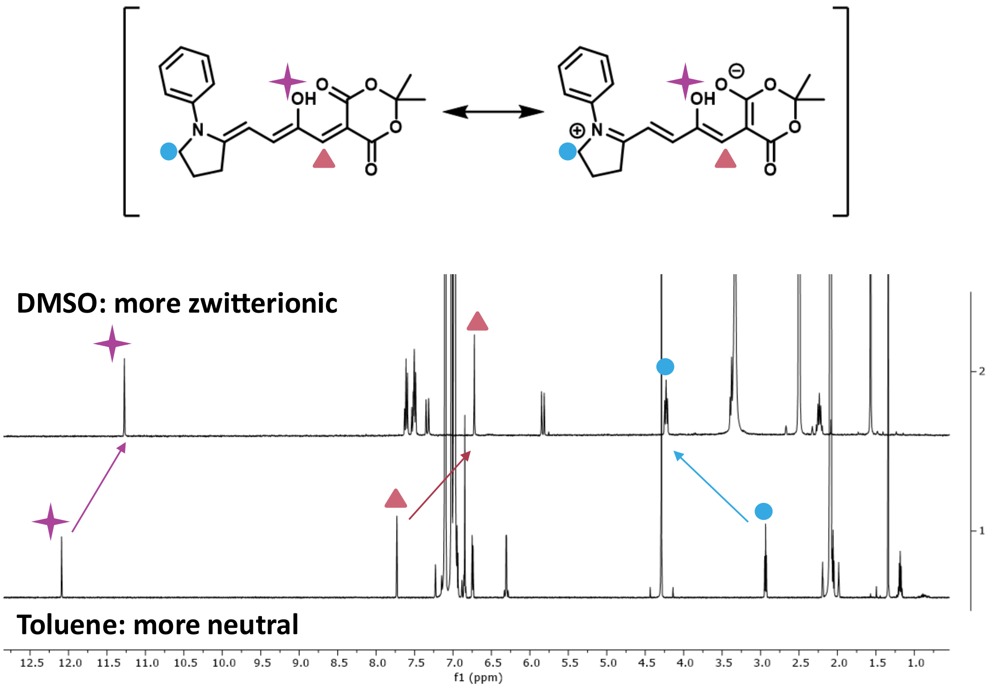
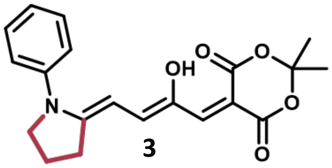


Figure S4. Overlayed equilibrated ^{1}H NMR of **3** in toluene and DMSO showing the peaks shifting corresponding to increased polarity in DMSO resulting in more charge separated ground state.

The ^{1}H NMR shifts of **3** change dramatically between toluene and DMSO, though in all solvents there is only one species present. This appears to be due to stabilization of the charge separated resonance structure in more polar solvents. In DMSO, hydrogens that are either next to the nitrogen or have resonance structures with positive charge are shifted downfield and hydrogens next to the carbon acid or on carbons with a resonance structure with a negative charge are shifted upfield.

Additional photoswitching studies of **3**

In order to see whether the ratio of **A** to **B/B'** was consistent over the time of irradiation, we selected the UV-Vis taken every 50 seconds from the first point the light turned on (250 s) for 8 points (until 600 s, a total of 350 s of irradiation). The spectra normalized based on the λ_{max} of the initial spectra were plotted and the **B/B'** shoulder is visible even after 10 minutes of irradiation (**Figure S5a**). In order to observe how the ratio of **A** to **B/B'** changes over time, we plotted the spectra with the **A** peak normalized to 1 (**Figure S5b**). In this case, it is clear that the ratio of **A** to **B/B'** does not change significantly over the time of irradiation, indicating that a photothermal stationary state is reached between the two isomers followed by slow thermal draining of **B/B'** to the colorless isomer.



3

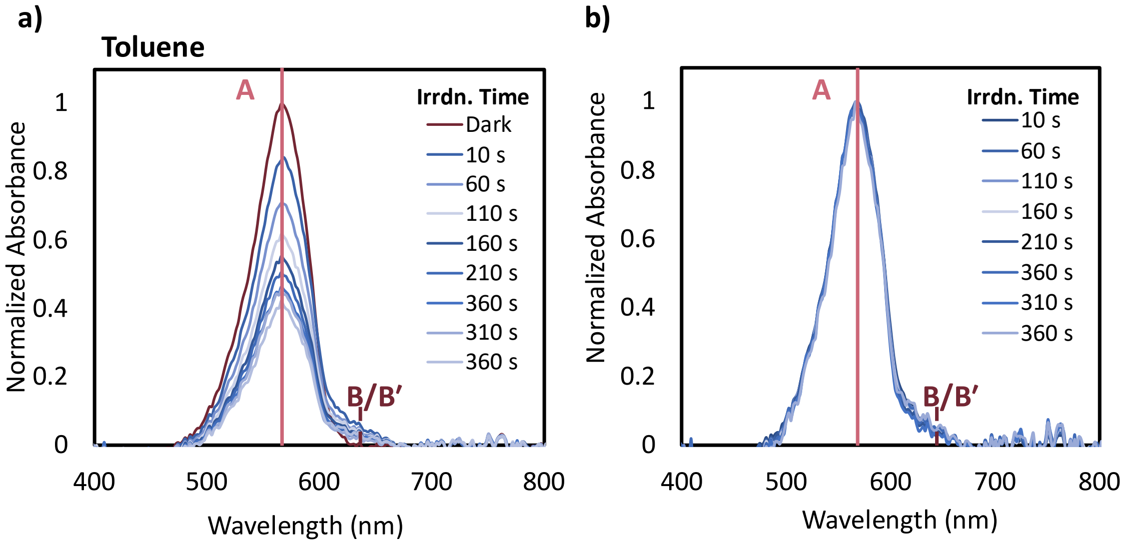


Figure S5. 10 µM solution of **3** in toluene at various points during irradiation showing that the ratio between the λ_{max} and the peak around 640 nm corresponding to **B/B'** stays consistent throughout the irradiation normalized (a) by dividing by the λ_{max} of the initial time point and (b) by dividing by the λ_{max} of each time point.

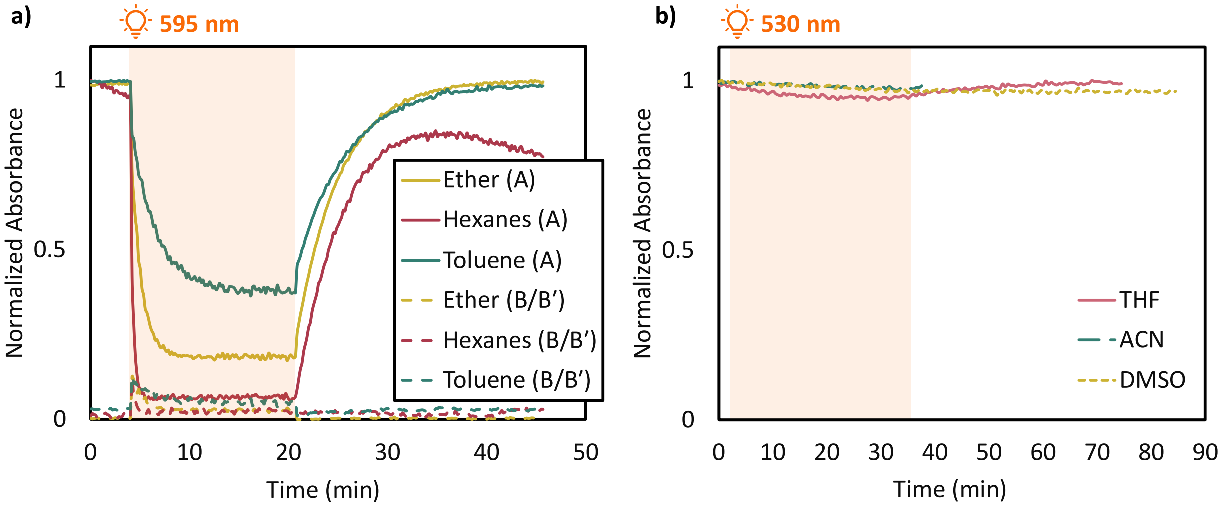


Figure S6. (a) Normalized time dependent UV-Vis studies of 10 µM **3** in diethyl ether (yellow), hexanes (red), and toluene (teal) following the λ_{max} of the **A** isomer (solid line corresponding to peak ~ 560 nm, depending on solvent) and the **B** isomer (dotted line corresponding to shoulder at 640 nm) over time. Time points were taken every 10 seconds with 25 prepoints before irradiation, 100 points during irradiation with a 530 nm LED, and 150 points after irradiation (b) normalized time dependent UV-Vis studies of 10 µM **3** in tetrahydrofuran (pink), acetonitrile (teal), and dimethyl sulfoxide (yellow) taken every 30 seconds with 5 points before irradiation, 60 points during irradiation with 530 nm LED, and up to 100 points post irradiation. Data was normalized by dividing by the absorbance at the λ_{max} at time zero.

We investigated the ability of 10 µM solutions of **3** to switch in a variety of solvents including nonpolar solvents such as diethyl ether and hexanes (**Figure S6a**) and more polar solvents such as tetrahydrofuran, acetonitrile, and dimethyl sulfoxide (**Figure S6b**). **3** switches reasonably well in nonpolar solvents. In hexanes, **3** isomerizes almost completely to the closed form in less than 5 minutes, though the absorbance declined linearly in the dark, likely due to precipitation of the compound which is poorly soluble in hexanes. There is minimal switching observed in more polar solvents such as acetonitrile and dimethyl sulfoxide, though there is a small amount of reversible switching (≈5%) observed in THF.

Solvatochromism of **3-5**

Solvatochromic analysis was performed for the DASA derivatives in this study. Small amounts of DASA were dissolved in ten solvents to compare to previously tested derivatives. Solvents chosen were toluene, diethyl ether, tetrahydrofuran (THF), chloroform, dichloromethane (DCM), acetone, dimethyl sulfoxide (DMSO), acetonitrile (ACN), and methanol (MeOH). Solvents were taken from ACS reagent grade solvents, used without further purification. The λ_{max} of each DASA was plotted against the Dimroth-Reichardt solvent polarity scale (E_T^N).[5]

Solvent (E_T^N)	**1** λ_{max} (nm)	**2** λ_{max} (nm)	**3** λ_{max} (nm)	**4** λ_{max} (nm)	**5** λ_{max} (nm)
Toluene (0.099)	588	602	567	596	595
Diethyl ether (0.117)	578	590	557	588	589
THF (0.207)	587	597	559	604	604
Ethyl acetate (0.228)	581	593	553	600	599
Chloroform (0.259)	590	601	558	604	603
DCM (0.309)	590	599	556	604	604
Acetone (0.355)	584	592	545	595	598
DMSO (0.444)	589	593	540	593	598
ACN (0.460)	582	588	539	588	593
MeOH (0.762)	578	581	529	575	581
Slope (nm)	**-7 ± 8**	**-24 ± 8**	**-56 ± 7**	**-32 ± 12**	**-20 ± 11**

Table S1. Solvatochromic data of DASA derivatives investigated in this study. Solvatochromic slopes of **1**[6] and **2**[7] are taken from literature.

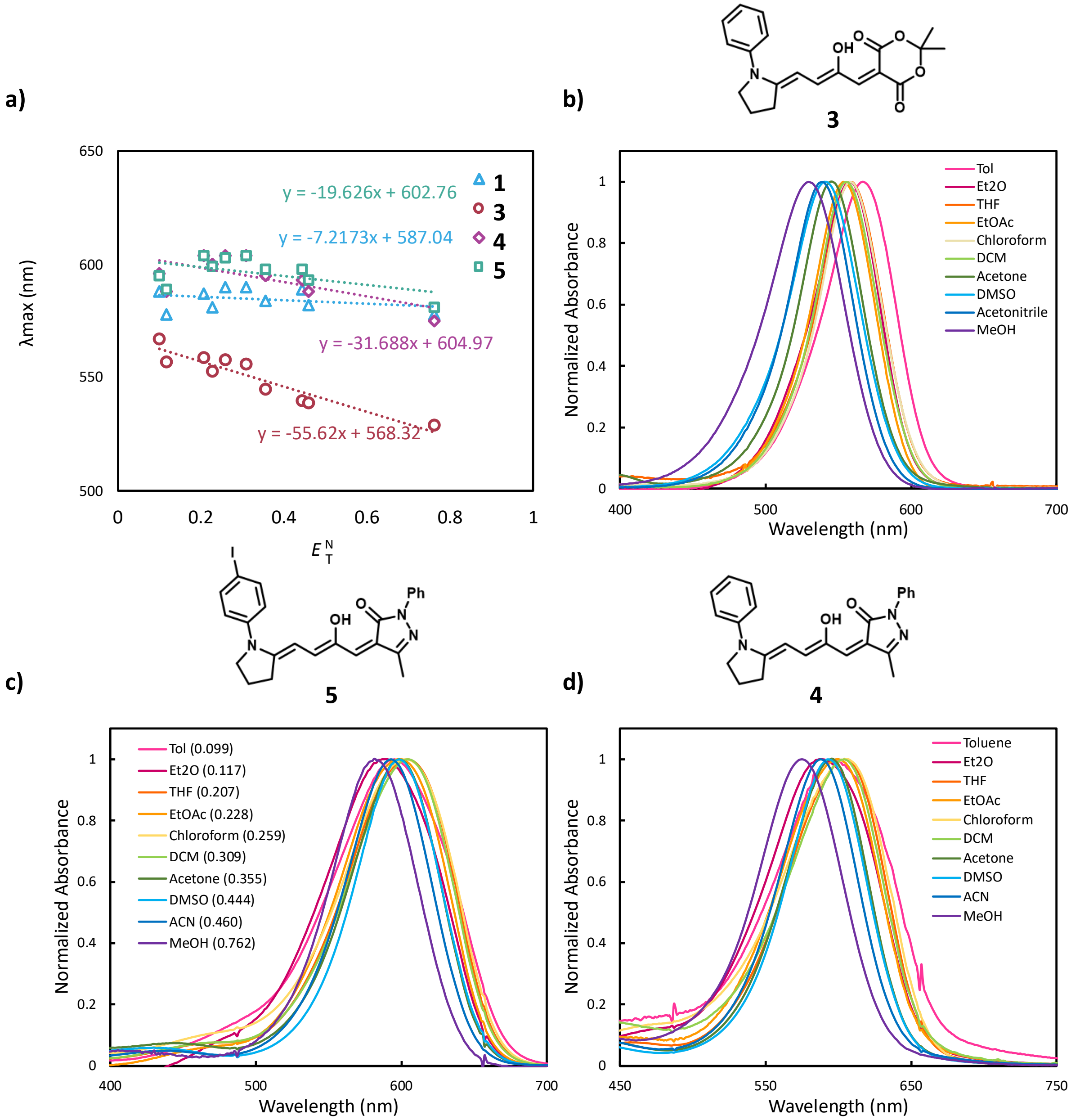


Figure S7. (a) Solvatochromic slope analysis of **1, 3, 4,** and **5** in toluene, diethyl ether, THF, DCM, chloroform, ethyl acetate, acetone, acetonitrile, DCM, and methanol. UV-Vis traces of **3** (b), **4** (d), and **5** (c) in the solvents listed above. Data was normalized by dividing by the absorbance at the λ_{max} at time zero.

