Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

An Easily Accessible Isospiropyran Switch

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SUPPORTING INFORMATION

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General Information

All chemicals were purchased from commercial sources and used as received unless stated otherwise. All solvents were dried prior to use according to standard literature procedures. Chromatographic purifications were performed with silica gel 60 (SiO_2, Sorbent Technologies 40-75μm, 200 x 400 mesh). Thin-layer chromatography (TLC) was performed on silica-gel plate w/UV254 (200 μm). Chromatograms were visualized by UV-light or stained with I_2 in SiO_2. All NMR samples were contained in class B glass NMR tubes (Wilmad Lab Glass). NMR experiments were performed with Bruker 600 and 700 MHz spectrometers. Chemical shifts are expressed in parts per million (δ, ppm) while coupling constant values (J) are given in Hertz (Hz). Residual solvent protons were used as internal standards: for ^{1}H NMR spectra $CDCl_3$ = 7.26 ppm and $(CD_3)_2SO$ = 2.50 ppm, while for ^{13}C NMR spectra $CDCl_3$ = 77.16 ppm and $(CD_3)_2SO$ = 39.52 ppm; $CDCl_3$ and $(CD_3)_2SO$ were purchased from Cambridge Isotope Laboratories. HRMS was measured on a Bruker ESI-TOF instrument. UV-vis experiments were performed with a Perkin Elmer Lambda 950 UV-vis spectrometer. All UV-vis samples were contained in Starna Cells Inc. UV quartz windows with a useable range of 170-2700 nm.

Synthetic Procedures

Isospiropyran 1: To a 100 mL round-bottom flask under an atmosphere of nitrogen, was added 5'-bromo-2'-hydroxyacetophenone (1.6 g, 7.4 mmol) and 30 mL of anhydrous ethanol. To the resulting solution was added $SiCl_4$ (4.2 mL, 36.6 mmol) dropwise with stirring over the course of 5 minutes, which was accompanied by a temporary inconsequential warming of the reaction mixture. During the addition, the solution gradually transitioned from colorless to dark red. After the addition, the reaction mixture was allowed to stir at room temperature overnight. The system was then diluted with 30 mL of CH_2Cl_2 and washed with 30 mL of cold water. The aqueous layer was further extracted with 2 x 30 mL CH_2Cl_2. The combined organic layers were then washed once with saturated $NaHCO_3$ (aq) and once with brine before being dried over Na_2SO_4. After vacuum filtration, the solvent was removed under reduced pressure to provide the crude product mixture. The crude mixture was then re-dissolved in minimal acetonitrile and stirred vigorously to induce the precipitation of 1.0 g (69%) of compound **1** as a light blue solid. M.p. decomposing at higher (rapid at >100 ºC) temperatures. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.790 (1H, d; J = 2.4 Hz), 7.523 (1H, d; J = 2.4 Hz), 7.499 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.370 (1H, dd; J = 9.0 Hz, J = 2.4 Hz), 7.360 (1H, d; J = 2.4 Hz), 7.286 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.076 (1H, d; J = 9.0 Hz), 6.833 (1H, d; J = 8.4 Hz), 6.645 (1H, d; J = 8.4 Hz), 6.561 (1H, s), 5.784 (1H, s), 5.545 (1H, d; J = 1.8 Hz), 2.117 (3H, d; J = 1.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 153.6, 149.9, 148.2, 146.5, 134.2, 133.2, 132.9, 132.3, 130.8, 128.3, 126.7, 125.0, 124.2, 123.6, 120.8, 119.4, 118.5, 118.3, 117.4, 113.8, 112.7, 102.8, 72.2, 18.1. HRMS (ESI): *m/z* calcd for $C_{24}H_{15}O_3Br_3$ 588.8644 $[M + H]^+$, found 588.8643. For 2D NMR characterization of isospiropyran **1**, see Figures S4-S8. For X-ray characterization of **1**, see Figure 2C.

Additional Notes Pertaining to the Preparation Isospiropyran 1: The induced precipitation from acetonitrile seemed to work best when the reaction was worked up sooner rather than later after stirring overnight, despite no apparent change in the crude ^{1}H NMR spectra. If the homogenous acetonitrile solution does not lead to precipitation, we found that the subsequent addition of an equal volume of hexanes with vigorous stirring could sometimes induce a slower but equally pure appearance of the desired solid. Any product remaining in the filtrate could also be isolated via column chromatography (SiO_2, hexanes:ethyl acetate = 4:1).

Compound 1a: By adding one molar equivalent of CH_3SO_3H to a 60 mM solution of **1** in $CDCl_3$, compound **1a** become the dominant species. M.p. decomposing at higher (rapid at >100 ºC) temperatures. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.963 (1H, br s), 8.429 (1H, d; J = 2.4 Hz), 8.200 (1H, dd; J = 9.0 Hz, J = 2.4 Hz), 8.125 (1H, d; J = 2.4 Hz), 7.955 (1H, d; J = 9.0 Hz), 7.543 (1H, dd; J = 9.0 Hz, J = 1.8 Hz), 7.307 (1H, d; J = 8.4 Hz), 7.232 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.189 (1H, d; J = 9.0 Hz), 7.132 (1H, br s), 6.700 (1H, d; J = 2.4 Hz), 2.522 (3H, br s). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 169.5, 163.7, 163.3, 162.2, 155.5, 154.0, 142.4, 140.9, 133.6, 130.9, 129.5, 128.7, 128.1, 124.0, 123.6, 122.1, 121.9, 121.1, 120.9, 119.0, 115.8, 113.0, 111.0, 28.1. HRMS (ESI): *m/z* calcd for $C_{24}H_{15}O_3Br_3$ 588.8644 $[M + H]^+$, found 588.8645. For 2D NMR characterization of **1a**, see Figures S11-S13. For X-ray characterization of **1a**, see Figure 4.

Compound 5: As described in the main text, heating a d_6-DMSO solution of **1** at 65 ˚C led to the formation of **5**. So far, we have been unable to isolate this compound in a pure form. ^{1}H NMR (600 MHz, d_6-DMSO): δ (ppm) 10.362 (1H, s), 9.713 (1H, s), 7.992 (1H, d; J = 2.4 Hz), 7.635 (1H, d; J = 2.4 Hz), 7.481 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.345 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.280 (1H, dd; J = 8.4 Hz, J = 2.4 Hz), 7.235 (1H, d; J = 2.4 Hz), 7.220 (1H, d; J = 8.4 Hz), 7.073 (1H, br s), 6.886 (1H, d; J = 8.4 Hz), 6.817 (1H, d; J = 8.4 Hz), 6.565 (1H, br s), 5.581 (1H, m), 5.540 (1H, d; J = 1.8 Hz). HRMS (ESI): *m/z* calcd for $C_{24}H_{15}O_3Br_3$ 588.8644 $[M + H]^+$, found 588.8579. For 2D NMR characterization of **5**, see Figures S17-S18.

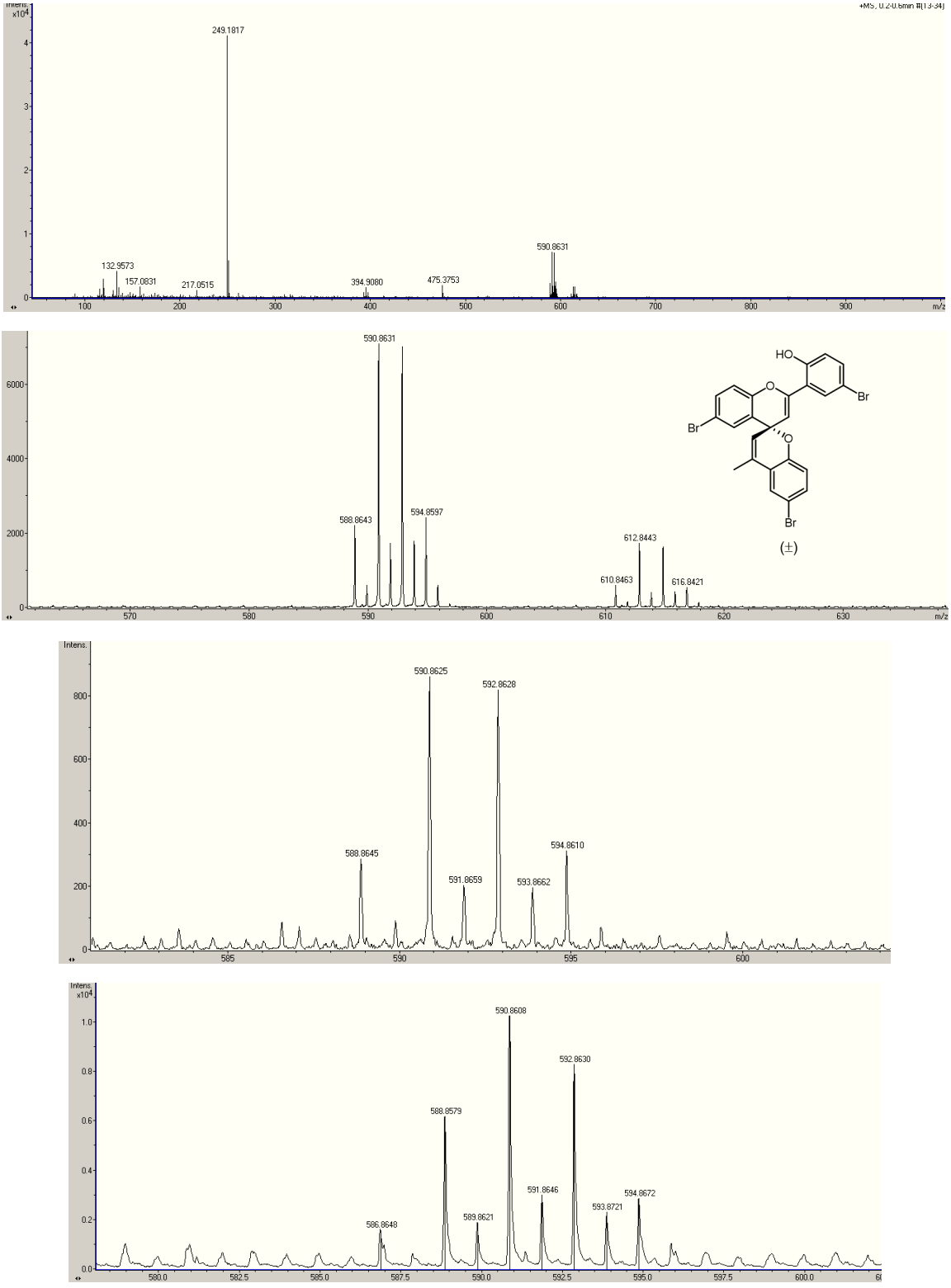


Figure S1. Top: full HRMS-ESI spectrum of isospiropyran **1**. Second: a view of the $[M+H]^+$ and $[M+Na]^+$ peaks observed for **1**. Identical peak-patterns were observed for compounds $\mathbf{1_a}$ (third) and **5** (bottom).

