Supporting Information

Stereocontrolled desymmetrization of 2,5-cyclohexadienones via organocatalytic domino sulfa-1,6-/1,4-addition or sulfa-1,6-/1,4-/sulfa-1,4-addition reactions

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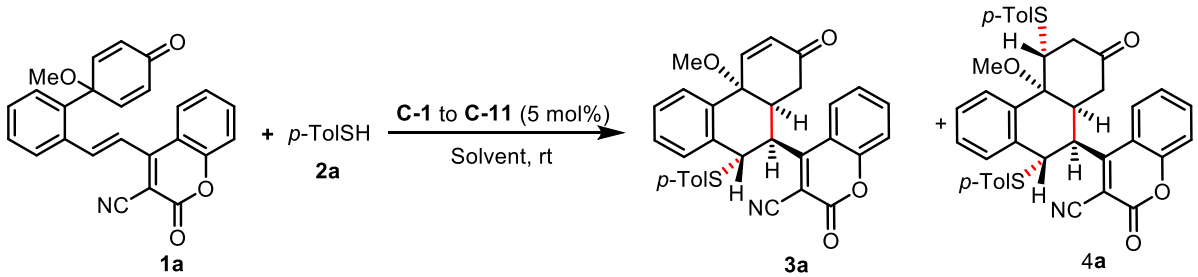
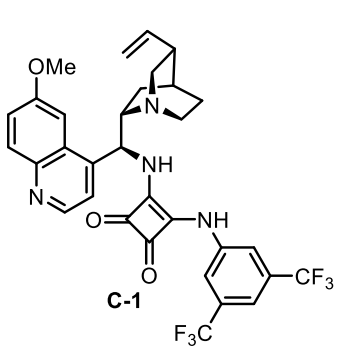
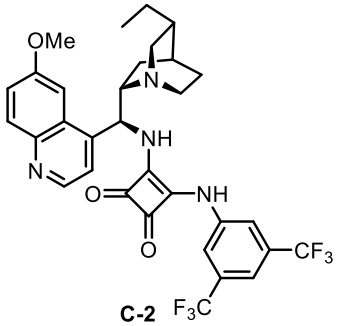
S1. General Information:

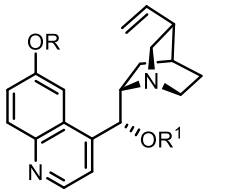
Unless otherwise noted, all commercially available compounds were purchased from Sigma-Aldrich, Tokyo Chemical Industry Co., Ltd. (TCI) Chemicals, Spectrochem Pvt. Ltd., and BLD Pharmatech (India) Pvt. Ltd. (BLD pharma), Chempure Pvt. Ltd. and used as received without further purification. The catalysts **C-1**[1], **C-2**[2], **C-4**[3], **C-5**[1], **C-6**[4], **C-7**[1], **C-8**[4], **C-9**[5], were prepared from methods known in the literature. The catalyst **C-3, C-10, C-11** are commercially available and used as it is. All the solvents for routine isolation of products and chromatography were laboratory reagent grade and distilled before use. Analytical thin-layer chromatography (TLC) was performed on the TLC Silica Gel 60 F254 Aluminium Sheets (MERCK), and UV light (254 nm) was used for the visualization. The flash column chromatography was performed on Combiflash NextGen 300 using silica gel (230 - 400 mesh), and the column chromatography was performed on the glass column using silica gel (100 - 200 mesh). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on the JEOL JNM-ECZ500R/S3 500MHz NMR Spectrometer at 500 MHz, 125 MHz and 471 MHz, respectively, and TMS/solvent's residual peak was used as an internal reference. NMR data are reported as follows: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), br s (broad singlet), br m (broad multiplet), d (doublet), t (triplet), m (multiplet), dd (double doublet); and coupling constants (*J*) are expressed in Hertz (Hz). Structural assignments were made with additional information from gCOSY and gHSQC experiments. Enantiomeric excess were measured on an Agilent 1260 Infinity II HPLC instrument by using Diacel Chiralpak IA, IB, IF and IG columns. Optical rotations were measured on a Rudolph Research Analytical, Autopol I. Melting points were measured on a Buchi melting point M-565 apparatus. High-resolution mass spectra (HRMS) were recorded on a Waters Xevo Q-TOF Mass Spectrometer using the electrospray ionization (ESI) technique. Elemental analysis was performed on Elementar unicu-CHNS-120 UNICUBE.

S2. Optimization Studies:

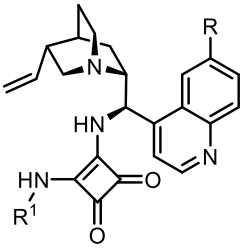




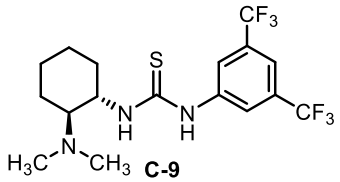


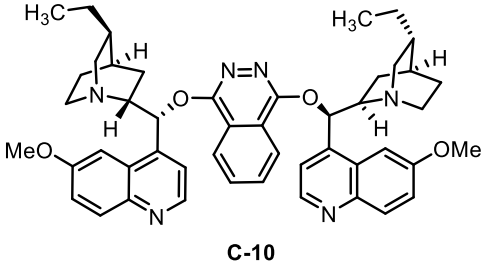


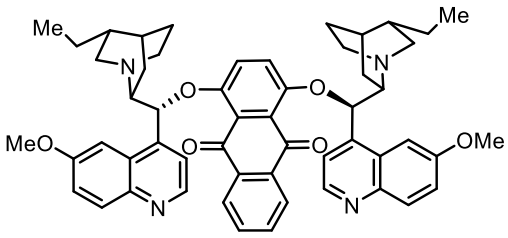
C-3: R = Me, R^1 = H
C-4: R = H, R^1 = Bn



C-5: R = H, R^1 = 3,5-$(CF_3)_2(C_6H_3)$
C-6: R = H, R^1 = CH_2[3,5-$(CF_3)_2(C_6H_3)$]
C-7: R = OMe, R^1 = 3,5-$(CF_3)_2(C_6H_3)$
C-8: R = OMe, R^1 = CH_2[3,5-$(CF_3)_2(C_6H_3)$]







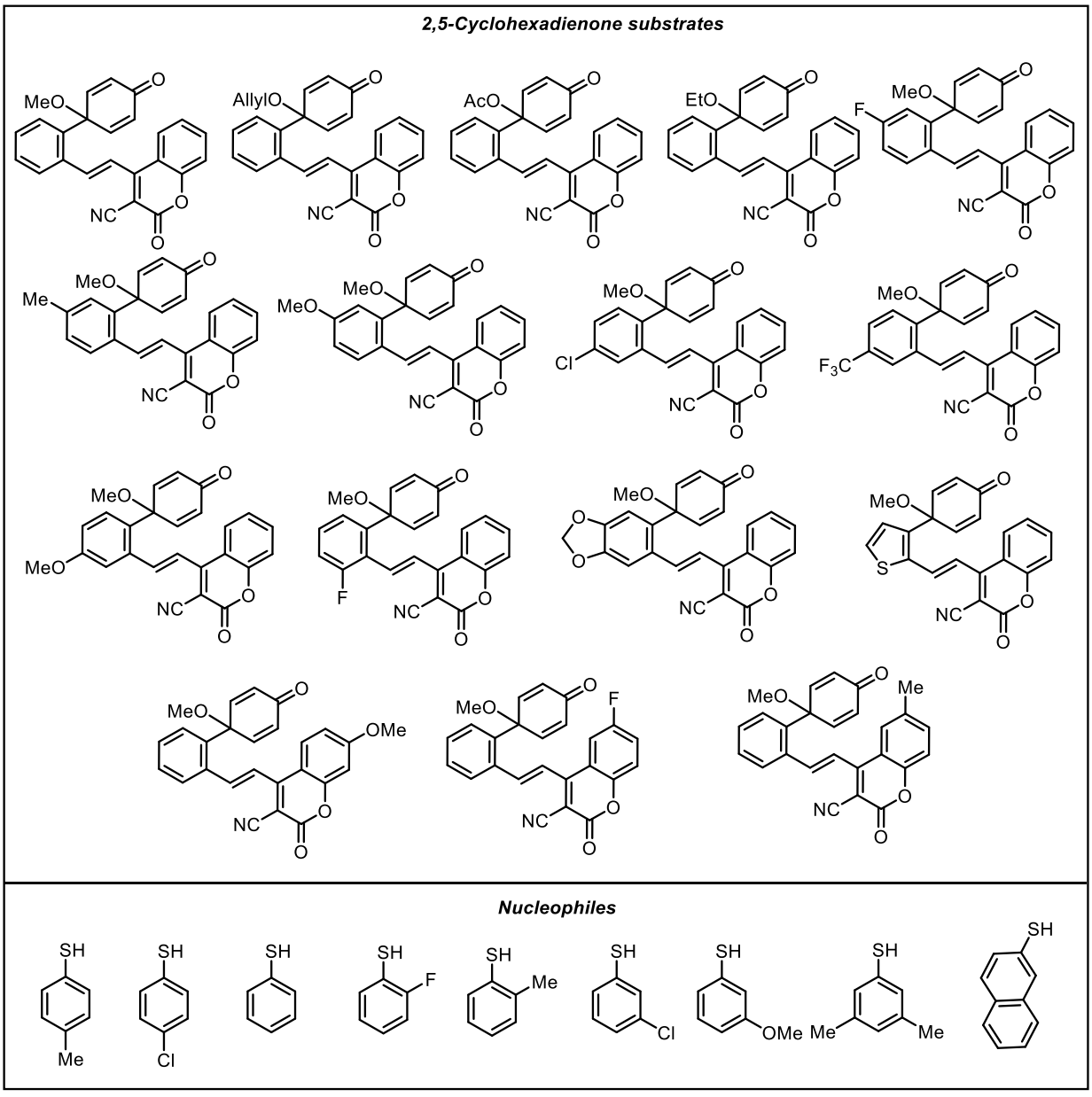
Entry	C-1 to C-11	Solvent	Time (h)	3a/4a	Yield (%)[a]	dr[b]	er[c]
1	**C-1**	Toluene	48	**4a**	93	>20:1	84.0:16.0
2	**C-2**	Toluene	48	**4a**	81	>20:1	80.0:20.0
3	**C-3**	Toluene	96	**4a**	81	>20:1	27.5:72.5
4	**C-4**	Toluene	48	**4a**	47	>20:1	45.5:54.5
5	**C-5**	Toluene	96	**4a**	72	>20:1	27.5:72.5
6	**C-6**	Toluene	48	**4a**	88	>20:1	30.5:69.5
7	**C-7**	Toluene	72	**4a**	84	>20:1	20.0:80.0
8	**C-8**	Toluene	48	**4a**	85	>20:1	28.0:72.0
9	**C-9**	Toluene	72	**4a**	91	>20:1	65.5:34.5
10	**C-10**	Toluene	72	**4a**	42	>20:1	84.5:15.5
11	**C-11**	Toluene	72	**4a**	79	>20:1	53.0:47.0
12	**C-1**	CH_2Cl_2	48	**4a**	80	>20:1	85.0:15.0
13	**C-1**	THF	48	**4a**	69	>20:1	82.5:17.5
14	**C-1**	o-xylene	48	**4a**	78	>20:1	83.0:17.0
15	**C-1**	$CHCl_3$	48	**4a**	78	>20:1	82.5:17.5

16	**C-1**	Diethyl ether	72	**4a**	69	>20:1	82.5:17.5
17	**C-1**	1,4-Dioxane	48	**4a**	77	>20:1	82.5:17.5
18	**C-1**	CH_3CN	24	**4a**	79	>20:1	96.5:3.5
19[d]	**C-1**	CH_3CN	12	**3a**	77	>20:1	93.5:6.5
20[e]	**C-1**	CH_3CN	12	**3a**	77	>20:1	96.5:3.5

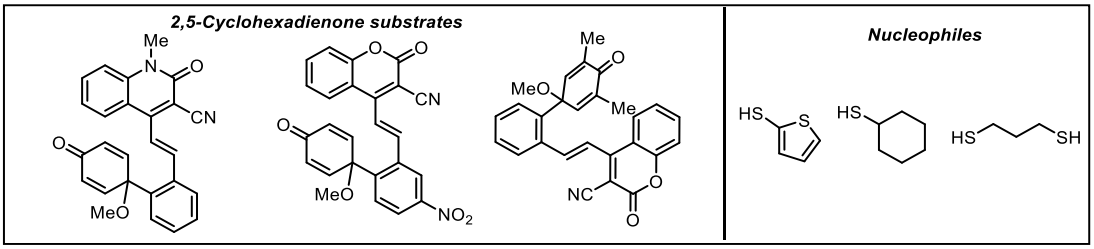
Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), **C-1** to **C-9** (5 mol%) in 1.0 mL of MeCN at rt [a]Yield refers to the isolated yield of the product. [b]dr was determined by HPLC using a chiral column. [c]er values (enantiomeric ratio) were determined by HPLC using a chiral column. [d]1.0 eq. of *p*-TolSH. [e]1.0 eq. of *p*-TolSH at -10 °C.

S3. Successful and Unsuccessful Substrates:

S3.1.1 Successful Substrates

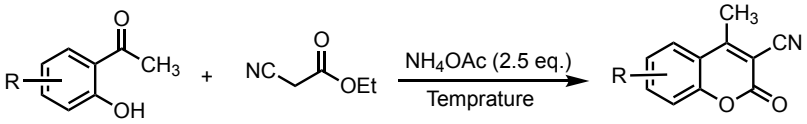


S.3.1.2 Unsuccessful Substrates:



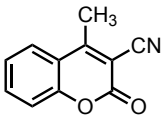
S4. Experimental Procedures and Characterization Data:

S4.1. General procedure for the synthesis of 3-cyano-4-methylcoumarins:[6]



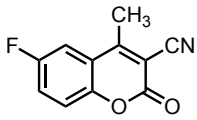
In a 250 mL round bottom flask, 2-hydroxyacetophenone derivative (20-30 mmol, 1.0 eq.), ethyl cyanoacetate (1.5 eq.), and ammonium acetate (2.5 eq.) were added at room temperature. Then the flask was fitted with a reflux condenser and the reaction mixture was heated to 80-150 °C for 5-7 hours. The mixture was then cooled to room temperature. The precipitates formed were filtered and washed with ethanol to afford 3-cyano-4-methylcoumarins.

4-Methyl-2-oxo-2*H*-chromene-3-carbonitrile



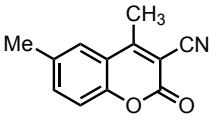
The reaction was performed at 20.0 mmol scale at 80 °C. White Solid; **Yield**: 1184 mg, 32%; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.99 (d, J = 8.5 Hz, 1H, Ar*H*), 7.82 – 7.79 (m, 1H, Ar*H*), 7.51 – 7.48 (m, 2H, Ar*H*), 2.74 (s, 3H, –CH_3); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 163.8, 156.8, 152.8, 135.4, 127.2, 125.4, 118.2, 117.0, 114.3, 101.4, 18.3.

6-Fluoro-4-methyl-2-oxo-2H-chromene-3-carbonitrile



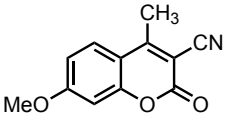
The reaction was performed at 20.0 mmol scale at 150 °C. White Solid**;** **Yield**: 410 mg, 10%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 3H, Ar*H*), 2.76 (s, 3H, –CH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 161.5, 159.2, 156.4, 149.6, 122.8, 119.6, 119.2, 113.23, 111.7, 103.8, 18.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –114.42.

4,6-Dimethyl-2-oxo-2H-chromene-3-carbonitrile



The reaction was performed at 20.0 mmol scale at 150 °C. Light Brown Solid; **Yield**: 1160 mg, 29%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.50 (m, 2H, Ar*H*), 7.29 (d, J = 9.0 Hz, 1H, Ar*H*), 2.77 (s, 3H, –CH_3), 2.47 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 162.4, 157.1, 151.6, 136.4, 135.5, 125.8, 118.0, 117.5, 113.7, 102.5, 21.1, 18.4.

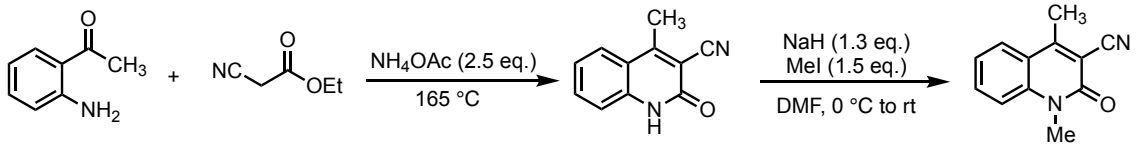
7-Methoxy-4-methyl-2-oxo-2*H*-chromene-3-carbonitrile



The reaction was performed at 30.0 mmol scale at 150 °C. Brown Solid; **Yield**: 1660 mg, 26%; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.90 (d, J = 9.0 Hz, 1H, Ar*H*), 7.09 – 7.05 (m, 2H, Ar*H*), 3.91 (s, 3H, ArOCH_3), 2.68 (s,

3H, –CH_3); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 165.6, 164.1, 157.9, 155.6, 129.1, 115.2, 114.2, 112.3, 101.5, 97.9, 57.0, 18.7.

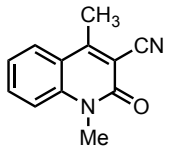
S4.2. Procedure for the synthesis of 1,4-dimethyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile:[7]



In a 50 mL round bottom flask, 2-aminoacetophenone (1.35g, 10.0 mmol, 1.0 eq.), ethyl cyanoacetate (1.70g, 15.0 mmol, 1.5 eq.), and ammonium acetate (1.93g, 25.0 mmol, 2.5 eq.) were added at room temperature. Then the flask was fitted with a reflux condenser and the reaction mixture was heated to 165 °C for 7 hours. The mixture was then cooled to room temperature. The precipitates formed were filtered and washed with ethanol to afford 4-methyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile.

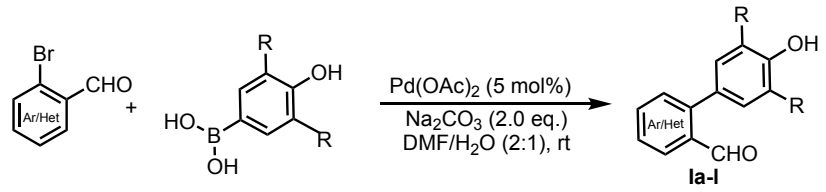
The dihydroquinoline-3-carbonitrile (921mg, 5.0 mmol, 1.0 eq.) was taken along with NaH (156mg, 6.5 mmol, 1.3 eq.) in an oven dried round bottom flask under argon. To this, dry DMF (20.0 mL) was added and the resulting solution was stirred at 0 °C for 30 minutes. Then a solution of methyl iodide (1.06g, 7.5 mmol, 1.5 eq.) in a dry DMF (6.0 mL) was added dropwise to the reaction mixture at 0 °C. The reaction was warmed to room temperature and stirred for 12 hours. The reaction mixture was poured in ice-cold water, stirred for 15 minutes and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain light yellow oil, which was purified by silica gel column chromatography (hexane : ethyl acetate = 7 : 3 as eluent).

1,4-Dimethyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile



White Solid; **Yield**: 743 mg, 75%; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.99 (dd, J = 8.0, 1.5 Hz, 1H, ArH), 7.82 – 7.79 (m, 1H, ArH), 7.62 (d, J = 8.0 Hz, 1H, ArH), 7.42 – 7.39 (m, 1H, ArH), 3.63 (s, 3H, –NCH_3), 2.73 (s, 3H, –CH_3); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 158.0, 157.2, 139.9, 134.2, 127.3, 123.1, 118.9, 115.7 (2C), 105.6, 29.8, 18.2.

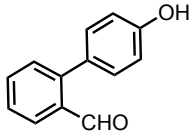
S4.3. General procedure for the synthesis of aldehydes Ia-l:[8]



Ia-l

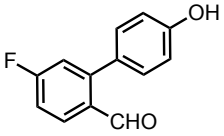
To a solution of substituted 2-bromo benzaldehyde derivatives (10.0 mmol, 1.0 eq.) and Na_2CO_3 (2.12g, 20.0 mmol, 2.0 eq.) in DMF/H_2O (v:v = 2:1, 25.0 mL) was added 4-hydroxy phenylboronic acid (10.0 mmol, 1.0 eq.). The reaction mixture was stirred at room temperature for 5 minutes. Palladium (II) acetate (5 mol %) was then added, and the reaction mixture was allowed to stir at room temperature until complete consumption of the aldehyde (monitored by TLC). After completion of the reaction, water was added, and the reaction mixture was extracted with ethyl acetate (4 × 30 mL). The combined organic phase was washed with water and brine, and dried over anhydrous Na_2SO_4. The organic phase was filtered and concentrated under vacuum to yield the crude product, which was purified by column chromatography (silica gel, hexane : ethyl acetate = 9 :1 to 7 : 3 as eluent) to afford **Ia-l**.

4'-Hydroxy-(1,1'-biphenyl)-2-carbaldehyde (Ia)



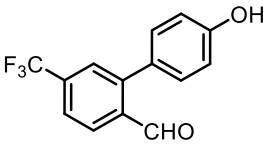
Yellow solid; **mp**: 111 – 112 °C; **Yield**: 1916 mg, 97%; $\mathbf{R_f}$: 0.35 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.99 (d, *J* = 1.0 Hz, 1H, –C*H*O), 8.03 – 8.01 (m, 1H, Ar*H*), 7.65 – 7.62 (m, 1H, Ar*H*), 7.49 – 7.43 (m, 2H, Ar*H*), 7.26 – 7.24 (m, 2H, Ar*H*), 6.97 – 6.96 (m, 2H, Ar*H*), 6.34 (br s, 1H, –O*H*); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 193.8, 156.4, 146.1, 134.0, 133.6, 131.6 (2C), 130.9, 129.9, 127.8, 127.5, 115.6 (2C); **HRMS** (ESI, m/z) calcd for $C_{13}H_{10}O_2Na^+$ $[M+Na]^+$: 221.0573, found: 221.0585.

5-Fluoro-4'-hydroxy-(1,1'-bipheny)-2-carbaldehyde (Ib)



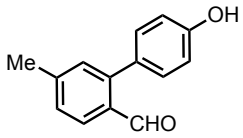
White solid; **mp**: 147 – 148 °C; **Yield**: 1768 mg, 82%; $\mathbf{R_f}$: 0.32 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (s, 1H, –C*H*O), 8.06 (dd, *J* = 9.0 Hz, 6.0 Hz, 1H, Ar*H*), 7.26 – 7.24 (m, 2H, Ar*H*), 7.17 – 7.11 (m, 2H, Ar*H*), 6.98 – 6.96 (m, 2H, Ar*H*) , 6.07 (br s, 1H, –O*H*); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 191.6, 165.7, 156.5, 148.8, 131.5 (2C), 130.9, 130.4, 129.0, 117.5, 115.7 (2C), 115.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –103.22; **HRMS** (ESI, m/z) calcd for $C_{13}H_{10}O_2F^+$ $[M+H]^+$: 217.0660, found: 217.0663.

4'-Hydroxy-5-[trifluoromethyl]-[1,1'-biphenyl]-2-carbaldehyde (Ic)



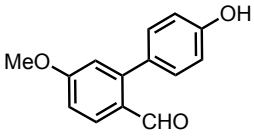
White solid; **mp**: 153 – 154 °C; **Yield**: 1900 mg, 71%; **R_f**: 0.46 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.02 (d, *J* = 0.5 Hz, 1H, –C*H*O), 8.12 – 8.10 (m, 1H, Ar*H*), 7.72 – 7.71 (m, 2H, Ar*H*), 7.29 – 7.27 (m, 2H, Ar*H*), 7.01 – 6.98 (m, 2H, Ar*H*), 5.76 (s, 1H, –O*H*); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 192.2, 156.7, 146.2, 136.0, 135.2, 131.7 (2C), 128.7, 128.6, 127.9, 124.2, 122.5, 115.9 (3C); **^{19}F NMR** (471 MHz, $CDCl_3$) δ –63.03; **HRMS** (ESI, m/z) calcd for $C_{14}H_{10}F_3O_2$+ $[M+H]^+$: 267.0627, found: 267.0617.

4'-Hydroxy-5-methyl-(1,1'-biphenyl)-2-carbaldehyde (Id)



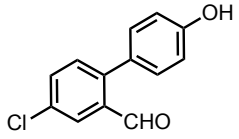
White solid; **mp**: 172 – 173 °C; **Yield**: 2075 mg, 98%; **R_f**: 0.29 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.93 (s, 1H, –C*H*O), 7.93 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.29 – 7.27 (m, 1H, Ar*H*), 7.25 – 7.23 (m, 3H, Ar*H*), 6.95 – 6.93 (m, 2H, Ar*H*), 5.78 (br s, 1H, –O*H*), 2.46 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 193.0, 156.1, 146.1, 144.9, 131.6 (2C), 131.5 (2C), 130.2, 128.5, 127.9, 115.5 (2C), 22.0; **HRMS** (ESI, m/z) calcd for $C_{14}H_{12}O_2Na^+$ $[M+Na]^+$: 235.0730, found: 235.0755.

4'-Hydroxy-5-methoxy-(1,1'-biphenyl)-2-carbaldehyde (Ie)



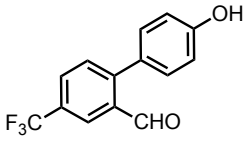
Brown solid; **mp**: 145 – 146 °C; **Yield**: 1442 mg, 63%; **R_f**: 0.22 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.84 (d, *J* = 1.0 Hz, 1H, –C*H*O), 8.02 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.30 – 7.25 (m, 2H, Ar*H*), 7.00 – 6.97 (m, 1H, Ar*H*), 6.95 – 6.93 (m, 2H, Ar*H*), 6.87 (d, *J* = 2.5 Hz, 1H, Ar*H*), 5.87 (d, *J* = 2.0 Hz, 1H, –O*H*), 3.91 (s, 3H, –CH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 192.0, 163.9, 156.3, 148.7, 131.5 (2C), 130.3, 130.1, 127.4, 115.5 (2C), 115.3, 113.9, 55.8; **HRMS** (ESI, m/z) calcd for $C_{14}H_{12}O_3Na^+$ $[M+Na]^+$: 251.0679, found: 251.0678.

4-Chloro-4'-hydroxy-(1,1'-biphenyl)-2-carbaldehyde (If)



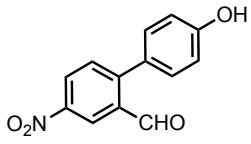
White solid; **mp**: 143 – 144 °C; **Yield**: 1956 mg, 84%; **R_f**: 0.33 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.92 (s, 1H, –C*H*O), 7.97 (d, *J* = 2.3 Hz, 1H, Ar*H*), 7.58 (dd, *J* = 8.3 Hz, 2.3 Hz, 1H, Ar*H*), 7.39 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.24 – 7.20 (m, 2H, Ar*H*), 6.96 – 6.95 (m, 2H, Ar*H*); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 191.8, 156.4, 144.1, 134.8, 134.1, 133.7, 132.4, 131.6 (2C), 129.0, 127.6, 115.8 (2C); **MS** (EI): m/z = 232; Anal. calcd for $C_{13}H_9ClO_2$: C, 67.11; H, 3.90, found: C, 67.17; H, 4.06.

4'-Hydroxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carbaldehyde (Ig)



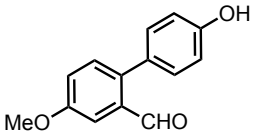
White solid; **mp**: 124 – 125 °C; **Yield**: 2183 mg, 82%; $\mathbf{R_f}$: 0.61 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.02 (d, *J* = 0.5 Hz, 1H, –C*H*O), 8.11 (dd, *J* = 8.5 Hz, 1.0 Hz, 1H, Ar*H*), 7.73 – 7.70 (m, 2H, Ar*H*), 7.30 – 7.27 (m, 2H, Ar*H*), 7.00 – 6.97 (m, 2H, Ar*H*), 5.38 (br s, 1H, –O*H*); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 191.9, 156.6, 146.0, 136.1, 134.9, 131.7 (2C), 128.9, 128.6, 127.9, 124.2, 123.6, 115.9 (2C); **^{19}F NMR** (471 MHz, $CDCl_3$) δ –63.02; **HRMS** (ESI, m/z) calcd for $C_{14}H_{10}F_3O_2$ $[M+H]^+$: 267.0627, found: 267.0618

4'-Hydroxy-4-nitro-(1,1'-biphenyl)-2-carbaldehyde (Ih)



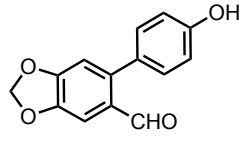
Yellow solid; **mp**: 174 – 175 °C; **Yield**: 1716 mg, 71%; $\mathbf{R_f}$: 0.28 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.03 (s, 1H, –O*H*), 9.91 (s, 1H, –C*H*O), 8.53 (d, 1H, *J* = 2.5 Hz, Ar*H*), 8.48 (dd, 1H, *J* = 8.5 Hz, 3.0 Hz, Ar*H*), 7.79 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.39 – 7.36 (m, 2H, Ar*H*), 6.96 .0 – 6.94 (m, 2H, Ar*H*); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 190.6, 158.9, 150.6, 146.3, 133.5, 132.5, 131.8 (2C), 127.5, 125.9, 122.4, 115.8 (2C); **HRMS** (ESI, m/z) calcd for $C_{13}H_9NNaO_4^+$ $[M+Na]^+$: 266.0419, found: 266.0403.

4'-Hydroxy-4-methoxy-(1,1'-biphenyl)-2-carbaldehyde (Ii)



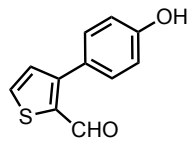
Yellow solid; **mp**: 148 – 149 °C; **Yield**: 1850 mg, 81%; $\mathbf{R_f}$: 0.30 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.95 (s, 1H, –C*H*O), 7.50 (d, *J* = 3.0 Hz, 1H, Ar*H*), 7.36 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.23 – 7.19 (m, 3H, Ar*H*), 6.94 – 6.93 (m, 2H, Ar*H*), 5.75 (br s, 1H, –O*H*), 3.90 (s, 3H, ArOCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 193.2, 159.0, 155.9, 139.2, 134.4, 132.3, 131.7 (2C), 129.9, 121.9, 115.5 (2C), 109.9, 55.8; **HRMS** (ESI, m/z) calcd for $C_{14}H_{12}O_3Na^+$$[M+Na]^+$: 251.0674, found: 251.0678.

6-(4-Hydroxyphenyl)benzo[d][1,3]dioxole-5-carbaldehyde (Ij)



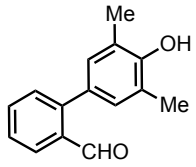
White solid; **mp**: 173 – 174 °C; **Yield**: 1088 mg, 45%; $\mathbf{R_f}$: 0.18 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.75 (s, 1H, –C*H*O), 7.46 (s, 1H, Ar*H*), 7.22 – 7.21 (m, 2H, Ar*H*), 6.92 – 6.90 (m, 2H, Ar*H*), 6.83 (s, 1H, Ar*H*), 6.10 (s, 2H, –OCH_2O–), 5.27 (s, 1H, –O*H*); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 191.3, 156.1, 152.4, 147.7, 131.6 (2C), 130.0, 128.8, 115.5 (2C), 110.4, 106.4, 102.2, 31.1; **HRMS** (ESI, m/z) calcd for $C_{14}H_{11}O_4^+$ $[M+H]^+$: 243.0652, found: 243.0660.

2-(4-Hydroxyphenyl)thiophene-3-carbaldehyde (Ik)



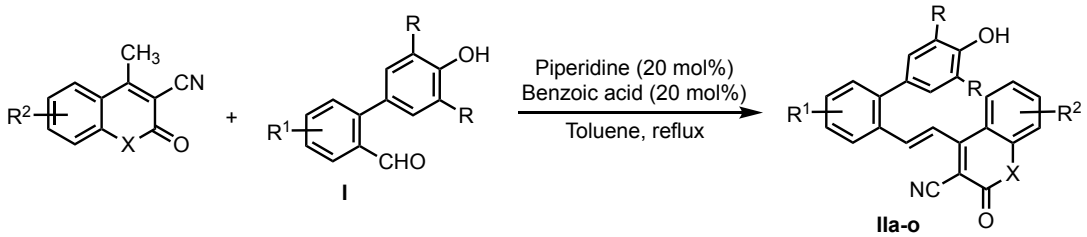
Yellow solid; **mp**: 103 – 104 °C; Yield: 1500 mg, 73%; $\mathbf{R_f}$: 0.61 (hexane : ethyl acetate = 7 : 3); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.86 (d, *J* = 1.5 Hz, 1H, –C*H*O), 7.74 (dd, *J* = 5.0 Hz, 1.5 Hz, 1H, Ar*H*), 7.37 – 7.35 (m, 2H, Ar*H*), 7.20 (d, *J* = 5.0 Hz, 1H, Ar*H*), 6.98 – 6.97 (m, 2H, Ar*H*), 6.10 (br s, 1H, –O*H*); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.1, 156.9, 152.2, 137.6, 134.8, 131.2 (2C), 130.8, 126.4, 116.0 (2C); **HRMS** (ESI, m/z) calcd for $C_{11}H_9O_2S^+$ $[M+H]^+$: 205.0318, found: 205.0322.

4'-Hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-2-carbaldehyde (Il)



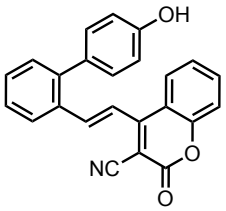
White solid; **mp**: 154 – 155 °C; **Yield**: 200 mg, 9%; $\mathbf{R_f}$: 0.53 (hexane : ethyl acetate = 4 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.00 (d, *J* = 1.0 Hz, 1H, –C*H*O), 7.99 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H, Ar*H*), 7.62 – 7.58 (m, 1H, Ar*H*), 7.46 – 7.41 (m, 2H, Ar*H*), 7.00 (s, 2H, Ar*H*), 4.80 (1H, –O*H*), 2.31 (s, 6H, 2 × –C*H*$_3$); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 193.2, 152.6, 146.2, 133.8, 133.6, 130.9, 130.6 (2C), 129.7, 127.6, 127.3, 125.9, 123.3, 16.1 (2C); **HRMS** (ESI, m/z) calcd for $C_{15}H_{15}O_2$ $[M+H]^+$: 227.1067, found: 227.1069.

S.4.4. General procedure for the synthesis of IIa-o:



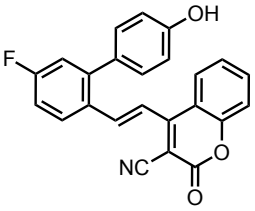
Chromene-3-carbonitrile or dihydroquinoline-3-carbonitrile (1.0 eq.), benzaldehyde derivative **I** (1.0 eq.) and benzoic acid (20 mol%) in toluene (10 mL/mmol) were placed in a round bottom flask equipped with an Dean-Stark receiver and magnetic stirring bar. After adding piperidine (20 mol%), the reaction mixture was heated to reflux for 2-12 hours on an oil bath. After the completion of reaction (indicated by TLC), the mixture was cooled to room temperature, diluted with ethyl acetate (30 mL/mmol) and washed with water. The separated organic layer was dried with anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the desired condensation products **IIa-o** were purified by column chromatography or crystallization.

(*E*)-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIa)



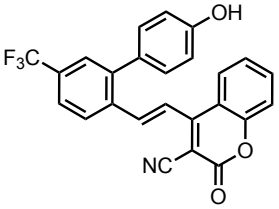
The reaction was performed at 13.42 mmol scale. Yellow solid; **m.p.**: 226 – 227 °C; **Yield**: 4000 mg, 82%; $\mathbf{R_f}$: 0.24 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.67 (br s, 1H), 8.17 – 8.15 (m, 1H), 8.06 (dd, J = 8.0, 1.5 Hz, 1H), 7.80 – 7.77 (m, 1H), 7.71 – 7.68 (m, 1H), 7.53 – 7.43 (m, 5H), 7.39 – 7.35 (m, 1H), 7.21 – 7.19 (m, 2H), 6.88 – 6.84 (m, 2H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 159.4, 157.5, 157.1, 152.9, 142.7, 141.1, 135.2, 132.2, 131.0 (2C), 130.6, 130.2, 129.9, 127.5, 127.4, 127.1, 125.2, 119.9, 117.2, 115.6, 115.4 (2C), 115.0, 97.5; **HRMS** (ESI, m/z) calcd for $C_{24}H_{16}NO_3^+$ $[M+H]^+$: 366.1125, found: 366.1129.

(*E*)-4-[2-(5-Fluoro-4'-hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIb)



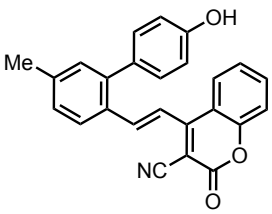
The reaction was performed at 5.00 mmol scale. Yellow solid; **m.p.**: 128 – 129 °C; **Yield**: 1400 mg, 73%; $\mathbf{R_f}$: 0.21 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.72 (s, 1H), 8.31 – 8.24 (m, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.81 – 7.78 (m, 1H), 7.71 – 7.67 (m, 1H), 7.50 – 7.42 (m, 3H), 7.37 – 7.33 (m, 1H), 7.24 – 7.20 (m, 3H), 6.86 (d, J = 8.5 Hz, 2H); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, DMSO-d_6) δ 159.3, 157.5, 157.5, 152.9, 145.1, 139.8, 135.2, 131.0 (2C), 129.8, 128.9, 128.7, 127.5, 125.2, 119.8, 117.4, 117.2, 116.8, 115.4 (2C), 115.3, 115.0, 114.7, 97.5; **^{19}F NMR** (471 MHz, DMSO-d_6) δ –110.26; **HRMS** (ESI, m/z) calcd for $C_{24}H_{15}FNO_3^+$ $[M+H]^+$: 384.1030, found: 384.1036.

(*E*)-4-[2-(4'-Hydroxy-5-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIc)



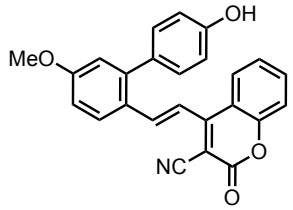
The reaction was performed at 6.00 mmol scale. Yellow solid; **m.p.**: 209 – 210 °C; **Yield**: 1820 mg, 70%; $\mathbf{R_f}$: 0.25 (hexane: ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.72 (br s, 1H), 8.33 (d, J = 8.5 Hz, 1H), 8.01 (dd, J = 8.0, 1.5 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.62 (d, J = 2.5 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.24 – 7.21 (m, 2H), 6.84 – 6.83 (m, 2H); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, DMSO-d_6) δ 159.1, 157.7, 157.4, 153.0, 143.1, 139.0, 136.1, 135.3, 131.2 (2C), 129.8, 129.3, 128.6, 128.5, 128.3, 127.6, 127.0, 125.3, 123.8, 122.8, 117.3, 115.6 (2C), 114.9, 98.4; **^{19}F NMR** (471 MHz, DMSO-d_6) δ –61.11; **HRMS** (ESI, m/z) calcd for $C_{25}H_{15}F_3NO_3^+$ $[M+H]^+$: 434.0999, found: 434.1001.

(*E*)-4-[2-(4'-Hydroxy-5-methyl-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IId)



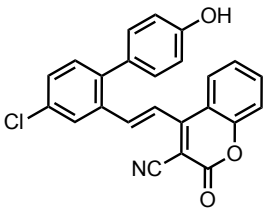
The reaction was performed at 4.00 mmol scale. Yellow solid; **m.p.**: 218 – 219 °C; **Yield**: 982 mg, 65%; $\mathbf{R_f}$: 0.25 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.57 (br s, 1H), 8.04 (m, 2H), 7.78 – 7.74 (m, 1H), 7.62 – 7.59 (m, 1H), 7.52 – 7.49 (m, 1H), 7.46 – 7.41 (m, 2H), 7.29– 7.27 (m, 1H), 7.18 – 7.16 (m, 3H), 6.85 – 6.82 (m, 2H), 2.39 (s, 3H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 159.4, 157.4, 157.0, 152.9, 142.9, 141.4, 140.1, 135.0, 131.0, 130.9, 129.9, 129.5, 128.1, 127.4, 126.9, 126.9, 125.1, 118.5, 117.3, 117.2, 115.5, 115.2, 114.9, 96.9, 21.0; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_3^+$ $[M+H]^+$: 380.1281, found: 380.1284.

(*E*)-4-[2-(4'-Hydroxy-5-methoxy-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIe)



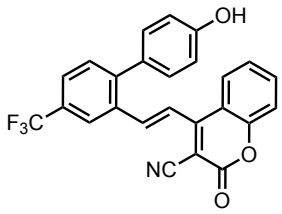
The reaction was performed at 4.05 mmol scale. Yellow solid; **m.p.**: 121 – 122 °C; **Yield**: 1430 mg, 89%; $\mathbf{R_f}$: 0.24 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.74 (br s, 1H), 8.16 (d, J = 9.0 Hz, 1H), 8.09 (dd, J = 8.0, 1.0 Hz, 1H), 7.79 – 7.76 (m, 1H), 7.60 – 7.51 (m, 2H), 7.48 – 7.42 (m, 2H), 7.23 – 7.20 (m, 2H), 7.07 (dd, J = 8.5, 2.5 Hz, 1H), 6.88 (d, J = 2.5 Hz, 1H), 6.87 – 6.84 (m, 2H), 3.86 (s, 3H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 160.7, 159.4, 157.7, 157.3, 152.9, 145.0, 141.3, 135.1, 131.0 (2C), 129.8, 127.4, 125.1, 125.0, 117.4, 117.2, 117.1, 115.3 (2C), 115.3, 114.9, 114.1, 96.3, 79.2, 55.5; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_4^+$ $[M+H]^+$: 396.1230, found: 396.1238.

(*E*)-4-[2-(4-Chloro-4'-hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIf)



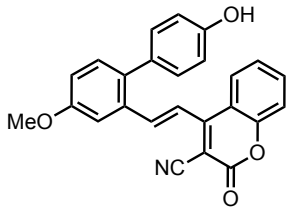
The reaction was performed at 8.00 mmol scale. Yellow solid; **m.p.**: 232 – 233 °C; **Yield**: 2200 mg, 69%; $\mathbf{R_f}$: 0.27 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.82 (br s, 1H), 8.28 (d, J = 2.5 Hz, 1H), 8.10 (dd, J = 8.5, 1.5 Hz, 1H), 7.84 (d, J = 16.0 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.53 (dd, J = 8.0, 2.0 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.41 – 7.37 (m, 2H), 7.20 – 7.17 (m, 2H), 6.87 – 6.84 (m, 2H); **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 159.2, 157.4, 157.4, 152.9, 141.4, 139.2, 135.2, 133.9, 132.3, 131.0 (2C), 129.8, 128.7, 127.7, 126.5, 125.2, 121.5, 117.3, 117.2, 115.6, 115.5 (2C), 114.9, 97.9; **HRMS** (ESI, m/z) calcd for $C_{24}H_{15}ClNO_3^+$ $[M+H]^+$: 400.0735, found: 400.0744.

(*E*)-4-[2-(4'-Hydroxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIg)



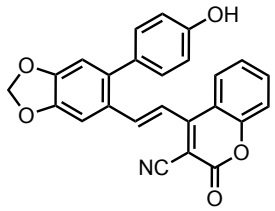
The reaction was performed at 7.00 mmol scale. Yellow solid; **m.p.**: 223 – 224 °C; **Yield**: 1577 mg, 52%; **R_f**: 0.24 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d_6*) δ 9.77 (s, 1H), 8.52 (s, 1H), 8.11 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.96 (d, *J* = 16.5 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.50 – 7.45 (m, 3H), 7.26 – 7.23 (m, 2H), 6.89 – 6.86 (m, 2H); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, DMSO-*d_6*) δ 159.3, 157.7, 157.4, 153.0, 146.1, 139.0, 135.4, 135.3, 133.0, 131.6, 131.1 (2C), 128.6, 127.8, 127.0, 126.1, 125.2, 124.0, 122.1, 117.4, 117.2, 115.5 (2C), 114.9, 98.2; **^{19}F NMR** (471 MHz, DMSO-*d_6*) δ –60.62; **HRMS** (ESI, m/z) calcd for $C_{25}H_{15}F_3NO_3^+$ $[M+H]^+$: 434.0999, found: 434.1005.

(*E*)-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-7-methoxy-2-oxo-2*H*-chromene-3-carbonitrile (IIh)



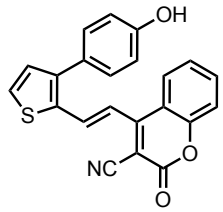
The reaction was performed at 7.00 mmol scale. Yellow solid; **m.p.**: 216 – 217 °C; **Yield**: 1650 mg, 60%; **R_f**: 0.18 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d_6*) δ 9.65 (br s, 1H), 8.08 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.67 (d, *J* = 2.5 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.16 – 7.13 (m, 2H), 7.09 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.84 – 6.81 (m, 2H), 3.90 (s, 3H); **^{13}C{^{1}H}NMR** (125 MHz, DMSO-*d_6*) 159.4, 158.5, 157.5, 156.8, 152.9, 141.0, 135.7, 135.2, 133.1, 131.8, 131.1 (2C), 129.7, 127.6, 125.2, 120.1, 117.4, 117.2, 116.8, 115.3 (2C), 115.0, 111.2, 97.5, 55.6; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_4^+$ $[M+H]^+$: 396.1230, found: 396.1236.

(*E*)-4-[2-(6-(4-Hydroxyphenyl)benzo[d][1,3]dioxol-5-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIi)



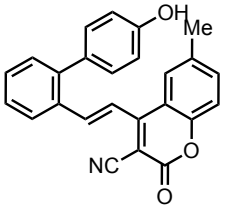
The reaction was performed at 5.00 mmol scale. Yellow solid; **m.p.**: 199 – 200 °C; **Yield**: 1023 mg, 50%; **R_f**: 0.28 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d_6*) δ 9.64 (br s, 1H), 8.11 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.83 (s, 1H), 7.78 – 7.75 (m, 1H), 7.65 – 7.62 (m, 1H), 7.49 – 7.42 (m, 3H), 7.16 – 7.14 (m, 2H), 6.90 (s, 1H), 6.83 – 6.81 (m, 2H), 6.16 (s, 2H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-*d_6*) δ 159.4, 157.7, 157.0, 152.8, 149.3, 147.3, 141.2, 139.2, 135.1, 131.2 (2C), 129.7, 127.4, 126.1, 125.1, 117.4 (2C), 117.2, 115.3 (2C), 115.2, 110.1, 105.8, 101.9, 96.3; **HRMS** (ESI, m/z) calcd for $C_{25}H_{16}NO_5^+$ $[M+H]^+$: 410.1023, found: 410.1016.

(*E*)-4-[2-(2-(4-Hydroxyphenyl)thiophen-3-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIj)



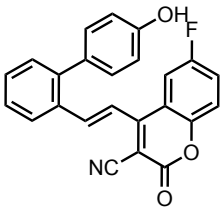
The reaction was performed at 5.00 mmol scale. Red solid; **m.p.**: 93 – 94 °C; **Yield**: 1113 mg, 60%; $\mathbf{R_f}$: 0.29 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.79 (br s, 1H), 8.08 – 8.06 (m, 1H), 7.87 – 7.86 (m, 1H), 7.81 – 7.76 (m, 2H), 7.51 – 7.46 (m, 2H), 7.39 – 7.33 (m, 3H), 7.29 – 7.27 (m, 1H), 6.88 – 6.86 (m, 2H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 158.2, 157.7, 157.7, 152.8, 146.2, 135.8, 135.1, 133.1, 130.6 (2C), 130.5, 129.7, 127.1, 125.4, 125.3, 117.4, 117.3, 117.2, 115.7 (2C), 115.5, 96.2; **HRMS** (ESI, m/z) calcd for $C_{22}H_{14}NO_3S^+$ $[M+H]^+$: 372.0689, found: 372.0696.

(*E*)-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-6-methyl-2-oxo-2*H*-chromene-3-carbonitrile (IIk)



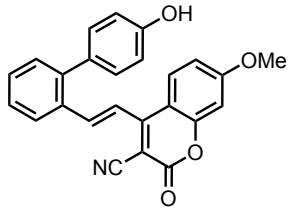
The reaction was performed at 6.00 mmol scale. Yellow solid; **m.p.**: 110 – 111 °C; **Yield**: 1893 mg, 83%; $\mathbf{R_f}$: 0.28 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.64 (s, 1H), 8.16 – 8.14 (m, 1H), 7.85 – 7.84 (m, 1H), 7.69 – 7.65 (m, 1H), 7.60 (dd, J = 8.5, 1.0 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.40 – 7.36 (m, 2H), 7.21 – 7.19 (m, 2H), 6.86 – 6.83 (m, 2H), 2.40 (s, 3H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-d_6) δ 159.3, 157.7, 157.1, 151.1, 142.7, 141.0, 136.1, 134.8, 132.2, 131.0 (2C), 130.6, 130.2, 130.0, 127.4, 127.2, 126.9, 120.0, 117.0 (2C), 115.4 (2C), 115.1, 97.3, 20.3; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_3^+$ $[M+H]^+$: 380.1281, found:

(*E*)-6-Fluoro-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIl)



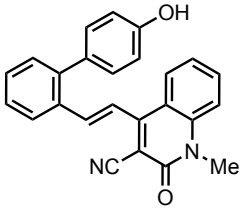
The reaction was performed at 1.92 mmol scale. Orange solid; **m.p.**: 200 – 201 °C; **Yield**: 450 mg, 61%; $\mathbf{R_f}$: 0.30 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.89 (br s, 1H), 8.22 – 8.20 (m, 1H), 8.02 (dd, J = 9.5, 3.0 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.58 – 7.47 (m, 4H), 7.39 – 7.37 (m, 1H), 7.21 – 7.19 (m, 2H), 6.86 – 6.83 (m, 2H); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, DMSO-d_6) δ 158.5 (2C), 157.4, 157.1, 149.3, 142.9, 141.4, 132.1, 131.0 (2C), 130.6, 130.4, 129.8, 127.3 (2C), 122.3, 119.5, 119.3, 118.5, 115.3 (2C), 114.9, 112.9, 98.2; **^{19}F NMR** (471 MHz, DMSO-d_6) δ –116.37; **HRMS** (ESI, m/z) calcd for $C_{24}H_{15}FNO_3^+$ $[M+H]^+$: 384.1030, found: 384.1033.

(*E*)-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-7-methoxy-2-oxo-2*H*-chromene-3-carbonitrile (IIm)



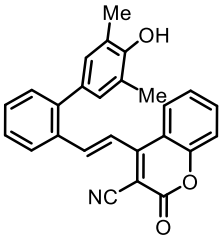
The reaction was performed at 4.00 mmol scale. Yellow solid; **m.p.**: 210 – 211 °C; **Yield**: 1180 mg, 75%; $\mathbf{R_f}$: 0.21 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d*$_6$) δ 9.65 (br s, 1H), 8.12 – 8.10 (m, 1H), 7.95 – 7.92 (m, 1H), 7.63 – 7.57 (m, 1H), 7.51 – 7.44 (m, 3H), 7.37 – 7.35 (m, 1H), 7.20 – 7.18 (m, 2H), 7.08 – 7.06 (m, 1H), 7.01 – 6.97 (m, 1H), 6.87 – 6.84 (m, 2H), 3.90 – 3.89 (m, 3H); **^{13}C{^{1}H}NMR** (125 MHz, DMSO-*d*$_6$) δ 165.0, 159.3, 158.0, 157.1, 155.4, 142.7, 140.8, 132.2, 131.0 (2C), 130.5, 130.2, 129.9, 128.9, 127.4, 127.0, 120.0, 115.3 (2C), 113.5, 110.8 (2C), 101.2, 93.5, 56.4; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_4^+$ $[M+H]^+$: 396.1230, found: 396.1233.
380.1289.

(*E*)-4-[2-(4'-Hydroxy-[1,1'-biphenyl]-2-yl)vinyl]-1-methyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile (IIn)



The reaction was performed at 3.00 mmol scale. Yellow solid; **m.p.**: 290 – 291 °C; **Yield**: 954 mg, 84%; $\mathbf{R_f}$: 0.10 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d*$_6$) δ 9.62 (s, 1H), 8.12 – 8.10 (m, 1H), 8.02 (d, *J* = 7.5 Hz, 1H), 7.80 (t, *J* = 7.0 Hz, 1H), 7.69 (d, *J* = 16.5 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.48 – 7.47 (m, 2H), 7.39 – 7.35 (m, 2H), 7.23 – 7.19 (m, 3H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.64 (s, 3H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-*d*$_6$) δ 158.4, 157.0, 155.5, 142.2, 140.2, 138.9, 134.2, 132.7, 131.0 (2C), 130.5, 130.1, 129.6, 127.9, 127.4, 126.8, 123.0, 121.3, 118.1, 116.0, 115.8, 115.3 (2C), 102.4, 30.0; **HRMS** (ESI, m/z) calcd for $C_{25}H_{19}N_2O_2^+$ $[M+H]^+$: 379.1441, found: 379.1456.

(*E*)-4-[2-(4'-Hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (IIo)



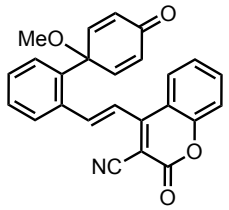
The reaction was performed at 0.97 mmol scale. Viscous orange oil; **Yield**: 370 mg, 97%; $\mathbf{R_f}$: 0.31 (hexane : ethyl acetate : 7 : 3); **^{1}H NMR** (500 MHz, DMSO-*d*$_6$) δ 8.14 – 8.12 (m, 1H), 8.00 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.95 – 7.93 (m, 1H), 7.77 – 7.74 (m, 1H), 7.65 – 7.58 (m, 2H), 7.54 (s, 1H), 7.51 – 7.44 (m, 3H), 7.42 – 7.39 (m, 1H), 6.92 (s, 2H), 2.20 (s, 6H); **^{13}C{^{1}H} NMR** (125 MHz, DMSO-*d*$_6$) δ 167.4, 159.4, 157.5, 153.0 (2C), 143.3, 141.1, 135.1, 132.8,

132.1, 130.7, 130.3, 130.1, 129.6, 129.3, 128.6, 127.4, 127.3, 125.1, 124.3, 119.6, 117.3, 115.0, 97.5, 16.7 (2C); **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_3^+$ $[M+H]^+$: 394.1438, found: 394.1436.

S4.5. General procedure for the synthesis of 2,5-cyclohexadienone substrates 1a-r:

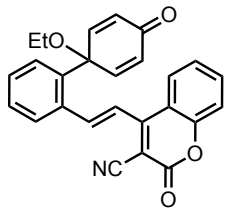
To a solution of hydroxy-biphenyl-2-oxo-2*H*-chromene-3-carbonitrile derivative or corresponding dihydroquinoline-3-carbonitrile (1.0 eq.) in the alcohol/acid (8.0 mL/mmol) was added $PhI(OAc)_2$ (1.5 eq.) at 0 ˚C. The mixture was stirred at room temperature until complete consumption of starting material (monitored by TLC). Then the solvent was removed under reduced pressure, and the residue was directly purified by column chromatography (silica gel, chloroform : ethyl acetate : = 19 : 1) to afford **1a-r**. *[Please note that for the substrates **1j,** and **1h** extra signal have been observed in ^1H and ^{13}C NMR spectra possibly due to the rotamers]*.

(*E*)-4-[2-(1'-Methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1a)



The reaction was performed at 1.54 mmol scale. Pale yellow solid; **m.p.**: 185 – 186 °C; **Yield**: 435 mg, 71%; $\mathbf{R_f}$: 0.34 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.97 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.82 – 8.00 (m, 1H, Ar*H*), 7.76 – 7.73 (m, 1H, Ar*H*), 7.48 – 7.39 (m, 5H, Ar*H*), 7.21 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.04 – 7.01 (m, 2H, –C*H*=CHC(O)), 6.47 – 6.44 (m, 2H, –CH=C*H*C(O)), 3.42 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.1, 158.8, 157.6, 153.8, 148.6 (2C), 143.8, 137.8, 135.3, 135.0, 130.8 (2C), 130.7, 129.6, 129.4, 127.2, 126.8, 125.5, 120.1, 118.2, 117.4, 114.4, 98.4, 77.6, 52.7; **HRMS** (ESI, m/z) calcd for $C_{25}H_{18}NO_4^+$ $[M+H]^+$: 396.1230, found: 396.1248.

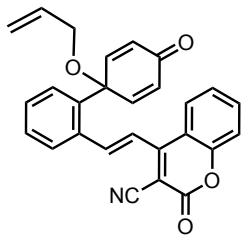
(*E*)-4-[2-(1'-Ethoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1b)



The reaction was performed at 2.00 mmol scale. Yellow solid; **m.p.**: 116 – 117 °C; **Yield**: 254 mg, 31%; $\mathbf{R_f}$: 0.45 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.80 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.94 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.80 – 7.72 (m, 2H, Ar*H*), 7.52 –

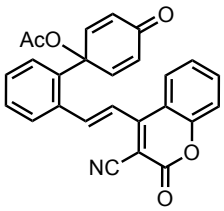
7.40 (m, 5H, Ar*H*), 7.18 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.07 – 7.05 (m, 2H, –C*H*=CHC(O)), 6.43 – 6.41 (m, 2H, –CH=C*H*C(O)), 3.60 – 3.56 (m, 2H, –OC*H*$_2$CH$_3$), 1.18 – 1.554 (m, 3H, –OCH$_2$C*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.2, 158.7, 157.6, 153.8, 149.1 (2C), 144.2, 138.0, 135.3 (2C), 130.7, 130.4 (2C), 129.5, 129.5, 127.1, 126.8, 125.5, 120.2, 118.2, 117.3, 114.5, 98.2, 77.2, 60.7, 15.9; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_4^+$ $[M+H]^+$: 410.1387, found: 410.1408.

(*E*)-4-[2-(1'-(Allyloxy)-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1c)



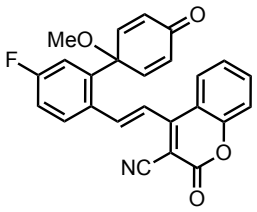
The reaction was performed at 1.64 mmol scale. Light yellow solid; **m.p.**: 170 – 171 °C; **Yield**: 256 mg, 37%; **R$_f$**: 0.41 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.92 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.80 – 7.78 (m, 1H, Ar*H*), 7.75 – 7.72 (m, 1H, Ar*H*), 7.50 – 7.39 (m, 5H, Ar*H*), 7.18 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.09 – 7.05 (m, 2H, –C*H*=CHC(O)), 6.45 – 6.41 (m, 2H, –CH=C*H*C(O)), 5.88 – 5.80 (m, 1H, –OCH$_2$C*H*=CH$_2$), 5.23 – 5.19 (m, 1H, –OCH$_2$CH=C*H*$_2$), 5.04 – 5.01 (m, 1H, –OCH$_2$CH=C*H*$_2$), 4.07 – 4.05 (m, 2H, –OC*H*$_2$CH=CH$_2$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.0, 158.8, 157.5, 153.8, 148.7 (2C), 144.1, 137.7, 135.2, 135.2, 134.1, 130.7, 130.5 (2C), 129.6, 129.5, 127.1, 126.8, 125.5, 120.2, 118.1, 117.7, 117.3, 114.5, 98.3, 77.3, 66.0; **HRMS** (ESI, m/z) calcd for $C_{27}H_{20}NO_4^+$ $[M+H]^+$: 422.1387, found: 422.1393.

(*E*)-2'-[2-(3-Cyano-2-oxo-2H-chromen-4-yl)vinyl]-4-oxo-[1,1'-biphenyl]-1(4*H*)-yl acetate (1d)



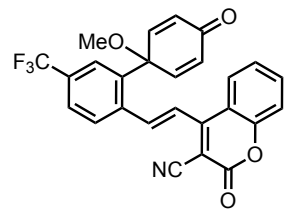
The reaction was performed at 2.00 mmol scale. Light yellow solid; **m.p.**: 163 – 164 °C; **Yield**: 268 mg, 32%; **R$_f$**: 0.16 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.89 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.77 – 7.74 (m, 2H, Ar*H*), 7.52 – 7.42 (m, 5H, Ar*H*), 7.30 – 7.27 (m, 2H, –C*H*=CHC(O)), 7.21 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 6.39 – 6.36 (m, 2H, –CH=C*H*C(O)), 2.04 (s, 3H, C*H*$_3$C(O)); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 184.9, 168.9, 157.7, 157.4, 153.8, 145.5 (2C), 142.9, 136.3, 135.5, 134.7, 131.0, 130.0, 129.9, 129.2 (2C), 126.6, 126.3, 125.7, 121.5, 118.3, 117.3, 114.5, 98.3, 78.0, 21.8.; **HRMS** (ESI, m/z) calcd for $C_{26}H_{21}N_2O_5^+$ $[M+NH^4]^+$: 441.1445, found: 441.1452.

(*E*)-4-[2-(5-Fluoro-1'-methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1e)



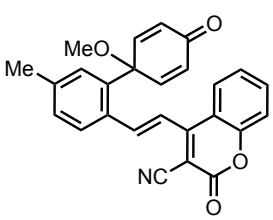
The reaction was performed at 1.64 mmol scale.Yellow solid; **m.p.**: 154 – 155 °C; **Yield**: 452 mg, 65%; $\mathbf{R_f}$: 0.34 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.92 – 7.90 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.80 – 7.72 (m, 2H, Ar*H*), 7.46 – 7.41 (m, 2H, Ar*H*), 7.28 – 7.26 (m, 1H, Ar*H*), 7.19 – 7.15 (m, 1H, Ar*H*), 7.13 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 6.96 – 6.93 (m, 2H, –C*H*=CHC(O)), 6.49 – 6.45 (m, 2H, –CH=C*H*C(O)), 3.40 (s, 3H, –OCH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 184.7, 158.6, 157.4, 153.9, 147.8 (2C), 142.3, 140.3, 135.3, 131.3 (3C), 131.0, 126.7, 125.5, 120.2, 118.2, 117.3, 116.5, 114.7, 114.4, 98.5, 77.4, 76.8, 52.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –107.83; **HRMS** (ESI, m/z) calcd for $C_{25}H_{17}FNO_4^+$ $[M+H]^+$: 414.1136, found: 414.1138.

(*E*)-4-[2-(1'-Methoxy-4'-oxo-5-(trifluoromethyl)-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1f)



The reaction was performed at 4.00 mmol scale. Light yellow solid; **m.p.**: 176 – 177 °C; **Yield**: 1300 mg, 70%; $\mathbf{R_f}$: 0.34 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.90 – 7.86 (m, 2H, Ar*H*), 7.82 (s, 1H, Ar*H*), 7.78 – 7.71 (m, 2H, Ar*H*), 7.47 – 7.42 (m, 2H, Ar*H*), 7.20 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 6.95 – 6.92 (m, 2H, –C*H*=CHC(O)), 6.51 – 6.48 (m, 2H, –CH=C*H*C(O)), 3.41 (s, 3H, –OCH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 184.6, 158.2, 157.2, 153.9, 147.6 (2C), 141.8, 138.7, 138.3, 135.6, 132.2, 131.6 (2C), 130.0, 126.6, 126.2, 125.6, 124.1, 123.6, 122.4, 118.3, 117.1, 114.1, 99.1, 76.7, 52.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –62.73. **HRMS** (ESI, m/z) calcd for $C_{26}H_{17}F_3NO_4^+$ $[M+H]^+$: 464.1104, found: 464.1114.

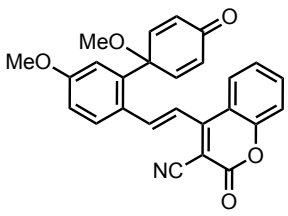
(*E*)-4-[2-(1'-Methoxy-5-methyl-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1g)



The reaction was performed at 4.00 mmol scale. Pale yellow solid; **m.p.**: 198 – 199 °C; **Yield**: 982 mg, 60%; $\mathbf{R_f}$: 0.31 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.98 – 7.96 (m, 1H, Ar*H*), 7.75 – 7.71 (m, 2H, Ar*H*), 7.45 – 7.41 (m, 2H, Ar*H*), 7.28 – 7.25 (m, 2H, Ar*H*), 7.20 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.04 – 7.00 (m, 2H, –C*H*=CHC(O)), 6.46 – 6.43 (m, 2H, –CH=C*H*C(O)), 3.41 (s, 3H, –OCH_3), 2.38 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.1, 158.8,

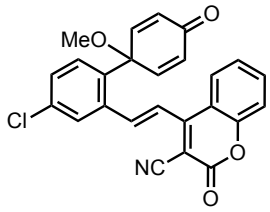
157.6, 153.8, 148.7 (2C), 143.7, 141.3, 137.7, 135.2, 132.1, 130.7 (2C), 130.2, 129.3, 127.9, 126.8, 125.4, 119.1, 118.1, 117.4, 114.5, 98.0, 77.6, 52.6, 21.6; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_4^+$ $[M+H]^+$: 410.1387, found: 410.1403.

(*E*)-4-[2-(1',5-Dimethoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1h)



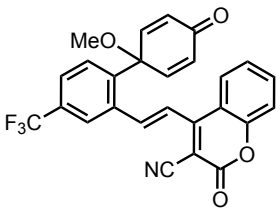
The reaction was performed at 2.78 mmol scale. Yellow solid; **m.p.**: 157 – 158 °C; **Yield**: 433 mg, 36%; $\mathbf{R_f}$: 0.28 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$)$_{major\ rotamer}$ δ 8.67 (*d*, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.96 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.82 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.74 – 7.70 (m, 1H, Ar*H*), 7.45 – 7.37 (m, 3H, Ar*H*), 7.14 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.02 – 7.00 (m, 1H, Ar*H,* 2H, –C*H*=CHC=O), 6.48 – 6.44 (m, 2H, –CH=C*H*C=O), 3.85 (s, 3H, ArOCH_3), 3.40 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$)$_{rotamers}$ δ 185.4, 185.0, 161.5, 160.7, 158.8, 157.8, 153.9, 148.7, 148.4 (2C), 143.3, 139.8, 138.3, 135.2, 135.1, 132.0, 131.0, 130.9 (2C), 130.9, 127.8, 127.3, 126.8, 125.3, 118.2, 117.9, 118.0, 117.5, 114.7, 114.1, 113.9, 113.7, 113.4, 55.7, 55.5, 52.6, 52.0; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_5^+$ $[M+H]^+$: 426.1336, found: 426.1343.

(*E*)-4-[2-(4-Chloro-1'-methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1i)



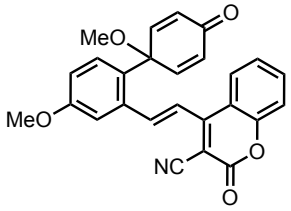
The reaction was performed at 5.00 mmol scale. White solid; **m.p.**: 185 – 186 °C; **Yield**: 1500 mg, 70%; $\mathbf{R_f}$: 0.37 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.92 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.77 – 7.74 (m, 2H, Ar*H*), 7.47 – 7.43 (m, 3H, Ar*H*), 7.37 (dd, *J* = 8.5, 2.0 Hz, 1H, Ar*H*), 7.18 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.00 – 6.95 (m, 2H, –C*H*=CHC(O)), 6.47 – 6.43 (m, 2H, –CH=C*H*C(O)), 3.39 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 158.3, 157.4, 153.8, 148.1 (2C), 142.0, 136.7, 136.3, 135.5, 135.4, 135.0, 131.1 (2C), 130.3, 129.1, 128.7, 126.7, 125.6, 121.1, 118.2, 117.3, 114.3, 98.8, 77.1, 52.6; **HRMS** (ESI, m/z) calcd for $C_{25}H_{17}ClNO_4^+$ $[M+H]^+$: 430.0841, found: 430.0838.

(*E*)-4-[2-(1'-Methoxy-4'-oxo-4-(trifluoromethyl)-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1j)



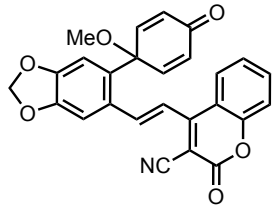
The reaction was performed at 3.00 mmol scale. Yellow solid; **m.p.**: 106 – 107 °C; **Yield**: 802 mg, 58%; $\mathbf{R_f}$: 0.42 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) *major rotamer* δ 8.61 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.98 (s, 1H, Ar*H*), 7.90 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.76 – 7.73 (m, 2H, Ar*H*), 7.67 – 7.66 (m, 1H, Ar*H*), 7.48 – 7.43 (m, 2H, Ar*H*), 7.21 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 6.98 – 6.95 (m, 2H, –C*H*=CHC(O)), 6.50 – 6.47 (m, 2H, –CH=C*H*C(O)), 3.40 (s, 3H, –OCH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$)*rotamers* δ 193.8, 184.6, 158.4, 158.2, 157.3, 157.1, 153.8, 153.7, 147.7, 142.6, 141.9, 141.4, 139.6, 138.5, 136.2, 135.9, 135.6, 135.5, 135.5, 133.5, 131.8, 131.5, 130.4, 128.0, 127.2, 126.9, 126.8, 126.6, 126.4, 126.0, 125.6, 124.4, 123.6, 123.0, 122.8, 121.6, 118.2, 118.2, 117.2, 117.1, 114.3, 114.0, 98.9, 91.3, 52.6, 50.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –62.73; **HRMS** (ESI, m/z) calcd for $C_{26}H_{17}F_3NO_4^+$ $[M+H]^+$: 464.1104, found: 464.1097.

(*E*)-4-[2-(1',4-Dimethoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1k)



The reaction was performed at 3.5 mmol scale. Light yellow solid; **m.p.**: 160 – 161 °C; **Yield**: 1200 mg, 81%; $\mathbf{R_f}$: 0.28 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.96 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.76 – 7.72 (m, 1H, Ar*H*), 7.46 – 7.41 (m, 2H, Ar*H*), 7.38 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.30 (d, *J* = 3.0 Hz, 1H, Ar*H*), 7.19 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.02 – 6.99 (m, 2H, –C*H*=CHC(O)), 6.91 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar*H*), 6.43 – 6.40 (m, 2H, –CH=C*H*C(O)), 3.88 (s, 3H, ArOCH_3), 3.39 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 160.1, 158.7, 157.5, 153.8, 149.0, 148.9 (2C), 143.5, 136.5, 135.3, 130.4 (2C), 129.9, 128.6, 126.8, 125.5, 120.3, 118.2, 117.3, 115.2, 115.1, 114.4, 98.4, 77.2, 55.7, 52.6; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_5^+$ $[M+H]^+$: 426.1336, found: 426.1351.

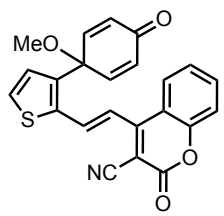
(*E*)-4-[2-(6-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)benzo[d][1,3]dioxol-5-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1l)



The reaction was performed at 2.00 mmol scale. Yellow solid; **m.p.**: 201 – 201 °C; **Yield**: 450 mg, 51%; $\mathbf{R_f}$: 0.50 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.92 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.74 – 7.71 (m, 1H, Ar*H*), 7.45 – 7.40 (m, 2H, Ar*H*), 7.29 (s, 1H, Ar*H*), 7.12 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 6.98 (s, 1H, Ar*H*), 6.98 – 6.96 (m, 2H, –C*H*=CHC(O)), 6.44 – 6.41 (m, 2H, –CH=C*H*C(O)),

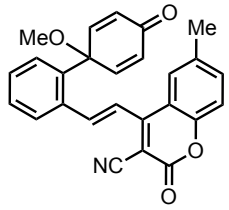
6.06 (s, 2H, –OC*H*$_2$O–), 3.38 (s, 3H, –OC*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 184.8, 158.5, 157.6, 153.7, 149.8, 148.6, 148.4 (2 C), 142.8, 135.0, 133.0, 130.6 (2C), 129.0, 126.5, 125.3, 118.2, 118.1, 117.3, 114.5, 108.0, 107.5, 102.3, 97.6, 77.2, 52.4; **HRMS** (ESI, m/z) calcd for $C_{26}H_{18}NO_6^+$ $[M+H]^+$: 440.1129, found: 440.1129.

(*E*)-4-[2-(3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)thiophen-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1m)



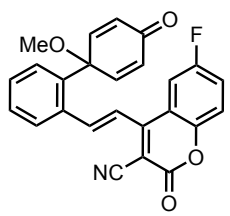
The reaction was performed at 4.00 mmol scale. Yellow solid; **m.p.**: 186 – 187 °C; **Yield**: 1108 mg, 69%; **R$_f$**: 0.31 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 16.5, 1.0 Hz, 1H, ArC*H*=CH–), 7.91 – 7.89 (m, 1H, Ar*H*), 7.74 – 7.71 (m, 1H, Ar*H*), 7.46 – 7.42 (m, 2H, Ar*H*), 7.38 – 7.37 (m, 1H, Ar*H*), 7.16 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.00 – 6.97 (m, 2H, –C*H*=CHC(O)), 6.90 (d, *J* = 5.0 Hz, 1H, Ar*H*), 6.45 – 6.42 (m, 2H, –CH=C*H*C(O)), 3.44 (s, 3H, –OC*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 184.9, 157.8, 157.7, 153.6, 148.8 (2C), 140.8, 138.2, 137.0, 135.2, 130.5 (2C), 128.5, 128.2, 126.3, 125.4, 118.1, 117.3 (2C), 114.8, 97.2, 76.6, 52.9; **HRMS** (ESI, m/z) calcd for $C_{23}H_{16}NO_4S^+$ $[M+H]^+$: 402.0795, found: 402.0801.

(*E*)-4-[2-(1'-Methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-6-methyl-2-oxo-2*H*-chromene-3-carbonitrile (1n)



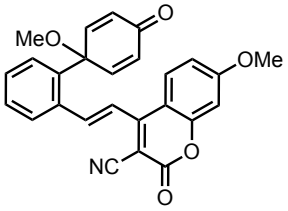
The reaction was performed at 4.74 mmol scale. Yellow solid; **m.p.**: 160 – 161 °C; **Yield**: 1480 mg, 76%; **R$_f$**: 0.34 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.83 – 7.82 (m, 1H, Ar*H*), 7.68 – 7.67 (m, 1H, Ar*H*), 7.55 – 7.53 (m, 1H, Ar*H*), 7.49 – 7.47 (m, 2H, Ar*H*), 7.42 – 7.39 (m, 1H, Ar*H*), 7.33 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.19 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 7.06 – 7.03 (m, 2H, –C*H*=CHC(O)), 6.46 – 6.43 (m, 2H, –CH=C*H*C(O)), 3.40 (s, 3H, –OC*H*$_3$), 2.47 (s, 3H, ArC*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.0, 158.6, 157.8, 151.9, 148.6 (2C), 143.3, 137.9, 136.4, 135.4, 135.1, 130.7 (2C), 130.6, 129.6, 129.3, 127.2, 126.3, 120.1, 117.8, 117.1, 114.7, 98.1, 77.5, 52.6, 21.2; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_4^+$ $[M+H]^+$: 410.1387, found: 410.1394.

(*E*)-6-Fluoro-4-[2-(1'-Methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1o)



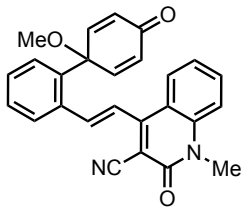
The reaction was performed at 1.09 mmol scale. Light yellow solid; **m.p.**: 152 – 153 °C; **Yield**: 260 mg, 58%; $\mathbf{R_f}$: 0.31 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.81 – 7.79 (m, 1H, Ar*H*), 7.68 – 7.66 (m, 1H, Ar*H*), 7.49 – 7.45 (m, 4H, Ar*H*), 7.43 – 7.40 (m, 1H, Ar*H*), 7.13 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.02 – 6.99 (m, 2H, –C*H*=CHC(O)), 6.47 – 6.44 (m, 2H, –CH=C*H*C(O)), 3.43 (s, 3H, –OCH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 185.0, 157.9, 157.1, 150.1, 148.6 (2C), 144.4, 137.8, 134.8, 130.9 (3C), 129.6, 129.6, 129.5, 127.3, 122.7, 119.9, 119.7, 118.1, 114.1, 112.5, 99.5, 77.7, 52.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –114.42; **HRMS** (ESI, m/z) calcd for $C_{25}H_{17}FNO_4^+$ $[M+H]^+$: 414.1136, found: 414.1140.

(*E*)-7-Methoxy-4-[2-(1'-methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1p)



The reaction was performed at 2.90 mmol scale. Yellow solid; **m.p.**: 190 – 191 °C; **Yield**: 1038 mg, 84%; $\mathbf{R_f}$: 0.22 (chloroform : ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 7.85 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.79 – 7.77 (m, 1H, Ar*H*), 7.47 – 7.44 (m, 2H, Ar*H*), 7.41 – 7.37 (m, 1H, Ar*H*), 7.14 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.03 – 7.00 (m, 2H, –C*H*=CHC(O)), 6.96 (dd, *J* = 9.5, 2.5 Hz, 1H, Ar*H*), 6.88 (d, *J* = 2.5 Hz, 1H, Ar*H*), 6.46 – 6.43 (m, 2H, –CH=C*H*C(O)), 3.95 (s, 3H, ArOCH_3), 3.41 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.1, 165.6, 158.7, 158.2, 156.3, 148.6 (2C), 143.3, 137.7, 135.2, 130.8 (2C), 130.5, 129.6, 129.5, 128.1, 127.1, 120.6, 114.9, 114.2, 110.9, 101.5, 94.8, 77.6, 56.3, 52.6; **HRMS** (ESI, m/z) calcd for $C_{26}H_{20}NO_5^+$ $[M+H]^+$: 426.1336, found: 426.1338.

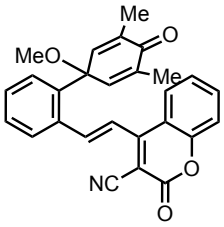
(*E*)-4-[2-(1'-Methoxy-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-1-methyl-2-oxo-1,2-dihydroquinoline-3-carbonitrile (1q)



The reaction was performed at 2.00 mmol scale. Pale yellow solid; **m.p.**: 122 – 123 °C; **Yield**: 596 mg, 73%; $\mathbf{R_f}$: 0.35 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 16.5 Hz, 1H, ArC*H*=CH–), 8.03 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.83 – 7.74 (m, 2H, Ar*H*), 7.48 – 7.44 (m, 3H, Ar*H*), 7.40 – 7.35 (m, 2H, Ar*H*), 7.21 (d, *J* = 16.5 Hz, 1H, ArCH=C*H*–), 7.05 (d, *J* = 10.0 Hz, 2H, –C*H*=CHC(O)), 6.43 (d, *J* = 10.0 Hz, 2H, –CH=C*H*C(O)), 3.80 (s, 3H, –NCH_3), 3.38 (s, 3H, –OCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 185.2, 159.1, 154.8, 148.8 (2C), 141.0, 140.8, 137.2, 135.7, 134.1, 130.7 (2C), 129.9, 129.5, 129.4, 127.8, 126.9,

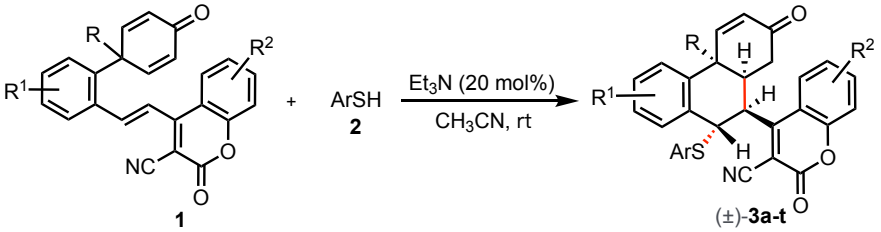
123.2, 122.0, 118.8, 115.7, 115.3, 104.2, 77.4, 52.5, 30.4; **HRMS** (ESI, m/z) calcd for $C_{26}H_{21}N_2O_3^+$ $[M+H]^+$: 409.1547, found: 409.1544.

(*E*)-4-[2-(1'-Methoxy-3',5'-dimethyl-4'-oxo-1',4'-dihydro-[1,1'-biphenyl]-2-yl)vinyl]-2-oxo-2*H*-chromene-3-carbonitrile (1r)



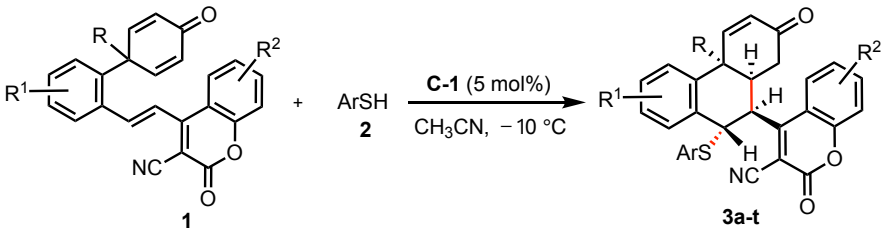
The reaction was performed at 0.98 mmol scale. Yellow solid; **m.p.**: 175 – 176 °C; **Yield**: 80 mg, 19%; $\mathbf{R_f}$: 0.75 (chloroform: ethyl acetate : 19 : 1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 16.0 Hz, 1H, ArC*H*=CH–), 7.97 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.79 – 7.77 (m, 1H, Ar*H*), 7.75 – 7.72 (m, 1H, Ar*H*), 7.49 – 7.39 (m, 5H, Ar*H*), 7.19 (d, *J* = 16.0 Hz, 1H, ArCH=C*H*–), 6.78 – 6.74 (m, 2H, –C*H*=CMeC(O)), 3.35 (s, 3H, –OCH_3), 1.95 (s, 6H, 2 × CH_3); **^{13}C{^{1}H}NMR** (125 MHz, $CDCl_3$) δ 186.6, 159.0, 153.9, 144.3, 144.3, 143.8 (2C), 139.2, 137.5, 135.2, 134.9, 130.6, 129.2, 129.2, 127.1, 126.9, 125.6, 125.4, 119.8, 118.2, 117.4, 114.4, 98.4, 77.6, 52.1, 16.1 (2C); **HRMS** (ESI, m/z) calcd for $C_{27}H_{21}KNO_4^+$ $[M+K]^+$: 462.1102, found: 462.1113.

S4.6. General procedure for the synthesis of racemic compounds via sulfa-1,6-addition/vinylogous 1,4-addition desymmetrization domino sequence:



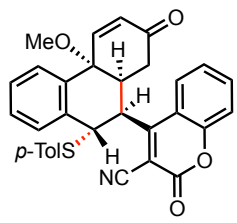
In a 10 mL reaction tube with a magnetic stirring bar, substrate **1** (0.05 mmol, 1.0 eq.) and Et_3N (20 mol, 1.4 uL) were stirred in CH_3CN (0.5 mL) at room temperature. After stirring for 5 minutes, thiol **2** (0.05 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 12-24 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 3 : 2 as eluent) to afford the product (±)-**3a-t**.

S4.7. General procedure for chiral squaramide catalyzed asymmetric sulfa-1,6-addition/vinylogous 1,4-addition desymmetrization domino sequence:

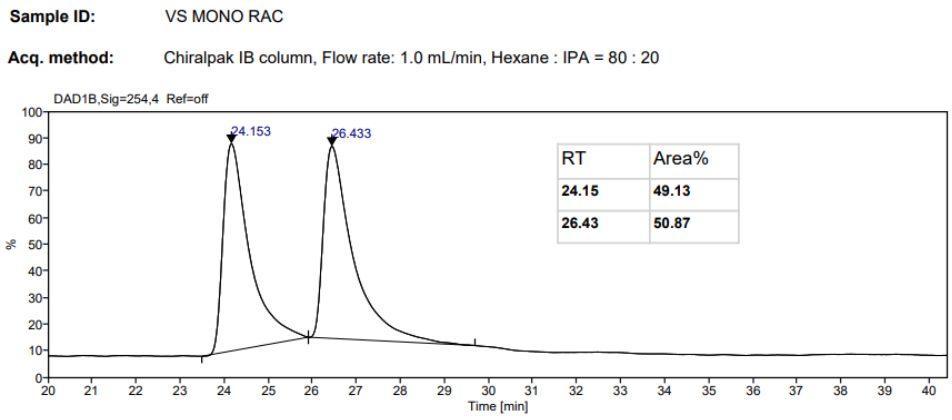


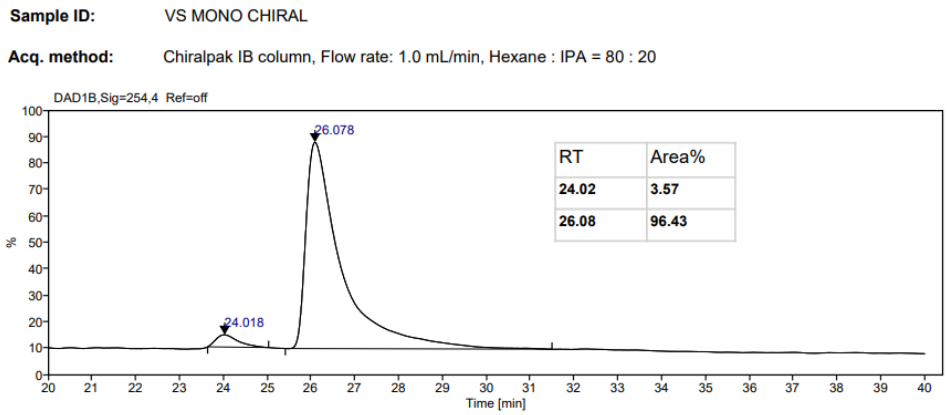
In a 10 mL reaction tube with a magnetic stirring bar, substrate **1** (0.1 mmol, 1.0 eq.) and **C-1** (5 mol%, 3.1 mg) were stirred in CH_3CN (1.0 mL) at −10 °C (maintained in a methanol bath). After stirring for 5 minutes, thiol **2** (0.1 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 6-24 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 3 : 2 as eluent) to afford the product **3a-t**.

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2H-chromene-3-carbonitrile (3a)



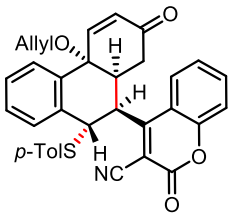
White solid; **m.p.**: 212 – 213 °C; **Yield**: 40 mg, 77%; **R_f**: 0.34 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30} = -64.8$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.85 – 7.83 (m, 1H, Ar*H*), 7.72 – 7.69 (m, 1H, Ar*H*), 7.56 – 7.51 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.42 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.38 – 7.32 (m, 2H, Ar*H*), 7.23 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.89 – 6.87 (m, 2H, Ar*H*), 6.80 – 6.78 (m, 2H, Ar*H*), 6.00 (dd, *J* = 10.0, 1.0 Hz, 1H, –CH=C*H*C(O)), 5.93 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.95 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 3.01 (s, 3H, –OCH_3), 2.73 – 2.68 (m, 1H, –C*H*CH_2–), 2.57 – 2.53 (m, 1H, –CHCH_2–), 2.40 – 2.34 (m, 1H, –CHCH_2–), 2.22 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 196.1, 162.6, 157.0, 153.6, 149.1, 139.8, 136.3, 136.3 (2C), 135.2, 132.1, 132.1, 130.2, 129.9, 129.6 (2C), 128.6, 127.4, 126.8, 125.7, 125.6, 118.2, 118.1, 114.8, 102.8, 75.9, 51.3, 47.1, 45.1, 40.8, 37.1, 21.2; **HRMS** (ESI, m/z) calcd for $C_{32}H_{29}N_2O_4S^+$ $[M+H]^+$: 537.1843, found: 537.1850.