Extinction coefficient of **4** and **5**

The extinction coefficients of **4** and **5** were determined in dichloromethane. No closed form is observed in the ^{1}H NMR of these compounds in dichloromethane. We assume an equilibrium of 95% to be on the conservative side. Solutions were prepared by allowing a 1 mM solution of each compound in dichloromethane to be equilibrated at least overnight. Aliquots of the stock solution were diluted to 10 mL with dry dichloromethane and the UV-Vis of those different concentrations was measured. The extinction coefficient was corrected by the assumed equilibrium of 95%, where the actual extinction coefficient is the measured slope of the absorbance/concentration divided by 0.95 to give extinction coefficients of 93,000 $M^{-1}cm^{-1}$ for **4** and 60,000 $M^{-1}cm^{-1}$ for **5.**

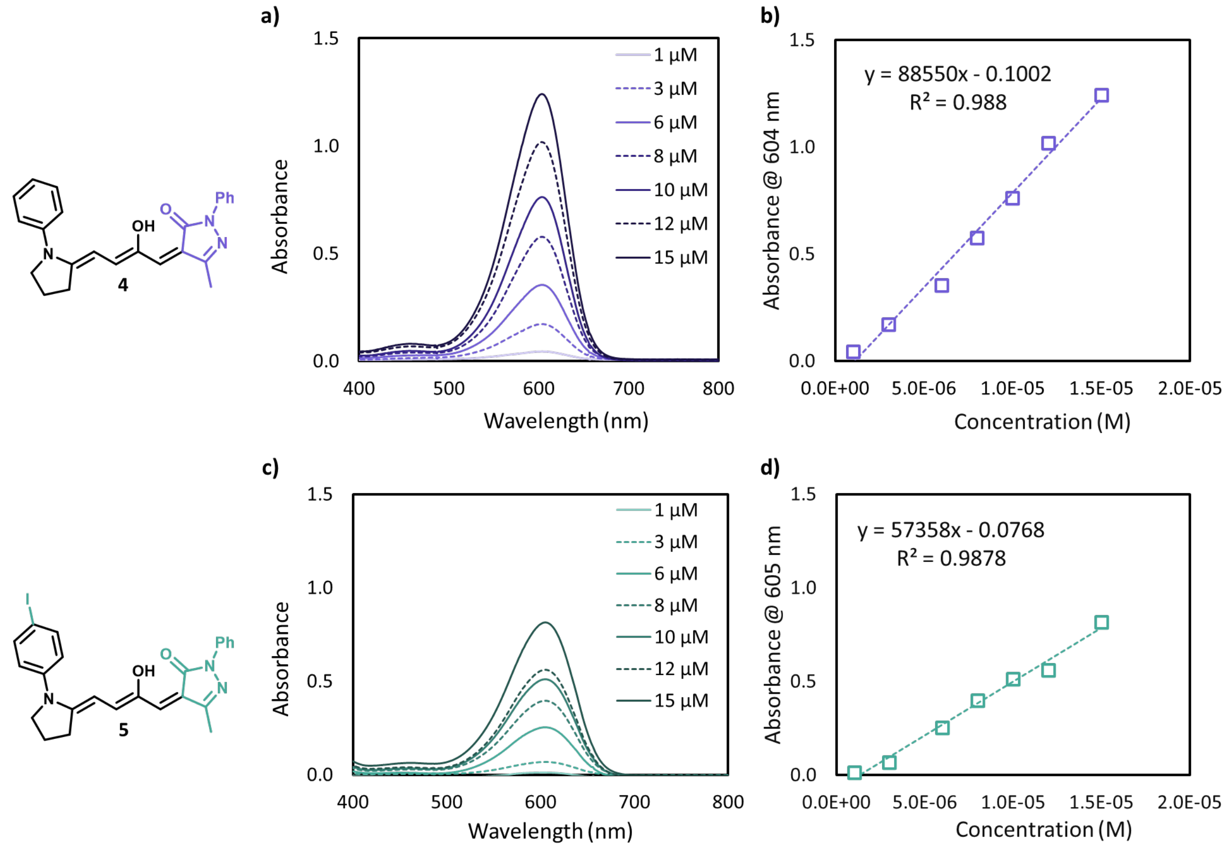


Figure S8. Concentration dependent UV-Vis data of **4** (a) and **5** (c), and the plotting of the absorbance at the λ_{max} versus the concentration of **4** (b) and **5** (d).

Determination of the equilibrium of **4** and **5** by ^{1}H NMR in deuterated methanol

The ^{1}H NMR of compound **4** was taken in deuterated methanol (fresh ampule from Cambride Isotopes) to determine the equilibrium between the open and closed forms. The solution was allowed to equilibrate for 12 hours after obtaining the NMR below. Open and closed form isomers are present.

DASA **4** is predominantly in the open isomer. We calculated the equilibrium by looking at the ratio of the multiplets centered around 4.35 ppm (open form, integration of 2 for 2 hydrogens) and 4.18 ppm (closed form, integration of 2.4 for 2 hydrogens). The ratio of these two peaks results in a calculated equilibrium of 89% open. It should be noted that there is precipitate visible even at concentrations less than 1 mM in deuterated methanol. Due to the saturation, there may be effects such as aggregation or different solubility of the isomers that influence the observed equilibrium at NMR concentrations. While this data shows there is significant open form present, the observed equilibrium does not directly correlate to the equilibrium at lower concentrations.[8]

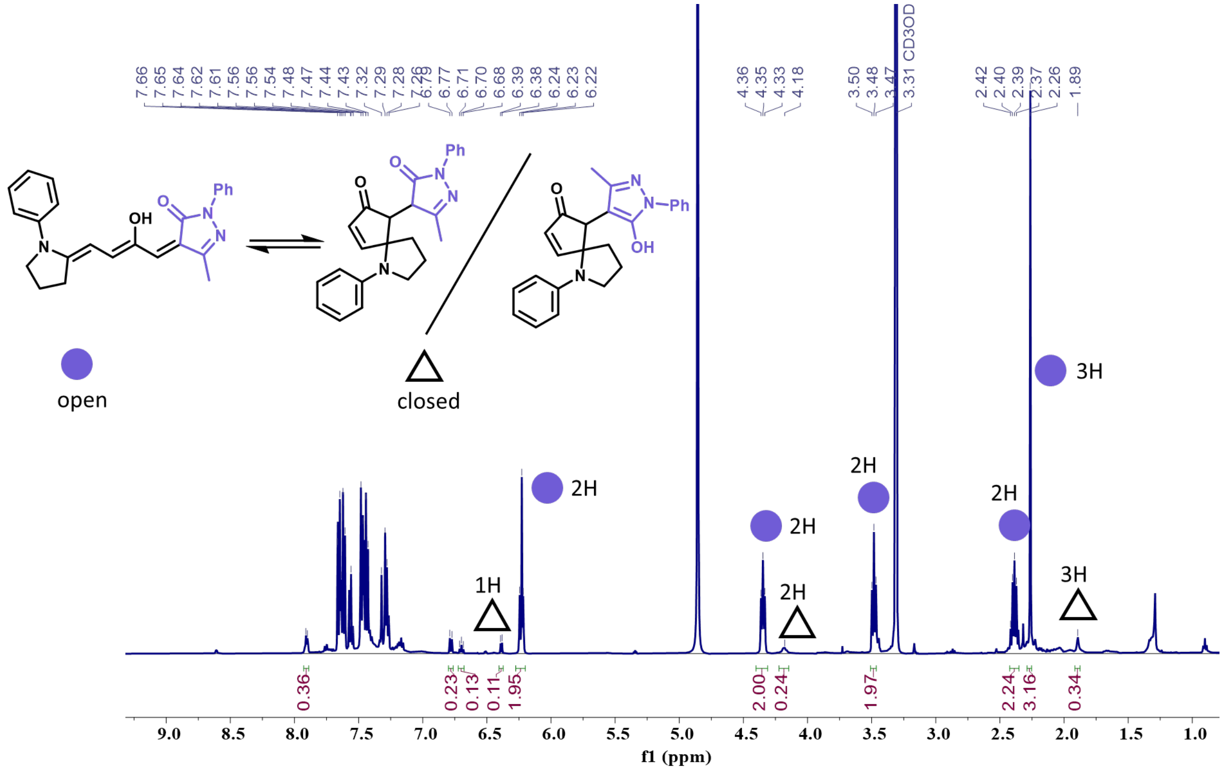


Figure S9. ^{1}H NMR of **4** in deuterated methanol showing a combination of open form indicated by the filled circle and closed form indicated by the unfilled triangles.

Impact of solvent on the equilibrium of **4** and **5** by UV-Vis

4 and **5** are poorly soluble in methanol at ^{1}H NMR concentrations, therefore we investigated the equilibrium of **4** and **5** in a variety of solvents using UV-Vis. To estimate their equilibrium, we prepared 1 mM stock solutions of each DASA in dichloromethane, in which the equilibrium is estimated to be at least 95% by ^{1}H NMR. Stock solutions were allowed to equilibrate overnight after which 20 µL of the solutions were injected into 2 mL of methanol in a cuvette. The solution was mixed using a pipette after which the UV-Vis was monitored until equilibrium was reached (approximately 30 minutes). The precent open form at equilibrium is estimated based on the following equation where A_{eq} is the absorbance of the equilibrated sample, A_0 is the initial absorbance, and 95% is the estimated initial percent of the open form.

$$\%\ \text{open form} = \left(\frac{A_{eq}}{A_0}\right)(95\%)$$

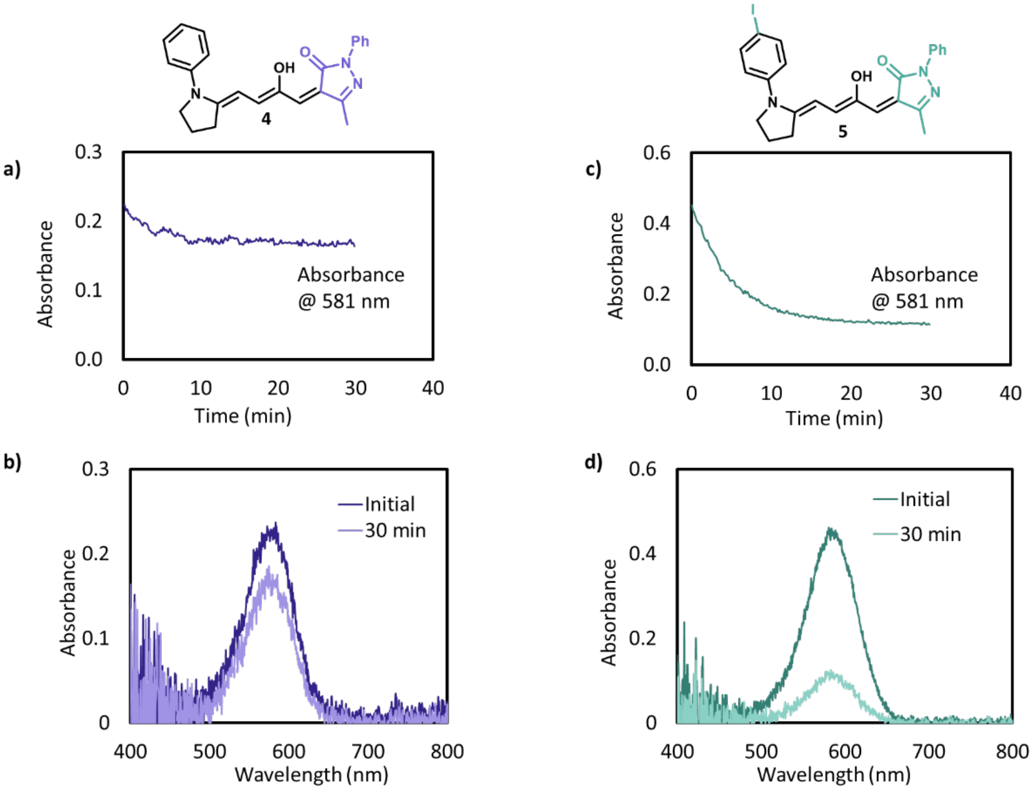


Figure S10. a) Absorbance at 581 nm of a solution of **4** monitored for 30 minutes after injection of an equilibrated solution in DCM into methanol. b) UV Vis of **4** immediately after injection into methanol and after allowed to equilibrate for 30 minutes. c) Absorbance at 581 nm of a solution of **5** monitored for 30 minutes after injection of equilibrated solution in DCM into methanol. d) UV-Vis of **5** immediately after injection into methanol and after allowed to equilibrate for 30 minutes.

	DASA 4	**DASA 5**
λ_{max}	581 nm	581 nm
A_0	0.223	0.452
A_{eq}	0.164	0.114
% open	**70%**	**24%**

Table S2. λ max, initial absorbance, absorbance of the equilibrated sample, and the estimated thermal equilibrium of the open form in methanol.

Photoswitching of 4 and 5 in toluene

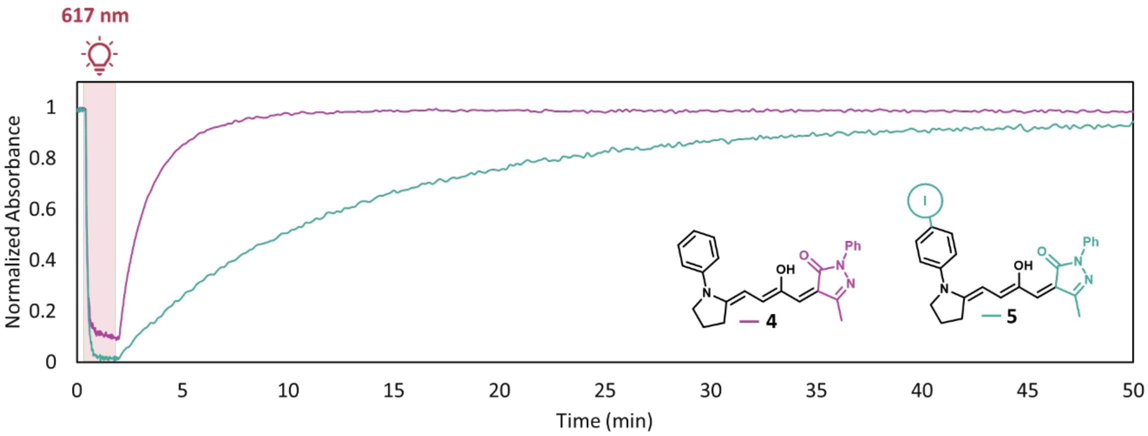
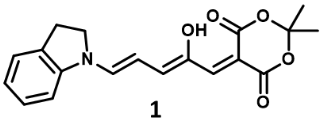


Figure S11. Time-dependent UV Vis traces of the absorbance at the λ_{max} for 10 µM solutions of **4** and **5** in toluene. Irradiation was done with a 617 nm LED. Data was normalized by dividing by the absorbance at the λ_{max} at time zero.