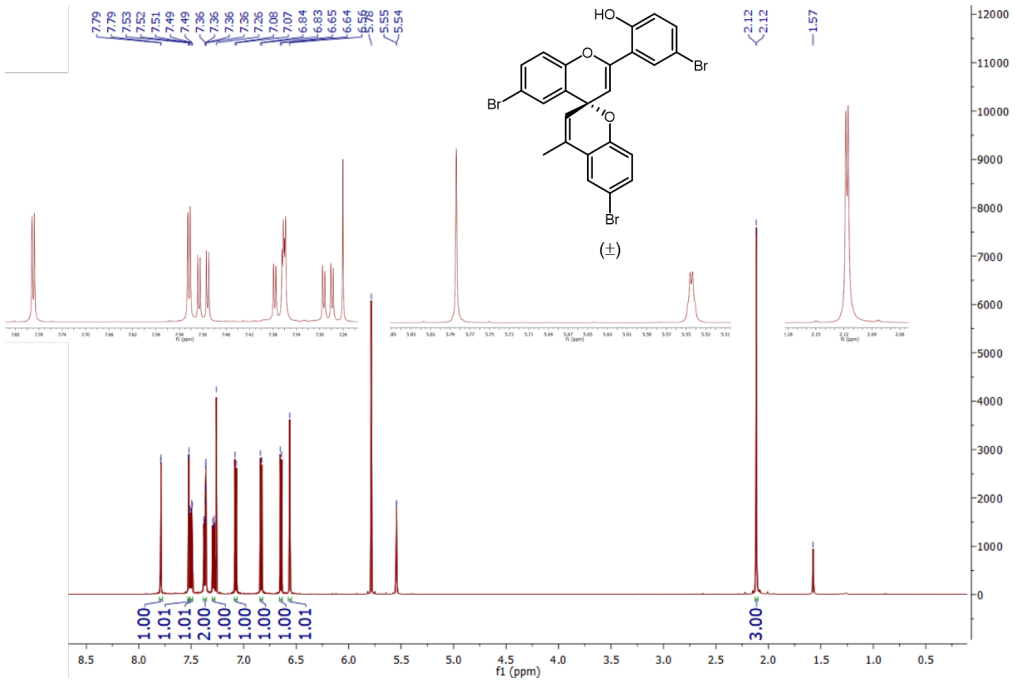


Figure S2. ^{1}H NMR spectrum (600 MHz, 298 K) of isospiropyran **1** in $CDCl_3$.

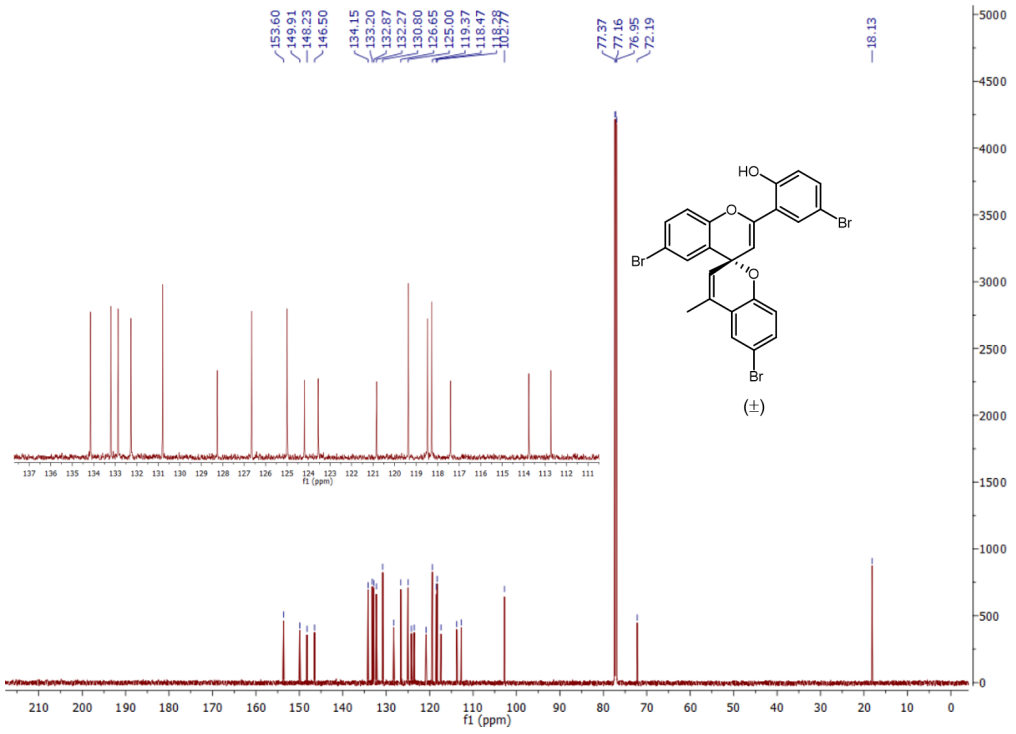


Figure S3. ^{13}C NMR spectrum (150 MHz, 298 K) of isospiropyran **1** in $CDCl_3$.

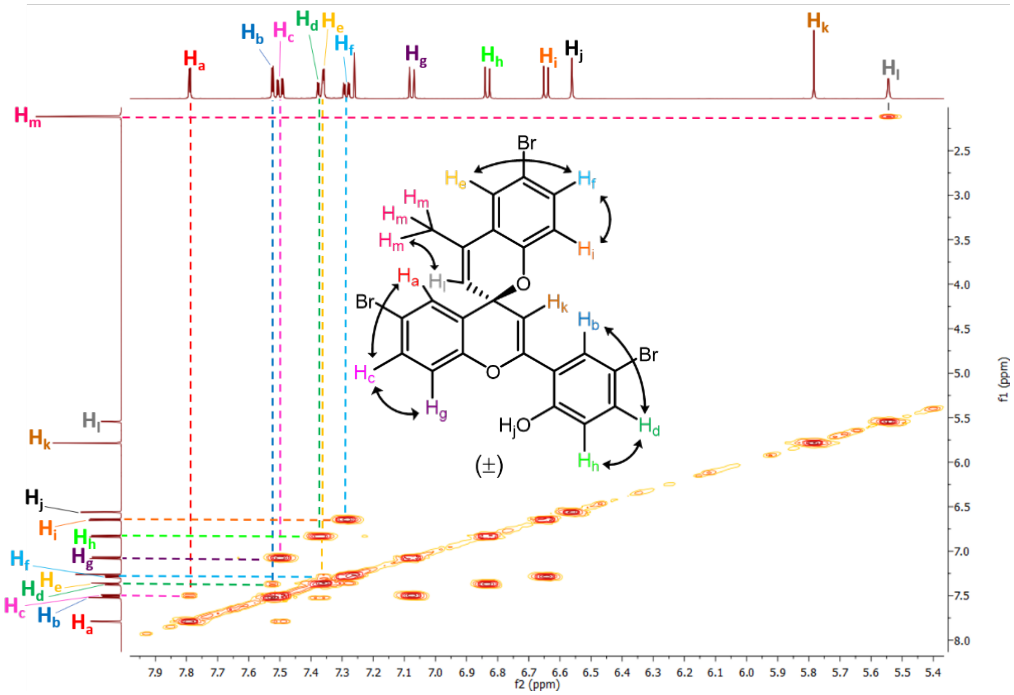


Figure S4. ^{1}H-^{1}H COSY NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in $CDCl_3$.

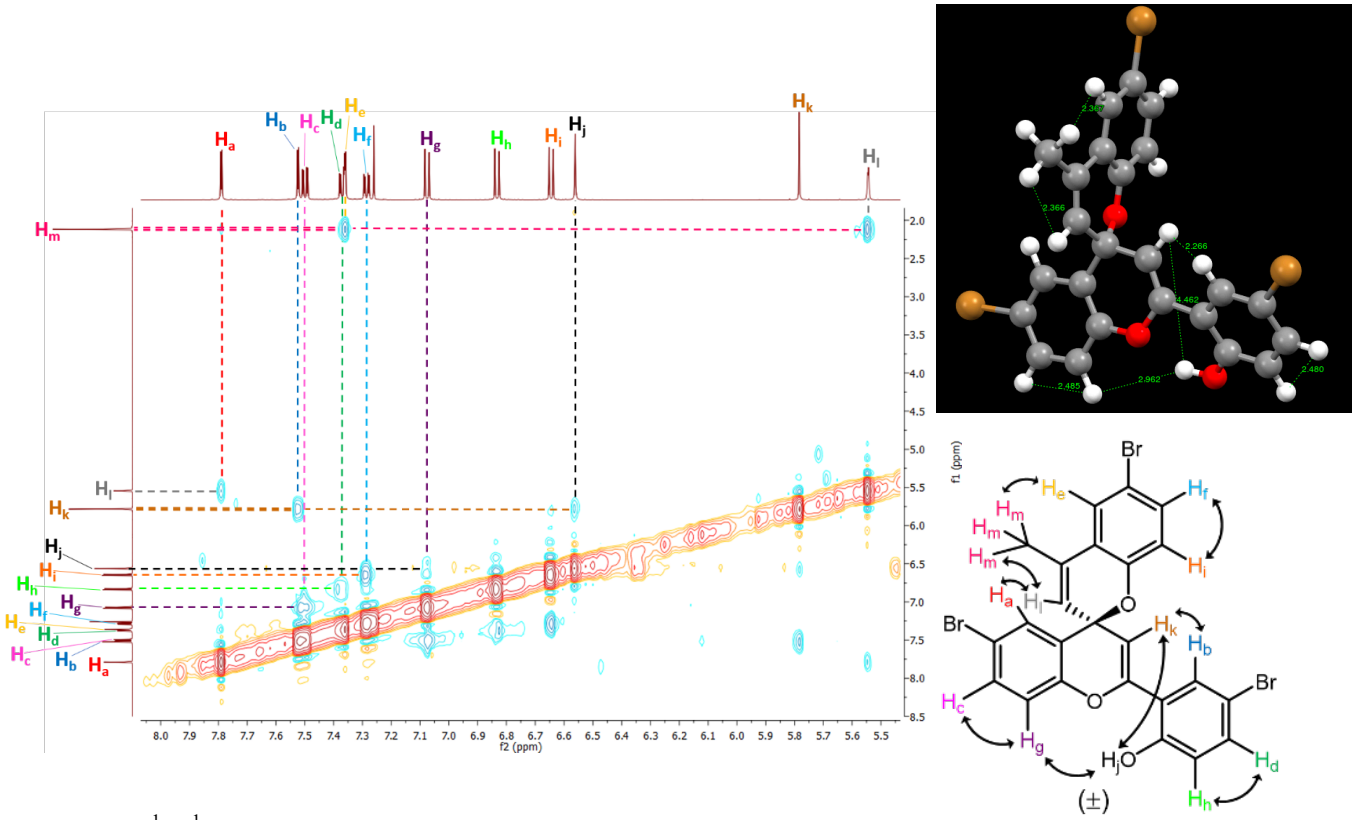


Figure S5. ^{1}H-^{1}H NOESY NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in $CDCl_3$. Energy-minimized structure (DFT; B3LYP: 6-311+G**) of **1** with interatomic distances.