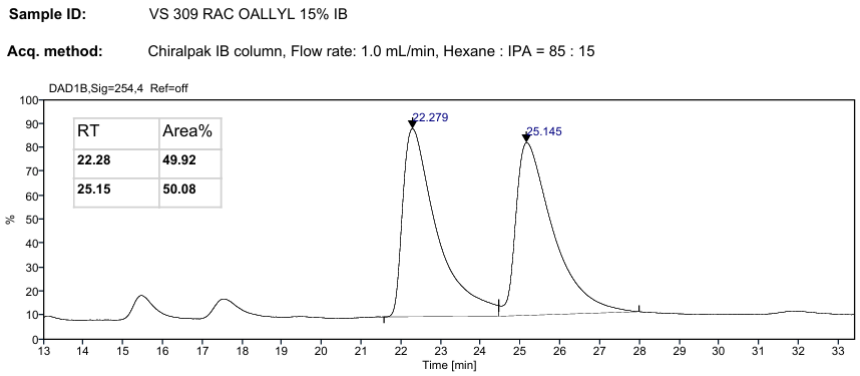


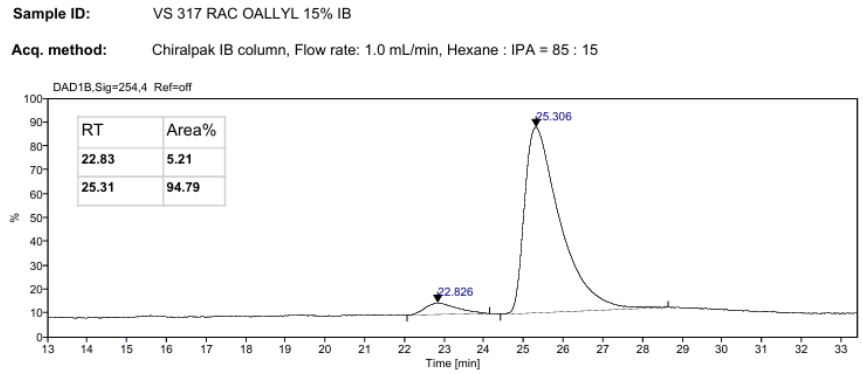
HPLC Data: 96.5 : 3.5 er; Daicel Chiralpak IB column, *n*-hexane : *i*-PrOH = 4: 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 24.02 min (minor), t_R = 26.08 min (major).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-(Allyloxy)-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3b)



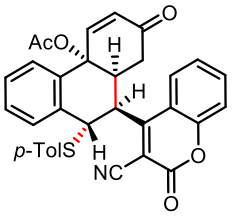
White solid; **m.p.**: 185 – 186 °C; **Yield**: 36 mg, 66%; **R**$_f$: 0.51 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –27.2 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.90 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.72 – 7.69 (m, 1H, Ar*H*), 7.57 – 7.54 (m, 1H, Ar*H*), 7.50 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.43 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.37 – 7.34 (m, 1H, Ar*H*), 7.31 – 7.26 (m, 2H, Ar*H*), 6.82 – 6.81 (m, 2H, Ar*H*), 6.76 – 6.74 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.99 – 5.97 (m, 1H, –CH=C*H*C(O)), 5.90 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 5.68 – 5.60 (m, 1H, –OCH$_2$C*H*=CH$_2$), 5.20 – 5.15 (m, 2H, –OCH$_2$CH=C*H*$_2$), 4.89 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.00 – 3.96 (m, 1H, –OC*H*$_2$CH=CH$_2$), 3.30 – 3.26 (m, 1H, –OC*H*$_2$CH=CH$_2$), 2.80 – 2.75 (m, 1H, –C*H*CH$_2$–), 2.61 – 2.57 (m, 1H, –CHC*H*$_2$–), 2.42 – 2.36 (m, 1H, –CHC*H*$_2$–), 2.20 (s, 3H, ArC*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.0, 162.4, 157.1, 153.6, 149.6, 139.9, 136.4, 136.3 (2C), 135.2, 134.2, 132.5, 132.1, 130.1, 129.8, 129.7 (2C), 128.4, 127.6, 126.2, 126.0, 125.4, 118.1, 118.0, 116.3, 114.8, 103.0, 76.0, 64.9, 47.0, 44.9, 40.6, 36.9, 21.2; **HRMS** (ESI, m/z) calcd for $C_{34}H_{31}N_2O_4S^+$ $[M+NH_4]^+$: 563.1999, found: 563.2010.



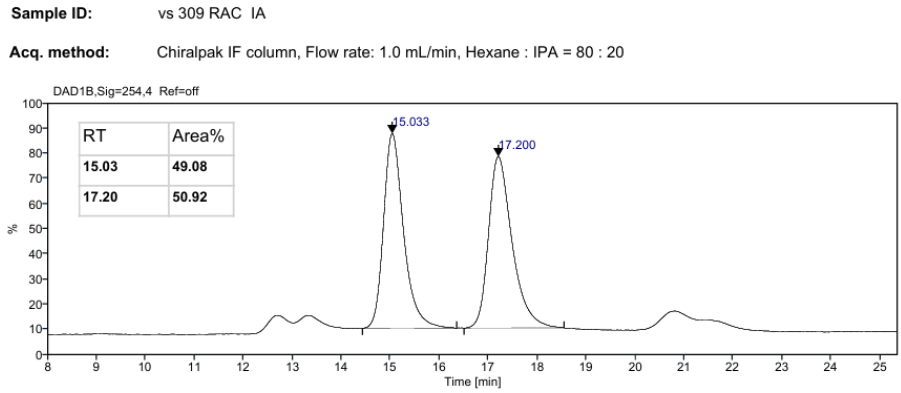


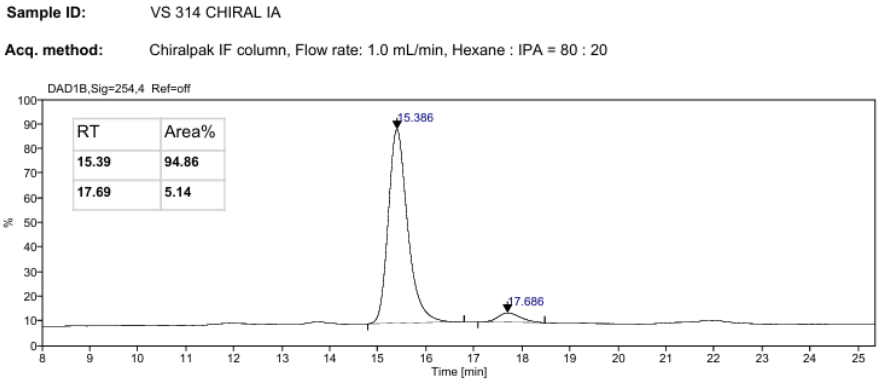
HPLC Data: 95.0 : 5.0 er; Daicel Chiralpak IB column, *n*-hexane : *i*-PrOH = 17 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 22.83 min (minor), t_R = 25.31 min (major).

[(4a*R*,9*S*,10*S*,10a*S*)-10-(3-Cyano-2-oxo-2H-chromen-4-yl)-2-oxo-9-(*p*-tolylthio)-1,9,10,10a-tetrahydrophenanthren-4a(2*H*)]-yl acetate (3c)



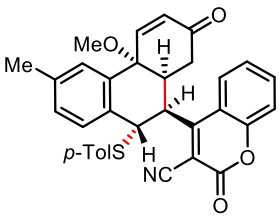
White solid; **m.p.**: 175 – 176 °C; **Yield**: 42 mg, 77%; **R**$_f$: 0.34 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –7.2 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.90 (d, *J* = 10.5 Hz, 1H, Ar*H*), 7.74 – 7.71 (m, 1H, Ar*H*), 7.60 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.56 – 7.53 (m, 1H, –C*H*=CHC(O), 1H, Ar*H*), 7.45 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.39 – 7.35 (m, 1H, Ar*H*), 7.31 – 7.28 (m, 1H, Ar*H*), 6.87 – 6.84 (m, 2H, Ar*H*), 6.81 – 6.79 (m, 2H, Ar*H*), 6.05 (dd, *J* = 10.5, 1.0 Hz, 1H, –CH=C*H*C(O)), 5.93 (d, *J* = 11.0 Hz, 1H, –C*H*SAr), 4.75 (dd, *J* = 11.0, 3.0 Hz, 1H, –C*H*CHSAr), 3.13 – 3.09 (m, 1H, –C*H*CH_2–), 2.60 – 2.56 (m, 1H, –CHCH_2–), 2.44 – 2.38 (m, 1H, –CHCH_2–), 2.21 (s, 3H, ArCH_3), 1.92 (m, 3H, –OC(O)CH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 194.9, 169.3, 161.4, 156.8, 153.6, 149.8, 139.9, 136.1 (2C), 135.5, 132.1, 131.5, 131.5, 130.3, 130.0, 129.7 (2C), 129.2, 127.8, 127.0, 125.2, 124.6, 118.6, 117.8, 114.6, 103.3, 80.0, 45.2, 45.0, 40.9, 37.2, 21.9, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{29}N_2O_5S^+$ $[M+NH_4]^+$: 565.1792, found: 565.1809.



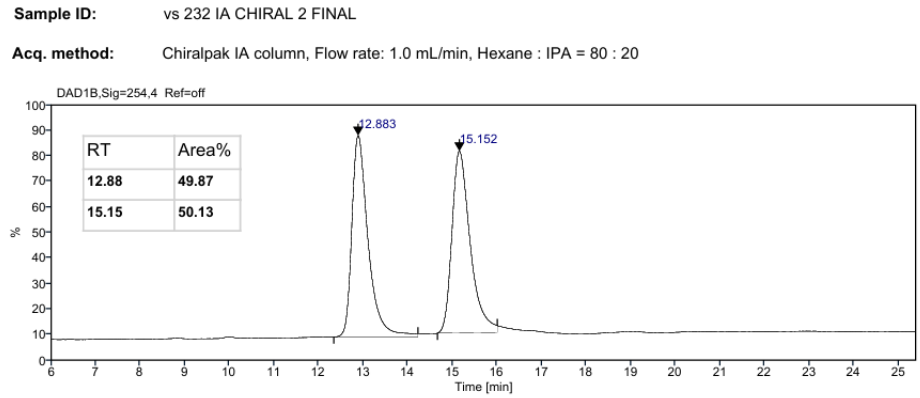


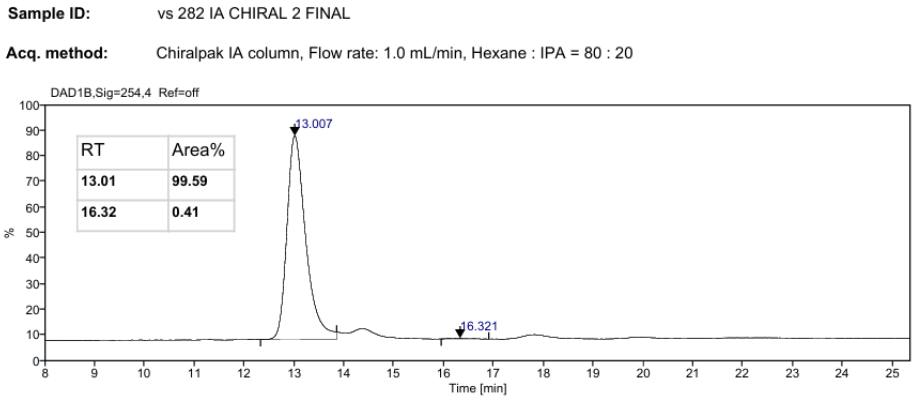
HPLC Data: 95.0 : 5.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 15.39 min (major), t_R = 17.69 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-3-methyl-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3d)



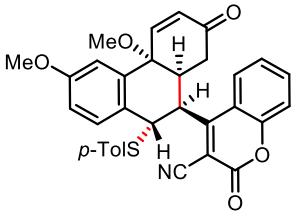
Yellow solid; **m.p.**: 220 – 221 °C; **Yield**: 26 mg, 49%; **R$_f$**: 0.40 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = 32.8 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.76 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.64 – 7.61 (m, 1H, Ar*H*), 7.44 (d, *J* = 10.0 Hz, 1H, –C*H*=CHC(O)), 7.34 – 7.33 (m, 1H, Ar*H*), 7.30 – 7.26 (m, 2H, Ar*H*), 6.94 (s, 1H, Ar*H*), 6.83 – 6.81 (m, 2H, Ar*H*), 6.72 – 6.71 (m, 2H, Ar*H*), 5.93 (d, *J* = 10.0 Hz, 1H, –CH=C*H*C(O)), 5.81 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.86 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 2.96 (s, 3H, –OCH_3), 2.63 – 2.59 (m, 1H, –C*H*CH_2–), 2.46 (dd, *J* = 16.5, 3.0 Hz, 1H, –CHCH_2–), 2.36 – 2.27 (m, 1H, –CHCH_2–, 3H, ArCH_3), 2.15 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 196.2, 162.7, 157.0, 153.6, 149.4, 139.7, 137.2, 136.2 (2C), 135.1, 133.1, 131.9, 131.8, 130.8, 130.6, 129.6 (2C), 129.1, 128.5, 127.0, 125.7, 125.6, 118.1, 114.8, 102.8, 76.0, 51.4, 47.2, 45.0, 40.9, 37.2, 21.4, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_4S^+$ $[M+NH_4]^+$: 551.1999, found: 551.2002.



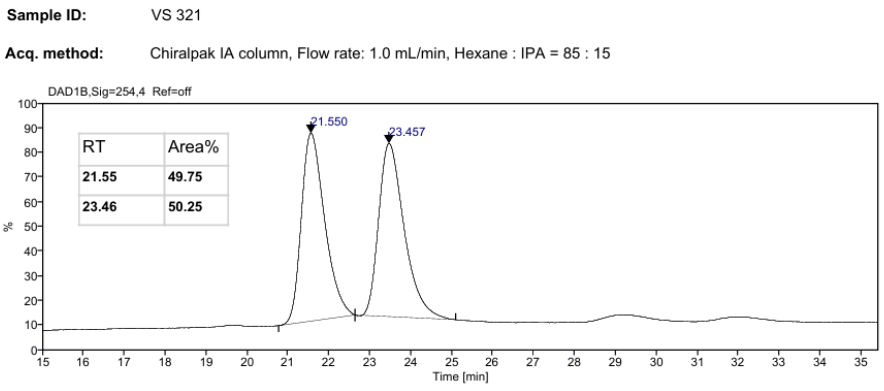


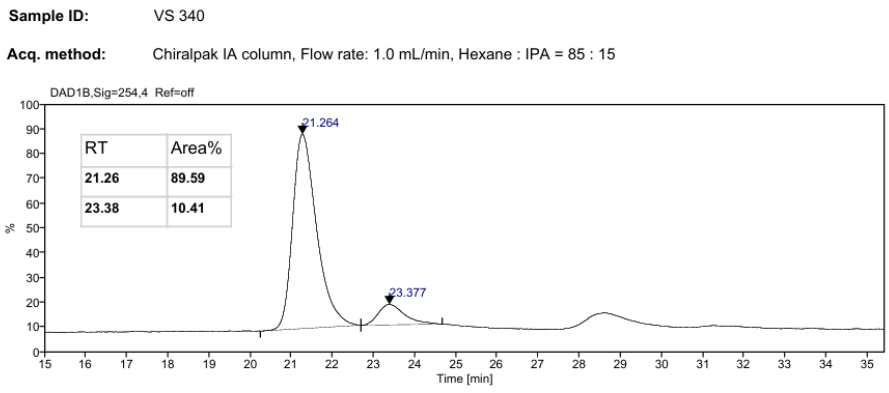
HPLC Data: >99.5 : 0.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 13.01 min (major), t_R = 16.32 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-3,4b-Dimethoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3e)



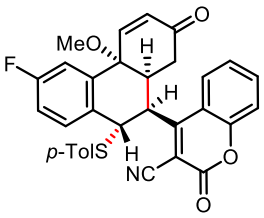
Yellow solid; **m.p.**: 175 – 176 °C; **Yield**: 37 mg, 67%; **R**$_f$: 0.30 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = 8.0 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.08 – 8.06 (m, 1H, Ar*H*), 7.83 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.71 – 7.68 (m, 1H, Ar*H*), 7.46 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.40 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.37 – 7.34 (m, 1H, Ar*H*), 7.09 (dd, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 6.91– 6.90 (m, 2H, Ar*H*), 6.80 – 6.79 (m, 2H, Ar*H*), 6.71 (d, *J* = 2.5 Hz, 1H, Ar*H*), 6.01 – 5.99 (m, 1H, –CH=C*H*C(O)), 5.88 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.93 (dd, *J* = 11.0, 3.5 Hz, 1H, –C*H*CHSAr), 3.87 (s, 3H, ArOCH_3), 3.04 (s, 3H, –OCH_3), 2.70 – 2.66 (m, 1H, –C*H*CH$_2$–), 2.55 – 2.51 (m, 1H, –CHCH_2–), 2.41 – 2.35 (m, 1H, –CHCH_2–), 2.22 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 196.1, 162.6, 158.3, 157.0, 153.5, 148.9, 139.8, 139.7, 136.2 (2C), 135.1, 133.3, 129.5 (2C), 128.7, 127.9, 127.0, 125.6, 125.6, 118.1 (2C), 116.1, 115.0, 114.8, 102.8, 75.9, 55.6, 51.4, 47.2, 44.8, 41.0, 37.2, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_5S^+$ $[M+NH_4]^+$: 567.1948, found: 567.1961.



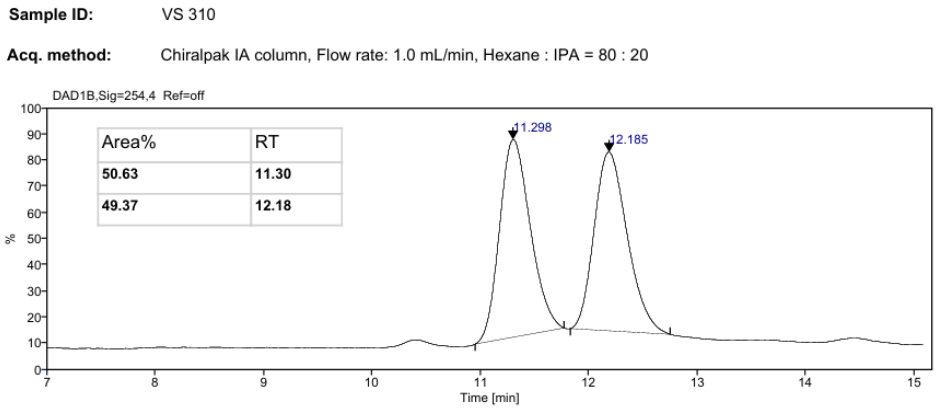


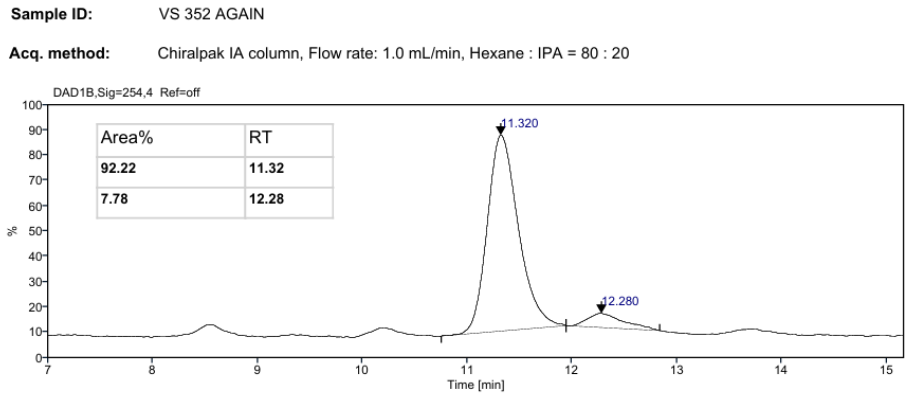
HPLC Data: 89.5 : 10.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 17 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 21.26 min (major), t_R = 23.38 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-3-Fluoro-4b-methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3f)



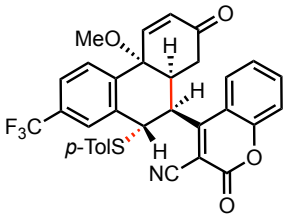
Yellow solid; **m.p.**: 163 – 164 °C; **Yield**: 34 mg, 63%; **R$_f$**: 0.40 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –26.4 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 – 8.15 (m, 1H, Ar*H*), 7.82 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.73 – 7.70 (m, 1H, Ar*H*), 7.45 – 7.42 (m, 1H, –C*H*=CHC(O), 1H, Ar*H*), 7.38 – 7.35 (m, 1H, Ar*H*), 7.28 – 7.24 (m, 1H, Ar*H*), 6.93 (dd, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 6.89 – 6.87 (m, 2H, Ar*H*), 6.82 – 6.81 (m, 2H, Ar*H*), 6.03 (d, *J* = 10.5 Hz, 1H, –CH=C*H*C(O)), 5.88 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.93 (dd, *J* = 11.5, 3.5 Hz, 1H, –C*H*CHSAr), 3.03 (s, 3H, –OCH_3), 2.74 – 2.70 (m, 1H, –C*H*CH_2–), 2.56 (dd, *J* = 16.5, 3.5 Hz, 1H, –CHCH_2–), 2.38 – 2.32 (m, 1H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 195.7, 162.3, 156.9, 153.6, 148.0, 140.0, 136.3 (2C), 135.3, 134.2, 134.0, 132.1, 129.7 (2C), 129.2, 126.5, 125.7, 125.6, 118.2, 118.0, 117.4, 116.6, 114.8, 102.9, 75.6, 51.4, 46.8, 44.6, 40.7, 37.0, 21.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –112.85; **HRMS** (ESI, m/z) calcd for $C_{32}H_{28}FN_2O_4S^+$ $[M+NH_4]^+$: 555.1748, found: 555.1739.



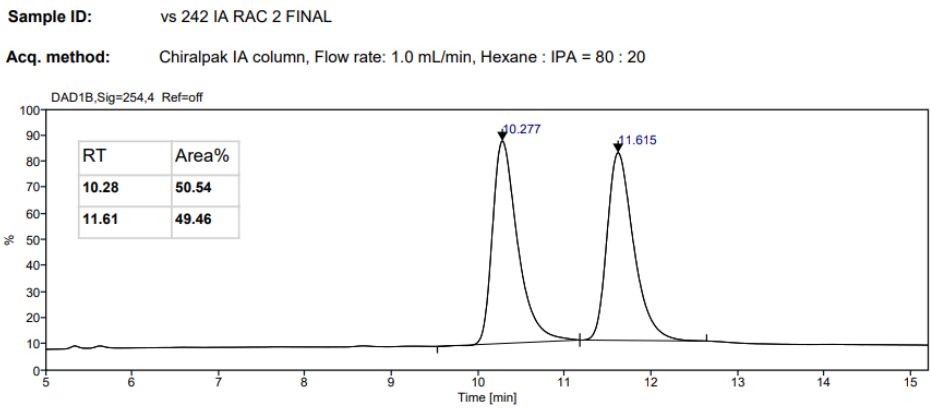


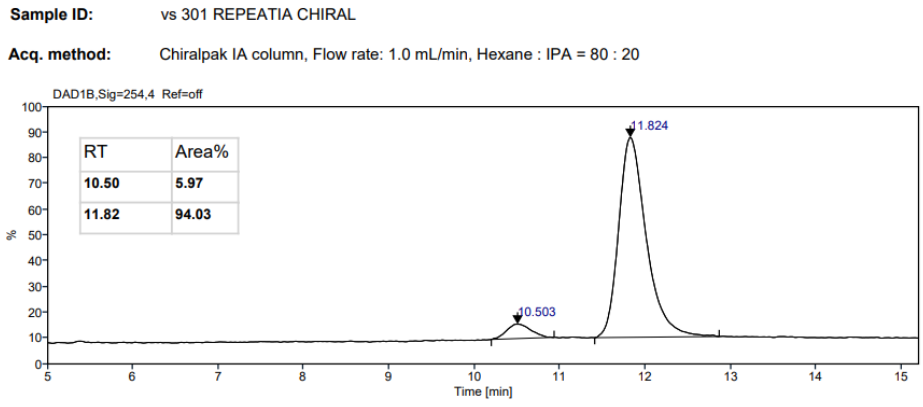
HPLC Data: 92.0 : 8.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 11.32 min (major), t_R = 12.28 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(*p*-tolylthio)-2-(trifluoromethyl)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3g)



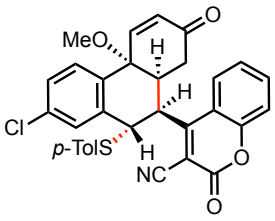
Yellow solid; **m.p.**: 115 – 116 °C; **Yield**: 45 mg, 77%; **R$_f$**: 0.26 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –29.60 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.45 – 8.44 (m, 1H, Ar*H*), 7.85 – 7.83 (m, 1H, Ar*H*), 7.75 – 7.72 (m, 1H, Ar*H*), 7.60 – 7.58 (m, 1H, Ar*H*), 7.50 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.44 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.40 – 7.37 (m, 2H, Ar*H*), 6.88 – 6.82 (m, 4H, Ar*H*), 6.05 (dd, *J*= 10.5, 1.0 Hz, 1H, –CH=C*H*C(O)), 5.93 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.98 – 4.95 (m, 1H, –C*H*CHSAr), 3.00 (s, 3H, –OCH_3), 2.79 – 2.74 (m, 1H, –C*H*CH_2–), 2.60 – 2.56 (m, 1H, –CHCH_2–), 2.36 – 2.30 (m, 1H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H}{^{19}F} NMR** (125 MHz, $CDCl_3$) δ 195.4, 161.9, 156.9, 153.7, 147.9, 140.3, 137.7, 136.4 (2C), 136.0, 135.4, 130.8, 129.8 (2C), 129.4, 129.1, 126.1, 125.8, 125.5, 124.0, 118.3, 118.0, 114.8, 102.9, 75.4, 51.4, 46.7, 44.8, 40.4, 36.9, 21.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –62.79. **HRMS** (ESI, m/z) calcd for $C_{33}H_{24}F_3KNO_4S^+$ $[M+K]^+$: 626.1010, found: 626.1019.



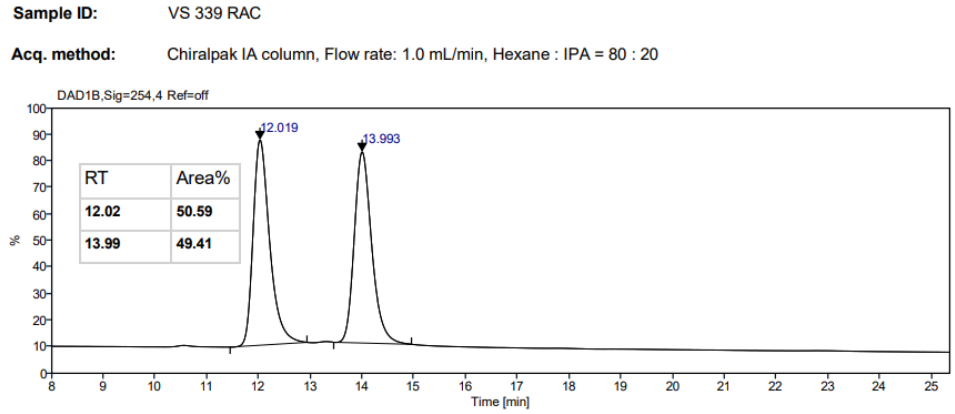


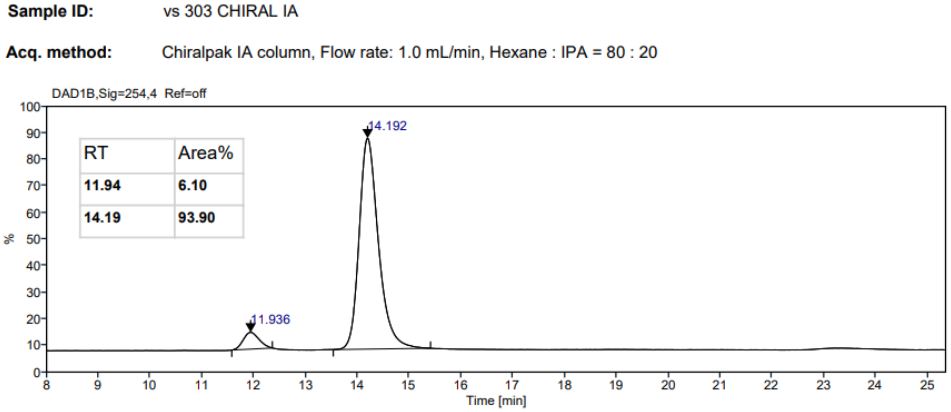
HPLC Data: 94.0 : 6.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 10.50 min (minor), t_R = 11.82 min (major).

4-[(4b*R*,8a*S*,9*S*,10*S*)-2-Chloro-4b-methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3h)



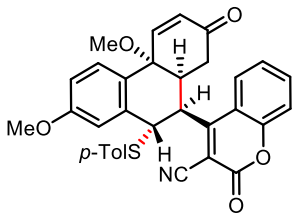
White solid; **m.p.**: 133 – 134 °C; **Yield**: 45 mg, 81%; **R$_f$**: 0.31 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –72.0 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 2.5, 1.0 Hz, 1H, Ar*H*), 7.81 – 7.79 (m, 1H, Ar*H*), 7.74 – 7.70 (m, 1H, Ar*H*), 7.47 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.43 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.38 – 7.35 (m, 1H, Ar*H*), 7.33 – 7.31 (m, 1H, Ar*H*), 7.18 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.89 – 6.87 (m, 2H, Ar*H*), 6.83 – 6.81 (m, 2H, Ar*H*), 6.01 (dd, *J* = 10.5, 1.5 Hz, 1H, CH=C*H*C(O)), 5.86 (d, 1H, *J* = 11.5 Hz, –C*H*SAr), 4.92 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 2.99 (s, 3H, –OCH_3), 2.73 – 2.69 (m, 1H, –C*H*CH_2–), 2.57 – 2.53 (m, 1H, –CHCH_2–), 2.37 – 2.31 (m, 1H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 195.6, 162.1, 156.9, 153.6, 148.3, 140.1, 138.5, 136.3 (2C), 136.0, 135.3, 131.9, 131.5, 130.7, 129.7 (2C), 129.0, 127.8, 126.2, 125.7, 125.5, 118.2, 118.0, 114.8, 102.8, 75.4, 51.2, 46.9, 44.7, 40.4, 37.0, 21.2; **HRMS** (ESI, m/z) calcd for $C_{32}H_{28}ClN_2O_4S^+$ $[M+H]^+$: 571.1453, found: 571.1461.



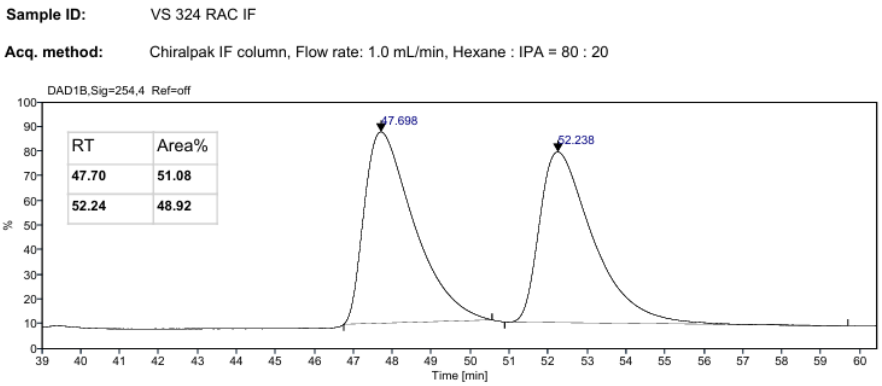


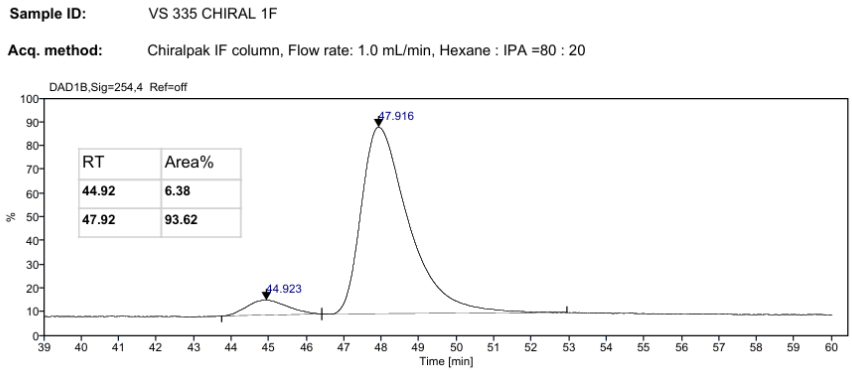
HPLC Data: 94.0 : 6.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 11.94 min (minor), t_R = 14.19 min (major).

4-[(4b*R*,8a*S*,9*S*,10*S*)-2,4b-Dimethoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3i)



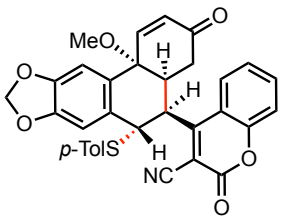
White solid; **m.p.**: 176 – 177 °C; **Yield**: 41 mg, 75%; **R_f**: 0.33 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = 16.8 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.64 – 7.61 (m, 1H, Ar*H*), 7.59 – 7.58 (m, 1H, Ar*H*), 7.41 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.34 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.29 – 7.26 (m, 1H, Ar*H*), 7.07 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.83 – 6.80 (m, 3H, Ar*H*), 6.74 – 6.72 (m, 2H, Ar*H*), 5.91 – 5.89 (m, 1H, –CH=C*H*C(O)), 5.81 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.83 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 3.85 (s, 3H, ArOCH_3), 2.92 (s, 3H, –OCH_3), 2.62 – 2.59 (m, 1H, –C*H*CH_2–), 2.49 – 2.45 (m, 1H, –CHCH_2–), 2.33 – 2.27 (m, 1H, –CHCH_2–), 2.16 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.2, 162.6, 160.4, 157.1, 153.6, 149.3, 139.8, 138.1, 136.1 (2C), 135.2, 131.5, 129.6 (2C), 128.2, 126.7, 125.7, 125.6, 124.2, 118.1 (2C), 115.5, 114.9, 114.7, 102.7, 75.7, 55.7, 51.1, 47.2, 45.2, 40.7, 37.2, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_5S^+$ $[M+NH_4]^+$: 567.1948, found: 567.1966.



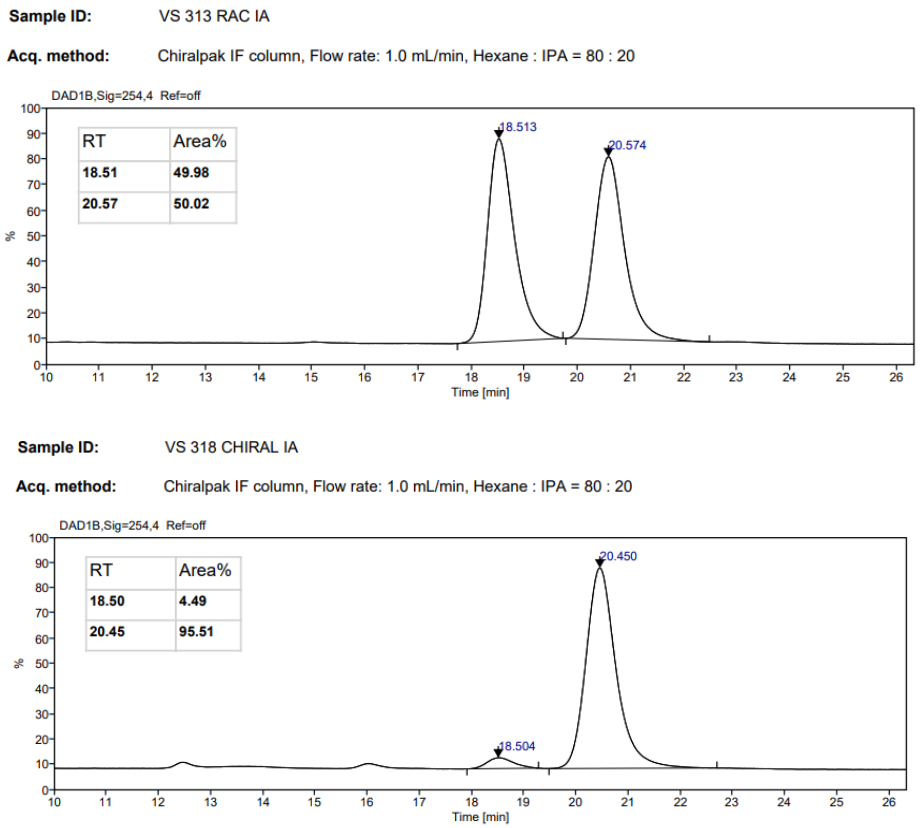


HPLC Data: 93.5 : 6.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 44.92 min (minor), t_R = 47.92 min (major).

4-[(4a*S*,5*S*,6*S*,11b*R*)-11b-Methoxy-3-oxo-6-(*p*-tolylthio)-3,4,4a,5,6,11b-hexahydrophenanthro[2,3-d][1,3]dioxol-5-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3j)

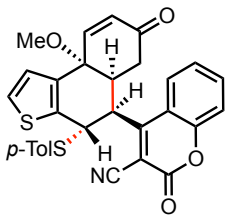


White solid; **m.p.**: 213 – 214 °C; **Yield**: 41 mg, 73%; **R$_f$**: 0.31 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –13.6 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 – 7.80 (m, 1H, Ar*H*), 7.72 – 7.68 (m, 1H, Ar*H*), 7.59 (d, *J* = 0.5 Hz, 1H, Ar*H*), 7.42 – 7.40 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.37 – 7.33 (m, 1H, Ar*H*), 6.94 – 6.91 (m, 2H, Ar*H*), 6.83 – 6.81 (m, 2H, Ar*H*,), 6.66 (s, 1H, Ar*H*), 6.10 (d, *J* = 1.0 Hz, 1H, –OCH_2O–), 6.04 (d, *J* = 1.5 Hz, 1H, –OCH_2O–), 5.97 (dd, *J* = 10.5, 1.0 Hz, 1H, –CH=C*H*C(O)), 5.82 – 5.80 (m, 1H, –C*H*SAr), 4.89 (dd, *J* = 11.5, 3.5 Hz, 1H, –C*H*CHSAr), 3.03 (s, 3H, –OCH_3), 2.68 – 2.63 (m, 1H, –C*H*CH_2–), 2.54 – 2.50 (m, 1H, –CHCH_2–), 2.43 – 2.37 (m, 1H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.1, 162.6, 157.0, 153.6, 149.0, 149.0, 147.2, 139.9, 136.2 (2C), 135.1, 130.6, 129.6 (2C), 128.6, 126.8, 125.7, 125.6, 125.5, 118.2, 118.1, 114.8, 111.2, 109.2, 102.8, 102.0, 75.9, 51.4, 47.2, 45.6, 40.9, 37.2, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{29}N_2O_6S^+$ $[M+H]^+$: 581.1741, found: 581.1741.

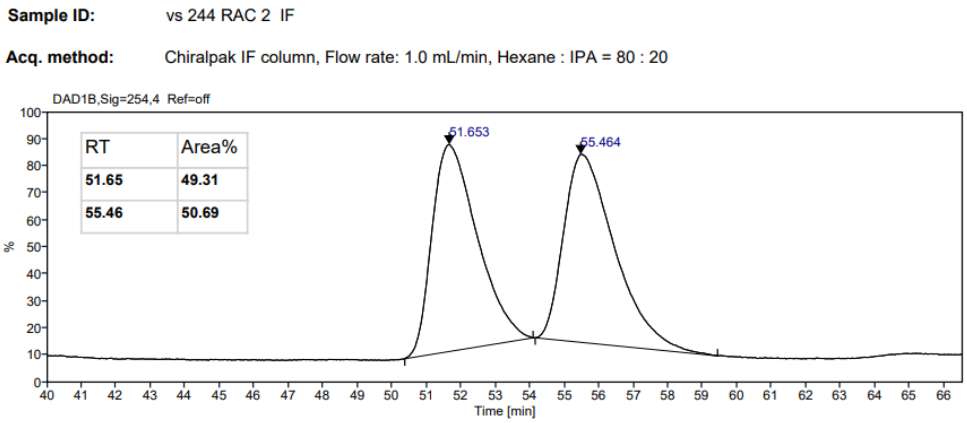


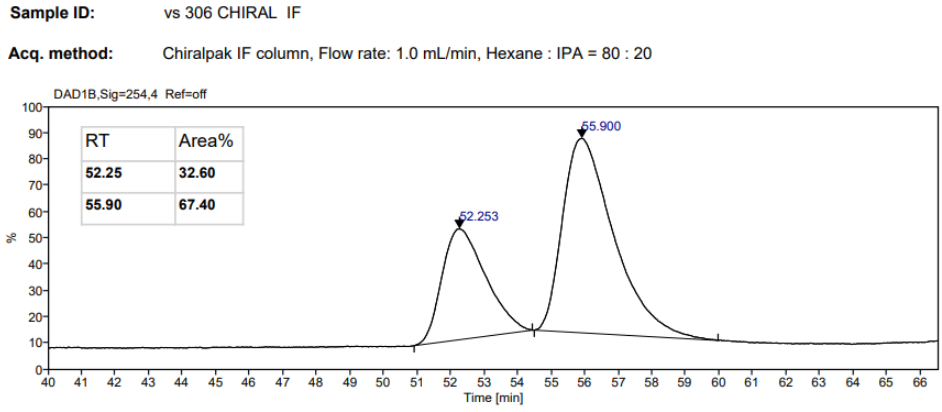
HPLC Data: 95.5 : 4.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 18.50 min (minor), t_R = 20.45 min (major).

4-[(4*S*,5*S*,5a*S*,9a*R*)-9a-Methoxy-7-oxo-4-(*p*-tolylthio)-4,5,5a,6,7,9a-hexahydronaphtho[2,1-b]thiophen-5-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3k)



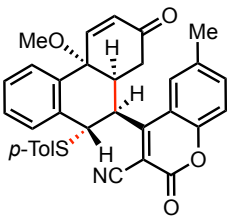
Yellow solid; **m.p.**: 133 – 134 °C; **Yield**: 34 mg, 65%; **R_f**: 0.34 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –23.2 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) 7.76 – 7.74 (m, 1H, Ar*H*), 7.72 – 7.68 (m, 1H, Ar*H*), 7.44 – 7.42 (m, 2H, Ar*H*), 7.34 – 7.32 (m, 1H, Ar*H*), 7.30 (d, *J* = 10.0 Hz, –C*H*=CHC(O)) 7.01 – 6.98 (m, 2H, Ar*H*), 6.90 (d, *J* = 5.5 Hz, 1H, Ar*H*), 6.87 – 6.85 (m, 2H, Ar*H*), 6.01 – 5.99 (m, 1H, –CH=C*H*C(O)), 5.93 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.62 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 3.08 (s, 3H, –OCH_3), 2.73 – 2.68 (m, 1H, –C*H*CH_2–), 2.62 – 2.57 (m, 1H, –CHCH_2–), 2.51 – 2.45 (m, 1H, –CHCH_2–), 2.26 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.0, 161.5, 156.9, 153.6, 147.1, 143.1, 140.2, 136.0 (2C), 135.2, 132.8, 129.7 (2C), 128.9, 126.8, 126.7, 125.9, 125.7, 125.6, 118.2, 118.0, 114.9, 103.2, 74.0, 51.6, 47.2, 41.9, 41.8, 37.1, 21.3; **HRMS** (ESI, m/z) calcd for $C_{30}H_{27}N_2O_4S_2^+$ $[M+H]^+$: 543.1407, found: 543.1425.



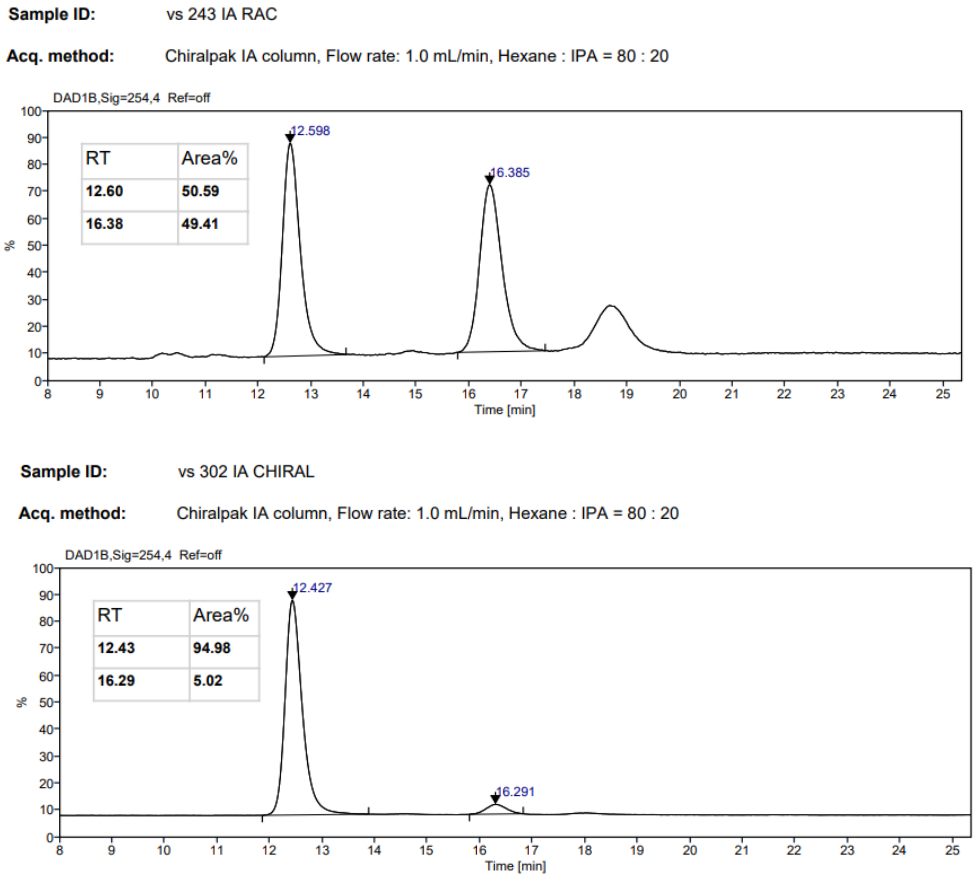


HPLC Data: 67.5 : 32.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 52.25 min (minor), t_R = 67.40 min (major).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-6-methyl-2-oxo-2*H*-chromene-3-carbonitrile (3l)

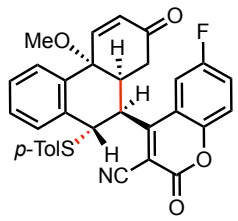


White solid; **m.p.**: 195 – 196 °C; **Yield**: 33 mg, 62%; **R**$_f$: 0.31 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –4.8 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.56 – 7.49 (m, 3H, Ar*H*, 1H, –C*H*=CHC(O)), 7.36 – 7.33 (m, 1H, Ar*H*), 7.30 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.25 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.82 – 6.78 (m, 4H, Ar*H*), 6.00 (dd, *J* = 10.5, 1.5 Hz, 1H, –CH=C*H*C(O)), 5.87 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.88 – 4.85 (m, 1H, –C*H*CHSAr), 3.03 (s, 3H, –OCH_3), 2.72 – 2.68 (m, 1H, –C*H*CH_2–), 2.62 – 2.56 (m, 1H, –CHCH_2–), 2.43 – 2.39 (m, 1H, –CHCH_2–), 2.37 (s, 3H, ArCH_3), 2.23 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.1, 162.4, 157.3, 151.8, 149.1, 139.7, 136.7, 136.2 (3C), 135.2, 132.3, 132.1, 130.1, 129.8, 129.4 (2C), 128.7, 127.4, 126.7, 125.6, 117.8, 117.7, 115.0, 102.6, 75.9, 51.2, 46.6, 44.8, 40.2, 37.1, 21.3, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_4S^+$ $[M+H]^+$: 551.1999, found: 551.2000.

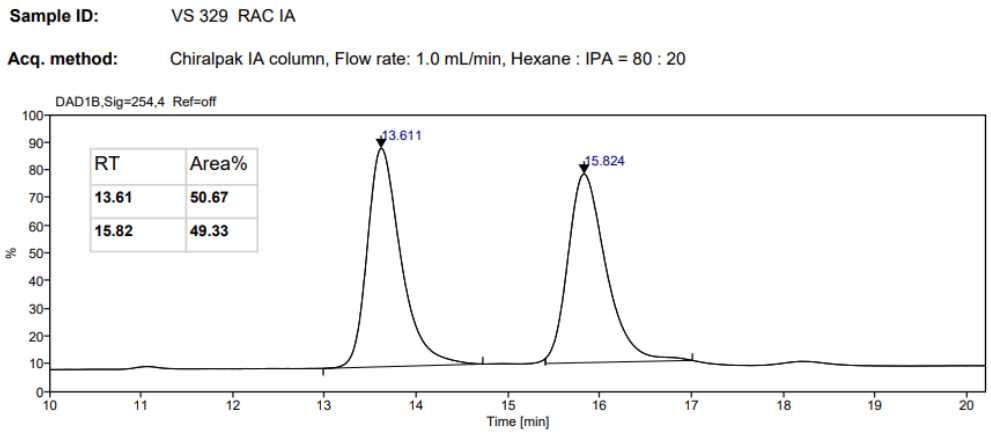


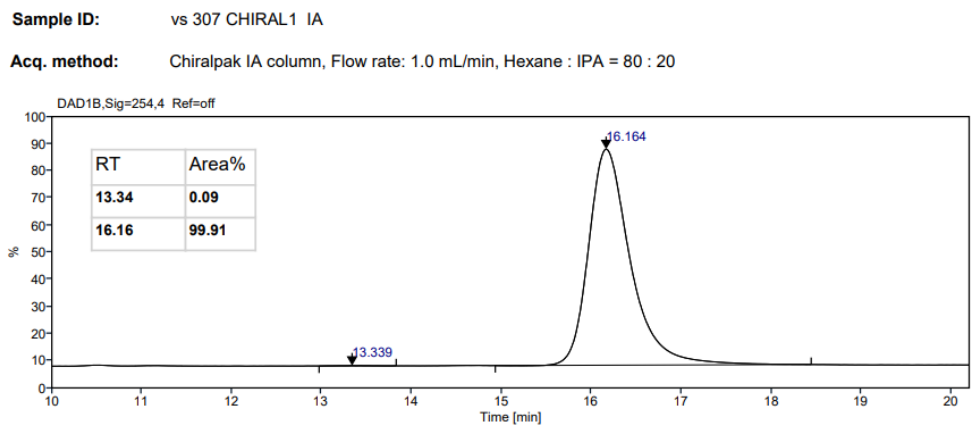
HPLC Data: 95.0 : 5.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 12.43 min (major), t_R = 16.29 min (minor).

6-Fluoro-4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3m)



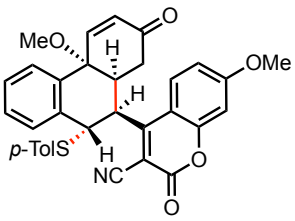
Light yellow solid; **m.p.**: 130 – 131 °C; **Yield**: 35 mg, 65%; **R**$_f$: 0.45 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –21.6 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.57 – 7.54 (m, 1H, Ar*H*), 7.52 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.48 – 7.46 (m, 1H, Ar*H*), 7.43 – 7.41 (m, 2H, Ar*H*), 7.37 – 7.33 (m, 1H, Ar*H*), 7.24 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.85 – 6.80 (m, 4H, Ar*H*), 6.01 (dd, *J* = 10.5, 1.5 Hz, 1H, –CH=C*H*C(O)), 5.87 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.74 (dd, *J* = 11.5, 2.5 Hz, 1H, –C*H*CHSAr), 3.04 (s, 3H, –OCH_3), 2.69 – 2.64 (m, 1H, –C*H*CH_2–), 2.58 – 2,54 (m, 1H, –CHCH_2–), 2.42 – 2.35 (m, 1H, –CHCH_2–), 2.23 (s, 3H, ArCH_3); **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 195.9, 161.5, 156.6, 149.8, 148.8, 140.0, 136.4, 136.0 (2C), 132.2, 132.0, 130.3, 129.9, 129.6, 129.6 (2C), 128.7, 127.5, 126.6, 122.6, 119.8, 119.1, 114.5, 111.6, 103.9, 75.8, 51.2, 46.9, 44.8, 40.8, 37.0, 21.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –114.10; **HRMS** (ESI, m/z) calcd for $C_{32}H_{28}FN_2O_4S^+$ $[M+H]^+$: 555.1748, found: 555.1757.



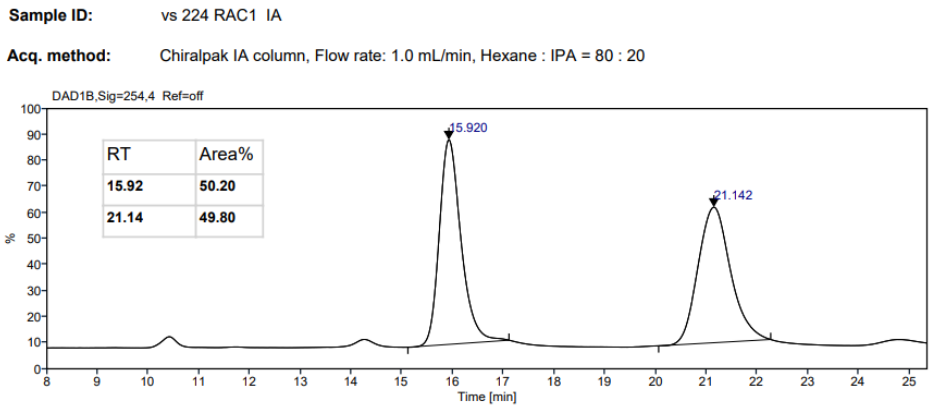


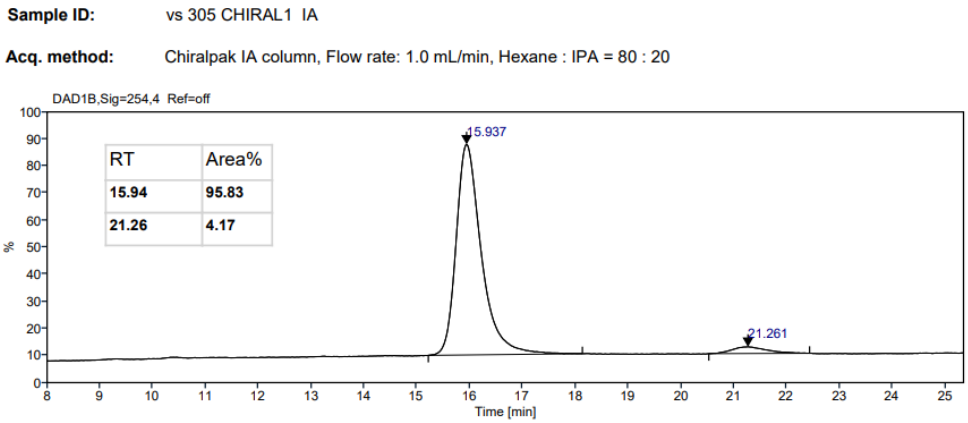
HPLC Data: >99.5 : 0.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 13.34 min (minor), t_R = 16.16 min (major).

7-Methoxy-4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(*p*-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3n)



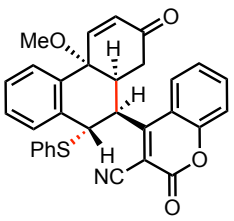
White solid; **m.p.**: 176 – 177 °C; **Yield**: 42 mg, 76%; **R$_f$**: 0.22 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –44.80 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.72 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.54 – 7.49 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.34 – 7.30 (m, 1H, Ar*H*), 7.22 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.92 – 6.82 (m, 6H, Ar*H*), 5.99 (dd, *J* = 10.5, 1.5 Hz, 1H, –CH=C*H*C(O)), 5.90 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.86 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 3.96 (s, 3H, ArOCH_3), 2.96 (s, 3H, –OCH_3), 2.69 – 2.65 (m, 1H, –C*H*CH$_2$–), 2.59 – 2.55 (m, 1H, –CHCH_2–), 2.40 – 2.33 (m, 1H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.2, 165.4, 162.5, 157.8, 156.0, 149.1, 139.7, 136.5, 136.3 (2C), 132.1, 132.0, 130.2, 129.7, 129.5 (2C), 128.6, 127.3, 127.1, 126.6, 115.4, 114.3, 111.7, 101.3, 98.8, 75.8, 56.3, 51.2, 47.3, 44.9, 40.6, 37.1, 21.2; **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_5S^+$ $[M+H]^+$: 567.1948, found: 567.1953.



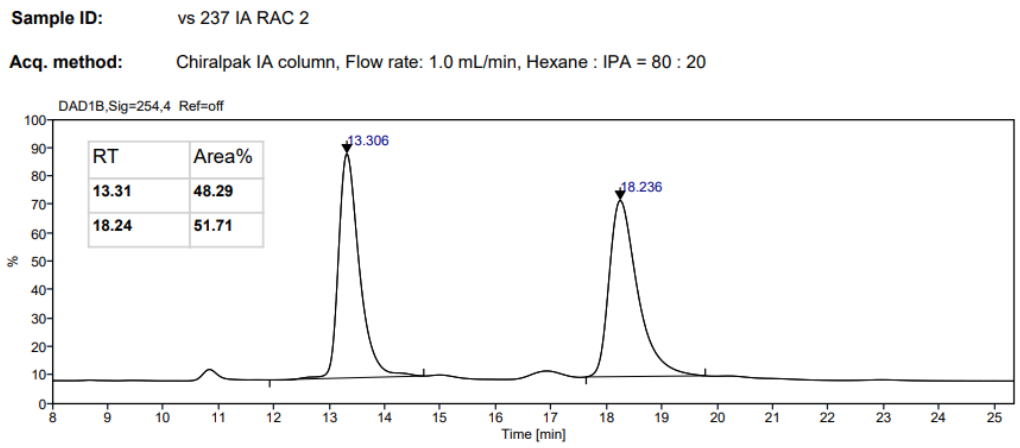


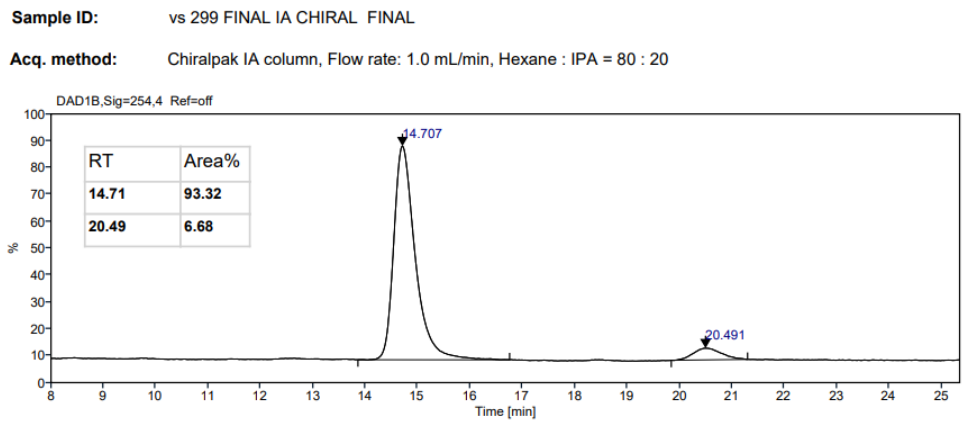
HPLC Data: 96.0: 4.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1 Flow rate: 1.0 mL/min; 254 nm, t_R = 15.94 min (major), t_R = 21.26 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(phenylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3o)



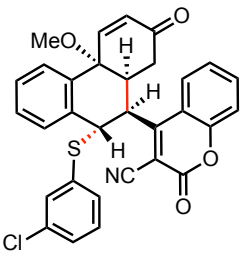
White solid; **m.p.**: 165 – 166 °C; **Yield**: 26 mg, 51%; **R**$_f$: 0.34 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30} = -31.2$ (*c* 0.25, $CHCl_3$; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.79 – 7.77 (m, 1H, Ar*H*), 7.72–7.68 (m, 1H, Ar*H*), 7.57 – 7.54 (m, 1H, Ar*H*), δ 7.51 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.43 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.36 – 7.31 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 7.02 – 6.95 (m, 4H, Ar*H*), 6.00 (d, *J* = 10.5 Hz, 1H, –CH=C*H*C(O)), 5.95 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.94 – 4.91 (m, 1H, –C*H*CHSAr), 2.99 (s, 3H, –OCH_3), 2.73 – 2.69 (m, 1H, –C*H*CH$_2$–), 2.60 – 2.56 (m, 1H, –CHCH_2–), 2.43 – 2.36 (m, 1H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.0, 162.5, 157.1, 153.6, 148.9, 136.5, 136.1 (2C), 135.2, 132.2, 132.1, 130.3, 130.2, 129.9, 129.5, 128.8 (2C), 128.7, 127.5, 125.7, 125.6, 118.3, 118.0, 114.8, 102.9, 75.9, 51.3, 47.1, 44.8, 40.4, 37.0; **HRMS** (ESI, m/z) calcd for $C_{31}H_{27}N_2O_4S^+$ $[M+NH_4]^+$: 523.1686, found: 523.1694.



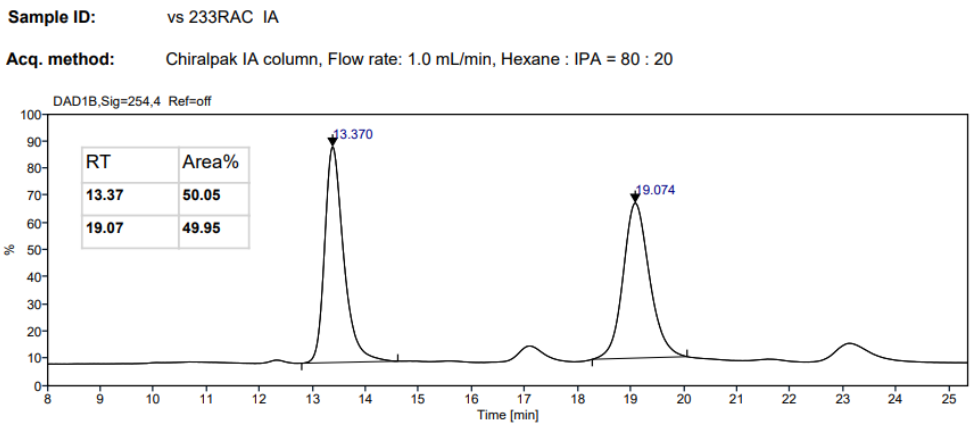


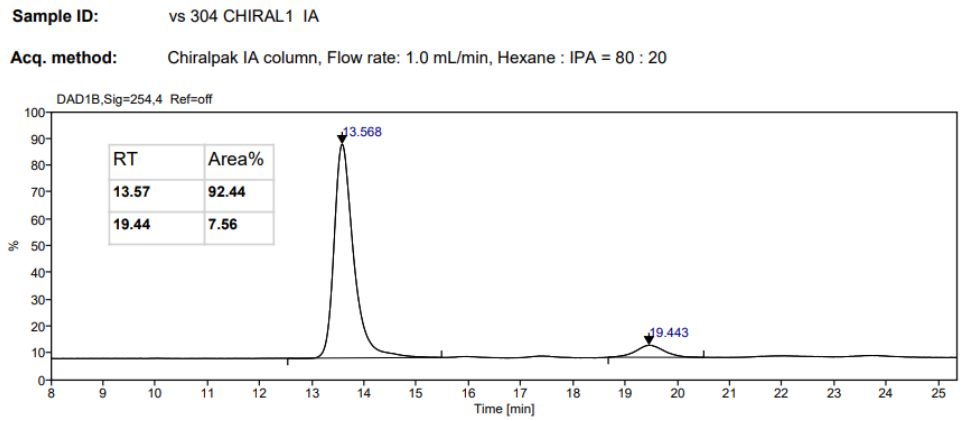
HPLC Data: 93.5 : 6.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 14.71 min (major), t_R = 20.49 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-10-((3-Chlorophenyl)thio)-4b-methoxy-7-oxo-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3p)



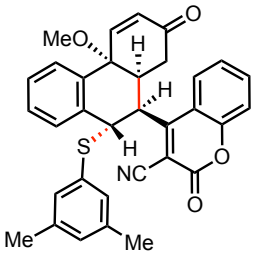
Light Yellow solid; **m.p.**: 184 – 185 °C; **Yield**: 46 mg, 85%; **R_f**: 0.32 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –3.2 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.79 – 7.77 (m, 1H, Ar*H*), 7.73 – 7.70 (m, 1H, Ar*H*), 7.59 – 7.56 (m, 1H, Ar*H*), 7.52 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.45 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.38 – 7.35 (m, 2H, Ar*H*), 7.26 – 7.24 (m, 1H, Ar*H*), 7.21 – 7.19 (m, 1H, Ar*H*), 6.90 (t, *J* = 8.0 Hz, 1H, 1H, Ar*H*), 6.90 – 6.86 (m, 2H, Ar*H*), 6.02 (d, *J* = 10.5 Hz, 1H, –CH=C*H*C(O)), 5.96 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.91 – 4.88 (m, 1H, –C*H*CHSAr), 3.03 (s, 3H, –OCH_3), 2.76 – 2.71 (m, 1H, –C*H*CH_2–), 2.62 – 2.58 (m, 1H, –CHCH_2–), 2.43 – 2.37 (m, 1H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 195.9, 162.2, 157.0, 153.6, 148.5, 136.0, 135.6, 135.4, 134.4, 134.0, 132.3, 132.0, 132.0, 130.4, 130.0, 129.9, 129.5, 128.8, 127.7, 126.0, 125.3, 118.4, 117.8, 114.8, 102.9, 75.8, 51.3, 47.1, 44.9, 40.2, 37.0; **HRMS** (ESI, m/z) calcd for $C_{31}H_{23}ClNO_4S^+$ $[M+H]^+$: 540.1031, found: 540.1043.



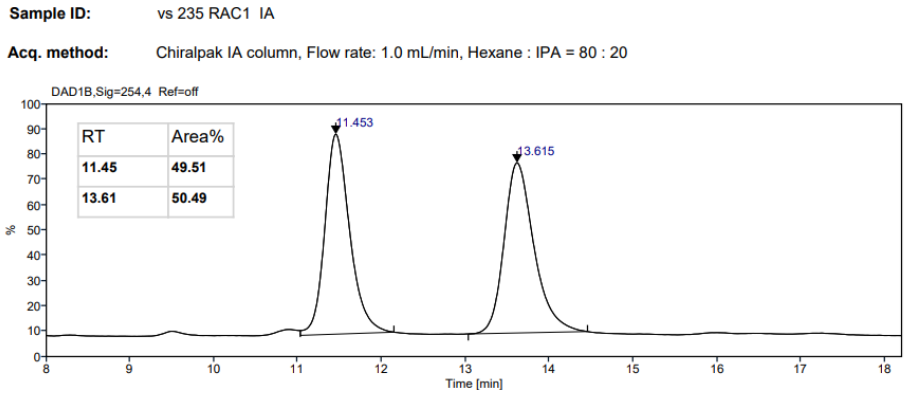


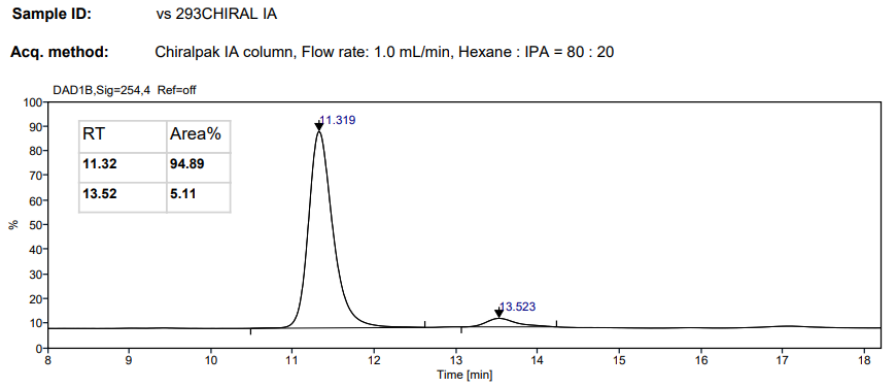
HPLC Data: 92.5 : 7.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 13.57 min (major), t_R = 19.44 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-10-((3,5-Dimethylphenyl)thio)-4b-methoxy-7-oxo-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3q)



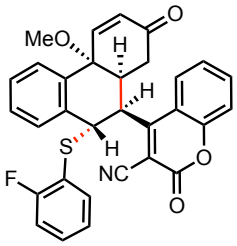
White solid; **m.p.**: 160 – 161 °C; **Yield**: 44 mg, 82%; **R_f**: 0.35 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30} = -13.6$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.88 – 7.86 (m, 1H, Ar*H*), 7.71 – 7.67 (m, 1H, Ar*H*), 7.57 – 7.53 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.42 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.39 – 7.33 (m, 2H, Ar*H*), 7.25 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.82 (s, 1H, Ar*H*), 6.66 – 6.65 (m, 2H, Ar*H*), 6.00 (dd, *J* = 10.5, 1.5 Hz, 1H, –CH=C*H*C(O)), 5.97 (d, *J* = 11.0 Hz, 1H, –C*H*SAr), 4.99 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 3.08 (s, 3H, –OCH_3), 2.71 – 2.66 (m, 1H, –C*H*CH_2–), 2.55 – 2.51 (m, 1H, –CHCH_2–), 2.40 – 2.34 (m, 1H, –CHCH_2–), 1.95 (s, 6H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.1, 162.3, 157.0, 153.5, 149.1, 138.8, 136.2, 134.9, 133.9 (3C), 132.1, 132.0, 131.3, 130.2, 129.9, 129.8 128.6, 127.4, 125.7, 125.5, 118.2, 118.1, 114.8, 102.5, 75.9, 51.4, 47.2, 45.1, 41.4, 37.1, 20.8 (2C); **HRMS** (ESI, m/z) calcd for $C_{33}H_{31}N_2O_4S^+$ $[M+H]^+$: 551.1999, found: 551.2013.



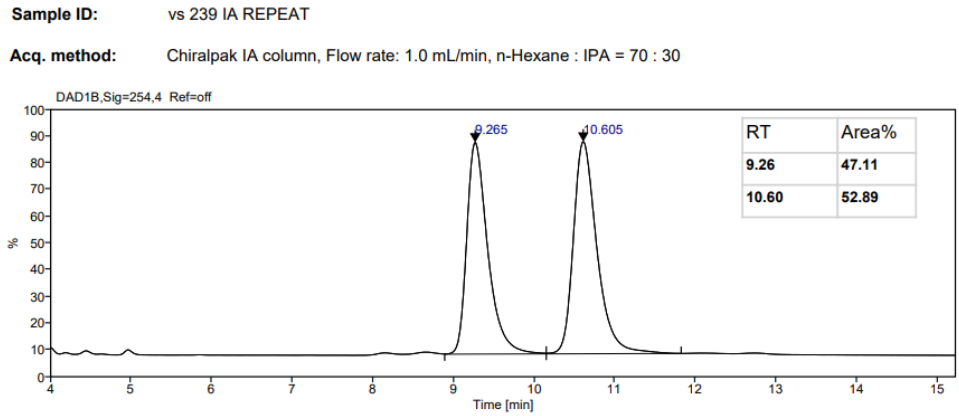


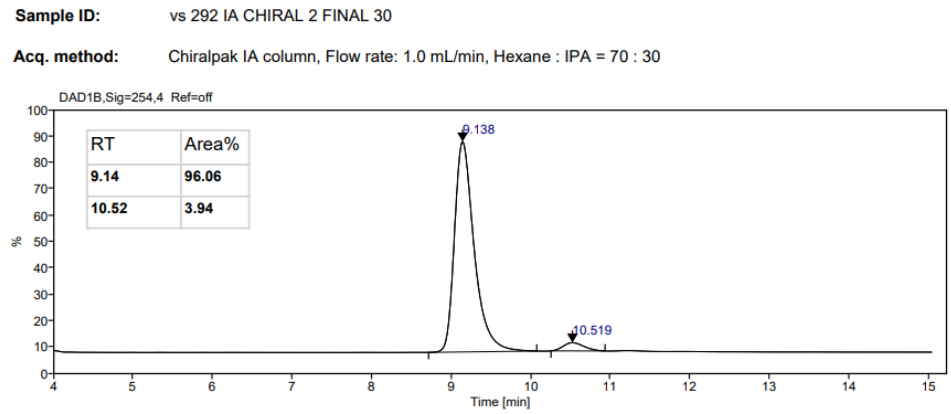
HPLC Data: 95.0 : 5.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 11.32 min (major), t_R = 13.52 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-10-((2-Fluorophenyl)thio)-4b-methoxy-7-oxo-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3r)



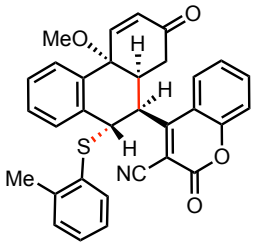
Yellow solid; **m.p.**: 99 – 100 °C; **Yield**: 34 mg, 65%; **R**$_f$: 0.20 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30} = -164.0$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.85 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.71 – 7.67 (m, 1H, Ar*H*), 7.57 – 7.52 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.40 – 7.34 (m, 3H, Ar*H*), 7.26 – 7.25 (m, 1H, Ar*H*), 7.21 – 7.17 (m, 1H, Ar*H*), 7.07 – 7.03 (m, 1H, Ar*H*), 6.83 – 6.76 (m, 2H, Ar*H*), 6.05 – 6.01 (m, 1H, –CH=C*H*C(O), 1H, –C*H*SAr), 5.00 (dd, *J* = 11.0, 3.5 Hz, 1H, –C*H*CHSAr), 3.13 (s, 3H, –OCH_3), 2.77 – 2.73 (m, 1H, –C*H*CH_2–), 2.54 – 2.50 (m, 1H, –CHCH_2–), 2.39 – 2.33 (m, 1H, –CHCH_2–); **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 196.0, 162.5, 157.0, 153.5, 149.1, 138.0, 135.8, 135.2, 132.0 (4C), 130.2, 130.0, 128.8, 127.7, 125.7, 125.5, 124.4, 118.1 (2C), 116.1, 114.7, 102.6, 76.0, 51.4, 47.2, 45.0, 41.5, 37.1; **^{19}F NMR** δ –103.56; **HRMS** (ESI, m/z) calcd for $C_{31}H_{26}FN_2O_4S^+$ $[M+H]^+$: 541.1592, found: 541.1603.



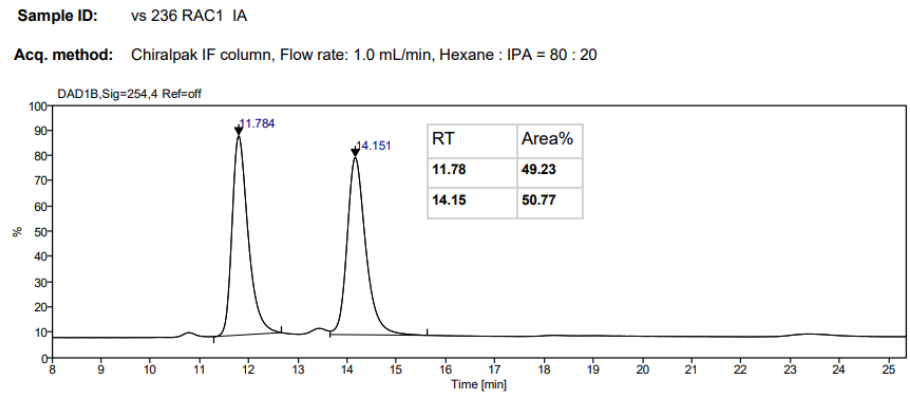


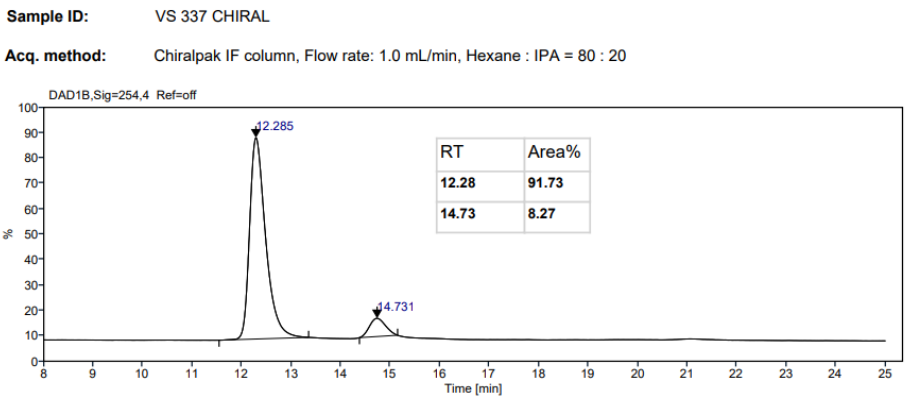
HPLC Data: 96.0 : 4.0 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 9.14 min (major), t_R = 10.52 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-10-(o-tolylthio)-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3s)



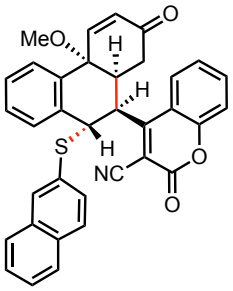
Pale yellow solid; **m.p.**: 133 – 134 °C; **Yield**: 42 mg, 81%; **R_f**: 0.41 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30} = -52.0$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.76 – 7.74 (m, 1H, Ar*H*), 7.68 – 7.65 (m, 1H, Ar*H*), 7.61 (d, *J* = 10.0 Hz, 1H, –C*H*=CHC(O), 7.54 – 7.50 (m, 1H, Ar*H*), 7.38 – 7.35 (m, 2H, Ar*H*), 7.32 – 7.29 (m, 2H, Ar*H*), 7.07 – 7.00 (m, 2H, Ar*H*), 6.92 (d, *J* = 7.5, 1H, Ar*H*), 6.76 – 6.73 (m, 1H, Ar*H*), 6.04 (dd, *J* = 10.5, 1.0, 1H, –CH=C*H*C(O)), 6.00 (d, *J* = 10.5 Hz, 1H, –C*H*SAr), 5.08 (dd, *J* = 10.5, 3.0 Hz, 1H, –C*H*CHSAr), 3.32 (s, 3H, –OCH_3), 2.75 –2.71 (m, 1H, –C*H*CH_2–), 2.53 – 2.48 (m, 1H, –CHCH_2–), 2.40 – 2.31 (m, 1H, –CHCH_2–), 2.16 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.0, 162.7, 156.9, 153.4, 149.3, 142.2, 136.3, 135.8, 135.1, 131.9, 131.7, 131.1, 130.9, 130.3, 130.1, 129.4, 128.8, 127.6, 126.2, 125.7, 125.3, 118.0 (2C), 114.8, 102.2, 76.1, 51.6, 47.2, 45.1, 41.5, 37.3, 20.9; **HRMS** (ESI, m/z) calcd for $C_{32}H_{29}N_2O_4S^+$ $[M+H]^+$: 537.1843, found: 537.1848.



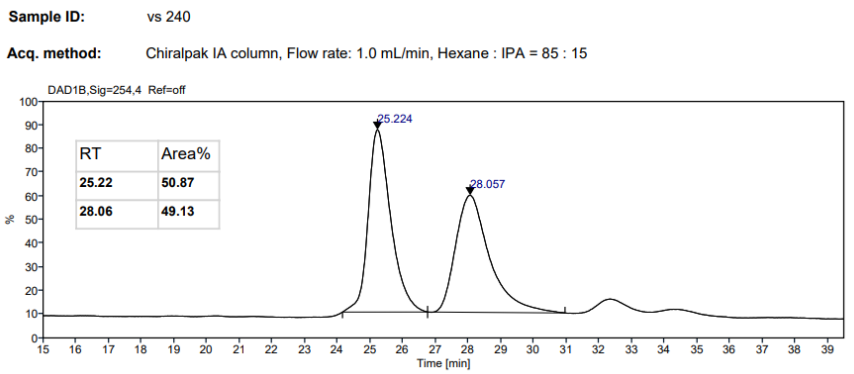


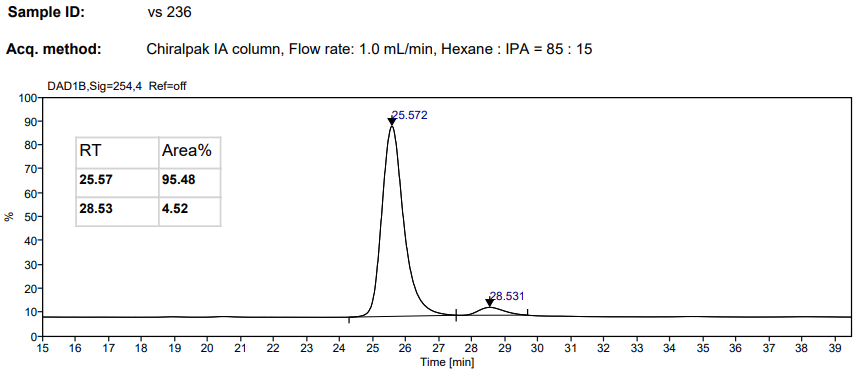
HPLC Data: 91.5 : 8.5; er Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 12.28 min (major), t_R = 14.73 min (minor).

4-[(4b*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-10-(naphthalen-2-ylthio)-7-oxo-4b,7,8,8a,9,10-hexahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (3t)



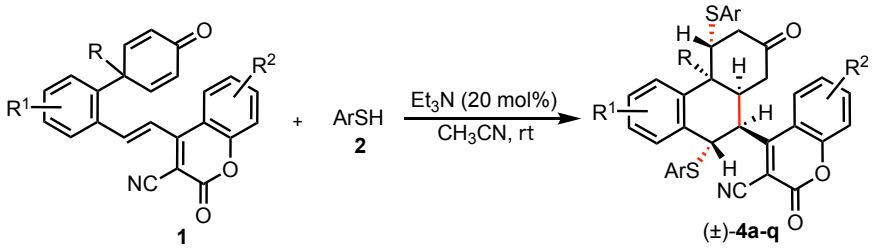
White solid; **m.p.**: 110 – 111 °C; **Yield**: 42 mg, 76%; **R_f**: 0.27 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –42.4 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.71 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.68 – 7.66 (dd, *J* = 9.0, 1.5 Hz, 1H, Ar*H*), 7.62 – 7.56 (m, 2H, Ar*H*), 7.53 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.49 – 7.45 (m, 1H, Ar*H*, 1H, –C*H*=CHC(O)), 7.42 – 7.41 (m, 1H, Ar*H*), 7.38 – 7.34 (m, 2H, Ar*H*), 7.30 – 7.28 (m, 1H, Ar*H*), 7.24 – 7.21 (m, 2H, Ar*H*), 7.19 – 7.15 (m, 1H, Ar*H*), 7.07 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 6.03 (d, *J* = 11.5 Hz, 1H, –CH=C*H*C(O)), 5.98 (d, *J* = 10.5 Hz, 1H, –C*H*SAr), 4.97 (m, 1H, –C*H*CHSAr), 2.82 (s, 3H, –OCH_3), 2.69 – 2.65 (m, 1H, –C*H*CH_2–), 2.57 – 2.53 (m, 1H, –CHCH_2–), 2.41 – 2.35 (m, 1H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.0, 162.4, 156.9, 153.4, 148.9 136.5, 136.2, 135.0, 133.2, 133.0, 132.2 (2C), 132.0, 130.3, 129.9, 128.6, 128.5, 127.6, 127.5 (3C), 127.3, 126.8, 125.6, 125.4, 118.2, 117.9, 114.9, 102.7, 75.8, 51.1, 47.0, 45.0, 40.6, 37.1; **HRMS** (ESI, m/z) calcd for $C_{35}H_{29}N_2O_4S^+$ $[M+H]^+$: 573.1843, found: 573.1861.





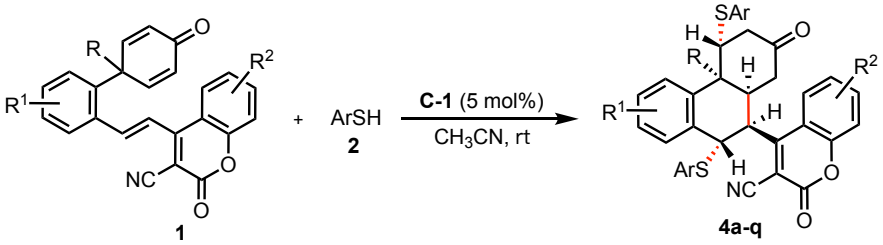
HPLC Data: 95.5 : 4.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 85 : 15, Flow rate: 1.0 mL/min; 254 nm, t_R = 25.57 min (major), t_R = 28.53 min (minor).

S4.8. General procedure for the synthesis of racemic compounds via sulfa-1,6-addition/vinylogous 1,4-addition/sulfa-1,4-addition desymmetrization domino sequence:



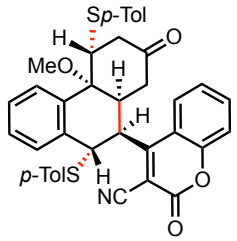
In a 10 mL reaction tube with a magnetic stirring bar, substrate **1** (0.05 mmol, 1.0 eq.) and Et_3N (20 mol%, 1.4 uL) were stirred in CH_3CN (0.5 mL) at room temperature. After stirring for 5 minutes, thiol **2** (0.15 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 24-48 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 7 : 3 as eluent) to afford the product (±)-**4a-q**.

S4.9. General procedure for chiral squaramide catalyzed asymmetric sulfa-1,6-addition/vinylogous 1,4-addition/ sulfa-1,4-addition desymmetrization domino sequence:

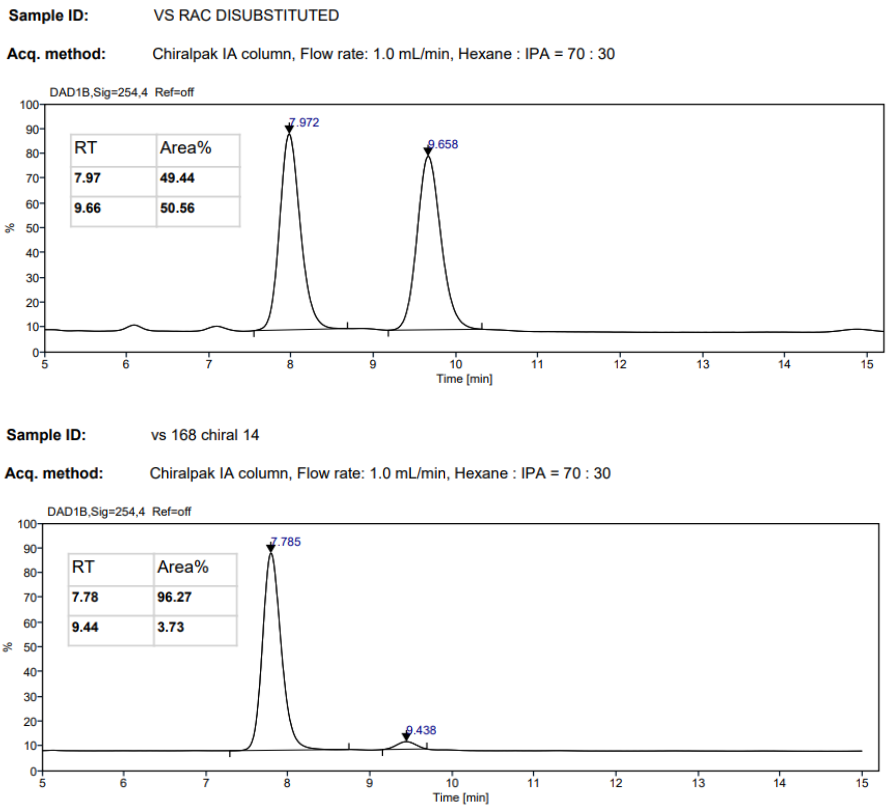


In a 10 mL reaction tube with a magnetic stirring bar, substrate **1** (0.1 mmol, 1.0 eq.) and **C-1** (5 mol%, 3.1mg) were stirred in CH_3CN (1.0 mL) at room temperature. After stirring for 5 minutes, substrate thiol **2** (0.3 mmol, 3.0 eq.) was added, and the stirring was continued at the same temperature for 24-96 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 7 : 3 as eluent) to afford the product **4a-q**.

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4a)

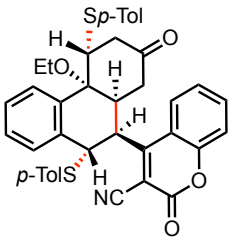


White solid; **m.p.**: 205 – 206 °C; **Yield**: 51 mg, 79%; **R**$_f$: 0.51 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -47.2$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.26 – 8.24 (m, 1H, Ar*H*), 7.92 – 7.90 (m, 1H, Ar*H*), 7.74 – 7.70 (m, 1H, Ar*H*), 7.58 – 7.55 (m, 1H, Ar*H*), 7.45 – 7.34 (m, 6H, Ar*H*), 7.16 – 7.14 (m, 2H, Ar*H*), 6.84 – 6.79 (m, 4H, Ar*H*), 5.95 (d, *J* = 11.5, Hz, 1H, –C*H*SAr), 5.03 (dd, *J* = 11.5, 3.5 Hz, 1H, –C*H*CHSAr), 4.55 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.14 – 3.08 (m, 1H, –C*H*CH$_2$–), 2.99 (s, 3H, –OC*H*$_3$), 2.48 – 2.44 (m, 1H, –CHC*H*$_2$–), 2.39 – 2.36 (m, 1H, –CHC*H*$_2$–), 2.34 – 2.32 (m, 3H, ArC*H*$_3$, 1H, –CHC*H*$_2$–), 2.30 – 2.26 (m, 1H, –CHC*H*$_2$–), 2.24 (s, 3H, ArC*H*$_3$); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.8, 163.3, 157.2, 153.6, 139.8, 139.3, 137.5, 136.3 (2C), 135.7 (2C), 135.2, 133.2, 130.7, 130.4 (2C), 129.7, 129.5 (2C), 128.0, 127.2, 126.8, 126.7, 125.9, 125.8, 118.3, 118.1, 115.0, 102.5, 77.4, 49.9, 49.2, 44.9, 44.5, 42.0, 40.6, 40.2, 21.4, 21.2; **HRMS** (ESI, m/z) calcd for $C_{39}H_{37}N_2O_4S_2^+$ $[M+NH_4]^+$: 661.2189, found: 661.2209.