Behavior of **1** in 75:25 THF:Water

A 1 mM solution of **1** was prepared in DCM and stored in the dark for 3 days to ensure equilibration. 20 µL of the stock solution was injected into a 2 mL mixture of 75:25 THF:Water to make a 10 µM solution and the absorbance of the λ_{max} was followed over time (**Figure S10**). The absorbance decreased until it was not significantly different from noise of the instrument (after around 5000 seconds) indicating conversion to the closed form. While **1** equilibrates to the closed form in the dark, it is also responsive to light, which can be ween with a change in the slope of the decline in absorbance upon irradiation with a 617 nm LED. Importantly, while it shows some response to light, **1** irreversibly closes in 75:25 THF:Water, highlighting the improvement in compatibility allowed through the tethered amine for compound **5**.



1

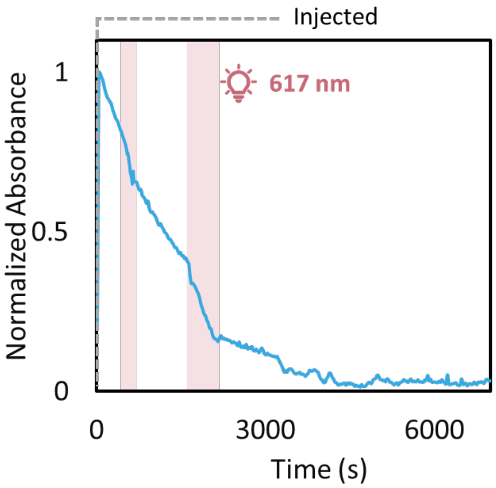


Figure S12. Normalized absorbance of the λ_{max} of a 10 µM solution of **1** in 75:25 THF:Water, monitored in the dark with occasional irradiation of 617 nm. Data was normalized by dividing by the absorbance at the λ_{max} at time zero.

Switching of **5** in aqueous solutions

Compound **5** demonstrates improved switching in polar protic solvents compared to many other DASA derivatives. The switching ability of 10 µM solutions of **5** in THF with various amounts of water (**Figure S11b**). The amount of water added slows down the forward switching, however reversible switching of a 10 µM solution of **5** is still evident in 60:40 THF:Water.

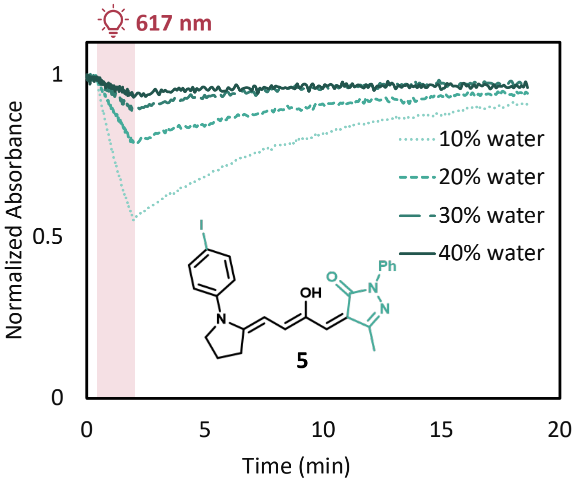


Figure S13. Time-dependent UV Vis traces of the normalized absorbance at the λ_{max} for 10 µM solutions of **5** in THF:water mixtures. For each sample, 1 s time points were taken with 25 points before irradiation, 95 points during irradiation with a 617 nm LED, and 5 s time points were taken after irradiation for 200 points. Data was normalized by dividing by the absorbance at the λ_{max} at time zero.

Characterization of new compounds

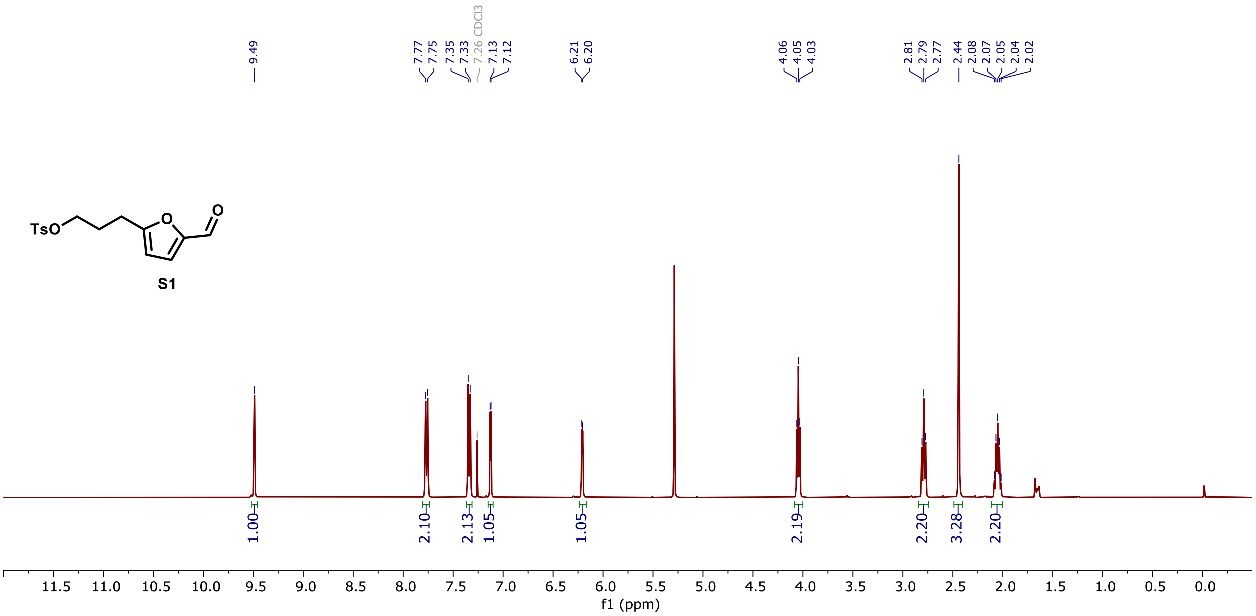


Figure S14. ^{1}H NMR of **S1** in CDCl$_3$ (400 MHz)

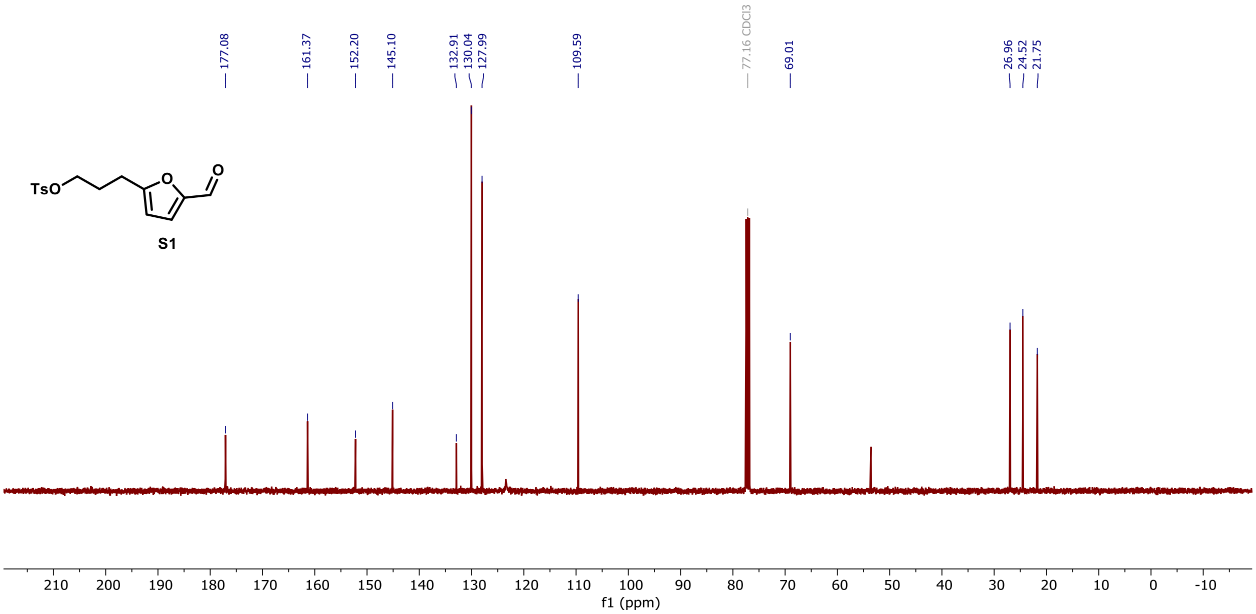


Figure S15. ^{13}C NMR of **S1** in CDCl$_3$ (100 MHz)

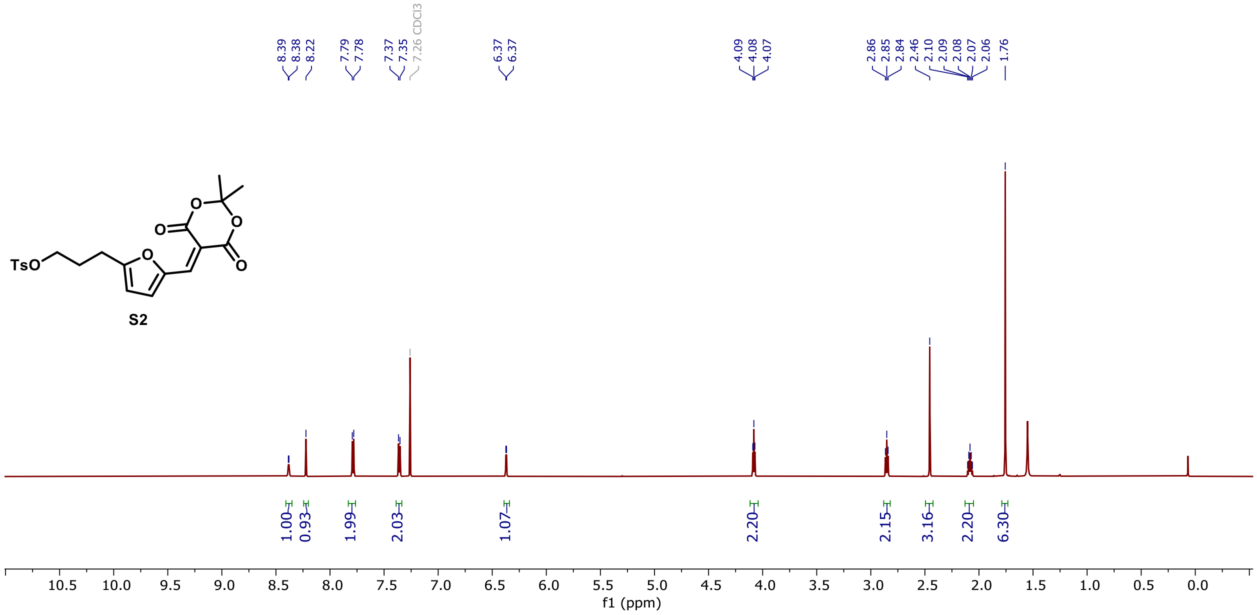


Figure S16. ^{1}H NMR of **S2** in $CDCl_3$ (600 MHz)

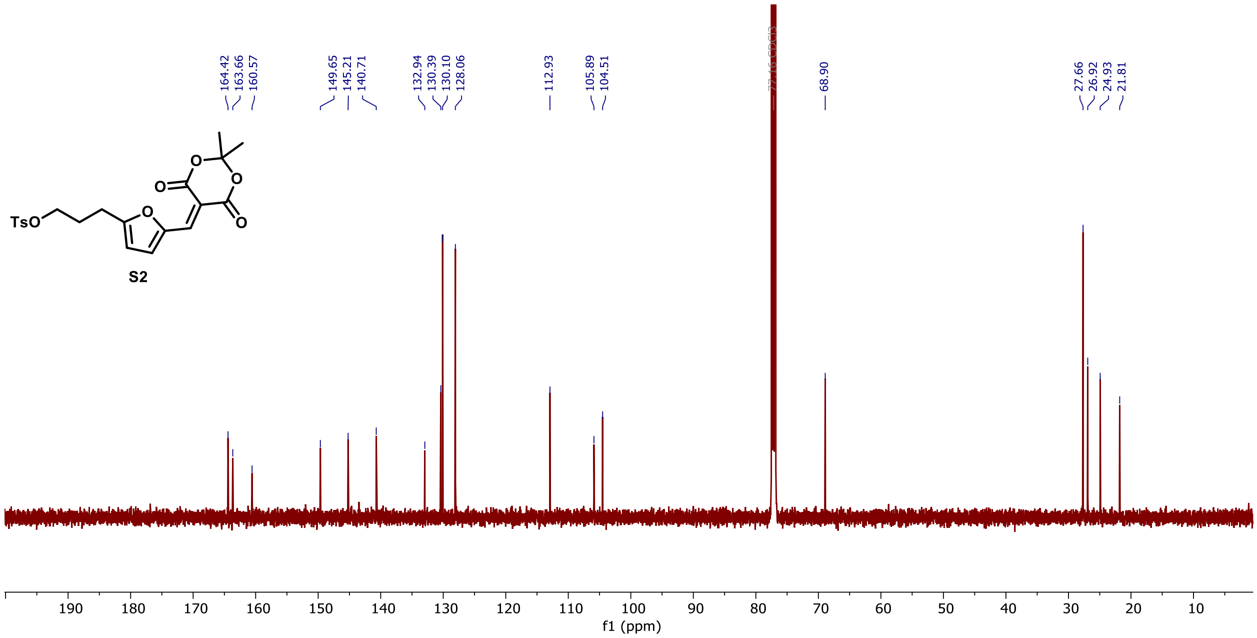


Figure S17. ^{13}C NMR of **S2** in $CDCl_3$ (500 MHz)