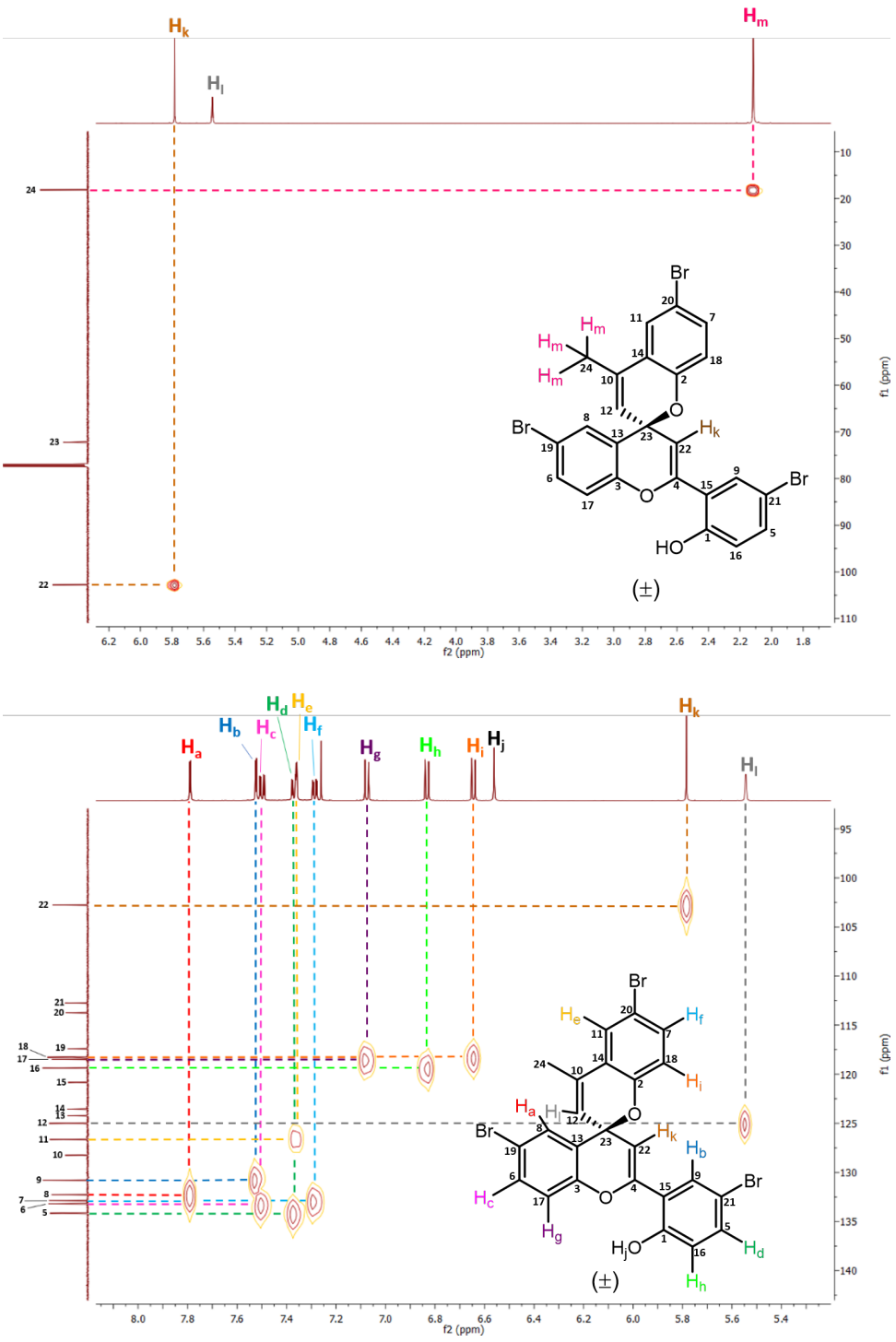
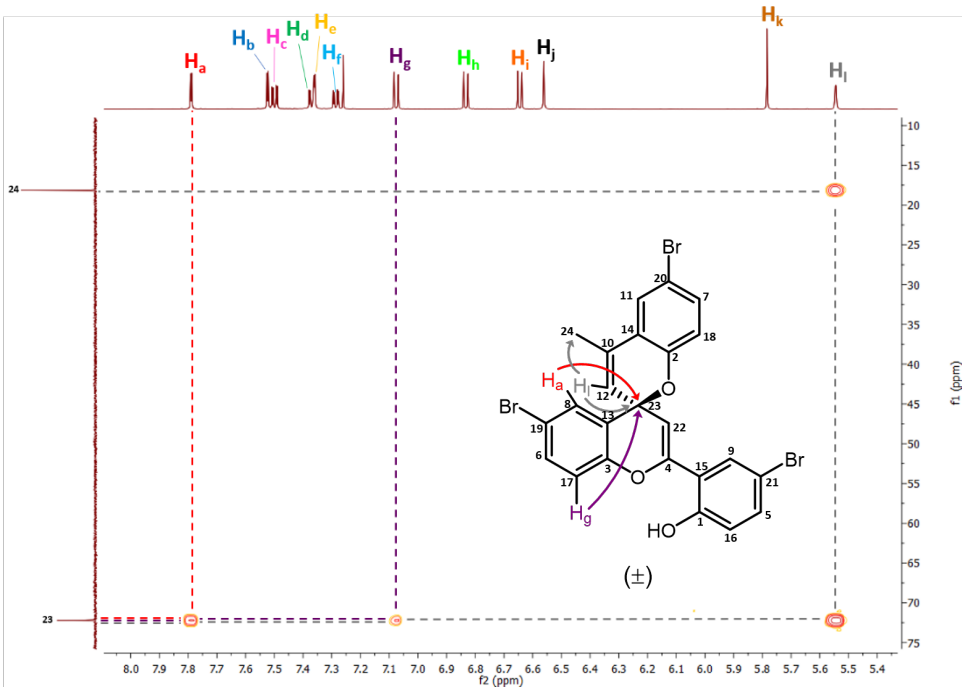
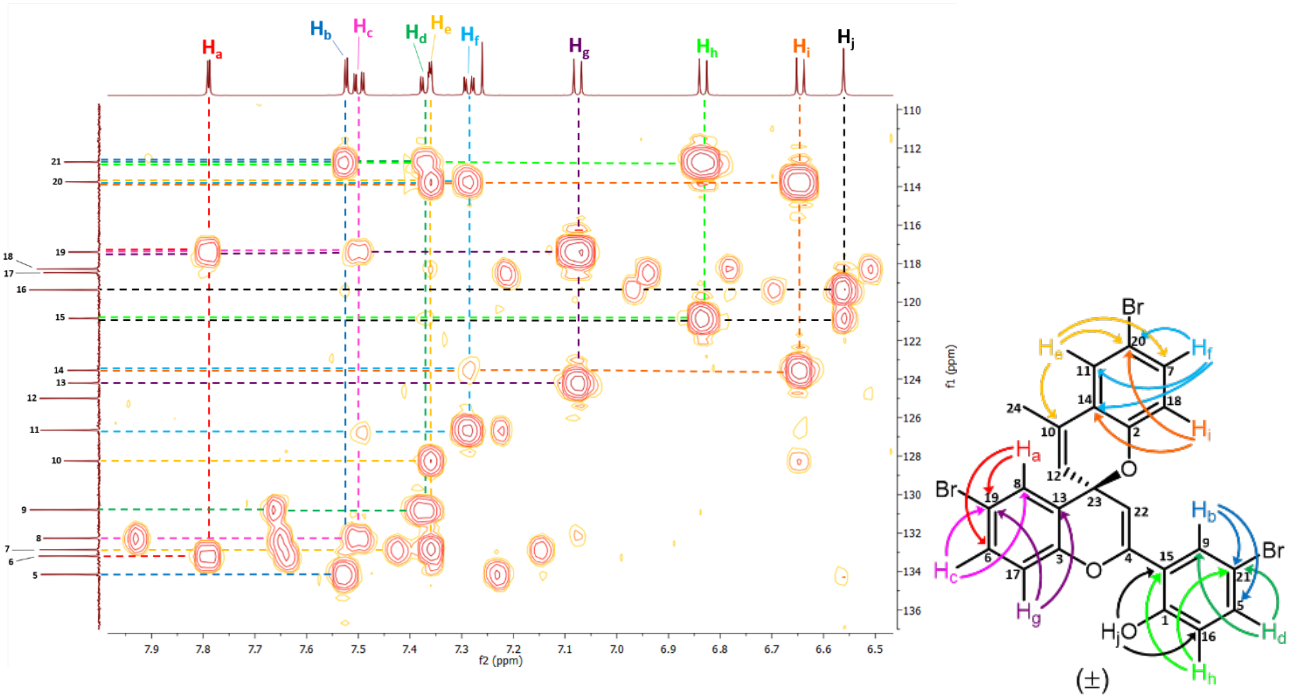


Figure S6. Two different regions of ^{1}H-^{13}C HSQC NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in $CDCl_3$.


Ha
Hb
Hc
Hd
He
Hf
Hg
Hh
Hi
Hj
Hk
Hl
f2 (ppm)
f1 (ppm)
Br
HO
(±)


Ha
Hb
Hc
Hd
He
Hf
Hg
Hh
Hi
Hj
f2 (ppm)
f1 (ppm)
Br
HO
(±)