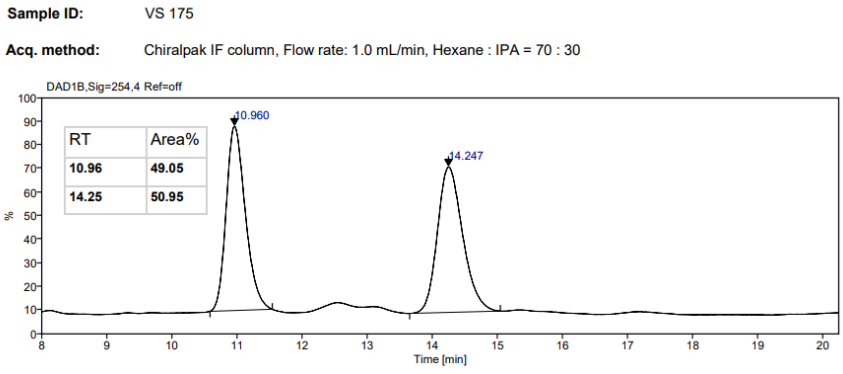


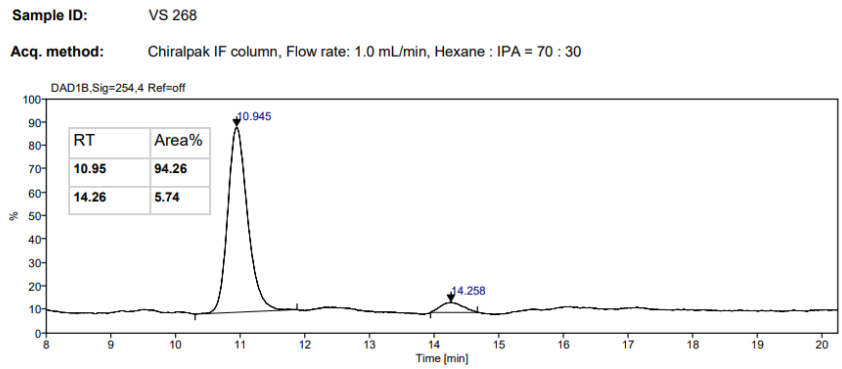
HPLC Data: 96.5 : 3.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 70 : 30, Flow rate: 1.0 mL/min; 254 nm, t_R = 7.78 min (major), t_R = 9.44 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Ethoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10 octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4b)



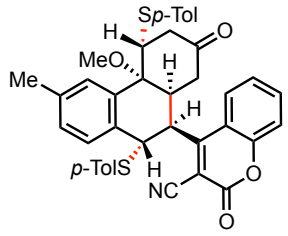
Yellow solid; **m.p.**: 190 – 191 °C; **Yield**: 36 mg, 55%; **R_f**: 0.47 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –47.2 (*c* 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H, Ar*H*), 8.04 – 8.02 (m, 1H, Ar*H*), 7.72 – 7.69 (m, 1H, Ar*H*), 7.57 – 7.54 (m, 1H, Ar*H*), 7.44 – 7.40 (m, 2H, Ar*H*), 7.38 – 7.35 (m, 2H, Ar*H*), 7.33 – 7.31 (m, 2H, Ar*H*), 7.13 (d, *J* = 7.5 Hz, 2H, Ar*H*), 6.79 – 6.75 (m, 4H, Ar*H*), 5.91 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.01 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.61 (t, *J* = 4.0 Hz, 1H, –C*H*SAr), 3.67 – 3.63 (m, 1H, –OCH_2CH$_3$), 3.15 – 3.12 (m, 1H, –C*H*CH$_2$–), 2.83 – 2.78 (m, 1H, –OCH_2CH$_3$), 2.51 – 2.47 (m, 1H, –CHCH_2–), 2.40 – 2.37 (m, 1H, –CHCH_2–), 2.33 (s, 3H, ArCH_3), 2.29 – 2.28 (m, 1H, –CHCH_2–), 2.25 – 2.24 (m, 1H, –CHCH_2–), 2.21 (s, 3H, ArCH_3), 0.94 (t, *J* = 7.0 Hz, 3H, –OCH$_2$CH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.8, 163.2, 157.2, 153.7, 139.8, 139.1, 137.5, 136.4 (2C), 135.5 (2C), 135.1, 133.2, 131.6, 130.3 (2C), 129.9, 129.6 (2C), 129.5, 128.3, 127.4, 126.6, 126.3, 125.5, 118.4, 118.1, 115.0, 102.7, 77.1, 57.7, 49.8, 45.0, 44.8, 41.8, 40.7, 40.0, 21.3, 21.2, 14.8; **HRMS** (ESI, m/z) calcd for $C_{40}H_{39}N_2O_4S_2^+$ $[M+NH_4]^+$: 675.2346, found: 675.2365.





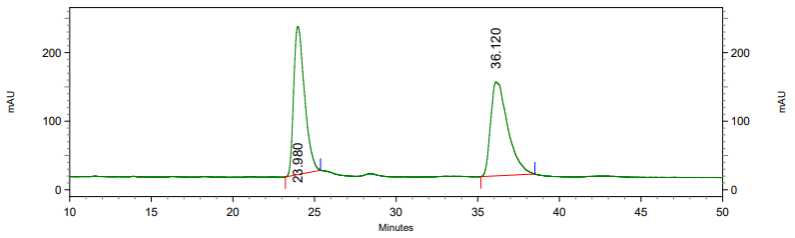
HPLC Data: 94.5 : 5.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 10.95 min (major), t_R = 14.26 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-3-methyl-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4c)



Yellow solid; **m.p.**: 234 – 235 °C; **Yield**: 50 mg, 76%; **R**$_f$: 0.41 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -2.4$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.91 – 7.89 (m, 1H, Ar*H*), 7.73 – 7.69 (m, 1H, Ar*H*), 7.43 – 7.36 (m, 5H, Ar*H*), 7.17 – 7.14 (m, 3H, Ar*H*), 6.86 – 6.84 (m, 2H, Ar*H*), 6.80 – 6.78 (m, 2H, Ar*H*), 5.91 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.01 (dd, *J* = 12.0, 3.5 Hz, 1H, –C*H*CHSAr), 4.53 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.12 – 3.06 (m, 1H C*H*CH$_2$–), 3.01 (s, 3H, –OC*H*$_3$), 2.46 – 2.42 (m, 3H, ArC*H*$_3$, 1H, –CHC*H*$_2$–), 2.38 – 2.32 (m, 3H, ArC*H*$_3$, 3H, –CHC*H*$_2$–), 2.23 (s, 3H, ArC*H*$_3$); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.9, 163.4, 157.2, 153.6, 139.7, 139.3, 137.0, 136.3 (2C), 135.8 (2C), 135.1, 134.2, 133.0, 130.6, 130.5, 130.4 (2C), 129.5 (2C), 128.1, 127.1, 127.0, 126.0, 125.8, 118.4, 118.0, 115.0, 102.5, 77.4, 50.0, 49.3, 44.8, 44.6, 42.1, 40.8, 40.3, 21.6, 21.4, 21.2; **HRMS** (ESI, m/z) calcd for $C_{40}H_{39}N_2O_4S_2^+$ $[M+NH_4]^+$: 675.2346, found: 675.2354.

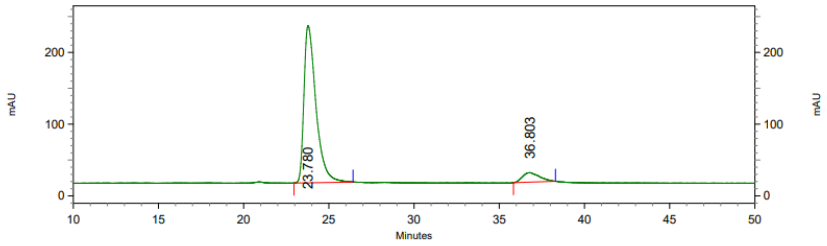
Sample ID: VS 170
Acq. Method: Chiralpak IF column, Flow rate: 1 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

Retention Time	Area %
23.98	50.01
36.12	49.99

Sample ID: VS 259
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

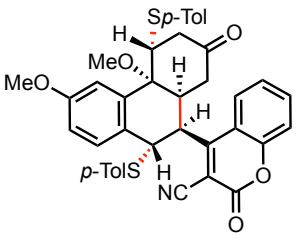


VWD: Signal A, 254 nm Results

RT	Area %
23.78	92.22
36.80	7.78

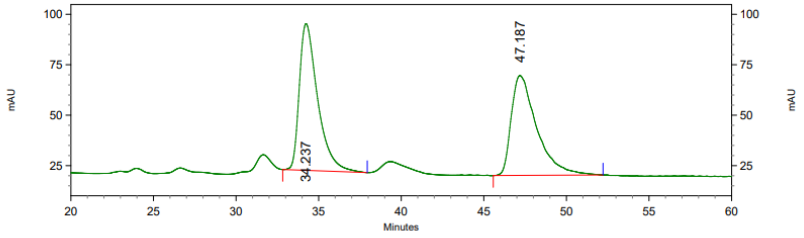
HPLC Data: 92.0 : 8.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 23.78 min (major), t_R = 36.80 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-3,4b-Dimethoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4d)



Yellow solid; **m.p.**: 183 – 184 °C; **Yield**: 49 mg, 73%; **R**$_f$: 0.45 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -30.4$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 – 7.88 (m, 1H, Ar*H*), 7.73 – 7.69 (m, 2H, Ar*H*), 7.43 – 7.39 (m, 2H, Ar*H*), 7.35 – 7.34 (m, 2H, Ar*H*), 7.30 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.15 – 7.13 (m, 2H, Ar*H*), 6.92 – 6.89 (m, 1H, Ar*H*), 6.87 – 6.80 (m, 4H, Ar*H*), 5.91 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.00 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 4.52 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.93 (s, 3H, ArOCH_3), 3.10 – 3.05 (m, 1H, –C*H*CH$_2$–), 2.99 (s, 3H, –OCH_3), 2.47 – 2.43 (m, 1H, –CHCH_2–), 2.40 – 2.36 (m, 1H, –CHCH_2–), 2.33 (s, 3H, ArCH_3), 2.32 – 2.26 (m, 2H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.9, 163.3, 160.2, 157.2, 153.6, 139.7, 139.3, 139.2, 136.2 (2C), 135.7 (2C), 135.2, 130.3 (2C), 129.5 (2C), 128.3, 128.1, 126.7, 126.0, 125.8, 122.9, 118.3, 118.1, 116.5, 115.0, 114.6, 102.5, 77.2, 55.7, 49.8, 49.4, 45.0, 44.5, 42.0, 40.6, 40.2, 21.3, 21.2; **HRMS** (ESI, m/z) calcd for $C_{40}H_{35}KNO_5S_2^+$ $[M+K]^+$: 712.1588, found: 712.1596.

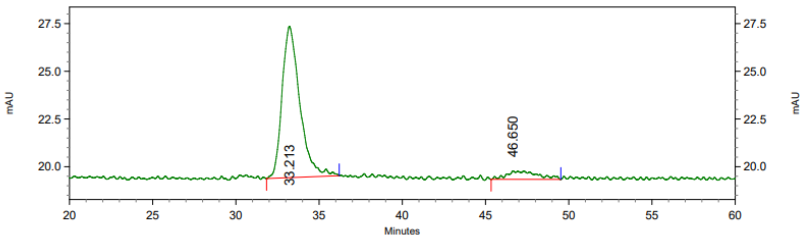
Sample ID: VS 183
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
34.24	51.33
47.19	48.67

Sample ID: VS 261
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

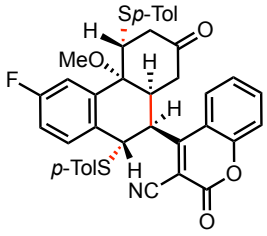


VWD: Signal A, 254 nm Results

RT	Area %
33.21	91.18
46.65	8.82

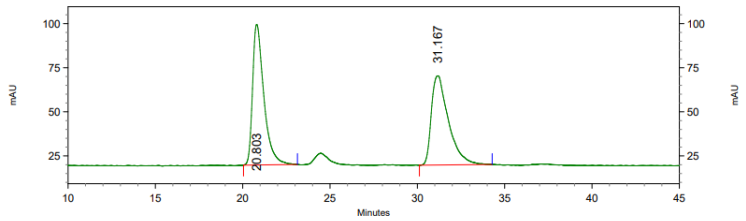
HPLC Data: 91.0 : 9.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 33.21 min (major), t_R = 46.65 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-3-Fluoro-4b-methoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4e)



Yellow solid; **m.p.**: 208 – 209 °C; **Yield**: 35 mg, 53%; **R$_f$**: 0.47 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –1.4 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.26 – 8.23 (m, 1H, Ar*H*), 7.90 – 7.88 (m, 1H, Ar*H*), 7.74 – 7.71 (m, 1H, Ar*H*), 7.45 – 7.41 (m, 2H, Ar*H*), 7.36 – 7.34 (m, 2H, Ar*H*), 7.31 – 7.27 (m, 1H, Ar*H*), 7.16 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.07 (dd, *J* = 10.0, 2.5 Hz, 1H, Ar*H*), 6.86 – 6.80 (s, 4H, Ar*H*), 5.91 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.99 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.41 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.13 – 3.09 (m, 1H, –C*H*CH_2–), 3.00 (s, 3H, –OCH_3), 2.49 – 2.44 (m, 1H, –CHCH_2–), 2.38 – 2.33 (m, 3H, ArCH_3, 2H, –CHCH_2–), 2.30 – 2.28 (m, 1H, –CHCH_2–), 2.25 (s, 3H, ArCH_3); **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 204.2, 163.0, 157.1, 153.6, 140.0, 139.5, 136.4 (2C), 135.7 (2C), 135.3 (2C), 133.3, 133.2, 130.4 (2C), 129.6 (2C), 127.7, 126.5, 125.9, 125.8 (2C), 118.3, 118.2, 117.2, 115.0, 113.5, 102.6, 77.1, 50.1, 49.1, 44.4, 44.3, 41.9, 40.5, 40.1, 21.4, 21.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –112.82; **HRMS** (ESI, m/z) calcd for $C_{39}H_{36}FN_2O_4S_2^+$ $[M+NH_4]^+$: 679.2095, found: 679.2086.

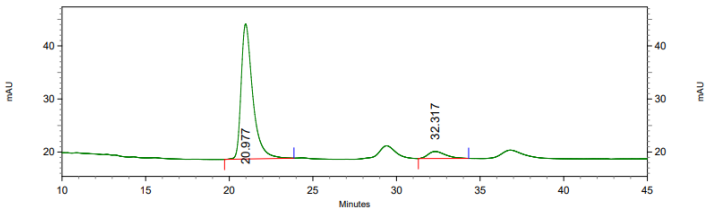
Sample ID: VS 176
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
20.80	50.95
31.17	49.05

Sample ID: VS 260
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

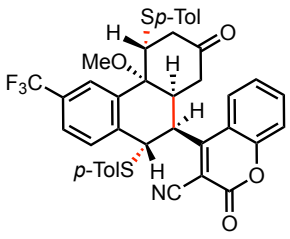


VWD: Signal A, 254 nm Results

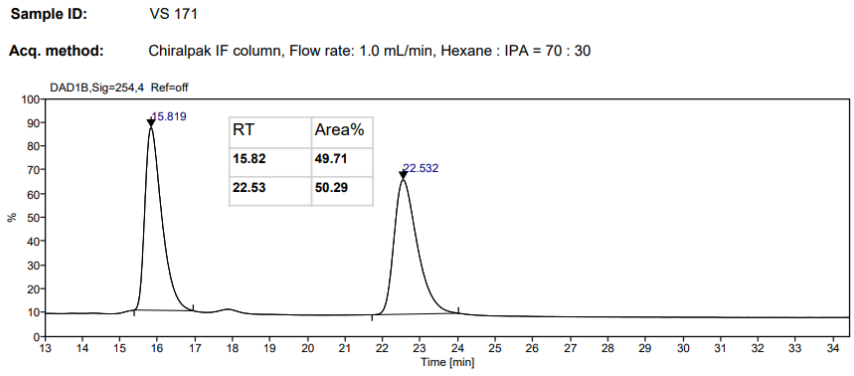
RT	Area %
20.98	92.83
32.32	7.17

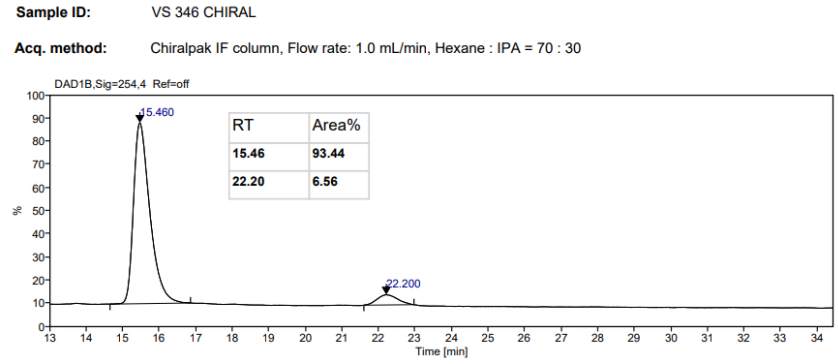
HPLC Data: 93.0 : 7.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 20.98 min (major), t_R = 32.32 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-5,10-bis(*p*-tolylthio)-3-(trifluoromethyl)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4f)



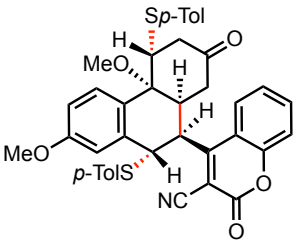
White solid; **m.p.**: 205 – 206 °C; **Yield**: 40 mg, 56%; **R$_f$**: 0.51 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -15.2$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.88 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.83 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 7.75 – 7.72 (m, 1H, Ar*H*), 7.56 (s, 1H, Ar*H*), 7.46 – 7.42 (m, 2H, Ar*H*), 7.39 – 7.38 (m, 2H, Ar*H*), 7.19 – 7.17 (m, 2H, Ar*H*), 6.83 (s, 4H, Ar*H*), 5.97 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.04 (dd, *J* = 11.5, 3.5 Hz, 1H, –C*H*CHSAr), 4.49 (t, *J* = 4.0 Hz, 1H, –C*H*SAr), 3.22 – 3.15 (m, 1H, –C*H*CH_2–), 2.99 (s, 3H, –OCH_3), 2.50 – 2.46 (m, 1H, –CHCH_2–), 2.42 –2.37 (m, 1H, –CHCH_2–), 2.35 (s, 3H, ArCH_3), 2.32 –2.29 (m, 1H, –CHCH_2–), 2.25 (m, 3H, ArCH_3), 2.21 – 2.17 (m, 1H, –CHCH_2–) ; **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 203.8, 162.6, 157.0, 153.7, 142.2, 140.2, 139.7, 136.3 (2C), 136.0 (2C), 135.3, 134.1, 132.0, 130.5 (2C), 129.9, 129.7 (2C), 128.7, 127.4, 126.4, 126.2, 125.9, 125.7, 123.4, 118.3, 118.2, 115.0, 102.7, 77.4, 49.9, 49.0, 44.7, 44.2, 41.9, 40.2, 40.1, 21.4, 21.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –62.21; **HRMS** (ESI, m/z) calcd for $C_{40}H_{36}F_3N_2O_4S_2^+$ $[M+NH_4]^+$: 729.2063, found: 729.2084.





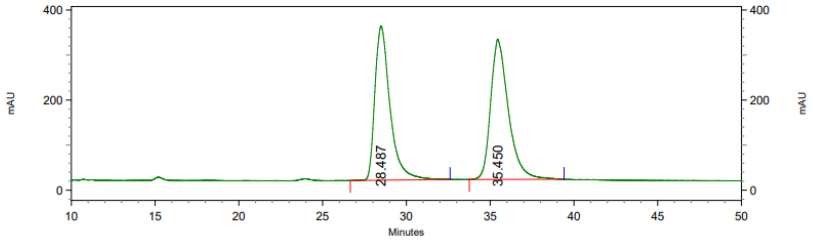
HPLC Data: 93.5 : 6.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 15.46 min (major), t_R = 22.20 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-2,4b-Dimethoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4g)



Pale yellow solid; **m.p.**: 223 – 224 °C; **Yield**: 45 mg, 67%; $\mathbf{R_f}$: 0.34 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –34.4 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.90 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.72 – 7.69 (m, 1H, Ar*H*), 7.43 – 7.40 (m, 2H, Ar*H*), 7.34 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.15 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.11 (dd, *J* = 9.0, 3.0 Hz, 1H, Ar*H*), 6.90 – 6.85 (m, 3H, Ar*H*), 6.81 – 6.80 (m, 2H, Ar*H*), 5.91 (d, *J* = 11.0 Hz, 1H, –C*H*SAr), 4.99 (dd, *J* = 11.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.47 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.89 (s, 3H, ArOCH_3), 3.10 – 3.03 (m, 3H, –OCH_3, 1H, –C*H*CH_2–), 2.46 – 2.34 (m, 4H, –CHCH_2–, 3H, ArCH_3), 2.23 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.8, 163.4, 158.4, 157.2, 153.6, 139.7, 139.3, 136.3 (2C), 135.7 (2C), 135.1, 134.5, 132.1, 130.4 (2C), 129.5 (2C), 129.0, 128.0, 127.0, 126.0, 125.8, 118.4, 118.1, 115.0, 113.8, 113.7, 102.5, 55.7, 50.1, 49.3, 44.6, 44.6, 42.0, 40.8, 40.3, 21.4, 21.2; **HRMS** (ESI, m/z) calcd for $C_{40}H_{39}N_2O_5S_2^+$ $[M+NH_4]^+$: 691.2295, found: 691.2299.

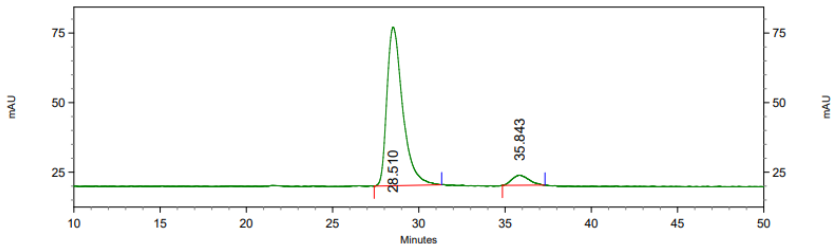
Sample ID: VS 182
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
28.49	48.40
35.45	51.60

Sample ID: VS 258
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

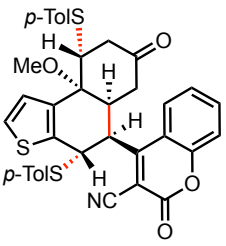


VWD: Signal A, 254 nm Results

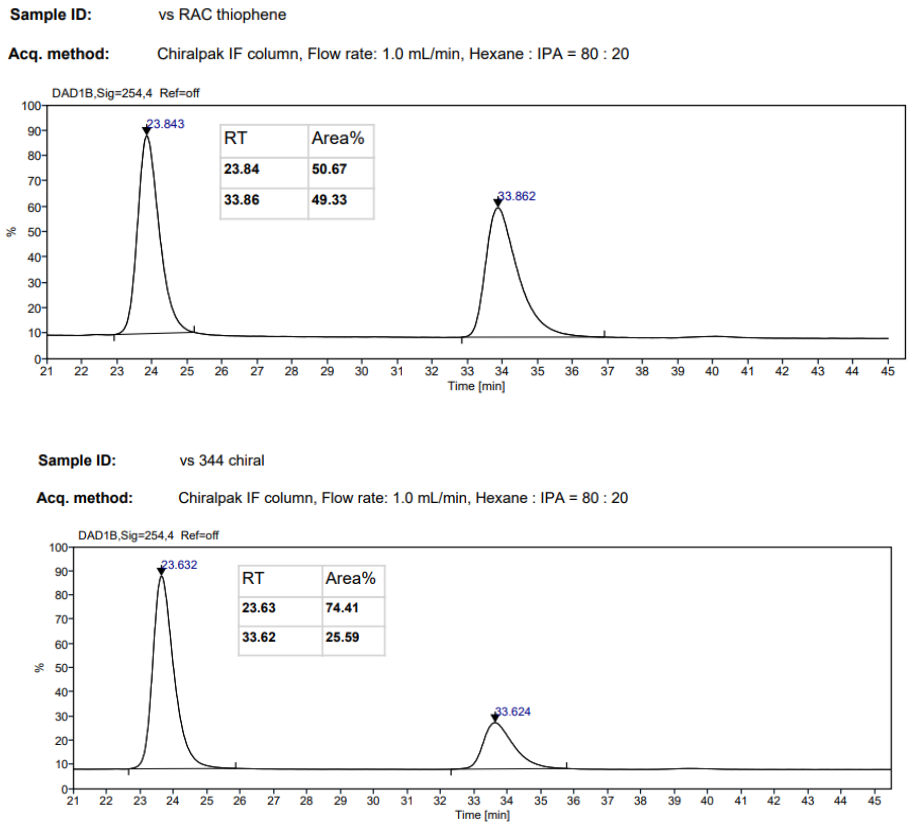
RT	Area %
28.51	93.69
35.84	6.31

HPLC Data: 93.5 : 6.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 28.51 min (major), t_R = 35.84 min (minor).

4-[(4*S*,5*S*,5a*S*,9*R*,9a*R*)-9a-Methoxy-7-oxo-4,9-bis(*p*-tolylthio)-4,5,5a,6,7,8,9,9a-octahydronaphtho[2,1-b]thiophen-5-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4h)

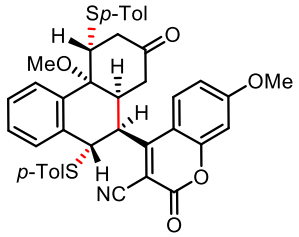


Pale yellow solid; **m.p.**: 222 – 223 °C; **Yield**: 33 mg, 51%; **R**$_f$: 0.30 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –36.8 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 – 7.82 (m, 1H, Ar*H*), 7.73 – 7.70 (m, 1H, Ar*H*), 7.47 – 7.46 (m, 1H, Ar*H*), 7.43 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.40 – 7.37 (m, 1H, Ar*H*), 7.34 – 7.32 (m, 2H, Ar*H*), 7.15 – 7.13 (m, 2H, Ar*H*), 7.00 (d, *J* = 5.5 Hz, 1H, Ar*H*), 6.98 – 6.95 (m, 2H, Ar*H*), 6.88 – 6.86 (m, 2H, Ar*H*), 5.97 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 4.74 (dd, *J* = 11.5, 2.5 Hz, 1H, –C*H*CHSAr), 4.37 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.06 (s, 3H, –OCH_3), 3.04 – 3.00 (m, 1H, –C*H*CH$_2$–), 2.52 – 2.42 (m, 2H, –CHCH_2–), 2.33 – 2.31 (m, 3H, ArCH_3, 2H, –CHCH_2–), 2.27 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.5, 162.3, 157.0, 153.6, 144.0, 140.1, 139.2, 136.0 (2C), 135.6 (2C), 135.2, 133.6, 130.3 (2C), 129.7, 127.8, 126.7 (2C), 126.0 (2C), 125.8, 125.2, 118.2, 118.1, 115.1, 102.7, 76.1, 50.4, 50.0, 45.5, 42.0, 41.8, 41.5, 39.9, 21.3 (2C); **HRMS** (ESI, m/z) calcd for $C_{37}H_{35}N_2O_4S_3^+$ $[M+NH_4]^+$: 667.1753, found: 667.1774.

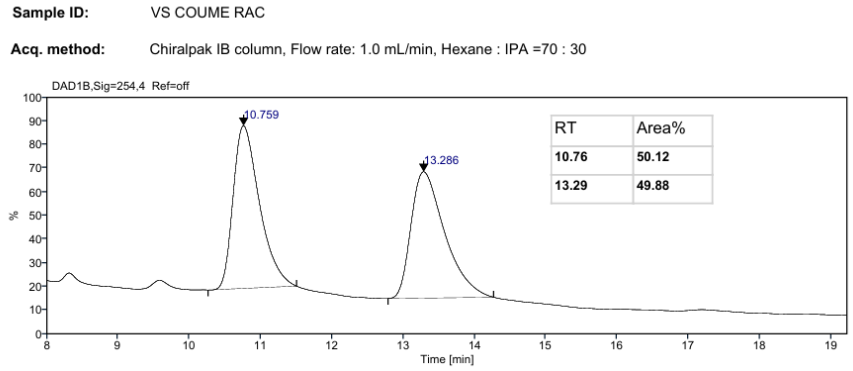


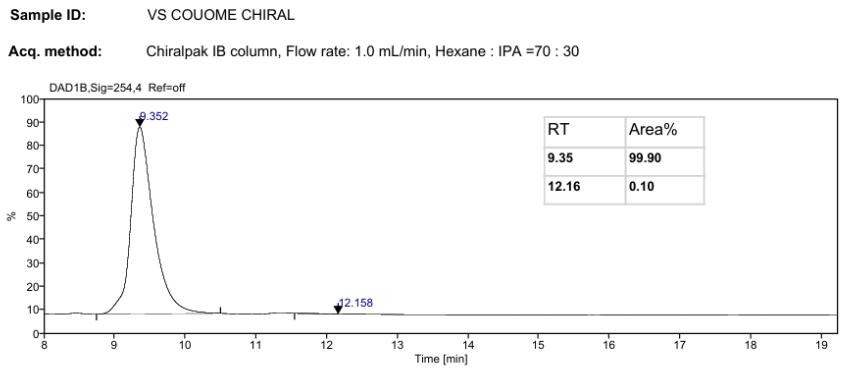
HPLC Data: 74.5: 25.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 80 : 20, Flow rate: 1.0 mL/min; 254 nm, t_R = 23.63 min (major), t_R = 33.62 min (minor).

7-Methoxy-4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-methoxy-7-oxo-5,10-bis(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4i)



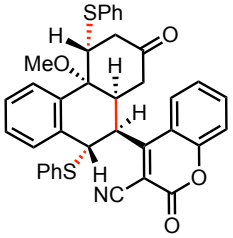
White solid; **m.p.**: 184 – 185 °C; **Yield**: 52 mg, 77%; **R**$_f$: 0.38 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –13.6 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 – 7.89 (m, 1H, Ar*H*), 7.73 – 7.70 (m, 2H, Ar*H*), 7.44 – 7.39 (m, 2H, Ar*H*), 7.36 – 7.33 (m, 2H, Ar*H*), 7.30 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.15 –7.13 (m, 2H, Ar*H*), 6.91 (dd, *J* = 8.5, 2.5 Hz, 1H, Ar*H*), 6.86 – 6.85 (m, 2H, Ar*H*), 6.82 – 6.80 (m, 2H, Ar*H*), 5.91 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.00 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.53 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.93 (s, 3H, –ArCH_3), 3.10 – 3.06 (m, 1H, –C*H*CH_2–), 2.98 (s, 3H, –OCH_3), 2.48 – 2.43 (m, 1H, –CHCH_2–), 2.38 (d, *J* = 14.0 Hz, 1H, –CHCH_2–), 2.33 – 2.30 (m, 3H, ArCH_3, 2H, –CHCH_2–), 2.24 (s, 3H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 205.0, 163.3, 160.2, 157.2, 153.5, 139.7, 139.2, 139.2, 136.2 (2C), 135.6 (2C), 135.1, 130.3 (2C), 129.5 (2C), 128.3, 128.1, 126.7, 126.0, 125.8, 122.9, 118.3, 118.0, 116.5, 115.0, 114.5, 102.4, 77.4, 55.7, 49.8, 49.4, 45.0, 44.5, 41.9, 40.6, 40.2, 21.3, 21.2; **HRMS** (ESI, m/z) calcd for $C_{40}H_{39}N_2O_5S_2^+$ $[M+NH_4]^+$: 691.2295, found: 691.2302.



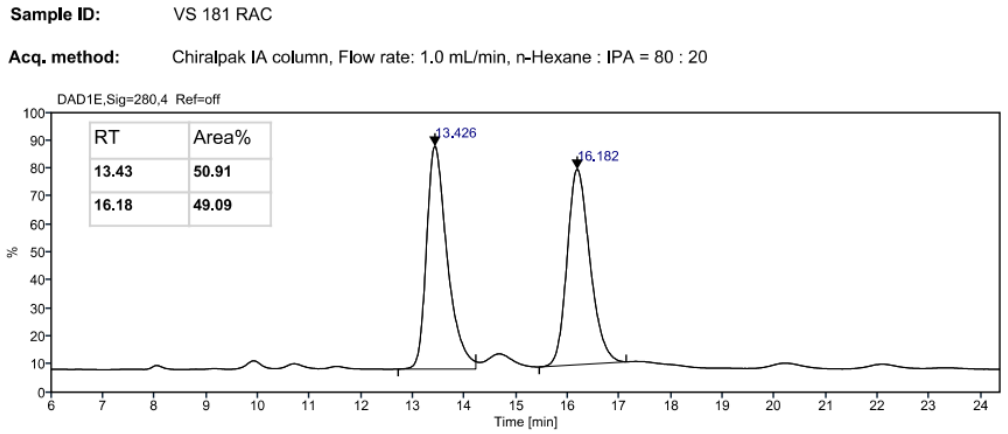


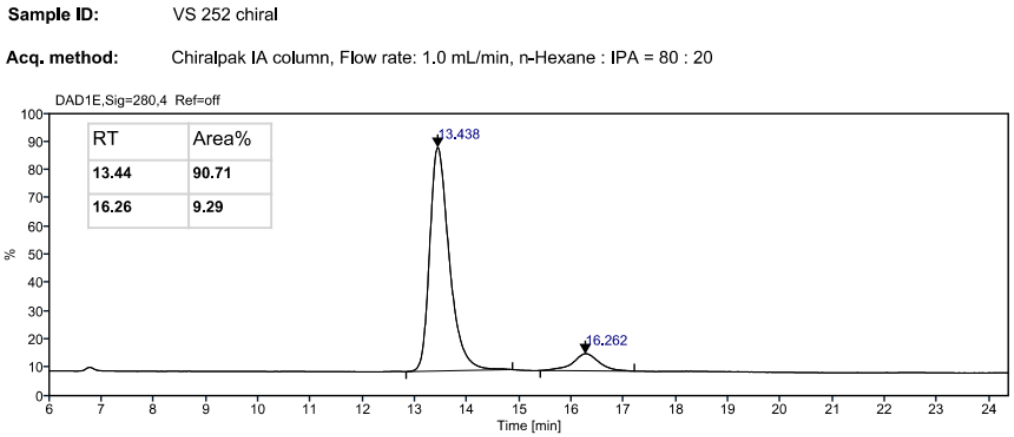
HPLC Data: >99.5 : 0.5 er; Daicel Chiralpak IB column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 9.35 min (major), t_R = 12.16 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-5,10-bis(phenylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4j)



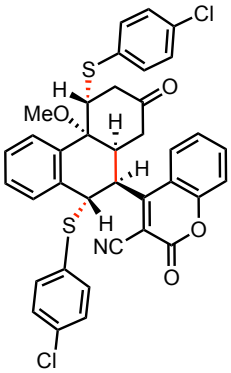
Yellow solid; **m.p.**: 155 – 156 °C; **Yield**: 52 mg, 85%; **R_f**: 0.39 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -23.2$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.29 – 8.27 (m, 1H, Ar*H*), 7.86 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.74 – 7.70 (m, 1H, Ar*H*), 7.60 – 7.57 (m, 1H, Ar*H*), 7.47 – 7.33 (m, 9H, Ar*H*), 7.24 – 7.20 (m, 1H, Ar*H*), 7.03 – 6.99 (m, 2H, Ar*H*), 6.92 – 6.90 (m, 2H, Ar*H*), 5.98 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 5.01 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 4.62 (t, 1H, *J* = 3.5 Hz –C*H*SAr), 3.13 – 3.09 (m, 1H, –C*H*CH_2–), 2.95 (s, 3H, –OCH_3), 2.51 – 2.47 (m, 1H, –CHCH_2–), 2.41 – 2.29 (m, 3H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.6, 163.2, 157.3, 153.6, 137.5, 136.1 (2C), 135.4 (2C), 135.3, 133.3, 131.8, 130.7, 130.1, 129.8, 129.6 (2C), 129.4, 128.9, 128.8 (2C), 127.3, 126.8, 125.9 (2C), 118.2 (2C), 115.0, 102.6, 77.4, 49.9, 49.1, 44.6, 44.5, 42.0, 40.3, 40.1; **HRMS** (ESI, m/z) calcd for $C_{37}H_{30}NO_4S_2^+$ $[M+H]^+$: 616.1611, found: 616.1601.



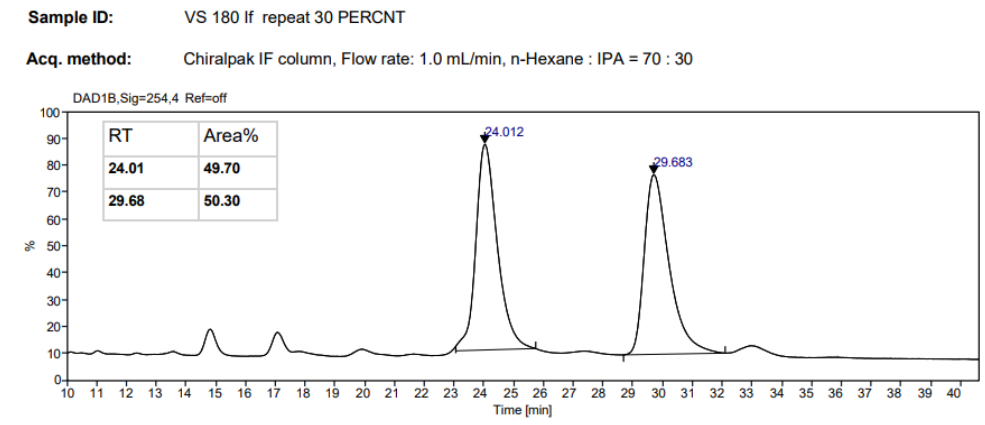


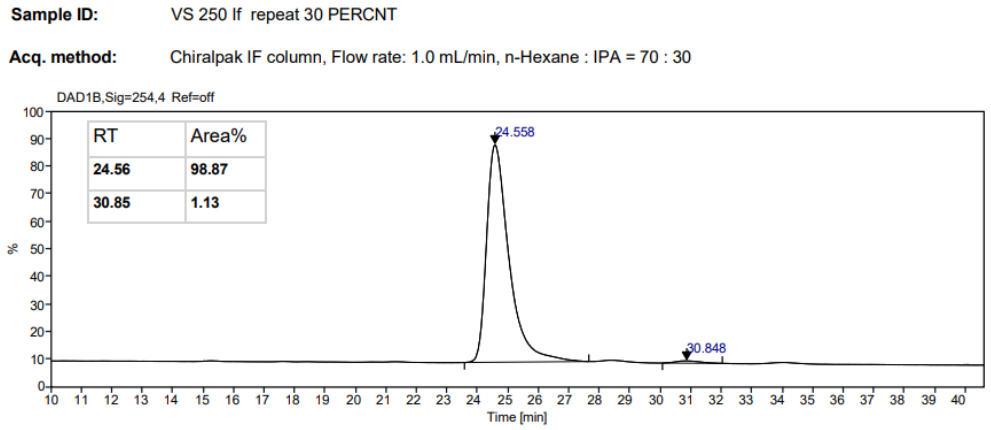
HPLC Data: 90.5: 9.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 13.44 min (major), t_R = 16.26 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-5,10-Bis((4-chlorophenyl)thio)-4b-methoxy-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4k)



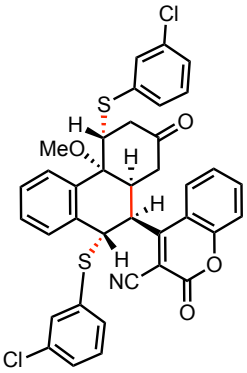
Yellow solid; **m.p.**: 184 – 185 °C; **Yield**: 42 mg, 61%; >20:1; $\mathbf{R_f}$: 0.54 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –48.4 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.5, 1.0 Hz, 1H, Ar*H*), 7.85 – 7.83 (m, 1H, Ar*H*), 7.77 – 7.74 (m, 1H, Ar*H*) 7.62 – 7.58 (m, 1H, Ar*H*), 7.49 – 7.38 (m, 6H, Ar*H*), 7.33 – 7.31 (m, 2H, Ar*H*), 7.01 – 7.00 (m, 2H, Ar*H*), 6.80 – 6.79 (m, 2H, Ar*H*), 5.96 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.92 (dd, *J* = 12.0, 3.5 Hz, 1H, –C*H*CHSAr), 4.60 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.14 – 3.09 (m, 1H, –C*H*CH_2–), 2.96 (s, 3H, –OCH_3), 2.52 – 2.48 (m, 1H, –CHCH_2–), 2.41 – 2.30 (m, 3H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.3, 162.8, 157.1, 153.6, 137.4 (2C), 137.2, 136.7 (2C), 135.9, 135.5, 135.4, 133.2, 130.7, 130.0, 129.9, 129.8 (2C), 128.9 (2C), 128.3, 127.6, 126.8, 126.0, 125.5, 118.4, 118.1, 114.9, 102.7, 77.4, 49.9, 49.1, 44.6, 44.4, 41.9, 40.0, 39.8; **HRMS** (ESI, m/z) calcd for $C_{37}H_{28}Cl_2NO_4S_2^+$ $[M+H]^+$: 684.0831, found: 684.0837.





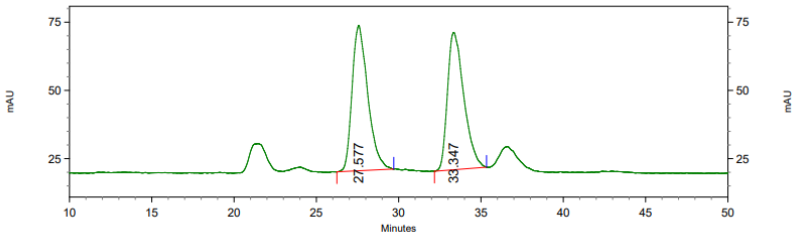
HPLC Data: 99.0 : 1.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 24.56 min (major), t_R = 30.85 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-5,10-Bis((3-chlorophenyl)thio)-4b-methoxy-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4l)



White solid; **m.p.**: 160 – 161 °C; **Yield**: 47 mg, 69%; $\mathbf{R_f}$: 0.31 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –4.0 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.86 – 7.84 (m, 1H, Ar*H*), 7.76 – 7.73 (m, 1H, Ar*H*), 7.63 – 7.60 (m, 1H, Ar*H*), 7.48 – 7.43 (m, 5H, Ar*H*), 7.33 – 7.27 (m, 3H, Ar*H*), 7.23 – 7.20 (m, 1H, Ar*H*), 6.98 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.83 – 6.82 (m, 1H, Ar*H*), 6.81 – 6.79 (m, 1H, Ar*H*), 5.99 (d, *J* = 12.0 Hz, 1H, –C*H*SAr), 4.96 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.68 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.14 – 3.10 (m, 1H, –C*H*CH_2–), 2.94 (s, 3H, –OCH_3), 2.51 (dd, *J* = 14.5, 4.5 Hz, 1H, –CHCH_2–), 2.41 (d, *J* = 14.0 Hz, 1H, –CHCH_2–), 2.36 – 2.35 (m, 2H, –CHCH_2–); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.0, 162.7, 157.1, 153.6, 137.1, 135.8, 135.5, 135.0, 134.4, 134.4, 134.2, 133.9, 133.2, 133.2, 131.8, 130.7, 130.6, 130.0, 129.8, 129.6, 129.1, 127.7, 126.9, 126.2, 125.4, 118.4, 118.0, 115.0, 102.6, 77.5, 50.1, 49.0, 44.7, 44.5, 42.1, 40.0 (2C); **HRMS** (ESI, m/z) calcd for $C_{37}H_{31}Cl_2N_2O_4S_2^+$ $[M+NH_4]^+$: 701.1097, found: 701.1097.

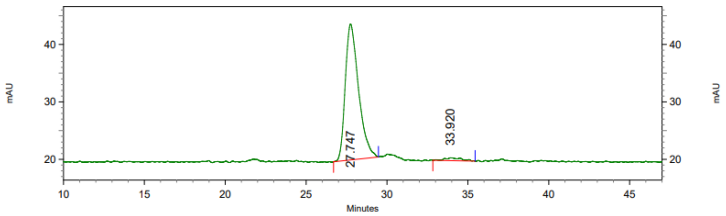
Sample ID: VS 186
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
27.58	50.42
33.35	49.58

Sample ID: VS 253
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

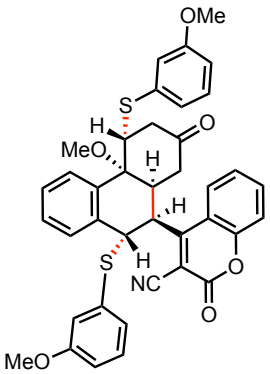


VWD: Signal A, 254 nm Results

RT	Area %
27.75	97.39
33.92	2.61

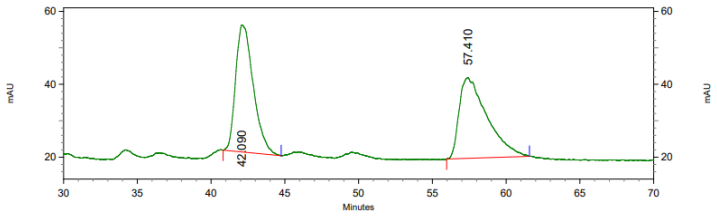
HPLC Data: 97.5 : 2.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 27.75 min (major), t_R = 33.92 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10S)-4b-Methoxy-5,10-bis((3-methoxyphenyl)thio)-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4m)



Yellow solid; **m.p.**: 96 – 97 °C; **Yield**: 42 mg, 62%; **R$_f$**: 0.58 (hexane : ethyl acetate = 3 : 2); $[\alpha]_D^{30}$ = –25.60 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.28 – 8.26 (m, 1H, Ar*H*), 7.88 (dd, *J* = 8.5, 1.5 Hz, 1H, Ar*H*), 7.73 – 7.70 (m, 1H, Ar*H*), 7.60 – 7.57 (m, 1H, Ar*H*), 7.45 – 7.39 (m, 4H, Ar*H*), 7.25 – 7.23 (m, 1H, Ar*H*), 7.05 – 7.03 (m, 1H, Ar*H*), 6.99 – 6.98 (m, 1H, Ar*H*), 6.96 – 6.93 (m, 1H, Ar*H*), 6.86 – 6.85 (m, 1H, Ar*H*), 6.77 – 6.75 (m, 1H, Ar*H*), 6.53 – 6.50 (m, 1H, Ar*H*), 6.40 (dd, *J* = 2.5, 1.5 Hz, 1H, Ar*H*), 6.00 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.01 (dd, *J* = 12.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.67 – 4.65 (m, 1H, –C*H*SAr), 3.80 (s, 3H, ArOCH_3), 3.40 (s, 3H, ArOCH_3), 3.13 – 3.09 (m, 1H, –C*H*CH$_2$–), 3.00 (s, 3H, –OCH_3), 2.51 – 2.46 (m, 1H, –CHCH_2–), 2.41 – 2.29 (m, 3H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.6, 163.1, 160.0, 159.4, 157.2, 153.6, 137.6, 135.2, 133.3, 132.9, 131.1, 130.8, 130.3, 129.8, 129.5, 128.3, 127.3, 127.1, 126.9, 125.9, 125.8, 120.5 (2C), 118.2, 118.1, 116.0, 115.0, 114.5, 102.5, 77.4, 55.5, 55.1, 50.0, 48.9, 44.8, 44.6, 42.0, 40.4, 40.1; **HRMS** (ESI, m/z) calcd for $C_{39}H_{33}KNO_6S_2^+$ [M+K]$^+$: 714.1381, found: 714.1396.

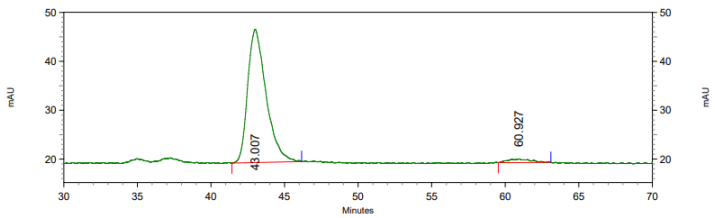
Sample ID: VS 187
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
42.09	50.01
57.41	49.99

Sample ID: VS 254
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

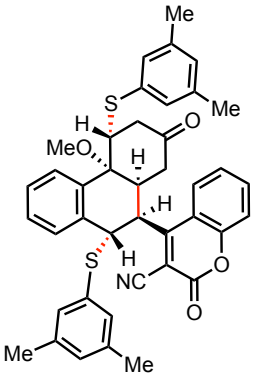


VWD: Signal A, 254 nm Results

RT	Area %
43.01	96.87
60.93	3.13

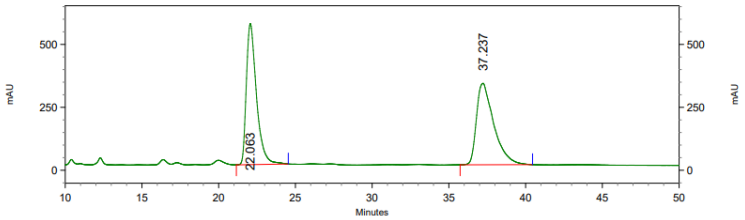
HPLC Data: 97.0 : 3.0 er:; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 43.01 min (major), t_R = 60.93 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-5,10-Bis((3,5-dimethylphenyl)thio)-4b-methoxy-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4n)



Pale yellow solid; **m.p.**: 148 – 149 °C; **Yield**: 60 mg, 89%; **R**$_f$: 0.47 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –56.0 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.96 (d, *J* = 7.0 Hz, 1H, Ar*H*), 7.72 – 7.69 (m, 1H, Ar*H*), 7.59 – 7.56 (m, 1H, Ar*H*), 7.46 – 7.38 (m, 4H, Ar*H*), 7.06 (s, 2H, Ar*H*), 6.95 (s, 1H, Ar*H*), 6.83 (s, 1H, Ar*H*), 6.63 (s, 2H, Ar*H*), 6.01 (d, *J* = 11.0 Hz, 1H, –C*H*SAr), 5.08 (dd, *J* = 11.0, 3.0 Hz, 1H, –C*H*CHSAr), 4.62 (t, *J* = 4.0 Hz, 1H, –C*H*SAr), 3.10 – 3.06 (m, 1H, –C*H*CH_2–, 3H, –OCH_3), 2.46 – 2.32 (m, 4H, –CHCH_2–), 2.30 (s, 6H, ArCH_3), 1.97 (s, 6H, ArCH_3); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.7, 163.0, 157.2, 153.5, 139.2 (2C), 138.7 (2C), 137.3, 134.9, 134.1 (2C), 133.3, 132.7 (2C), 131.3 (2C), 130.7 (2C), 129.9, 129.7, 127.2, 126.9, 125.9, 125.8, 118.3, 118.2, 115.0, 102.2, 77.4, 50.1, 48.8, 45.1, 44.5, 42.2, 41.3, 40.2, 21.3 (2C), 20.9 (2C); **HRMS** (ESI, m/z) calcd for $C_{41}H_{41}N_2O_4S_2^+$ $[M+NH_4]^+$: 689.2502, found: 689.2529.

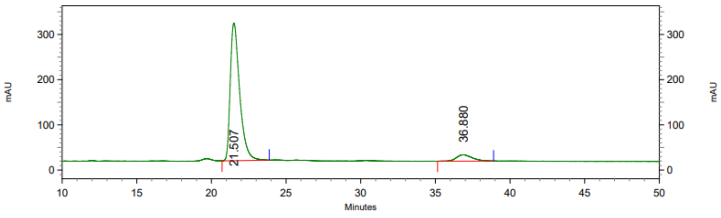
Sample ID: VS 192
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
22.06	50.34
37.24	49.66

Sample ID: VS 257
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

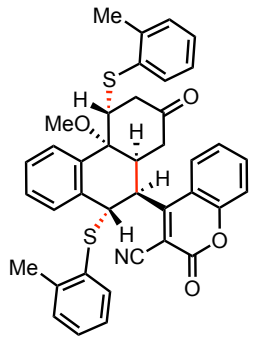


VWD: Signal A, 254 nm Results

RT	Area %
21.51	92.77
36.88	7.23

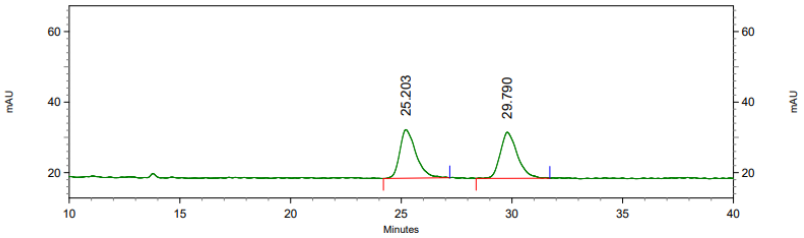
HPLC Data: 93.0 : 7.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 21.51 min (major), t_R = 36.88 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-5,10-bis(o-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4o)



Yellow solid; **m.p.**: 148 – 149 °C; **Yield**: 38 mg, 59%; **R_f**: 0.48 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –24.0 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.14 – 8.12 (m, 1H, Ar*H*), 7.85 – 7.83 (m, 1H, Ar*H*), 7.71 – 7.67 (m, 1H, Ar*H*), 7.57 – 7.54 (m, 1H, Ar*H*), 7.51 – 7.47 (m, 2H, Ar*H*), 7.44 – 7.35 (m, 3H, Ar*H*), 7.25 – 7.17 (m, 3H, Ar*H*), 7.04 – 7.00 (m, 2H, Ar*H*), 6.93 – 6.91 (m, 1H, Ar*H*), 6.75 – 6.72 (m, 1H, Ar*H*), 6.04 (d, *J* = 10.5 Hz, 1H, –C*H*SAr), 5.15 – 5.13 (dd, *J* = 11.0, 3.5 Hz, 1H, –C*H*CHSAr), 4.73 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.23 (s, 3H, –OCH_3), 3.21 – 3.17 (m, 1H, –C*H*CH_2–), 2.45 (s, 3H, ArCH_3), 2.42 – 2.30 (m, 4H, –CHCH_2–), 2.13 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.8, 163.3, 157.0, 153.4, 142.4, 137.3, 136.1, 135.8, 135.1, 132.9, 131.2, 131.0, 130.9, 130.8, 130.5, 130.0, 129.4, 128.9, 127.5, 127.0, 126.9, 126.1, 125.8, 125.6, 118.3, 118.0, 115.0, 102.0, 77.6, 77.4, 50.4, 48.4, 44.9, 44.7, 42.5, 41.4, 40.4, 21.1, 20.9; **HRMS** (ESI, m/z) calcd for $C_{39}H_{33}KNO_4S_2^+$ $[M+K]^+$: 682.1483, found: 682.1490.

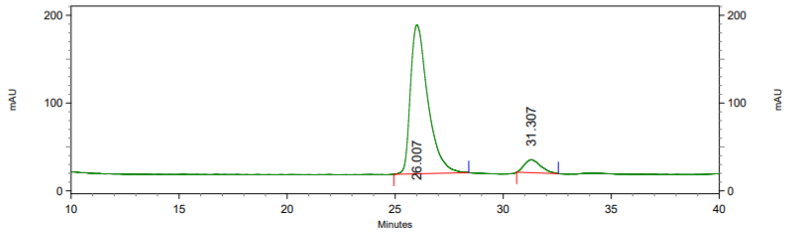
Sample ID: VS 189
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30



VWD: Signal A, 254 nm Results

RT	Area %
25.20	49.98
29.79	50.02

Sample ID: VS 255
Acq. Method: Chiralpak IF column, Flow rate: 1.0 mL/min, Hexane : IPA = 70 : 30

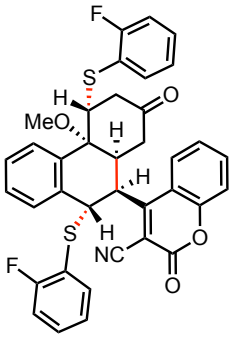


VWD: Signal A, 254 nm Results

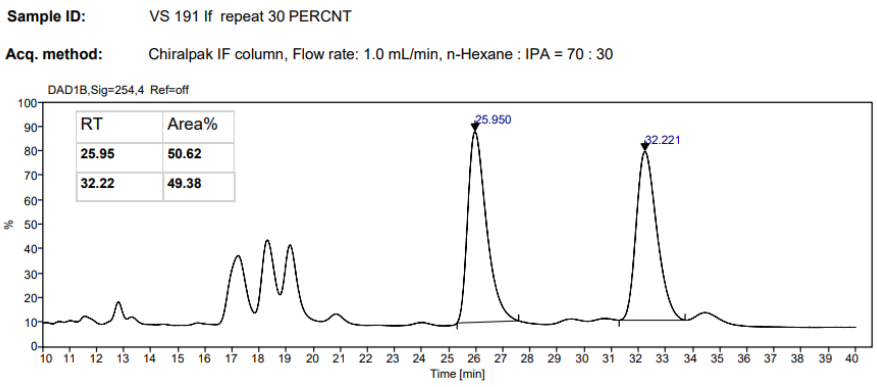
RT	Area %
26.01	92.45
31.31	7.55

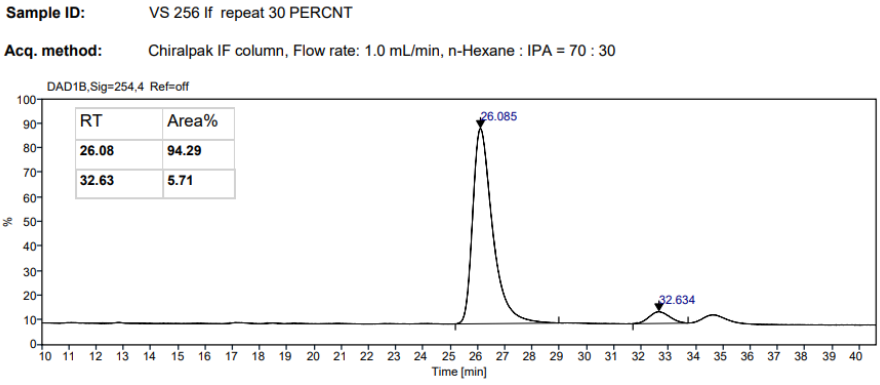
HPLC Data:; **er**: 92.5 : 7.5; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 26.01 min (major), t_R = 31.31 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-5,10-Bis((2-fluorophenyl)thio)-4b-methoxy-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4p)



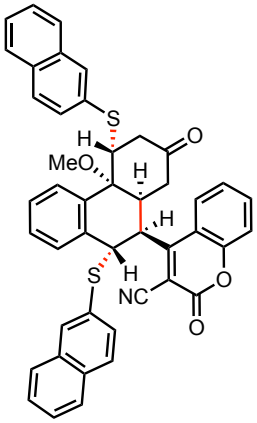
Pale yellow solid; **m.p.**: 152 – 153 °C; **Yield**: 47 mg, 72%; $\mathbf{R_f}$: 0.27 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -59.2$ (*c* 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.92 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.73 – 7.70 (m, 1H, Ar*H*), 7.59 – 7.56 (m, 1H, Ar*H*), 7.48 – 7.34 (m, 6H, Ar*H*), 7.23 – 7.18 (m, 1H, Ar*H*), 7.15 – 7.10 (m, 2H, Ar*H*), 6.98 – 6.95 (m, 1H, Ar*H*), 6.85 – 6.75 (m, 2H, Ar*H*), 6.07 (d, *J* = 11.0 Hz, 1H, –C*H*SAr), 5.06 (dd, *J* = 11.5, 3.5 Hz, 1H, –C*H*CHSAr), 4.89 (t, *J* = 4.0 Hz, 1H, –C*H*SAr), 3.23 – 3.19 (m, 1H, –C*H*CH_2–), 3.08 (s, 3H, –OCH_3), 2.47 – 2.43 (m, 1H, –CHCH_2–), 2.39 – 2.33 (m, 2H, –CHCH_2–), 2.26 – 2.21 (m, 1H, –CHCH_2–); **^{13}C{^{1}H}{^{19}F}** (125 MHz, $CDCl_3$) δ 204.3, 163.0, 157.1, 153.5, 138.1 (2C), 136.9, 135.2, 133.2, 132.0, 131.4, 130.5, 130.0, 127.6, 126.9, 125.8, 125.7, 125.1, 124.3, 118.5, 118.3, 118.1 (2C), 118.0, 116.2, 116.2, 116.0, 114.9, 102.4, 77.4, 50.2, 46.8, 44.8, 44.4, 42.3, 41.3, 40.1; **^{19}F NMR** (471 MHz, $CDCl_3$) δ –107.01, –103.51; **HRMS** (ESI, m/z) calcd for $C_{37}H_{31}F_2N_2O_4S_2^+$ $[M+NH_4]^+$: 669.1688, found: 669.1692.



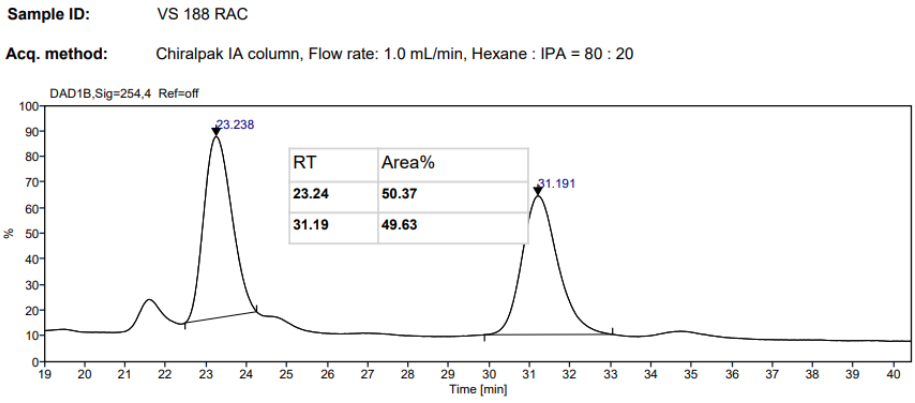


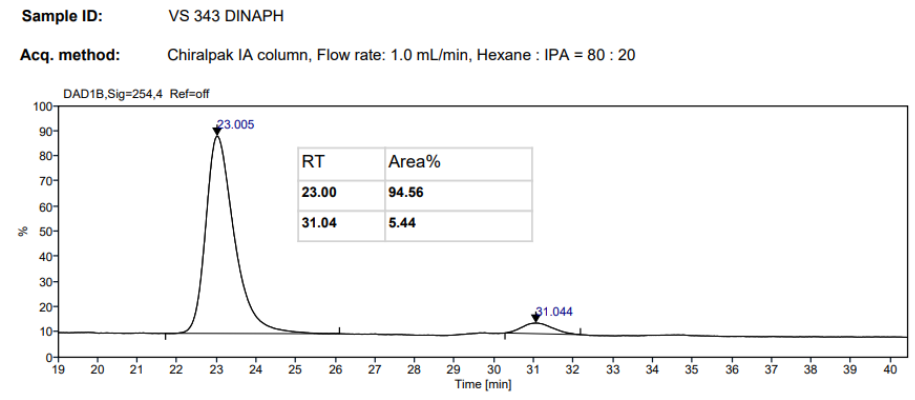
HPLC Data: 94.5 : 5.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 26.08 min (major), t_R = 32.63 min (minor).

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-5,10-bis(naphthalen-2-ylthio)-7-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (4q)



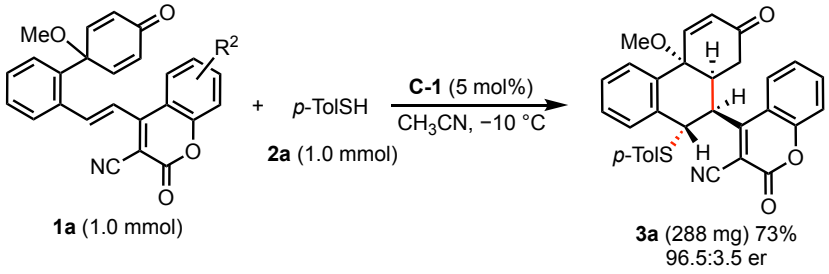
Pale yellow solid; **m.p.**: 207 – 208 °C; **Yield**: 46 mg, 64%; **R**$_f$: 0.33 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = –20.8 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 – 8.31 (m, 1H, Ar*H*), 7.91 – 7.90 (m, 1H, Ar*H*), 7.80 – 7.75 (m, 4H, Ar*H*), 7.72 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.66 – 7.60 (m, 2H, Ar*H*), 7.53 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.49 – 7.45 (m, 4H, Ar*H*), 7.41 – 7.33 (m, 5H, Ar*H*), 7.29 – 7.24 (m, 2H, Ar*H*), 7.00 (dd, *J* = 8.5, 2.0 Hz, 1H, Ar*H*), 6.07 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.07 (dd, *J* = 11.5, 2.5 Hz, 1H, –C*H*CHSAr), 4.68 (t, *J* = 4.0 Hz, 1H, –C*H*SAr), 3.14 – 3.09 (m, 1H, –C*H*CH$_2$–), 2.78 (s, 3H, –OC*H*$_3$), 2.52 – 2.48 (m, 1H, –CHC*H*$_2$–), 2.43 – 2.28 (m, 3H, –CHC*H*$_2$–); **^{13}C{^{1}H}** (125 MHz, $CDCl_3$) δ 204.5, 163.1, 157.1, 153.5, 137.4, 136.8, 135.1, 134.9, 133.8, 133.3 (2C), 133.0, 132.4, 131.5, 130.8, 129.8, 129.2, 128.9, 128.4, 127.8 (2C), 127.6 (2C), 127.4 (2C), 127.3, 127.1, 126.9, 126.9, 126.7, 125.8, 125.7, 118.2 (2C), 115.1, 102.5, 77.3, 49.8, 49.0, 45.0, 44.6, 42.1, 40.4, 40.3; **HRMS** (ESI, m/z) calcd for $C_{45}H_{37}N_2O_4S_2^+$ $[M+NH_4]^+$: 733.2189, found: 733.2198.





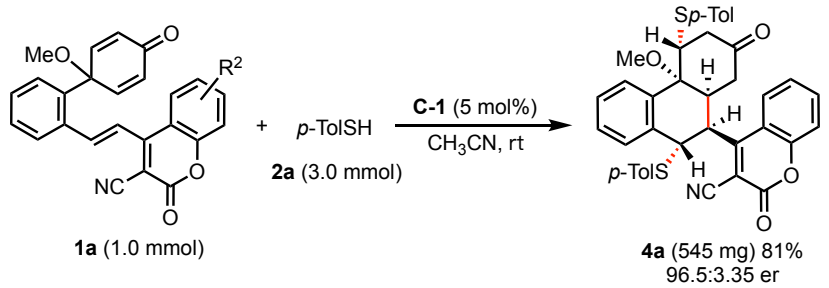
HPLC Data: dr: 94.5 : 5.5 er; Daicel Chiralpak IA column, *n*-hexane : *i*-PrOH = 4 : 1, Flow rate: 1.0 mL/min; 254 nm, t_R = 23.00 min (major), t_R = 31.04 min (minor).

S4.10. Procedure for scale up synthesis of 3a:



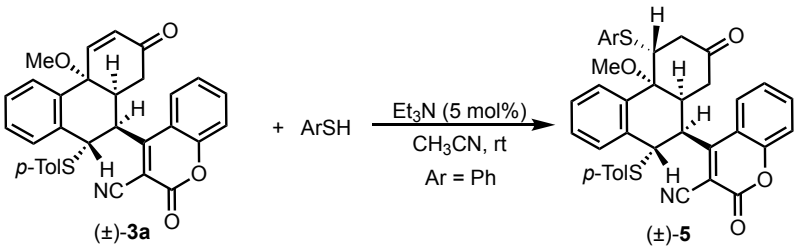
In a 25 mL reaction tube with a magnetic stirring bar, substrate **1a** (395mg, 1.0 mmol, 1.0 eq.) and **C-1** (5 mol%) were stirred in CH_3CN (10.0 mL) at −10 °C (maintained in a methanol bath). After stirring for 5 minutes, *p*-thiocresol **2a** (373mg, 1.0 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 12 hours. Then the excess of solvent evaporate under high vacuum and the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 3 : 2 as eluent) to afford the product **3a**.

S4.11. Procedure for scale up synthesis of 4a:



In a 25 mL reaction tube with a magnetic stirring bar, substrate **1a** (395mg, 1.0 mmol, 1.0 eq.) and **C-1** (5 mol%) were stirred in CH_3CN (10.0 mL) at room temprature. After stirring for 5 minutes, substrate *p*-thiocresol **2a** (373mg, 3.0 mmol, 3.0 eq.) was added, and the stirring was continued at the same temperature for 24 hours. Then the excess of solvent evaporate under high vacumm and the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 7 : 3 as eluent) to afford the product **4a**.

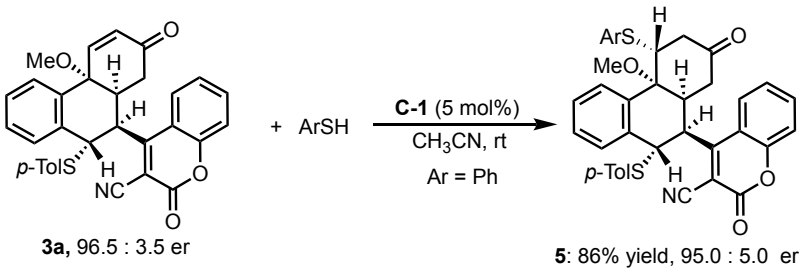
S4.12. Procedure for the synthesis of (±)-5:



In a 10 mL reaction tube with a magnetic stirring bar, the product (±)-**3a** (26 mg, 0.05 mmol, 1.0 eq.) and Et_3N (20 mol%, 1.4 uL) were stirred in CH_3CN (0.5 mL) at room temperature.

After stirring for 5 minutes, thiophenol **2a** (5.1 uL, 0.05 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 12 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 7 : 3 as eluent) to afford the product (±)-**5**.

S4.13. Procedure for the synthesis of 5:

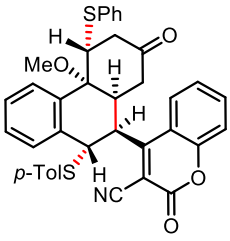


3a, 96.5 : 3.5 er

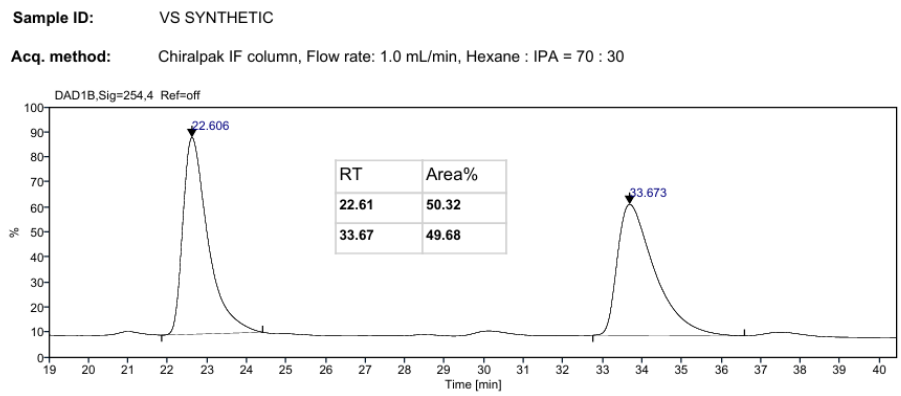
5: 86% yield, 95.0 : 5.0 er

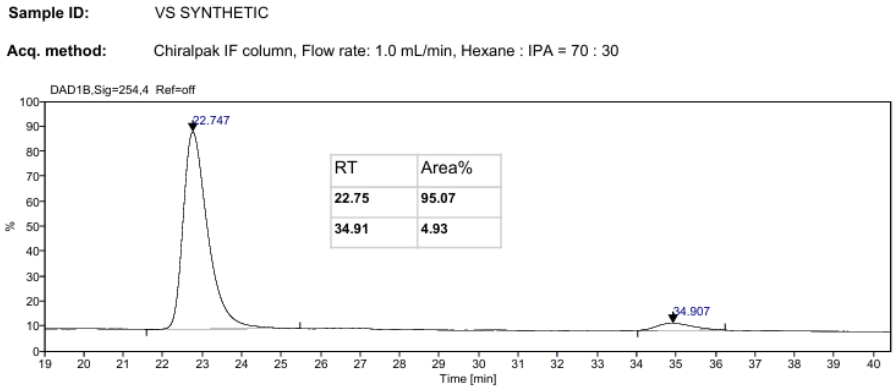
In a 10 mL reaction tube with a magnetic stirring bar, enantiopure product **3a** with 96:4 er (26 mg, 0.05 mmol, 1.0 eq.) and **C-1** (5 mol%, 1.6 mg) were stirred in CH_3CN (0.5 mL) at room temperature. After stirring for 5 minutes, thiophenol **2a** (5.1 uL, 0.05 mmol, 1.0 eq.) was added, and the stirring was continued at the same temperature for 24 hours. Then the crude product was directly purified by silica gel column chromatography (hexane: ethyl acetate = 7 : 3 as eluent) to afford the product **5**.

4-[(4b*R*,5*R*,8a*S*,9*S*,10*S*)-4b-Methoxy-7-oxo-5-(phenylthio)-10-(*p*-tolylthio)-4b,5,6,7,8,8a,9,10-octahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (5)



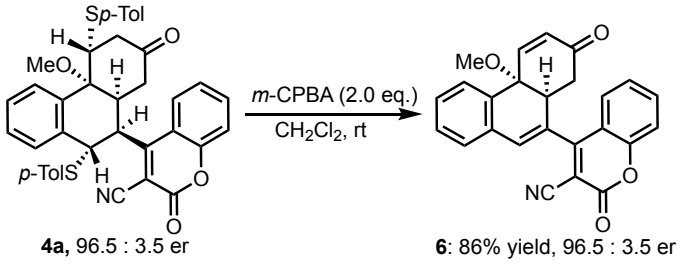
White solid; **m.p.**: 172 – 173 °C; **Yield**: 27 mg, 86%; $\mathbf{R_f}$: 0.41 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -40.8$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.92 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.76 – 7.71 (m, 1H, Ar*H*), 7.59 – 7.55 (m, 1H, Ar*H*), 7.48 – 7.33 (m, 9H, Ar*H*), 6.84 – 6.79 (m, 4H, Ar*H*), 5.96 (d, *J* = 11.5 Hz, 1H, –C*H*SAr), 5.04 (dd, *J* = 11.5, 3.0 Hz, 1H, –C*H*CHSAr), 4.62 (t, *J* = 3.5 Hz, 1H, –C*H*SAr), 3.14 – 3.07 (m, 1H, –C*H*CH_2–), 2.98 (s, 3H, –OCH_3), 2.49 – 2.45 (m, 1H, –CHCH_2–), 2.39 – 2.37 (m, 1H, –CHCH_2–), 2.34 – 2.29 (m, 2H, –CHCH_2–), 2.23 (s, 3H, ArCH_3); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 204.6, 163.2, 157.2, 153.6, 139.8, 137.5, 136.3 (2C), 135.4 (2C), 135.2, 133.3, 131.8, 130.7, 129.8, 129.6 (2C), 129.5 (2C), 128.9, 127.3, 126.8, 126.7, 125.9, 125.8, 118.3, 118.1, 115.0, 102.6, 77.4, 49.9, 49.2, 44.9, 44.5, 42.1, 40.6, 40.2, 21.2; **HRMS** (ESI, m/z) calcd for $C_{38}H_{35}N_2O_4S_2^+$ $[M+NH_4]^+$: 647.2033, found: 647.2054.





HPLC Data: 95.0 : 5.0 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 22.75 min (major), t_R = 34.91 min (minor).

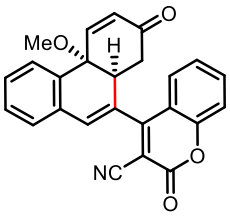
S4.14. Procedure for the synthesis of 6:



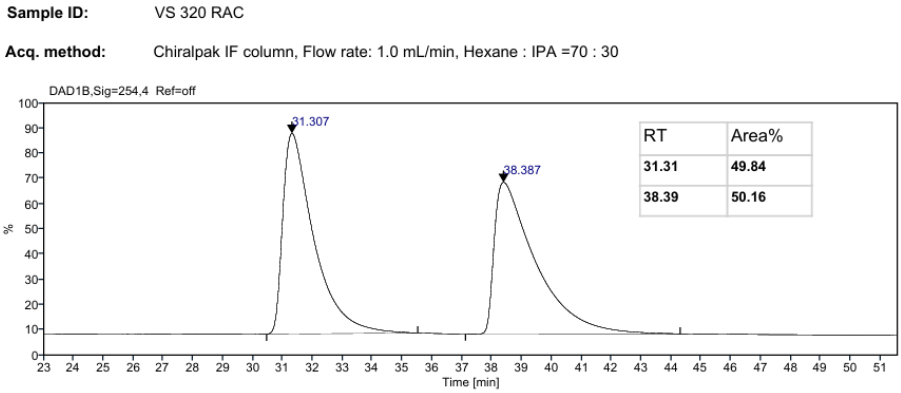
4a, 96.5 : 3.5 er **6**: 86% yield, 96.5 : 3.5 er

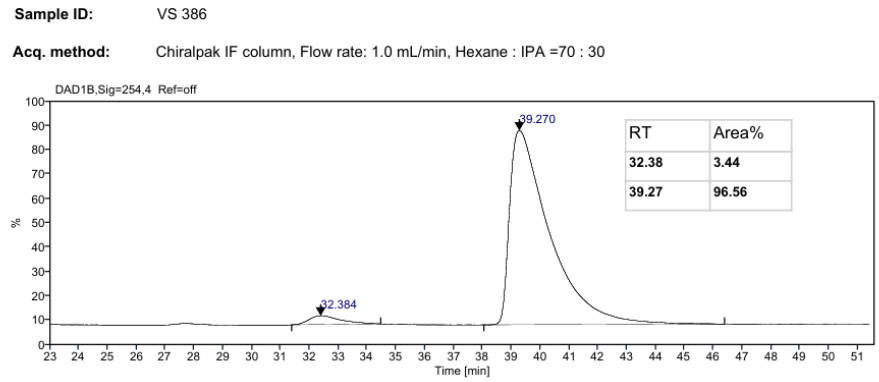
In a 10 mL reaction tube with a magnetic stirring bar, enantiopure product **4a** with 97:3 er (32 mg, 0.05 mmol, 1.0 eq.) was dissolved in DCM (0.5 mL). To this, *m*-CPBA (17 mg, 0.1mmol, 2.0 eq.) was added at room temperature. The mixture was stirred at the same temperature for 2 hours. After completion of the reaction, saturated solution of $NaHCO_3$ was added, and the reaction mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The organic phase was filtered and concentrated under vacuum to yield the crude product, which was purified by column chromatography (silica gel, hexane : ethyl acetate = 7 : 3 as eluent) to afford final product **6**.

4-[(4b*R*,8a*S*)-4b-Methoxy-7-oxo-4b,7,8,8a-tetrahydrophenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (6)



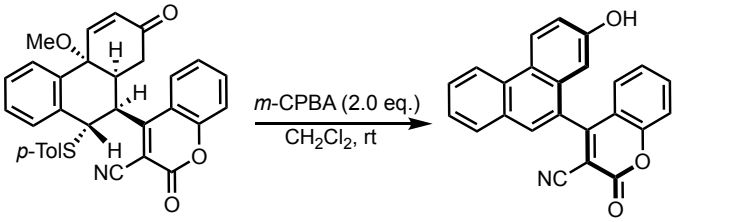
White solid; **m.p.**: 130 – 131 °C; **Yield**: 17 mg, 86%; **R_f**: 0.15 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30}$ = 35.2 (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 – 8.18 (m, 1H, Ar*H*), 7.71 – 7.68 (m, 1H, Ar*H*), 7.60 (d, *J* = 10.5 Hz, 1H, –C*H*=CHC(O)), 7.51 – 7.47 (m, 1H, Ar*H*), 7.44 – 7.36 (m, 5H, Ar*H*), 6.92 (s, 1H, ArC*H*=), 6.18 (dd, *J* = 10.5, 1.0 Hz, 1H, –CH=C*H*C(O)), 3.43 – 3.39 (m, 1H, –C*H*CH_2–), 3.18 (s, 3H, –OCH_3), 2.61 (dd, *J* = 17.0, 3.5 Hz, 1H, –CHCH_2–), 2.46 – 2.40 (m, 1H, –CHCH_2–); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 196.2, 162.4, 157.0, 153.9, 147.3, 135.4, 133.3, 131.5, 130.5, 130.3, 129.5, 129.2 (2C), 129.1 (2C), 125.8 (2C), 118.3, 117.7, 113.6, 101.9, 76.1, 51.1, 46.0, 38.6; **HRMS** (ESI, m/z) calcd for $C_{25}H_{21}N_2O_4^+$ $[M+NH_4]^+$: 413.1496, found: 413.1491.





HPLC Data: 96.5 : 3.5 er; Daicel Chiralpak IF column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 32.38 min (minor), t_R = 39.27 min (major).

S4.15. Procedure for the synthesis of 7:

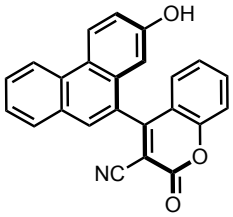


3a, 96.5 : 3.5 er

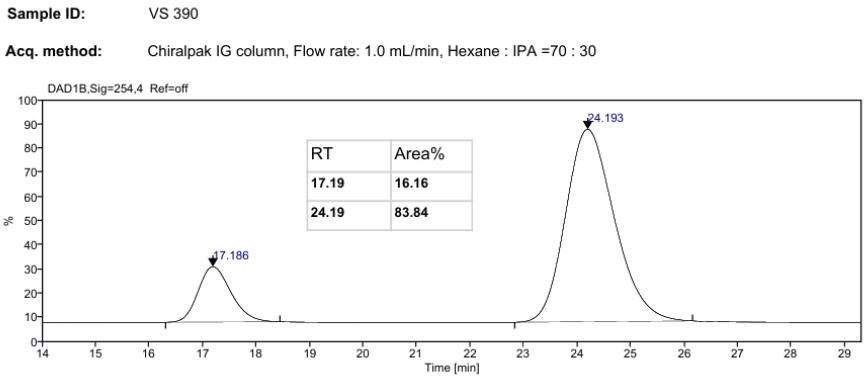
7: 88% yield, 87.0 : 13.0 er
>99.5 :0.5 er after crystallization

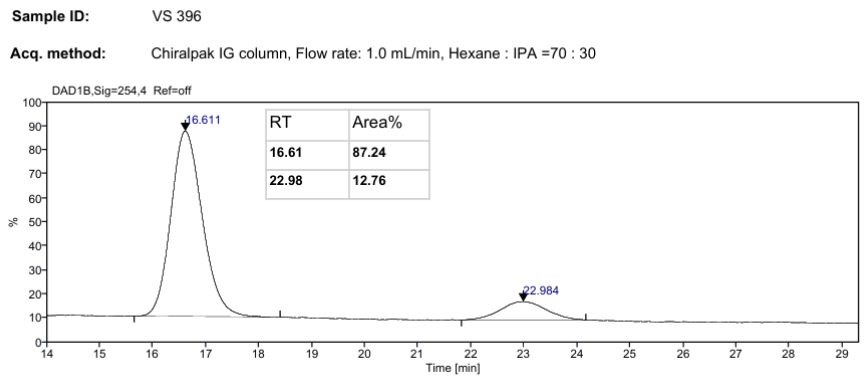
In a 10 mL reaction tube with a magnetic stirring bar, enantiopure product **4a** with 96:4 er (26 mg, 0.05 mmol, 1.0 eq.) was dissolved in DCM (0.5 mL). To this, *m*-CPBA (17 mg, 0.1 mmol, 2.0 eq.) was added at room temperature. The mixture was stirred at the same temperature for 2 hours. After completion of the reaction, saturated solution of $NaHCO_3$ was added, and the reaction mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The organic phase was filtered and concentrated under vacuum to yield the crude product, which was purified by column chromatography (silica gel, hexane : ethyl acetate = 7 : 3 as eluent) to afford final product **7**. For HPLC analysis the enantiomer of the **7** was synthesized by using poseudoenantiomeric catalyst **C-5**.

4-[7-Hydroxyphenanthren-9-yl]-2-oxo-2*H*-chromene-3-carbonitrile (7)

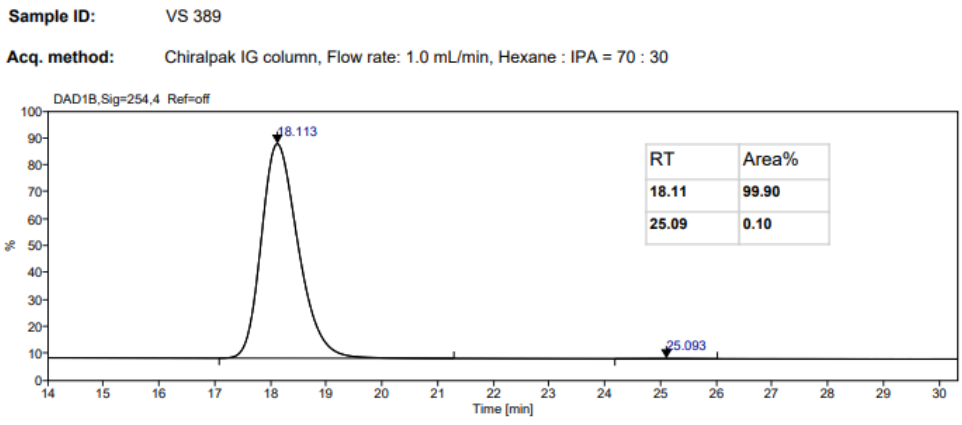


Yellow solid; **m.p.**: 270 – 271 °C; **Yield**: 16 mg, 88%; $\mathbf{R_f}$: 0.19 (hexane : ethyl acetate = 7 : 3); $[\alpha]_D^{30} = -23.2$ (*c* 0.25, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.66 – 8.63 (m, 2H, Ar*H*), 7.93 – 7.91 (m, 1H, Ar*H*), 7.79 (s, 1H, Ar*H*), 7.77 – 7.74 (m, 1H, Ar*H*), 7.69 – 7.61 (m, 2H, Ar*H*), 7.50 – 7.48 (m, 1H, Ar*H*), 7.27 – 7.25 (m, 1H, Ar*H*), 7.17 – 7.11 (m, 2H, Ar*H*), 6.80 (d, *J* = 2.5 Hz, 1H, Ar*H*), 5.91 (br s, –OH); **^{13}C{^{1}H} NMR** (125 MHz, $CDCl_3$) δ 164.6, 157.3, 155.3, 153.9, 135.6, 131.5, 130.3, 129.6, 129.5, 129.4, 129.0, 128.8, 127.7, 126.7, 125.7, 125.5, 124.9, 122.4, 118.8, 118.2, 117.7, 113.2, 109.5, 103.6; **HRMS** (ESI, m/z) calcd for $C_{24}H_{14}NO_3^+$ $[M+H]^+$: 364.0968, found: 364.0965.





HPLC Data: 87.0 : 13.0 er; Daicel Chiralpak IG column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 16.61 min (major), t_R = 22.98 min (minor).



HPLC Data after crystallization: >99.5 : 0.5 er; Daicel Chiralpak IG column, *n*-hexane : *i*-PrOH = 7 : 3, Flow rate: 1.0 mL/min; 254 nm, t_R = 18.11 min (major), t_R = 25.09 min (minor).

S5. Single Crystal X-Ray Data and ORTEP Representations:

Single Crystal X-Ray Data of 3a.

Single crystals of $C_{31}H_{25}N_2O_4S$ (**3a**) were obtained in a hexane : chloroform (3 : 1) solution. A suitable crystal was selected and mounted on a Bruker D8 venture diffractometer with monochromatic MoKα (λ = 0.71073). The crystal was kept at 298.0 K during data collection. The structure was solved and refined using Apex 4.

Crystal data for 3a	
Identification code	mo_MONO_VS_0m_a
Empirical formula	$C_{31}H_{25}N_2O_4S$
Formula weight	521.59 g/moL
Temperature/K	298.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.664(4)
b/Å	13.778(6)
c/Å	19.369(8)
α/°	90
β/°	90
γ/°	90
Volume/$Å^3$	2579.1(18)
Z	4
$\rho_{calc}g/cm^3$	1.343
μ/mm^{-1}	0.166
F(000)	1092.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.206 to 49.426
Index ranges	$-11 \leq h \leq 11$, $-16 \leq k \leq 16$, $-22 \leq l \leq 22$
Reflections collected	16029
Independent reflections	4296 [R_{int} = 0.0269, R_{sigma} = 0.0265]
Data/restraints/parameters	4296/0/345
Goodness-of-fit on F^2	1.127
Final R indexes [I>=2σ (I)]	R_1 = 0.0574, wR_2 = 0.1202
Final R indexes [all data]	R_1 = 0.0729, wR_2 = 0.1360
Largest diff. peak/hole / e $Å^{-3}$	0.29/-0.39
Flack parameter	0.01(3)

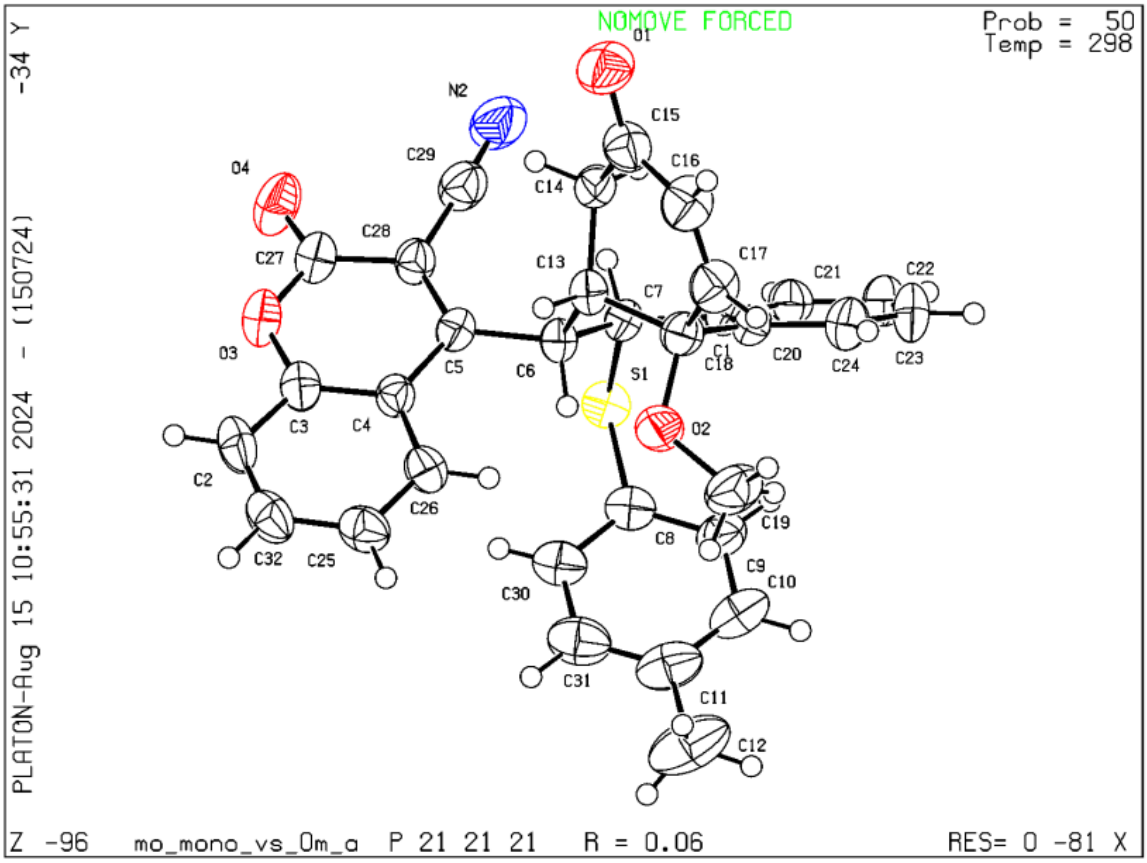


Figure S1: ORTEP representation of the crystal structure of compound **3a** (CCDC: 2382016). Thermal ellipsoids are drawn at 50% probability level.