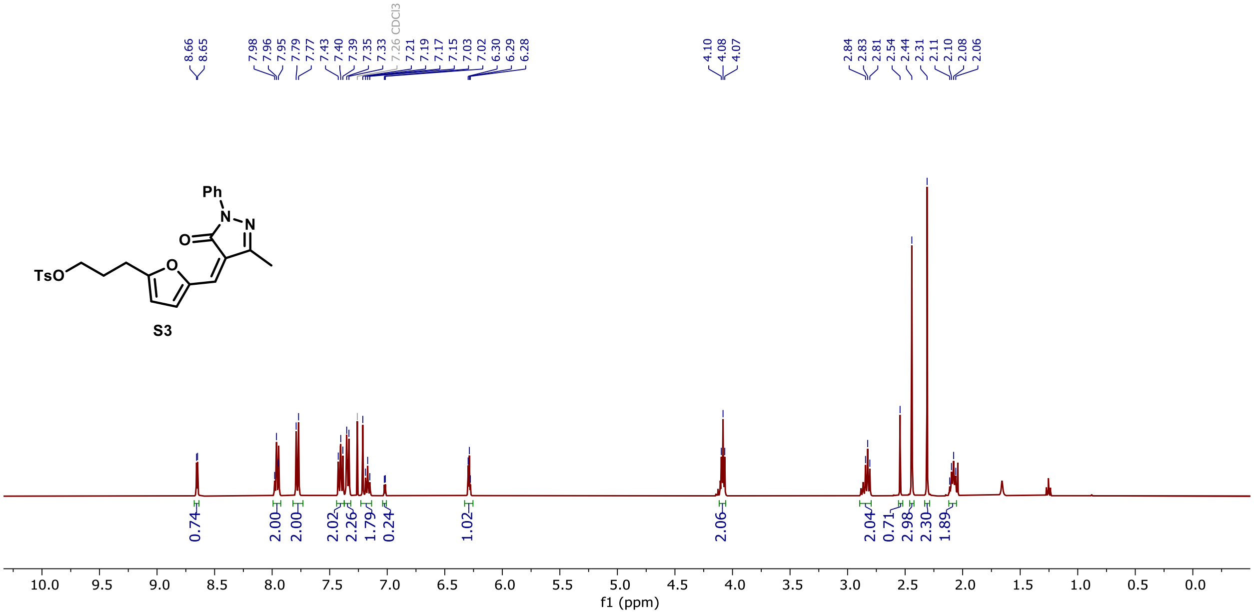


Figure S18. ^{1}H NMR of **S3** in $CDCl_3$ (400 MHz)

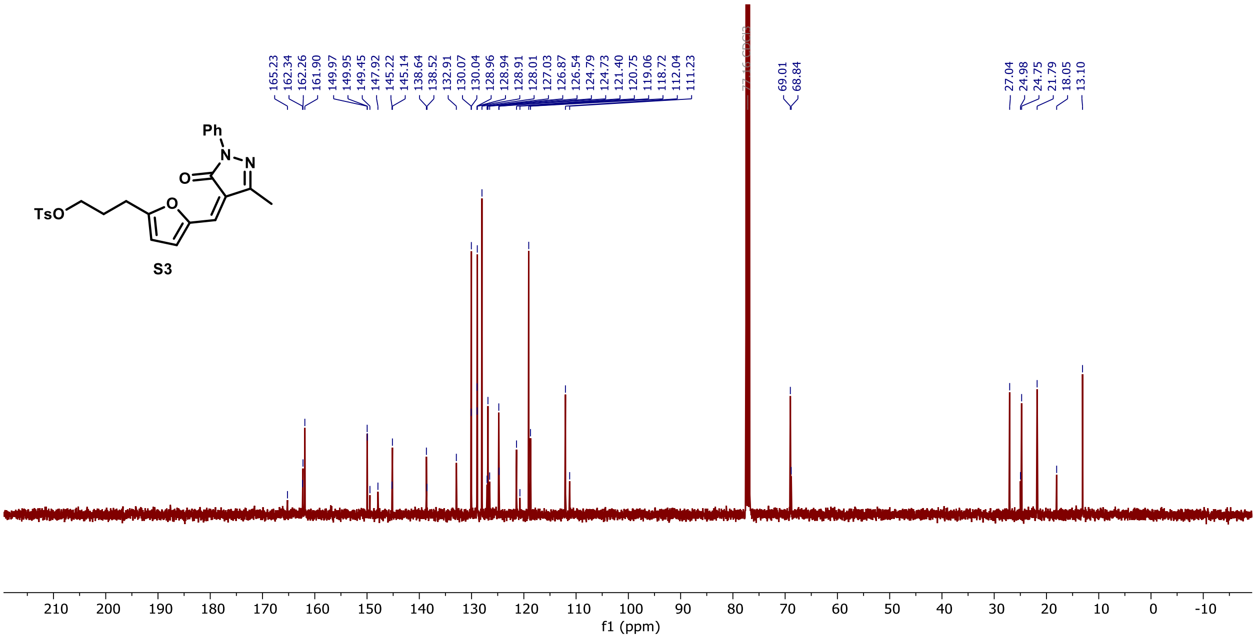


Figure S19. ^{13}C NMR of **S3** in $CDCl_3$ (100 MHz)

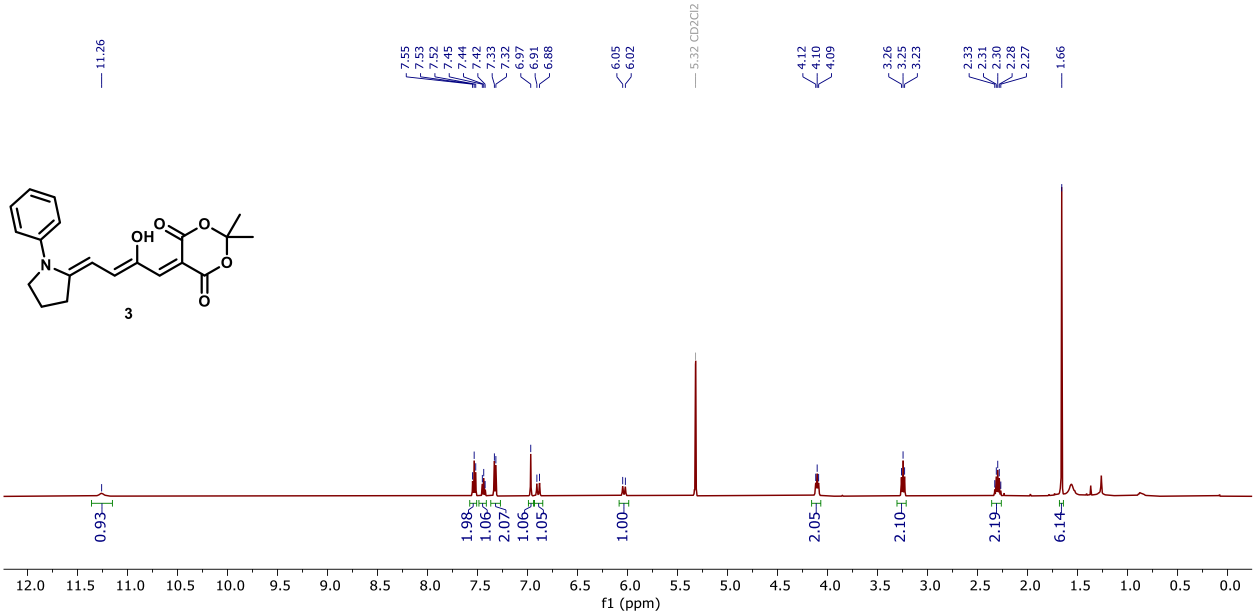


Figure S20. ^{1}H NMR of **3** in CD_2Cl_2 (500 MHz)

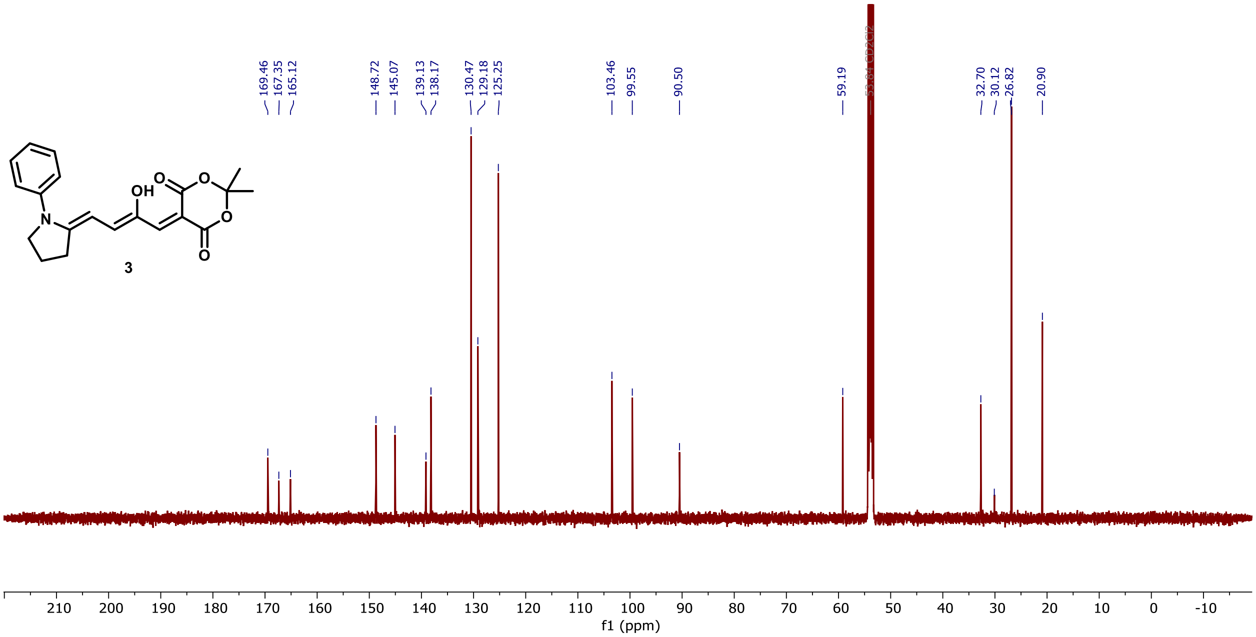


Figure S21. ^{13}C NMR of **3** in CD_2Cl_2 (125 MHz)

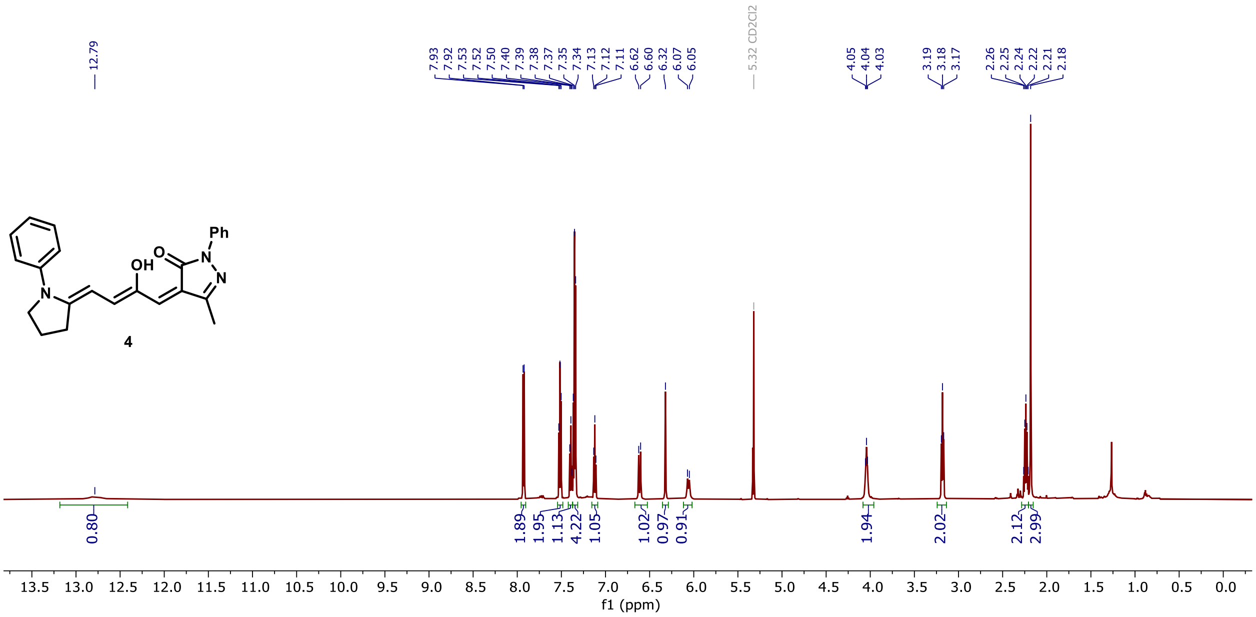


Figure S22. ^{1}H NMR of **4** in CD_2Cl_2 (600 MHz)

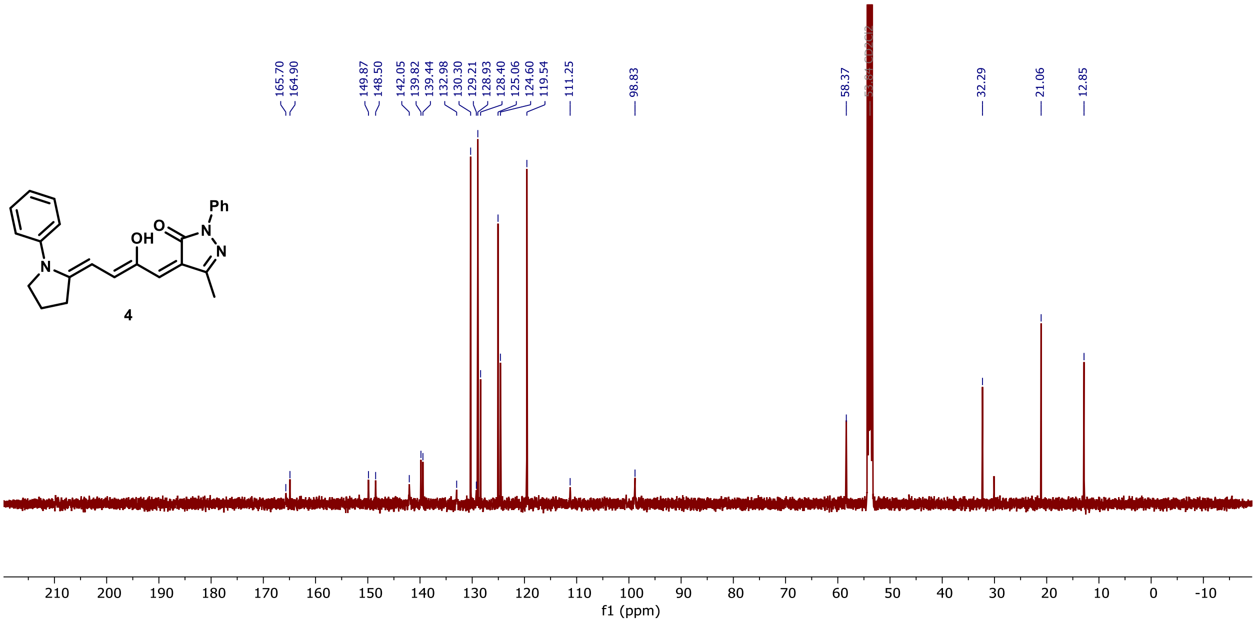


Figure S23. ^{13}C NMR of **4** in CD_2Cl_2 (125 MHz)