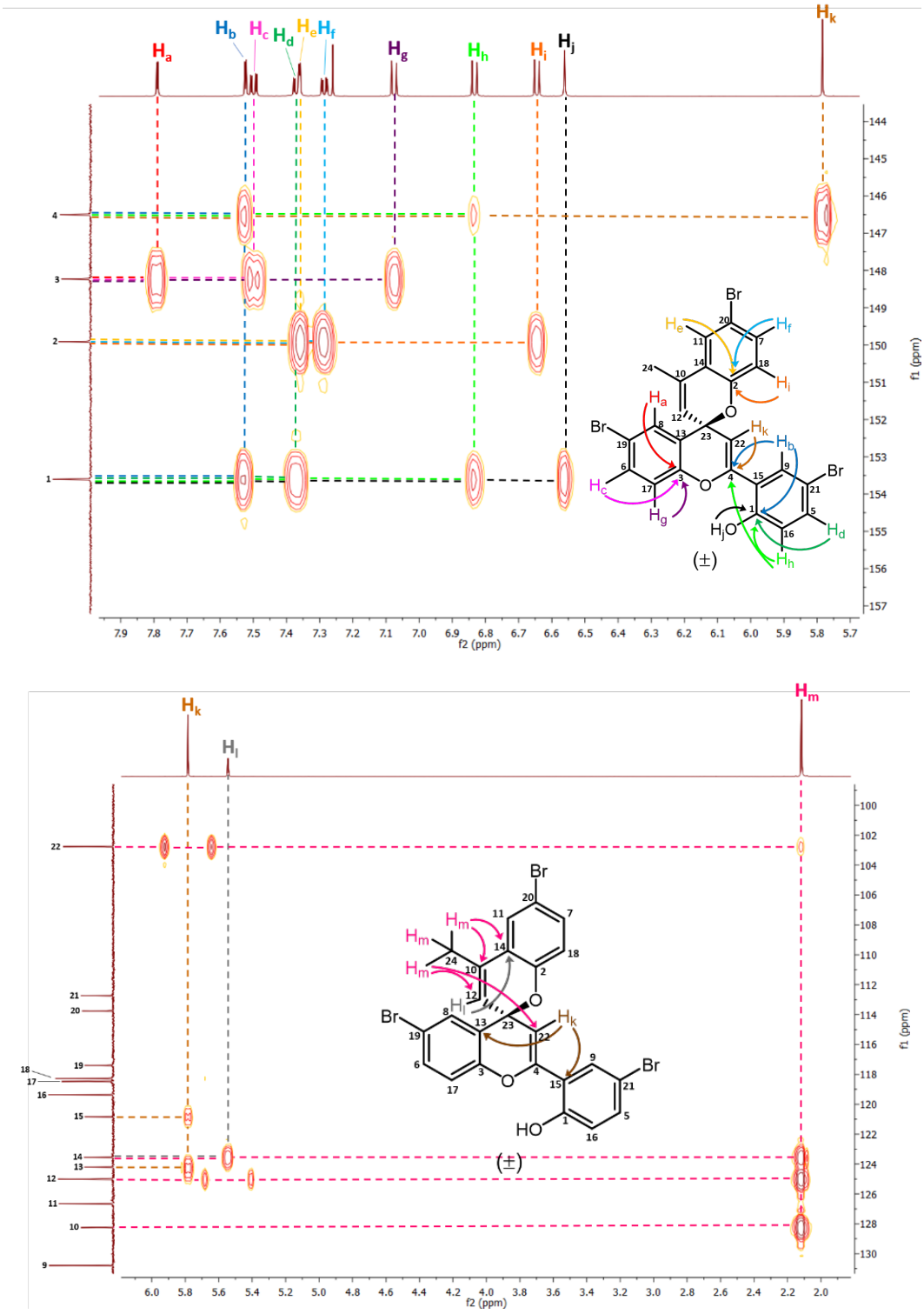
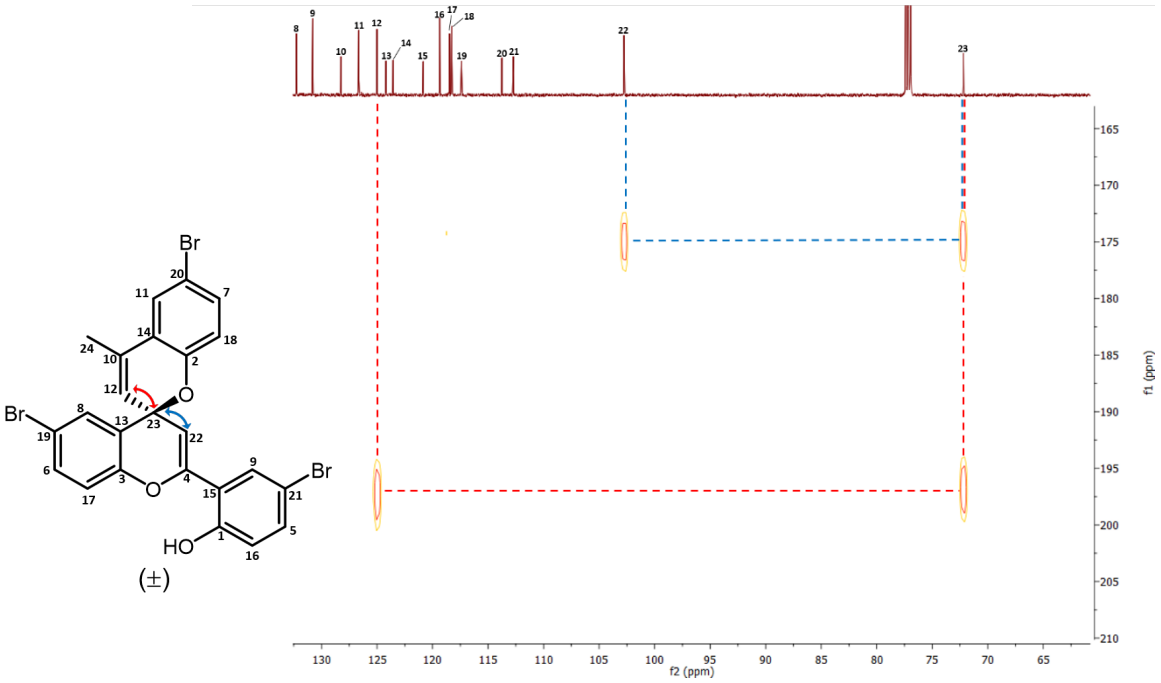
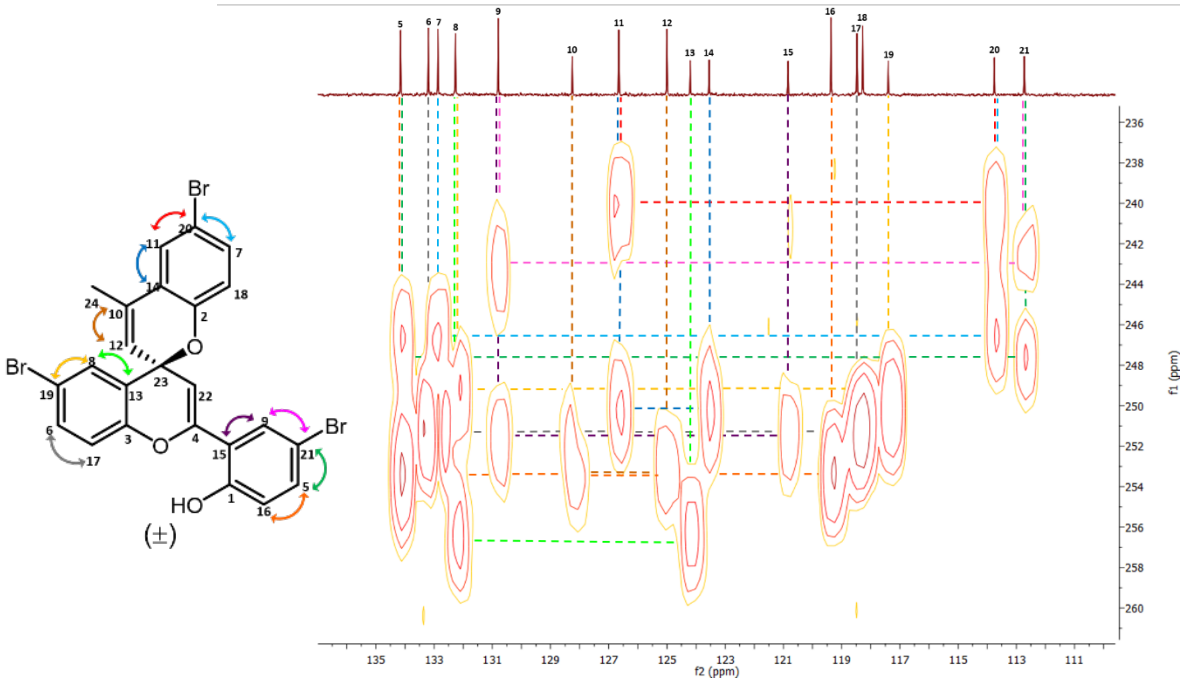


Figure S7. Four different regions of ^{1}H-^{13}C HMBC NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in $CDCl_3$.


Br
Br
HO
(±)
f2 (ppm)
f1 (ppm)


Br
Br
HO
(±)
f2 (ppm)
f1 (ppm)

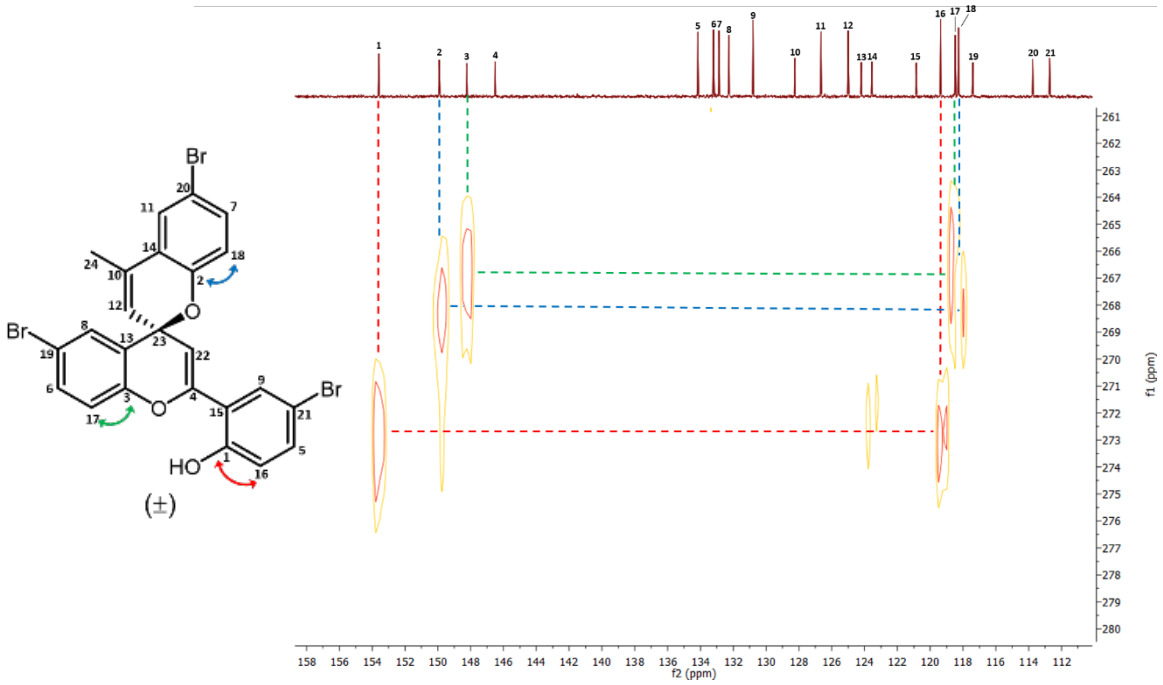


Figure S8. Three different regions of ^{13}C-^{13}C INADEQUATE NMR (700 MHz, 298 K) spectrum of isospiropyran **1** in $CDCl_3$.