Single Crystal X-Ray Data of 4a.

Single crystals of $C_{39}H_{33}NO_4S_2$ (**4a**) were obtained in a hexane : chloroform (3 : 1) solution. A suitable crystal was selected and mounted on a Bruker D8 venture diffractometer with monochromatic CuKα (λ = 1.54178). The crystal was kept at 200.0 K during data collection. The structure was solved and refined using Apex 4.

Crystal data for 4a	
Identification code	cu_VS_168_0m_a
Empirical formula	$C_{39}H_{33}NO_4S_2$
Formula weight	643.78 g/moL
Temperature/K	200.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	12.190(2)
b/Å	16.147(3)
c/Å	16.952(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3336.7(11)

Z	4
$\rho_{calc}g/cm^3$	1.282
μ/mm^{-1}	1.781
F(000)	1352.0
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.56 to 134.982
Index ranges	$-14 \leq h \leq 14$, $-19 \leq k \leq 19$, $-18 \leq l \leq 20$
Reflections collected	33778
Independent reflections	5923 [R_{int} = 0.0817, R_{sigma} = 0.0498]
Data/restraints/parameters	5923/4/419
Goodness-of-fit on F^2	1.066
Final R indexes [I>=2σ (I)]	R_1 = 0.0381, wR_2 = 0.1015
Final R indexes [all data]	R_1 = 0.0457, wR_2 = 0.1053
Largest diff. peak/hole / e $Å^{-3}$	0.29/-0.20
Flack parameter	0.10(2)

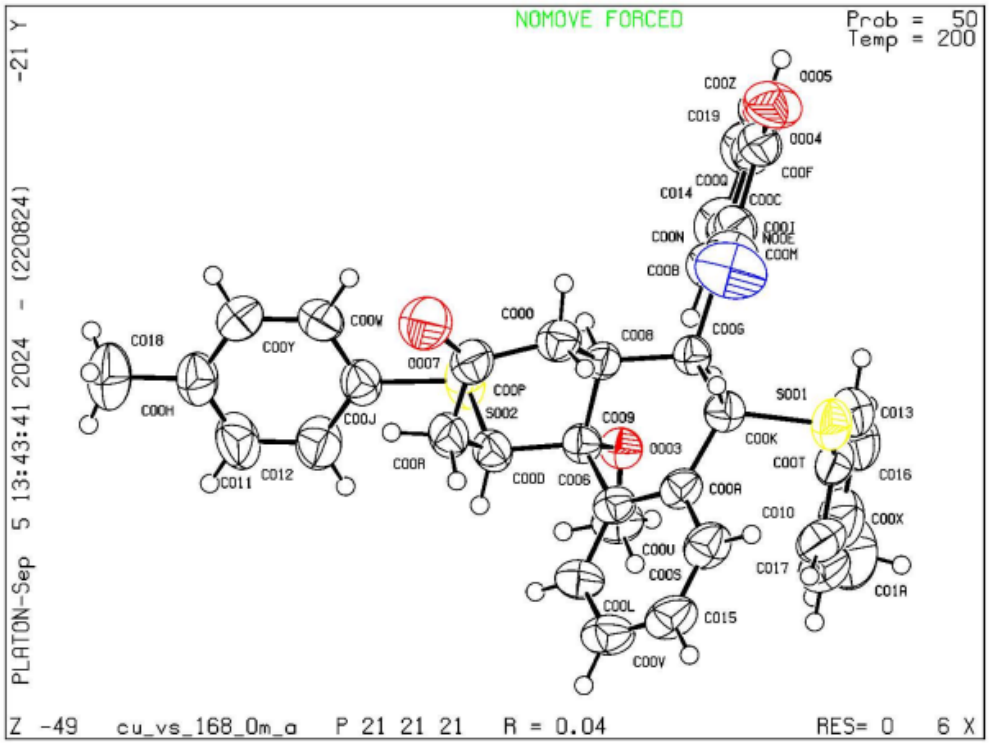


Figure S2: ORTEP representation of the crystal structure of compound **4a** (CCDC 2382203). Thermal ellipsoids are drawn at 50% probability level.

Single Crystal X-Ray Data of 7.

Single crystals of $C_{2.74}H_{1.49}N_{0.11}O_{0.34}$ (**7**) were obtained in a hexane : chloroform (3 : 1) solution. A suitable crystal was selected and mounted on a Bruker D8 venture diffractometer with monochromatic MoKα (λ = 0.71073). The crystal was kept at 100.0 K during data collection. The structure was solved and refined using Apex 4.

Crystal data for 14	
Identification code	mo_VS_389_0m_a
Empirical formula	$C_{2.74}H_{1.49}N_{0.11}O_{0.34}$
Formula weight	41.53 g/moL
Temperature/K	100.0.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	19.7206(8)
b/Å	9.0822(3)
c/Å	19.9389(8)
α/°	90
β/°	103.2230(10)
γ/°	90
Volume/Å^3	3476.5(2)
Z	70
ρ_{calc}g/cm^3	1.388
μ/mm^{-1}	0.092
F(000)	1504.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.248 to 56.55
Index ranges	$-24 \leq h \leq 23$, $-9 \leq k \leq 12$, $-25 \leq l \leq 26$
Reflections collected	21711
Independent reflections	13733 [R_{int} = 0.0663, R_{sigma} = 0.1040]
Data/restraints/parameters	13733/1/1014
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0892, wR_2 = 0.2273
Final R indexes [all data]	R_1 = 0.1161, wR_2 = 0.2732
Largest diff. peak/hole / e Å^{-3}	0.54/-0.44
Flack parameter	-1.4(9)

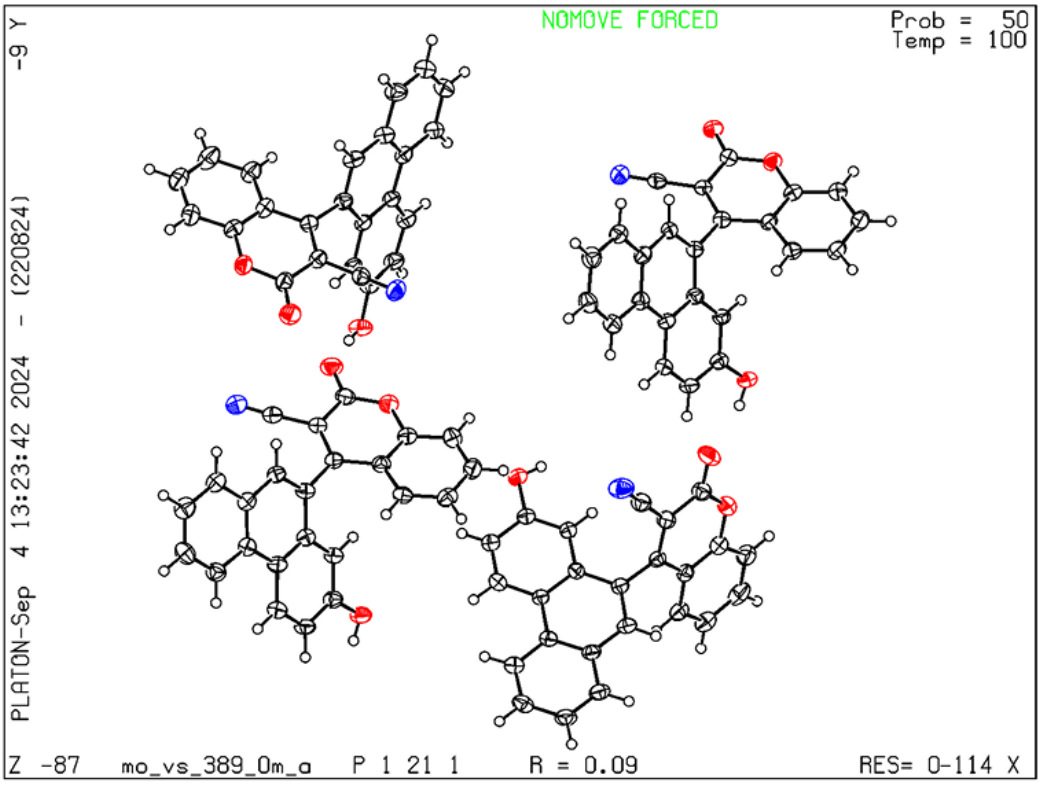


Figure S6: ORTEP representation of the crystal structure of compound **7** (CCDC: 2382041). Thermal ellipsoids are drawn at 50% probability level.

S6. References:

1. W. Yang and D.-M. Du, Highly enantioselective Michael addition of nitroalkanes to chalcones using chiral squaramides as hydrogen bonding organocatalysts, *Org. Lett*., 2010, **12**, 5450-5453.
2. C. Didaskalou, J. Kupai, L. Cseri, J. Barabas, E. Vass, T. Holtzl and G. Szekely, Membrane-grafted asymmetric organocatalyst for an integrated synthesis–separation platform, *ACS Cat.,* 2018, **8**, 7430-7438.
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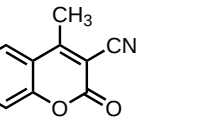
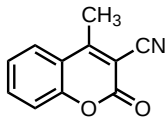
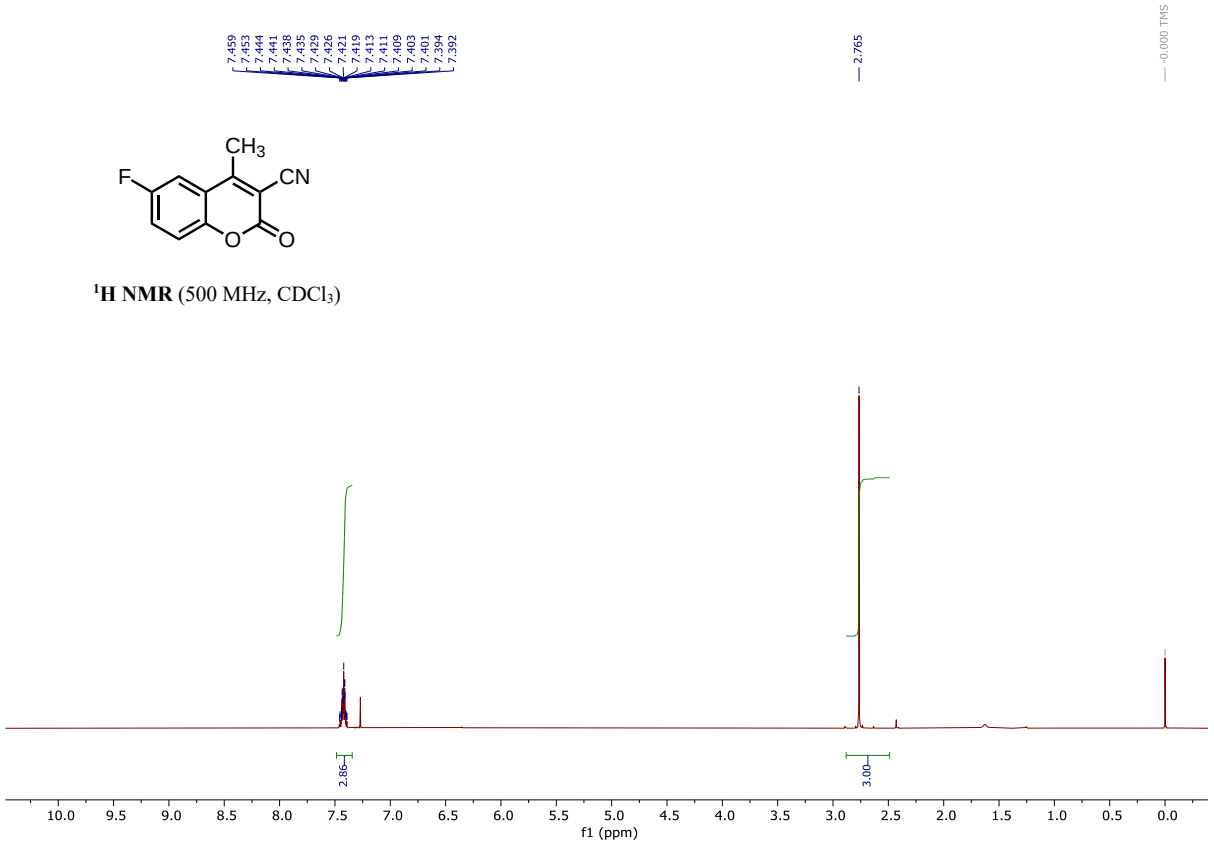
S7. NMR Spectra:



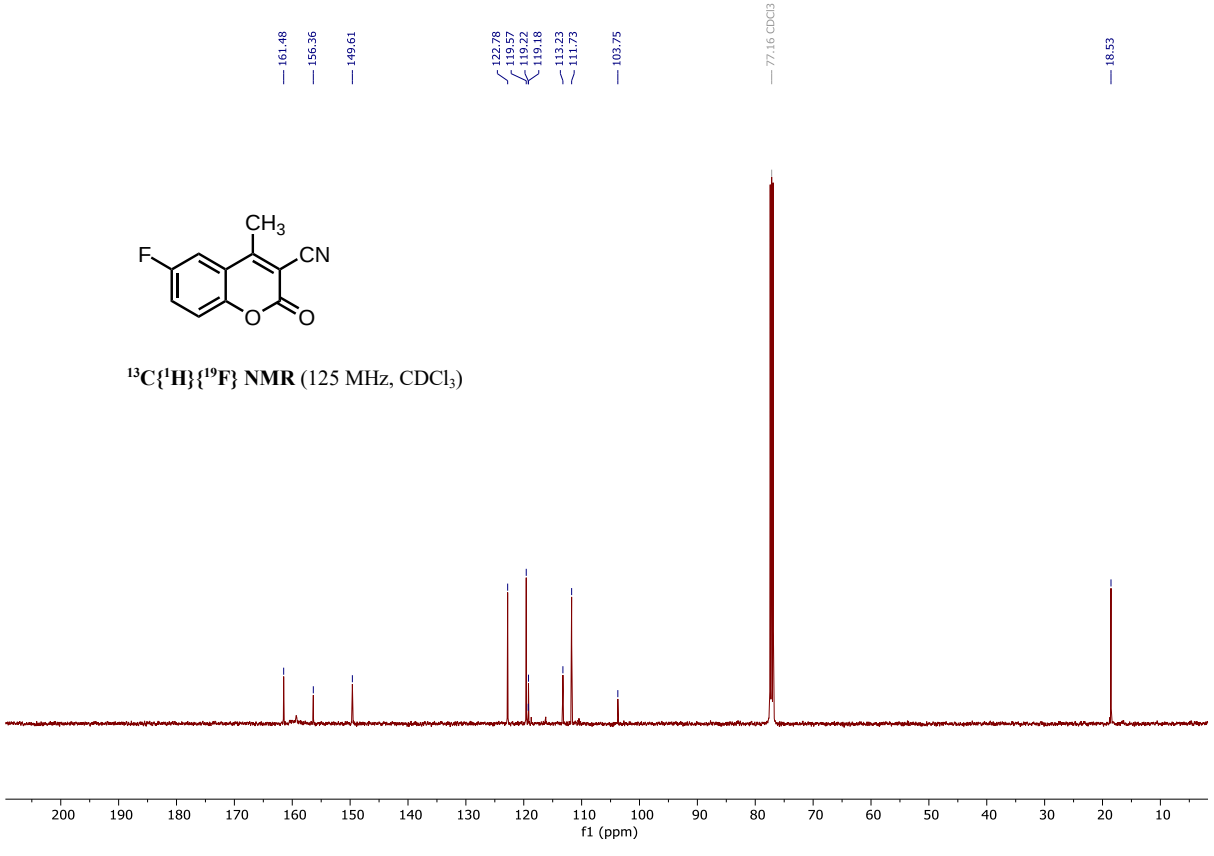
^{1}H NMR (500 MHz, DMSO-d_6)



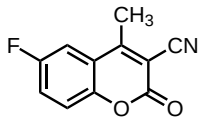
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)



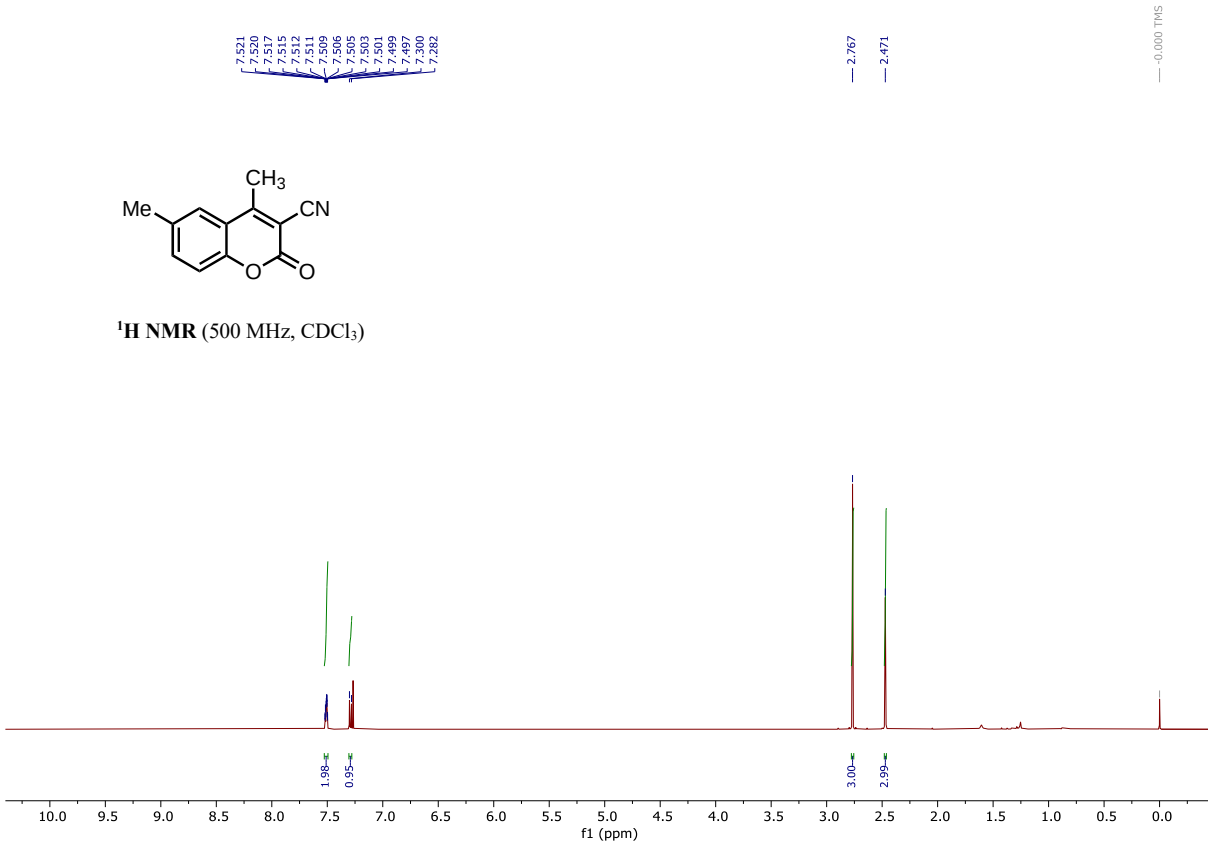
^{1}H NMR (500 MHz, $CDCl_3$)



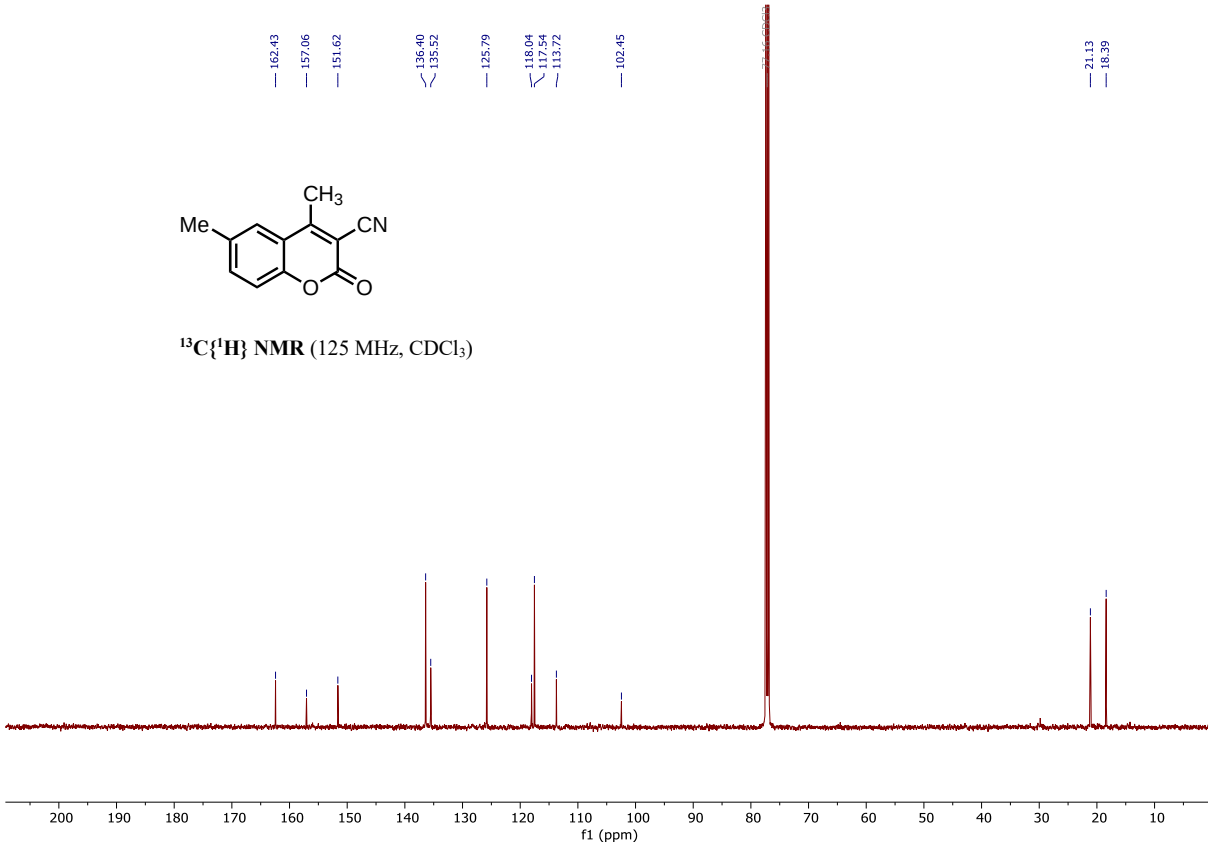
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



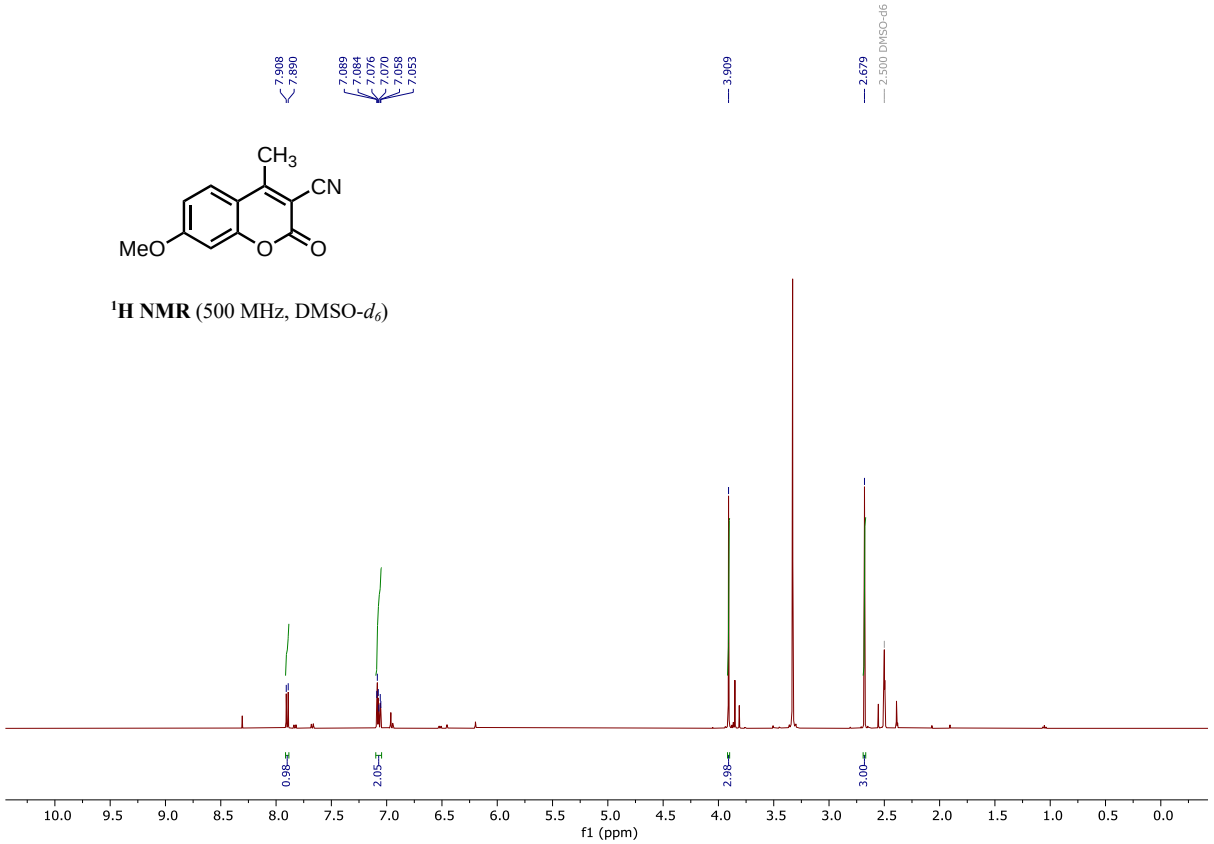
^{19}F NMR (471 MHz, $CDCl_3$)



^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



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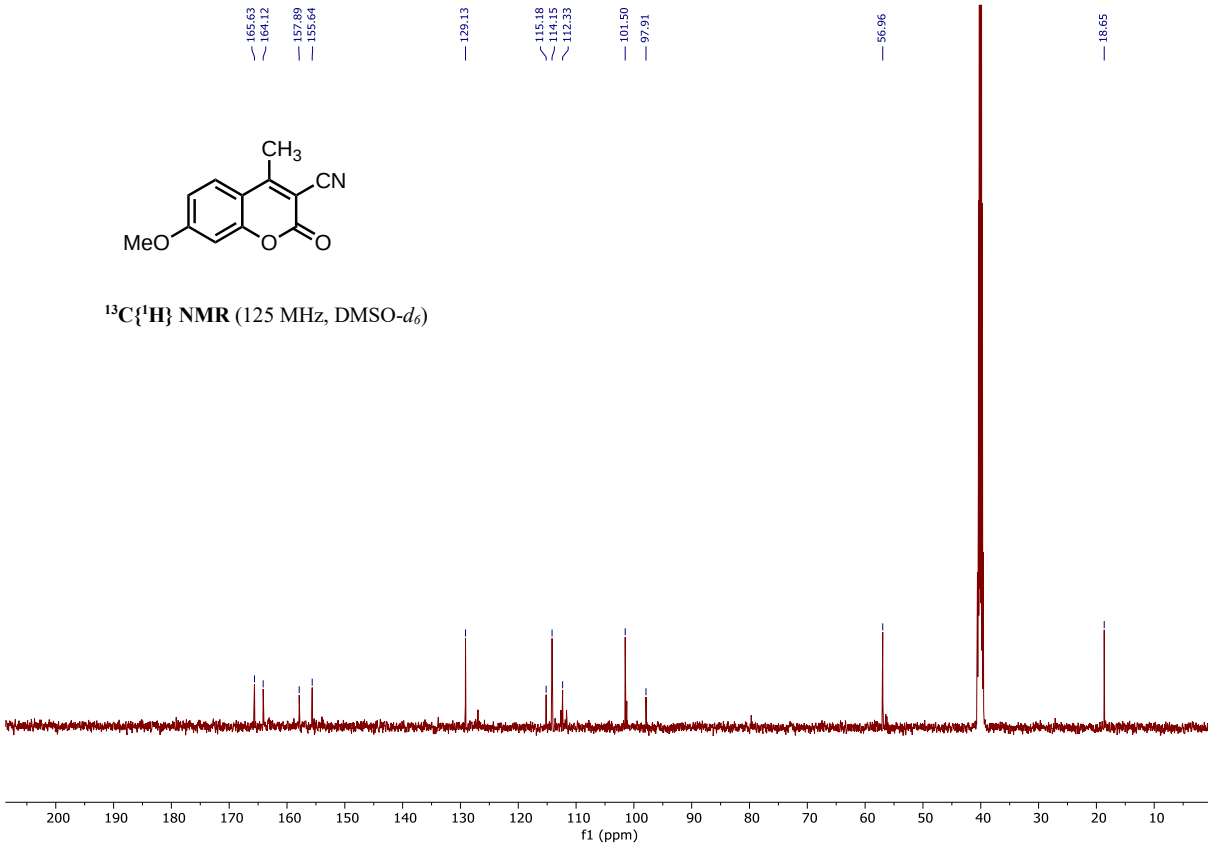

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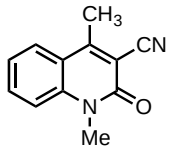

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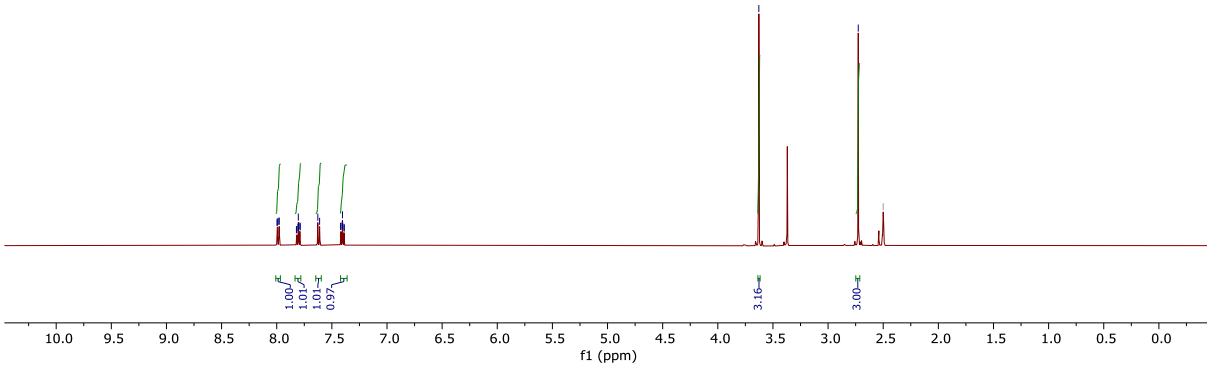
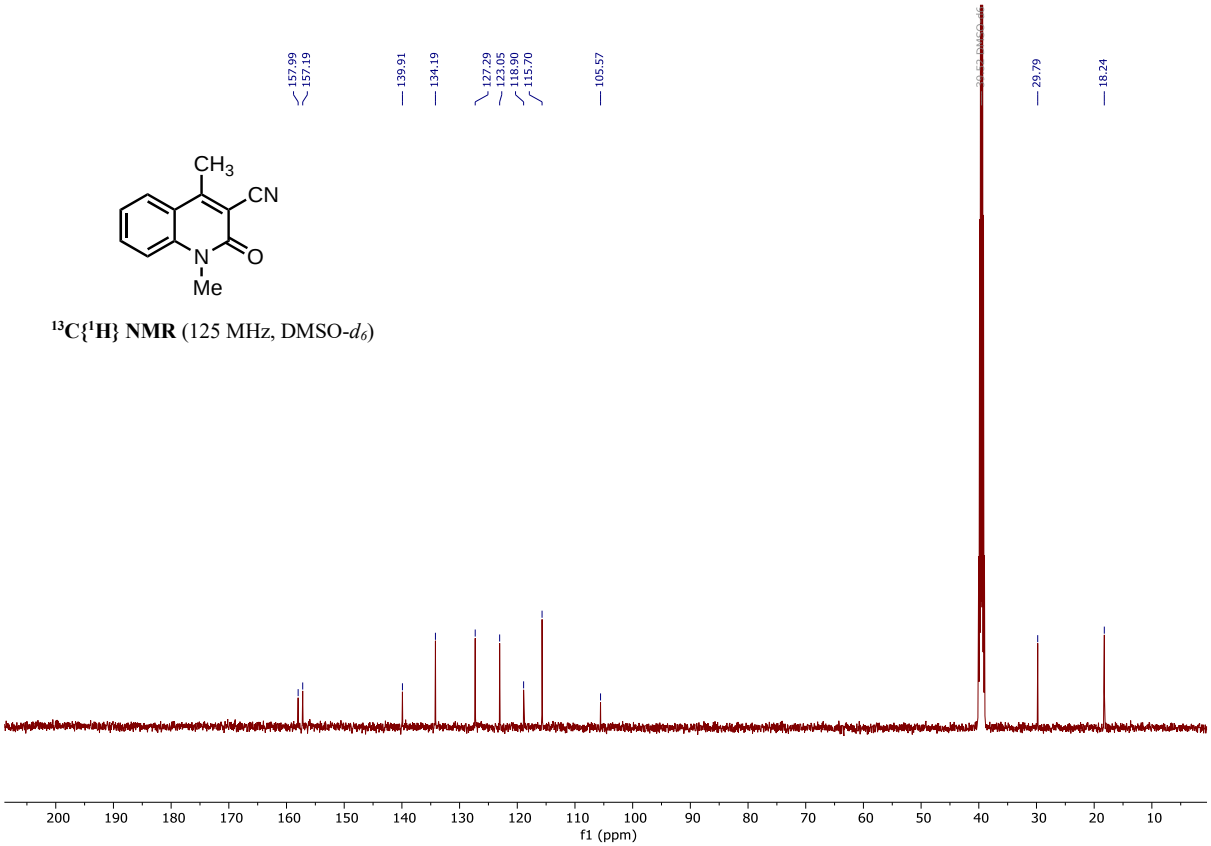
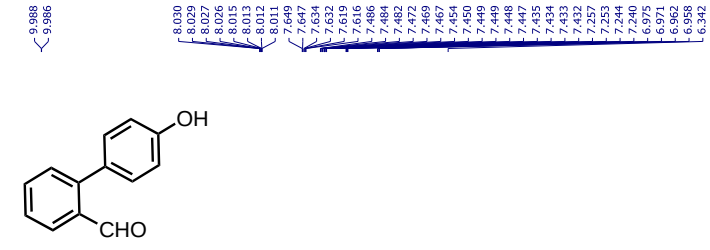


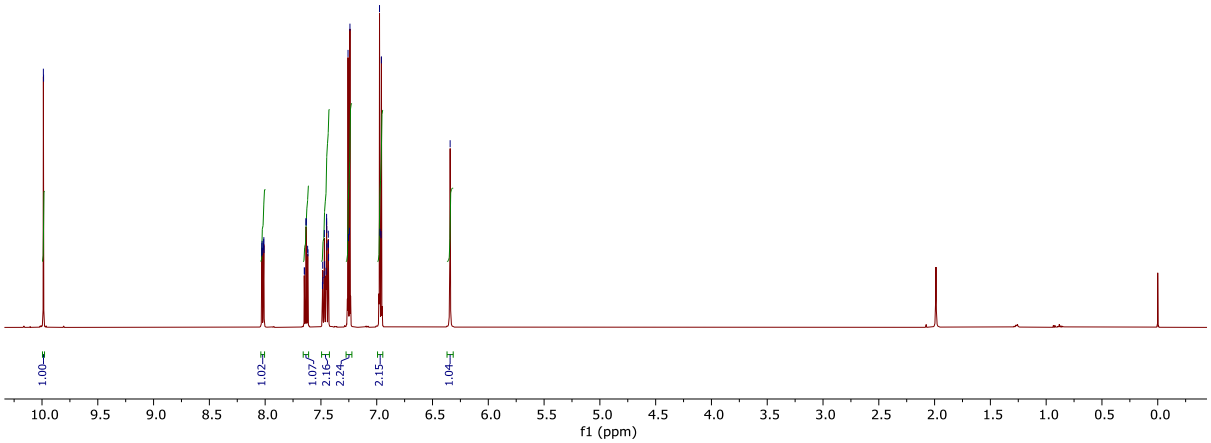


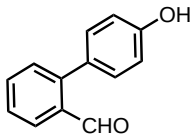
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)



Ia

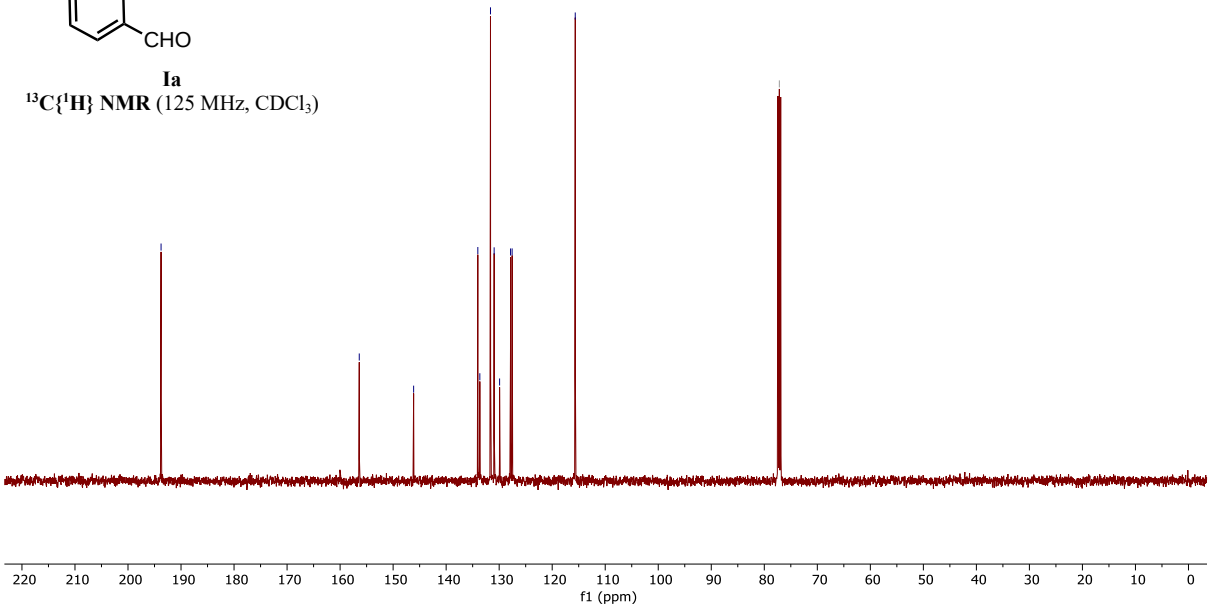
^{1}H NMR (500 MHz, $CDCl_3$)

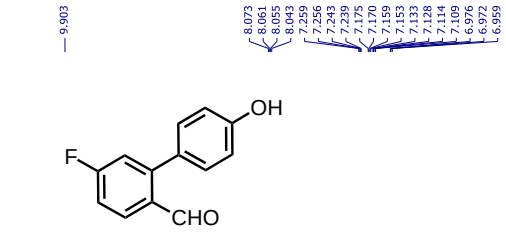




Ia

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)





Ib

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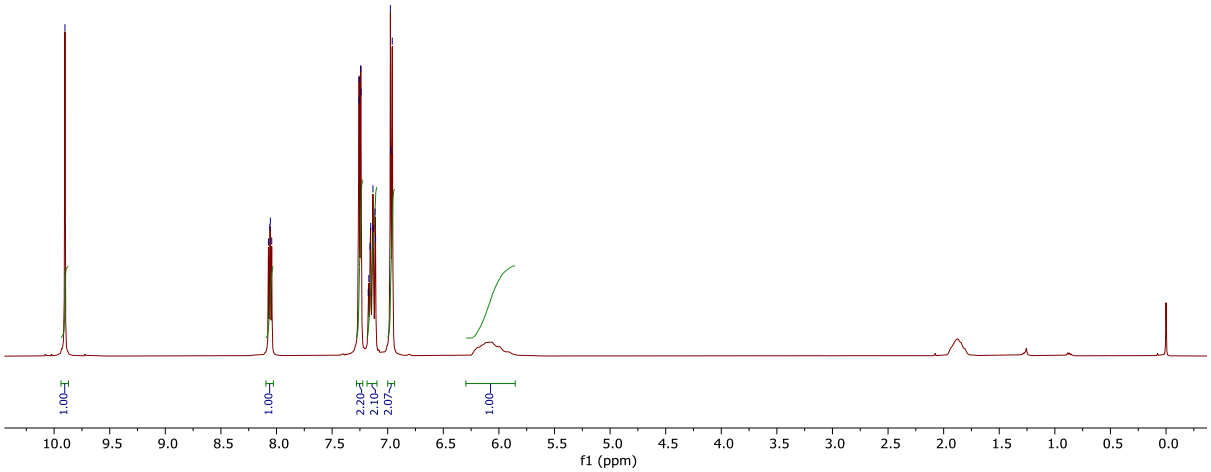

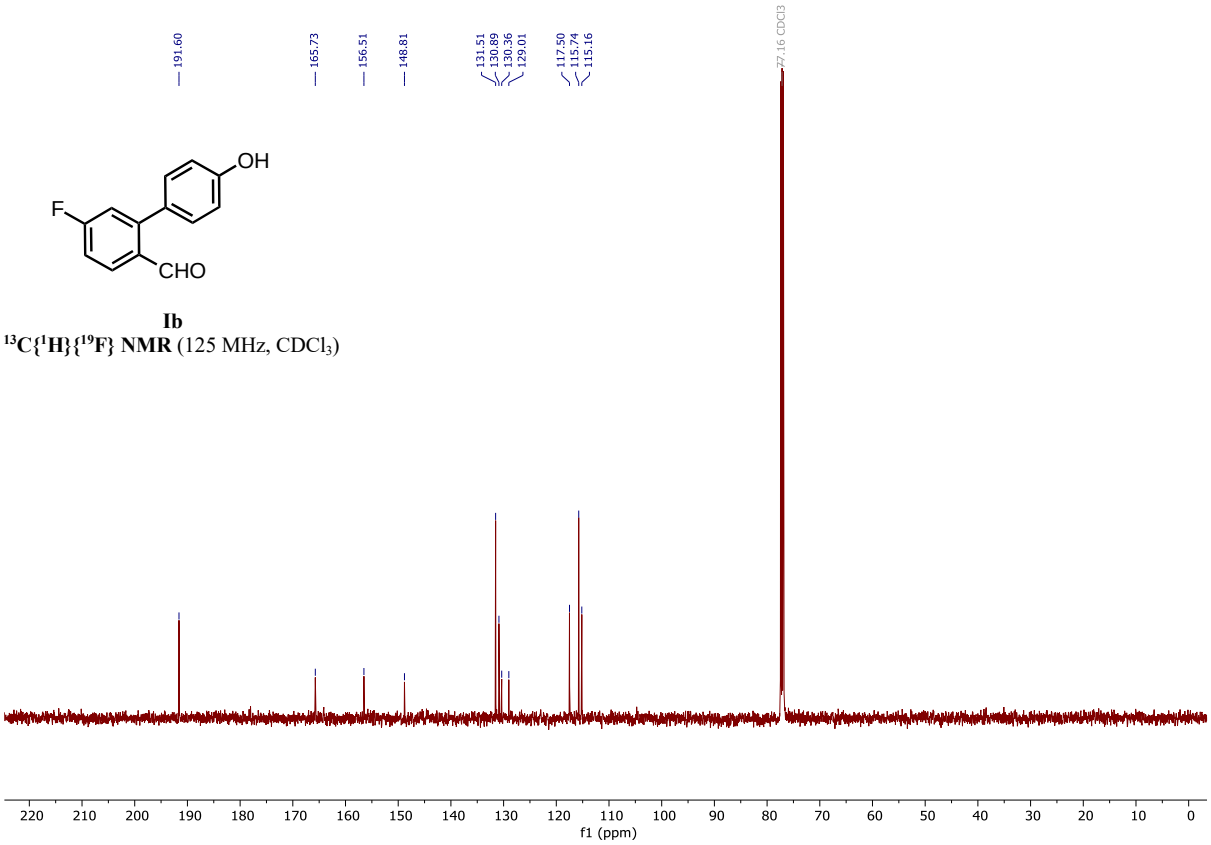

Ib

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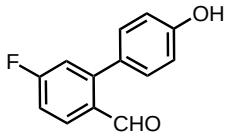
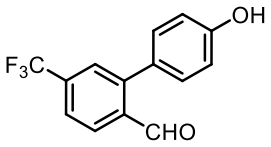


Ib

^{19}F NMR (471 MHz, $CDCl_3$)



Ic

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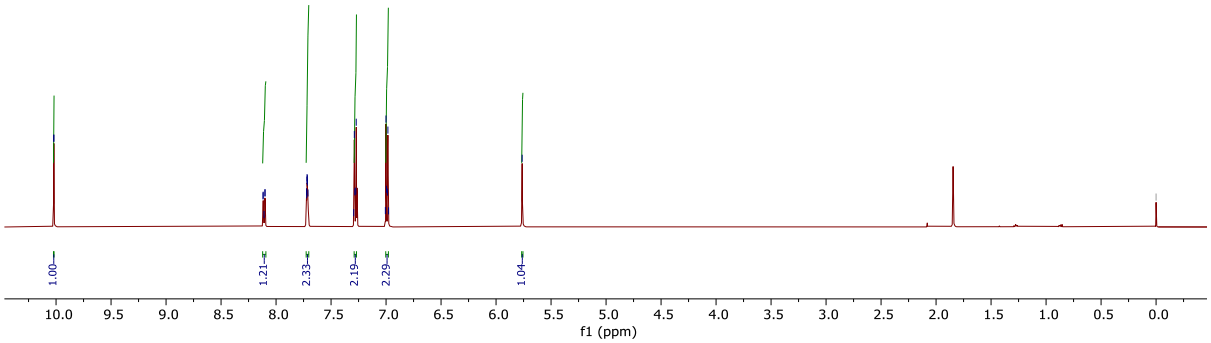
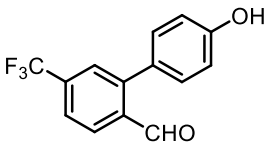
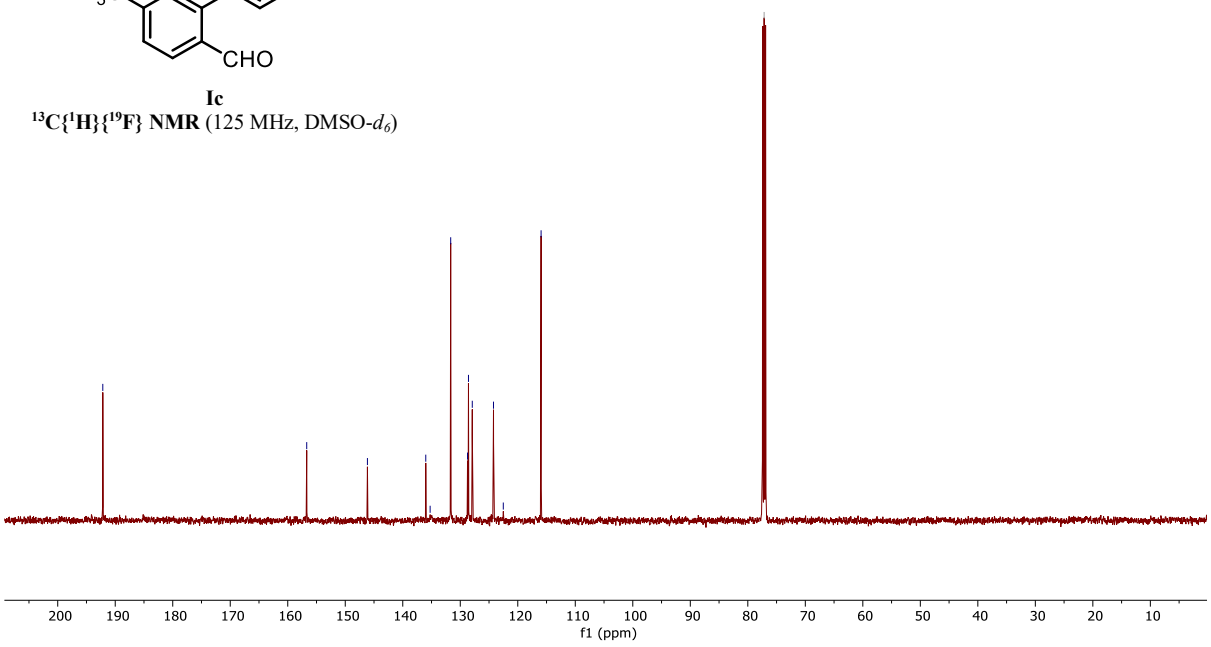
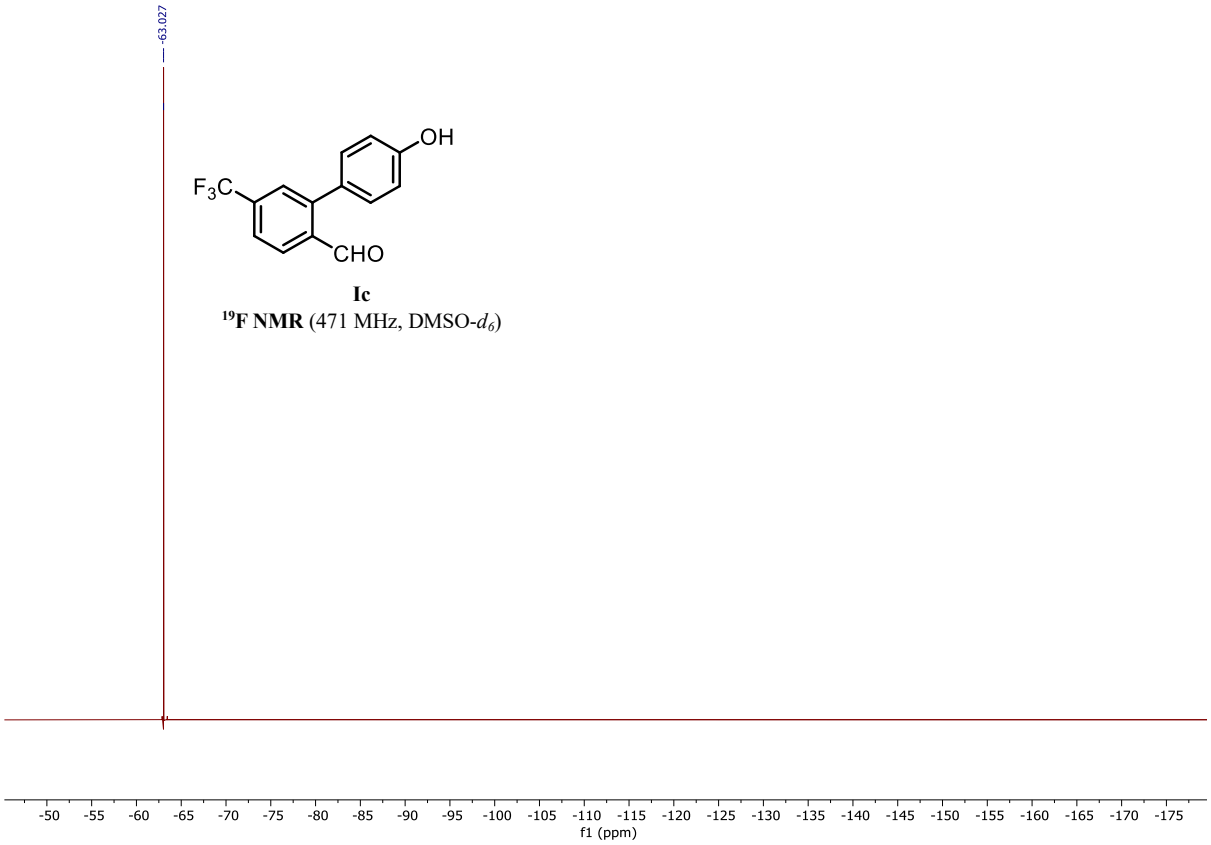




Ic

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, DMSO-d_6)





Ic

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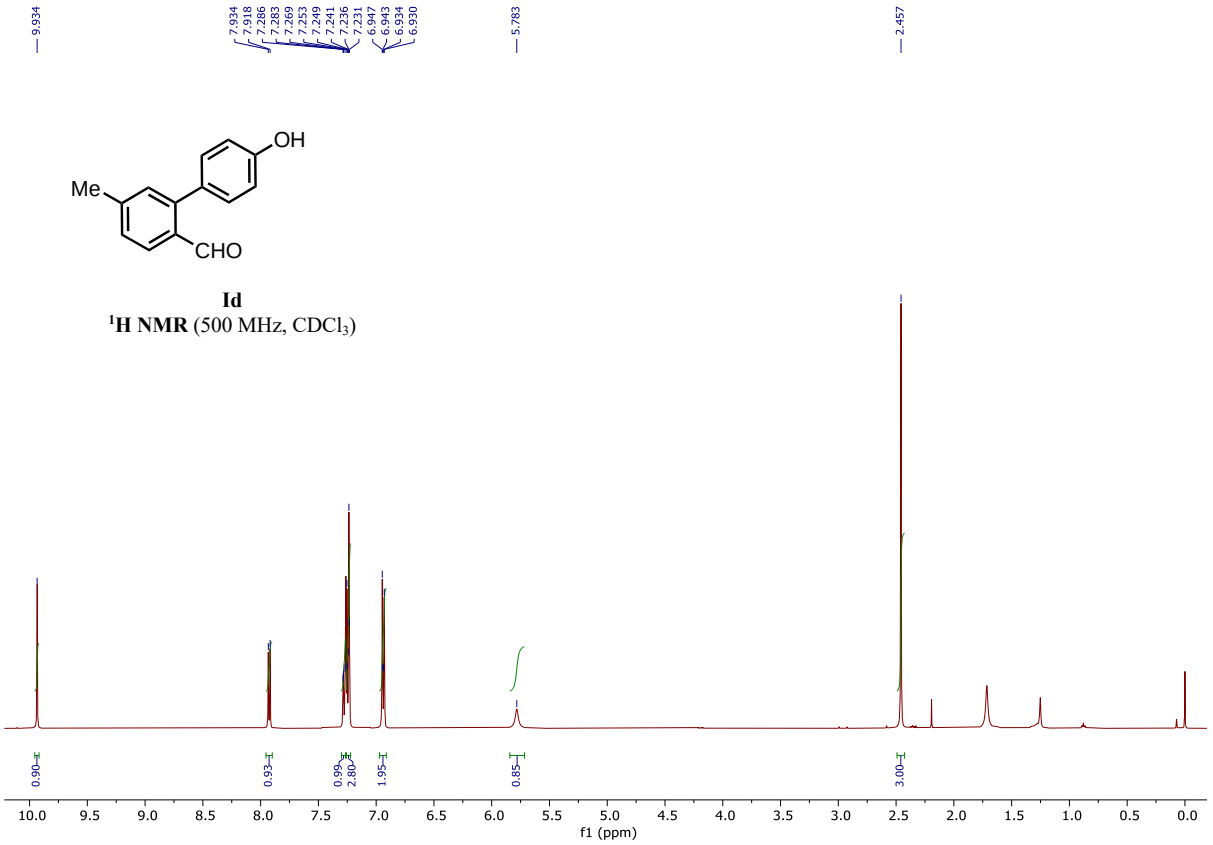

Id

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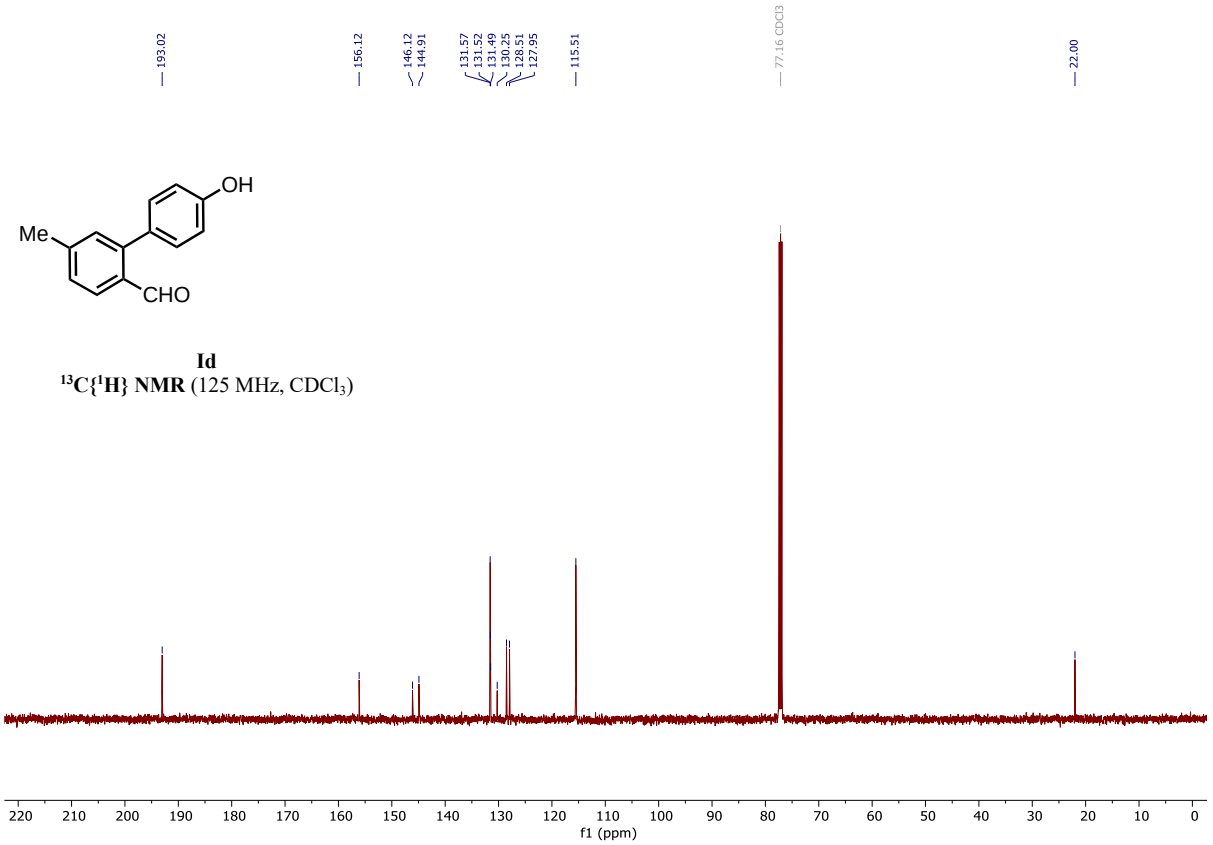

Id

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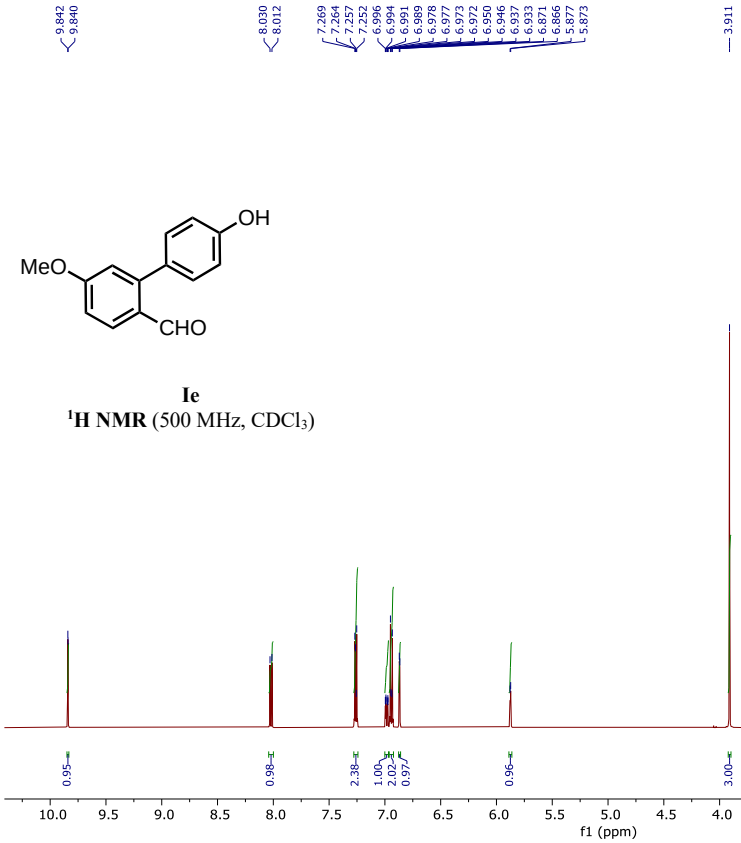

Ie

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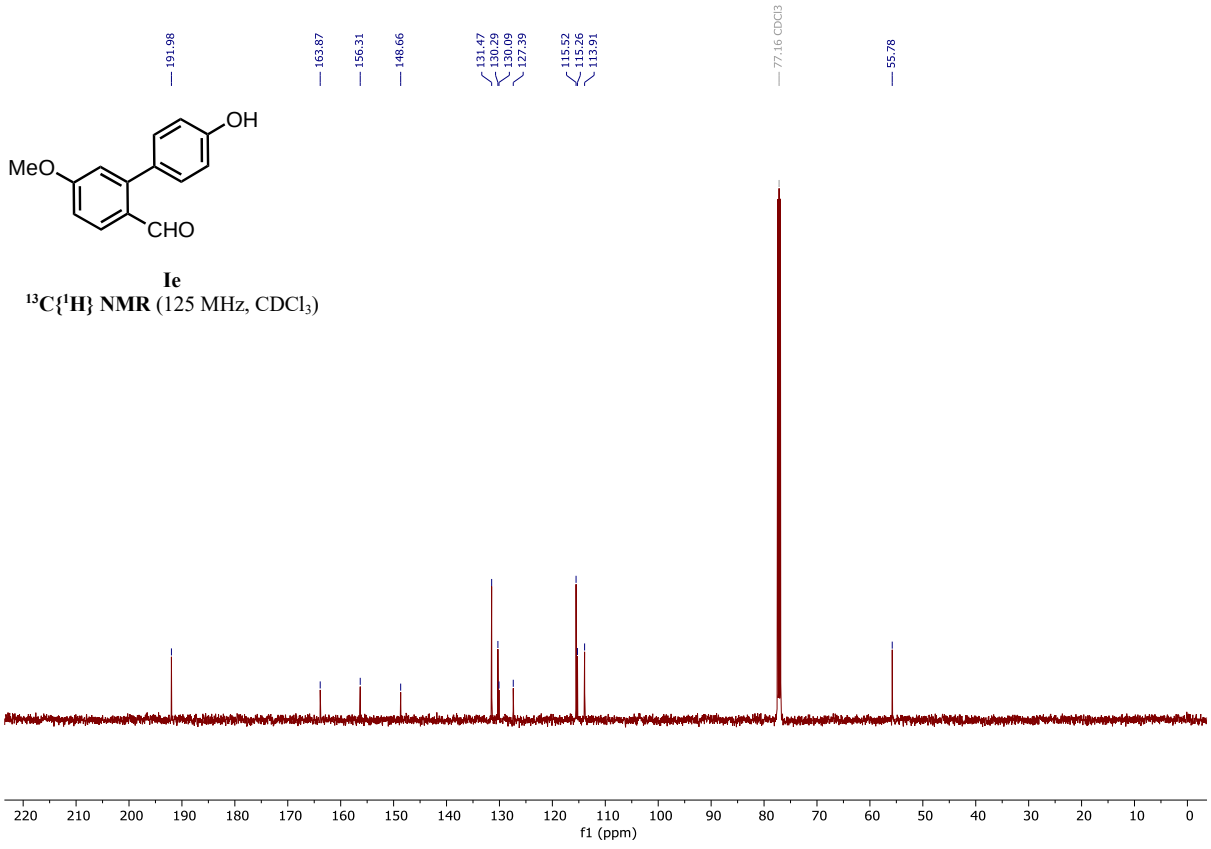
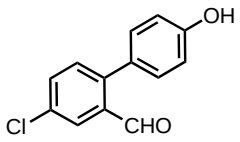


Ie

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



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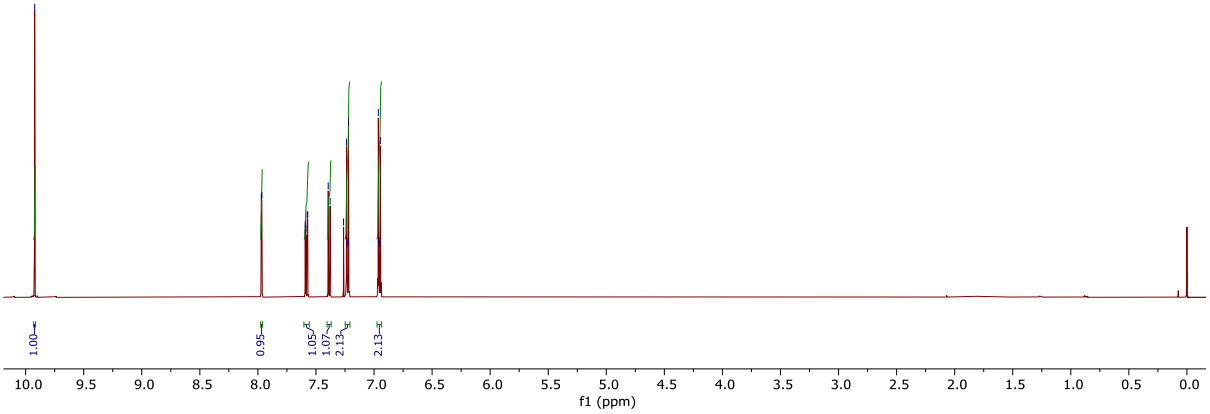

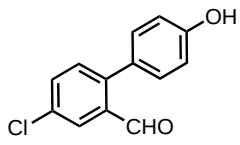

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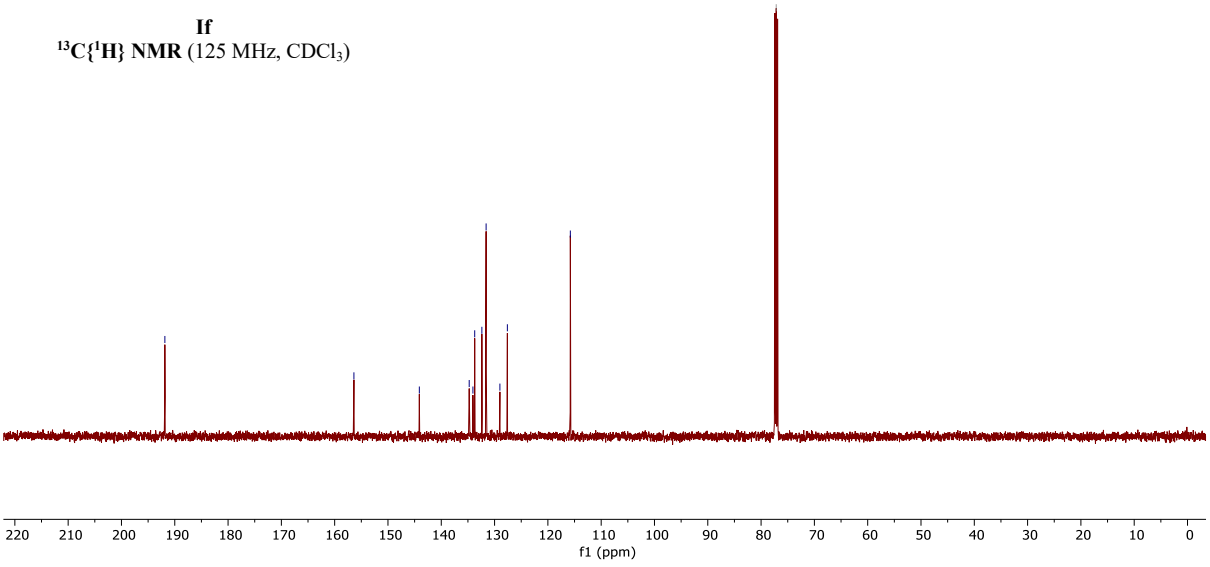

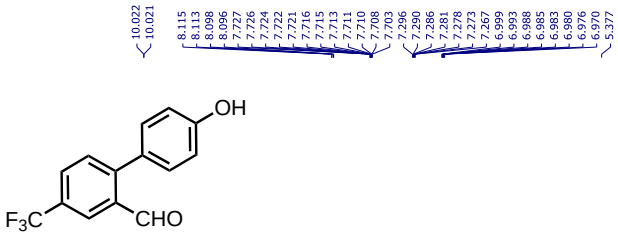

Ig

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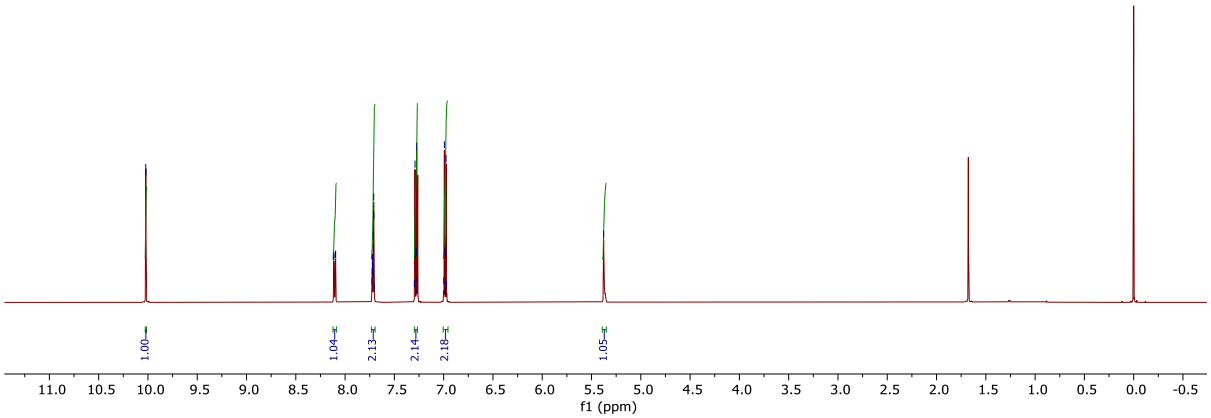
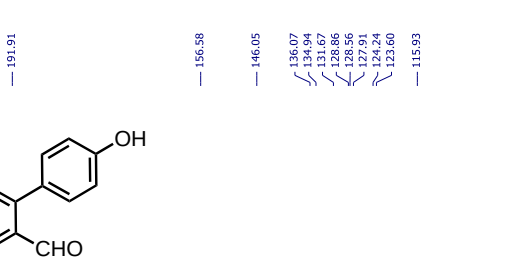
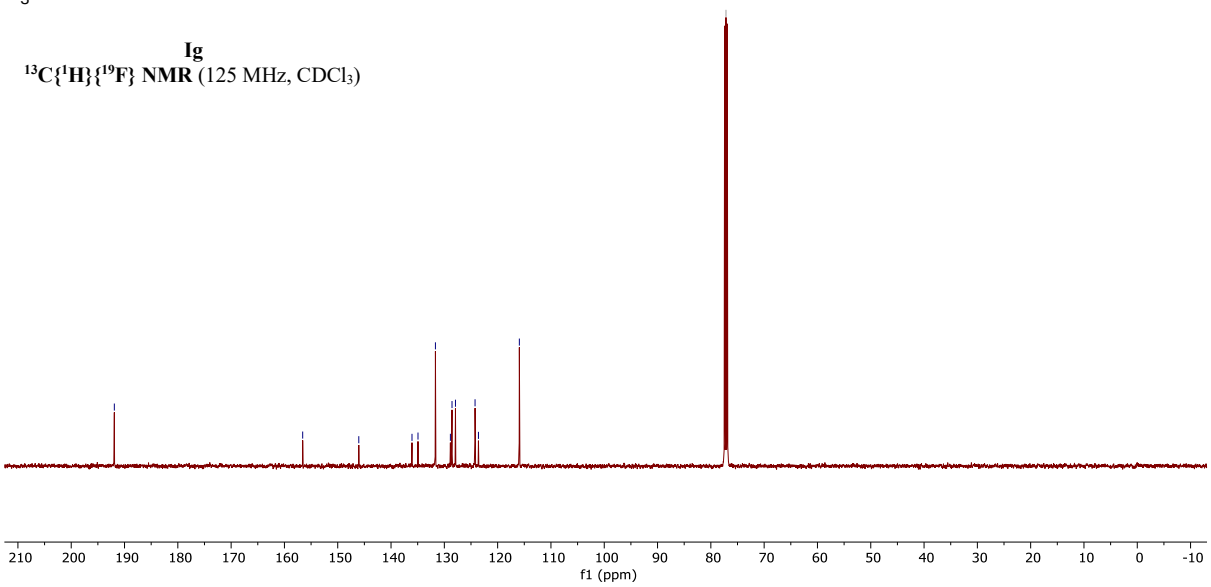
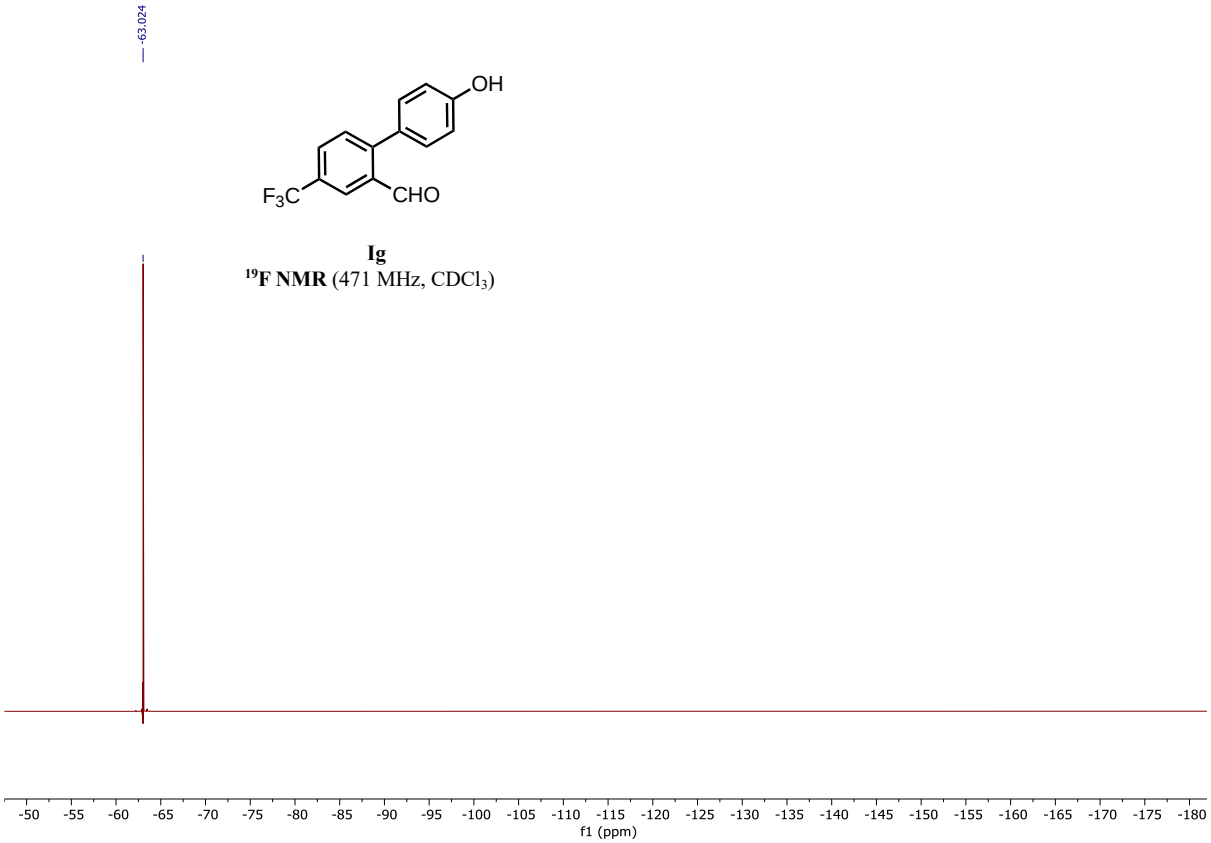




Ig

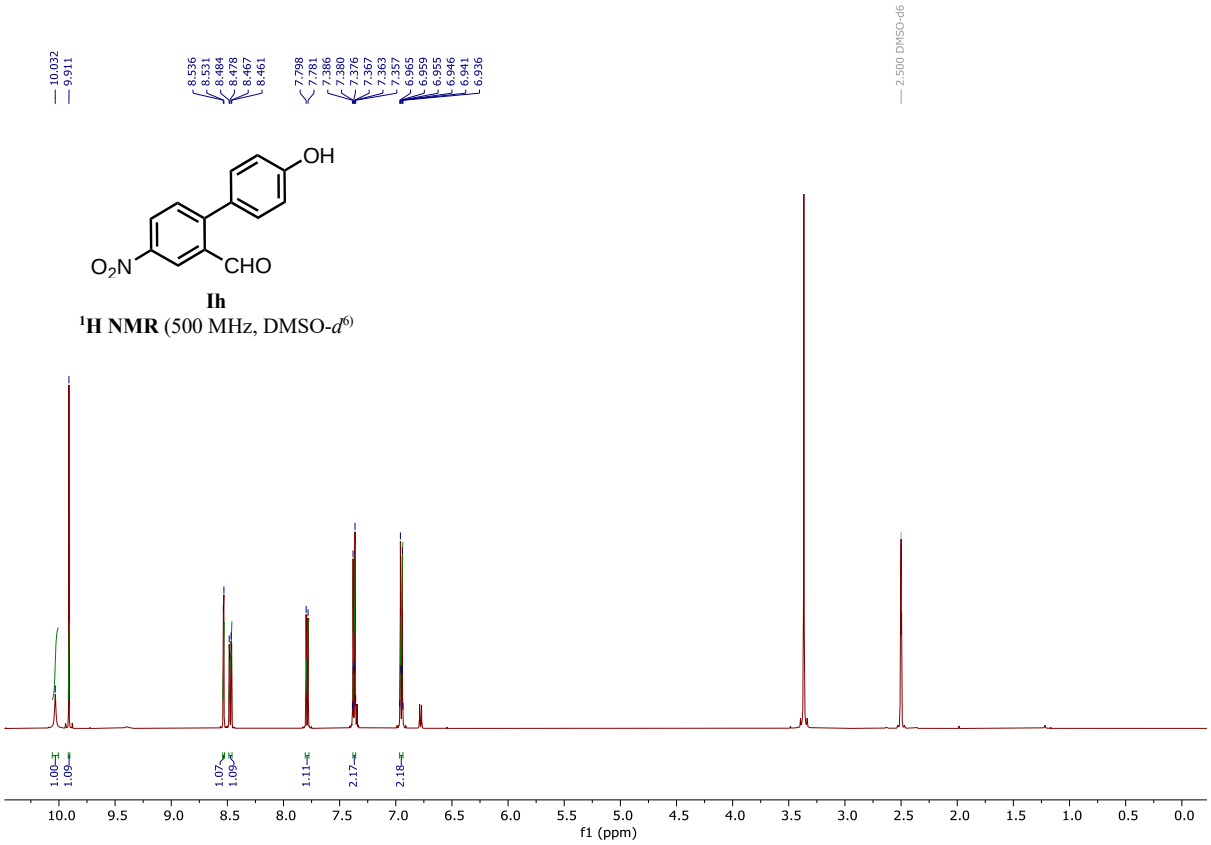
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)





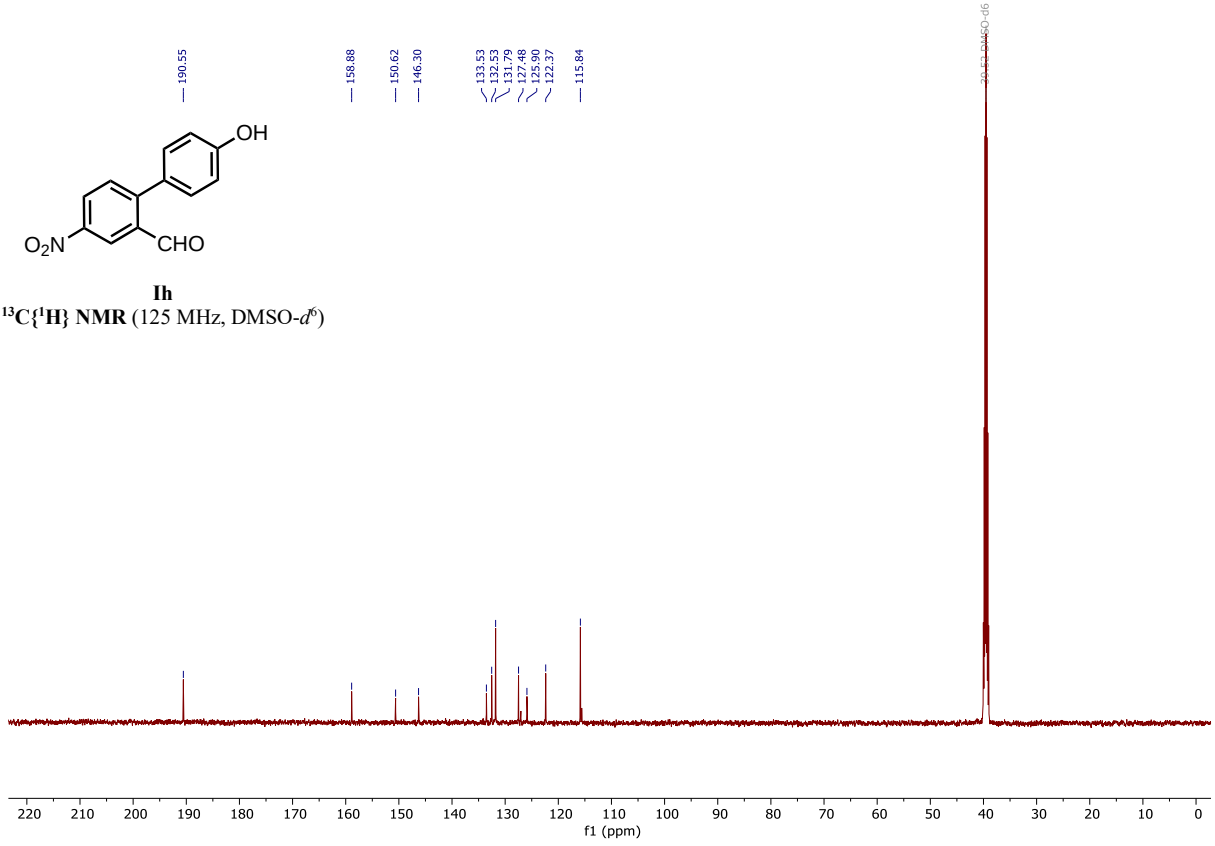
Ig

^{19}F NMR (471 MHz, $CDCl_3$)



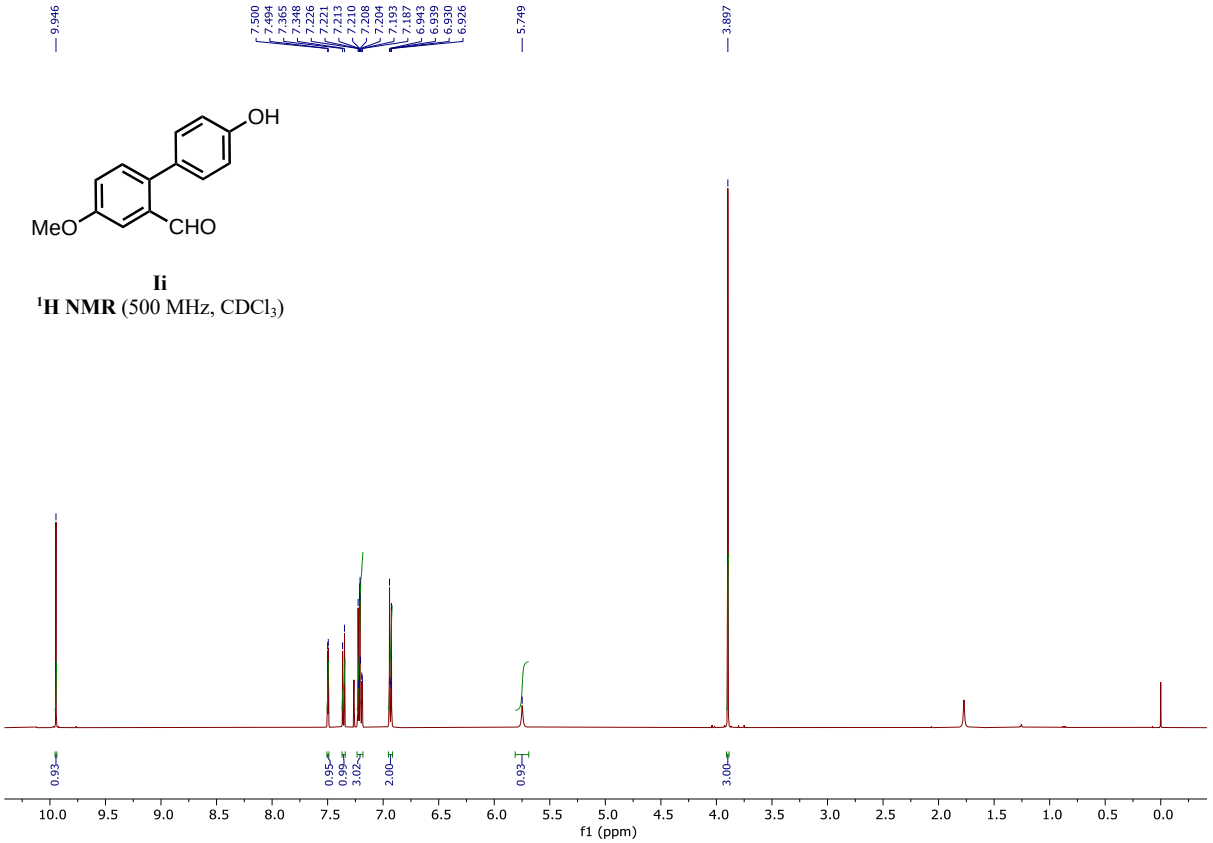
Ih

^{1}H NMR (500 MHz, DMSO-*d*^{6})