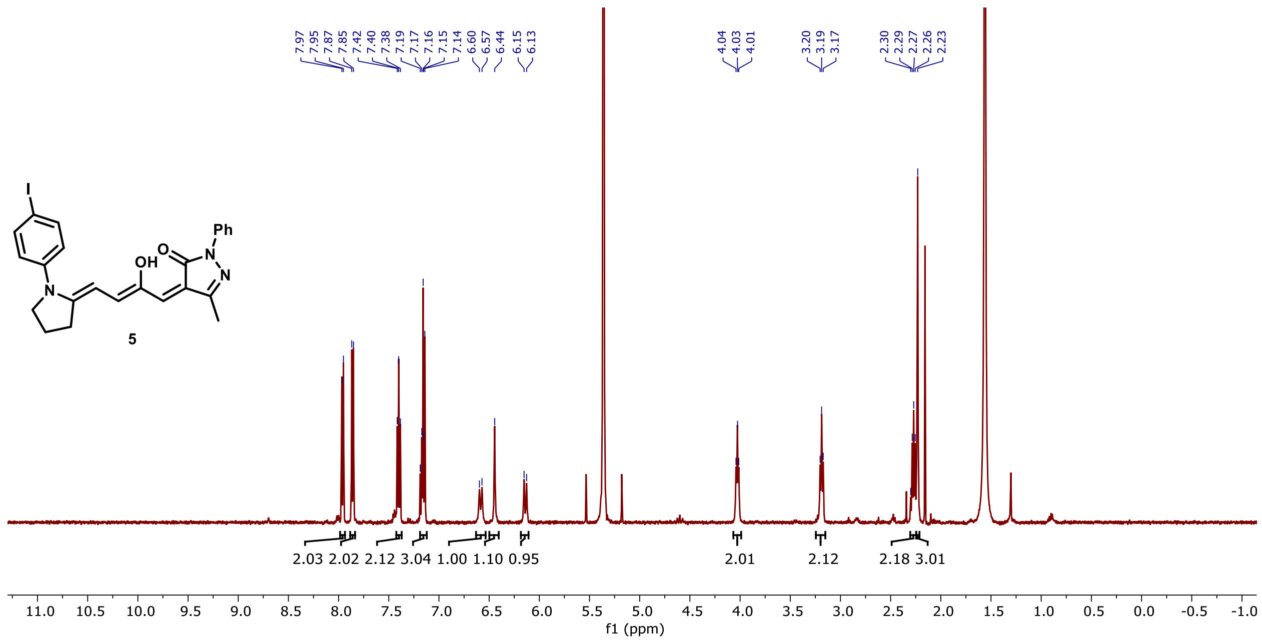


Figure S24. ^1H NMR of **5** in CD_2Cl_2 (600 MHz)

Since **5** is poorly soluble in every deuterated solvent we tried (acetone, acetonitrile, methanol, chloroform, dimethyl sulfoxide, and DCM) we were unable to get a resolved ^{13}C NMR after running for 10 h on a 500 MHz Bruker equipped with a cryoprobe. In order to extract more peaks, we ran an HMBC with non-uniform sampling. The HMBC was worked up using apodization along f2 (exponential = 5 Hz) and the carbon NMR was extracted, resulting in the appearance of more peaks, though significantly broadened and not all peaks are visible.

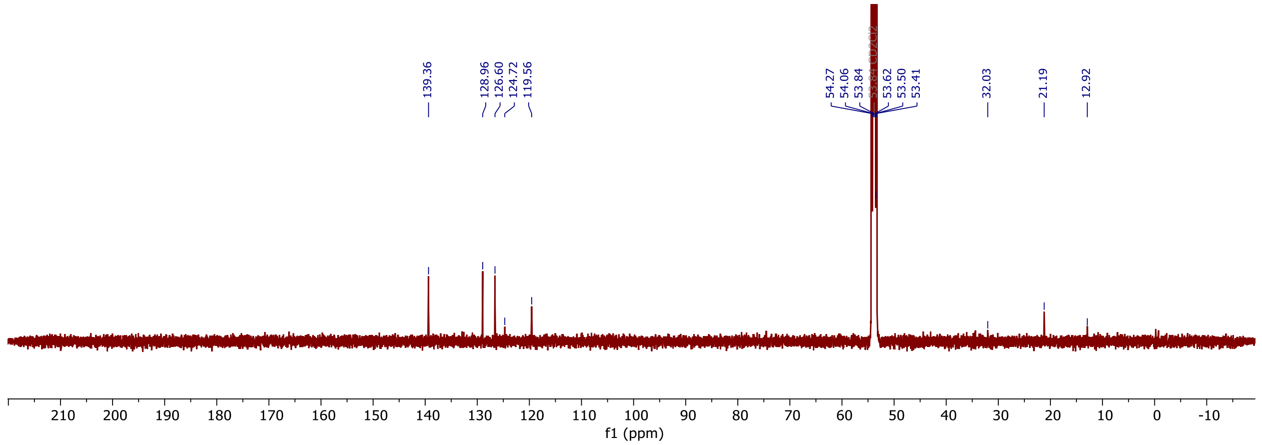


Figure S25. ^{13}C NMR of **5** (saturated) in CD_2Cl_2 run for approximately 10 h (125 Hz Bruker cryoprobe)

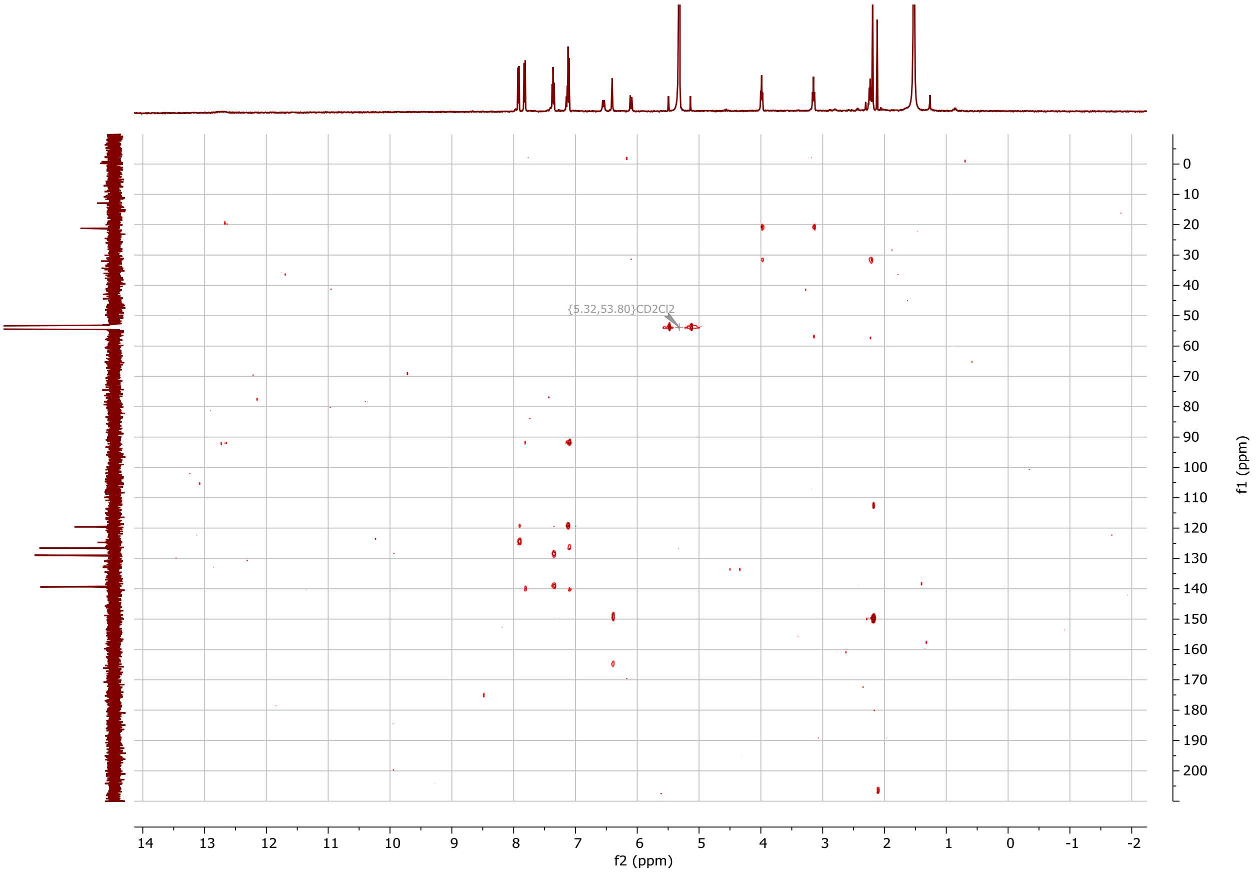


Figure S26. HMBC of **5** (saturated) in CD_2Cl_2 acquired using nonuniform sampling (64 scans)

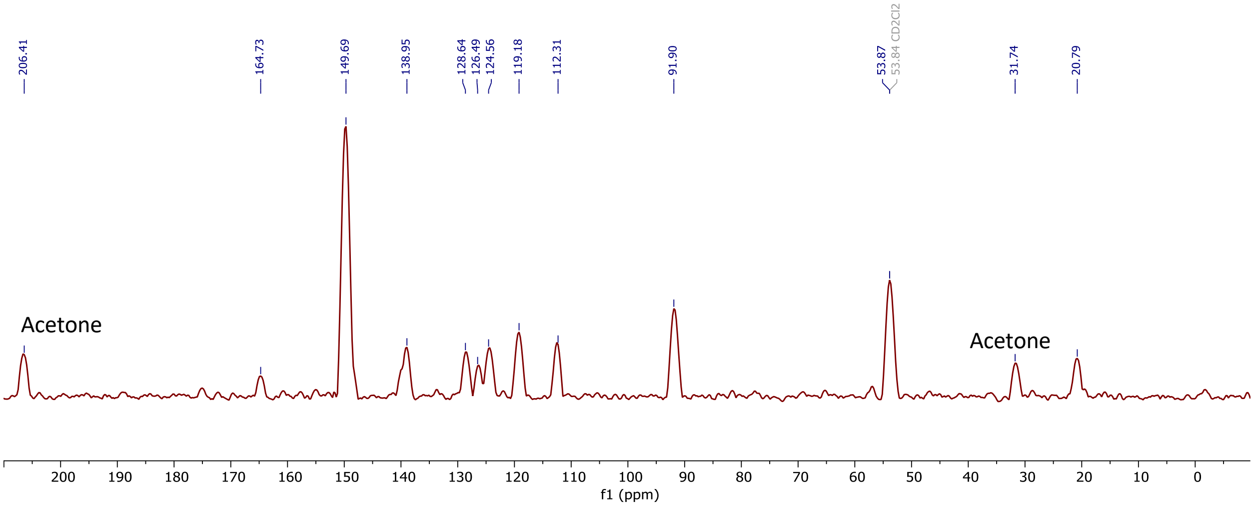


Figure S27. ^{13}C NMR of **5** extracted from HMBC. There are likely additional peaks under peaks around 149, 138, and 53 ppm that are hidden due to the broadening of the peaks

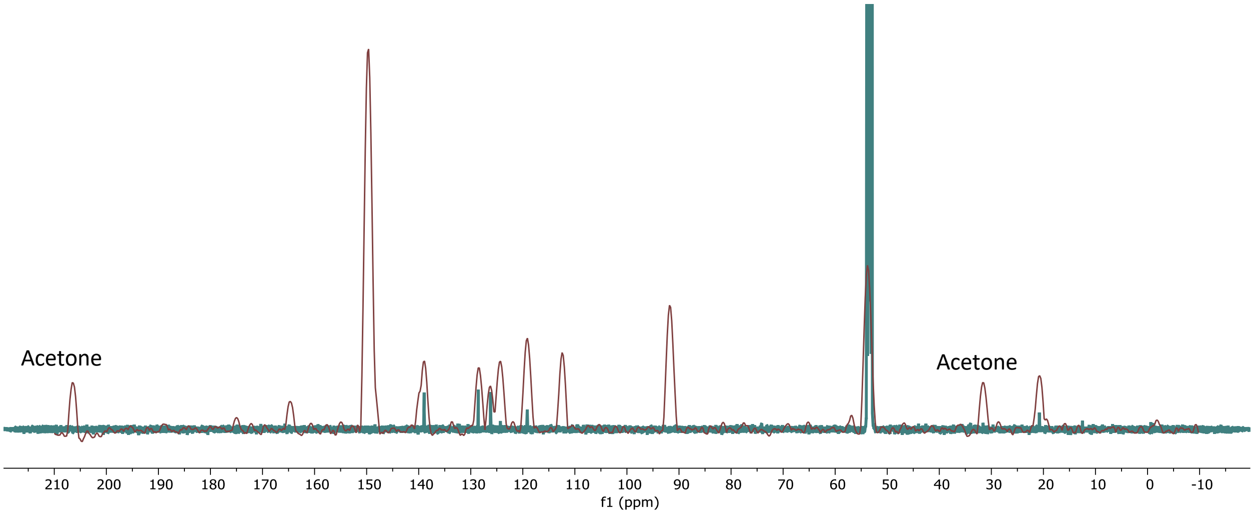


Figure S28. Overlay of ^{13}C NMR run normally and ^{13}C NMR extracted from the HMBC showing the original peaks of **5** as well as some additional peaks.

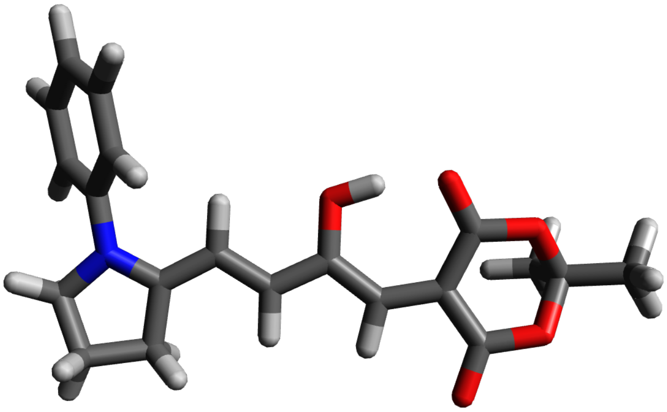
DFT Calculations of **3** and **4**

DFT calculations were conducted using Gaussian 16[9] using the Center for Scientific Computing at the California Nanosystems Institute (CNSI) at UCSB. Geometries were optimized using M06-2X/6-31+G(d,p) in chloroform using an SMD solvent model. Transition states were found doing relaxed scans around the coordinate of interest and doing a transition state search on the highest energy geometry. Frequencies were calculated of each point to ensure that the optimized isomers had zero negative frequencies and the transition states had one negative frequency.