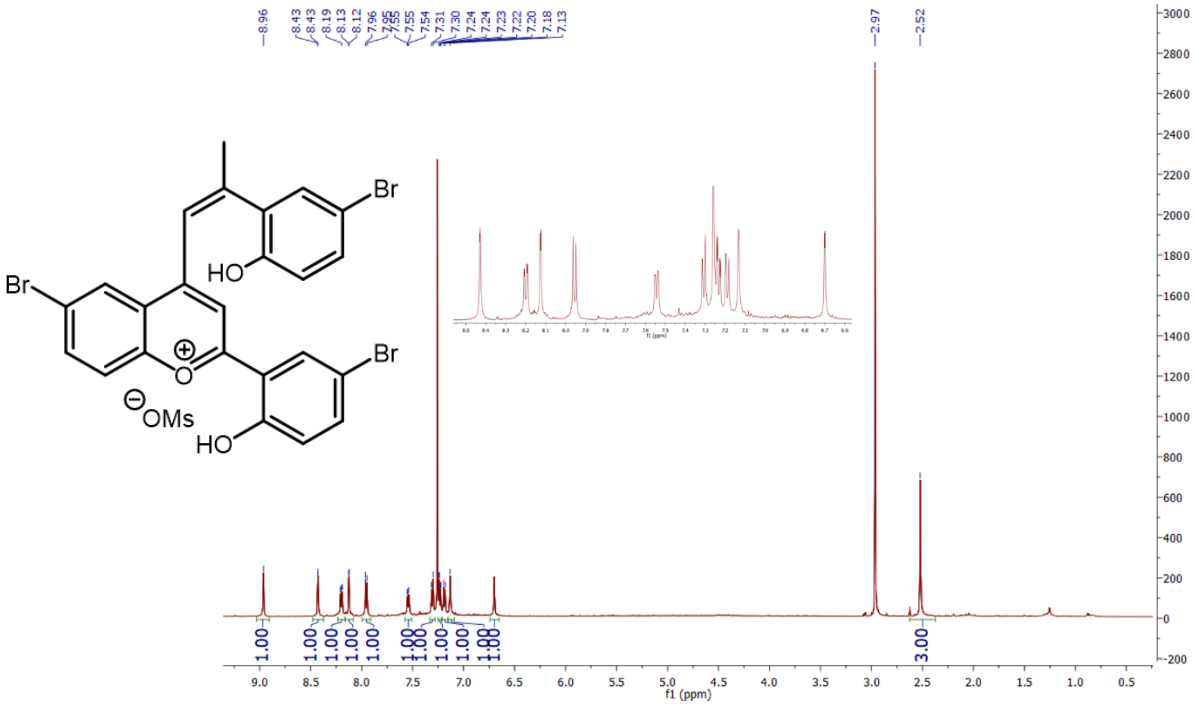


Figure S9. ^{1}H NMR spectrum (600 MHz, 298 K) of compound $\mathbf{1_a}$ in $CDCl_3$. The resonance at 2.97 ppm is from the mesylate counterion.

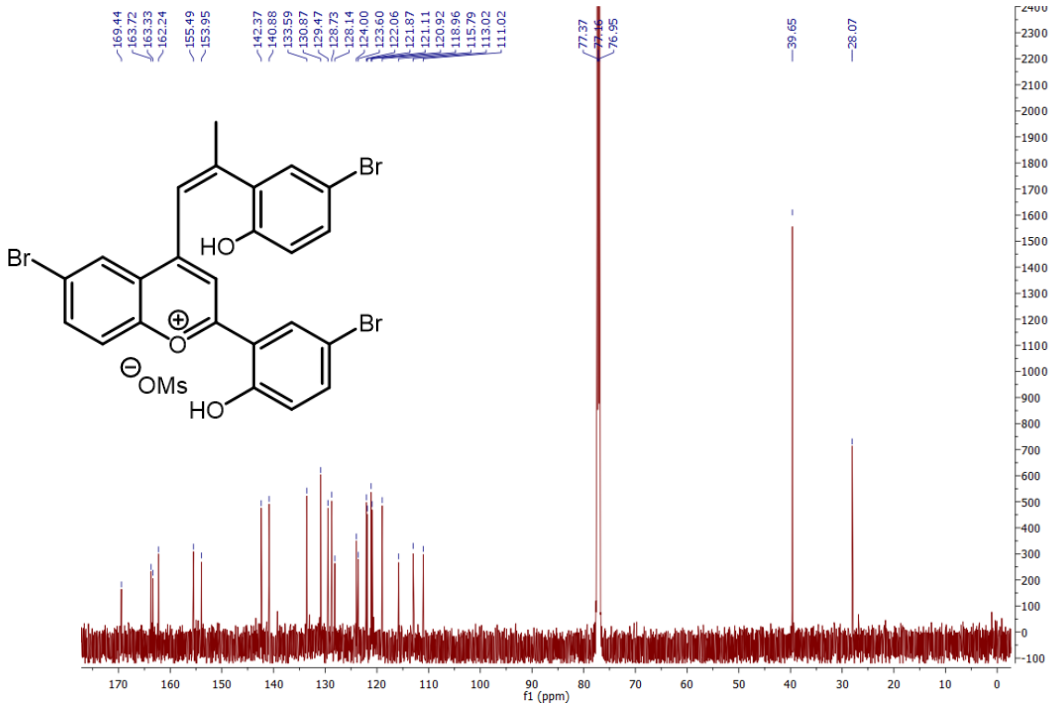


Figure S10. ^{13}C NMR spectrum (150 MHz, 298 K) of compound $\mathbf{1_a}$ in $CDCl_3$. The resonance at 39.65 ppm is from the mesylate counterion.

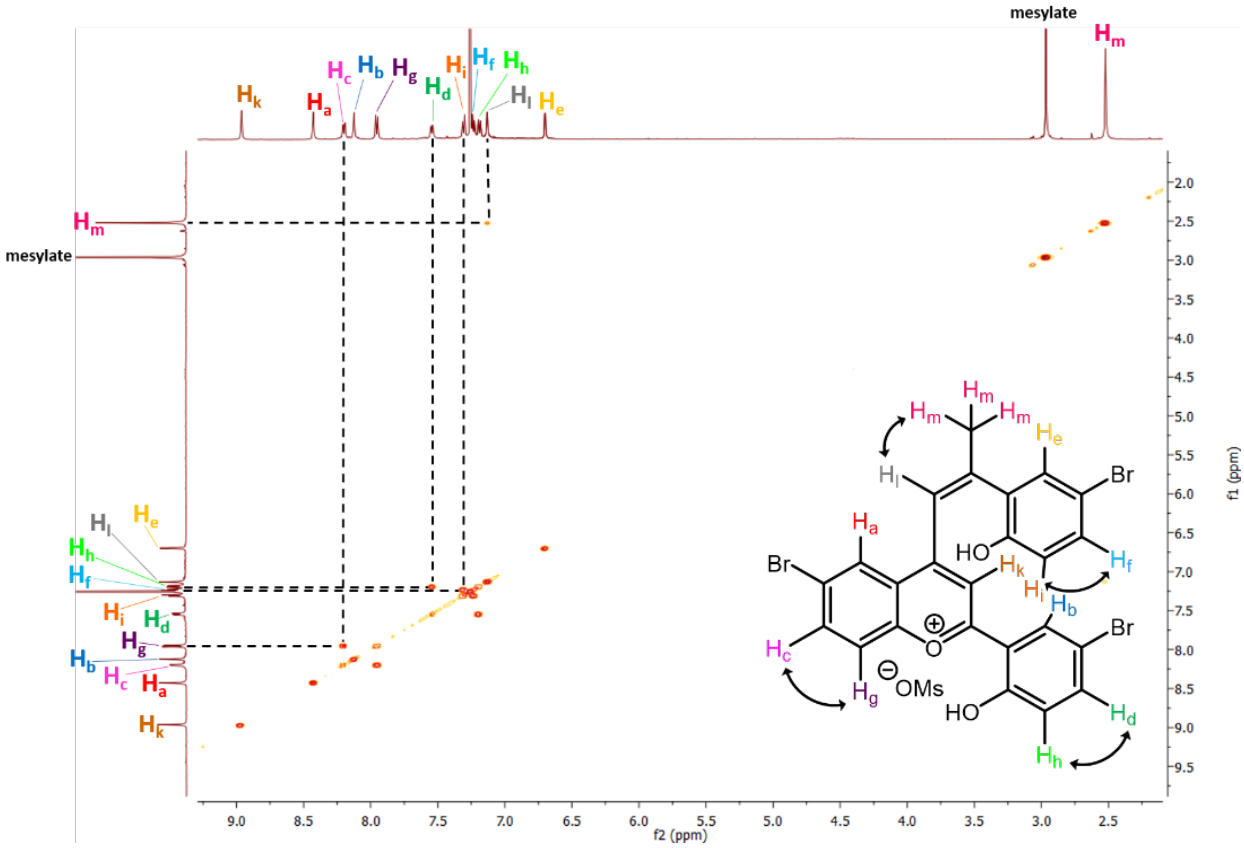


Figure S11. ^{1}H-^{1}H COSY NMR (600 MHz, 298 K) spectrum of compound $\mathbf{1_a}$ in $CDCl_3$.