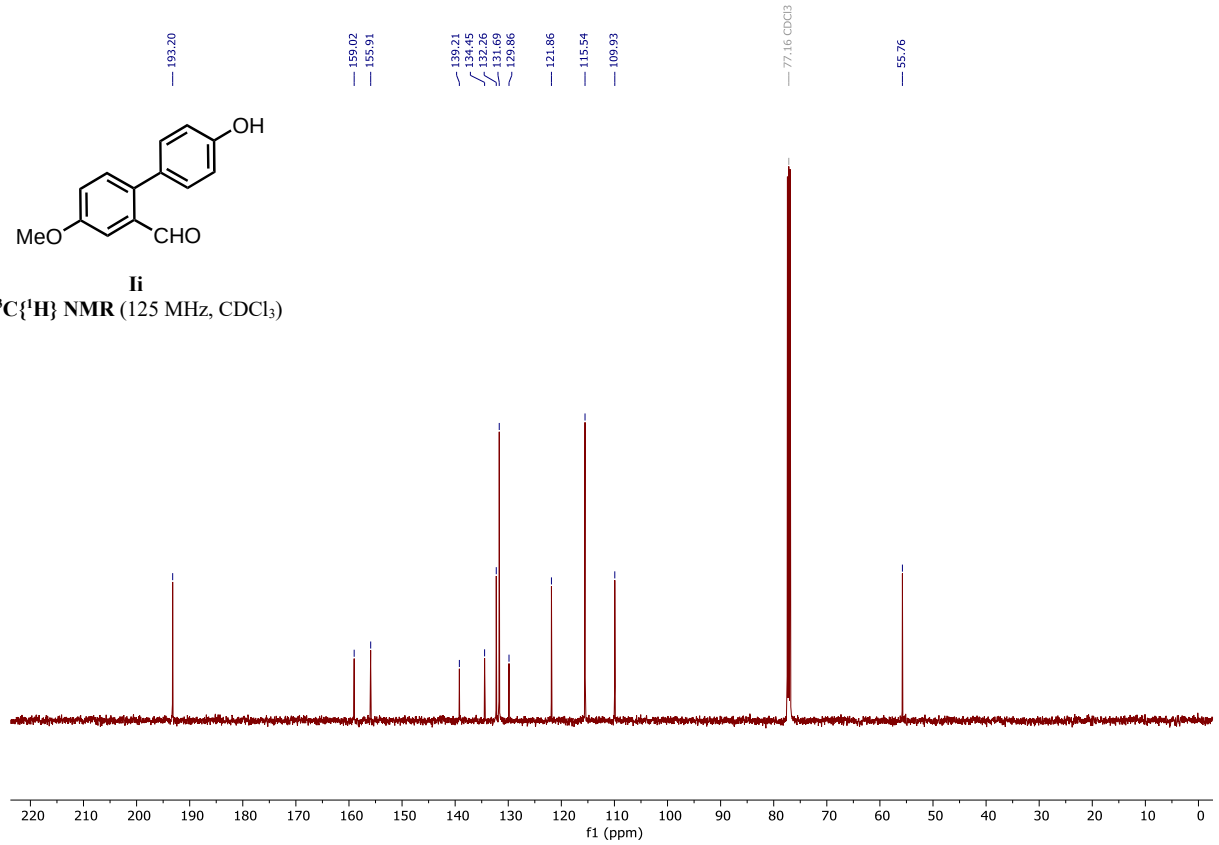
Ih

^{13}C{^{1}H} NMR (125 MHz, DMSO-*d*^{6})



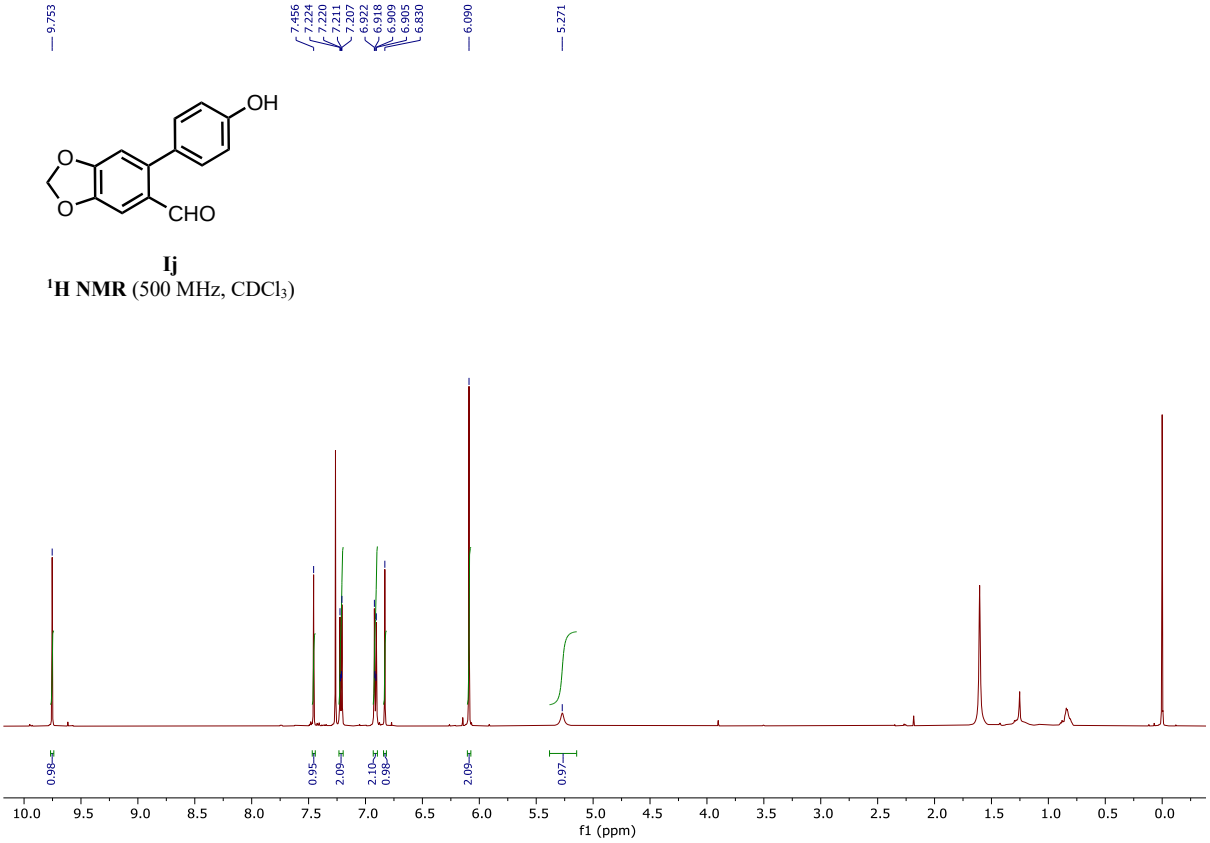
Ii

^{1}H NMR (500 MHz, $CDCl_3$)



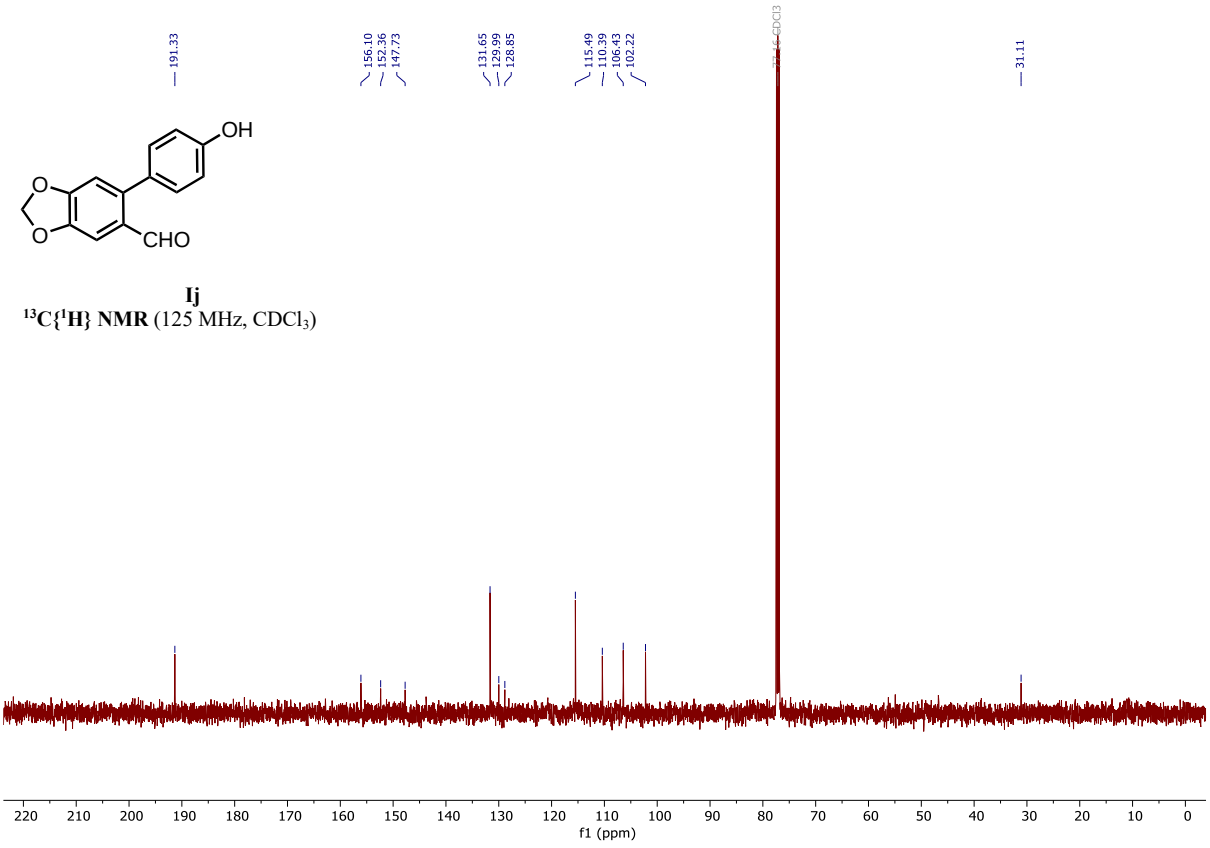
Ii

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



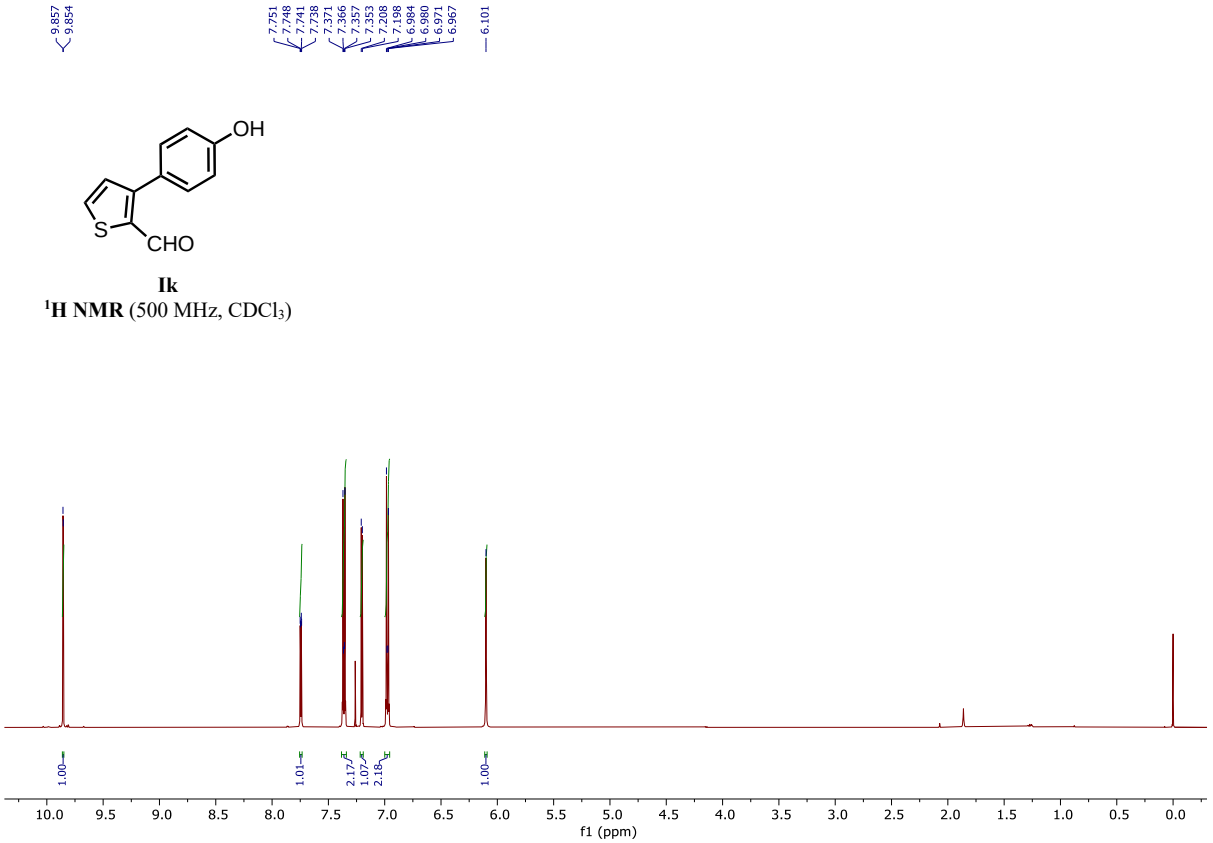
Ij

^{1}H NMR (500 MHz, $CDCl_3$)



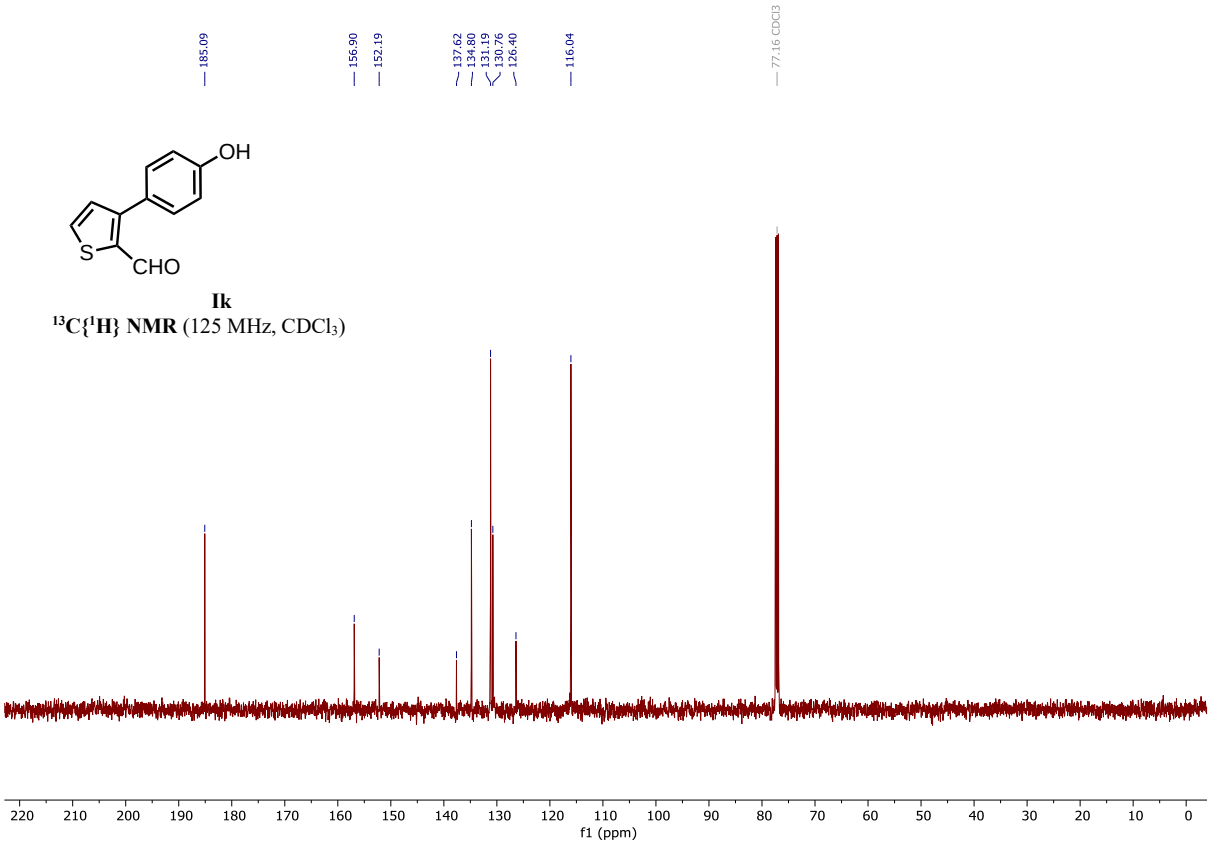
Ij

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



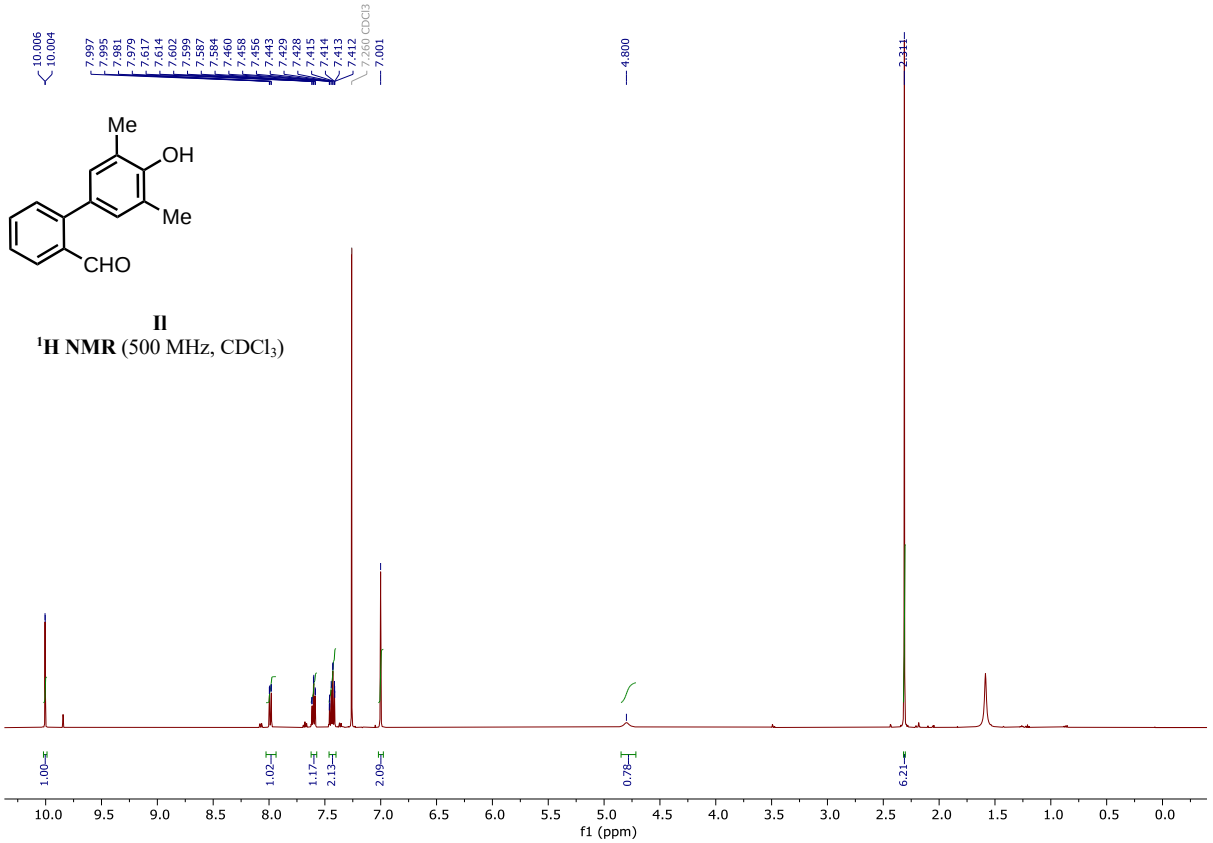
Ik

^{1}H NMR (500 MHz, $CDCl_3$)



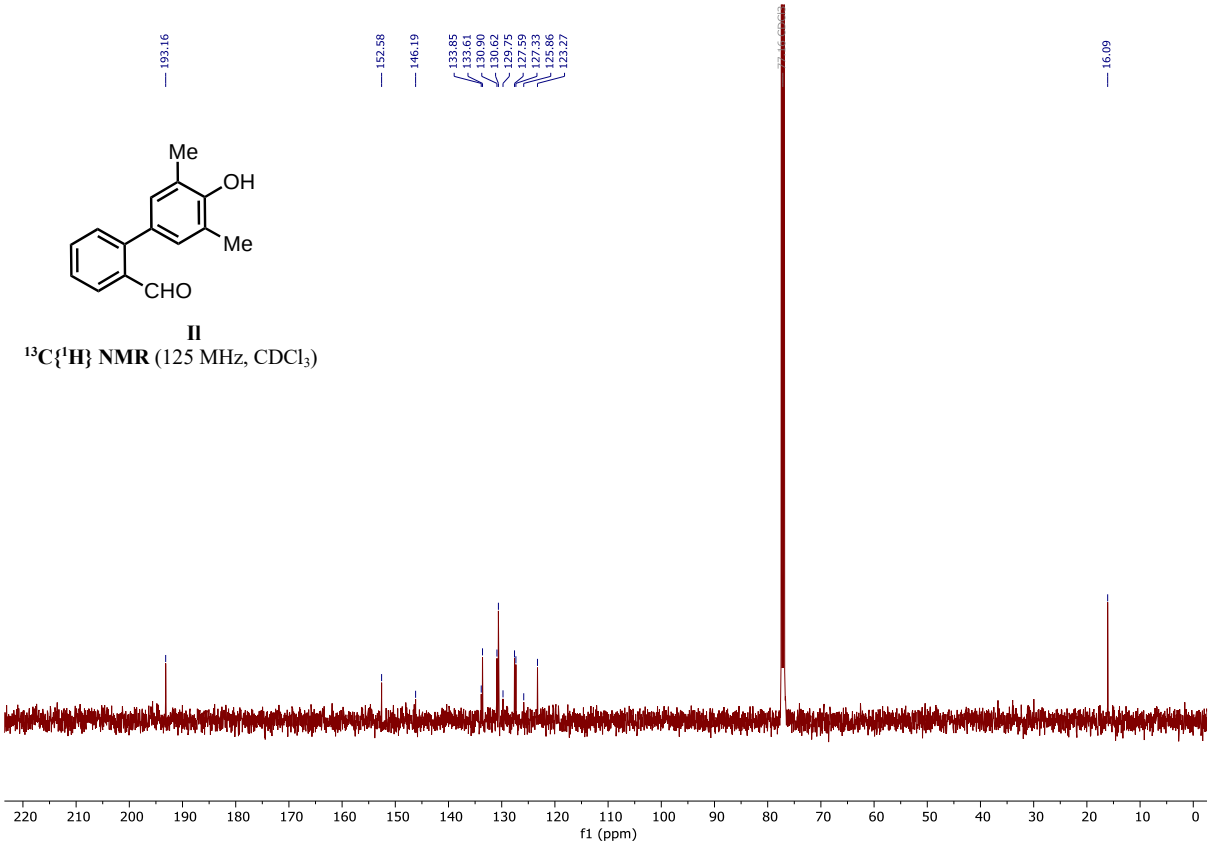
Ik

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



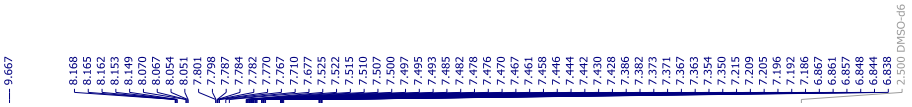
II

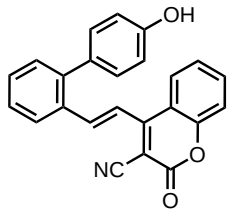
^{1}H NMR (500 MHz, $CDCl_3$)



II

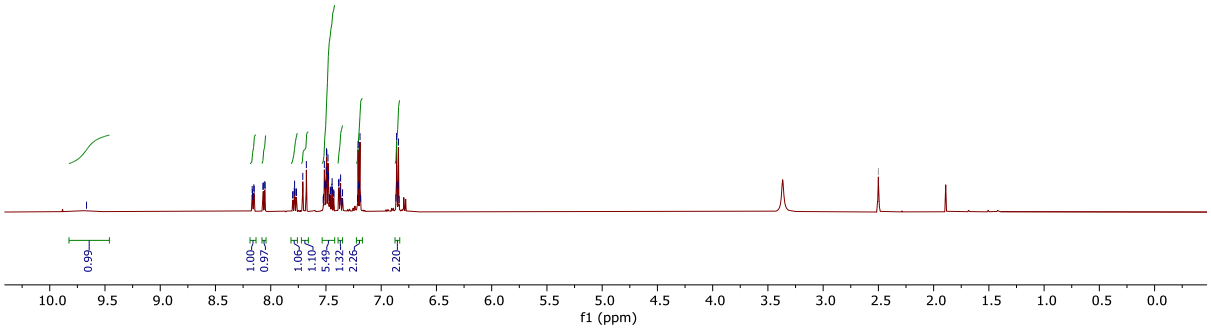
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

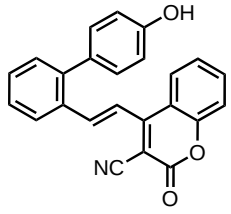




IIa

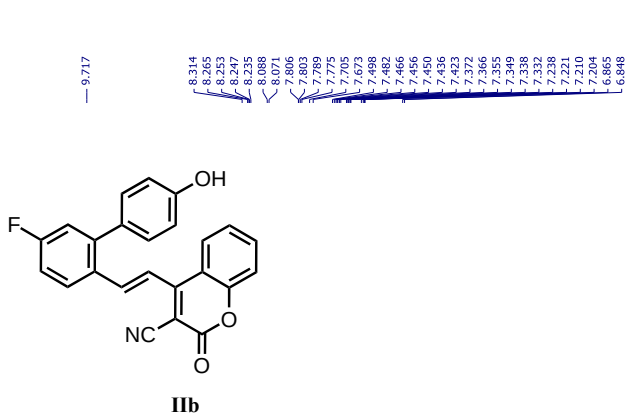
^{1}H NMR (500 MHz, DMSO-d_6)





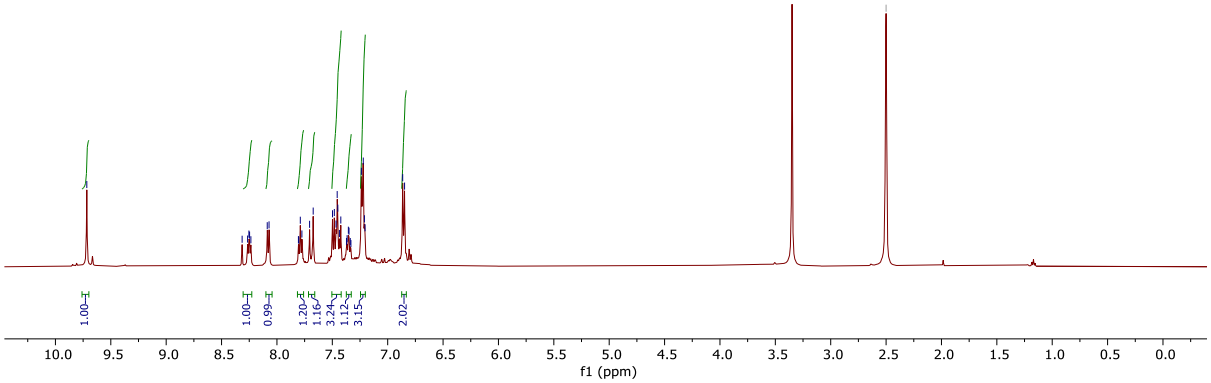
IIa

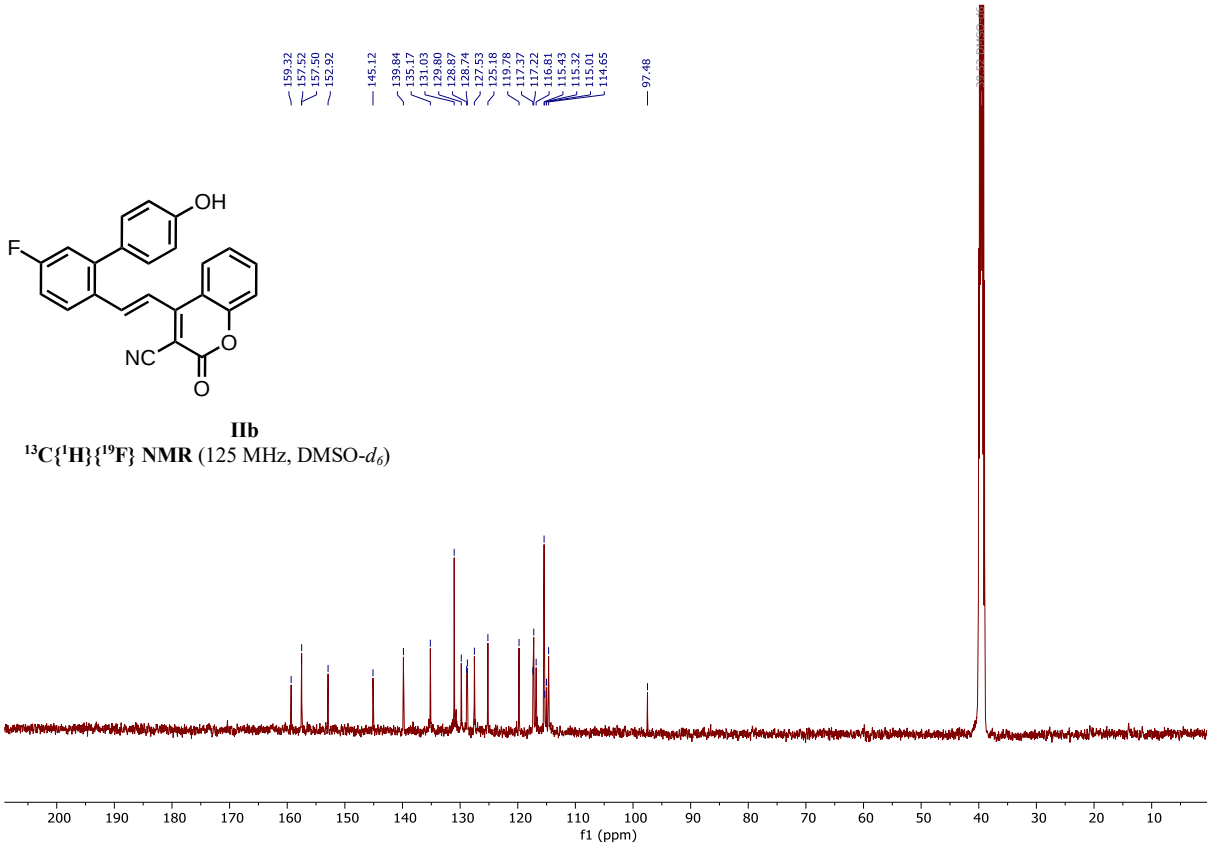
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)



IIb

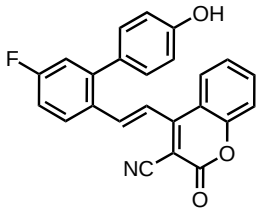
^{1}H NMR (500 MHz, DMSO-d_6)





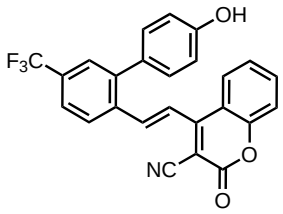
IIb

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, DMSO-d_6)



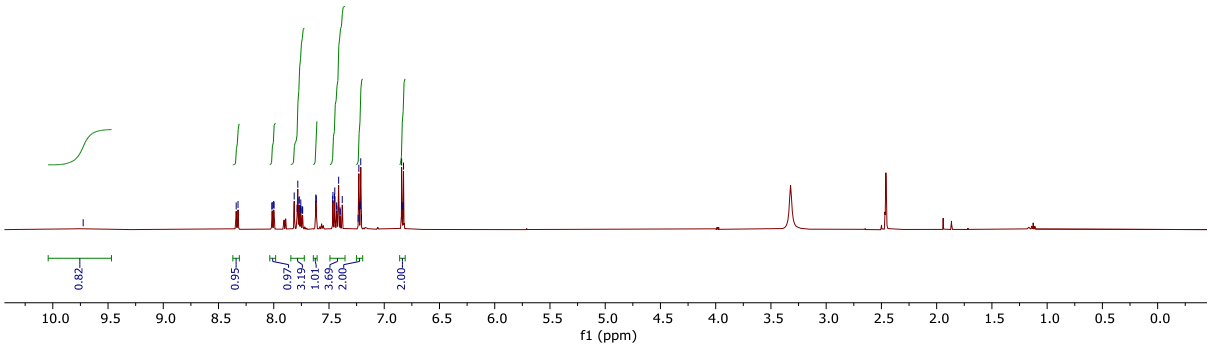
IIb

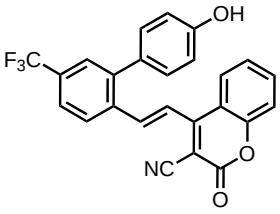
^{19}F NMR (471 MHz, DMSO-d_6)



IIc

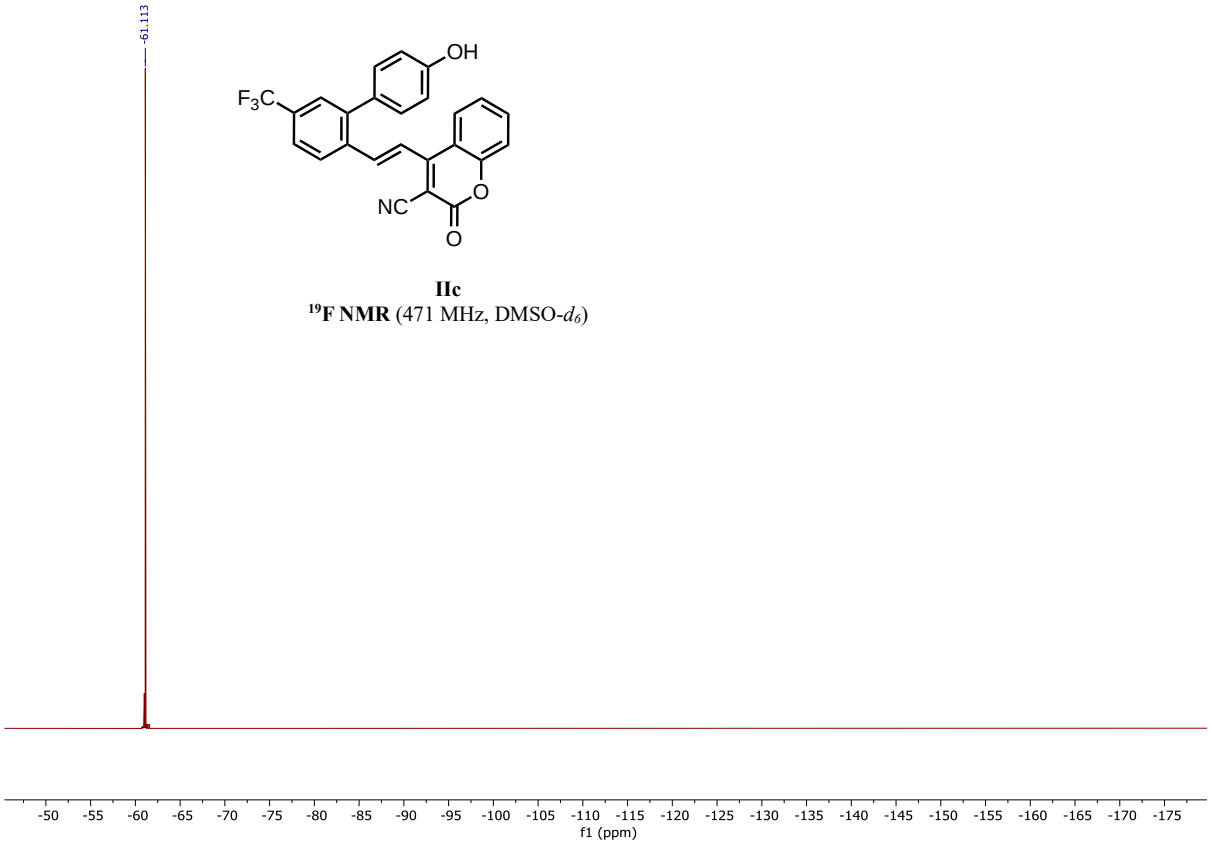
^{1}H NMR (500 MHz, DMSO-d_6)





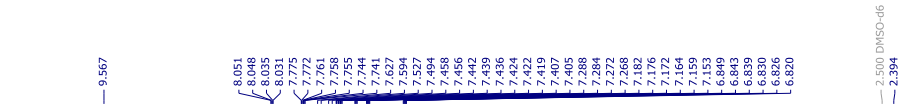
IIc

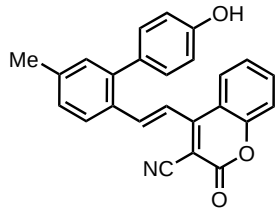
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, DMSO-d_6)



IIc

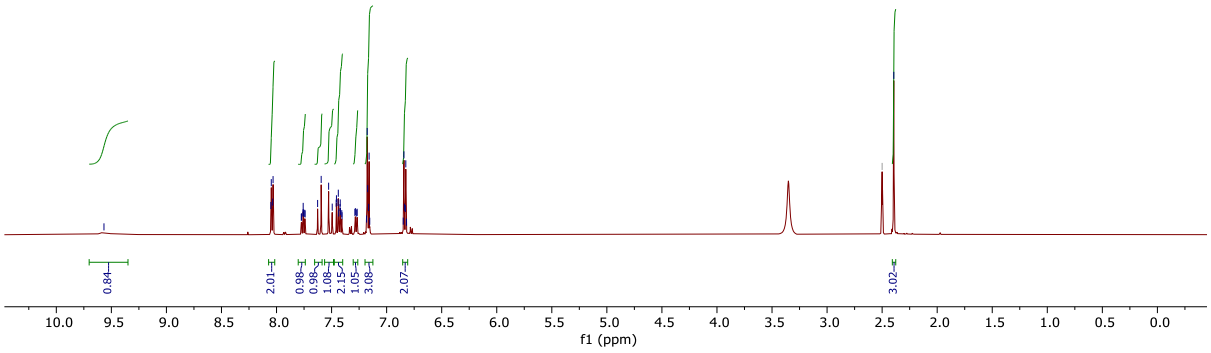
^{19}F NMR (471 MHz, DMSO-d_6)

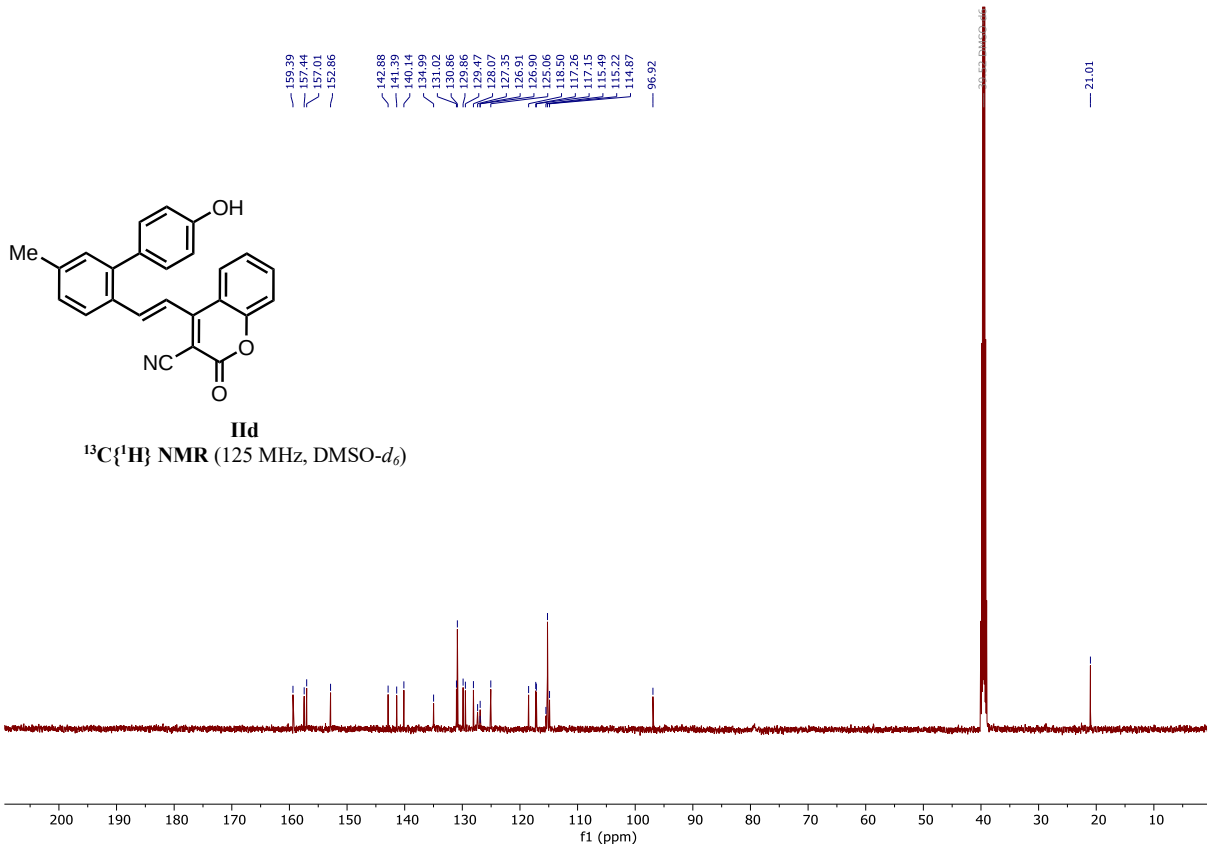




IId

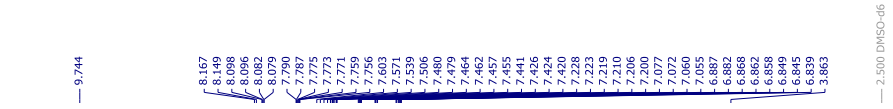
^{1}H NMR (500 MHz, DMSO-d_6)

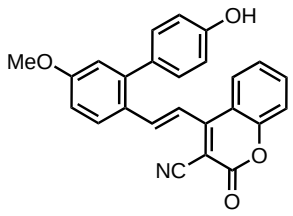




IId

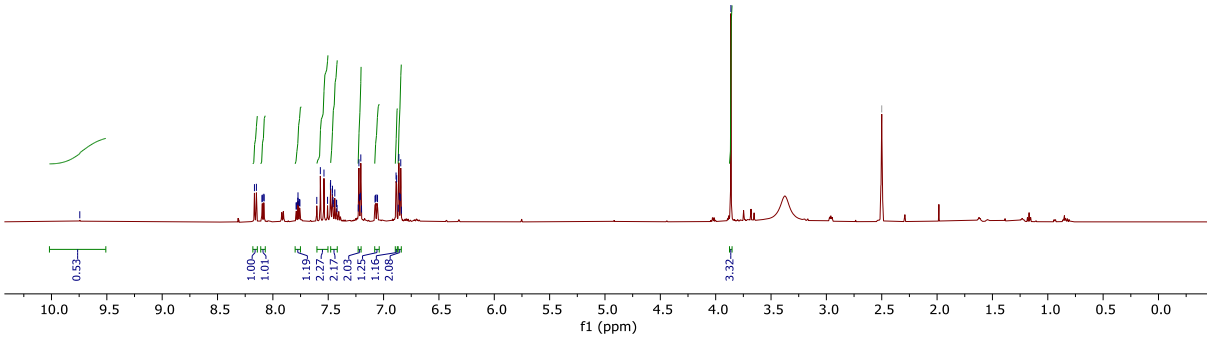
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

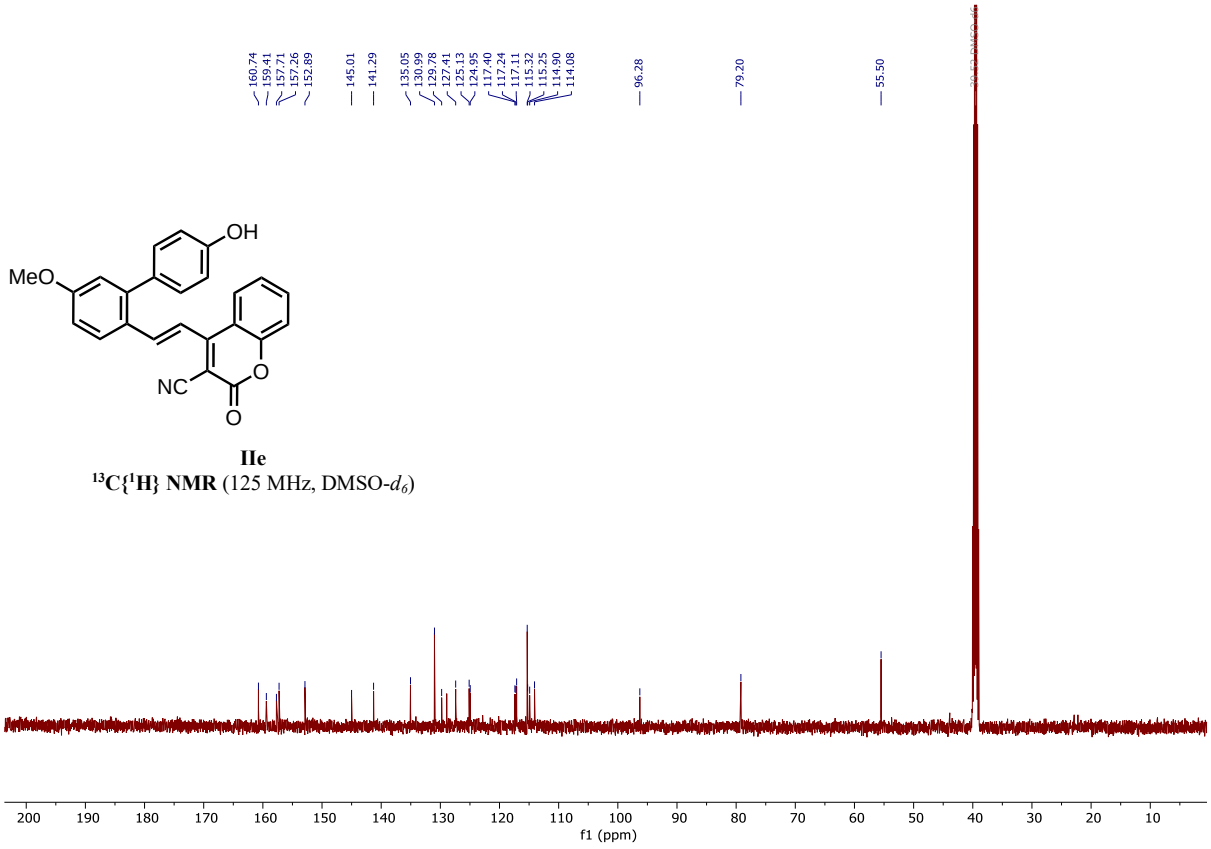




IIe

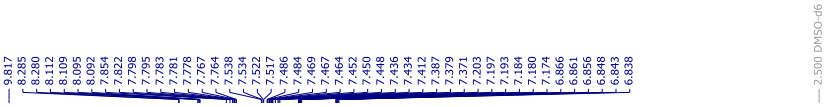
^{1}H NMR (500 MHz, DMSO-d_6)

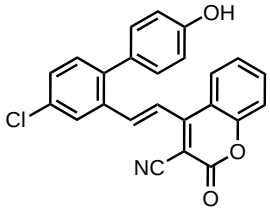




IIe

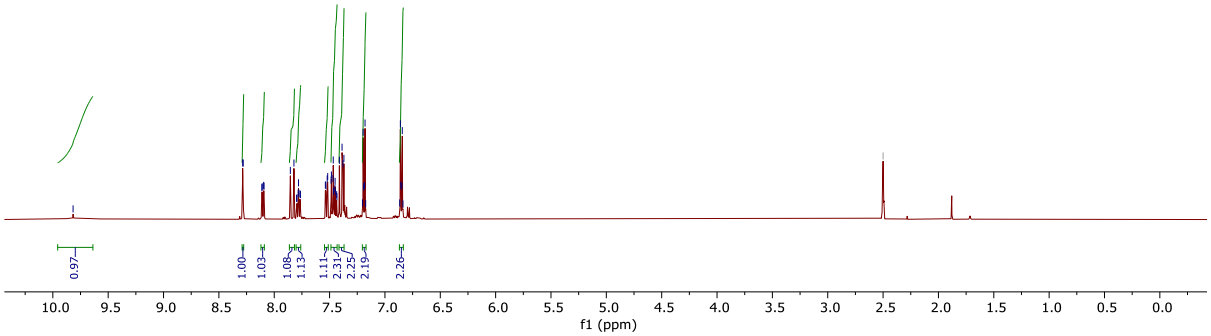
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

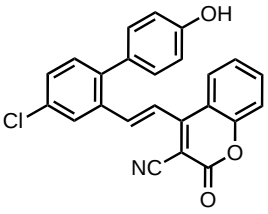




IIf

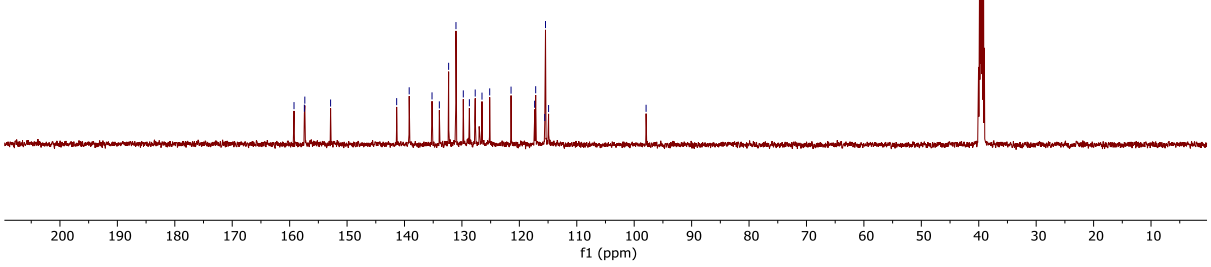
^{1}H NMR (500 MHz, DMSO-d_6)

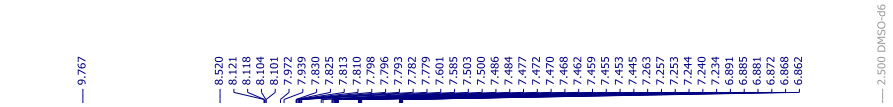


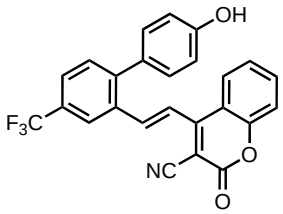


IIf

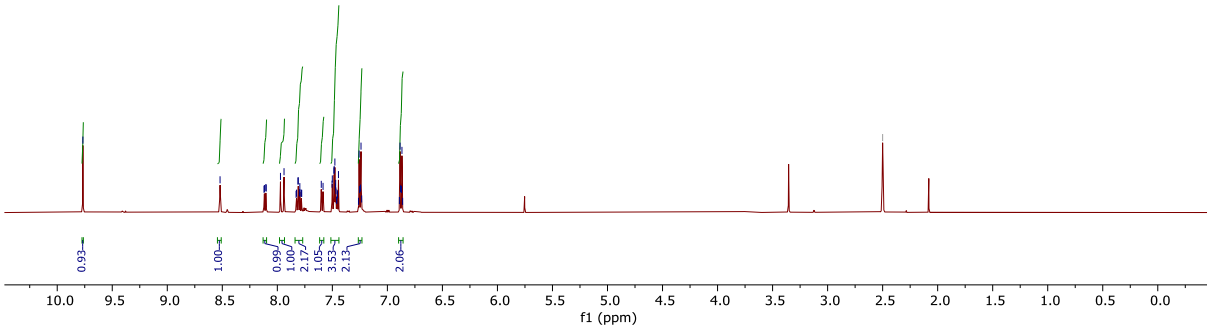
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

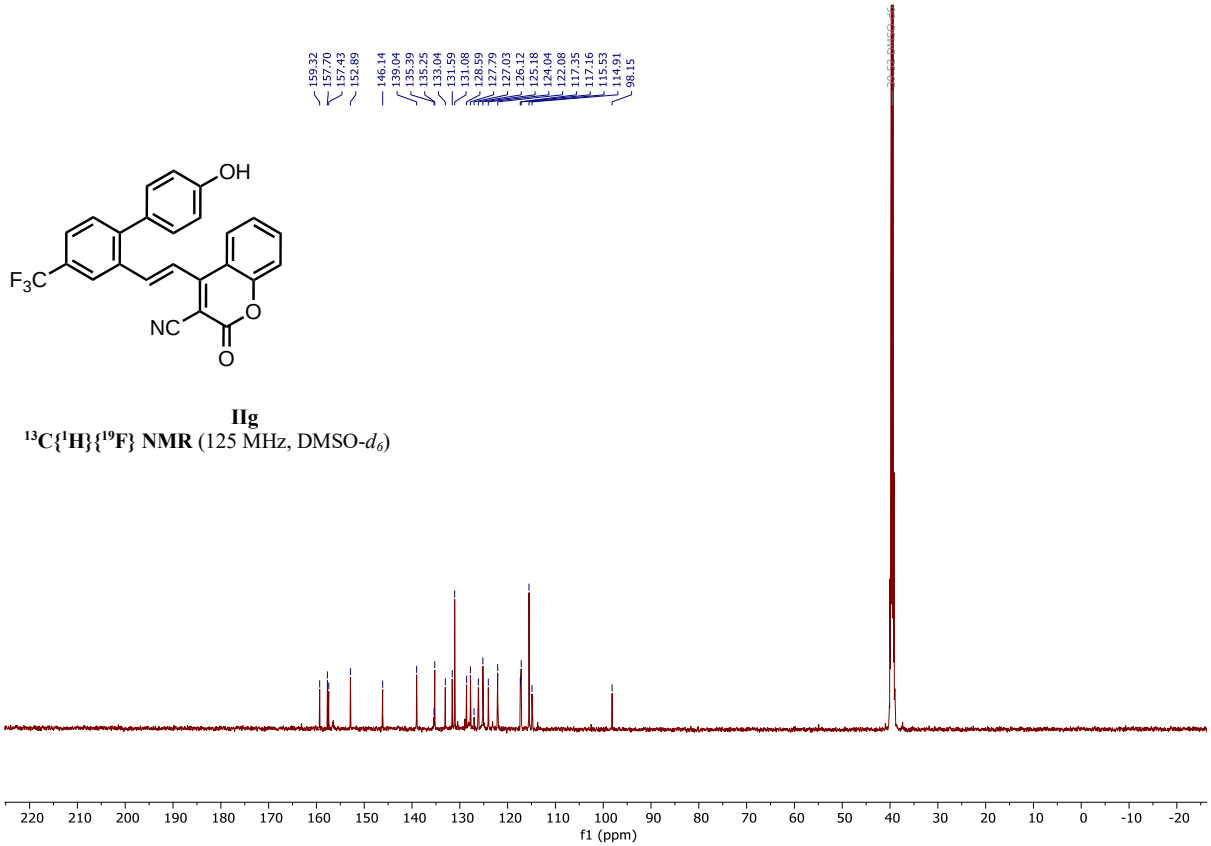




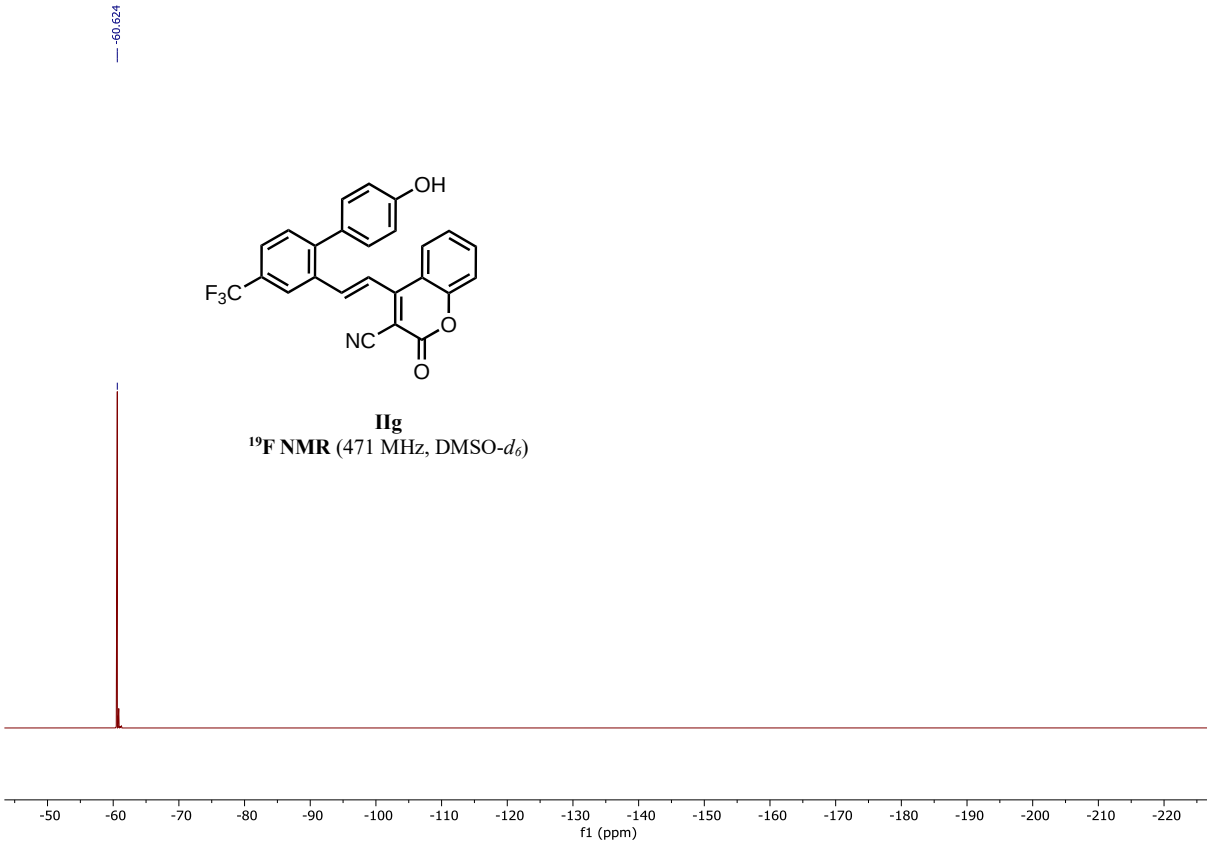


IIg
^{1}H NMR (500 MHz, DMSO-d_6)



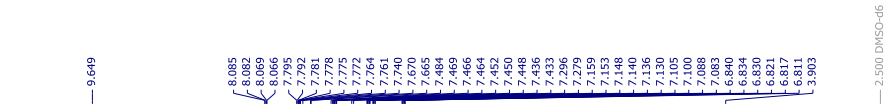


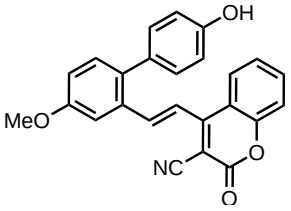
IIg
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, DMSO-d_6)



IIg

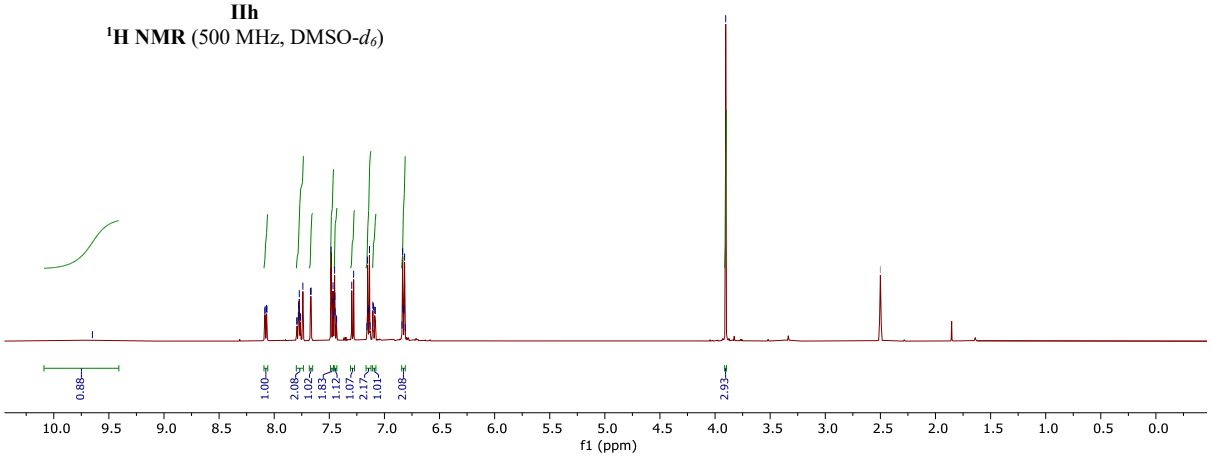
^{19}F NMR (471 MHz, DMSO-d_6)

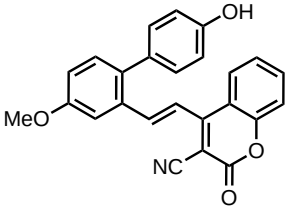




IIh

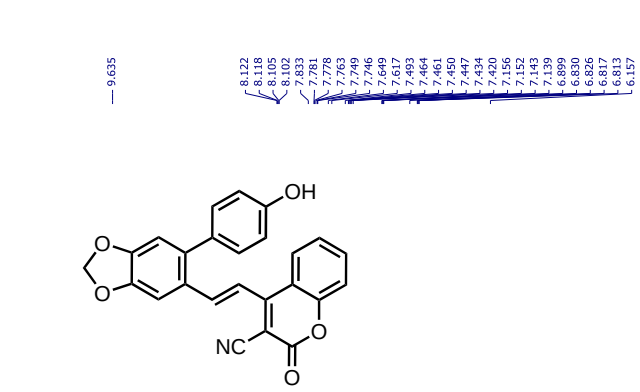
^{1}H NMR (500 MHz, DMSO-d_6)





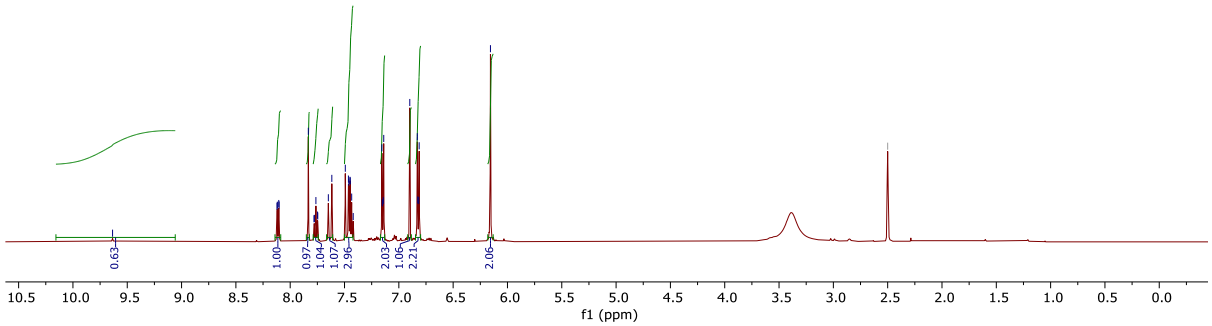
IIh

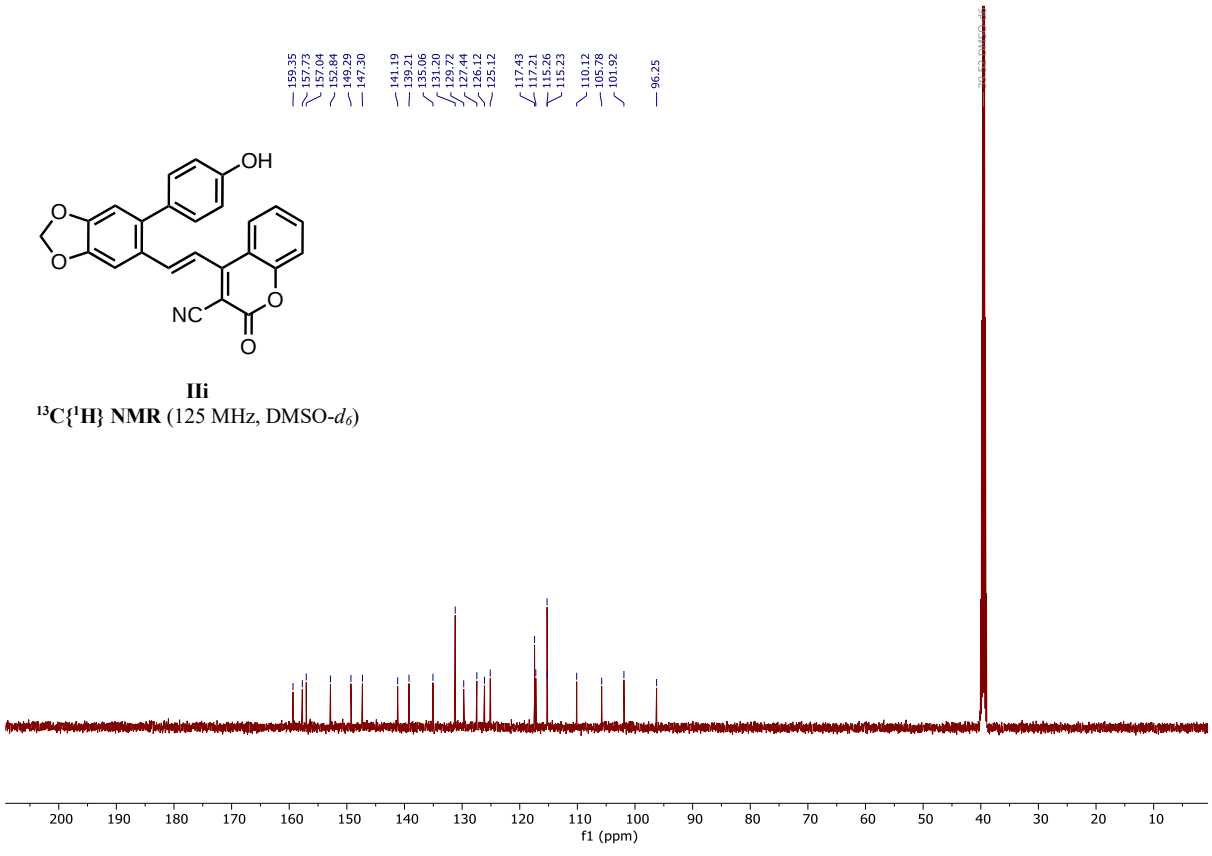
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)



IIi

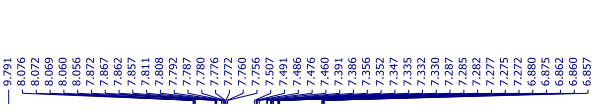
^{1}H NMR (500 MHz, DMSO-d_6)

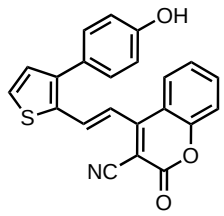




IIi

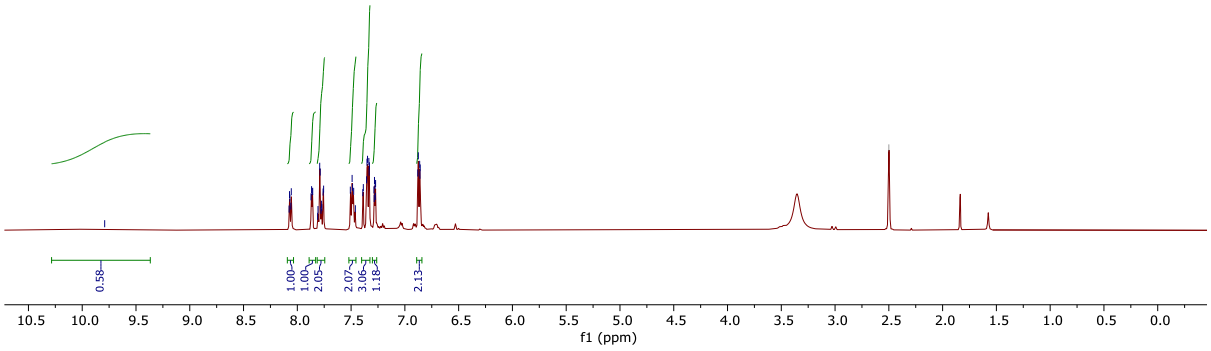
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

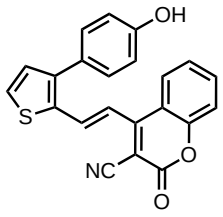




IIj

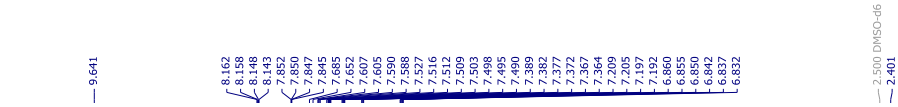
^{1}H NMR (500 MHz, DMSO-d_6)

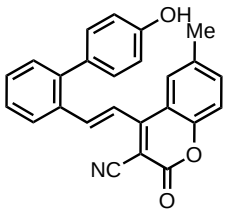




IIj

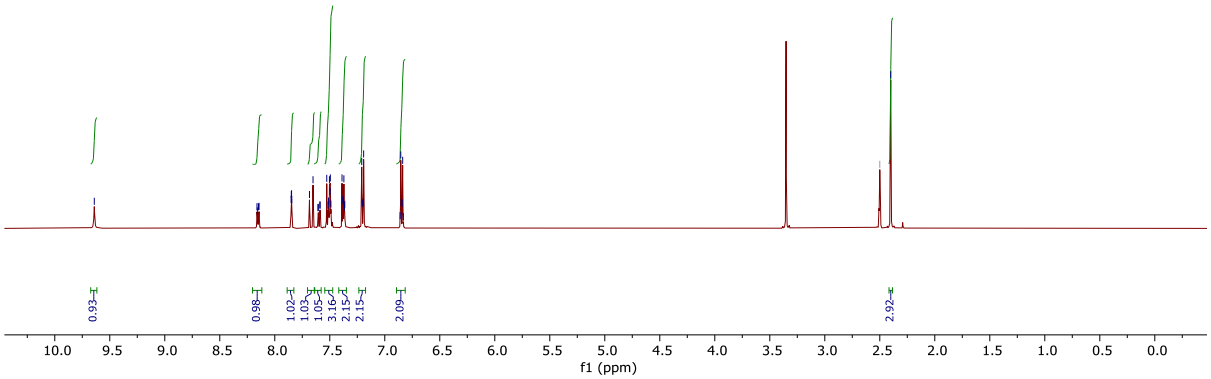
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

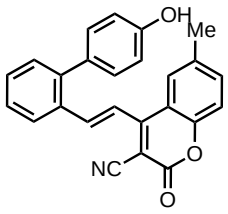




IIk

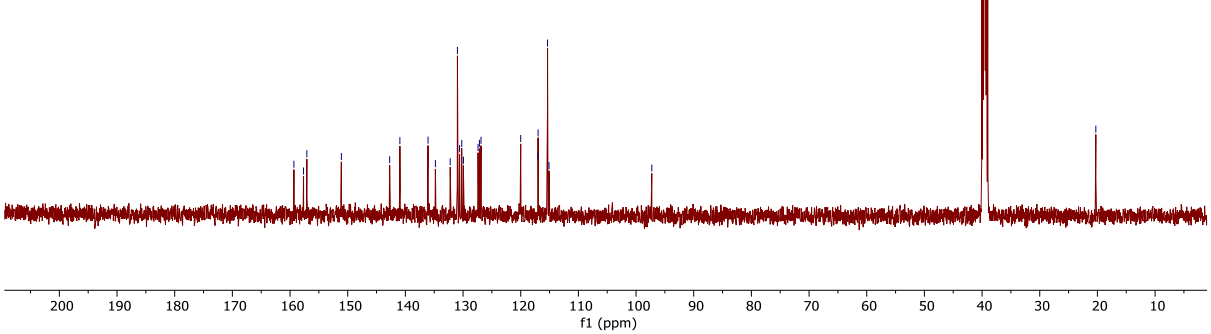
^{1}H NMR (500 MHz, DMSO-d_6)

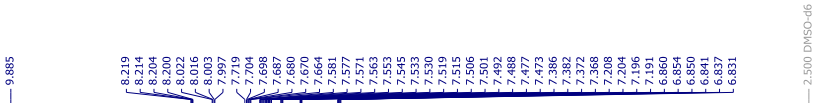


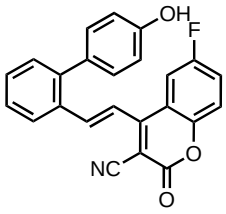


IIk

^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

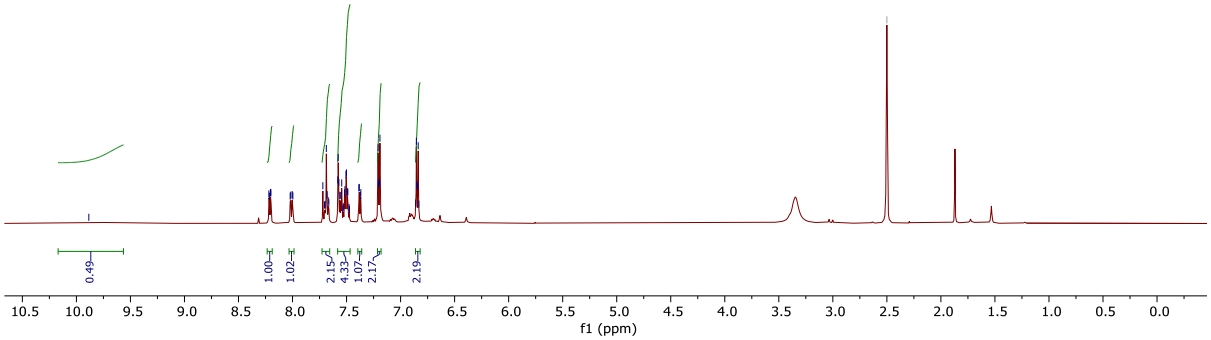


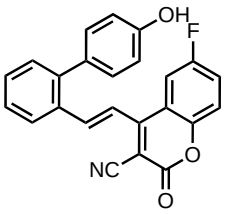




III

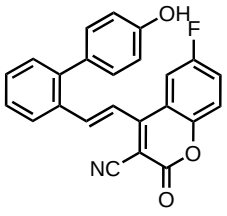
^{1}H NMR (500 MHz, DMSO-d_6)





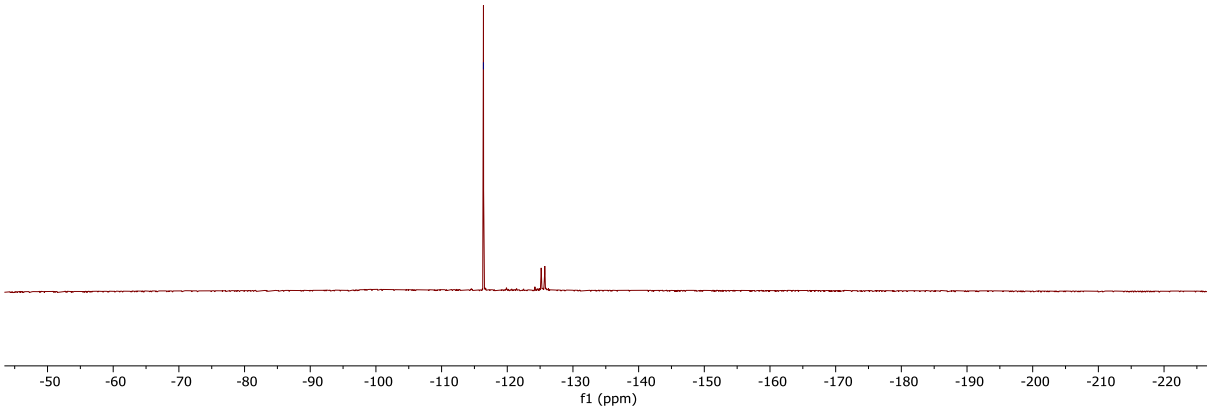
III

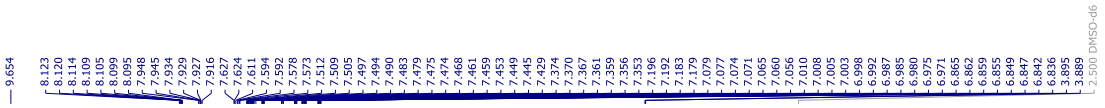
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, DMSO-d_6)

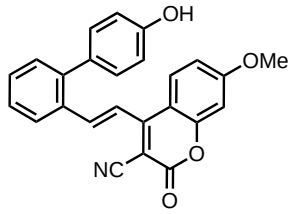


III

^{19}F NMR (471 MHz, DMSO-d_6)

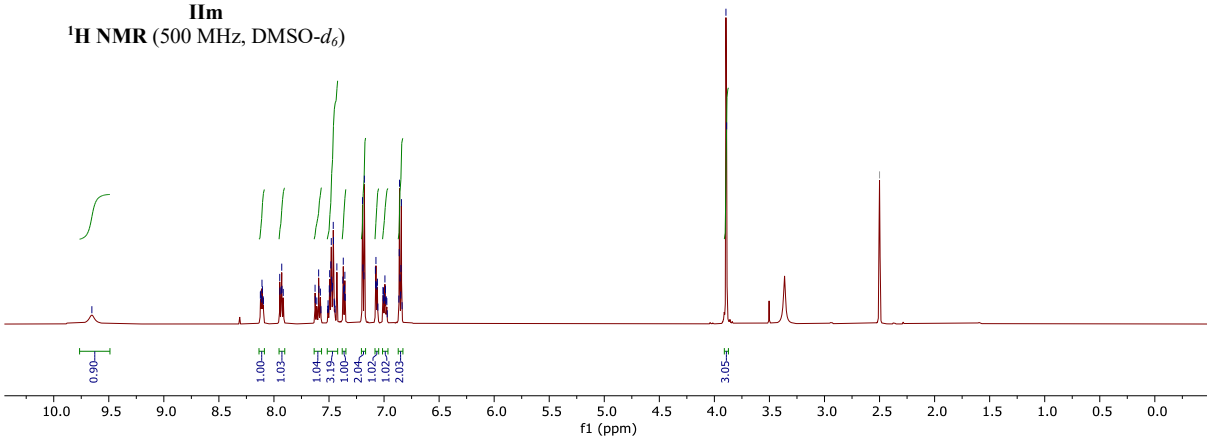


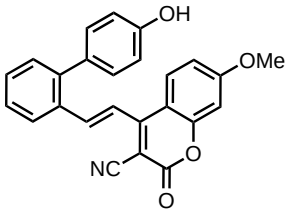




IIm

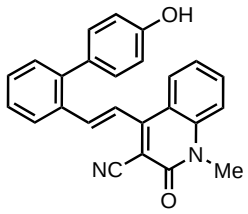
^{1}H NMR (500 MHz, DMSO-d_6)





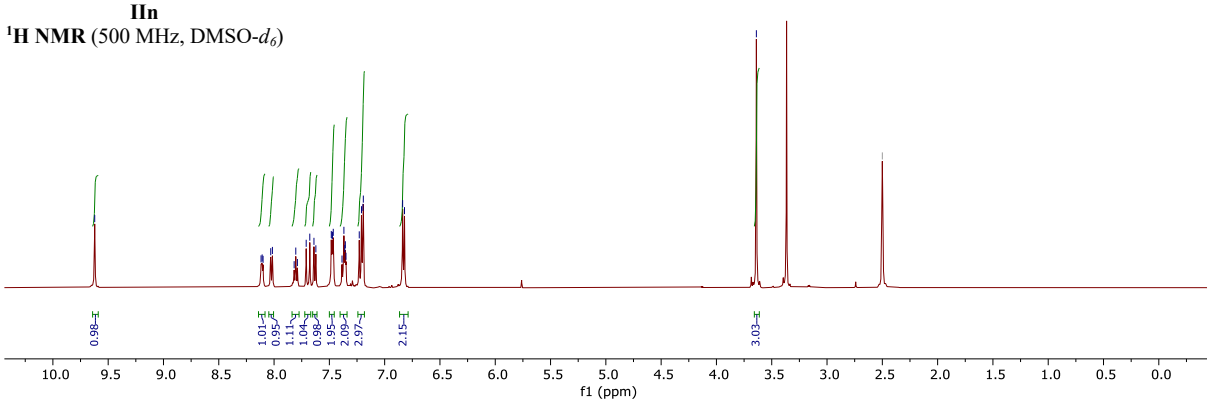
IIm

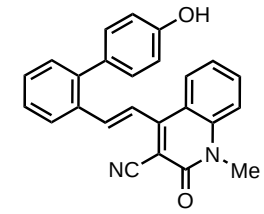
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)



IIn

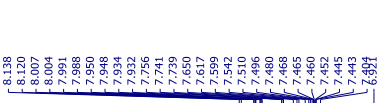
^{1}H NMR (500 MHz, DMSO-d_6)

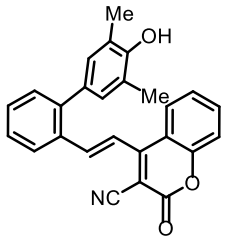




IIn

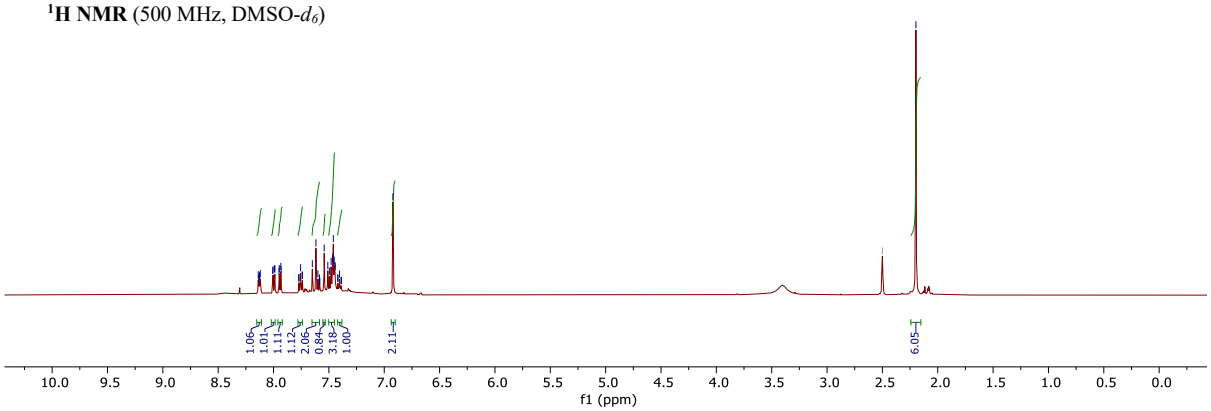
^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

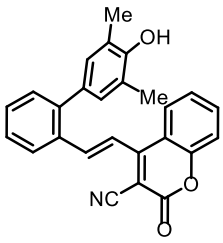




IIo

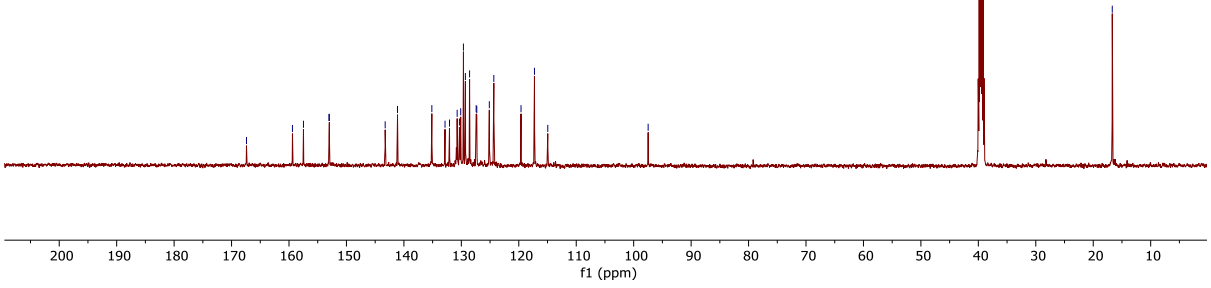
^{1}H NMR (500 MHz, DMSO-d_6)

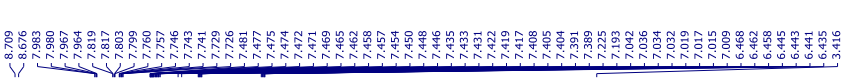


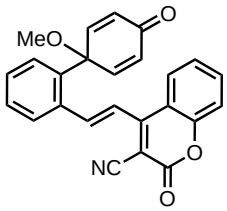


IIo

^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6)

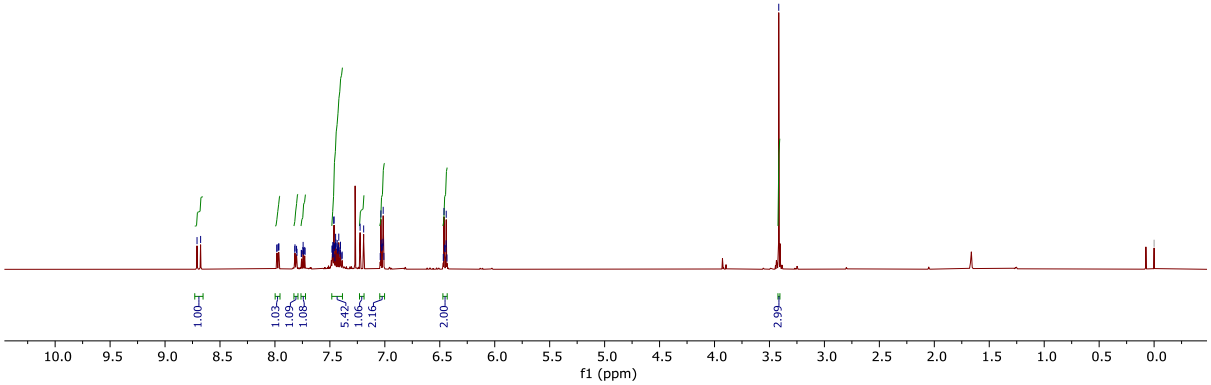


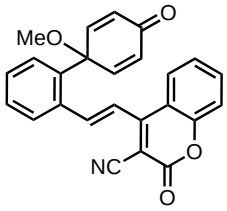




1a

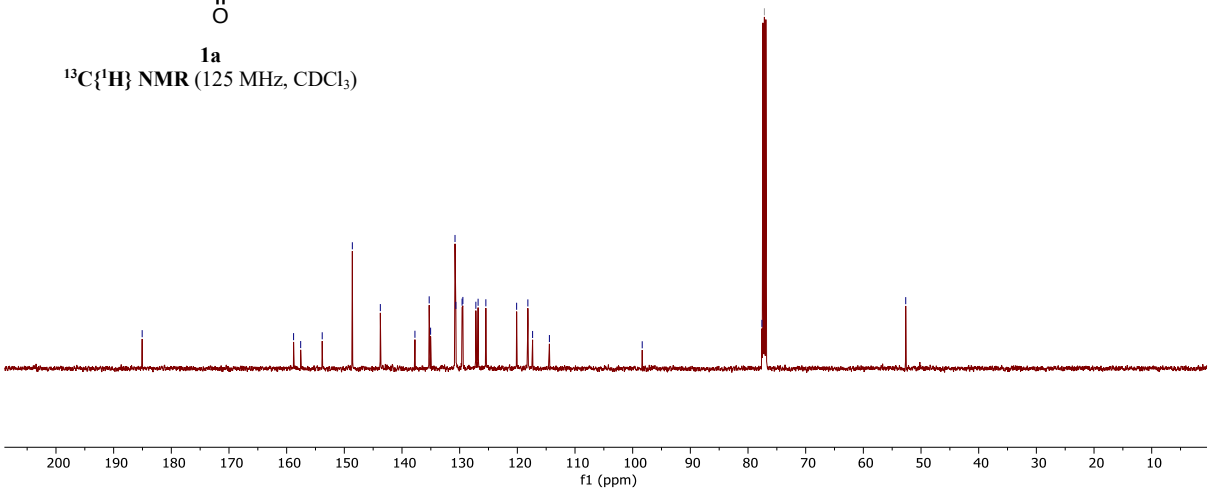
^{1}H NMR (500 MHz, $CDCl_3$)