Calculations of **3**

A

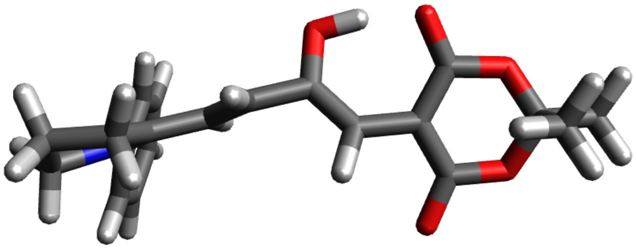
H	-4.46189	3.35851	-1.31186
H	5.81074	-1.45681	2.23000
H	4.58003	-0.17867	2.11932
C	5.59752	-0.46052	1.83557
H	6.29689	0.25546	2.27356
H	-6.04835	1.88438	-0.26376
C	-4.30276	3.24187	-0.23637
H	-4.56991	4.17488	0.26113
C	-5.11618	2.05726	0.27741
N	-4.19824	0.92377	0.05150
C	-2.91266	1.30413	-0.02312
C	-1.81424	0.44664	-0.07044
C	-0.51346	0.93974	-0.13548
C	-2.85573	2.81331	0.03620
H	-2.14097	3.22655	-0.67739
C	0.62637	0.12338	-0.13599
C	1.87062	0.74941	-0.20568
C	5.77212	-0.46910	0.32518
H	1.81476	1.83423	-0.24134
H	-1.96142	-0.62632	-0.02781
O	2.80713	-2.07188	-0.54373
O	0.42183	-1.21419	-0.03703
C	3.56634	-1.12463	-0.33245
C	3.18952	0.26367	-0.22162
O	4.88288	-1.42041	-0.26865
H	7.39299	-1.86562	0.25827
H	-5.33475	2.14408	1.34855
C	7.16425	-0.86272	-0.10887
C	4.24241	1.27520	-0.26409
H	1.27308	-1.68002	-0.24238
H	7.88802	-0.15543	0.30194
O	5.52740	0.82474	-0.21571
H	-2.53263	3.10402	1.04346
O	4.06780	2.47297	-0.38566



H	7.22594	-0.85237	-1.19941
H	-0.34131	2.01139	-0.17878
C	-4.68720	-0.41221	0.04466
C	-4.29478	-1.30310	-0.95768
C	-5.60479	-0.80629	1.02121
C	-4.80399	-2.59903	-0.96103
H	-3.60571	-0.97800	-1.73075
C	-6.11432	-2.10294	1.00342
H	-5.91125	-0.10589	1.79196
C	-5.71188	-3.00356	0.01812
H	-4.49541	-3.29052	-1.73870
H	-6.82315	-2.40894	1.76643
H	-6.10732	-4.01427	0.00949

Electronic energy: -1204.8498724 Hartree
Free energy: -1204.9272438 Hartree

A-B

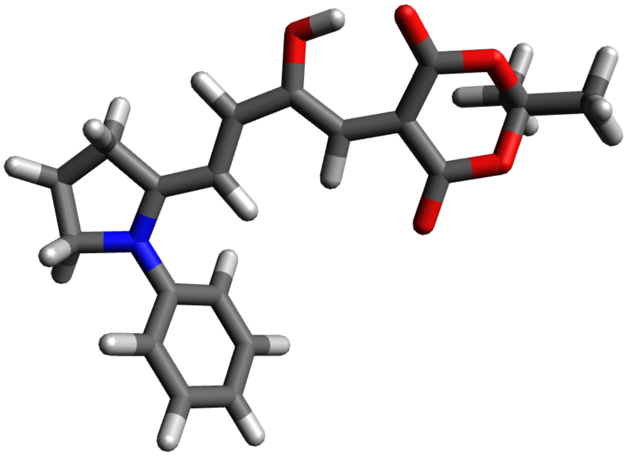


H	5.17806	-1.64858	-0.77242
H	6.70722	-1.37218	0.09142
H	-2.84029	-3.48590	0.28726
H	6.55241	-0.90424	-1.61974
H	-5.23537	-3.62741	-1.15937
H	-2.89482	-3.02457	-1.41857
C	6.02735	-0.96944	-0.66348
H	-0.75871	-2.64267	0.23869
C	-3.32443	-2.82091	-0.42969
H	-5.20632	-3.22063	0.56652
C	-4.85739	-2.91798	-0.42350
H	1.25856	-0.97734	-1.30109
C	-0.68616	-1.55956	0.34063
C	1.55718	-0.73282	-0.28463
C	0.64126	-0.96986	0.67155
C	5.57162	0.42251	-0.24405
O	3.27016	-0.58512	2.14993
C	2.89698	-0.15186	-0.15967
C	3.64360	-0.16036	1.03331
C	-3.06433	-1.37560	-0.11321
H	1.74342	-0.63351	2.19802
C	3.43802	0.48104	-1.32573
O	4.90534	0.36421	1.01474
H	7.40736	1.00917	0.69560
O	2.85829	0.65610	-2.39139
O	0.75059	-0.71098	2.00006
C	-5.31418	-1.48961	-0.71737
H	-5.45204	-1.29241	-1.78538

H	7.26743	1.48258	-1.01571
C	-1.78278	-0.79312	0.20961
O	4.71636	0.98375	-1.22974
C	6.72612	1.38426	-0.07183
H	-6.20739	-1.17709	-0.17525
N	-4.16089	-0.67996	-0.24911
H	-1.71291	0.28578	0.31372
H	6.34556	2.36284	0.23008
C	-4.30689	0.73349	-0.03911
H	-4.94565	1.08581	-2.06717
H	-3.71207	0.62289	2.02736
C	-4.74976	1.52736	-1.09487
C	-4.04198	1.26910	1.21930
C	-4.91453	2.89411	-0.88328
C	-4.20846	2.63807	1.41567
H	-5.24924	3.52535	-1.69991
H	-3.99930	3.06736	2.38996
C	-4.64355	3.44886	0.36780
H	-4.77173	4.51481	0.52629

Electronic energy: -1204.8162092 Hartree
Free energy: -1204.893220 Hartree

B



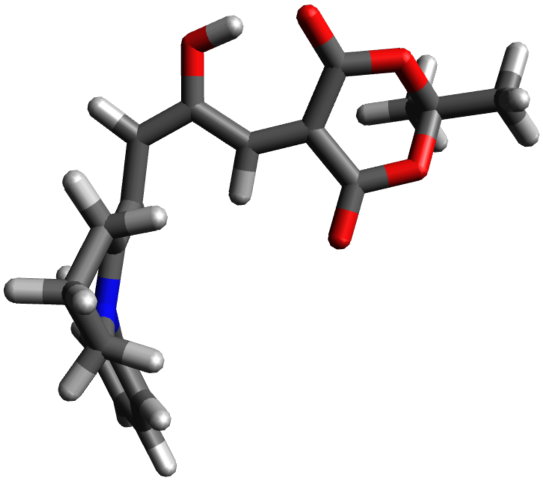
H	-5.19341	-2.56203	1.57564
H	5.92271	-0.10937	1.99612
H	4.16627	0.16477	2.02718
C	5.12488	0.57533	1.69903
H	5.28068	1.54015	2.18728
H	-6.11556	-0.60640	0.51919
C	-5.07550	-2.55761	0.48858
H	-5.73256	-3.31613	0.06158
C	-5.37070	-1.16200	-0.05364
N	-4.05952	-0.49658	0.06513
C	-3.03522	-1.36794	0.09292
C	-1.68771	-1.02310	0.02652
C	-0.69660	-2.00398	0.04746
C	-3.60185	-2.76938	0.11990
H	-3.07131	-3.41558	0.82089
C	0.69915	-1.86009	-0.02934
C	1.29172	-0.60372	-0.13604
C	5.16205	0.76707	0.19117
H	0.59559	0.22982	-0.12323
H	-1.42943	0.02475	-0.07562
O	3.70857	-2.24193	-0.79198
O	1.39513	-3.03057	0.07563

C	3.75921	-1.05070	-0.48511
C	2.62974	-0.18796	-0.22470
O	4.98762	-0.48854	-0.47225
H	7.28733	0.64947	-0.03449
H	-5.67588	-1.18874	-1.10669
C	6.47456	1.32793	-0.30296
C	2.85317	1.25722	-0.20807
H	2.30829	-2.88806	-0.27634
H	6.65174	2.30199	0.15824
O	4.14851	1.67690	-0.22480
H	-3.49590	-3.20149	-0.88263
O	1.98304	2.10681	-0.22467
H	6.44009	1.44170	-1.38878
H	-1.01554	-3.04137	0.14083
C	-3.95787	0.92151	0.02298
C	-3.19062	1.60079	0.97341
C	-4.67003	1.63020	-0.94738
C	-3.11660	2.99048	0.93033
H	-2.66574	1.04250	1.74269
C	-4.59728	3.02148	-0.97484
H	-5.26762	1.09690	-1.68060
C	-3.81708	3.70422	-0.04264
H	-2.51595	3.51582	1.66614
H	-5.14684	3.57007	-1.73343
H	-3.75767	4.78753	-0.07087

Electronic energy: -1204.8419464
Free energy: -1204.9210152

B-B′

H	-3.88550	2.98550	1.89847
H	5.34080	-1.66875	-1.83351
H	3.57340	-1.52567	-1.70512
C	4.47117	-1.92467	-1.22426
H	4.38286	-3.01160	-1.16296
H	-4.62901	0.72123	2.31661
C	-3.09177	2.30023	2.21084
H	-2.80140	2.54196	3.23477
C	-3.57471	0.86021	2.06440
N	-3.36542	0.60624	0.63501
C	-2.29045	1.34984	0.15267
C	-1.61669	1.18824	-1.00420
C	-0.49866	2.08176	-1.37810
C	-1.92086	2.35745	1.22452
H	-1.74309	3.35096	0.80487
C	0.82110	1.86796	-1.14000

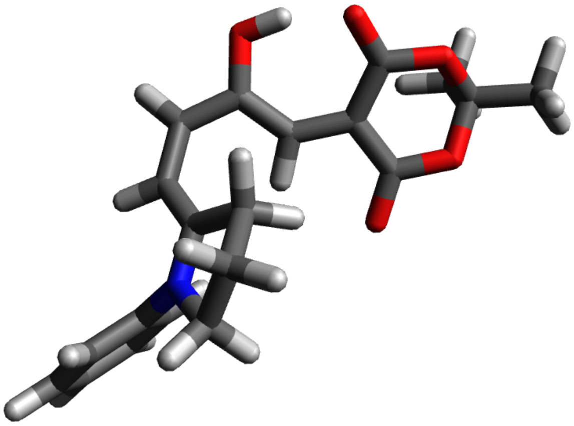


C	1.21074	0.69469	-0.38398
C	4.65651	-1.36332	0.17383
H	0.35638	0.08505	-0.09654
H	-1.88852	0.40895	-1.71040
O	3.92491	1.99056	-0.45815
O	1.71860	2.74628	-1.64860
C	3.73372	0.82508	-0.15481
C	2.41081	0.19607	0.02281
O	4.80129	0.06629	0.11735
H	6.77425	-1.62629	0.29316
H	-2.97108	0.17796	2.68104
C	5.88673	-1.88266	0.87535
C	2.36048	-1.08011	0.78975
H	2.59394	2.62428	-1.21960
H	5.81812	-2.96841	0.96869
O	3.54392	-1.69464	1.00454
H	-0.99050	2.03216	1.70695
O	1.35572	-1.55542	1.26093
H	5.96109	-1.43616	1.86926
H	-0.72317	2.99523	-1.93350
C	-3.95978	-0.49713	0.00323
C	-4.26828	-0.46642	-1.36631
C	-4.31153	-1.62995	0.75207
C	-4.88718	-1.55672	-1.97001
H	-4.04994	0.42333	-1.94655
C	-4.93980	-2.71220	0.13836
H	-4.08724	-1.66883	1.81306
C	-5.22439	-2.68837	-1.22555
H	-5.12149	-1.51283	-3.02968
H	-5.20077	-3.58151	0.73486
H	-5.70960	-3.53468	-1.70121

Electronic energy: -1204.8218224 Hartree
Free energy: -1204.8982527 Hartree

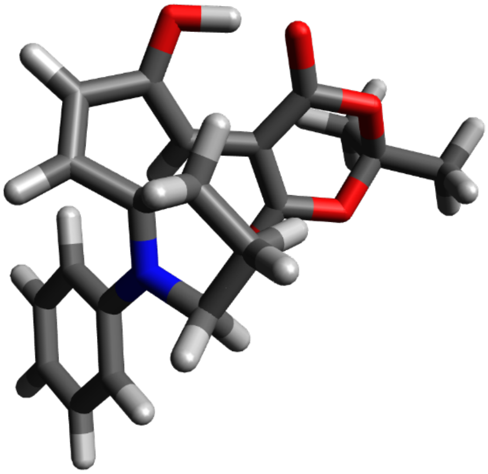
B’

H	-2.32918	1.65397	3.18440
H	5.84963	-0.67757	-1.80111
H	4.09903	-0.80989	-2.08227
C	4.94355	-1.22076	-1.52248
H	5.06182	-2.27437	-1.78626
H	-3.89321	-0.13873	2.83231
C	-1.85633	0.70387	2.91860
H	-1.33609	0.31060	3.79268
C	-2.90715	-0.26293	2.38166
N	-2.95647	0.09530	0.95072
C	-1.88341	0.79272	0.54310
C	-1.83543	1.44156	-0.69986
C	-0.74835	2.12989	-1.23661
C	-0.92592	0.89194	1.71261
H	-0.36834	1.83041	1.70480
C	0.61772	1.89769	-1.00462
C	1.03247	0.63667	-0.57631
C	4.72806	-1.10340	-0.02202
H	0.24146	-0.10786	-0.56023
H	-2.77967	1.51294	-1.23430
O	3.49872	2.15395	0.08612
O	1.46892	2.89284	-1.38607
C	3.45912	0.92461	0.04509
C	2.28971	0.12219	-0.22881
O	4.60166	0.27199	0.35372
H	6.79289	-1.12139	0.54004
H	-2.60507	-1.31342	2.47384
C	5.87526	-1.65953	0.78769
C	2.34421	-1.31016	0.05504
H	2.31609	2.77473	-0.89423
H	6.00567	-2.71888	0.55607
O	3.56367	-1.82338	0.37469
H	-0.20494	0.06806	1.67284
O	1.38719	-2.06162	0.08337
H	5.66331	-1.54459	1.85309
H	-0.97170	2.93713	-1.93435
C	-4.00159	-0.38186	0.10867
C	-5.32962	-0.09713	0.43069
C	-3.69225	-1.15546	-1.01303
C	-6.35230	-0.58604	-0.38012
H	-5.55614	0.51045	1.30206
C	-4.72049	-1.63331	-1.82069
H	-2.65399	-1.37909	-1.24114
C	-6.05082	-1.35116	-1.50636
H	-7.38534	-0.36227	-0.13308
H	-4.48092	-2.23503	-2.69179
H	-6.84993	-1.72899	-2.13638