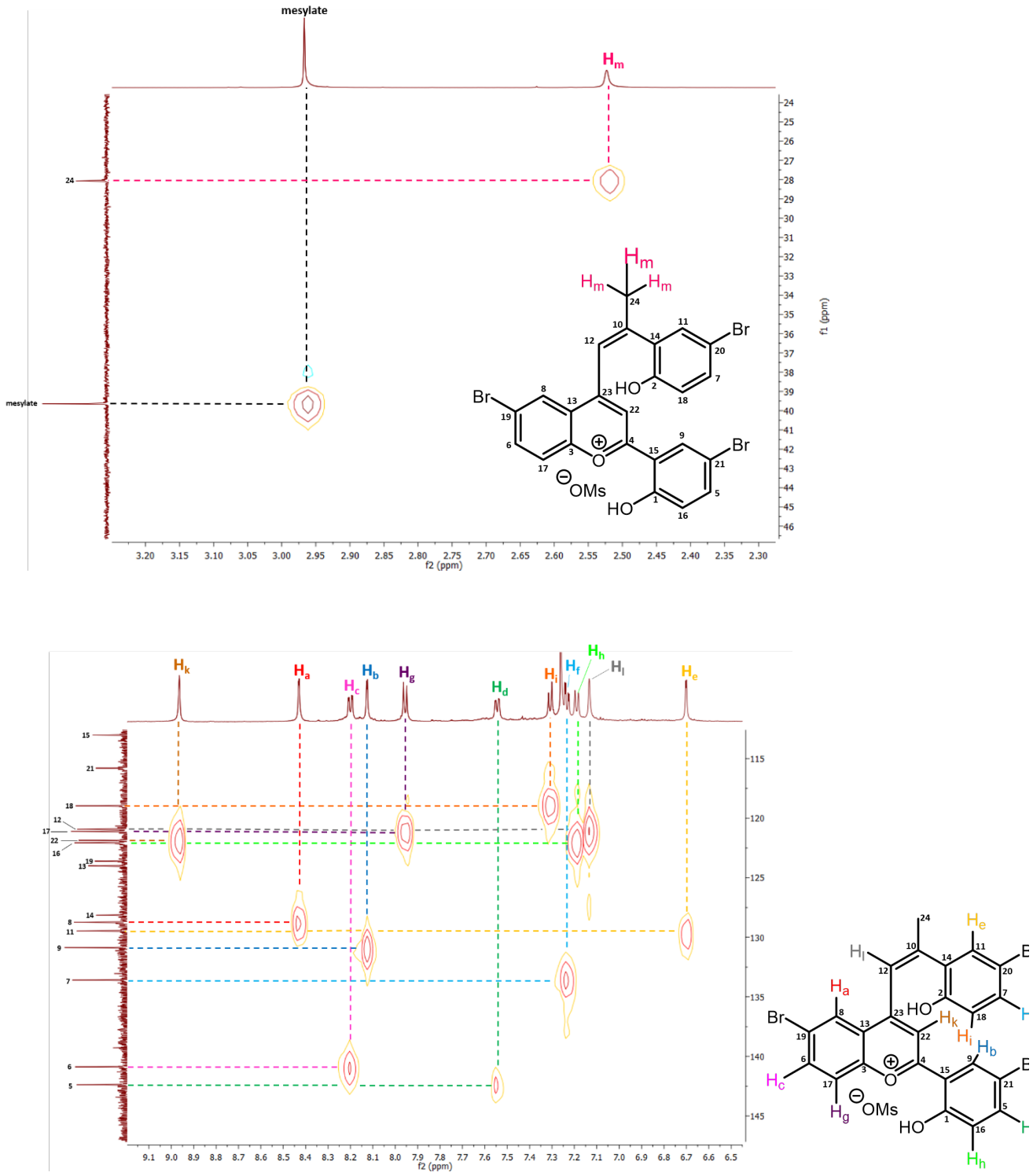
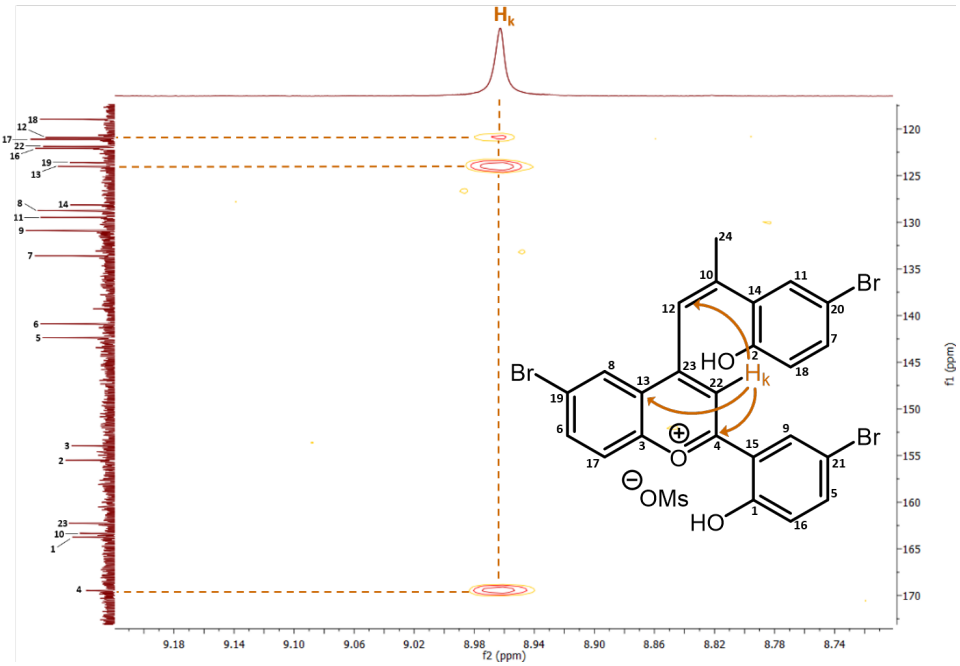
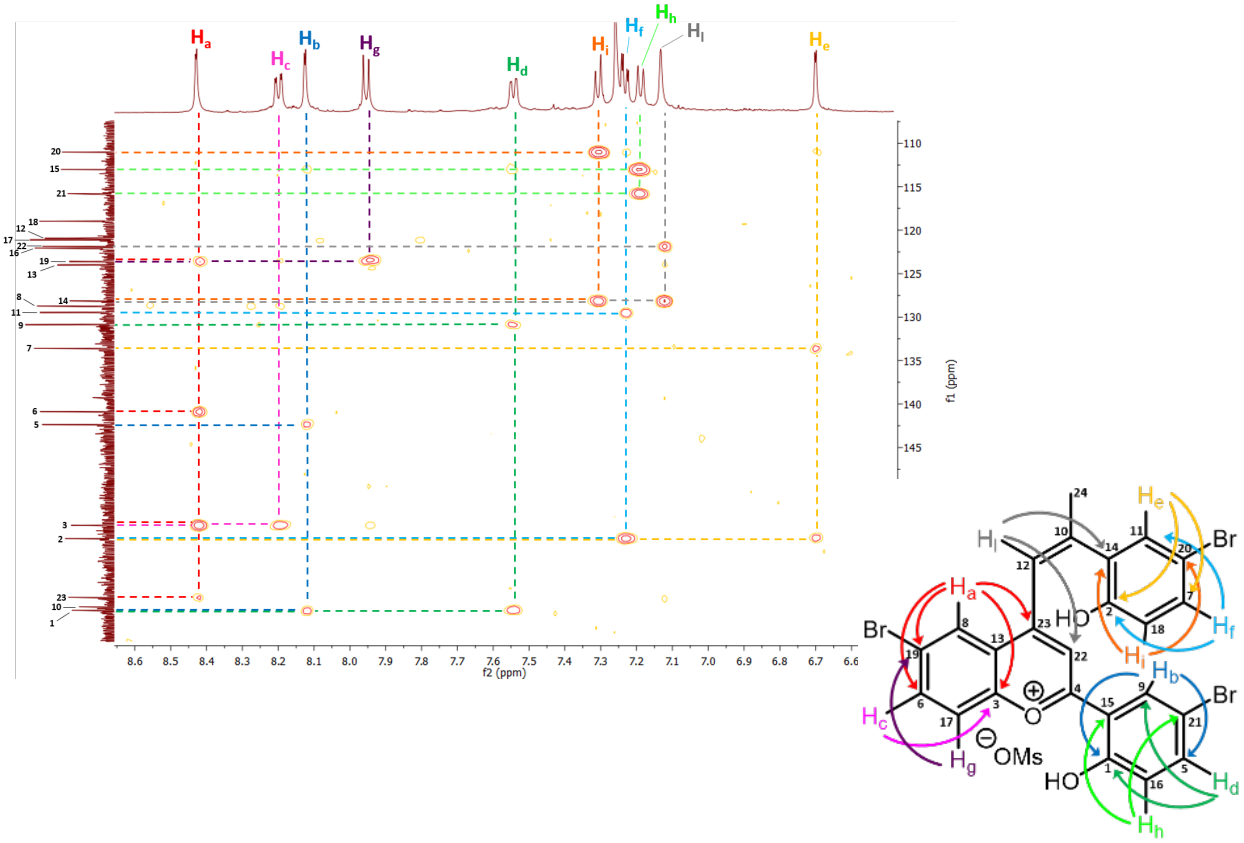


Figure S12. Two different regions of ^{1}H-^{13}C HSQC NMR (600 MHz, 298 K) spectrum of compound **1**$_{a}$ in $CDCl_3$.


Hk
f2 (ppm)
f1 (ppm)
Br
HO
OMs


Ha
Hb
Hc
Hd
He
Hf
Hg
Hh
Hi
Hl
f2 (ppm)
f1 (ppm)
Br
HO
OMs

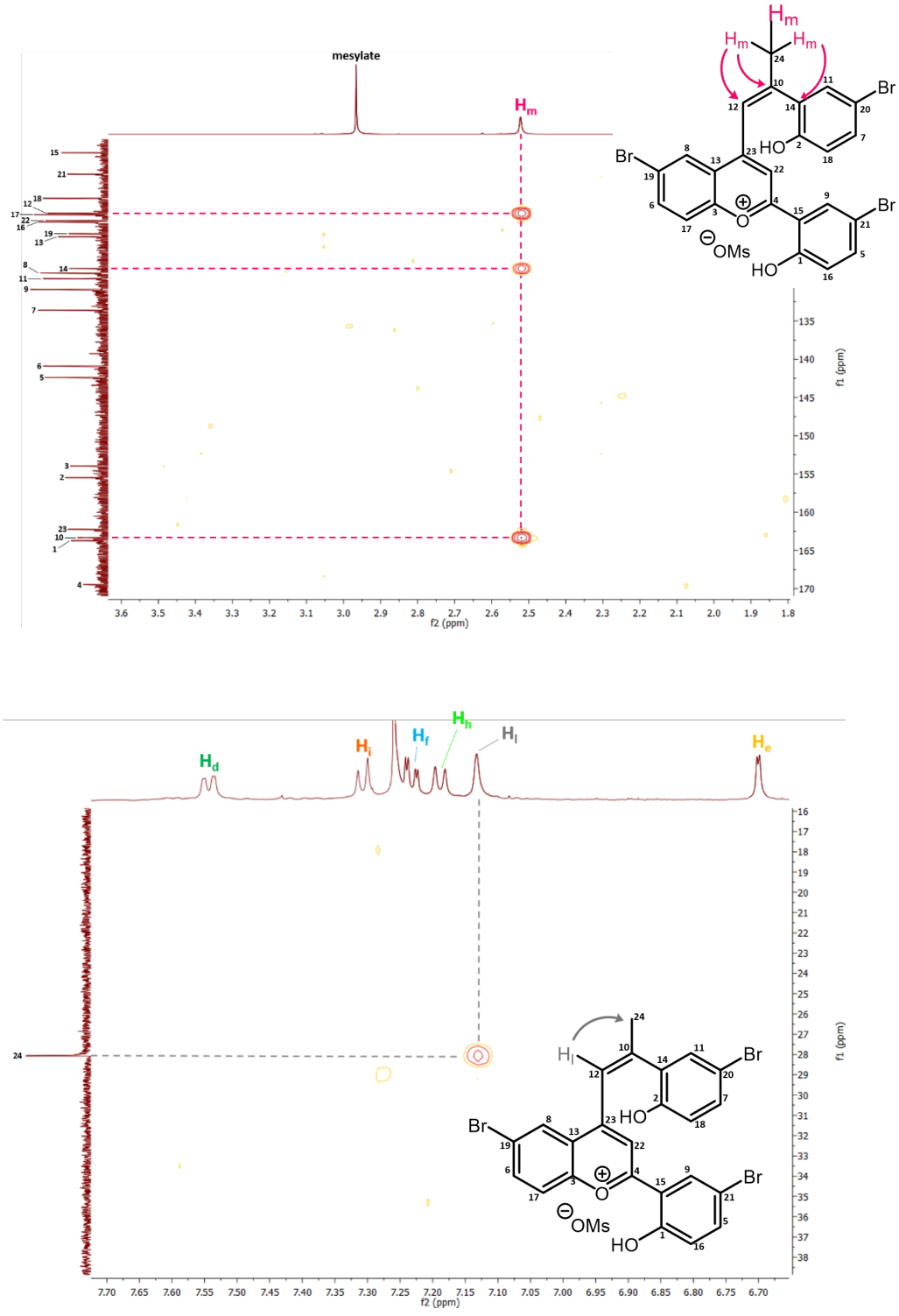


Figure S13. Four different regions of ^{1}H-^{13}C HMBC NMR (600 MHz, 298 K) spectrum of compound **1**$_{a}$ in $CDCl_3$.