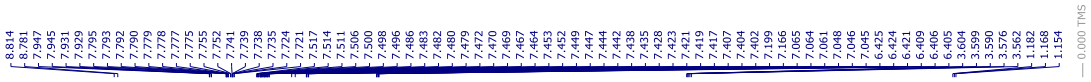


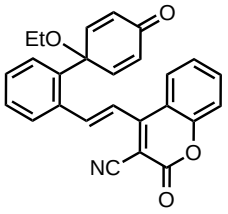


1a

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

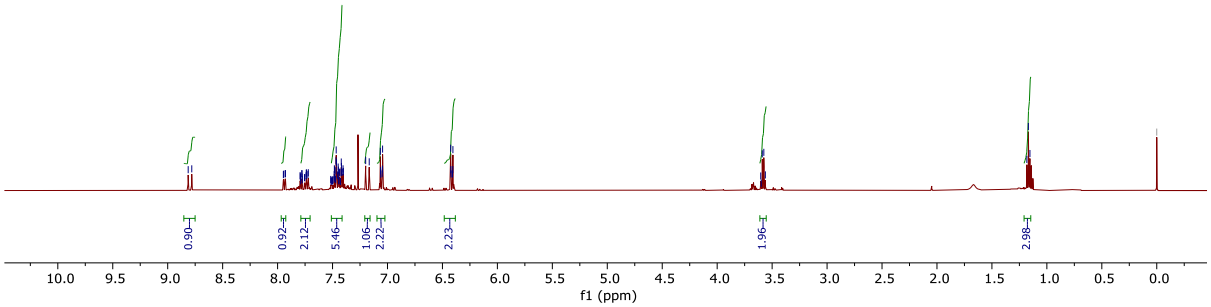


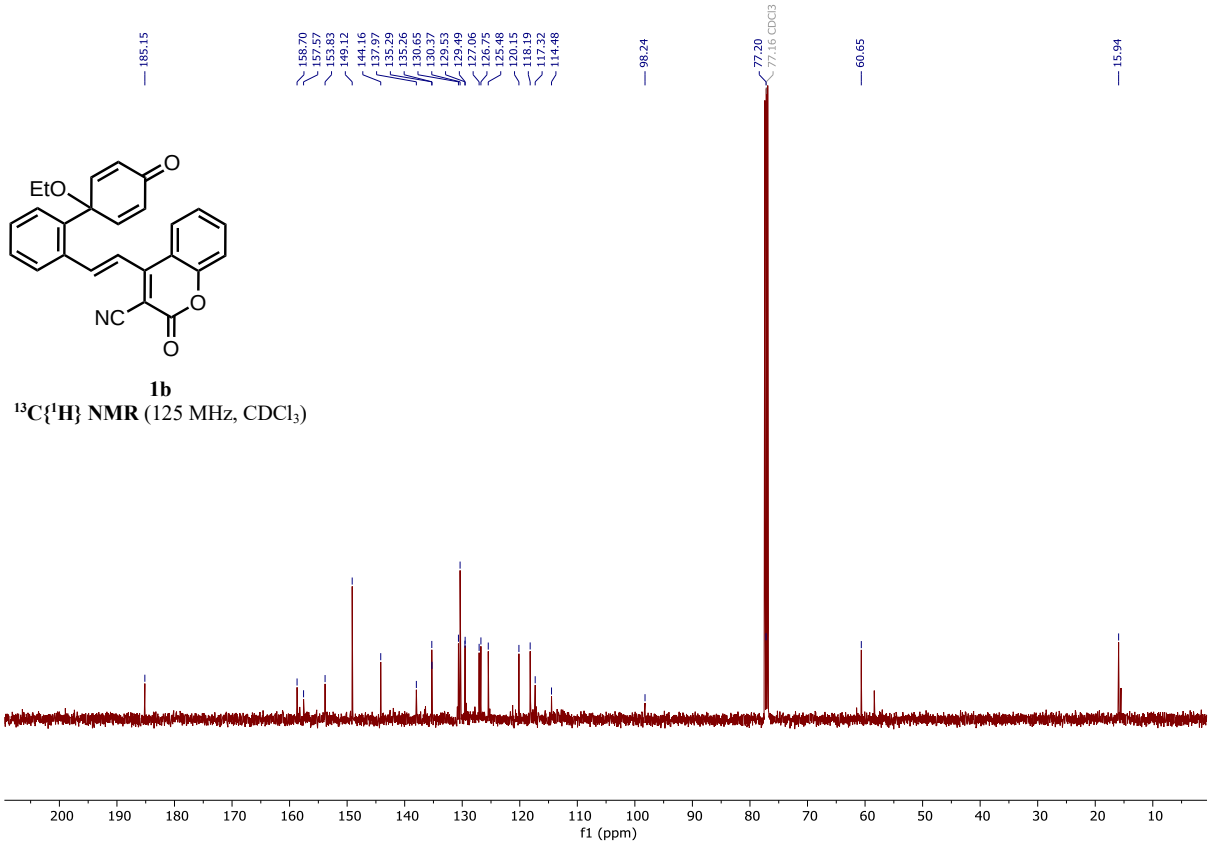




1b

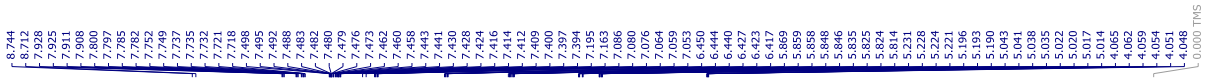
^{1}H NMR (500 MHz, $CDCl_3$)

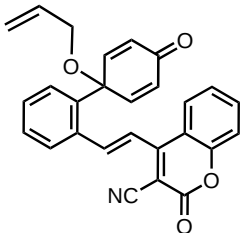




1b

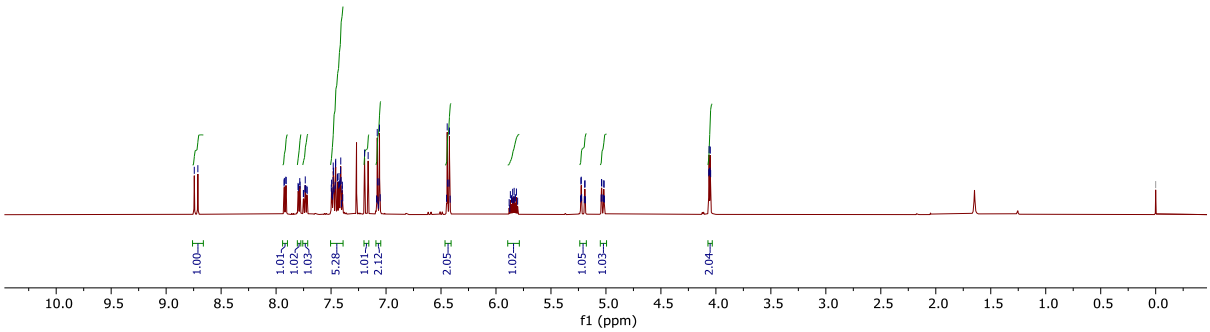
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

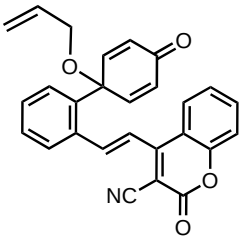




1c

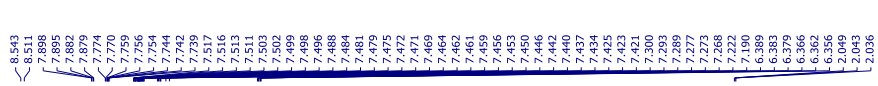
^{1}H NMR (500 MHz, $CDCl_3$)

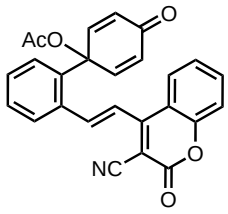




1c

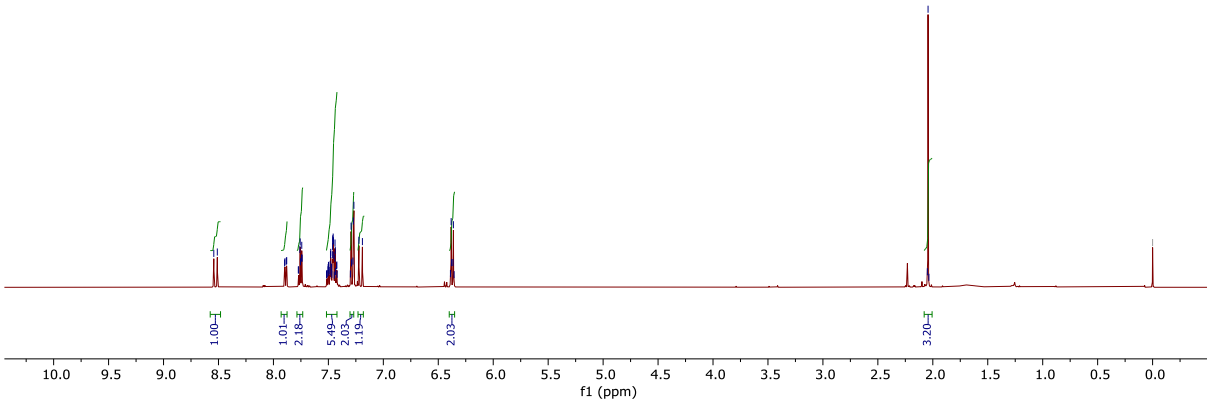
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

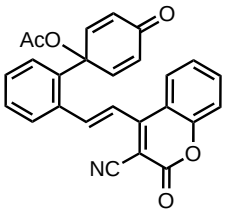




1d

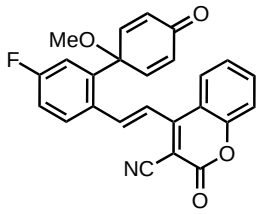
^{1}H NMR (500 MHz, $CDCl_3$)





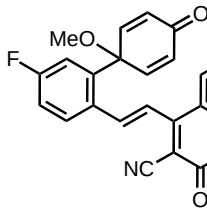
1d

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



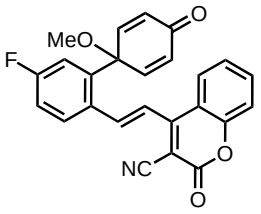
1e

^{1}H NMR (500 MHz, $CDCl_3$)



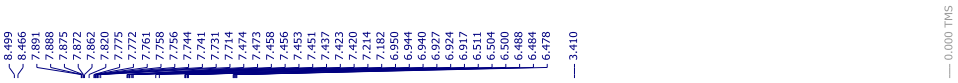
1e

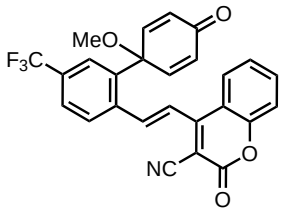
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



1e

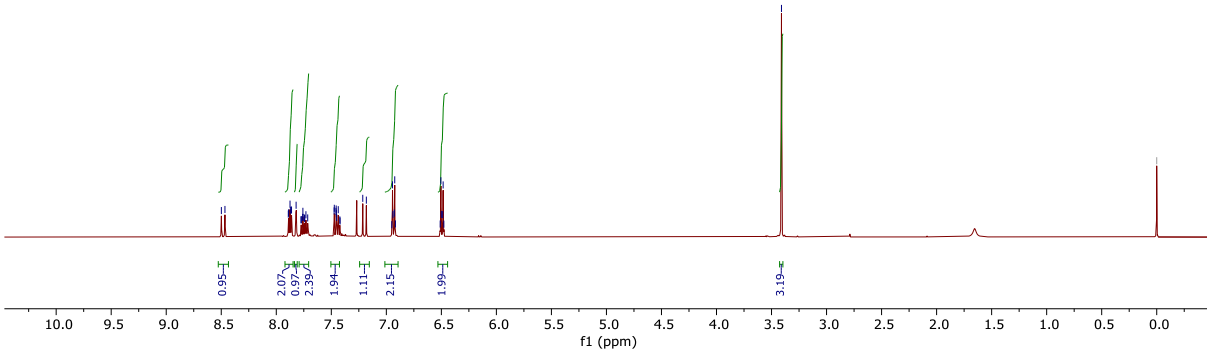
^{19}F NMR (471 MHz, $CDCl_3$)

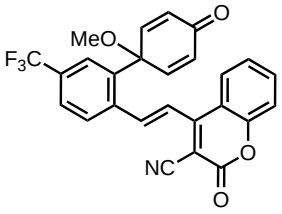




1f

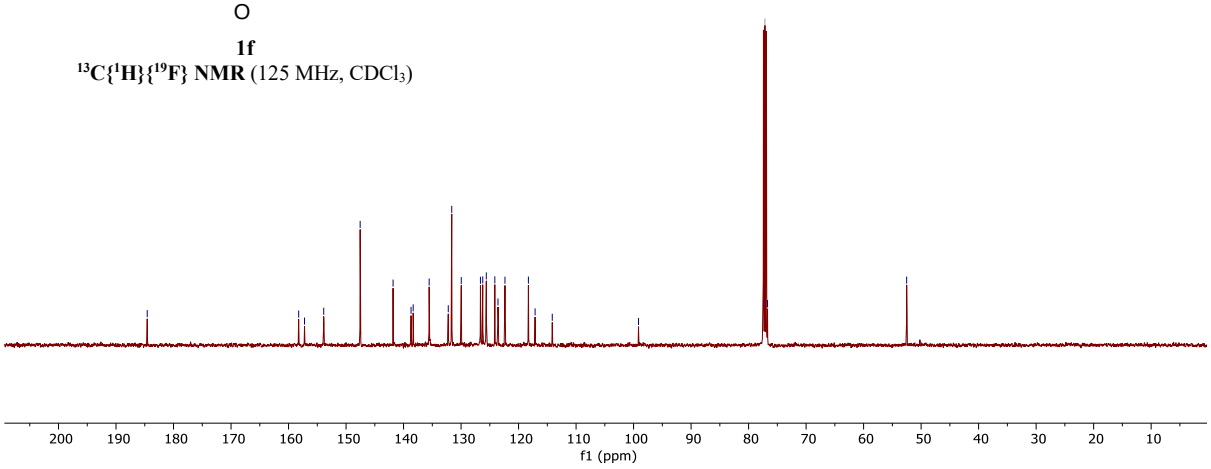
^{1}H NMR (500 MHz, $CDCl_3$)

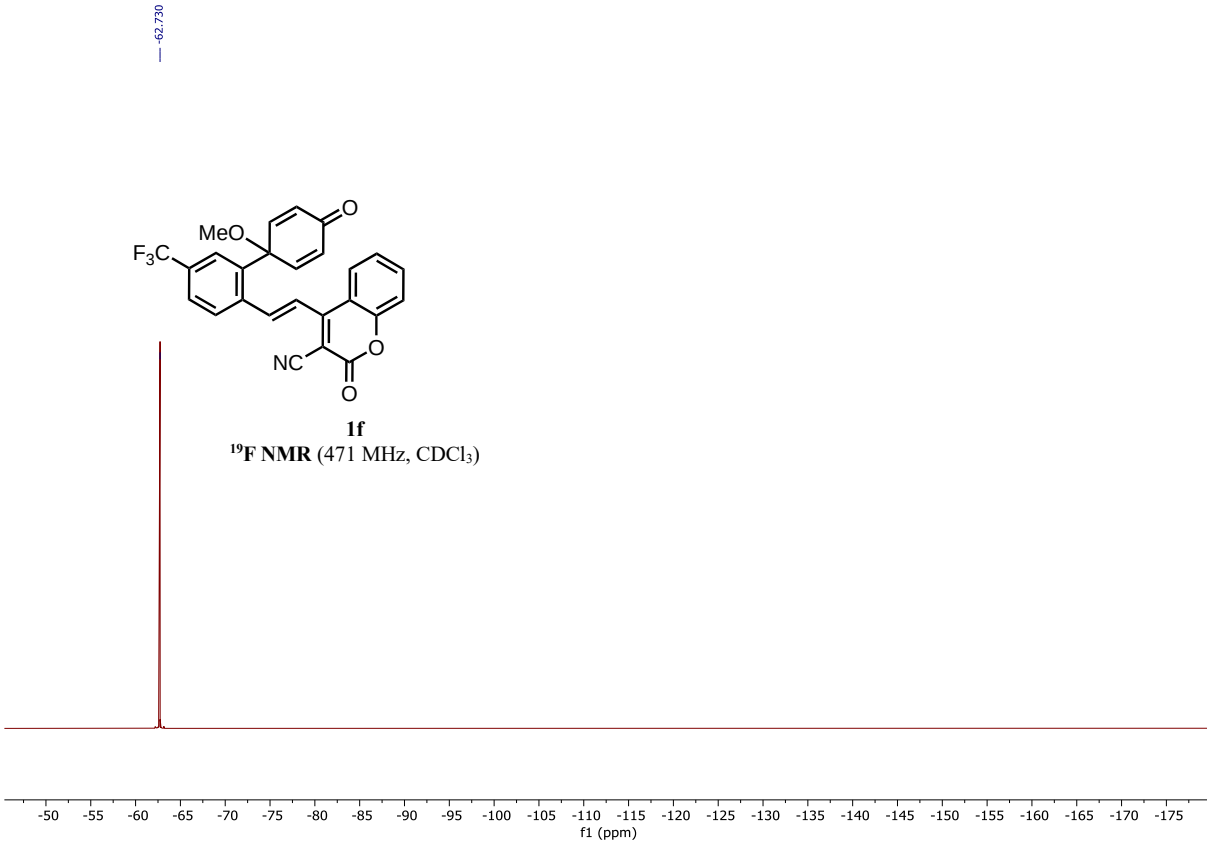




1f

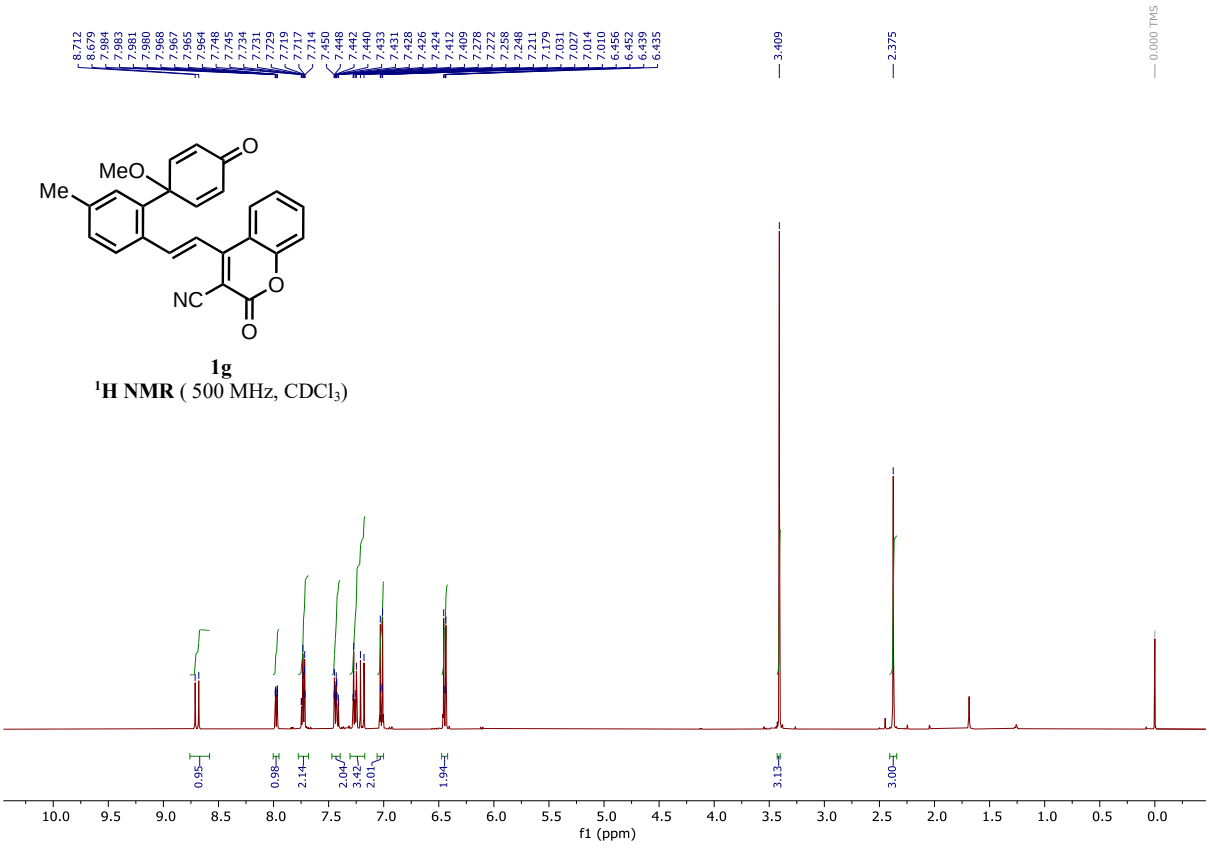
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)





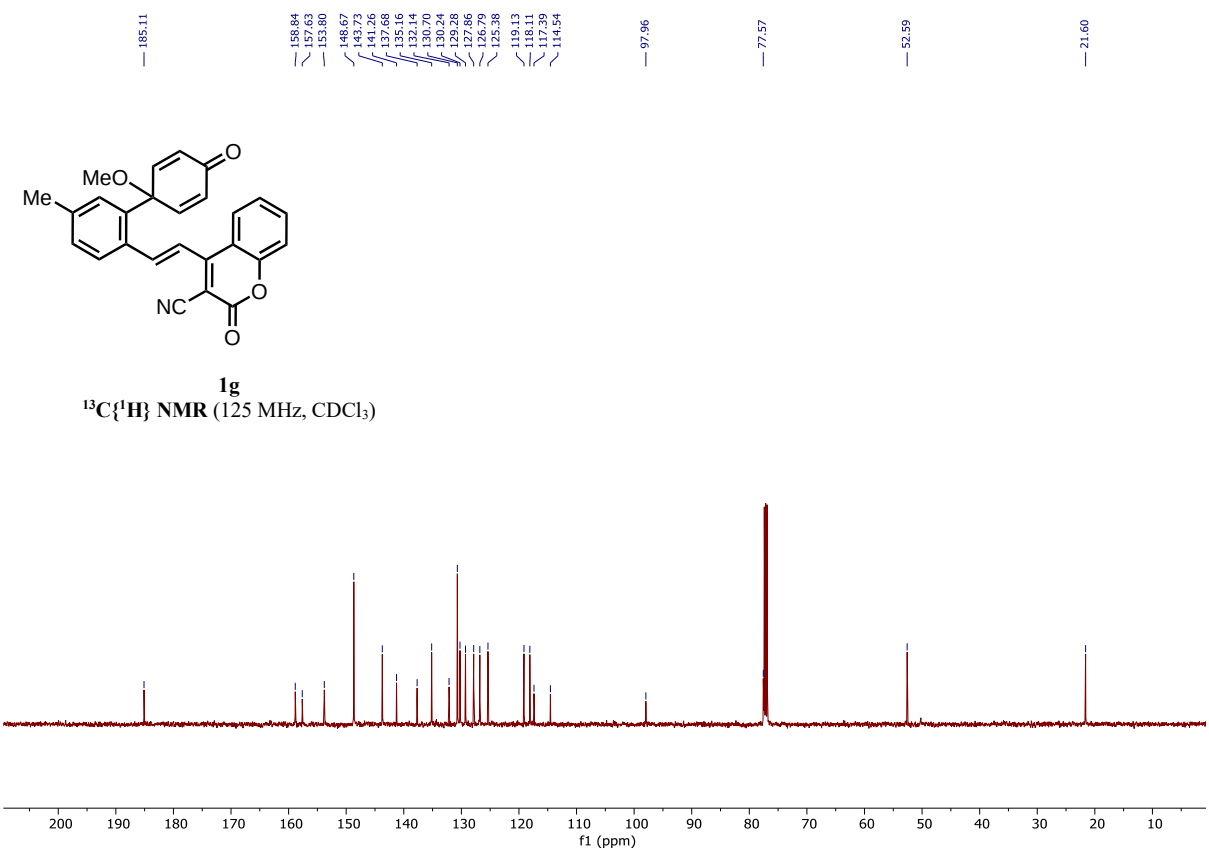
1f

^{19}F NMR (471 MHz, $CDCl_3$)



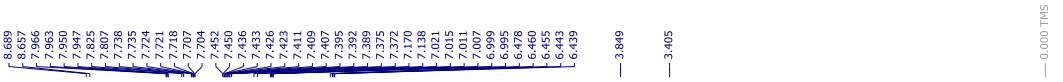
1g

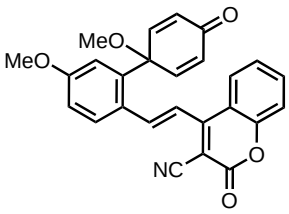
^{1}H NMR (500 MHz, $CDCl_3$)



1g

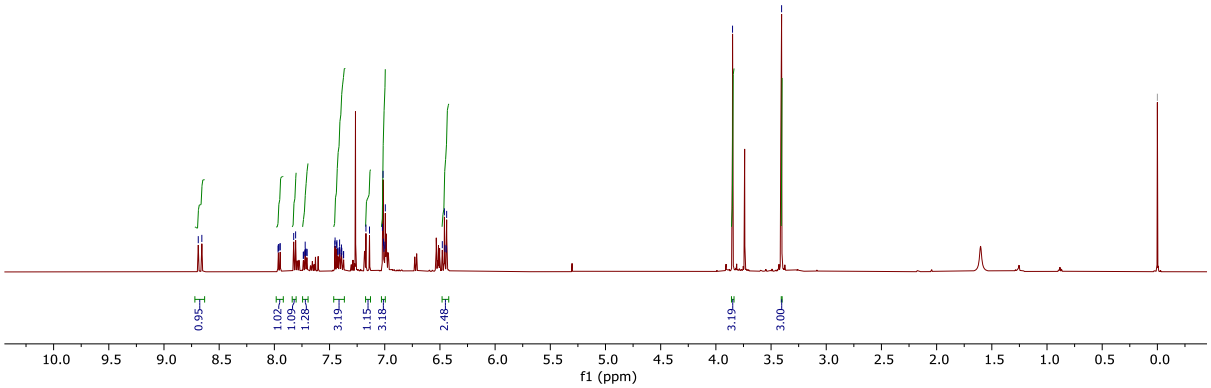
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

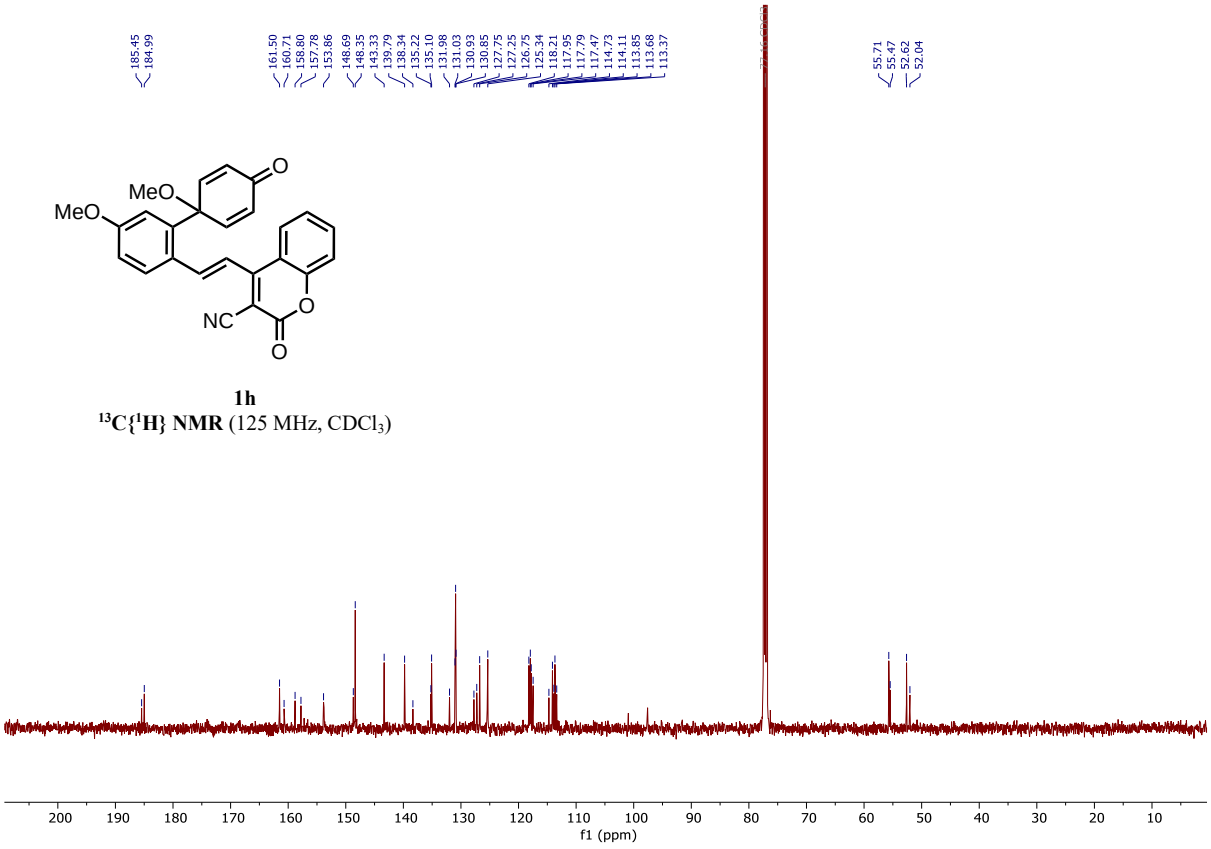




1h

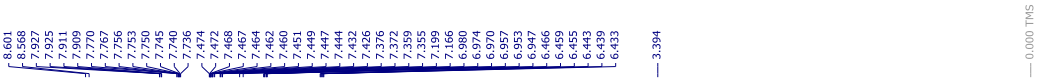
^{1}H NMR (500 MHz, $CDCl_3$)

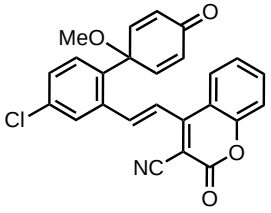




1h

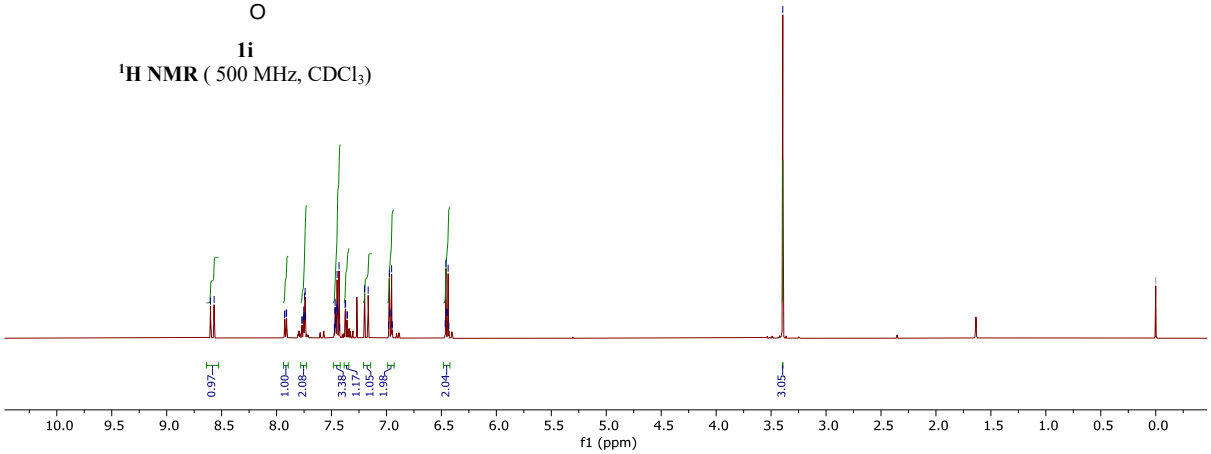
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

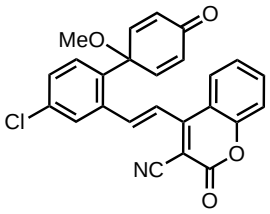




1i

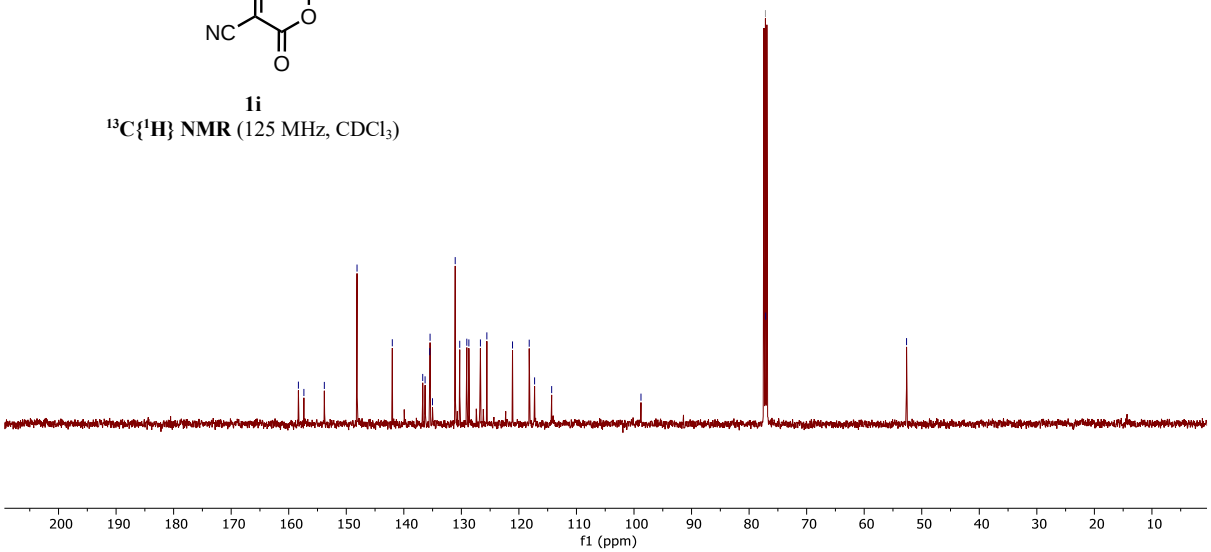
^{1}H NMR (500 MHz, $CDCl_3$)

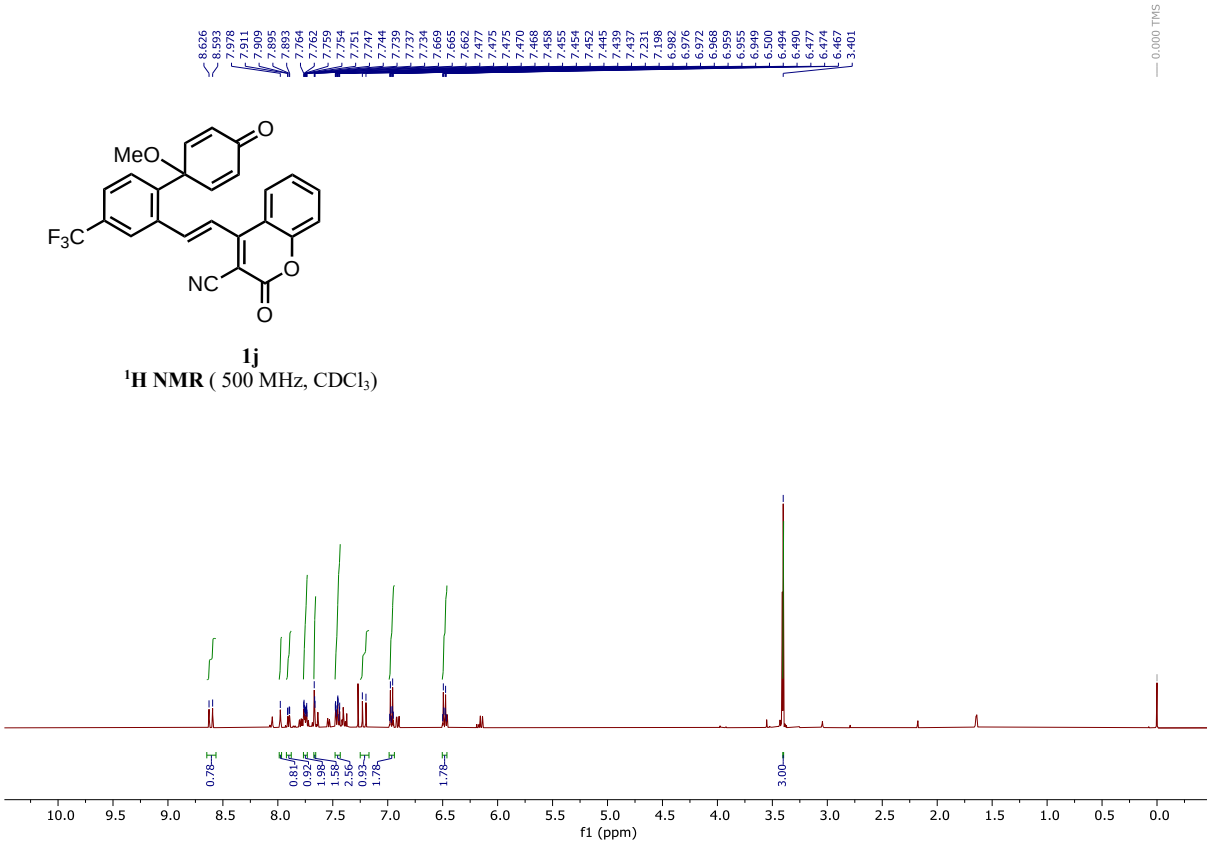




1i

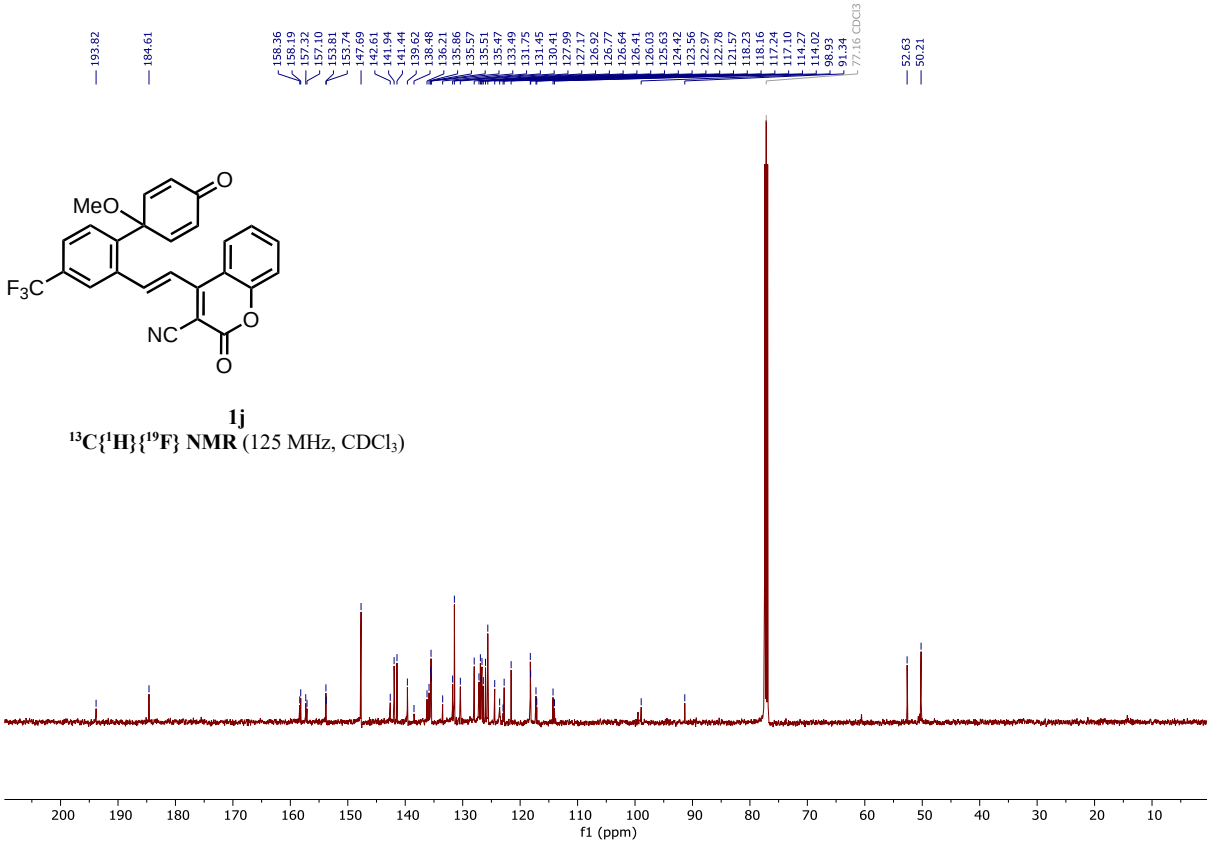
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)





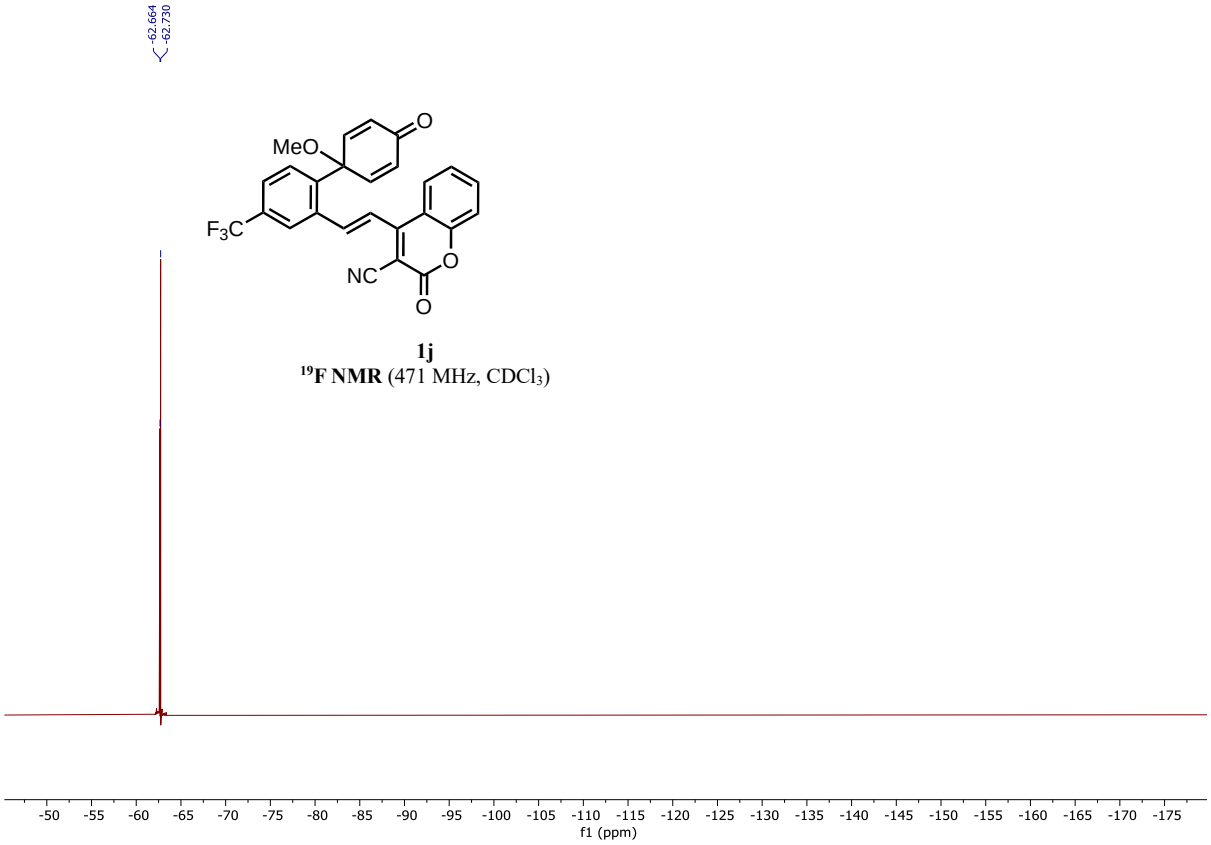
1j

^{1}H NMR (500 MHz, $CDCl_3$)



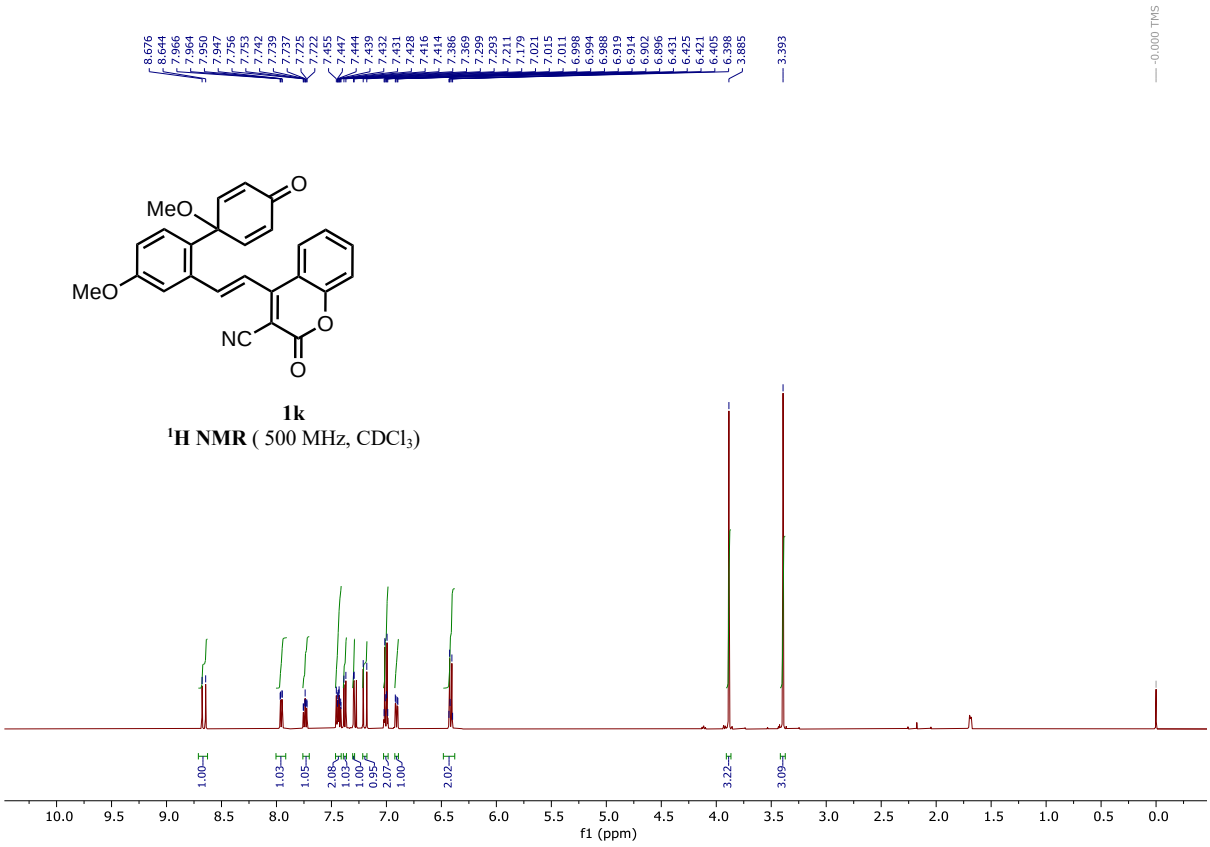
1j

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



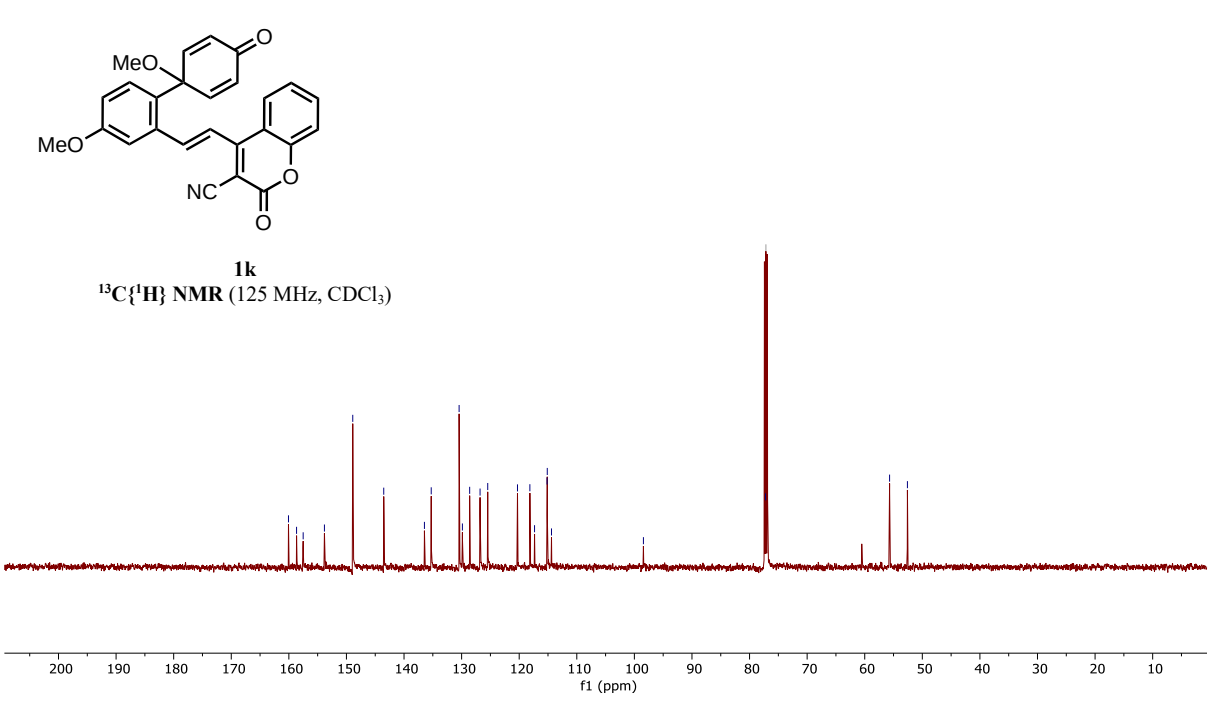
1j

^{19}F NMR (471 MHz, $CDCl_3$)



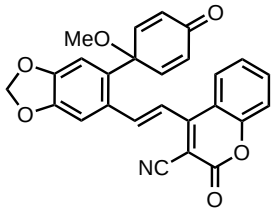
1k

^{1}H NMR (500 MHz, $CDCl_3$)



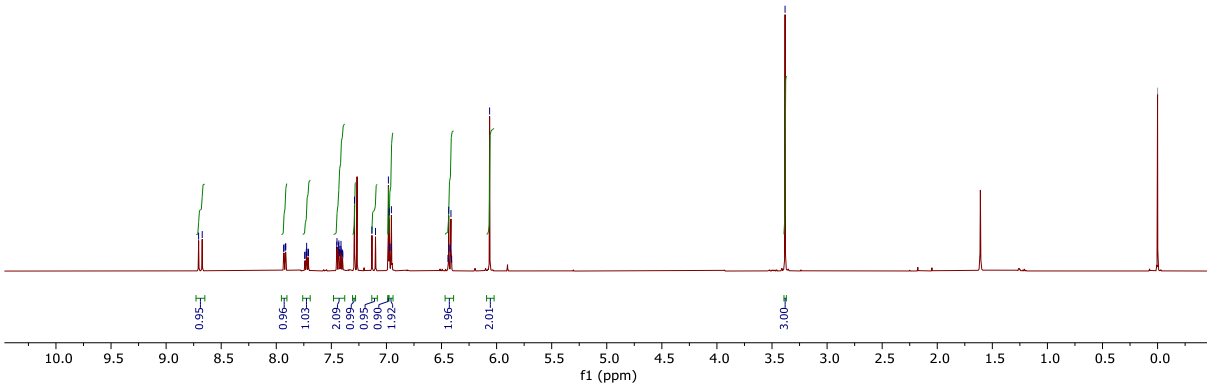
1k

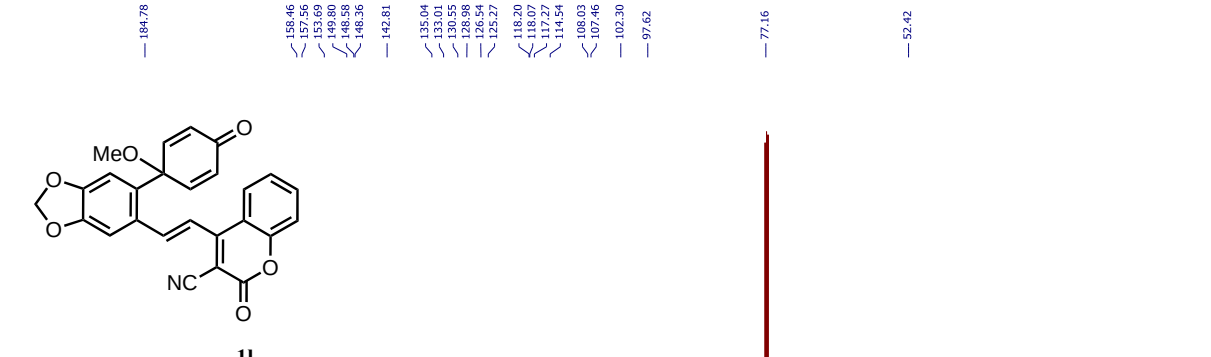
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



1l

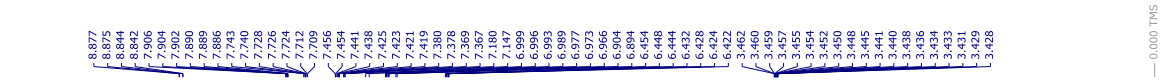
^{1}H NMR (500 MHz, $CDCl_3$)

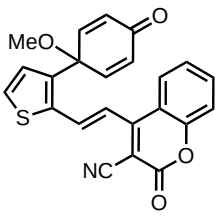




1l

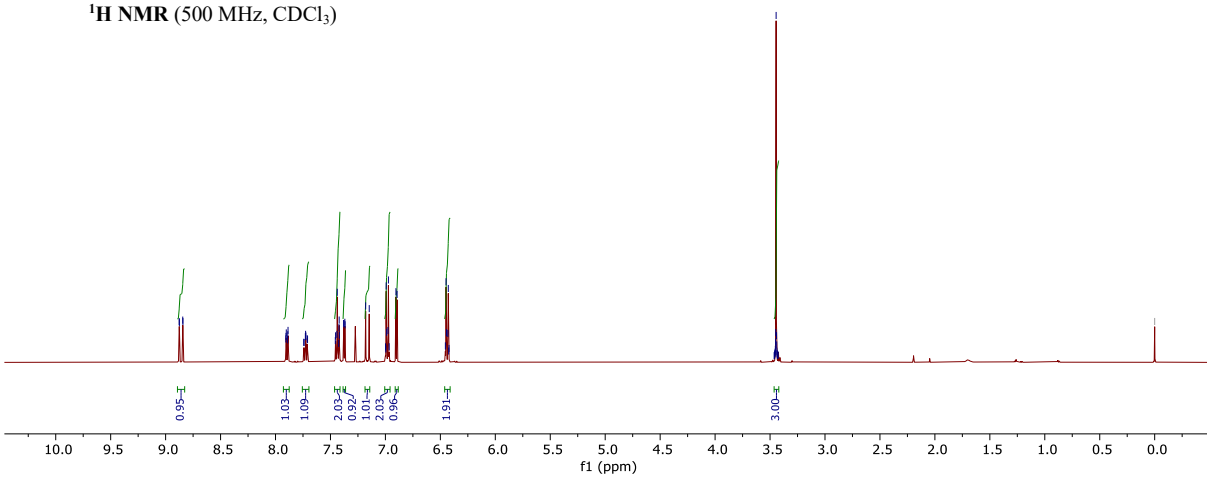
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

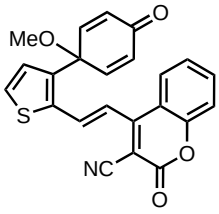




1m

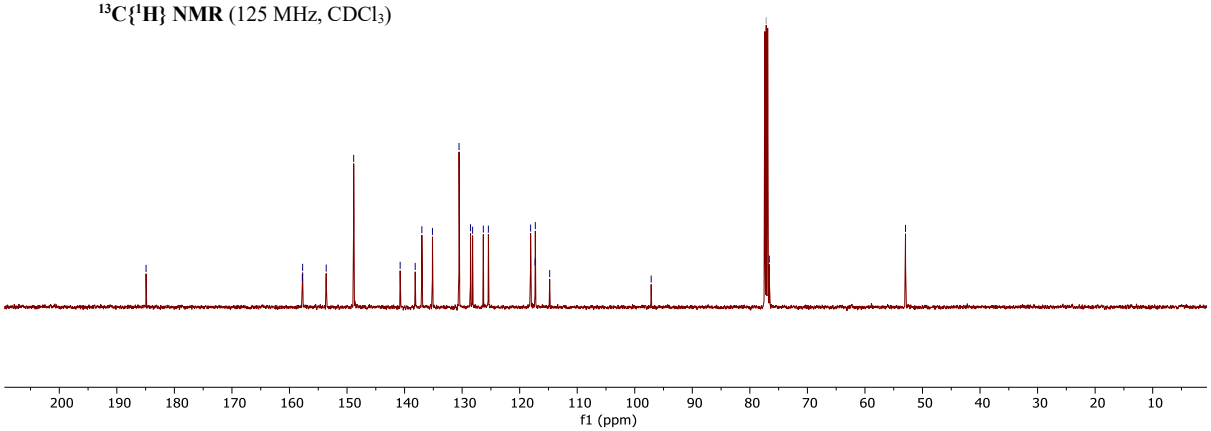
^{1}H NMR (500 MHz, $CDCl_3$)

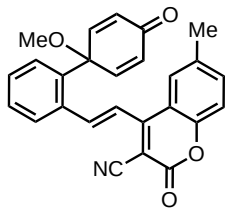




1m

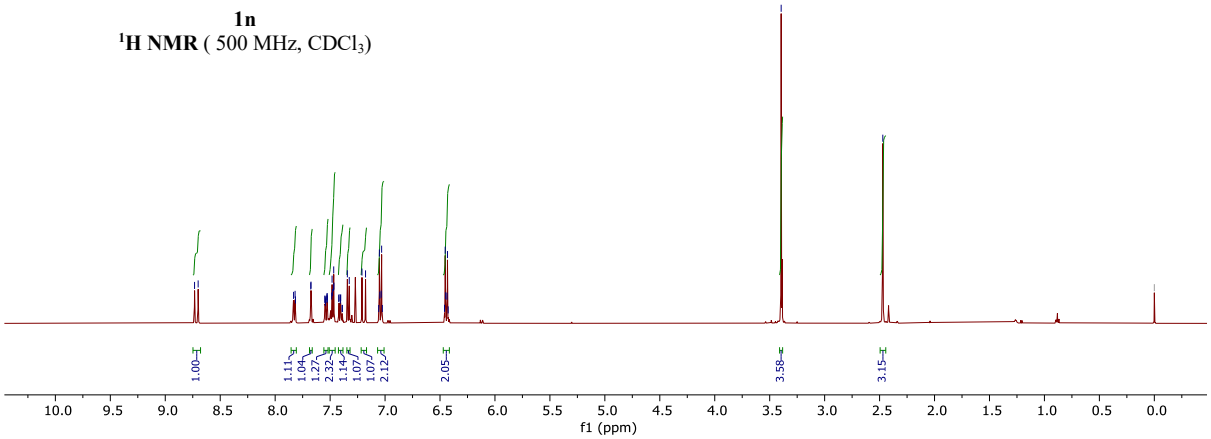
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

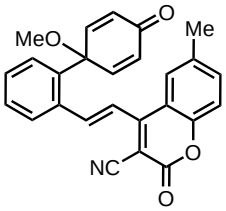




1n

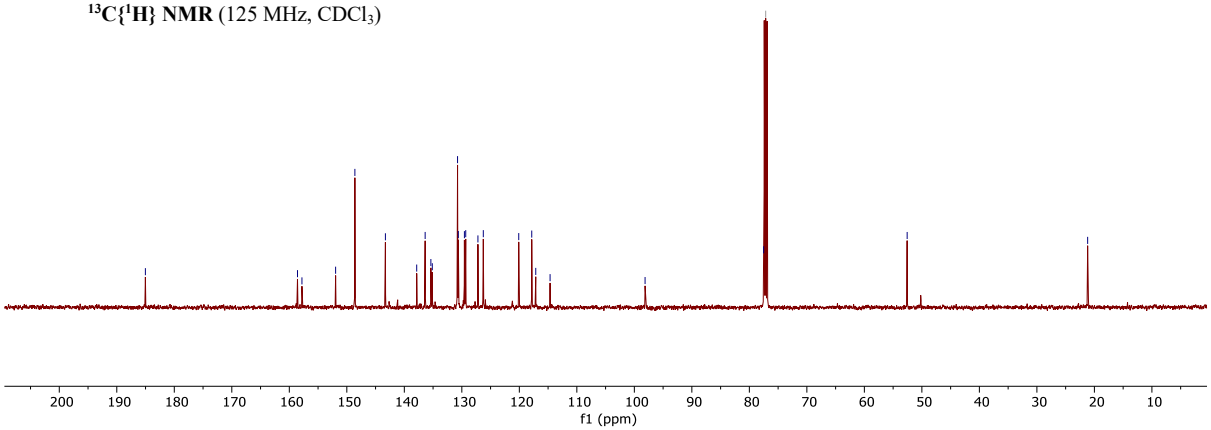
^{1}H NMR (500 MHz, $CDCl_3$)

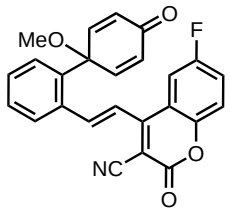




1n

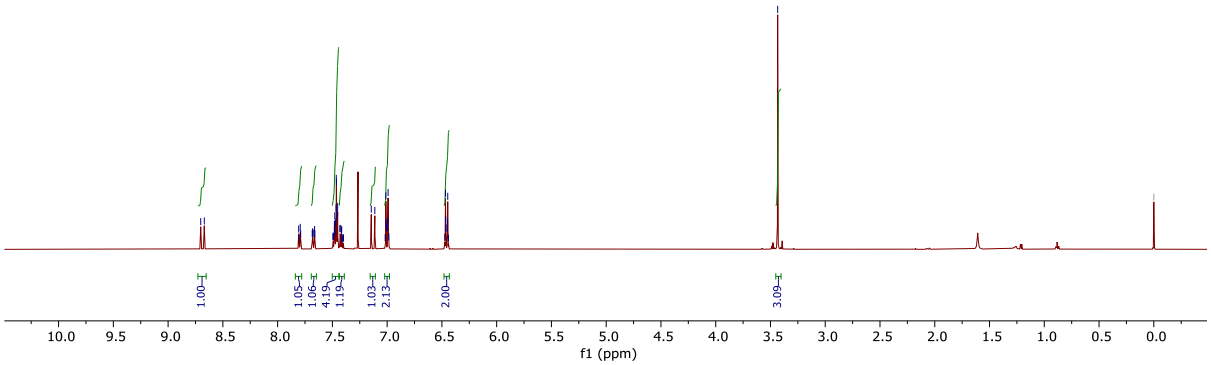
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

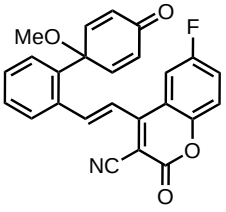




1o

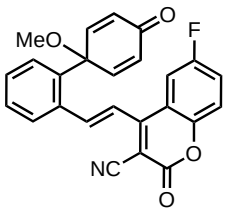
^{1}H NMR (500 MHz, $CDCl_3$)





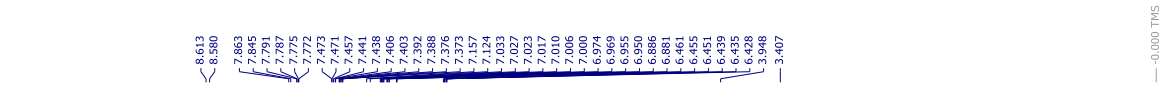
1o

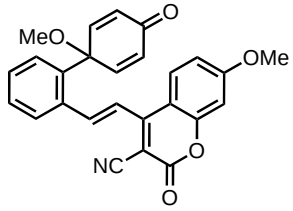
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



1o

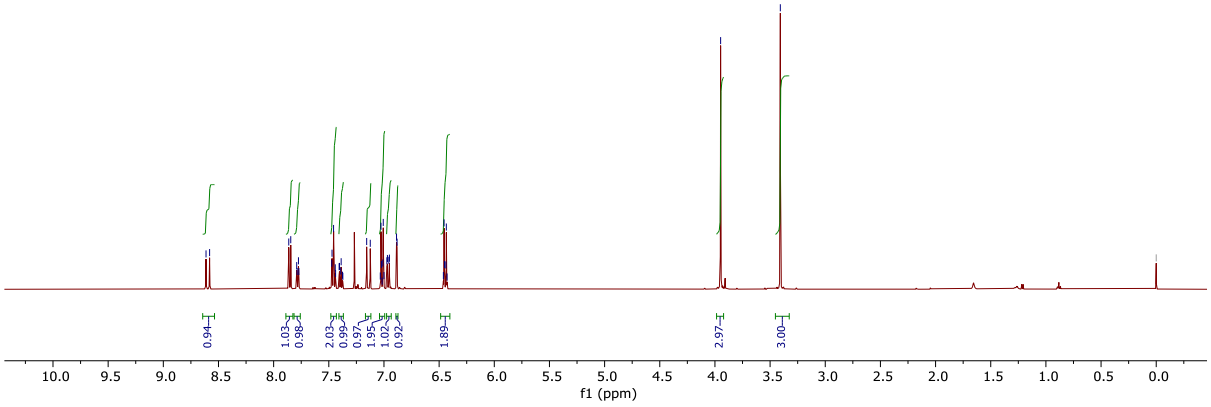
^{19}F NMR (471 MHz, $CDCl_3$)

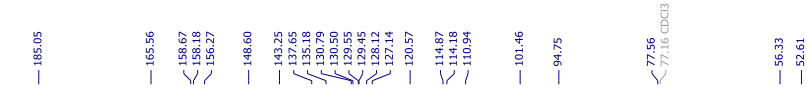


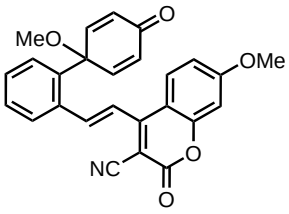


1p

^{1}H NMR (500 MHz, $CDCl_3$)

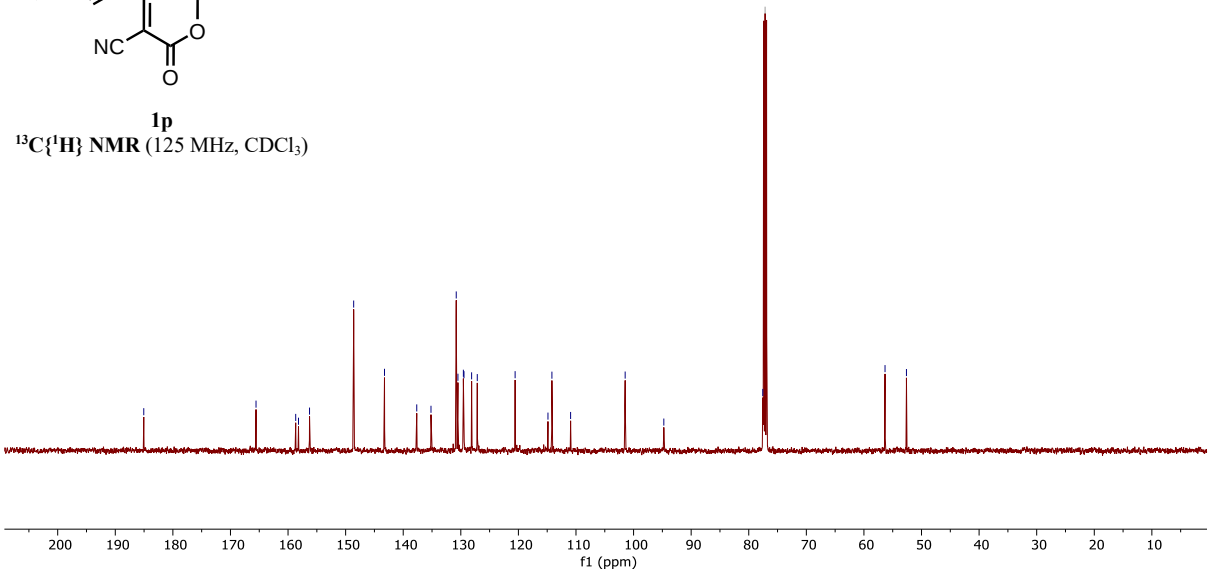


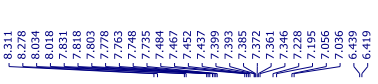


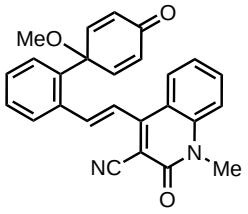


1p

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

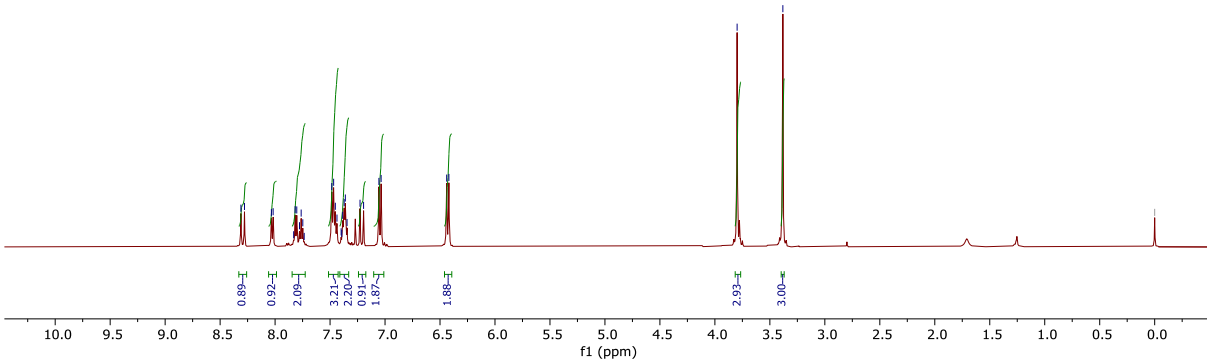


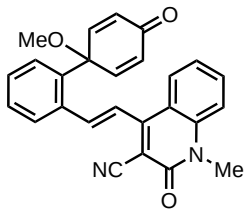




1q

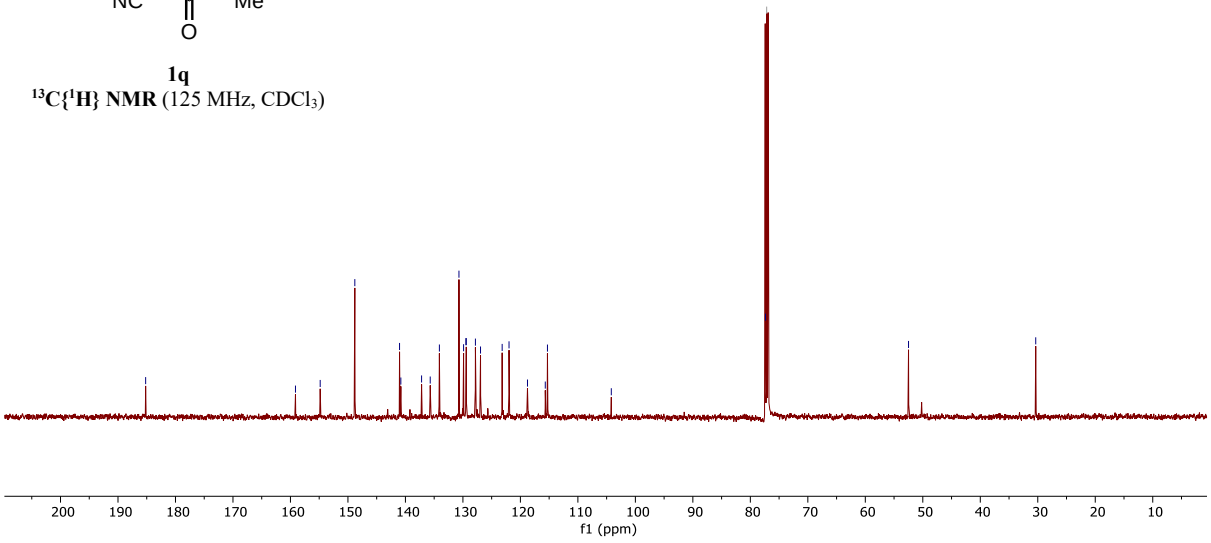
^{1}H NMR (500 MHz, $CDCl_3$)

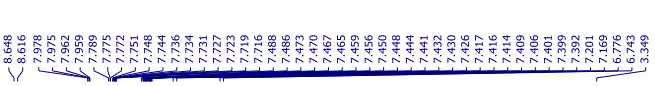


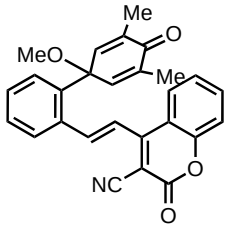


1q

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

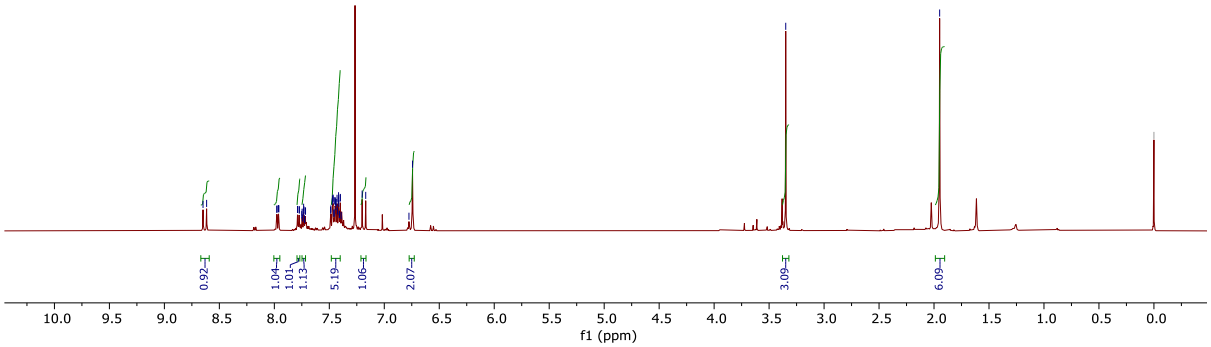


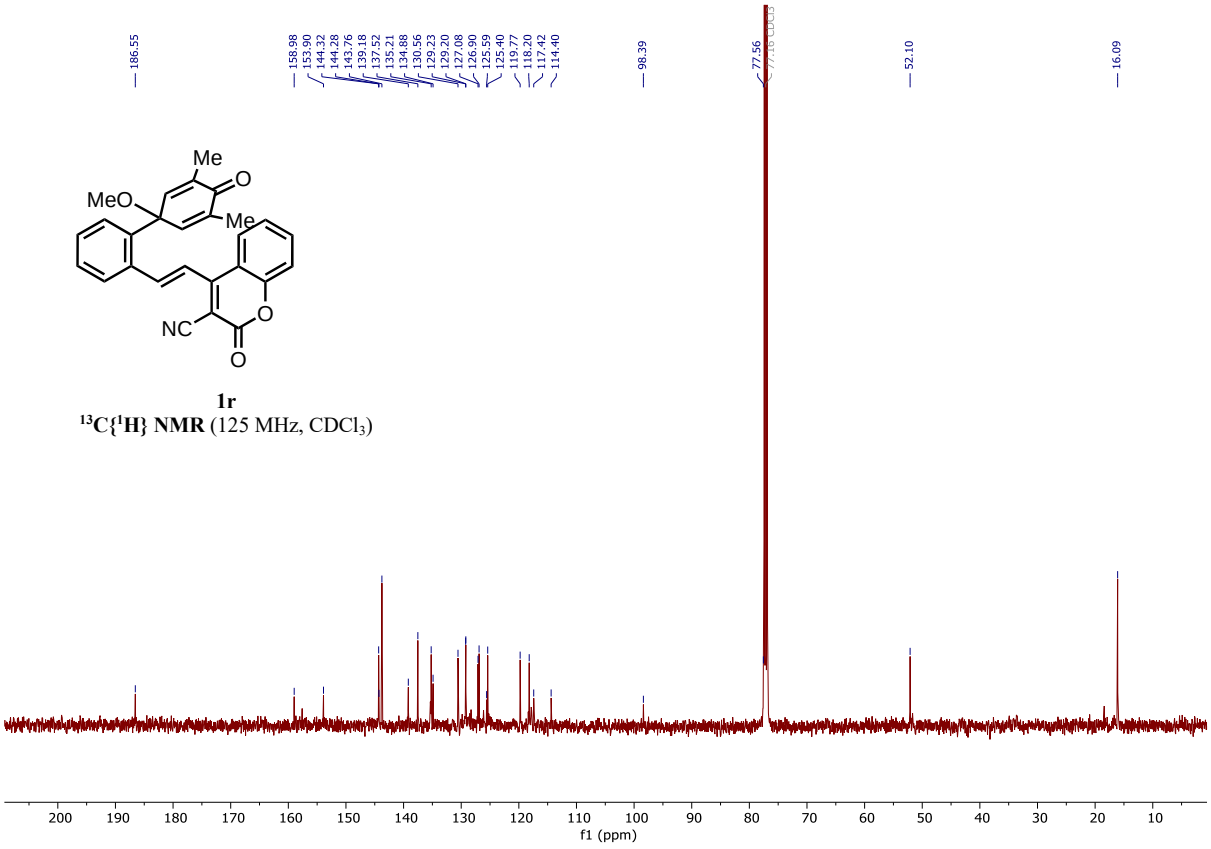




1r

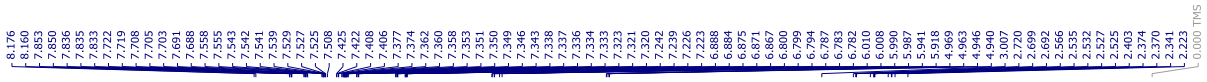
^{1}H NMR (500 MHz, $CDCl_3$)

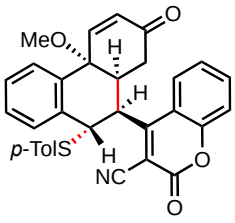




1r

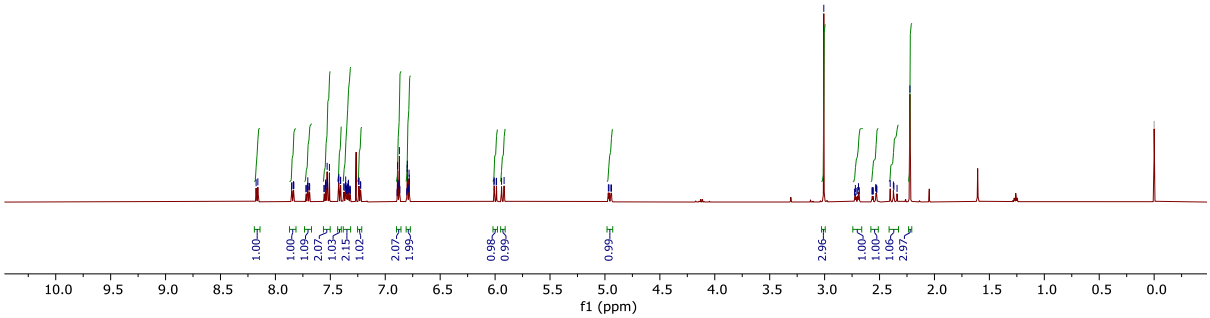
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

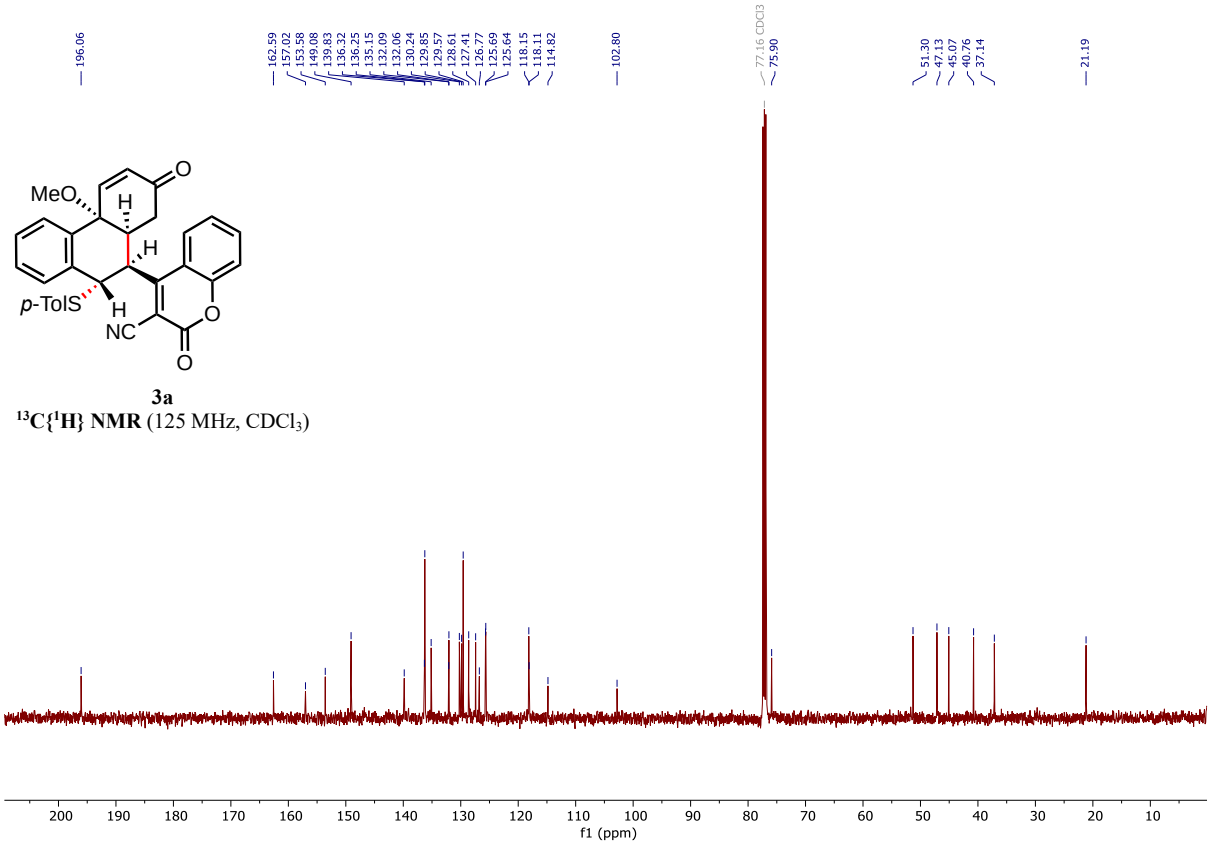




3a

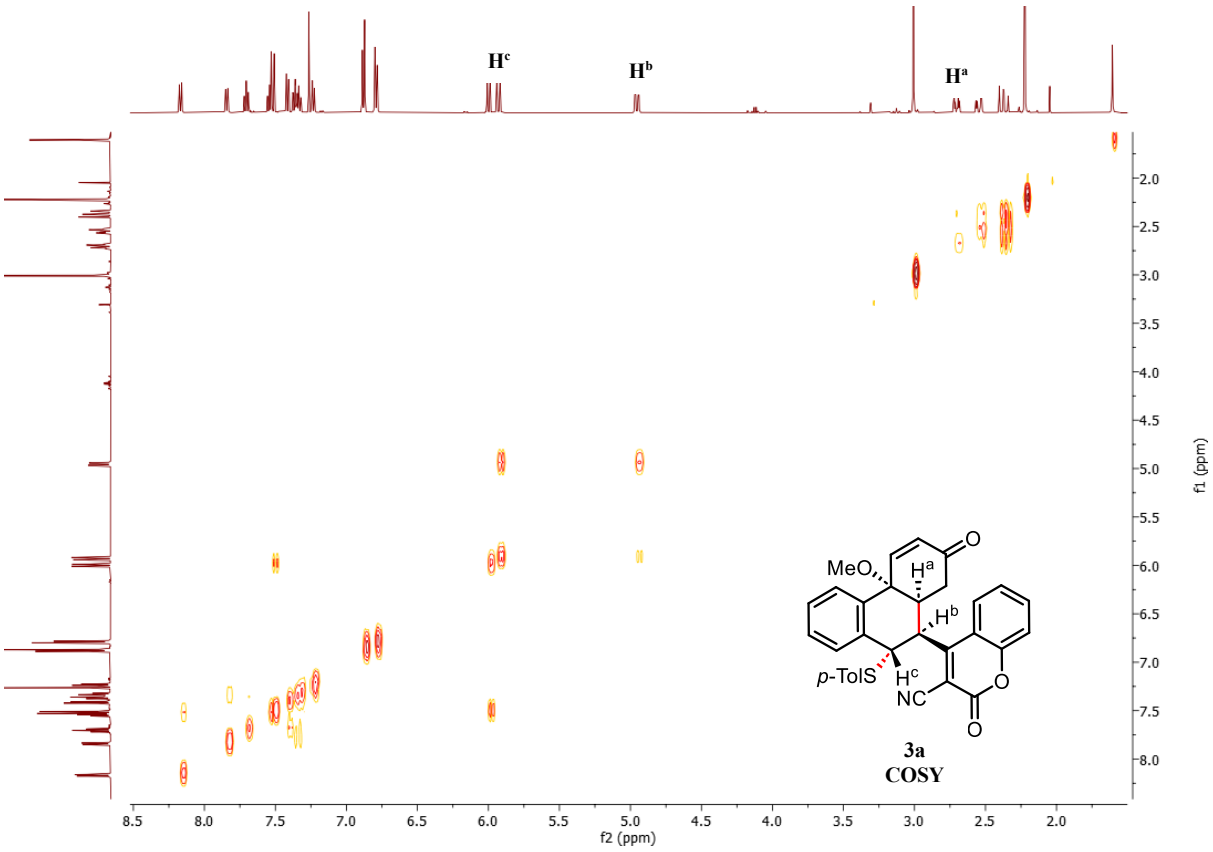
^{1}H NMR (500 MHz, $CDCl_3$)

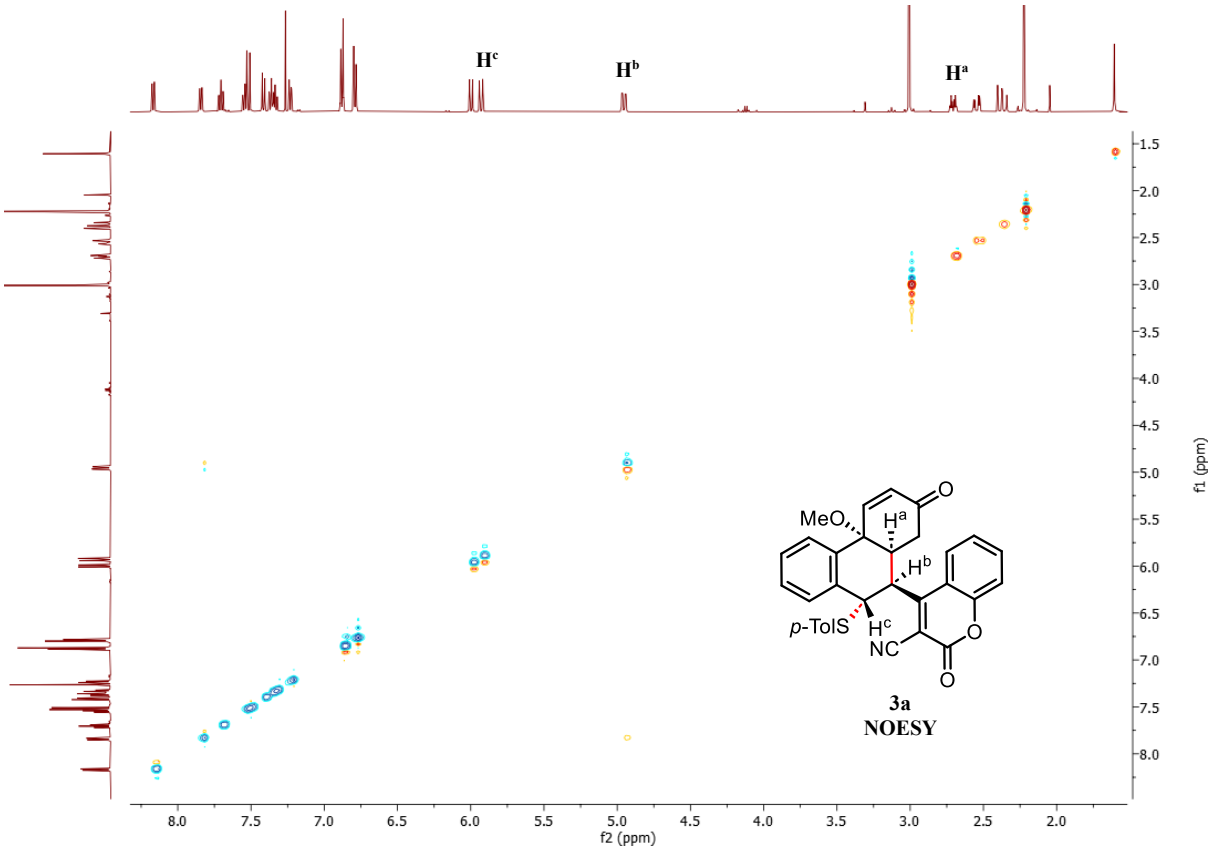


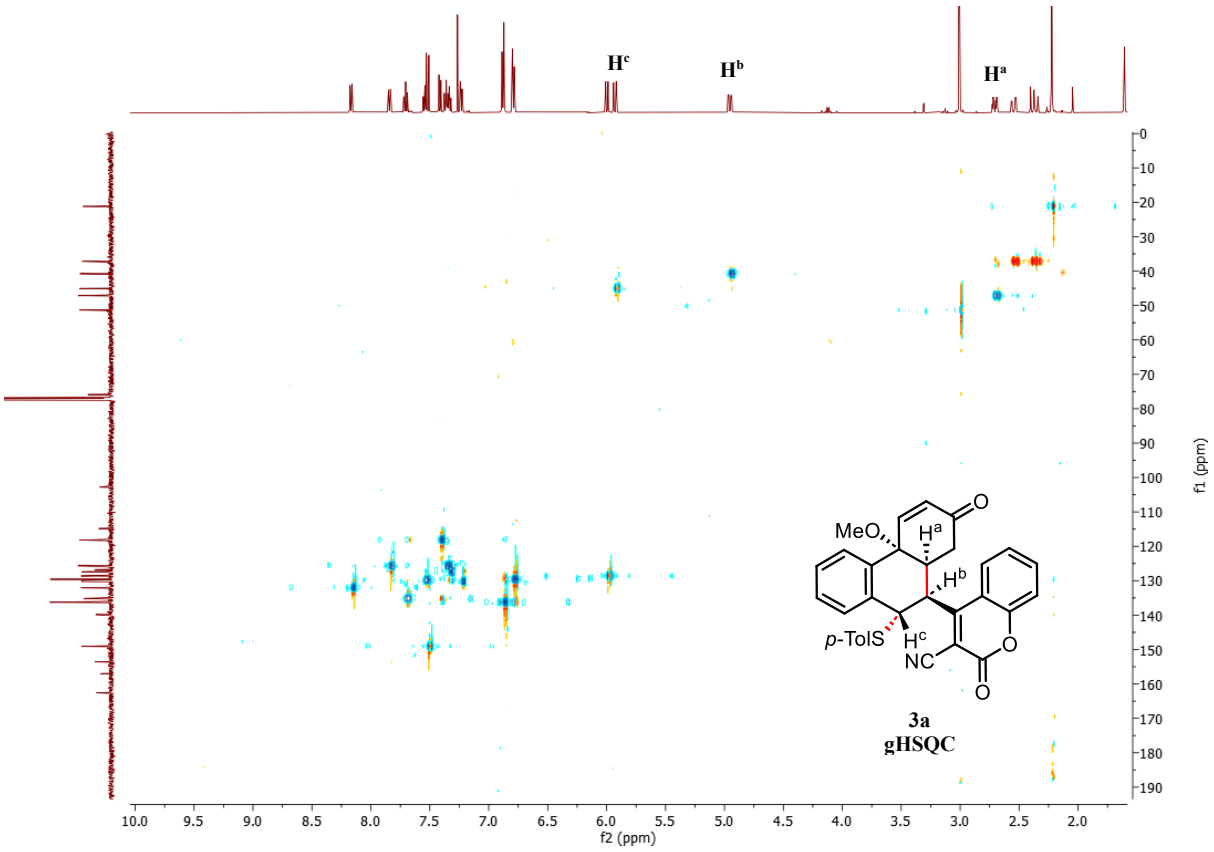


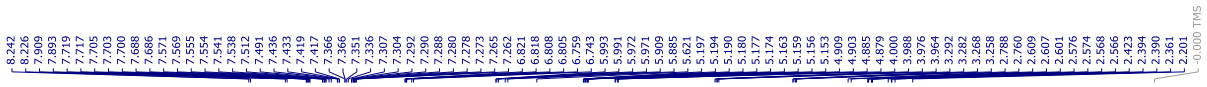
3a

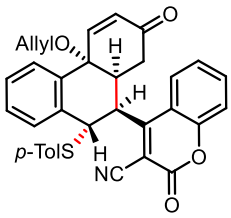
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)