Electronic energy: -1204.8353862 Hartree
Free energy: -1204.9124881 Hartree

B’-C

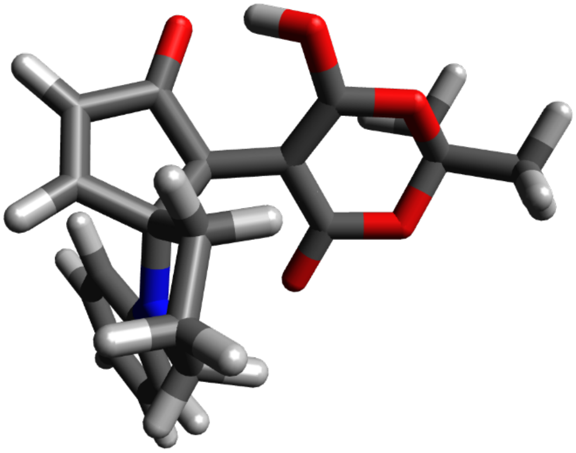


H	-0.05800	0.38449	3.71722
H	4.76380	-1.34060	-1.95985
H	3.04605	-1.01932	-2.29093
C	3.74152	-1.65603	-1.73810
H	3.60692	-2.69015	-2.06401
H	-2.21433	-0.39018	3.02322
C	-0.18023	0.31285	2.63528
H	0.70524	-0.17245	2.21897
C	-1.43771	-0.46649	2.25313
N	-1.90642	0.19578	1.02297
C	-1.20756	1.33650	0.73036
C	-1.84119	2.41805	-0.03786
C	-1.00734	3.09785	-0.85238
C	-0.39734	1.67882	1.98312
H	-1.02963	2.31244	2.61705
C	0.29667	2.47980	-0.90673
C	0.28100	1.07798	-0.66630
C	3.50059	-1.57029	-0.23869
H	-0.49159	0.54675	-1.21613
H	-2.90672	2.61275	0.06878
O	3.12642	1.87598	-0.06394
O	1.35254	3.23314	-1.00341
C	2.73248	0.67990	-0.08996
C	1.43122	0.22619	-0.36979
O	3.69011	-0.22567	0.21191
H	5.48149	-2.10912	0.37177
H	-1.23637	-1.52075	2.04690
C	4.45367	-2.42605	0.56220
C	1.13976	-1.18003	-0.22126
H	2.20900	2.68392	-0.65562
H	4.33994	-3.47186	0.26835
O	2.18617	-2.00800	0.08219
H	0.52318	2.22119	1.76095
O	0.02776	-1.68079	-0.27610
H	4.23391	-2.32341	1.62735
H	-1.23349	4.02953	-1.35870
C	-2.86616	-0.43481	0.20872
C	-3.62982	-1.48317	0.74624
C	-3.07511	-0.07326	-1.13261
C	-4.57420	-2.14390	-0.03499
H	-3.49437	-1.78747	1.77723
C	-4.02004	-0.74451	-1.90266

H	-2.51100	0.72708	-1.59604
C	-4.77887	-1.78272	-1.36437
H	-5.15129	-2.95028	0.40752
H	-4.15593	-0.44953	-2.93883
H	-5.51417	-2.30077	-1.97129

Electronic energy: --1204.8183692 Hartree
Free energy: -1204.8905822 Hartree

C



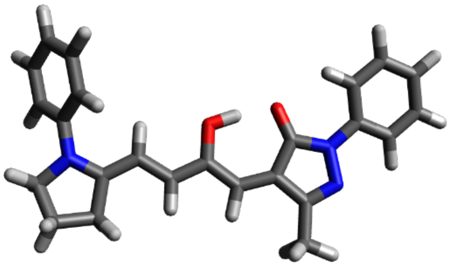
H	-1.89707	1.66738	3.35208
H	4.61286	-1.37959	-1.95619
H	2.85588	-1.20612	-2.17759
C	3.63485	-1.71437	-1.60314
H	3.54402	-2.79089	-1.76496
H	-2.65110	-0.57072	2.86017
C	-1.10177	0.95752	3.10164
H	-0.55565	0.70816	4.01403
C	-1.69792	-0.26615	2.41868
N	-1.90609	0.20298	1.05167
C	-0.96334	1.26051	0.68886
C	-1.67230	2.52289	0.24227
C	-1.08625	3.12932	-0.79949
C	-0.19140	1.51708	2.01146
H	0.05991	2.57325	2.13548
C	0.08599	2.34916	-1.19461
C	0.01361	0.98586	-0.52820
C	3.50800	-1.42684	-0.11658
H	-0.58075	0.38787	-1.23791
H	-2.55524	2.86986	0.77390
O	2.93335	1.98683	-0.38581
O	0.99508	2.75090	-1.92164
C	2.56006	0.73462	-0.20736
C	1.29273	0.22607	-0.28235
O	3.61989	-0.01477	0.11546
H	5.56423	-1.72608	0.39324
H	-1.00752	-1.12347	2.44903
C	4.58310	-2.08166	0.71563
C	1.13195	-1.18537	0.05368
H	2.29081	2.42833	-1.00114
H	4.53291	-3.16461	0.58451
O	2.25775	-1.88722	0.37749
H	0.74265	0.94653	1.98858
O	0.06572	-1.75658	0.13428
H	4.43456	-1.83656	1.76957
H	-1.35045	4.07260	-1.26216

C	-2.67001	-0.52816	0.15419
C	-3.13057	-1.81583	0.49757
C	-3.04503	-0.01572	-1.10429
C	-3.92941	-2.54528	-0.37691
H	-2.83932	-2.26158	1.44147
C	-3.83500	-0.76281	-1.97439
H	-2.74426	0.98168	-1.40334
C	-4.28967	-2.03266	-1.62324
H	-4.26116	-3.53649	-0.08015
H	-4.10427	-0.33388	-2.93573
H	-4.90847	-2.60888	-2.30334

Electronic energy: -1204.8371212 Hartree
Free energy: -1204.9101492 Hartree

Calculations of **4**

A

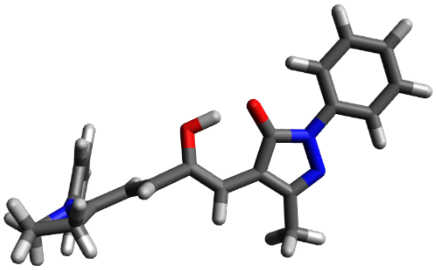


H	-5.77208	-2.85906	1.32314
H	-7.03658	-1.08714	0.29623
C	-5.61473	-2.77926	0.24393
H	-6.08502	-3.63422	-0.24345
C	-6.16800	-1.44834	-0.25787
N	-5.03070	-0.53432	-0.04352
C	-3.84795	-1.17990	0.00186
C	-2.59502	-0.58064	0.02636
C	-1.42056	-1.33997	0.05380
C	-4.11611	-2.66673	-0.06101
H	-3.48987	-3.22627	0.63594
C	-0.14068	-0.78169	0.03849
C	0.96343	-1.64330	0.06055
H	0.71349	-2.70231	0.08993
H	-2.50823	0.49938	-0.00694
O	-0.04684	0.56832	0.00638
H	-6.41693	-1.48785	-1.32545
H	0.91282	0.86436	-0.02324
H	-3.88617	-3.01554	-1.07532
H	-1.47689	-2.42442	0.08640
C	-5.22659	0.87252	-0.01547
C	-6.07287	1.46489	-0.95642
C	-4.62246	1.65089	0.97618
C	-6.30031	2.83888	-0.91155
H	-6.54280	0.85717	-1.72363
C	-4.84919	3.02414	1.00616
H	-3.98980	1.18031	1.72199
C	-5.68639	3.62287	0.06414
H	-6.95522	3.29582	-1.64689

H	-4.37610	3.62504	1.77648
H	-5.86247	4.69342	0.09391
C	2.32313	-1.33571	0.05181
C	3.40947	-2.28086	0.08324
N	4.57058	-1.68767	0.06623
N	4.31772	-0.32172	0.02858
C	2.96969	-0.04091	0.00721
O	2.47036	1.10852	-0.05079
C	3.30470	-3.76865	0.13693
H	2.76772	-4.08973	1.03519
H	2.76362	-4.15339	-0.73345
H	4.30434	-4.20749	0.15052
C	5.40738	0.57469	-0.03187
C	5.23761	1.94087	0.22859
C	6.67873	0.07608	-0.34483
C	6.33945	2.79199	0.16439
H	4.25792	2.32702	0.47427
C	7.76697	0.94182	-0.39942
H	6.80324	-0.98168	-0.54054
C	7.60700	2.30453	-0.14835
H	6.19753	3.84931	0.36788
H	8.74719	0.54322	-0.64384
H	8.45871	2.97593	-0.19403

Electronic energy: -1242.2137541 Hartree
Free energy: -1242.2966278 Hartree

A-B



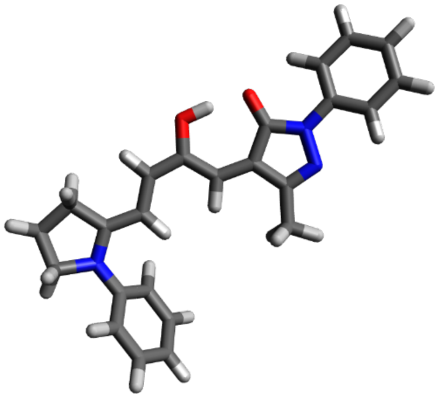
H	5.95763	-2.30379	-2.23378
H	6.98174	-0.61237	-0.88663
C	5.80600	-2.47085	-1.16491
H	6.36510	-3.35770	-0.86733
C	6.23902	-1.23182	-0.38276
N	4.97289	-0.46437	-0.26677
C	3.90957	-1.18878	-0.49241
C	2.55945	-0.70555	-0.32315
C	1.50434	-1.48378	-0.62128
C	4.30469	-2.59004	-0.86294
H	3.71929	-2.96443	-1.70452
C	0.10245	-0.99509	-0.49693
C	-0.66840	-1.29930	0.56625
H	-0.21467	-1.90935	1.34481
H	2.40952	0.29809	0.06380
O	-0.24887	-0.23989	-1.56113
H	6.58647	-1.46157	0.62947
H	-1.29434	-0.16522	-1.60143
H	4.09798	-3.23317	0.00143

H	1.65992	-2.48651	-1.02016
C	4.99874	0.92346	0.10137
C	5.66524	1.29803	1.26670
C	4.39858	1.86502	-0.73248
C	5.71175	2.64699	1.60997
H	6.12756	0.54655	1.89974
C	4.45023	3.21018	-0.37464
H	3.90252	1.54797	-1.64523
C	5.10426	3.60112	0.79336
H	6.22037	2.95016	2.51928
H	3.98112	3.95076	-1.01392
H	5.14232	4.65070	1.06663
C	-2.05310	-0.88865	0.75733
C	-2.82699	-0.95739	1.94170
N	-4.06428	-0.52494	1.76302
N	-4.12970	-0.15337	0.43785
C	-2.92817	-0.37348	-0.21988
O	-2.73345	-0.15655	-1.47149
C	-2.38186	-1.44486	3.28379
H	-2.06107	-2.49133	3.23698
H	-1.53708	-0.85640	3.65742
H	-3.20364	-1.36713	3.99973
C	-5.34843	0.31516	-0.08672
C	-5.41617	0.92428	-1.34881
C	-6.51715	0.18141	0.67799
C	-6.64239	1.38153	-1.82848
H	-4.51604	1.02730	-1.93950
C	-7.73101	0.64846	0.18323
H	-6.46007	-0.28681	1.65259
C	-7.80674	1.25022	-1.07331
H	-6.67945	1.85049	-2.80775
H	-8.62603	0.53570	0.78858
H	-8.75655	1.61072	-1.45600

Electronic energy: -1242.1789714 Hartree
Free energy: -1242.2605843 Hartree

B

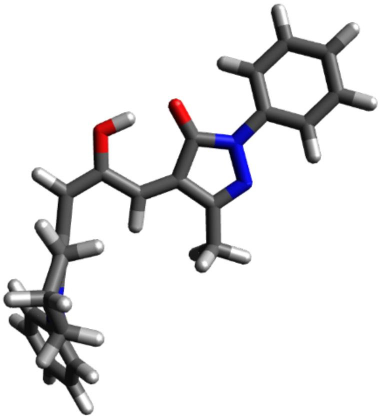
H	-5.95651	-2.95351	1.12128
H	-6.97348	-1.01343	0.12079
C	-5.74123	-2.84700	0.05437
H	-6.28095	-3.62195	-0.49146
C	-6.11802	-1.44154	-0.40558
N	-4.90332	-0.67233	-0.08341
C	-3.79507	-1.45105	-0.04309
C	-2.49178	-0.99096	0.02762
C	-1.40545	-1.88100	0.06179
C	-4.22695	-2.89417	-0.18334
H	-3.70247	-3.55046	0.51324
C	-0.03842	-1.60066	0.07169
C	0.44613	-0.28476	0.02330
H	-0.31544	0.49040	-0.01469
H	-2.32385	0.07973	0.02843
O	0.77865	-2.68887	0.12675
H	-6.30865	-1.40559	-1.48576
H	1.74208	-2.42527	0.10013
H	-3.99166	-3.22909	-1.20082
H	-1.62954	-2.94661	0.08360
C	-4.94493	0.74007	0.02757
C	-5.71068	1.47981	-0.87837
C	-4.27193	1.38975	1.06863
C	-5.78506	2.86576	-0.75257
H	-6.23926	0.97463	-1.68077
C	-4.34551	2.77539	1.17955
H	-3.71150	0.80810	1.79387
C	-5.09862	3.51904	0.26981
H	-6.37862	3.43437	-1.46174
H	-3.82327	3.27342	1.99069
H	-5.15631	4.59877	0.36335
C	1.75631	0.17745	0.01138
C	2.15833	1.56234	-0.04388
N	3.45413	1.69176	-0.04859
N	3.98423	0.40749	0.00964
C	3.00723	-0.56166	0.03666
O	3.21285	-1.79547	0.06308
C	1.26164	2.75412	-0.08635
H	0.61895	2.72744	-0.97212
H	0.61514	2.78761	0.79646
H	1.86240	3.66522	-0.11610
C	5.38680	0.24358	-0.02824
C	5.98423	-0.96528	0.35106
C	6.18377	1.31899	-0.44090
C	7.37183	-1.08656	0.30379
H	5.37030	-1.79467	0.67473
C	7.56797	1.17941	-0.47638
H	5.71406	2.25162	-0.72797