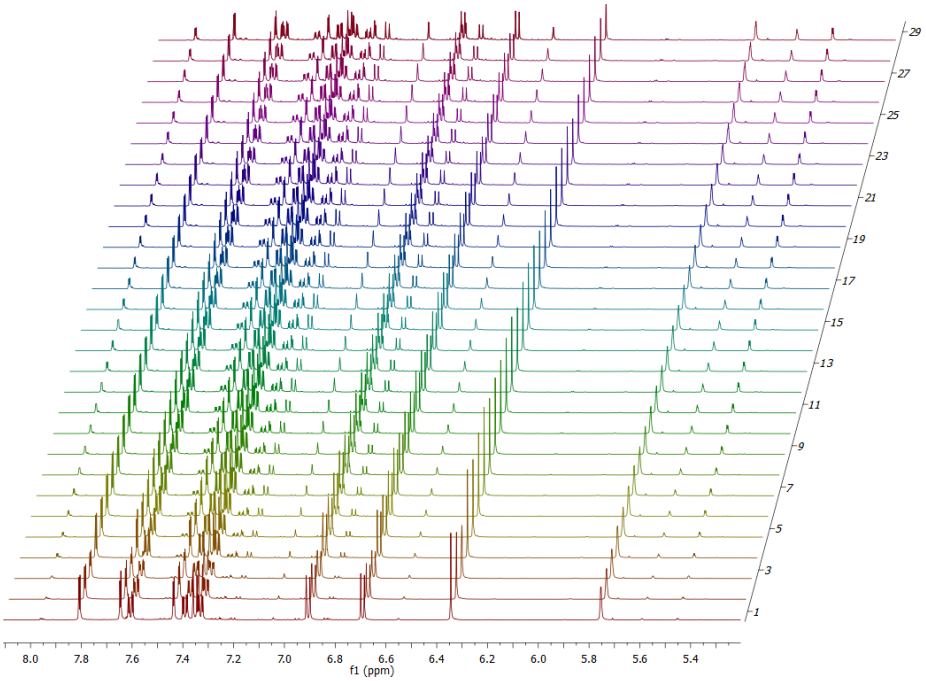


Figure S14. Partial ^{1}H spectra (600 MHz, 338 K) of isospiropyran **1** in d_6-DMSO at 65 ºC. Spectra were taken at 10-minute intervals for 280 minutes.

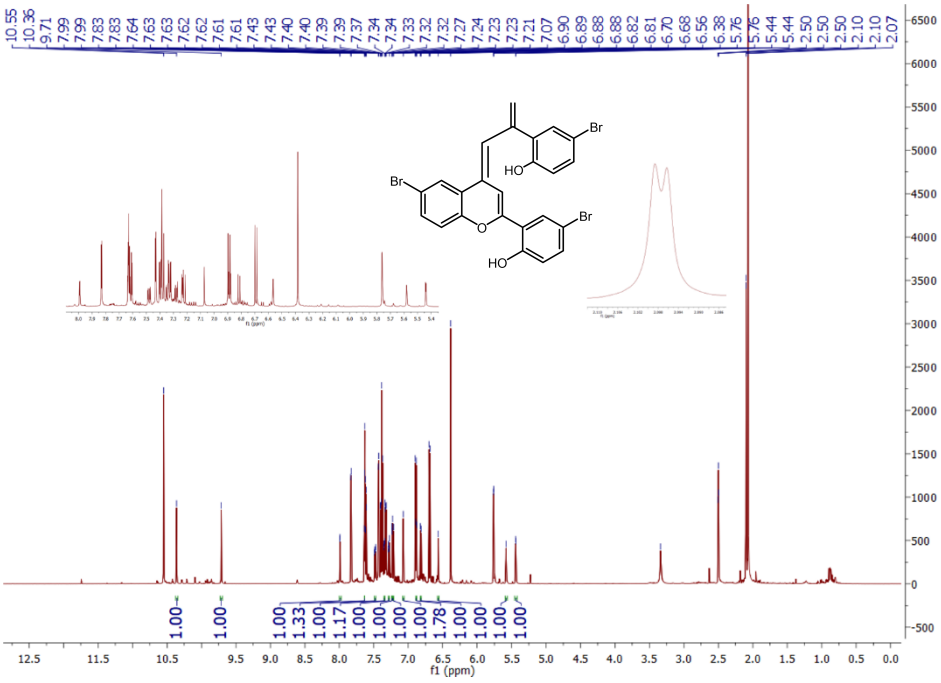


Figure S15. ^{1}H NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in d_6-DMSO after 5 hours at 65 ºC. Only resonances from compound **5** are integrated. A residual acetonitrile resonance appears at 2.10 ppm.

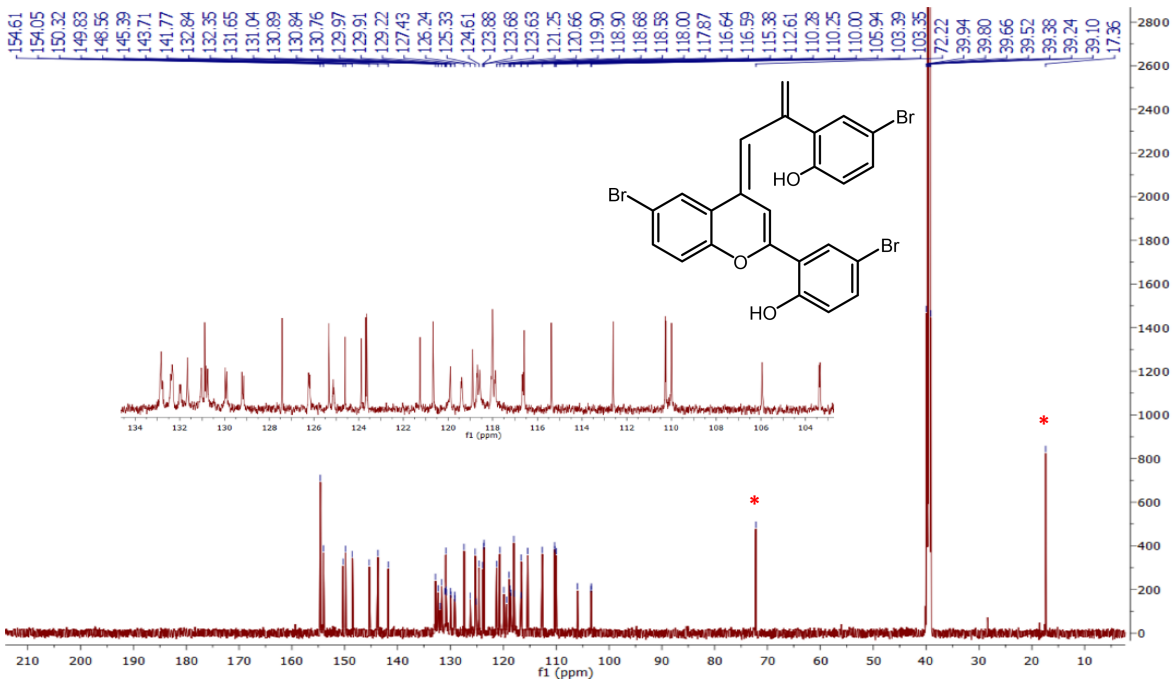


Figure S16. ^{13}C NMR (600 MHz, 298 K) spectrum of isospiropyran **1** in d_6-DMSO after 5 hours at 65 ºC. Two residual resonances from acetonitrile appear at 116.6 ppm and 1.9 ppm, while two resonances from sp^3 hybridized carbons in **1** are shown with stars.

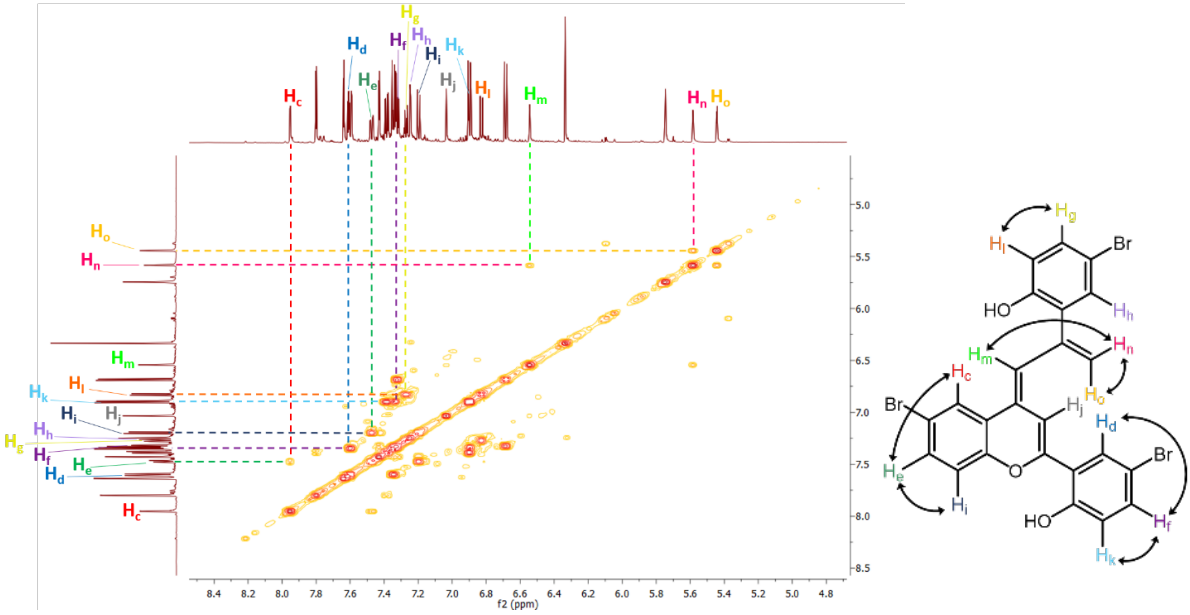


Figure S17. Partial ^{1}H-^{1}H COSY NMR (600 MHz, 338 K) spectrum of **1** in d_6-DMSO held at 65 ºC for 5 hours. The cross-signals from compound **5** are labeled.

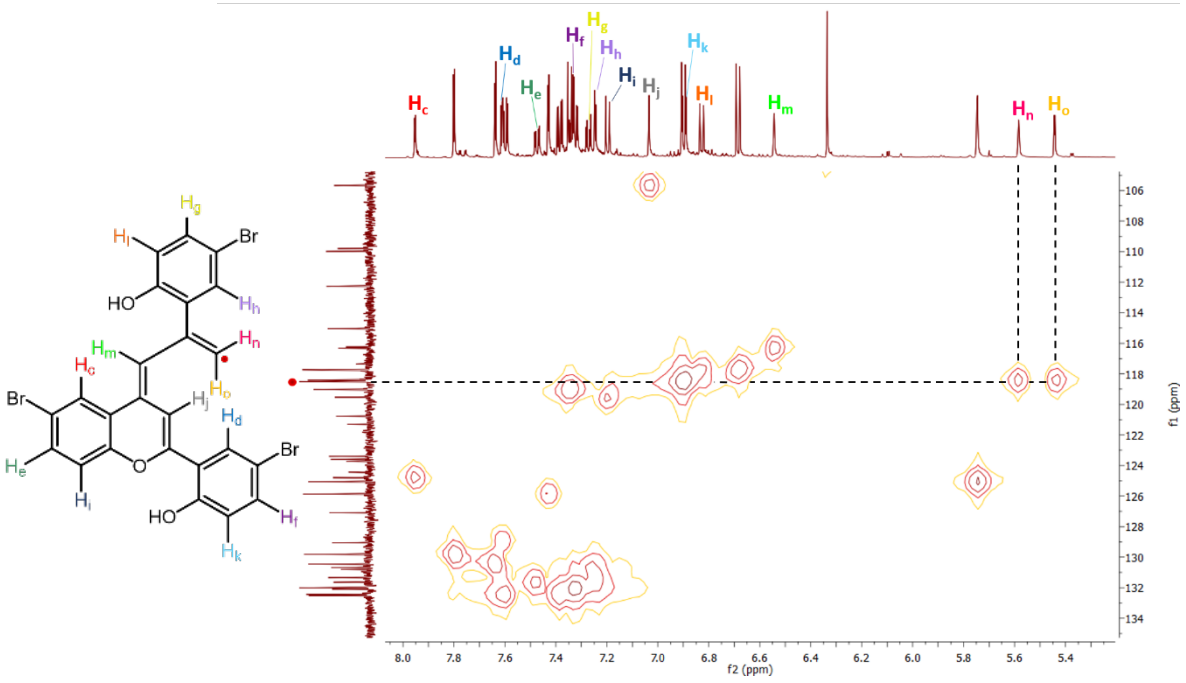


Figure S18. Partial ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, 338 K) of **1** in d_6-DMSO after 5 hours at 65 ºC. Only cross-signals from compound **5** are labeled. The cross peaks from diastereotopic and germinal $\mathbf{H_N}$–$\mathbf{H_O}$ protons of compound **5** are shown.