H^c
H^b
H^a
MeO
H^a
H^b
p-TolS
H^c
NC
O
O
O
3a
COSY
f2 (ppm)
f1 (ppm)


H^c
H^b
H^a
MeO
H^a
H^b
p-TolS
H^c
NC
O
O
O
3a
NOESY
f2 (ppm)
f1 (ppm)

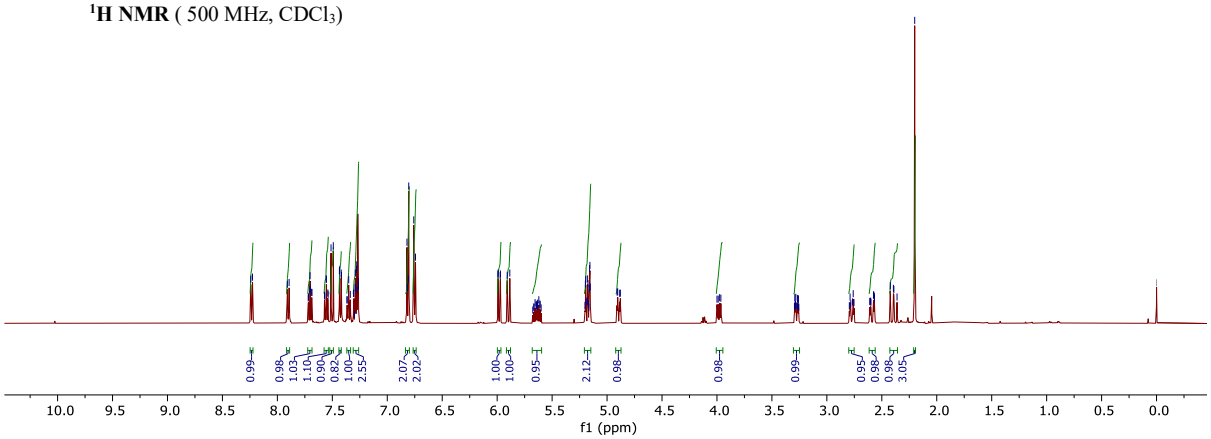

Hc
Hb
Ha
MeO
Ha
Hb
p-TolS
Hc
NC
O
O
O
3a
gHSQC
f2 (ppm)
f1 (ppm)

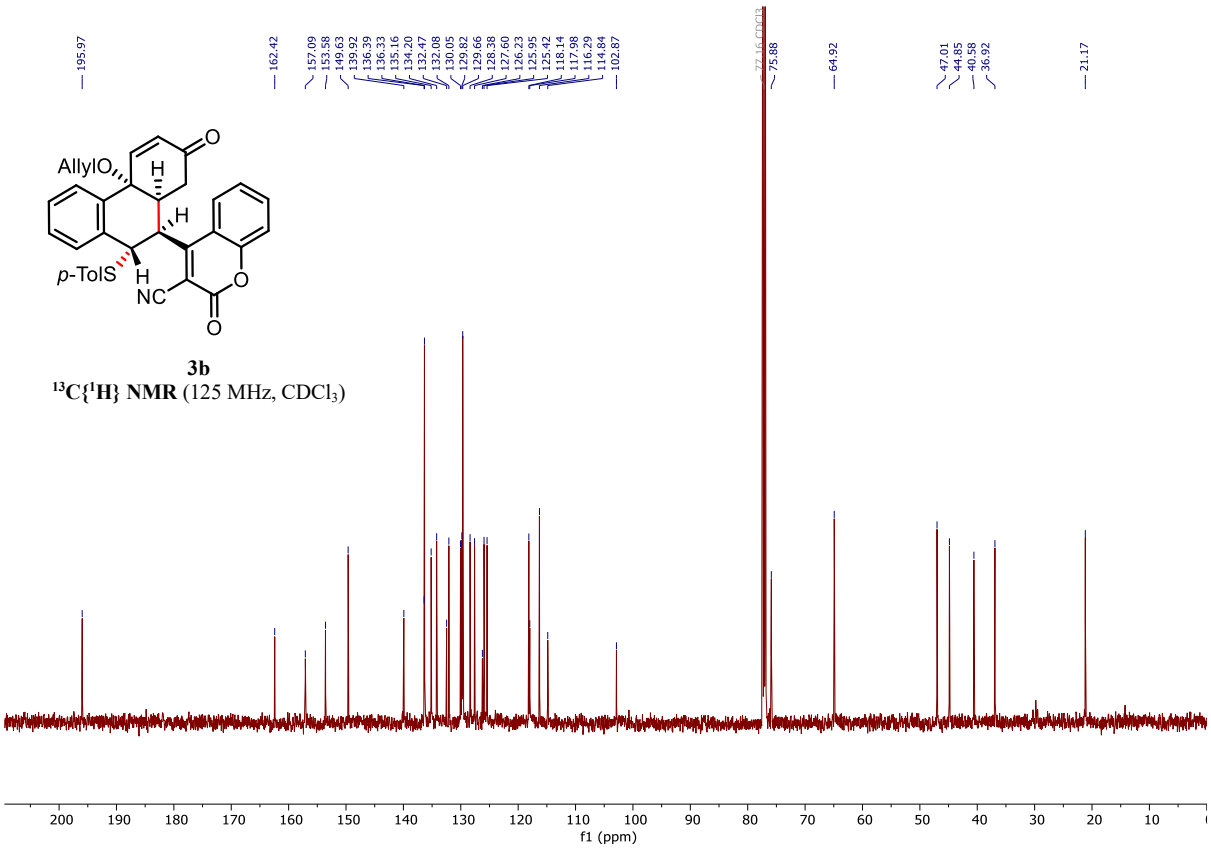




3b

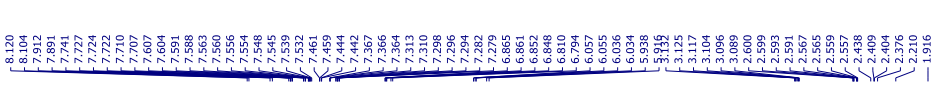
^{1}H NMR (500 MHz, $CDCl_3$)

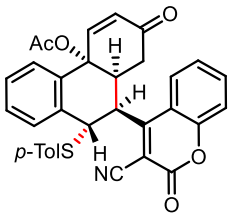




3b

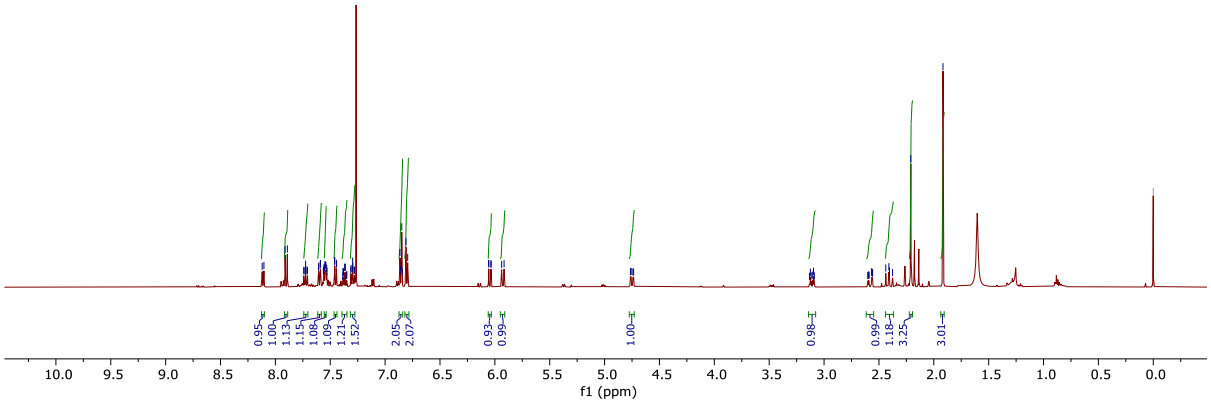
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

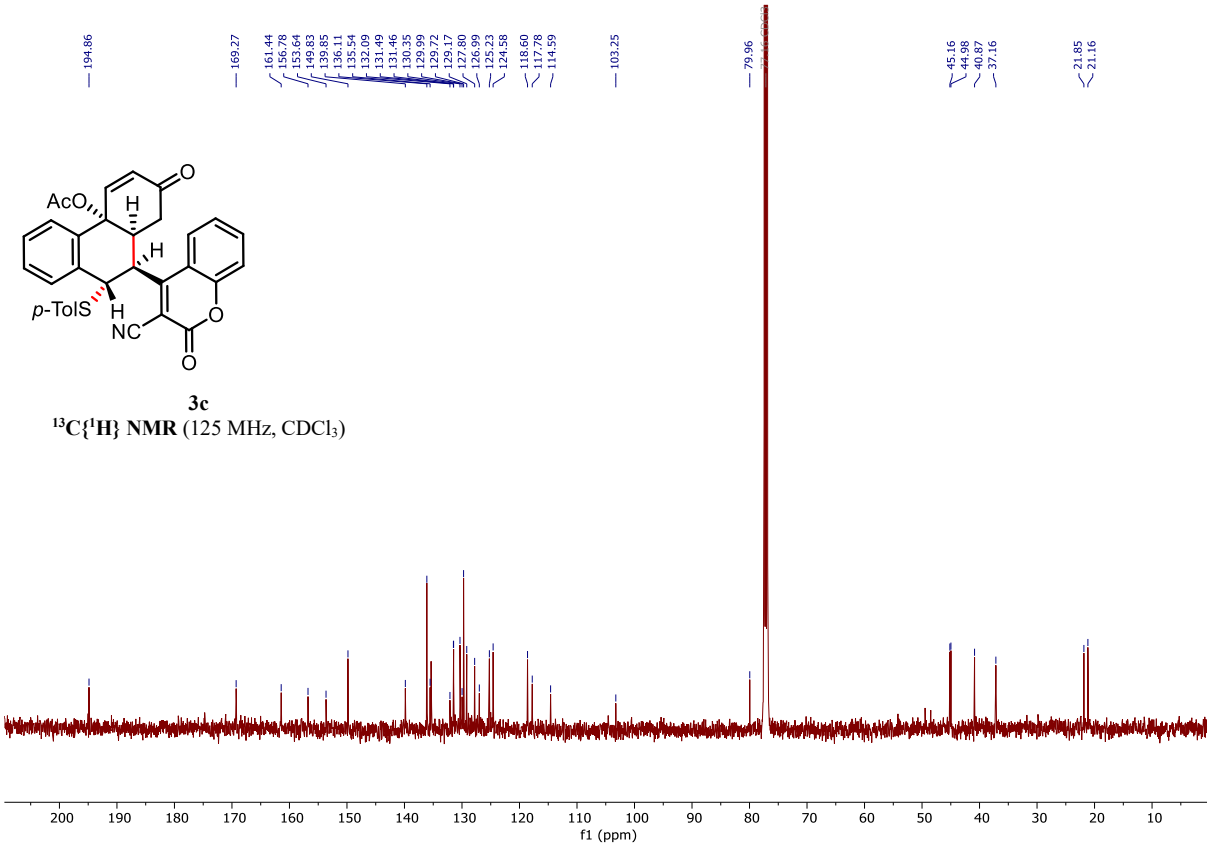




3c

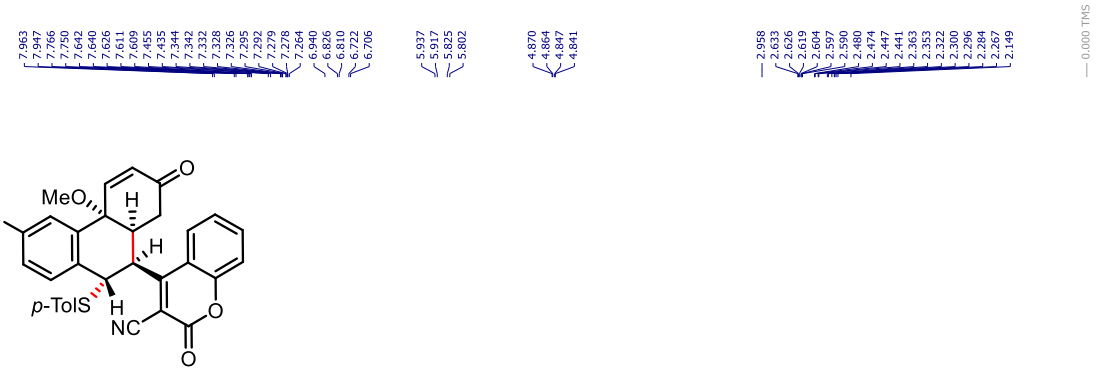
^{1}H NMR (500 MHz, $CDCl_3$)





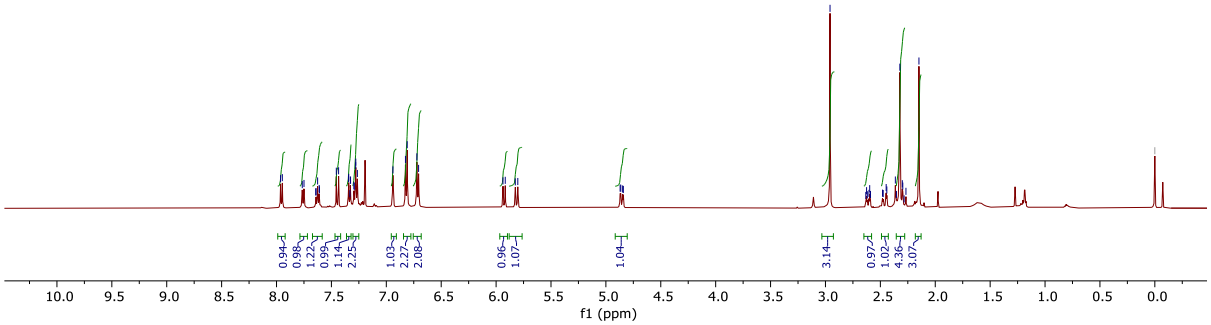
3c

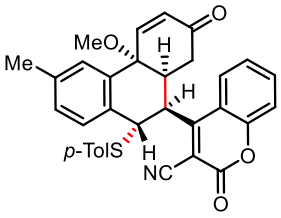
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



3d

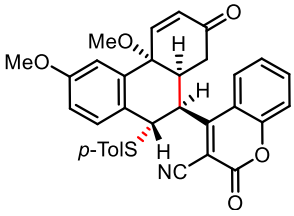
^{1}H NMR (500 MHz, $CDCl_3$)





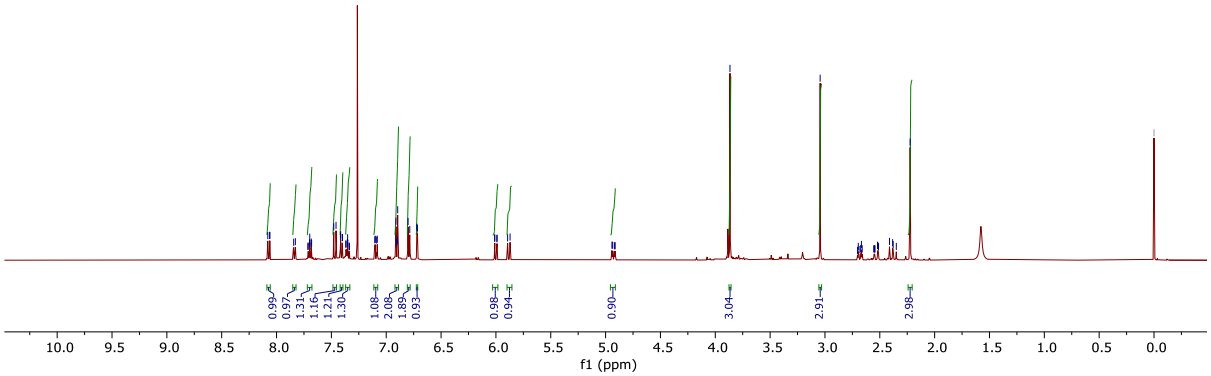
3d

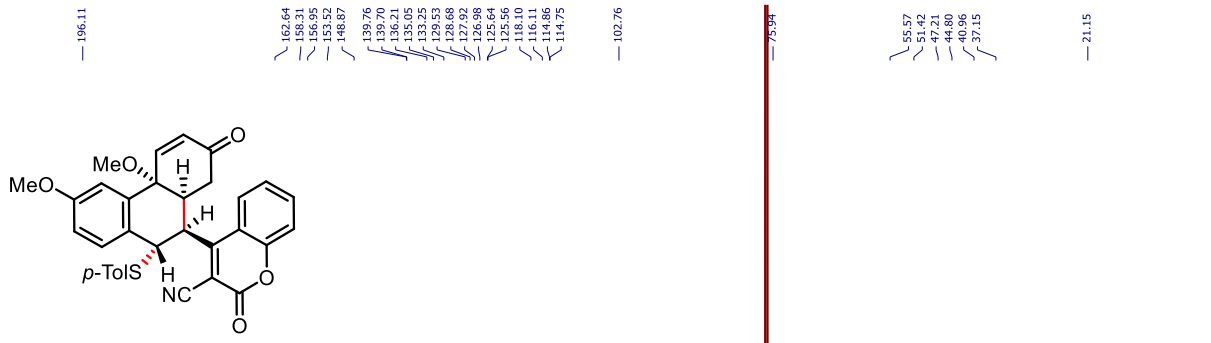
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



3e

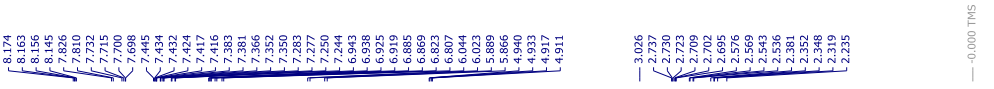
^{1}H NMR (500 MHz, $CDCl_3$)

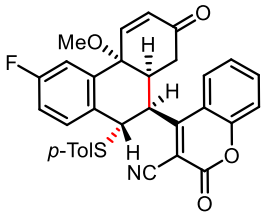




3e

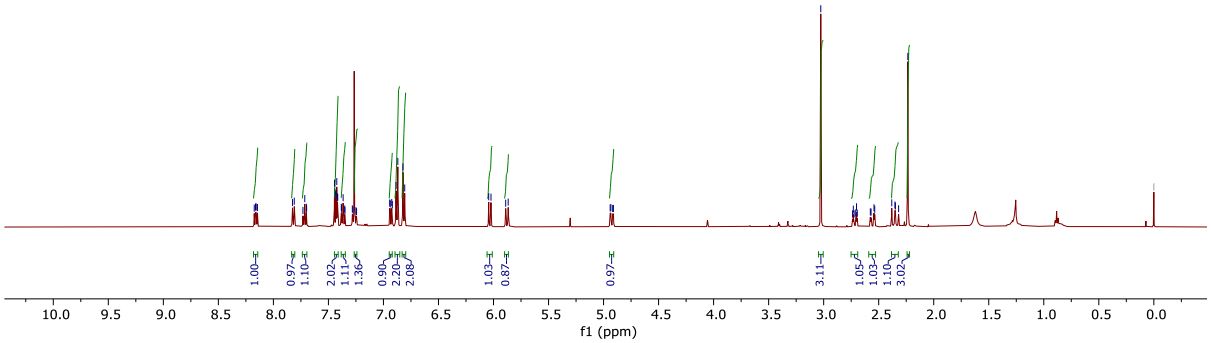
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

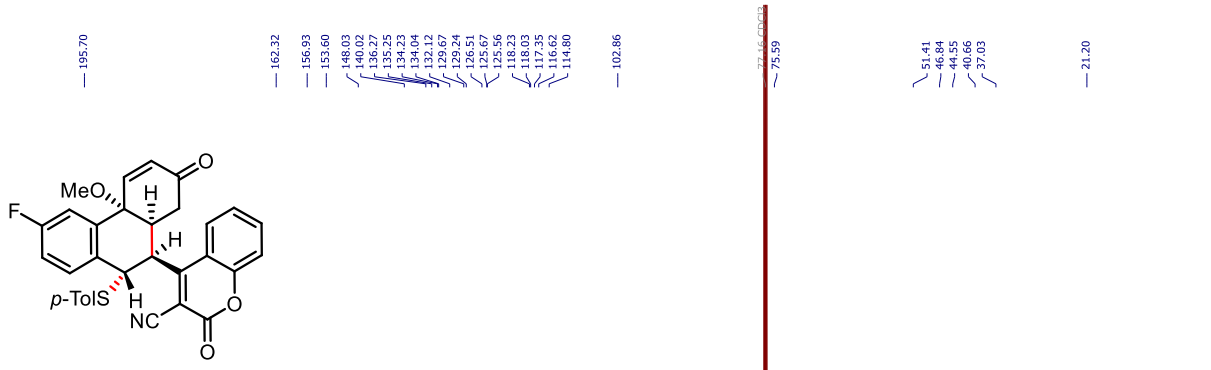




3f

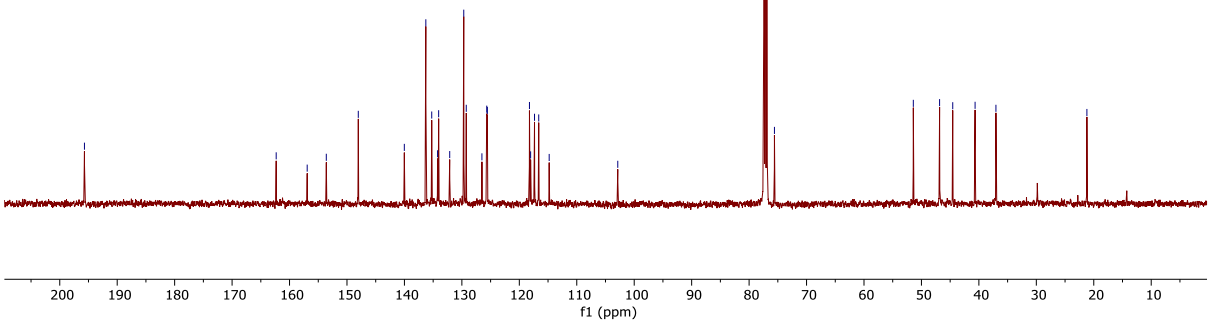
^{1}H NMR (500 MHz, $CDCl_3$)

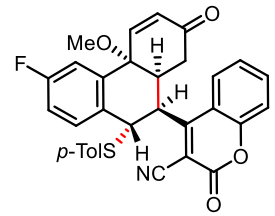




3f

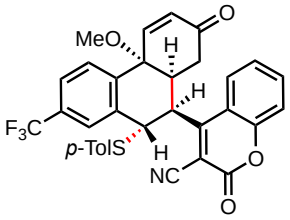
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)





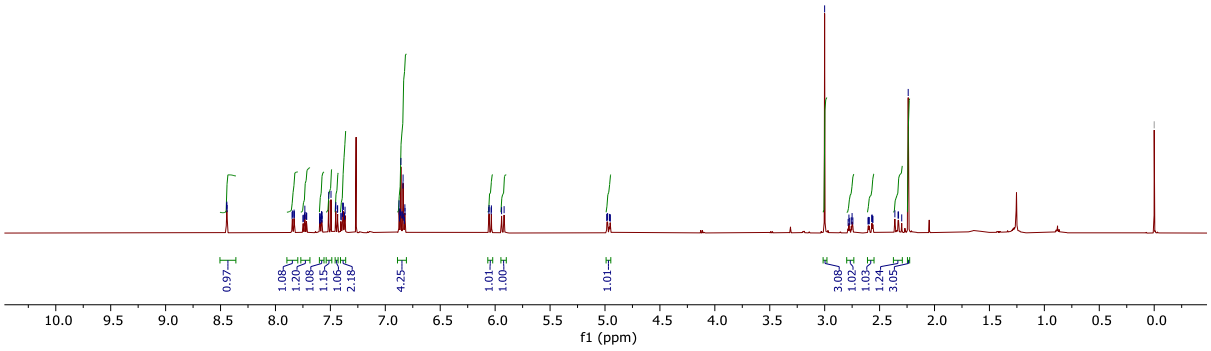
3f

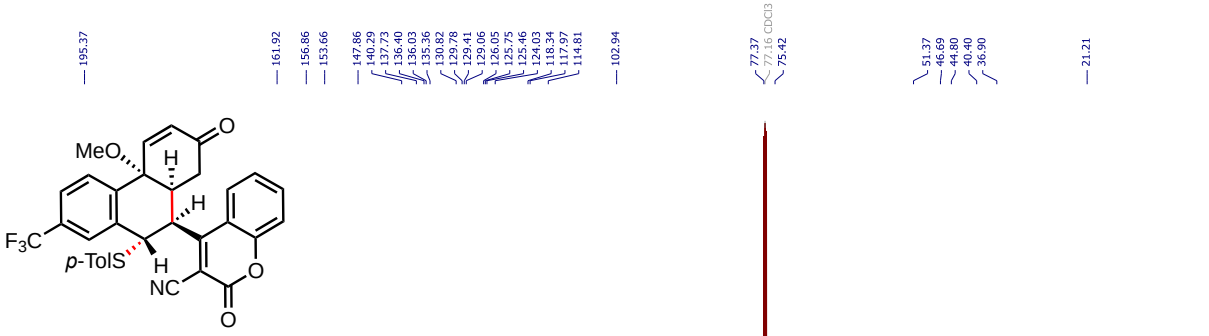
^{19}F NMR (471 MHz, $CDCl_3$)



3g

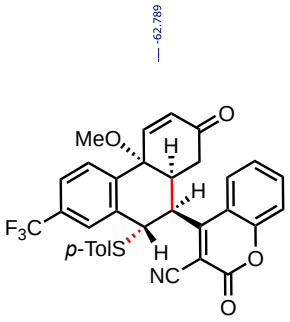
^{1}H NMR (500 MHz, $CDCl_3$)





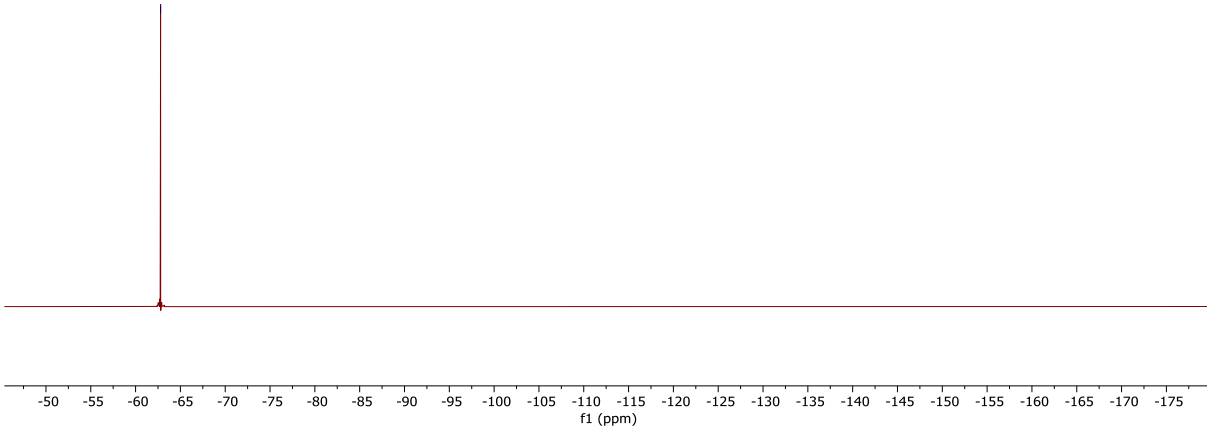
3g

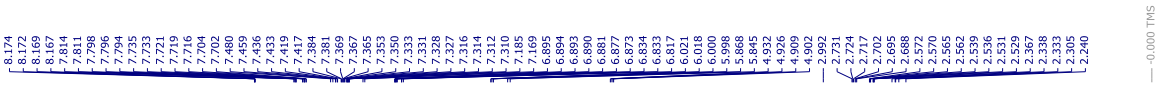
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)

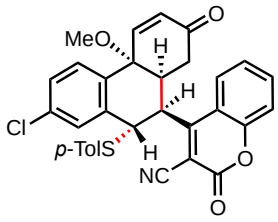


3g

^{19}F NMR (471 MHz, $CDCl_3$)

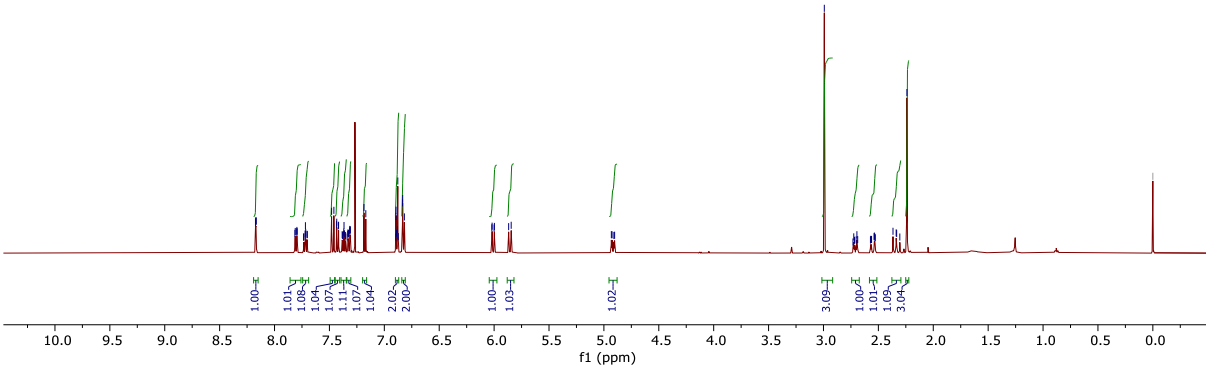


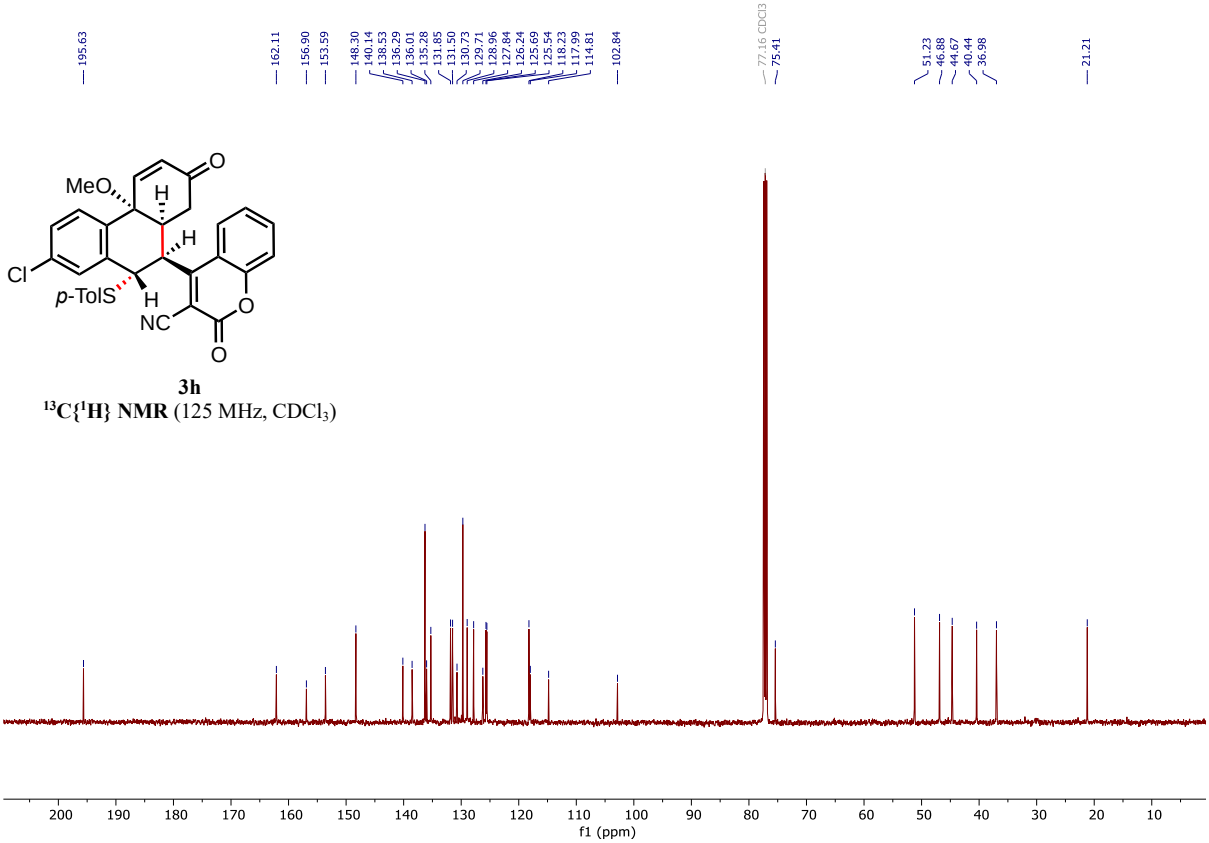




3h

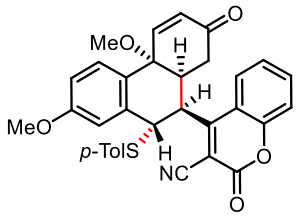
^{1}H NMR (500 MHz, $CDCl_3$)





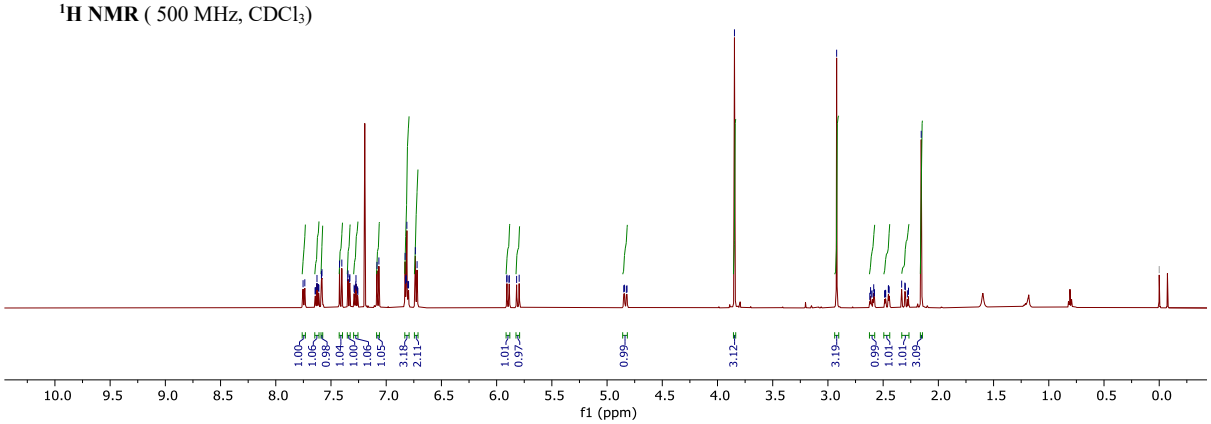
3h

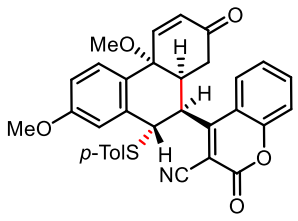
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



3i

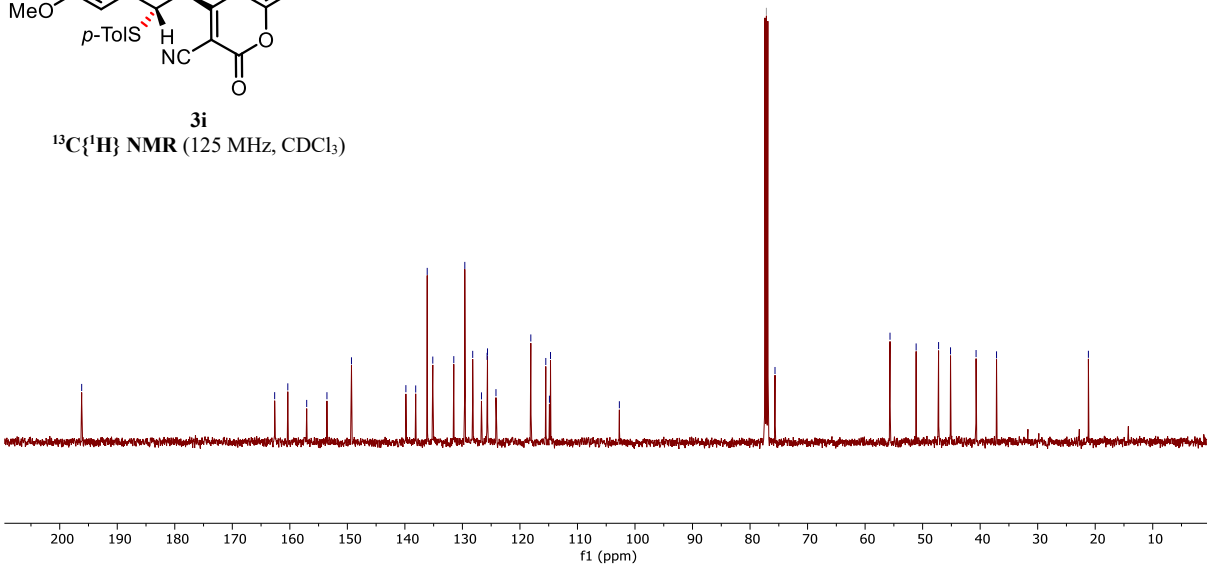
^{1}H NMR (500 MHz, $CDCl_3$)

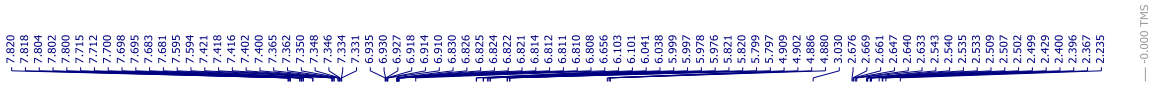


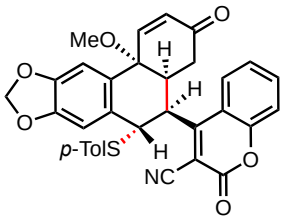


3i

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

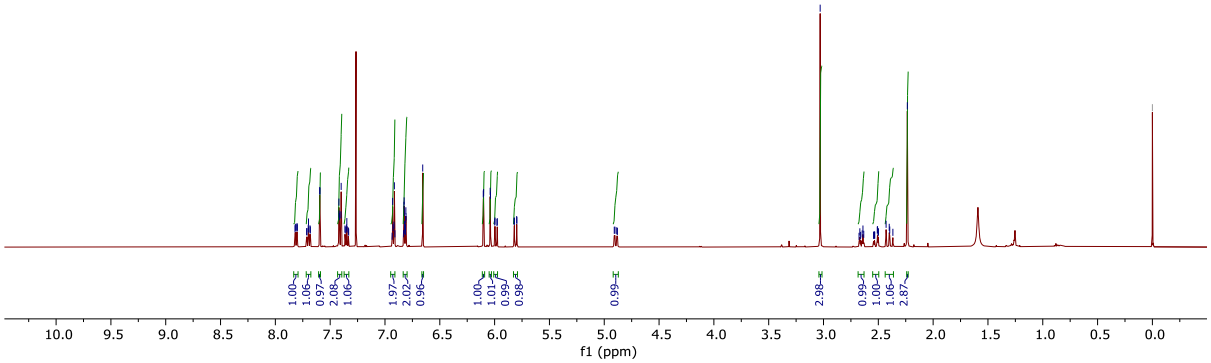


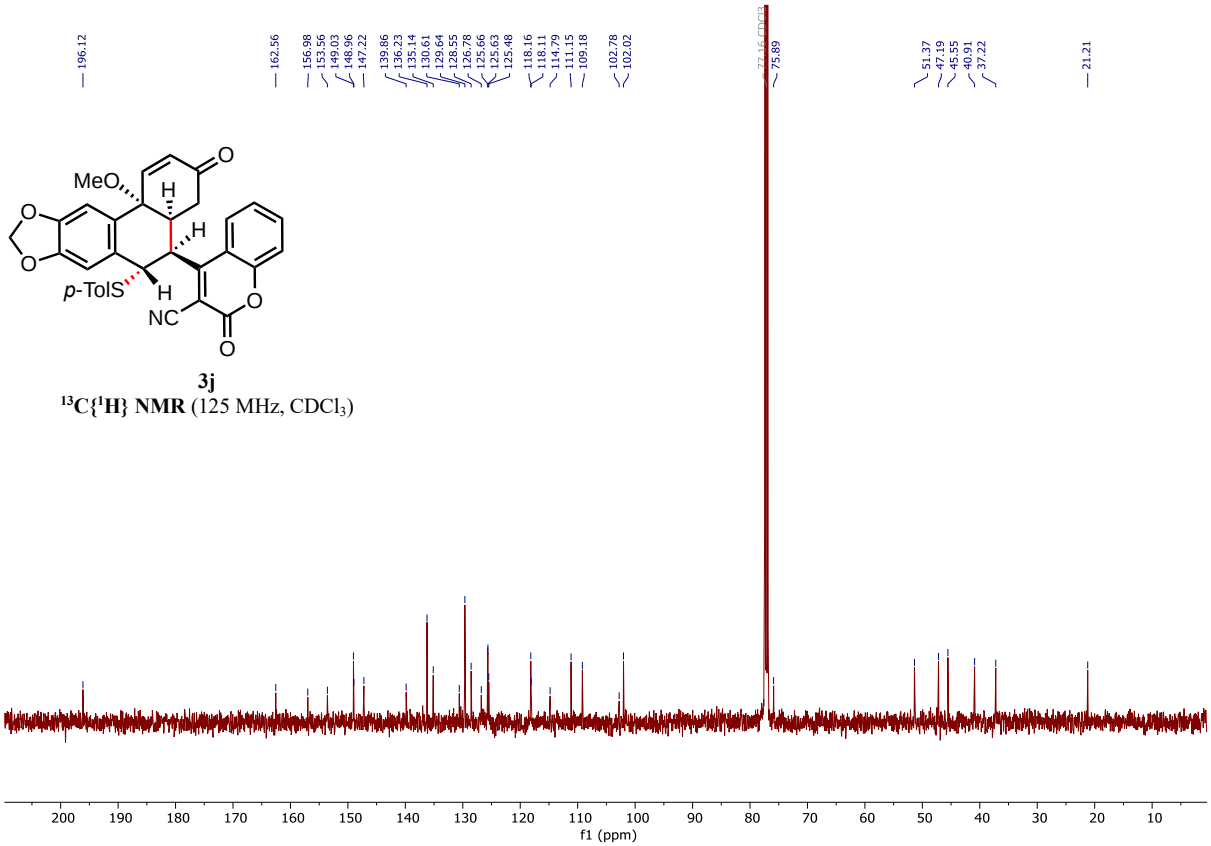




3j

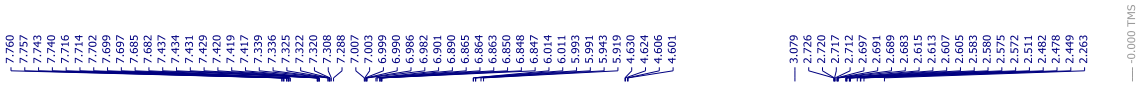
^{1}H NMR (500 MHz, $CDCl_3$)

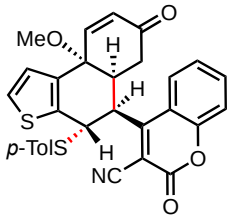




3j

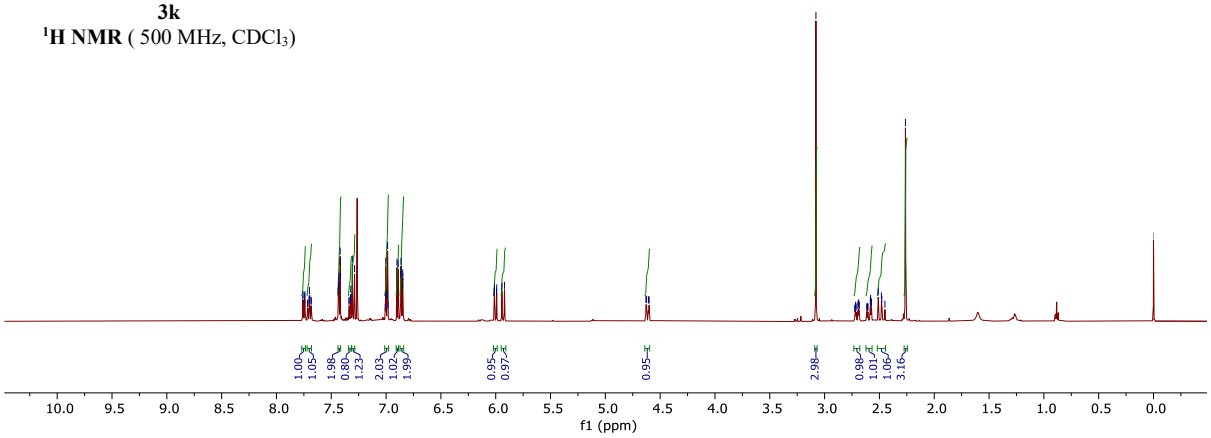
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

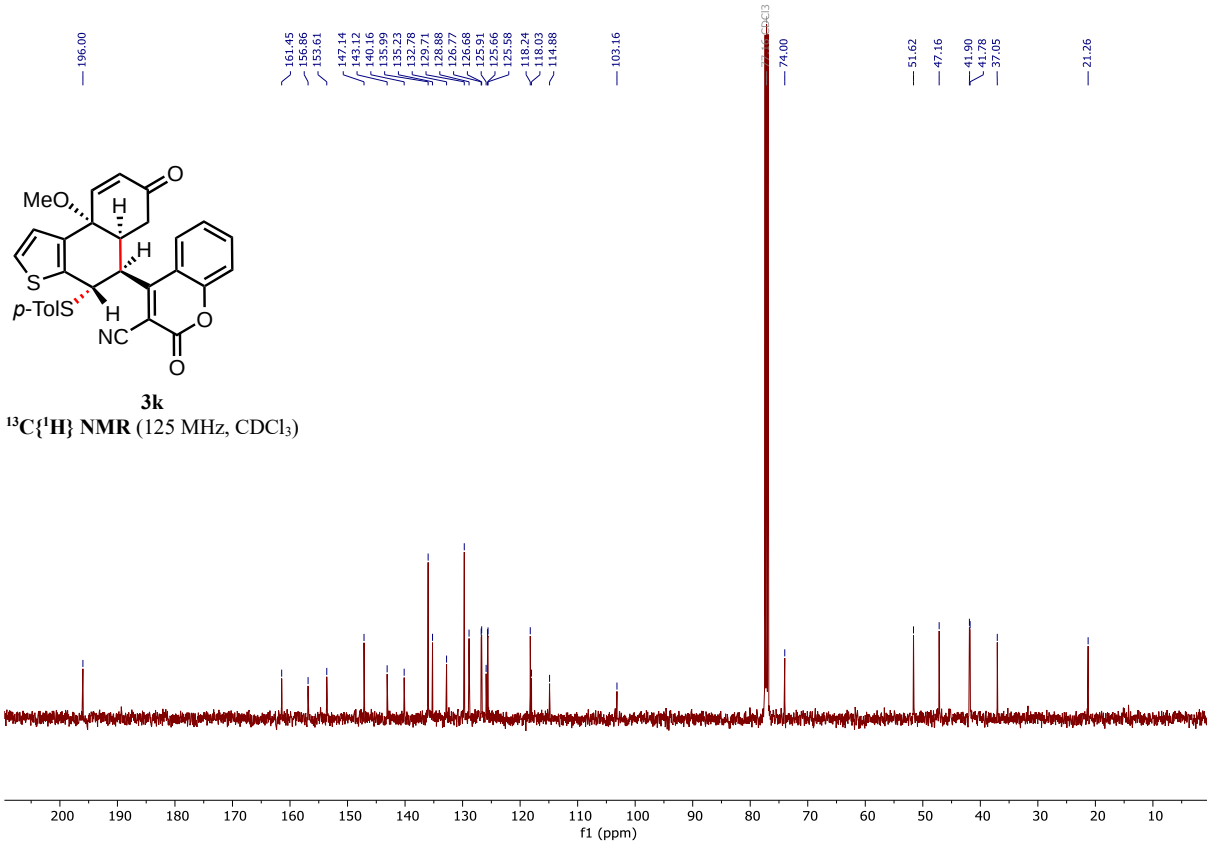




3k

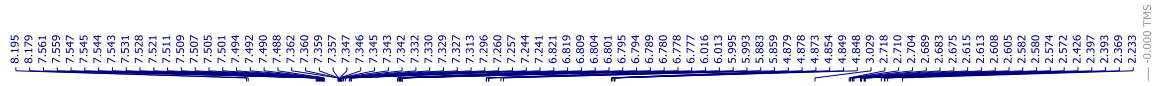
^{1}H NMR (500 MHz, $CDCl_3$)

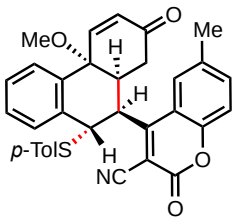




3k

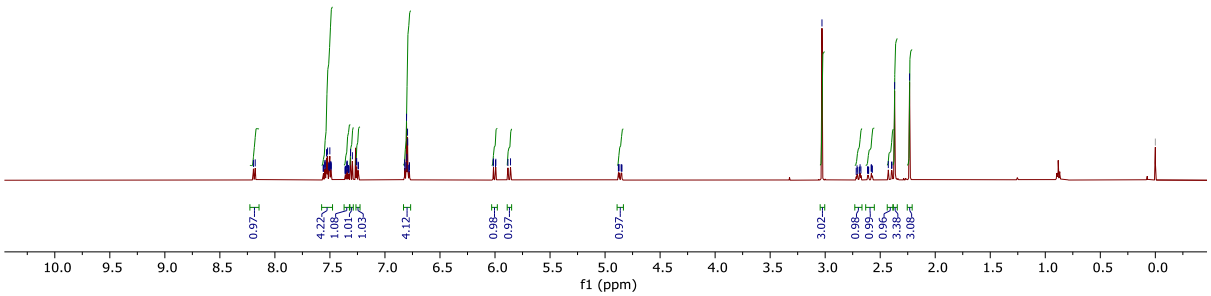
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

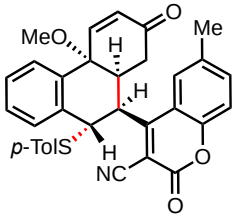




3l

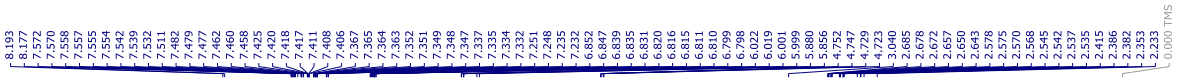
^{1}H NMR (500 MHz, $CDCl_3$)

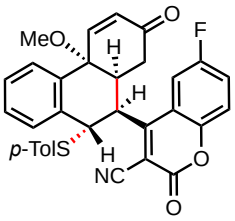




3l

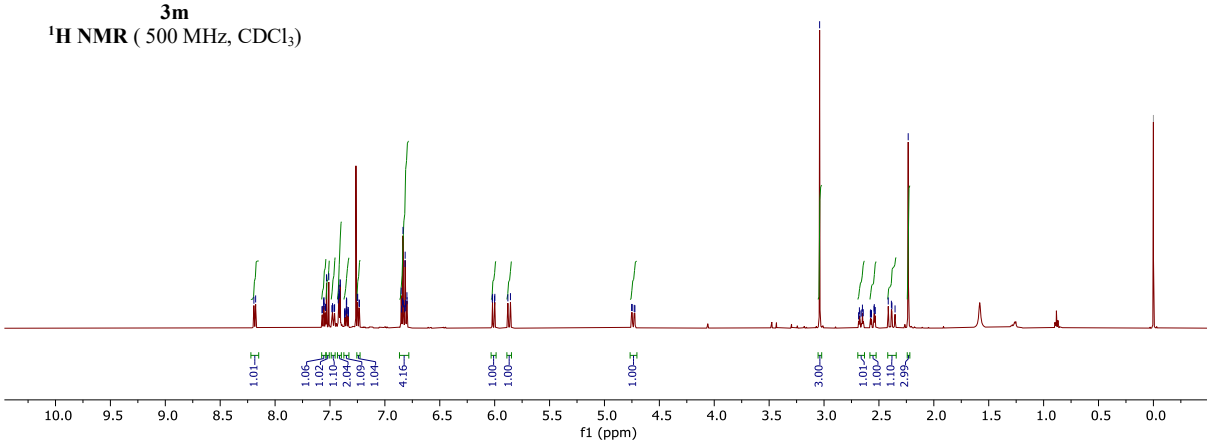
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

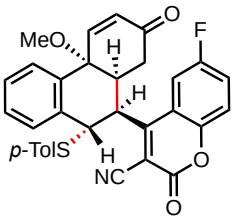




3m

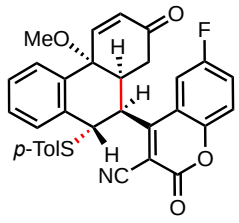
^{1}H NMR (500 MHz, $CDCl_3$)





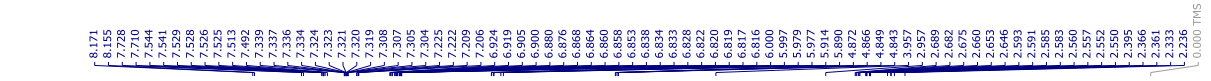
3m

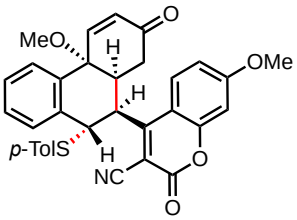
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



3m

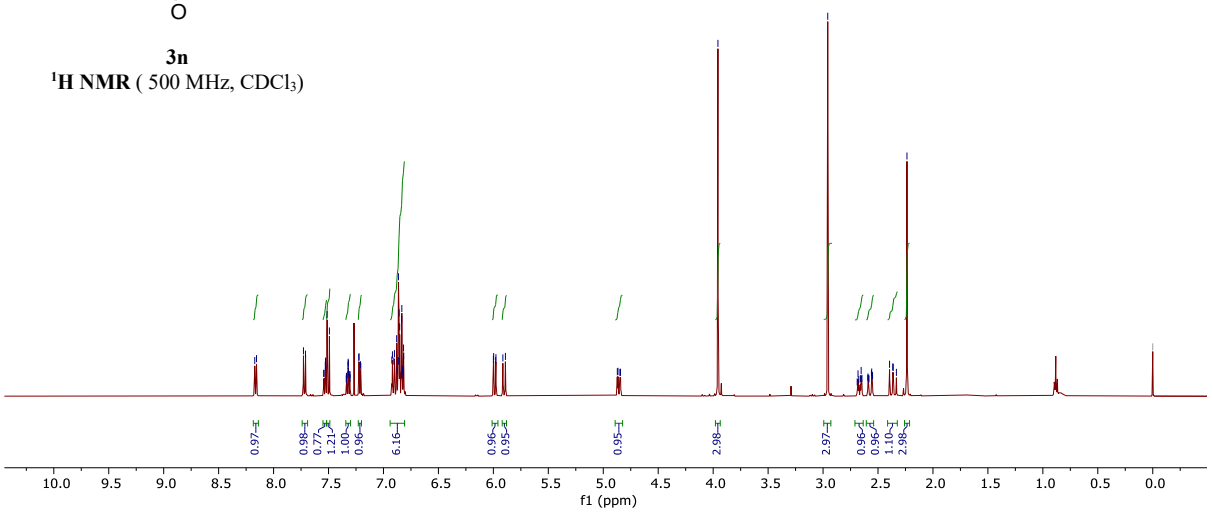
^{19}F NMR (471 MHz, $CDCl_3$)

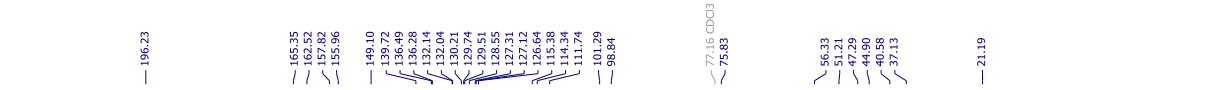


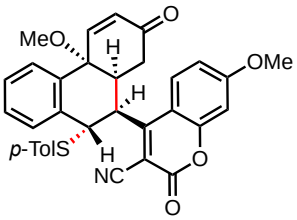


3n

^{1}H NMR (500 MHz, $CDCl_3$)

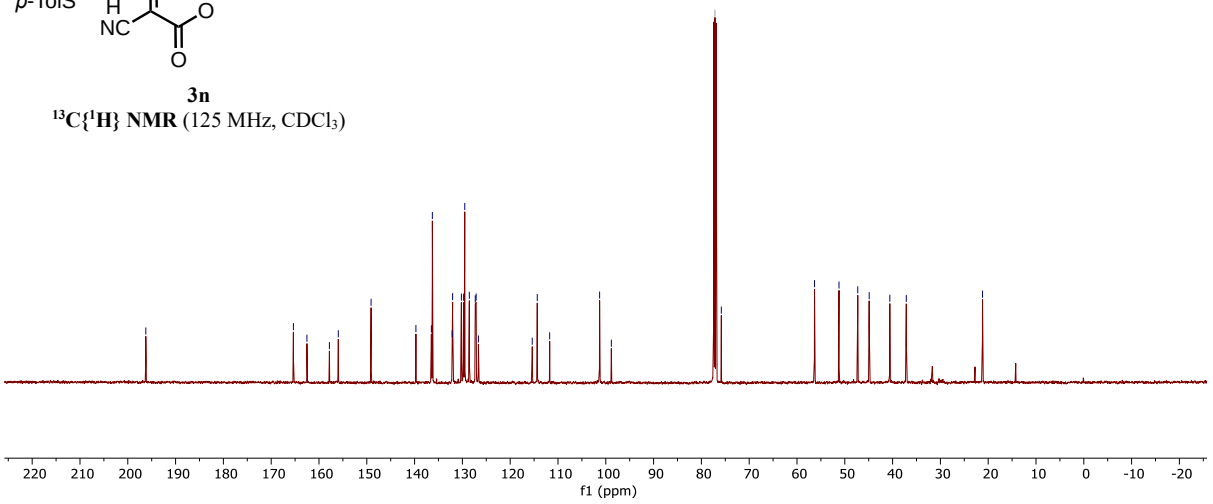


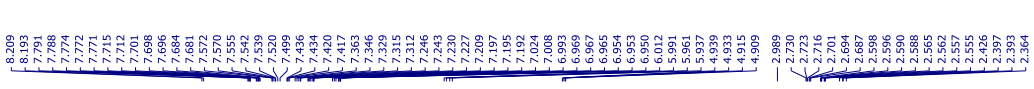


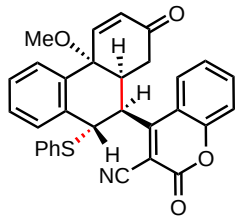


3n

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

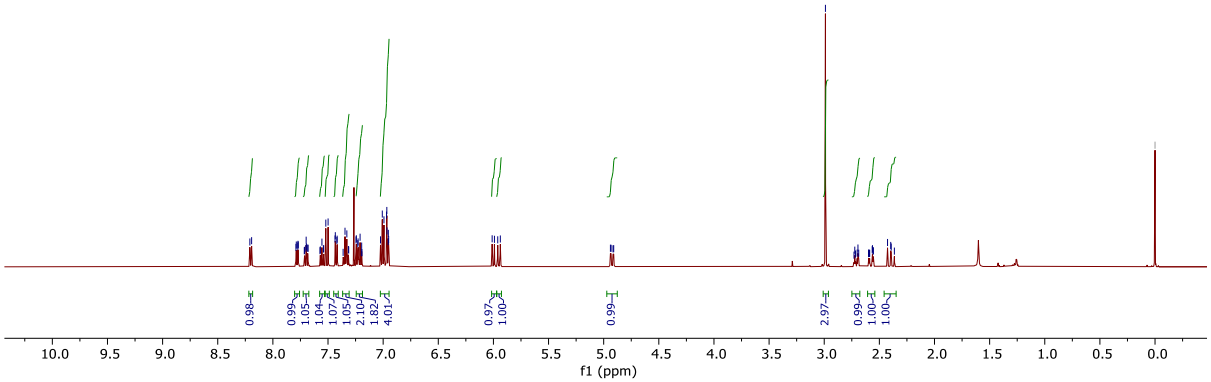


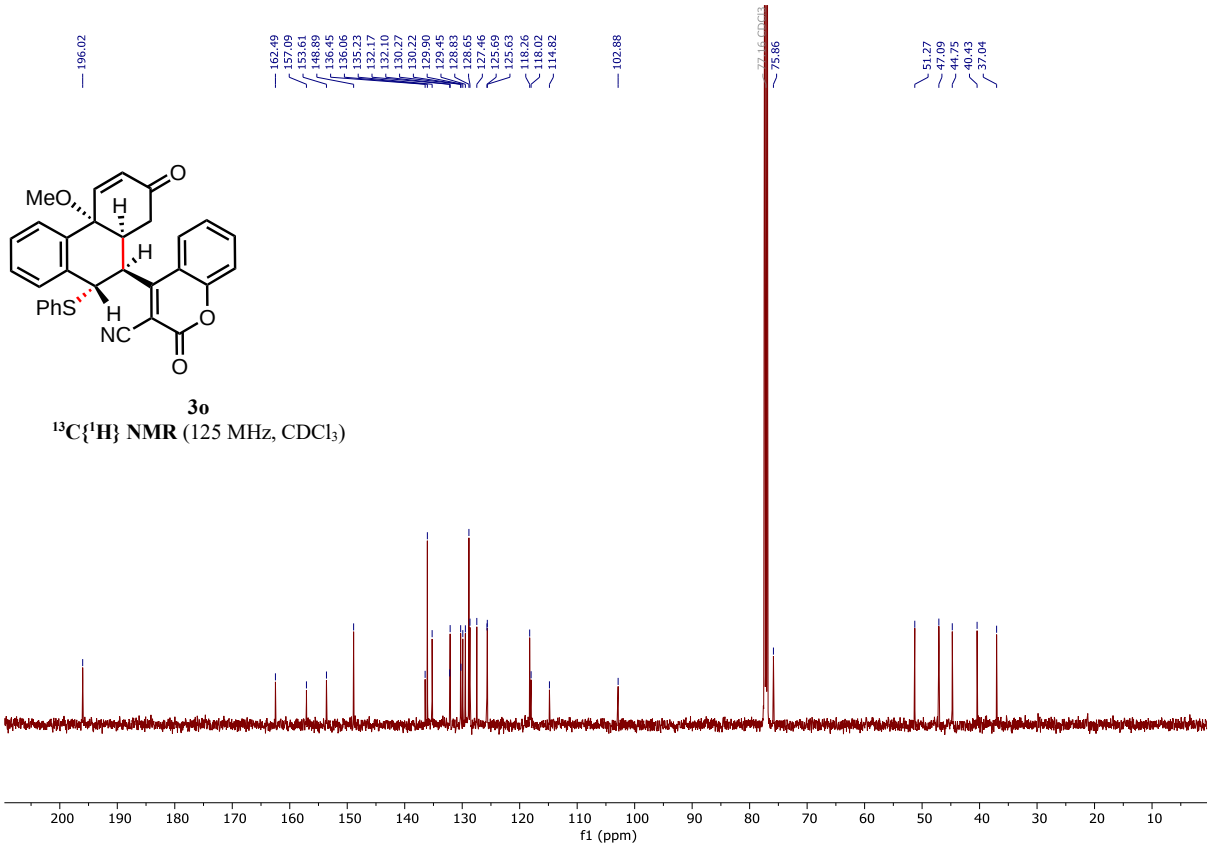




3o

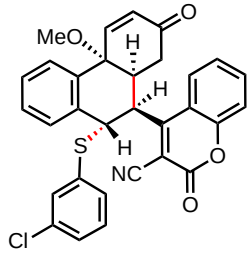
^{1}H NMR (500 MHz, $CDCl_3$)





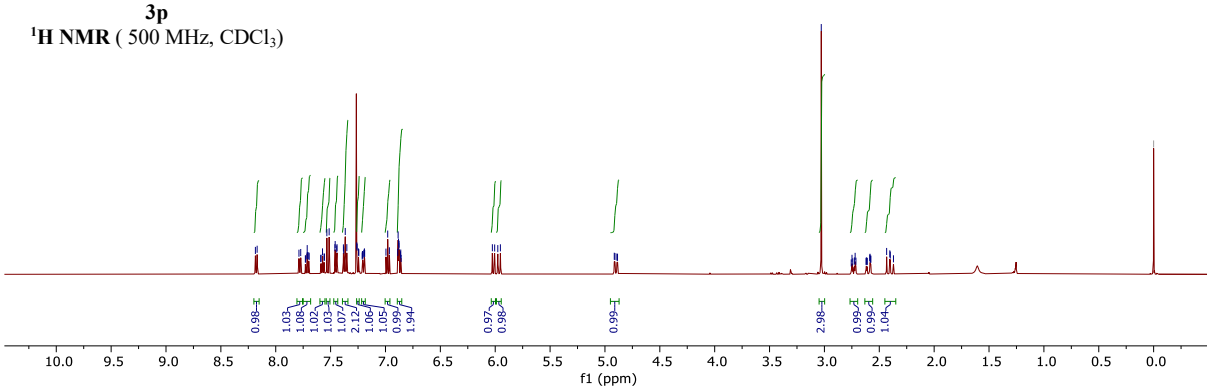
3o

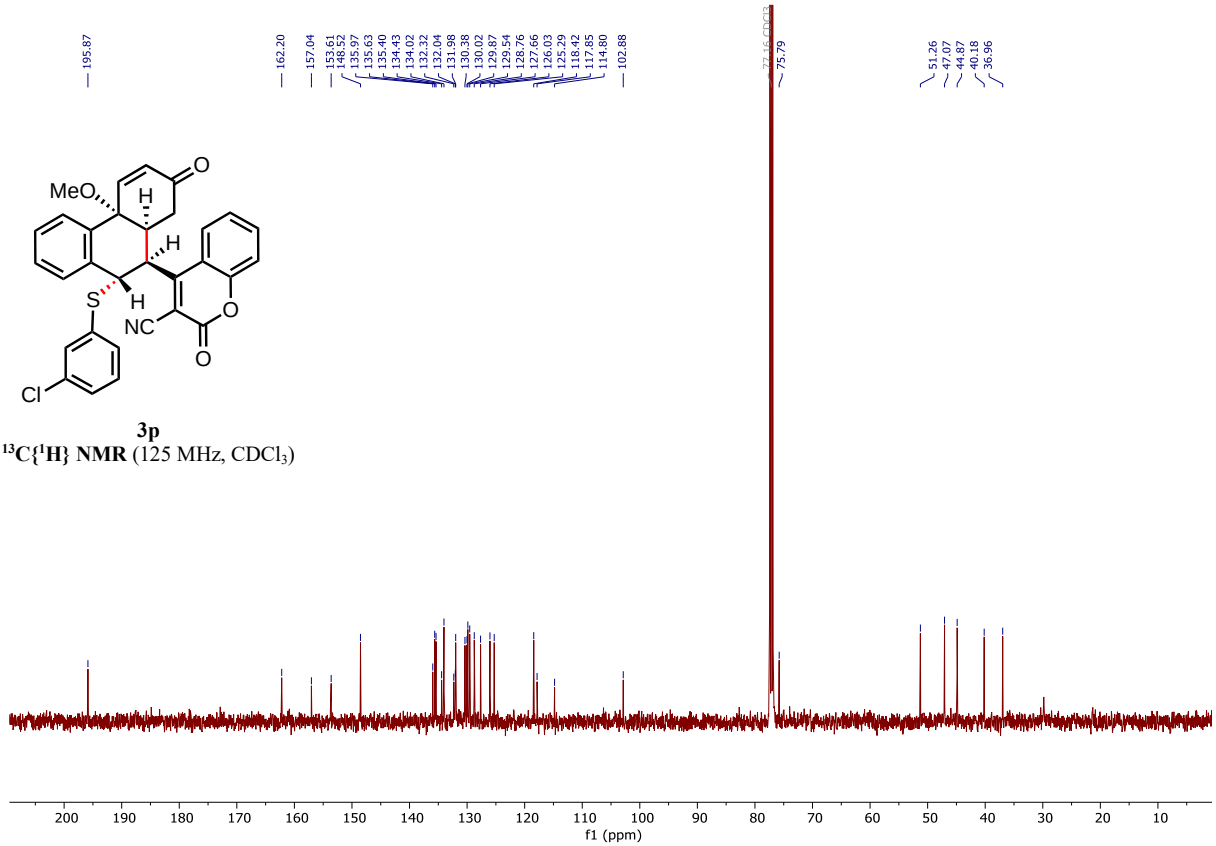
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



3p

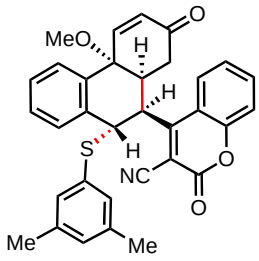
^{1}H NMR (500 MHz, $CDCl_3$)





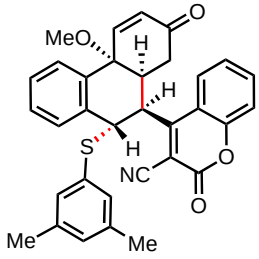
3p

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



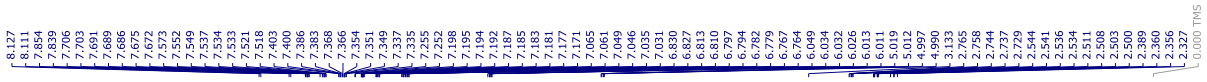
3q

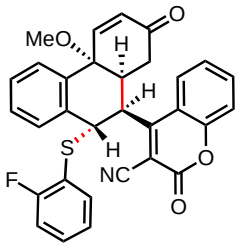
^{1}H NMR (500 MHz, $CDCl_3$)



3q

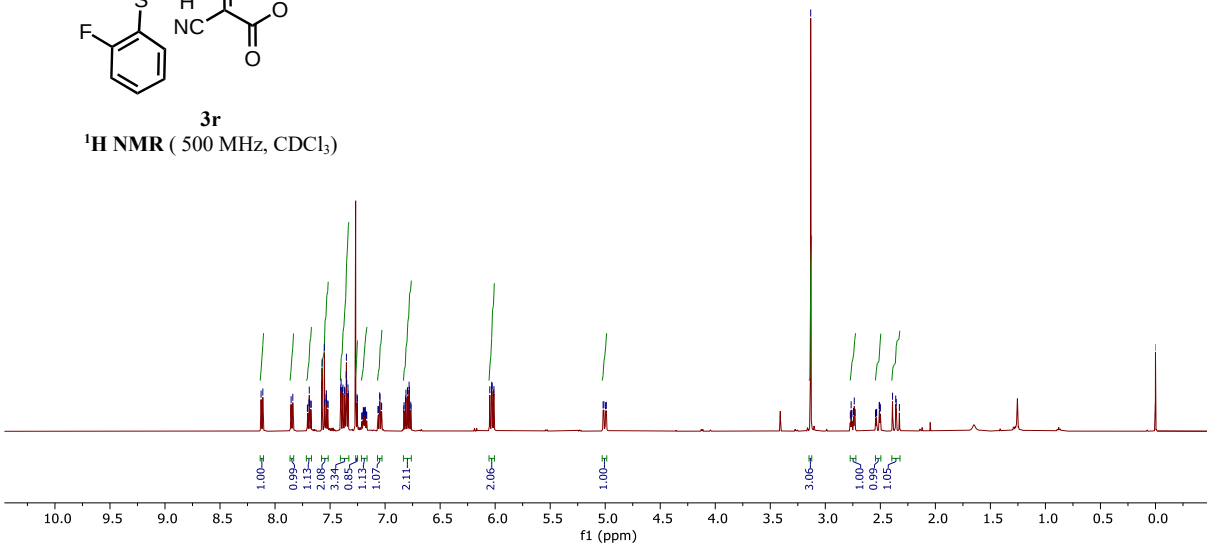
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

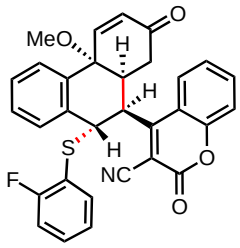




3r

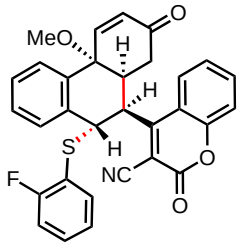
^{1}H NMR (500 MHz, $CDCl_3$)





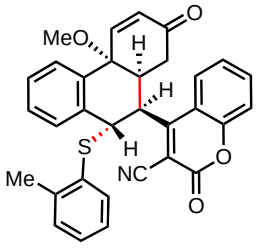
3r

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



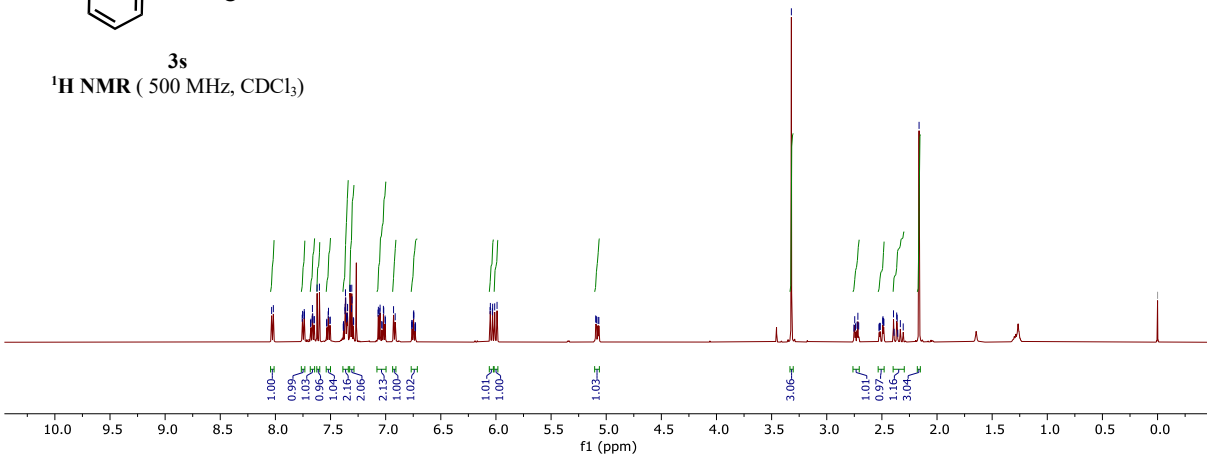
3r

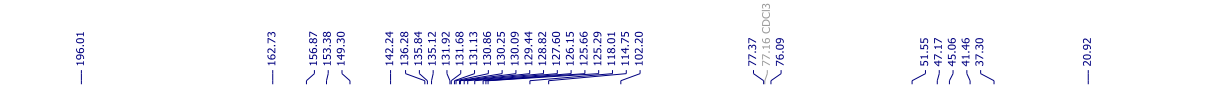
^{19}F NMR (471 MHz, $CDCl_3$)

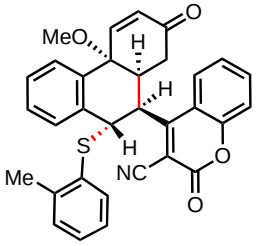


3s

^{1}H NMR (500 MHz, $CDCl_3$)

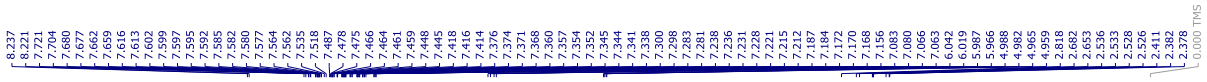


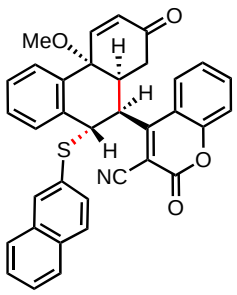




3s

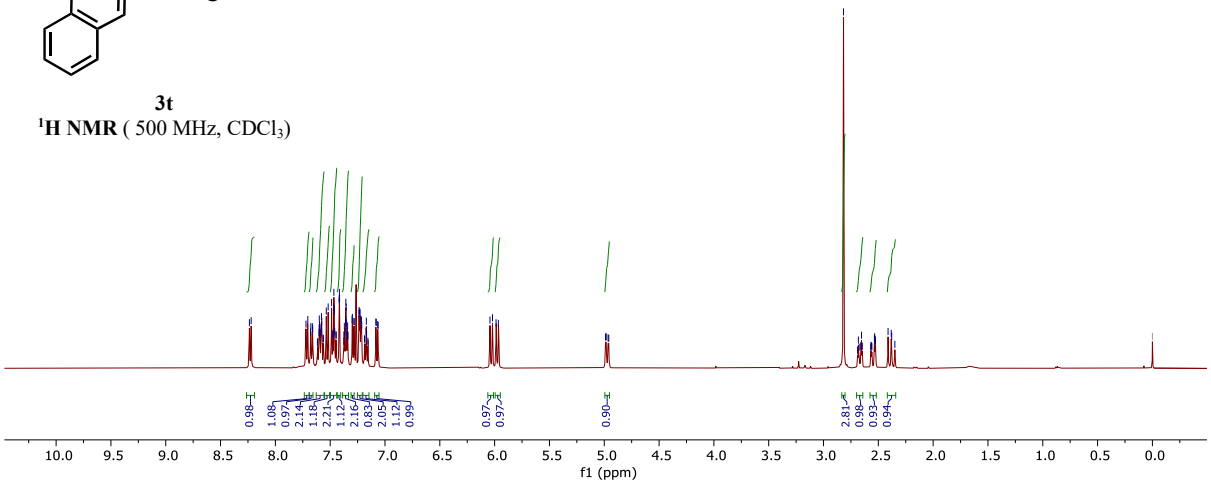
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

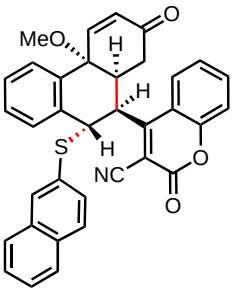




3t

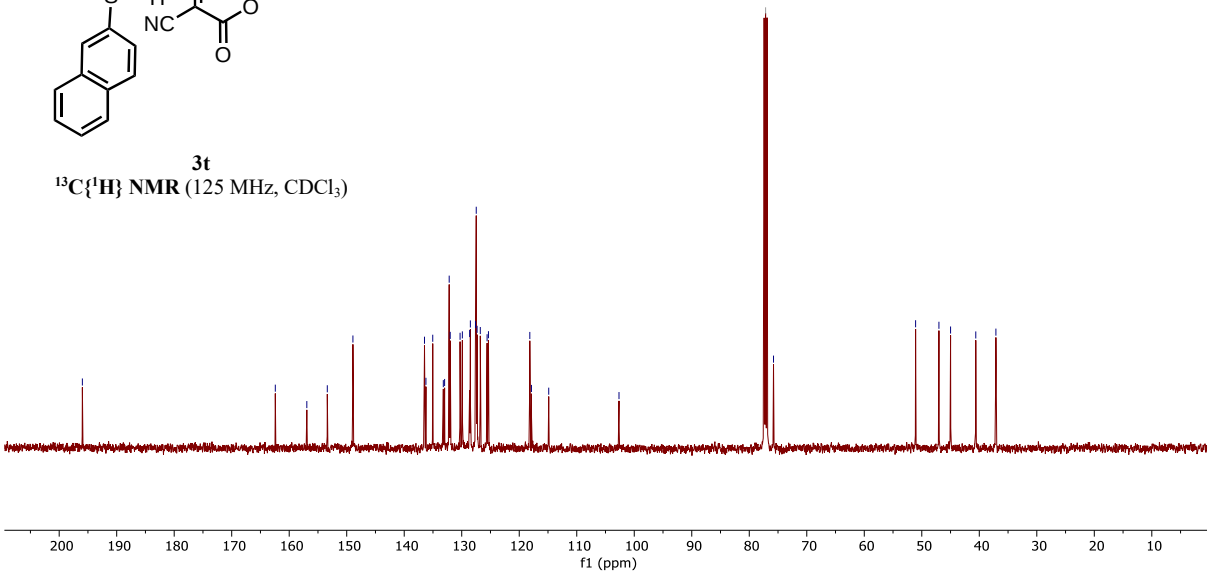
^{1}H NMR (500 MHz, $CDCl_3$)

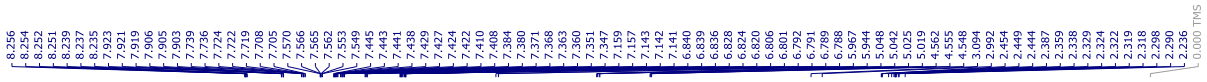


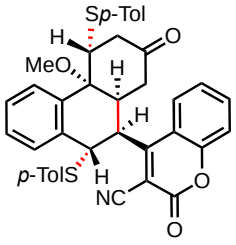


3t

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

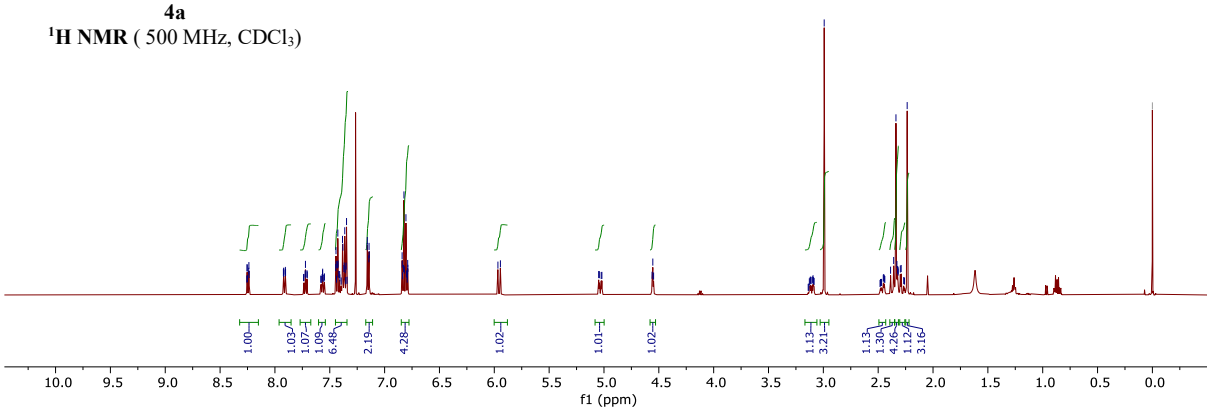


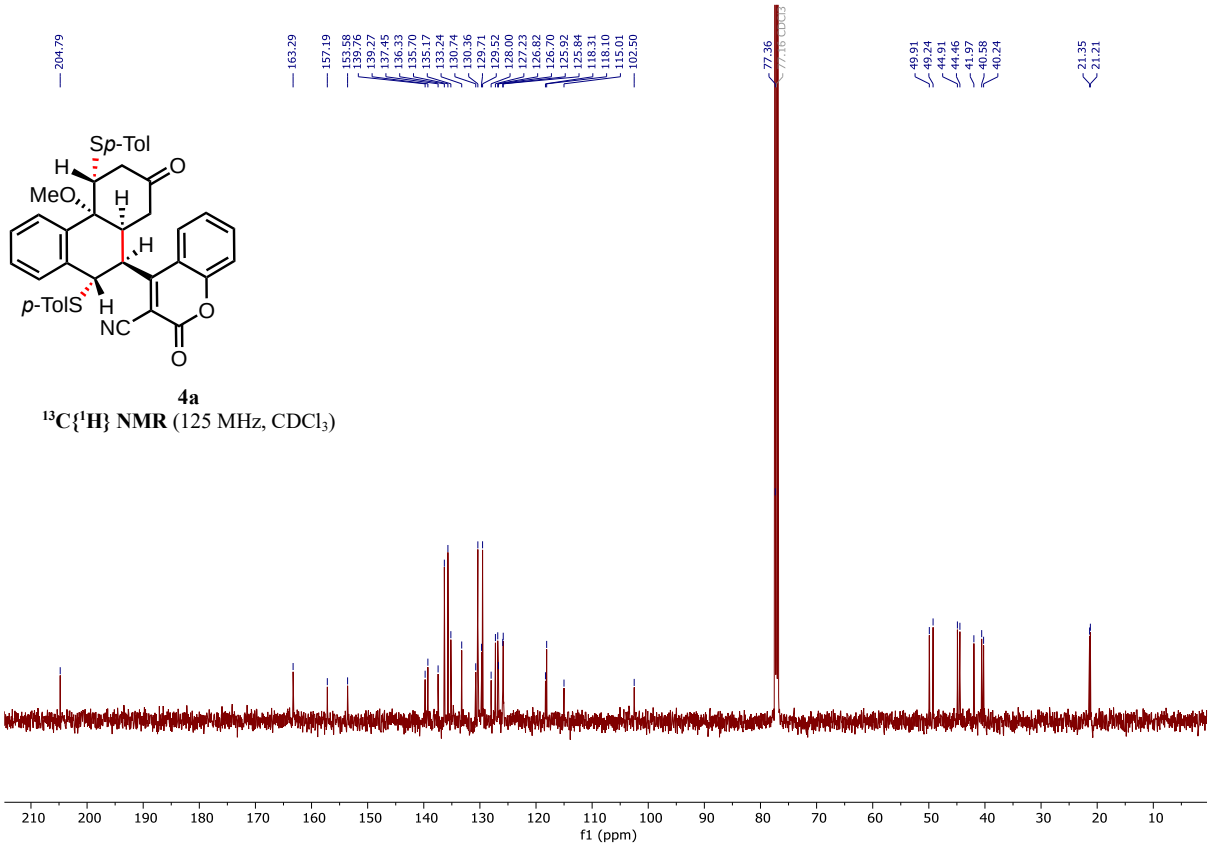




4a

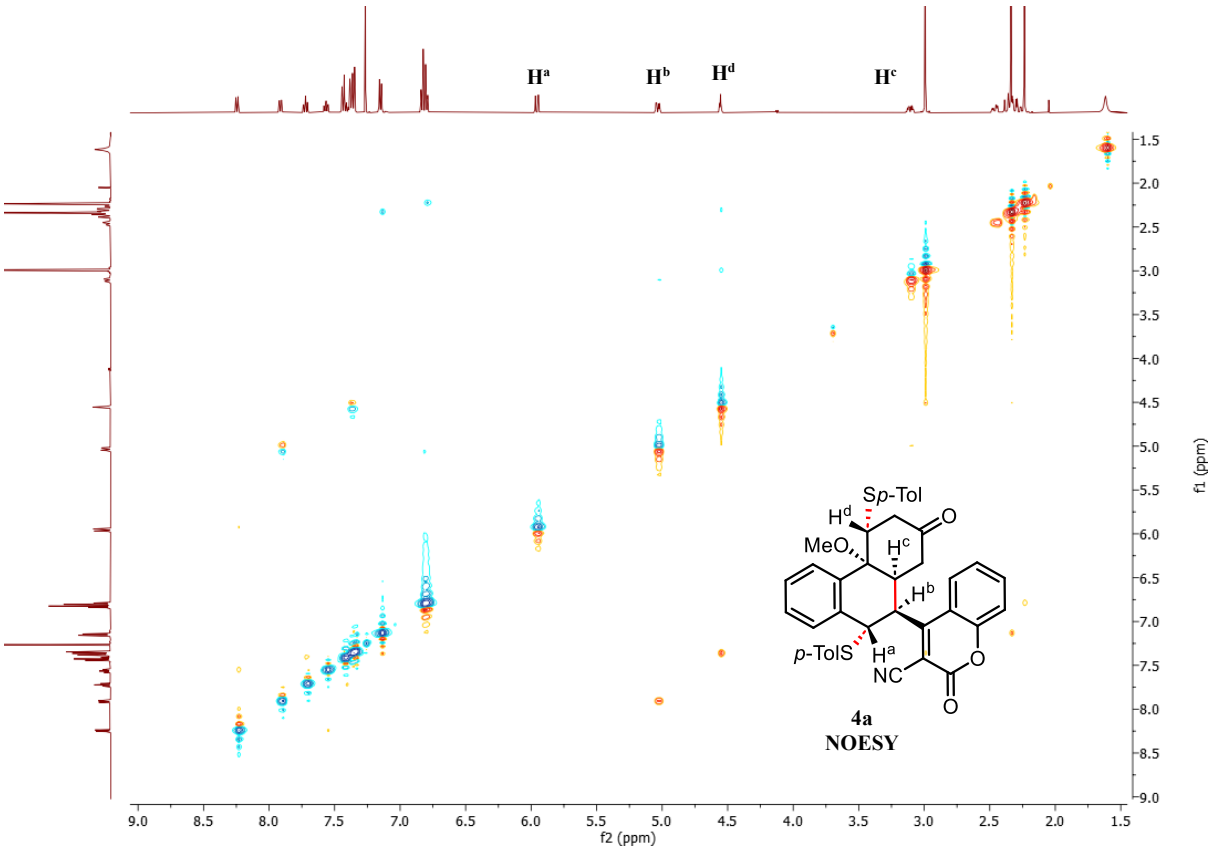
^{1}H NMR (500 MHz, $CDCl_3$)