C	8.17221	-0.02258	-0.10805
H	7.82651	-2.02750	0.59920
H	8.17573	2.01955	-0.79913
H	9.25212	-0.12748	-0.14005

Electronic energy: -1242.2061507 Hartree
Free energy: -1242.2901504 Hartree

B-B′

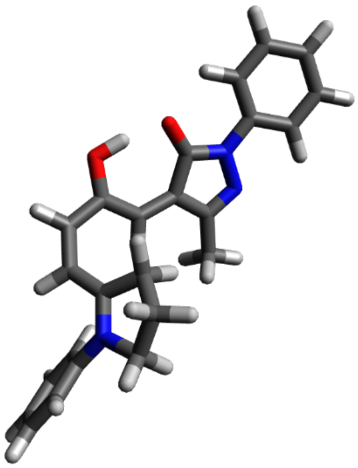


H	4.51691	-2.56058	2.57649
H	5.41123	-0.31323	2.54942
C	3.76510	-1.77458	2.69516
H	3.41854	-1.77365	3.73011
C	4.35989	-0.43356	2.27602
N	4.22427	-0.47406	0.81634
C	3.12007	-1.23998	0.44085
C	2.51466	-1.30240	-0.76262
C	1.35403	-2.19089	-0.99820
C	2.63260	-1.96482	1.68147
H	2.39559	-3.01101	1.47296
C	0.04634	-1.85182	-0.86941
C	-0.30432	-0.51093	-0.44204
H	0.56109	0.12389	-0.26043
H	2.88330	-0.72750	-1.60721
O	-0.90014	-2.77642	-1.15149
H	3.78745	0.40253	2.70560
H	-1.81885	-2.43367	-1.00091
H	1.71108	-1.48436	2.03402
H	1.53879	-3.21456	-1.33062
C	4.92730	0.42700	0.00296
C	5.34500	1.66214	0.52222
C	5.27916	0.09303	-1.31509
C	6.07751	2.54723	-0.26689
H	5.09404	1.93307	1.54264
C	6.00236	0.98905	-2.09639
H	5.01451	-0.88036	-1.71244
C	6.40312	2.22341	-1.58256
H	6.38937	3.49880	0.15371
H	6.26843	0.71033	-3.11188
H	6.97000	2.91640	-2.19595
C	-1.52279	0.05291	-0.24347
C	-1.76308	1.42878	0.18519
N	-3.02730	1.67540	0.28901
N	-3.71811	0.51204	-0.06096
C	-2.87894	-0.51790	-0.38450
O	-3.21877	-1.66525	-0.70515
C	-0.73129	2.46420	0.47141

H	-0.06534	2.13321	1.27446
H	-0.11940	2.65380	-0.41584
H	-1.21761	3.39340	0.77293
C	-5.13218	0.50654	0.01783
C	-5.88279	-0.47410	-0.64059
C	-5.77116	1.50727	0.75814
C	-7.27250	-0.44832	-0.54011
H	-5.38913	-1.24327	-1.21907
C	-7.16036	1.51833	0.84173
H	-5.18066	2.26537	1.25782
C	-7.91917	0.54146	0.19758
H	-7.85007	-1.21186	-1.05222
H	-7.64933	2.29748	1.41851
H	-9.00217	0.55332	0.26813

Electronic Energy: -1242.1888893 Hartree
Free energy: -1242.270595 Hartree

B’

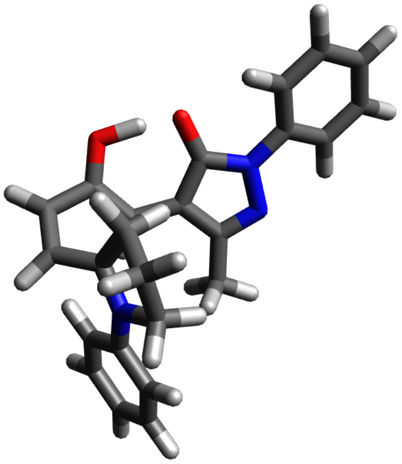


H	-2.85411	0.52432	3.55354
H	-4.58797	-0.95603	2.81712
C	-2.48836	-0.31900	2.96027
H	-1.94874	-1.00325	3.61634
C	-3.65751	-0.99330	2.24850
N	-3.77549	-0.19977	1.01137
C	-2.66971	0.54355	0.75335
C	-2.63880	1.55810	-0.19490
C	-1.52409	2.35404	-0.52581
C	-1.62997	0.18921	1.79516
H	-0.98870	1.03866	2.03795
C	-0.18212	1.98341	-0.52195
C	0.17329	0.62427	-0.62570
H	-0.66057	-0.05124	-0.80659
H	-3.59500	1.84662	-0.62539
O	0.73584	2.98441	-0.58469
H	-3.44785	-2.03876	1.98788
H	1.64524	2.64058	-0.36057
H	-0.98926	-0.62110	1.42799
H	-1.72381	3.38304	-0.82539
C	-4.89812	-0.33906	0.15283
C	-4.71460	-0.61949	-1.20583
C	-6.18974	-0.23161	0.67533
C	-5.82039	-0.77726	-2.03571
H	-3.70841	-0.71403	-1.60342
C	-7.29151	-0.40044	-0.16152
H	-6.33132	-0.00640	1.72801
C	-7.11199	-0.66970	-1.51747

H	-5.67136	-0.99472	-3.08886
H	-8.29252	-0.31228	0.24923
H	-7.97219	-0.79708	-2.16697
C	1.43137	0.04453	-0.59854
C	1.73487	-1.34721	-0.83381
N	3.00379	-1.59617	-0.68556
N	3.61488	-0.39043	-0.35576
C	2.71453	0.64742	-0.27674
O	2.98753	1.82830	0.02940
C	0.77050	-2.42058	-1.21219
H	-0.02094	-2.51872	-0.46156
H	0.29531	-2.19461	-2.17198
H	1.29404	-3.37499	-1.29502
C	5.00241	-0.37620	-0.08898
C	5.72119	0.82577	-0.06936
C	5.66046	-1.58997	0.14597
C	7.08950	0.79948	0.19405
H	5.21508	1.76312	-0.25588
C	7.02833	-1.59531	0.40259
H	5.09804	-2.51519	0.12366
C	7.75206	-0.40336	0.43157
H	7.63930	1.73585	0.20714
H	7.52841	-2.54210	0.58386
H	8.81836	-0.41274	0.63425

Electronic energy: -1242.1981781 Hartree
Free energy: -1242.2804475 Hartree

B’-C



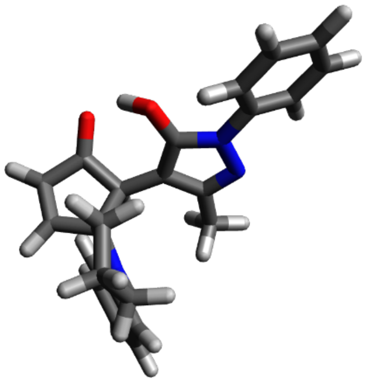
H	-2.43835	2.00744	3.32025
H	-3.19550	-0.24474	3.09050
C	-1.67519	1.32265	2.93831
H	-0.92623	1.15797	3.71447
C	-2.32886	0.02319	2.48365
N	-2.76417	0.34053	1.10695
C	-2.10158	1.42658	0.60099
C	-2.71682	2.34733	-0.33611
C	-1.87434	2.95188	-1.21469
C	-1.06914	1.85473	1.63839
H	-0.90198	2.93222	1.61668
C	-0.57543	2.32681	-1.26331
C	-0.59298	0.92544	-1.03036
H	-1.46148	0.37682	-1.38043
H	-3.79224	2.51297	-0.30087
O	0.50463	3.03142	-1.42224
H	-1.62534	-0.81975	2.47103
H	1.47691	2.46133	-1.07925

H	-0.11553	1.34323	1.45485
H	-2.11319	3.83581	-1.79695
C	-3.57409	-0.56461	0.38968
C	-3.94065	-0.35353	-0.95122
C	-3.98349	-1.75556	1.01424
C	-4.68685	-1.30879	-1.63544
H	-3.65395	0.54766	-1.47825
C	-4.73581	-2.69797	0.31801
H	-3.70605	-1.96732	2.03921
C	-5.09361	-2.48654	-1.01114
H	-4.95064	-1.12061	-2.67176
H	-5.03451	-3.60957	0.82666
H	-5.67684	-3.22510	-1.55116
C	0.56552	0.14415	-0.73372
C	0.63556	-1.27191	-0.55829
N	1.85356	-1.66887	-0.26324
N	2.62738	-0.52516	-0.24161
C	1.89279	0.59124	-0.52592
O	2.38864	1.77999	-0.62427
C	-0.49247	-2.24656	-0.64937
H	-1.22672	-2.07661	0.14608
H	-1.01833	-2.15308	-1.60533
H	-0.11086	-3.26572	-0.55701
C	4.01995	-0.63145	-0.01540
C	4.75860	0.46371	0.44545
C	4.65008	-1.85933	-0.24523
C	6.12801	0.32164	0.66175
H	4.26734	1.41074	0.62733
C	6.01702	-1.98522	-0.01524
H	4.06503	-2.69952	-0.59947
C	6.76507	-0.89725	0.43509
H	6.69641	1.17572	1.01761
H	6.49910	-2.94124	-0.19650
H	7.83169	-0.99930	0.60888

Electronic energy: -1242.184438 Hartree
Free energy: -1242.2640237 Hartree

C

H	-2.24085	1.94461	3.14321
H	-2.99225	-0.30888	3.04330
C	-1.45430	1.22235	2.90102
H	-0.80200	1.11251	3.76985
C	-2.08146	-0.09871	2.47942
N	-2.39001	0.10937	1.06066
C	-1.60194	1.17663	0.47776
C	-2.44952	2.31648	-0.03680
C	-1.91460	2.92353	-1.09591
C	-0.69339	1.63972	1.64798
H	-0.49040	2.71098	1.59191
C	-0.67368	2.22105	-1.40797
C	-0.79921	0.83750	-0.80885
H	-1.45890	0.27734	-1.47993
H	-3.34297	2.64494	0.48913
O	0.30891	2.67988	-1.97708
H	-1.38639	-0.93975	2.61849
H	1.80630	2.28414	-1.07076
H	0.26105	1.10680	1.60510
H	-2.22749	3.85641	-1.55494
C	-3.41293	-0.57445	0.41359
C	-3.86755	-0.19620	-0.86791
C	-4.04279	-1.69078	1.01664
C	-4.90012	-0.88696	-1.49501
H	-3.43233	0.65317	-1.37972
C	-5.08068	-2.36313	0.37834
H	-3.70793	-2.05455	1.97938
C	-5.52529	-1.97201	-0.88300
H	-5.22108	-0.55796	-2.47937
H	-5.53688	-3.21363	0.87738
H	-6.33164	-2.50201	-1.37878
C	0.45791	0.06600	-0.62655
C	0.60781	-1.35111	-0.62369
N	1.85495	-1.71855	-0.37877
N	2.55722	-0.56103	-0.23928
C	1.75536	0.51848	-0.42925
O	2.29288	1.74651	-0.42186
C	-0.45034	-2.38111	-0.82821
H	-1.12553	-2.42865	0.03007
H	-1.05494	-2.15628	-1.71249
H	0.01136	-3.36218	-0.95911
C	3.96009	-0.60247	-0.02755
C	4.60056	0.39631	0.70918
C	4.68524	-1.67443	-0.55343
C	5.97896	0.32332	0.90099
H	4.03033	1.21518	1.13086
C	6.05927	-1.74058	-0.34076
H	4.16783	-2.44113	-1.11862



C	6.71307	-0.74151	0.38101
H	6.47613	1.10136	1.47207
H	6.62081	-2.57501	-0.74956
H	7.78560	-0.79448	0.53934

Electronic energy: -1242.2167631 Hartree
Free energy: -1242.2942796 Hartree

References

(1) Yamamoto, H.; Sasaki, I.; Imagawa, H.; Nishizawa, M. Hg(OAc)2·0.1Sc(OTf)3-Catalyzed Cycloisomerization of 2-(4-Pentynyl)Furan. *Org. Lett.* **2007**, *9* (7), 1399–1402. https://doi.org/10.1021/OL070335M/SUPPL_FILE/OL070335MSI20070215_061316.PDF.

(2) Yan, C.; Theodorescu, D.; Miller, B.; Kumar, A.; Kumar, V.; Ross, D.; Wempe, M. F. Synthesis of Novel Ral Inhibitors: An in Vitro and in Vivo Study. *Bioorg. Med. Chem. Lett.* **2016**, *26* (23), 5815–5818. https://doi.org/10.1016/j.bmcl.2016.10.021.

(3) Stricker, F.; Peterson, J.; Read de Alaniz, J. Preparation of a Donor-Acceptor Stenhouse Adduct (DASA): 5-((2Z,4E)-5-(Diethylamino)-2-Hydroxypenta2,4-Dien-1-Ylidene)-2,2-Dimethyl-1,3-Dioxane-4,6-Dione. *Org. Synth.* **2022**, *99*, 79–91. https://doi.org/10.15227/orgsyn.99.0079.

(4) Clerc, M.; Stricker, F.; Ulrich, S.; Sroda, M.; Bruns, N.; Boesel, L. F.; Read de Alaniz, J. Promoting the Furan Ring Opening Reaction to Access New Donor–Acceptor Stenhouse Adducts with Hexafluoroisopropanol. *Angew. Chem. Int. Ed.* **2021**, anie.202100115. https://doi.org/10.1002/anie.202100115.

(5) Reichardt, C. Solvatochromic Dyes as Solvent Polarity Indicators. *Chem. Rev.* **1994**, *94* (8), 2319–2358. https://doi.org/10.1021/cr00032a005.

(6) Sroda, M. M.; Stricker, F.; Peterson, J. A.; Bernal, A.; Read de Alaniz, J. Donor–Acceptor Stenhouse Adducts: Exploring the Effects of Ionic Character. *Chem. – Eur. J.* **2021**, *27* (12), 4183–4190. https://doi.org/10.1002/chem.202005110.

(7) Peterson, J. A.; Stricker, F.; Read de Alaniz, J.; Li, R.; Chemcomm, /; Communication, C. Improving the Kinetics and Dark Equilibrium of Donor–Acceptor Stenhouse Adduct by Triene Backbone Design. *Chem. Commun.* **2022**, *58* (14), 2303–2306. https://doi.org/10.1039/D1CC06235B.

(8) Mallo, N.; Foley, E. D.; Iranmanesh, H.; Kennedy, A. D. W.; Luis, E. T.; Ho, J.; Harper, J. B.; Beves, J. E. Structure-Function Relationships of Donor-Acceptor Stenhouse Adduct Photochromic Switches. *Chem. Sci.* **2018**, *9* (43), 8242–8252. https://doi.org/10.1039/c8sc03218a.

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. a.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. a.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, a. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, a. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. a.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. a.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, a. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. G16_C01, 2016, Gaussian 16, Revision C.01, Gaussian, Inc., Wallin.