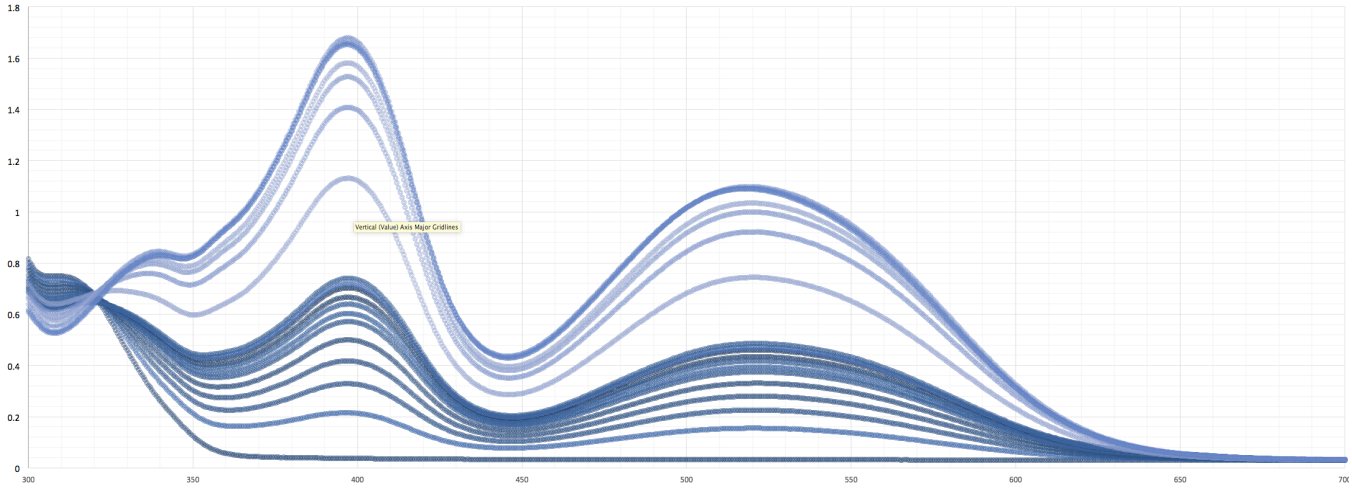
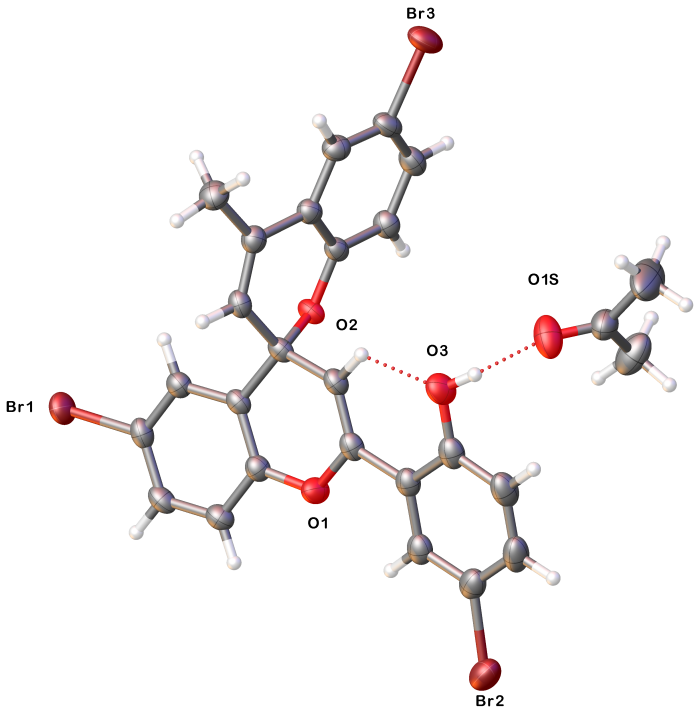


Figure S19. UV-Vis spectra of **1** (bottom) and $\mathbf{1}_a$ (top), obtained after incremental additions of CH_3SO_3H to 0.1 mM $CHCl_3$ solution of **1** at room temperature.

Crystallographic Data

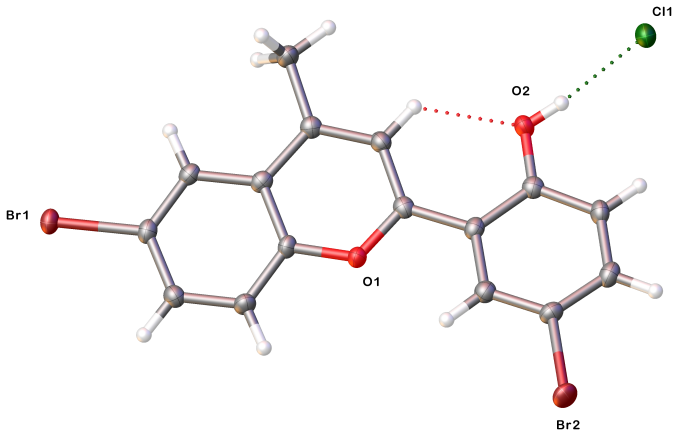
Table S1. Crystal data and structure refinement for isospiropyran **1**.



Report date	2019-05-13
Identification code	TN_ClosedAcetone
Empirical formula	C27 H21 Br3 O4
Molecular formula	C24 H15 Br3 O3, C3 H6 O
Formula weight	649.17
Temperature	100 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 11.7759(6) Å α= 90°.

	b = 8.8470(4) Å β= 90.994(2)°.
	c = 23.5375(11) Å γ = 90°.
Volume	2451.8(2) $Å^3$
Z	4
Density (calculated)	1.759 Mg/m^3
Absorption coefficient	4.968 mm^{-1}
F(000)	1280
Crystal size	0.168 x 0.086 x 0.074 mm^3
Crystal color, habit	Redish Orange Rod
Theta range for data collection	2.880 to 26.384°.
Index ranges	-14<=h<=14, -11<=k<=11, -29<=l<=29
Reflections collected	30295
Independent reflections	5015 [R(int) = 0.0274, R(sigma) = 0.0198]
Completeness to theta = 25.000°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.0932 and 0.0632
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5015 / 0 / 311
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0285, wR2 = 0.0643
R indices (all data)	R1 = 0.0404, wR2 = 0.0690
Extinction coefficient	n/a
Largest diff. peak and hole	0.685 and -0.694 $e.Å^{-3}$

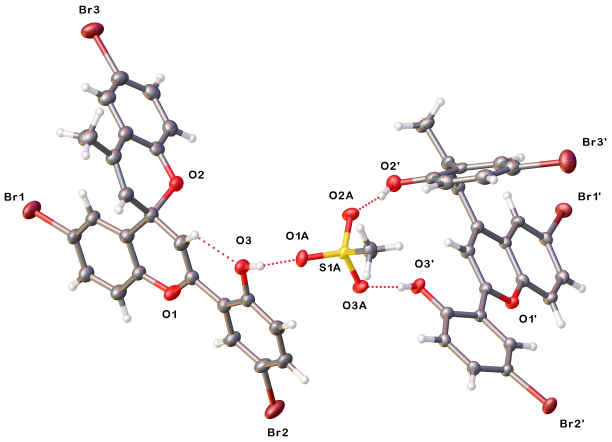
Table S2. Crystal data and structure refinement for compound **4**.



Report date	2019-05-13	
Identification code	TN_2BrHCl	
Empirical formula	C16 H11 Br2 Cl O2	
Molecular formula	C16 H11 Br2 O2, Cl	
Formula weight	430.52	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.6085(8) Å	α= 74.183(3)°.
	b = 9.1123(8) Å	β= 80.293(3)°.
	c = 10.0471(10) Å	γ = 85.184(3)°.
Volume	746.83(12) $Å^3$	
Z	2	
Density (calculated)	1.914 Mg/m^3	

Absorption coefficient	5.606 mm^{-1}
F(000)	420
Crystal size	0.152 x 0.144 x 0.088 mm^3
Crystal color, habit	Light Yellow Block
Theta range for data collection	3.276 to 26.404°.
Index ranges	-10<=h<=10, -11<=k<=11, -12<=l<=12
Reflections collected	45442
Independent reflections	3058 [R(int) = 0.0424, R(sigma) = 0.0239]
Completeness to theta = 25.000°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.093175 and 0.060453
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3058 / 0 / 192
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0217, wR2 = 0.0468
R indices (all data)	R1 = 0.0292, wR2 = 0.0491
Extinction coefficient	n/a
Largest diff. peak and hole	0.404 and -0.331 $e.Å^{-3}$

Table S3. Crystal data and structure refinement for compound **1a**.



Report date	2019-05-13	
Identification code	TN_OpenClosed	
Empirical formula	C49 H34 Br6 O9 S	
Molecular formula	C24 H15 Br3 O3, C24 H16 Br3 O3, C H3 O3 S	
Formula weight	1278.28	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 11.4092(9) Å	α= 109.501(2)°.
	b = 14.1314(10) Å	β= 99.298(3)°.
	c = 15.9669(12) Å	γ = 101.718(2)°.
Volume	2301.5(3) $Å^3$	
Z	2	
Density (calculated)	1.845 Mg/m^3	
Absorption coefficient	5.336 mm^{-1}	

F(000)	1252
Crystal size	0.105 x 0.093 x 0.017 mm^3
Crystal color, habit	Dark Red Plate
Theta range for data collection	2.780 to 26.391°.
Index ranges	-14<=h<=14, -17<=k<=17, -19<=l<=19
Reflections collected	62357
Independent reflections	9395 [R(int) = 0.0460, R(sigma) = 0.0318]
Completeness to theta = 25.000°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.0932 and 0.0598
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9395 / 0 / 592
Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0386, wR2 = 0.0939
R indices (all data)	R1 = 0.0572, wR2 = 0.1028
Extinction coefficient	n/a
Largest diff. peak and hole	1.127 and -1.076 $e.Å^{-3}$