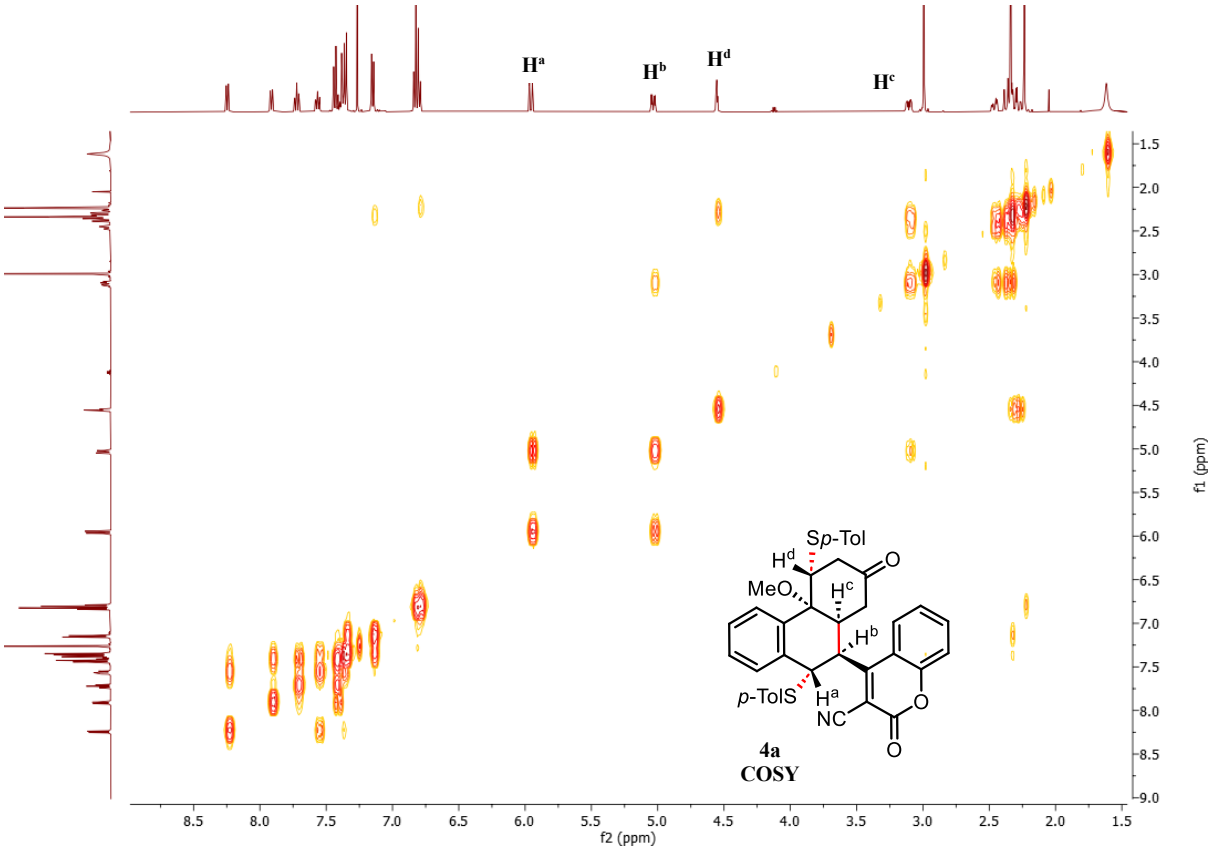


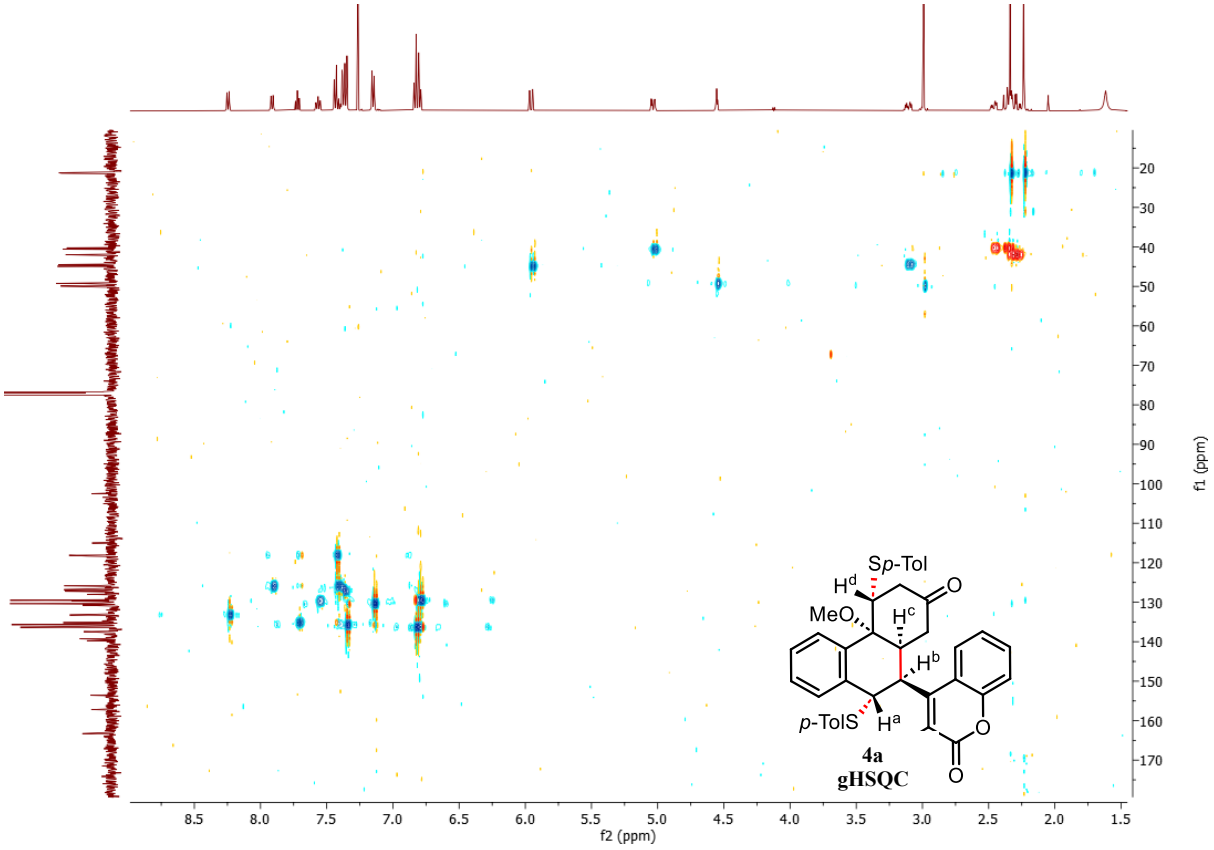


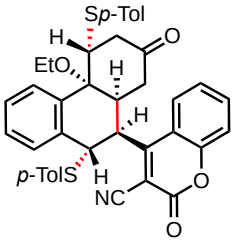
4a

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)


Ha
Hb
Hd
Hc
Sp-Tol
Hd
MeO
Hc
Hb
p-TolS
Ha
NC
O
O
O
4a
NOESY
f2 (ppm)
f1 (ppm)

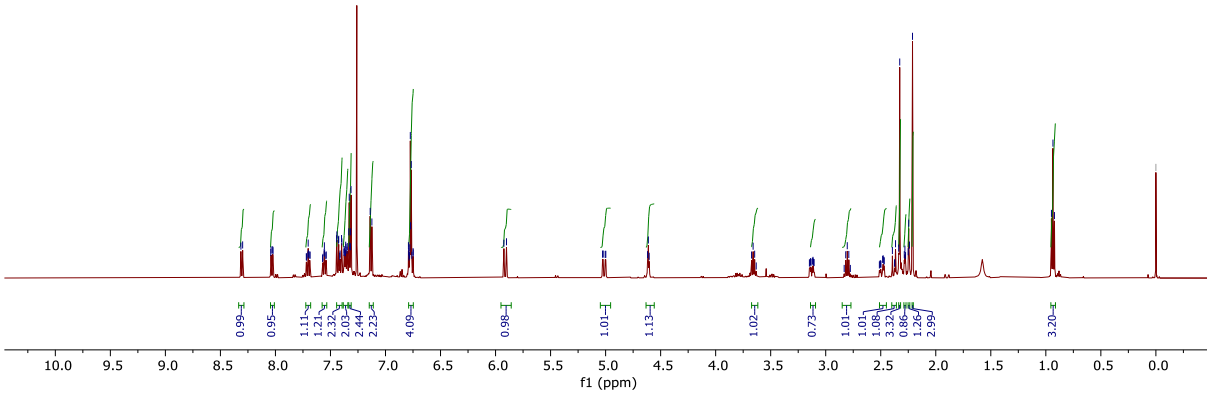

Ha
Hb
Hd
Hc
Sp-Tol
Hd
MeO
Hc
Hb
p-TolS
Ha
NC
O
O
O
4a
COSY
f2 (ppm)
f1 (ppm)

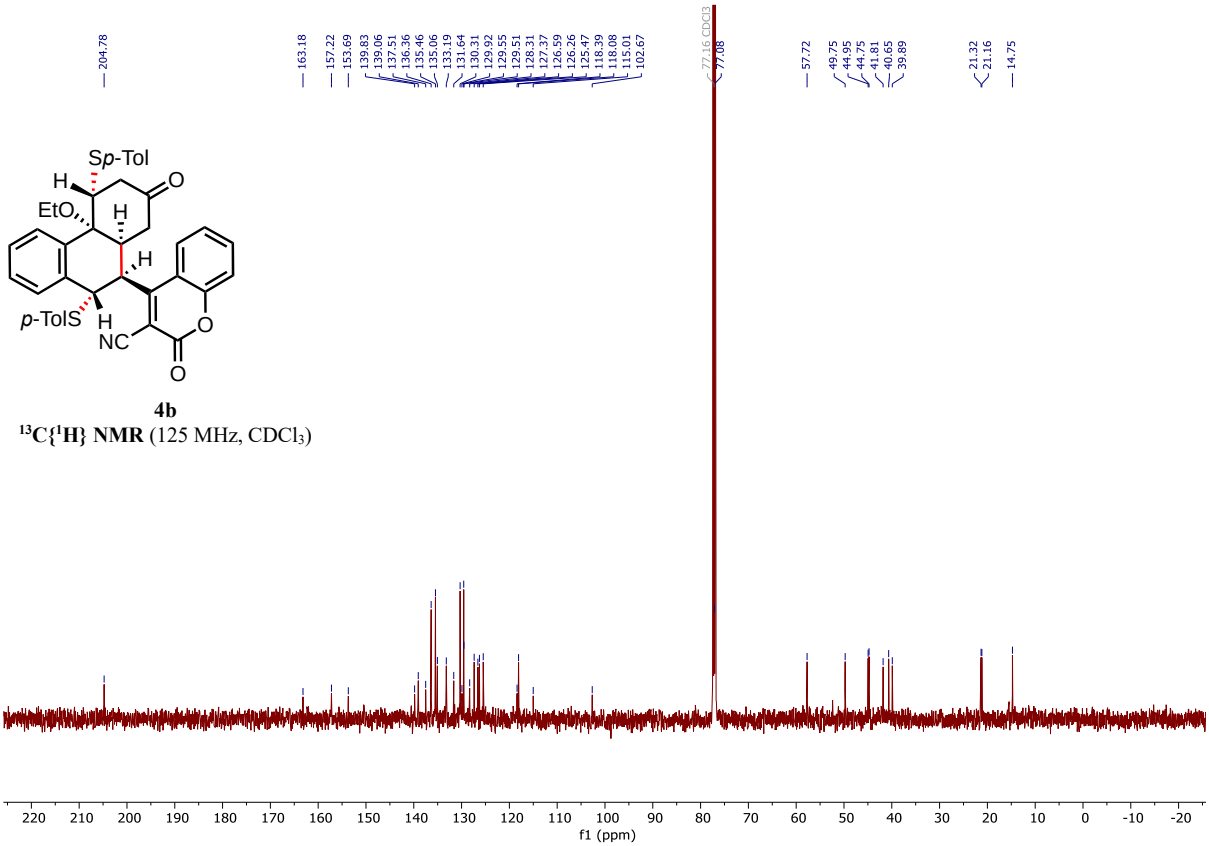

f2 (ppm)
f1 (ppm)
Sp-Tol
Hd
MeO
Hc
Hb
p-TolS
Ha
O
O
O
4a
gHSQC



4b

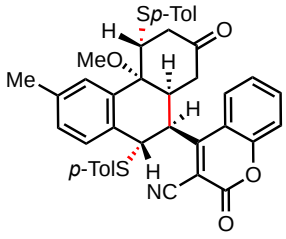
^{1}H NMR (500 MHz, $CDCl_3$)





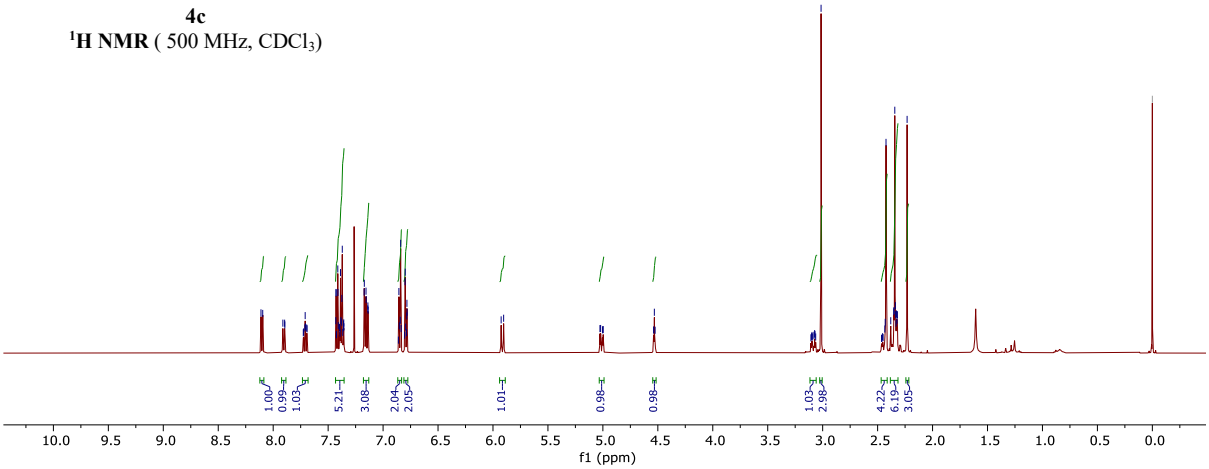
4b

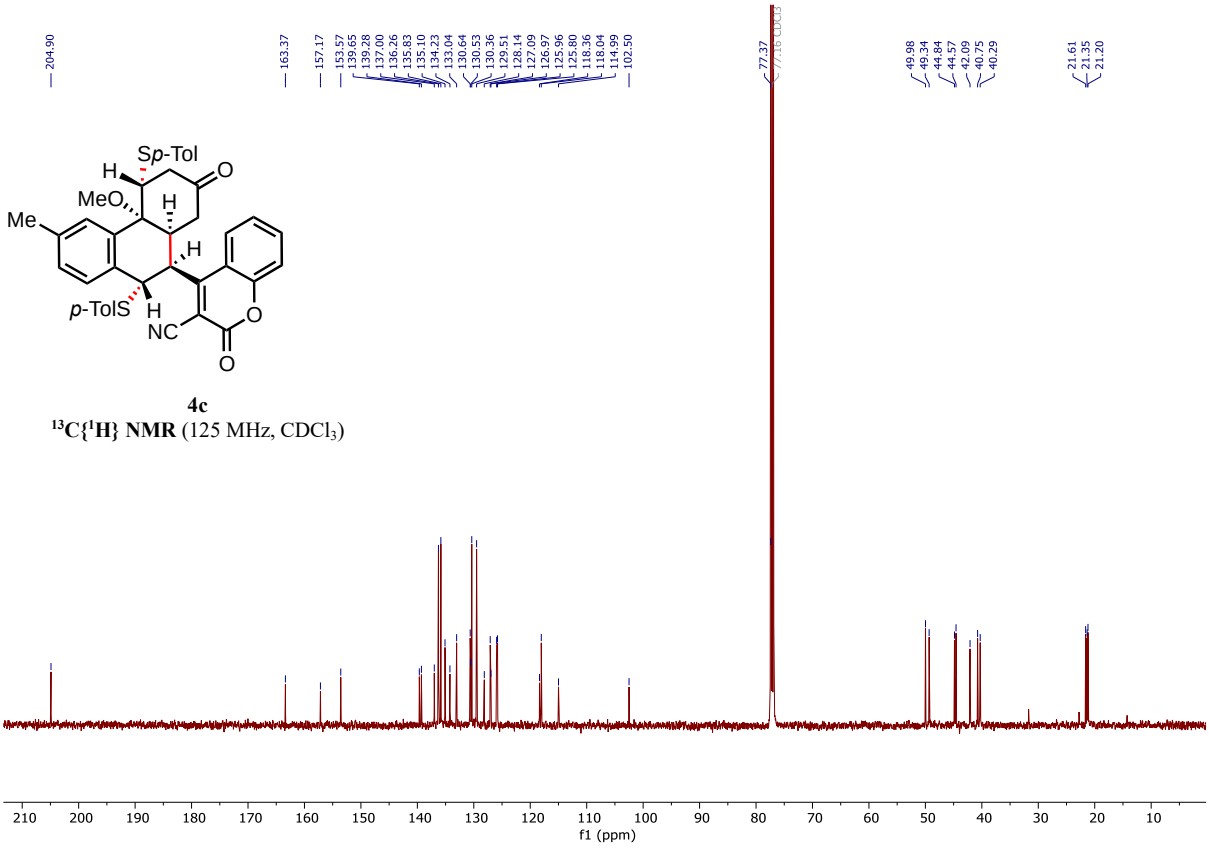
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



4c

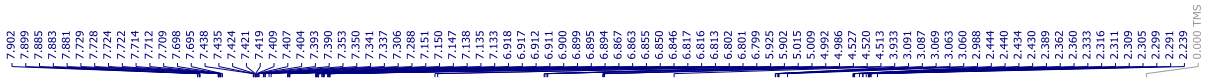
^{1}H NMR (500 MHz, $CDCl_3$)

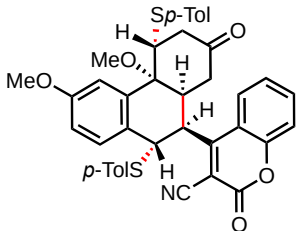




4c

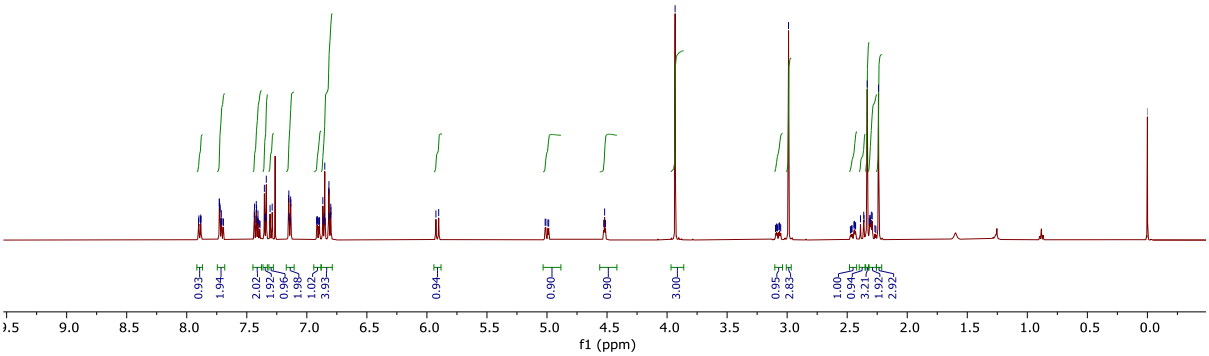
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

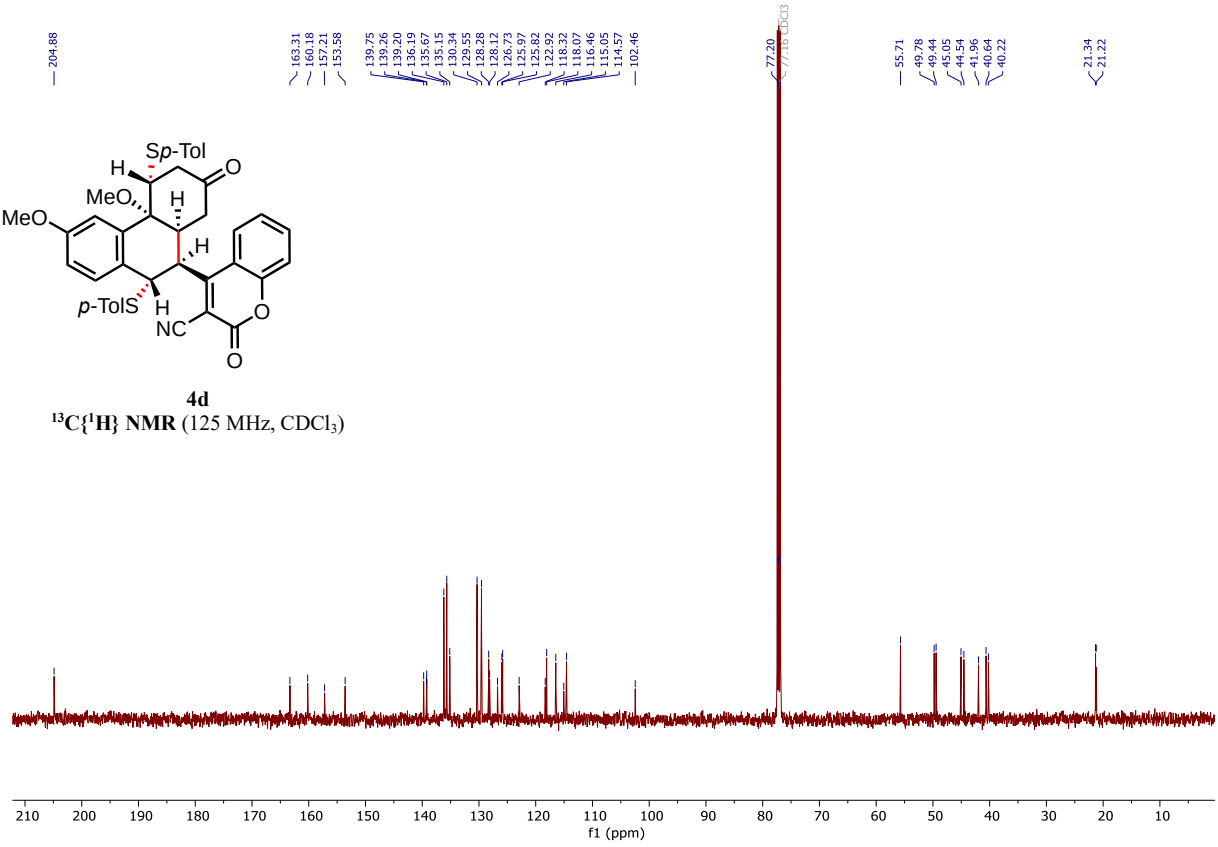




4d

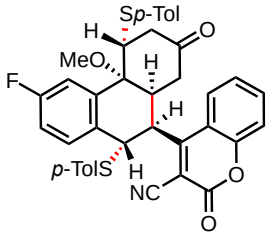
^{1}H NMR (500 MHz, $CDCl_3$)





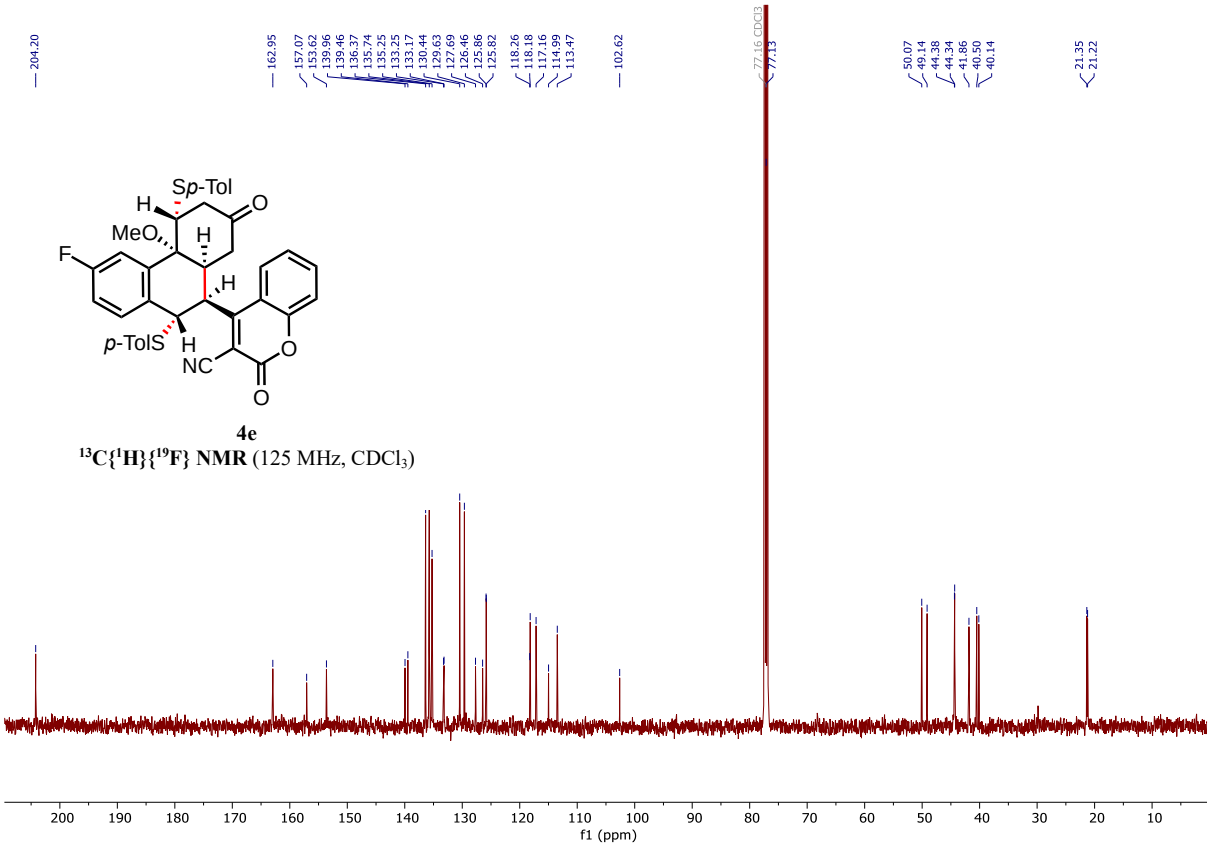
4d

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



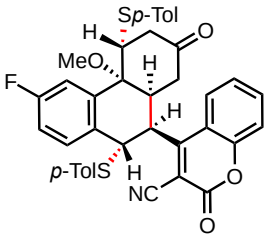
4e

^{1}H NMR (500 MHz, $CDCl_3$)



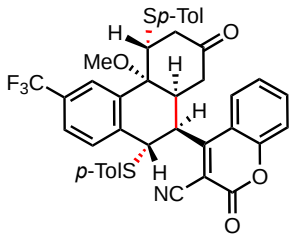
4e

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



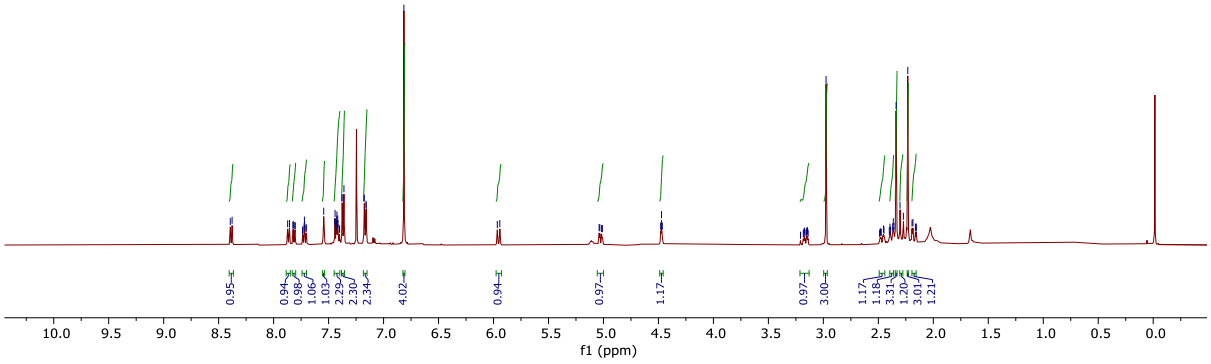
4e

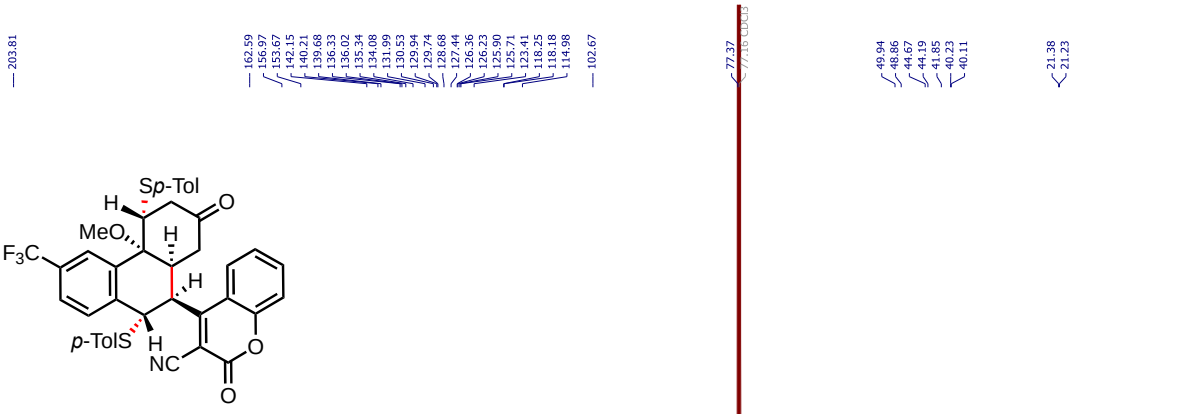
^{19}F NMR (471 MHz, $CDCl_3$)



4f

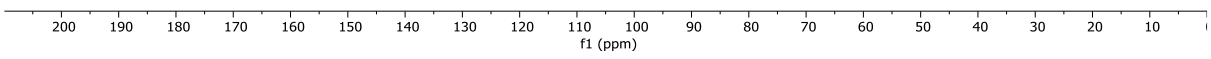
^{1}H NMR (500 MHz, $CDCl_3$)

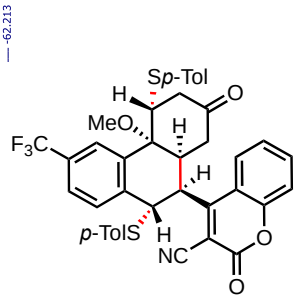




4f

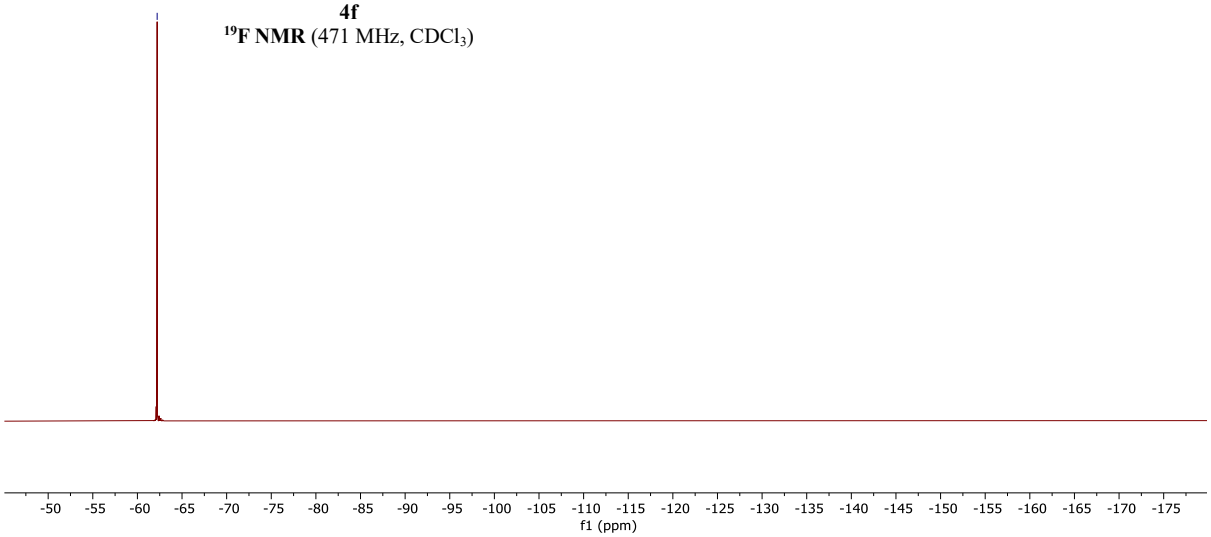
^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)

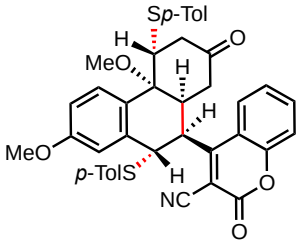




4f

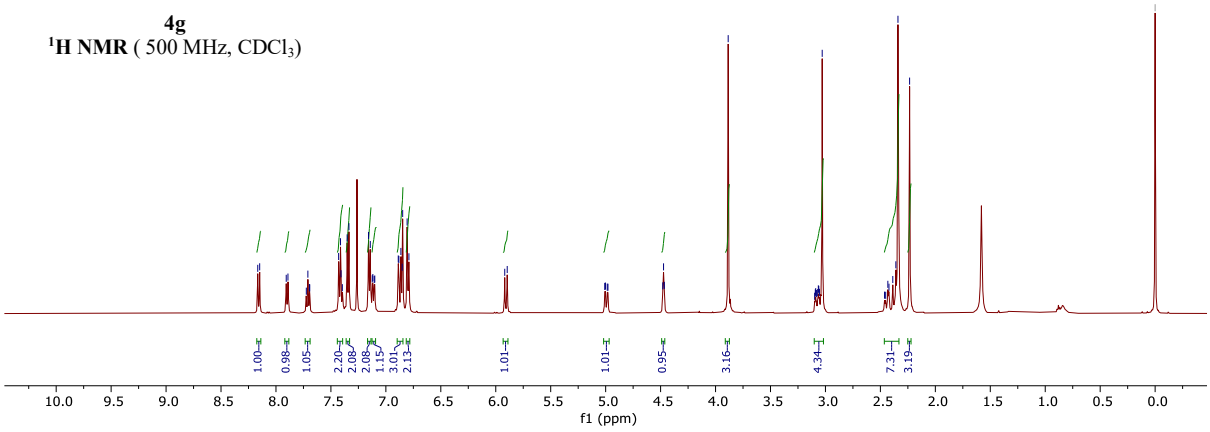
^{19}F NMR (471 MHz, $CDCl_3$)

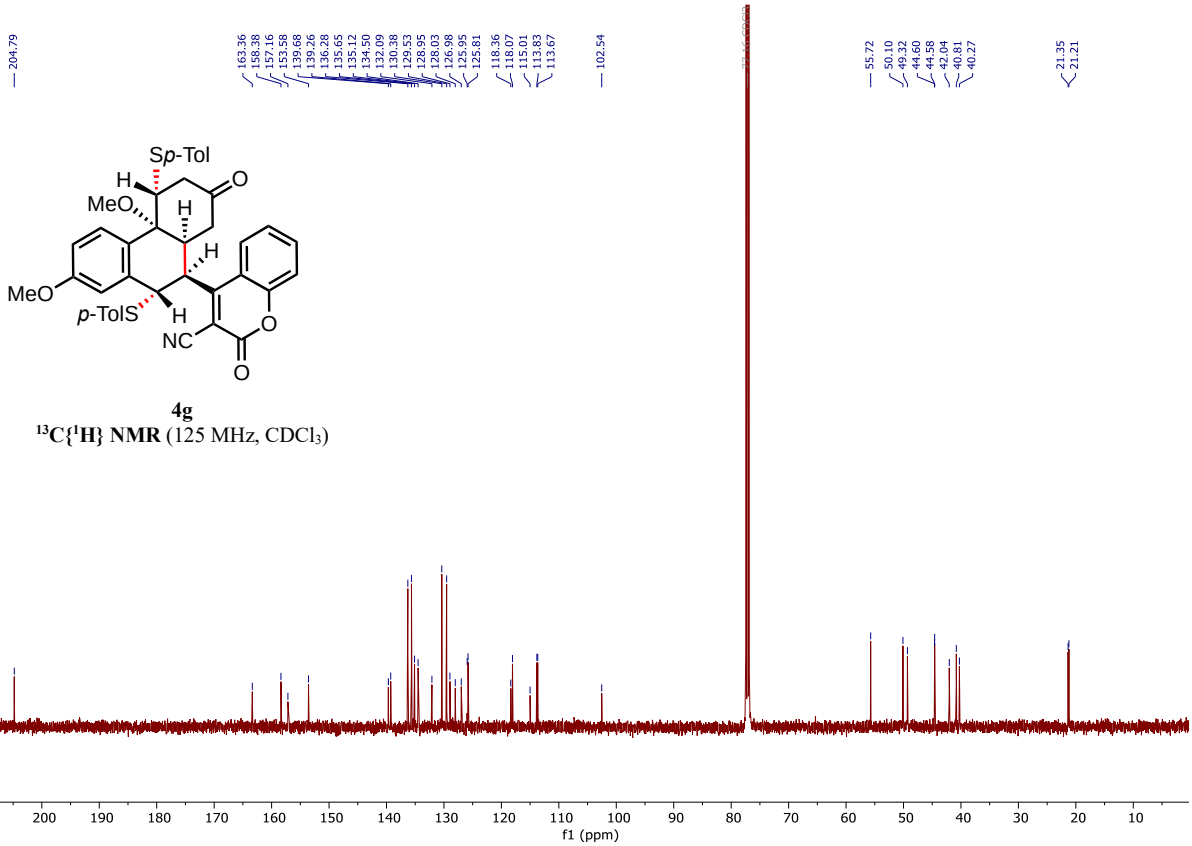




4g

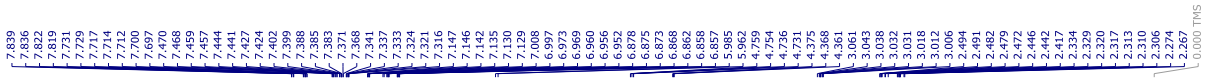
^{1}H NMR (500 MHz, $CDCl_3$)

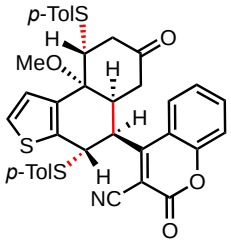




4g

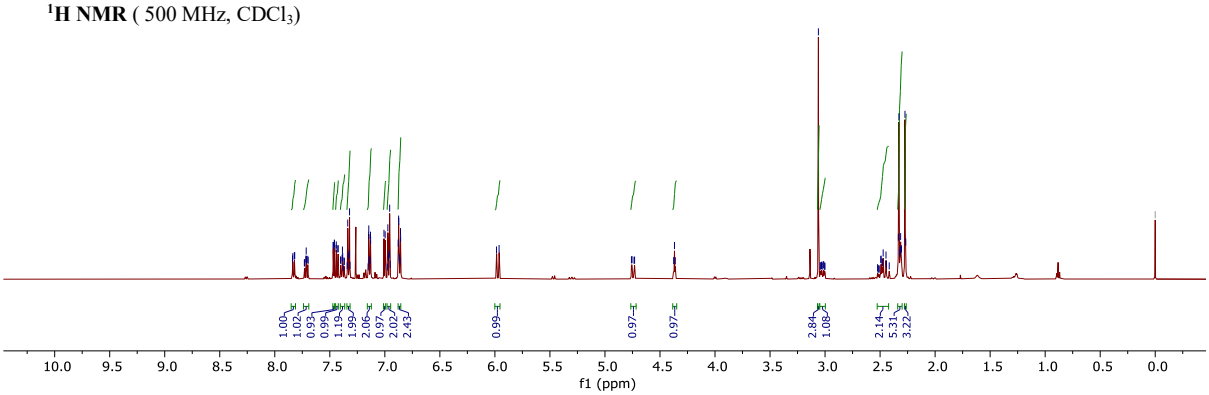
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

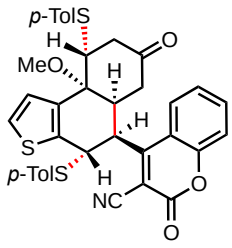




4h

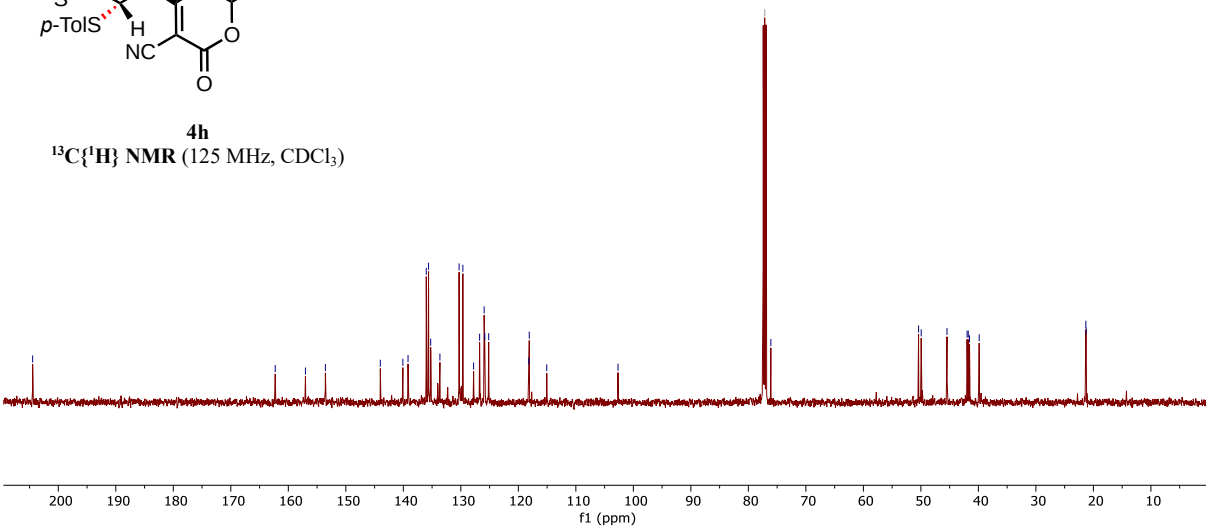
^{1}H NMR (500 MHz, $CDCl_3$)

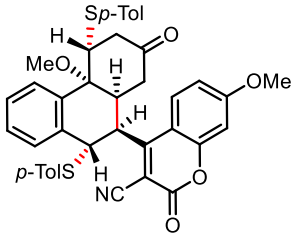




4h

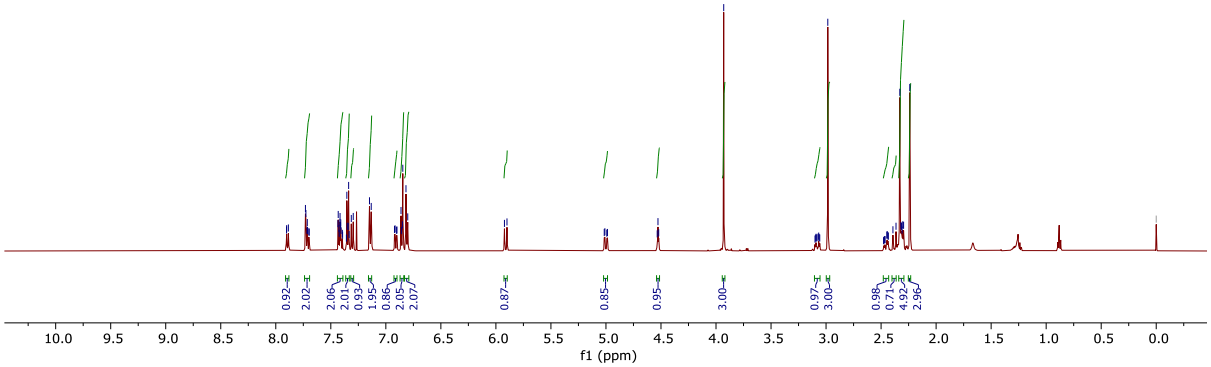
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

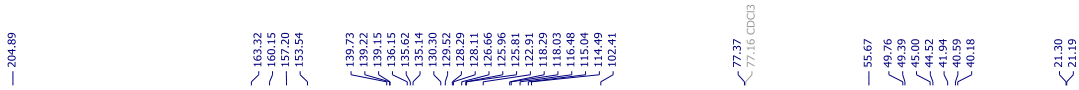


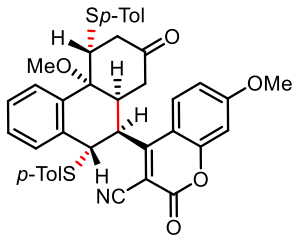


4i

^{1}H NMR (500 MHz, $CDCl_3$)

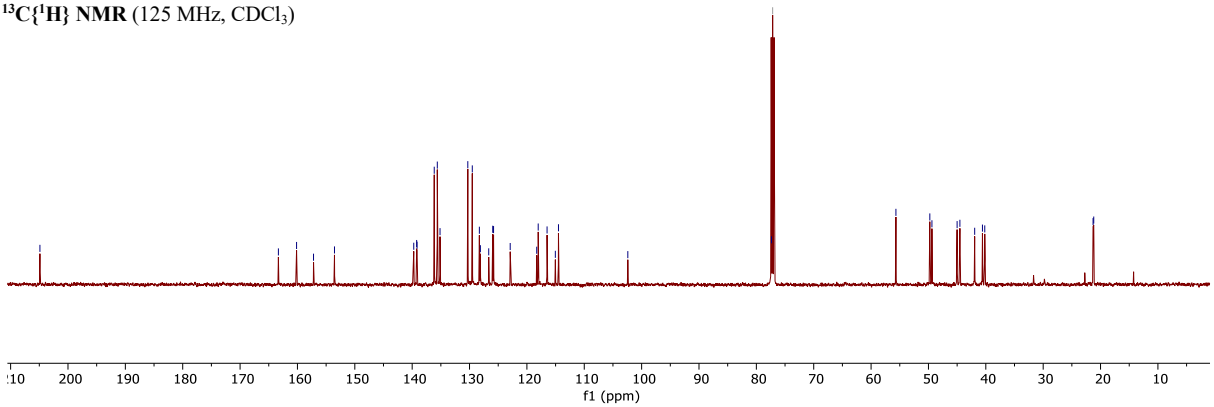


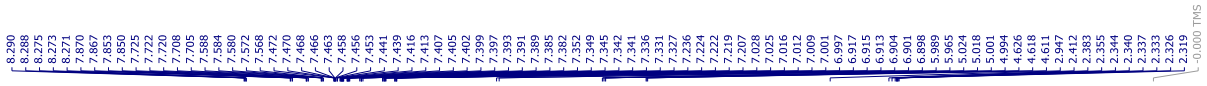


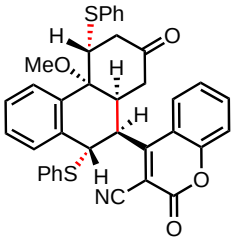


4i

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

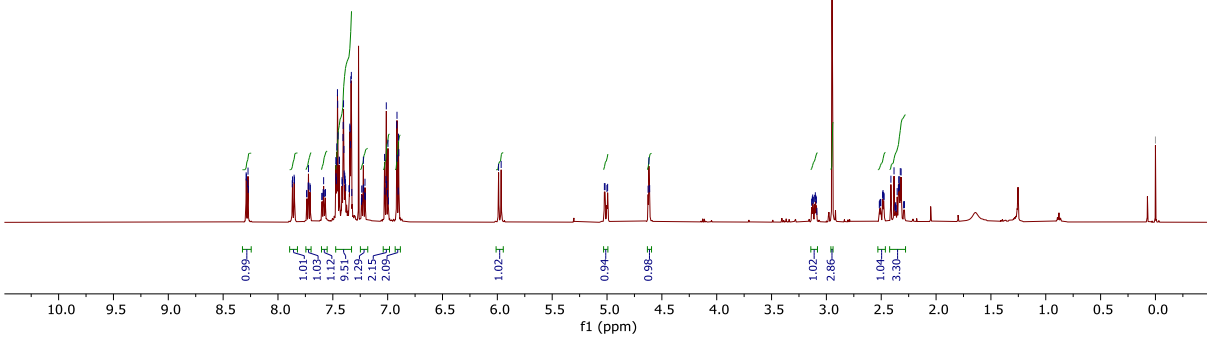


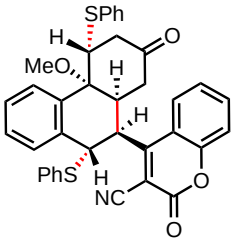




4j

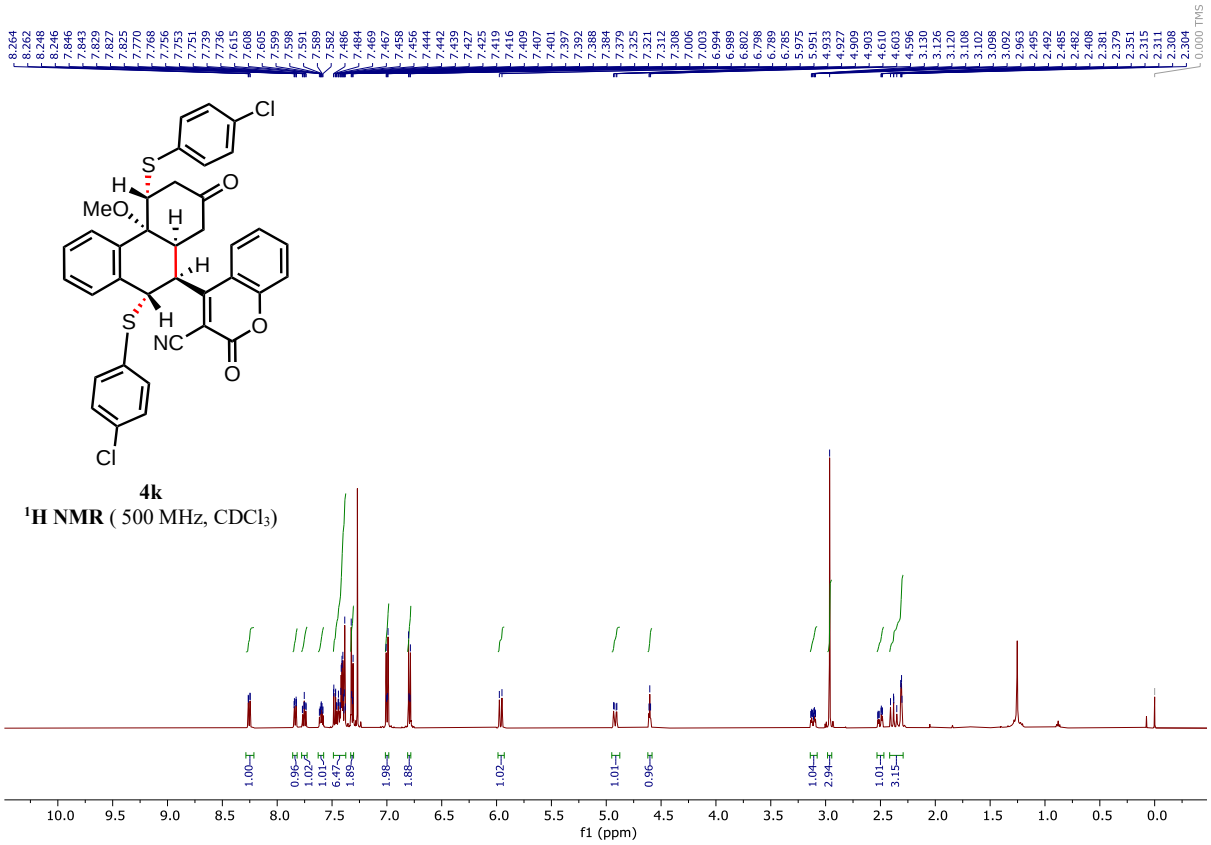
^{1}H NMR (500 MHz, $CDCl_3$)





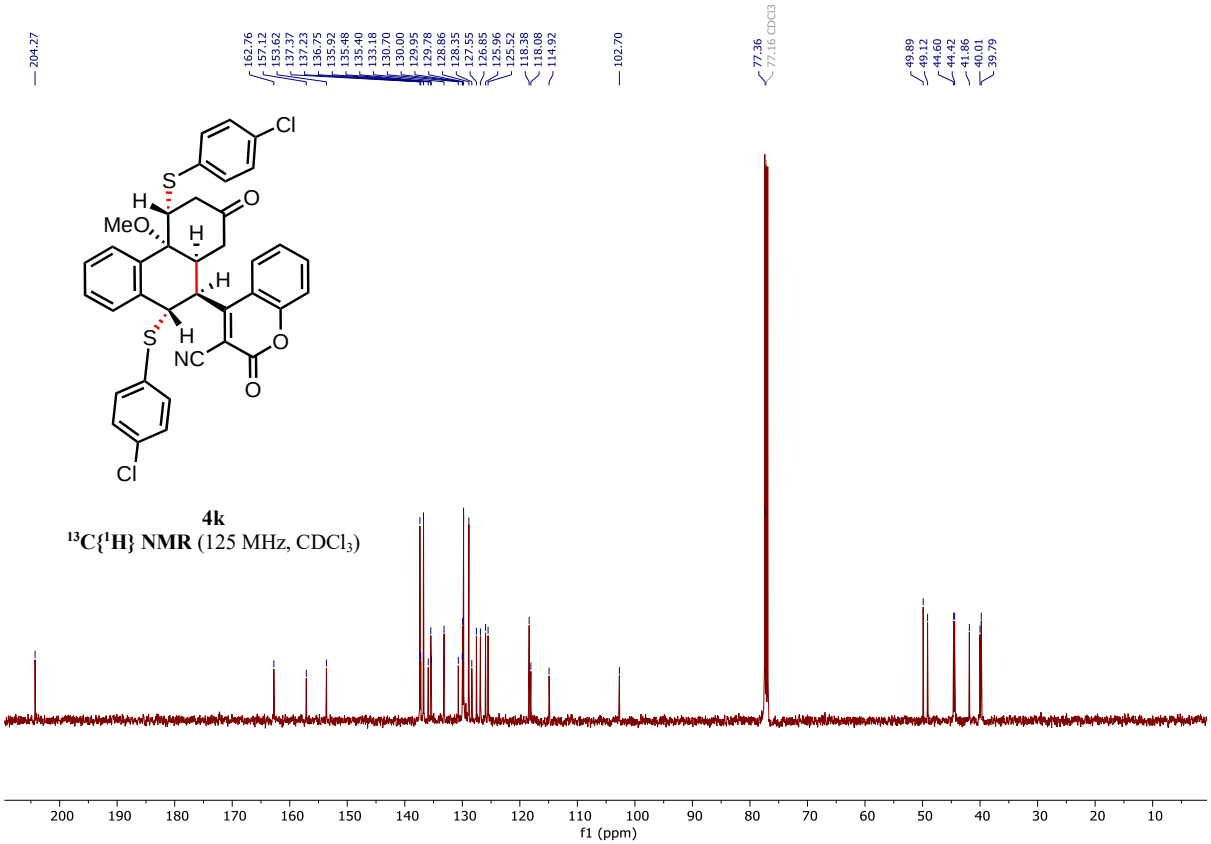
4j

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



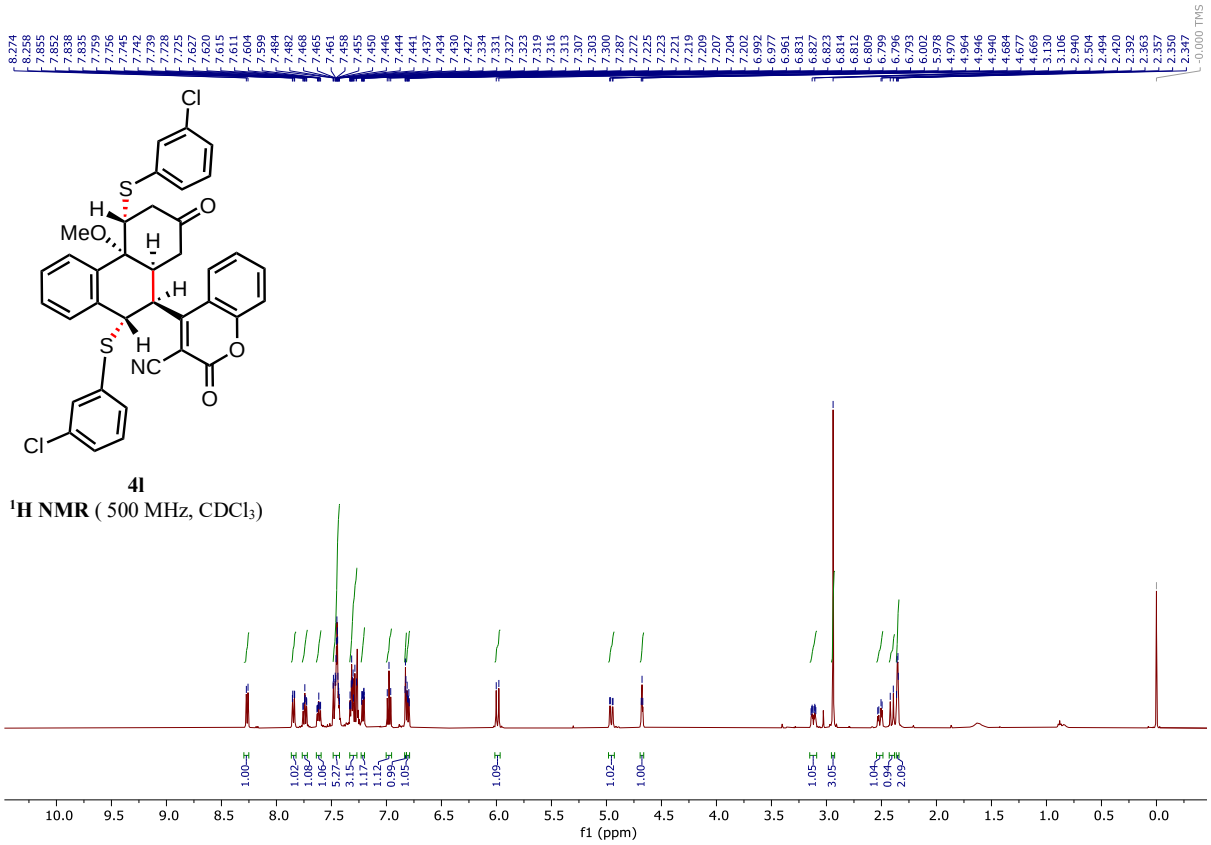
4k

^{1}H NMR (500 MHz, $CDCl_3$)



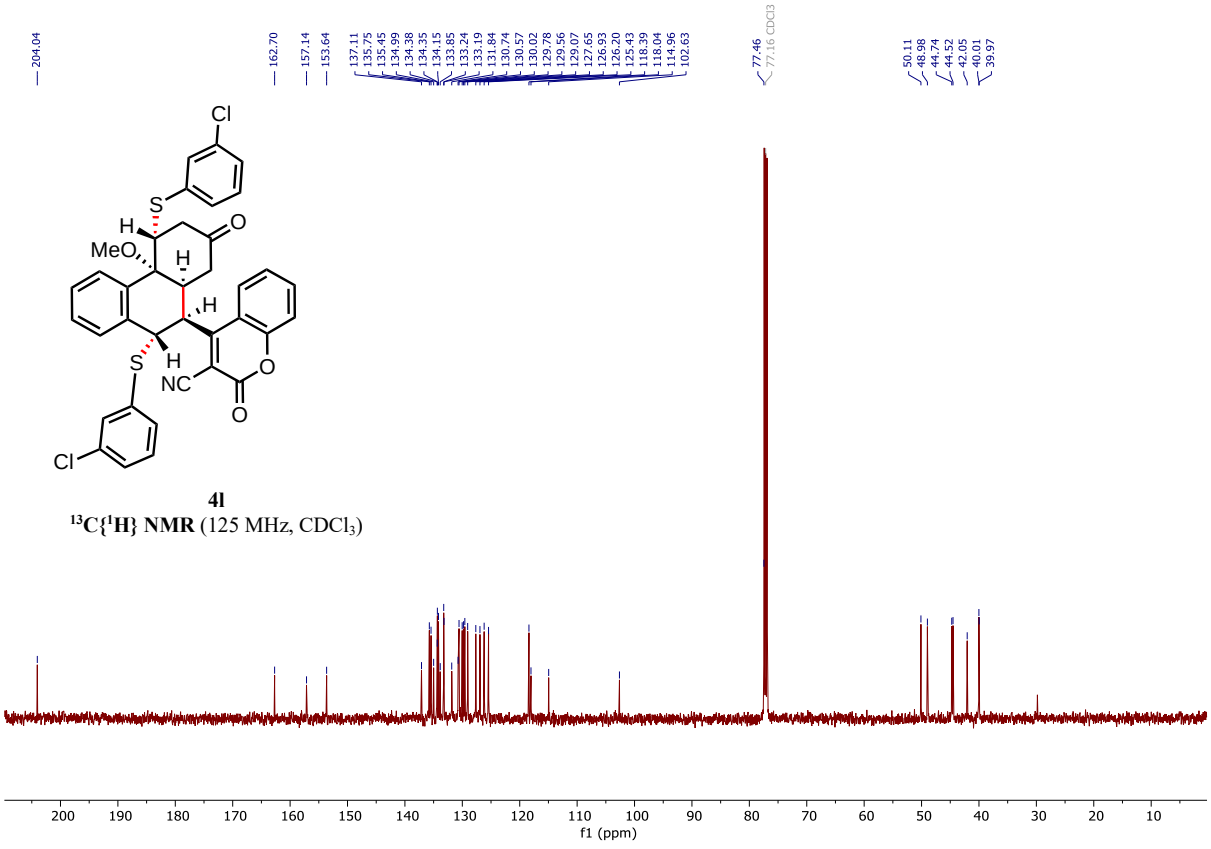
4k

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



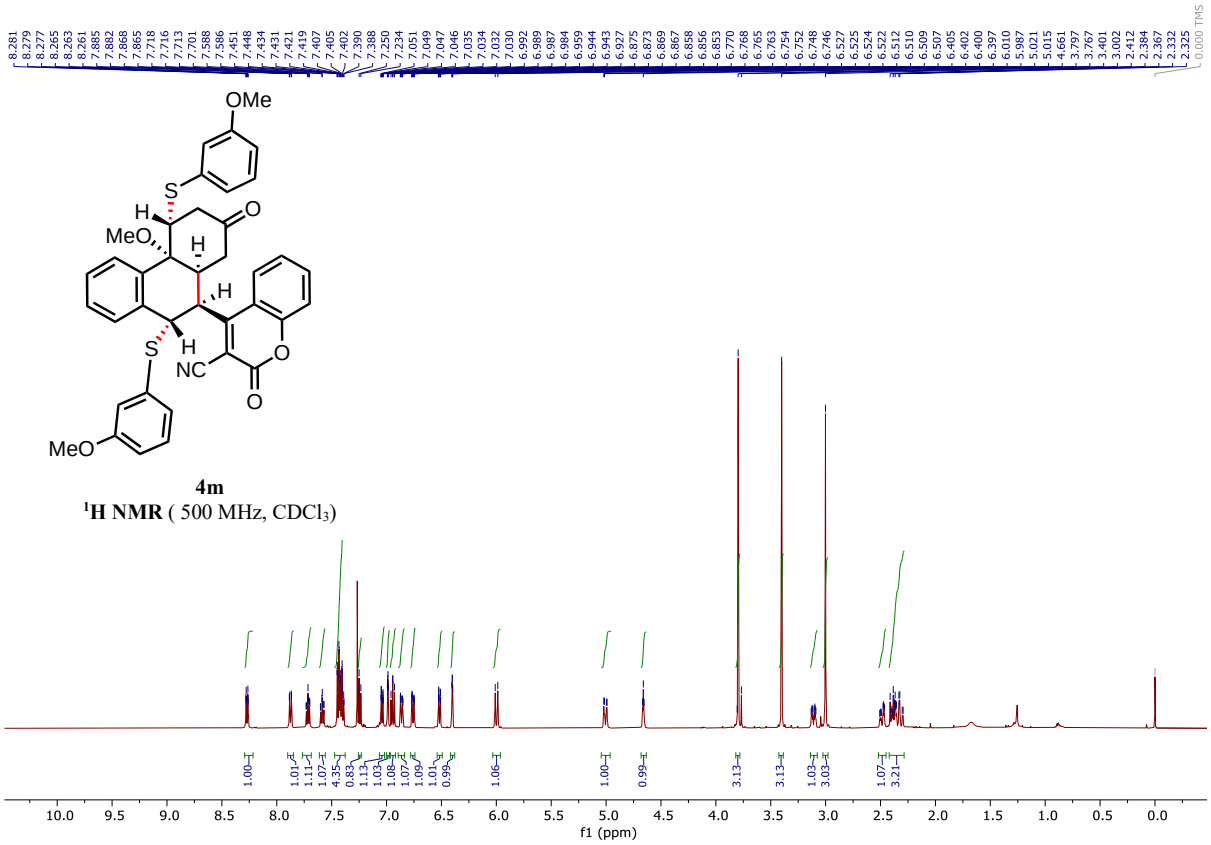
4l

^{1}H NMR (500 MHz, $CDCl_3$)



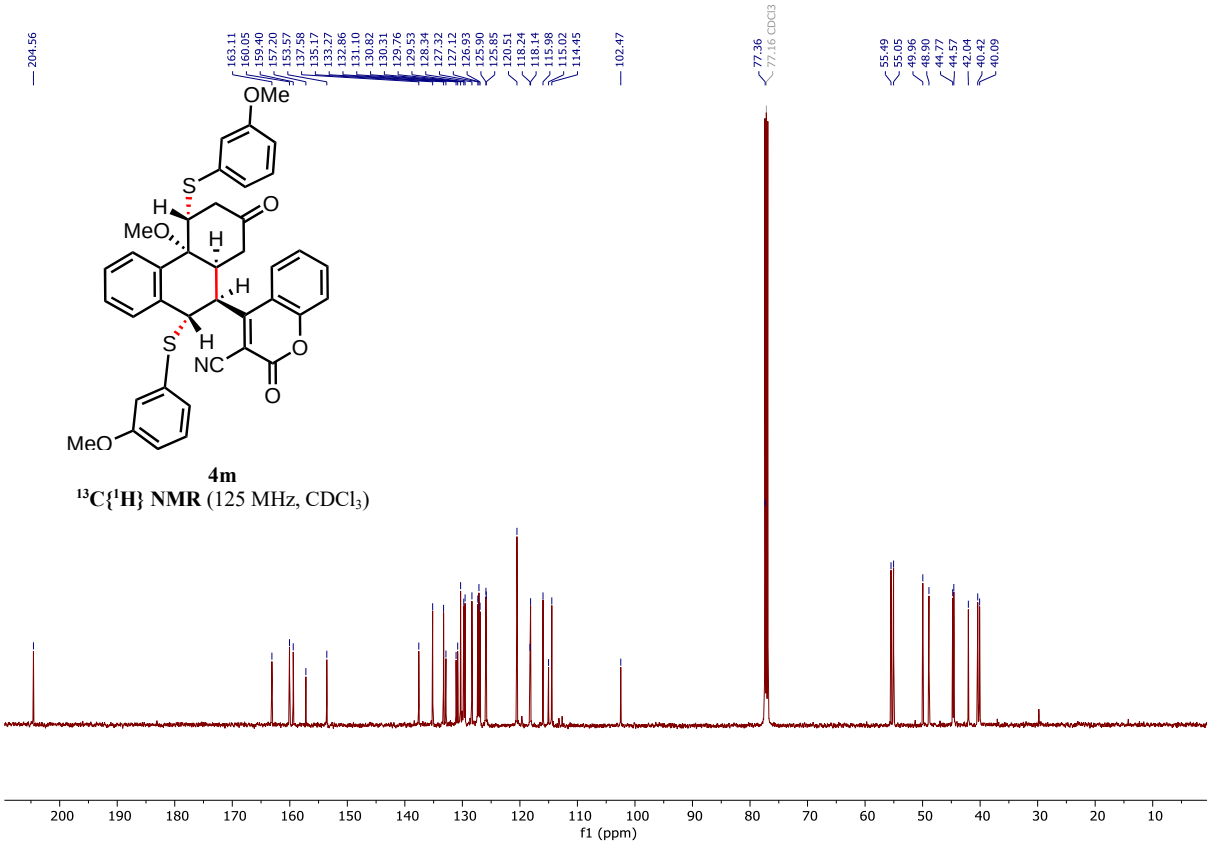
4l

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



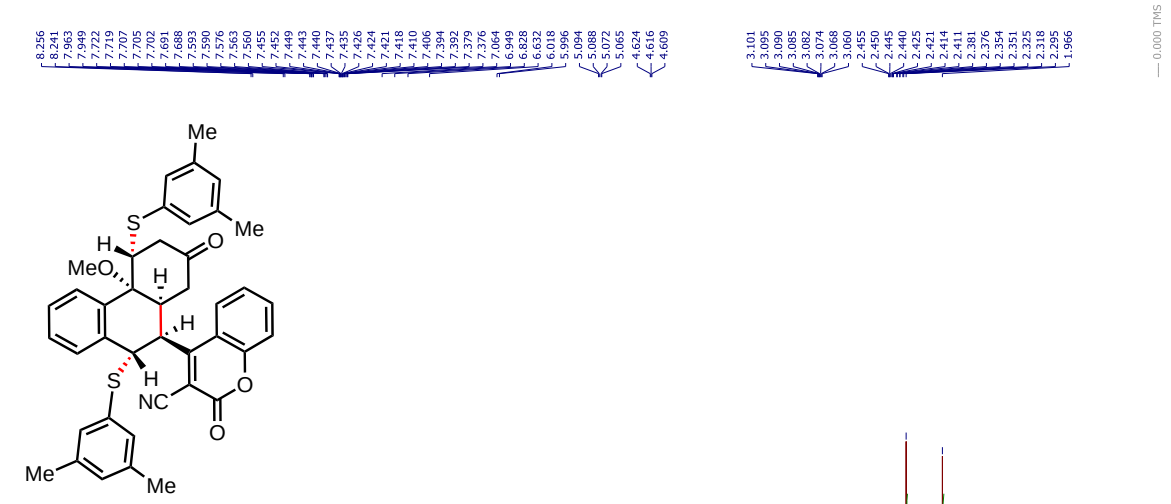
4m

^{1}H NMR (500 MHz, $CDCl_3$)



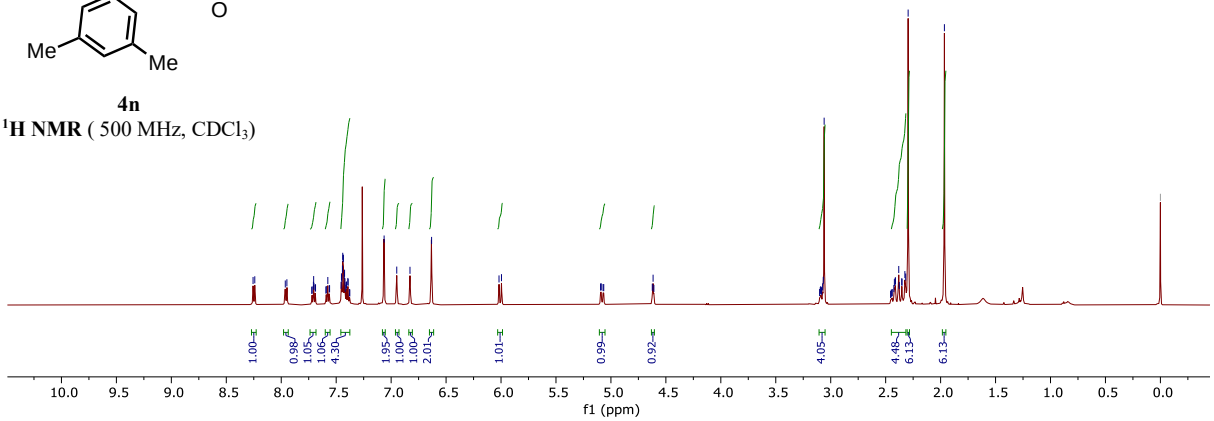
4m

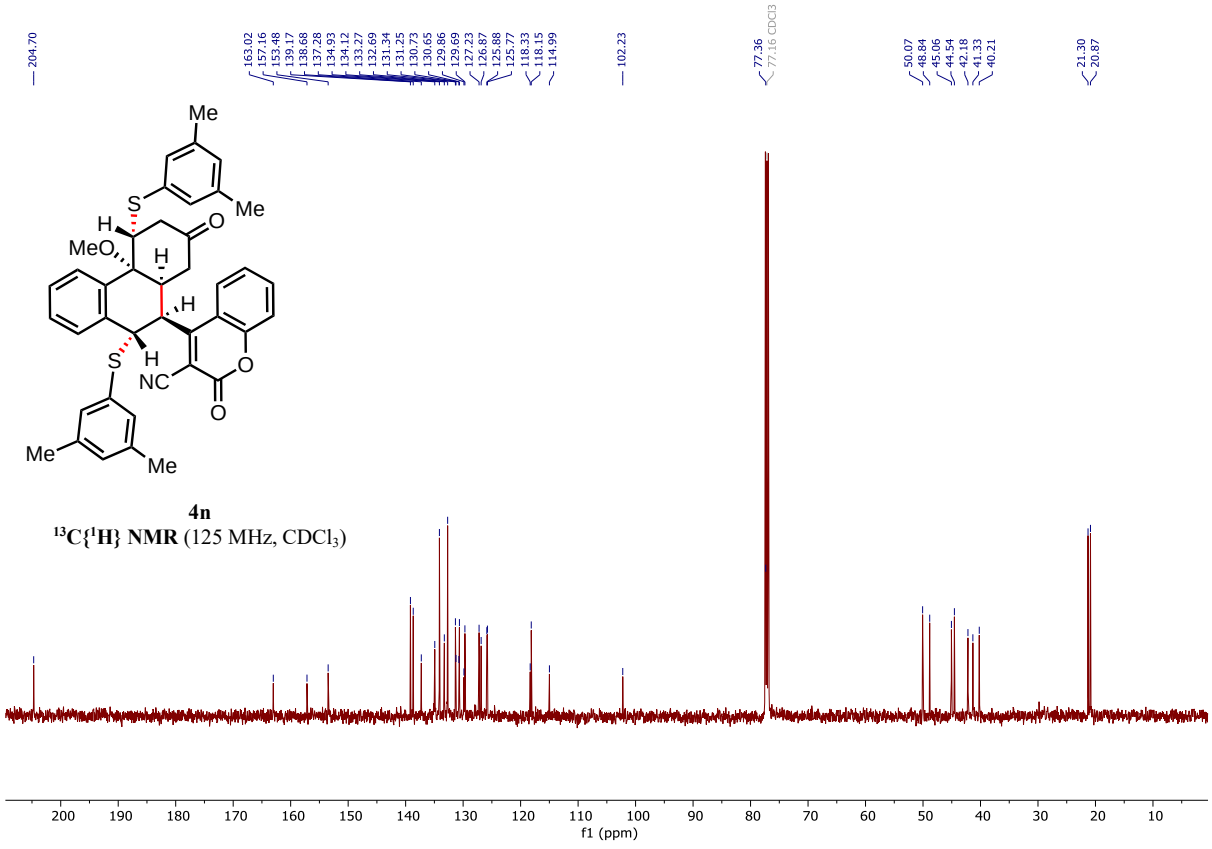
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



4n

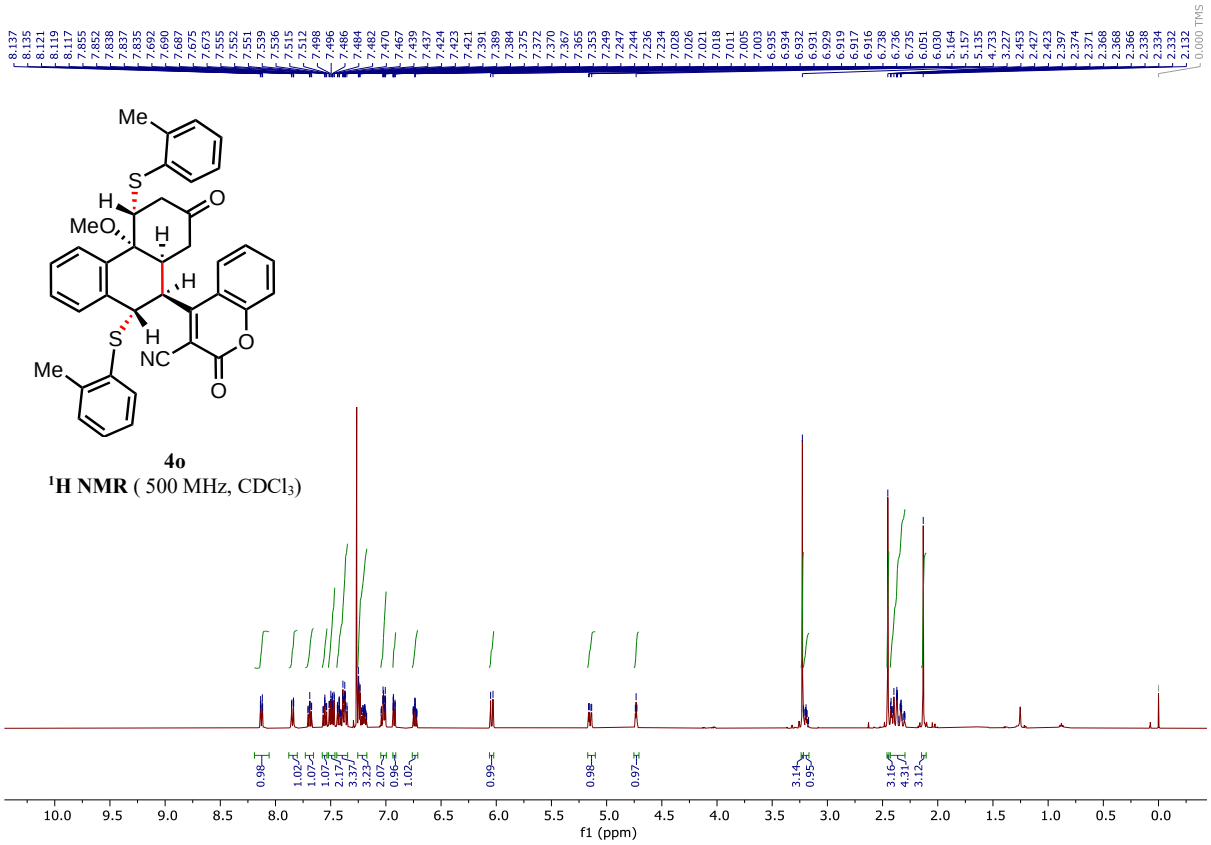
^{1}H NMR (500 MHz, $CDCl_3$)





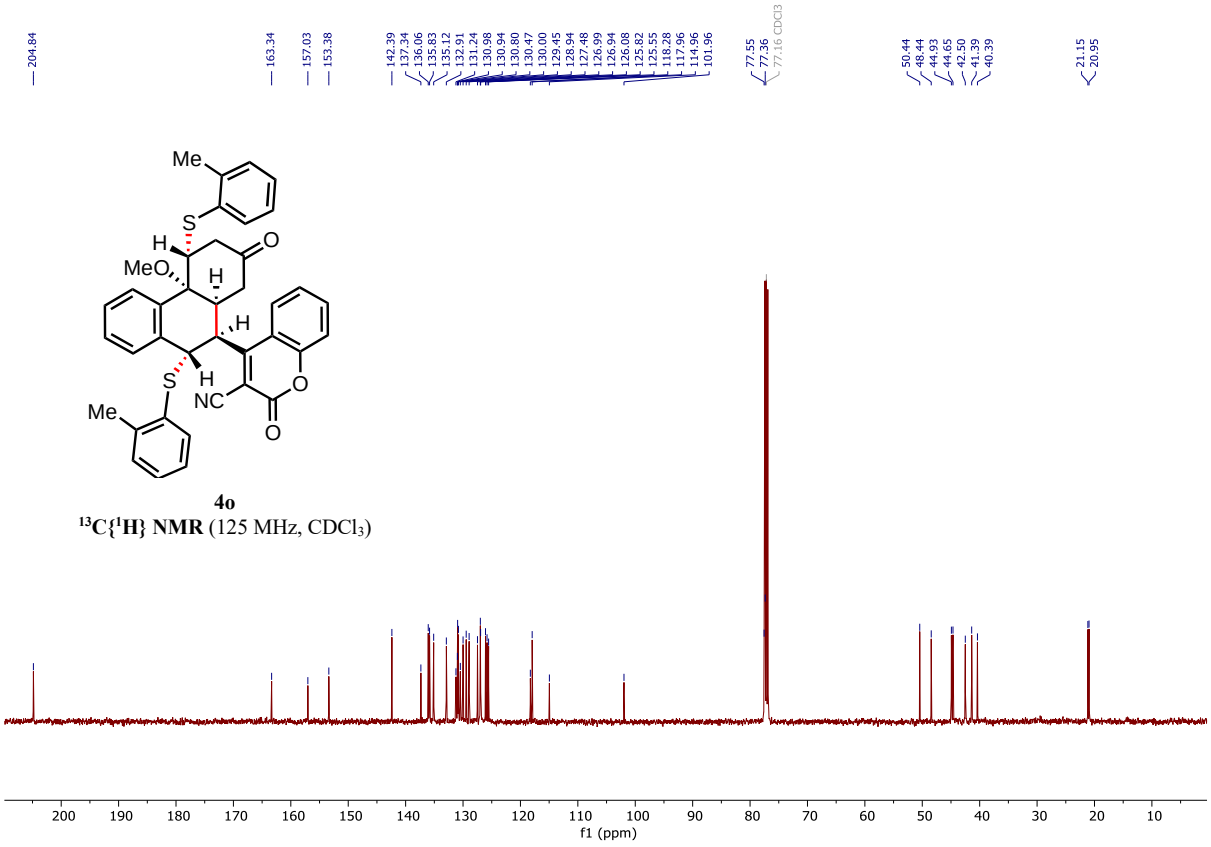
4n

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



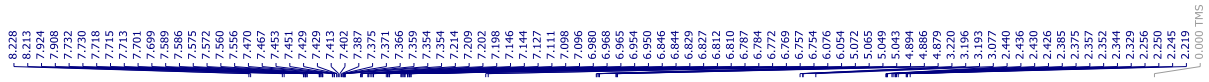
4o

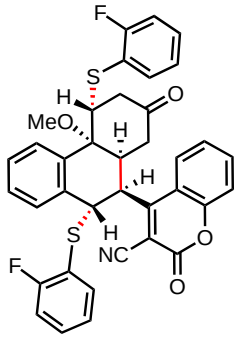
^{1}H NMR (500 MHz, $CDCl_3$)



4o

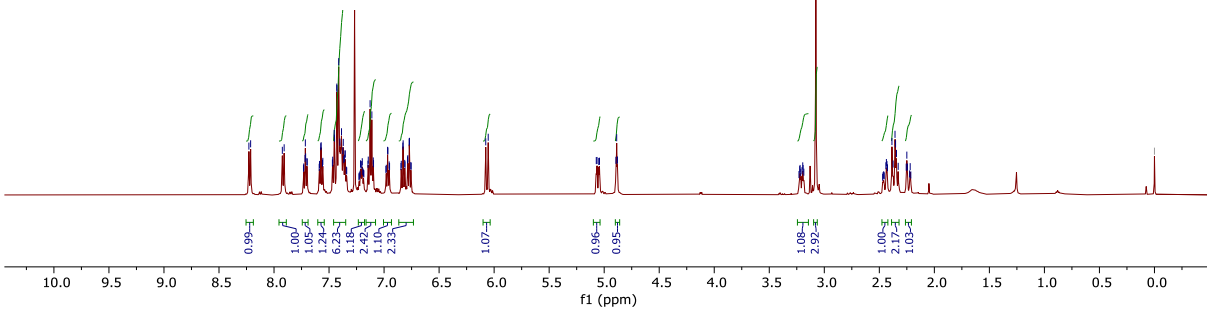
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

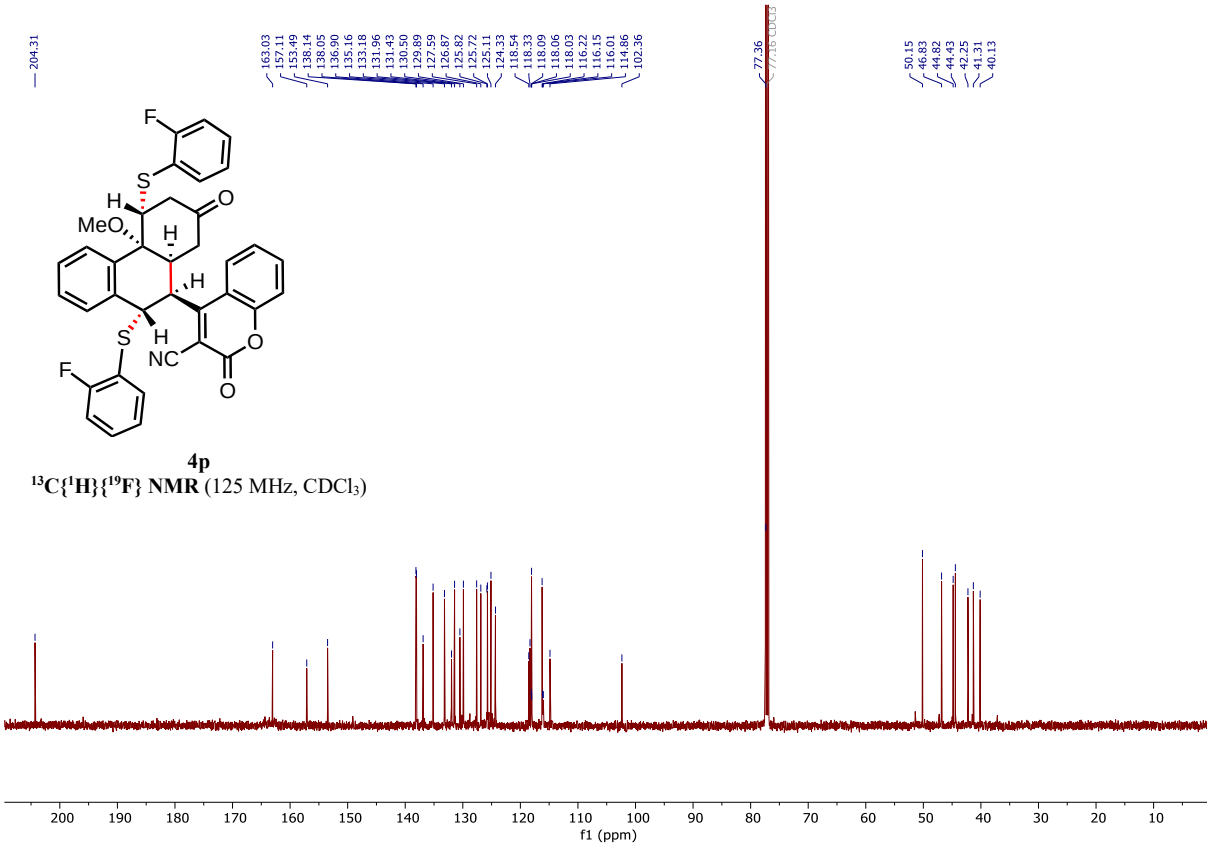




4p

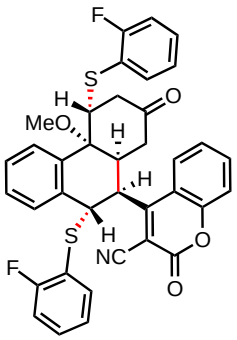
^{1}H NMR (500 MHz, $CDCl_3$)





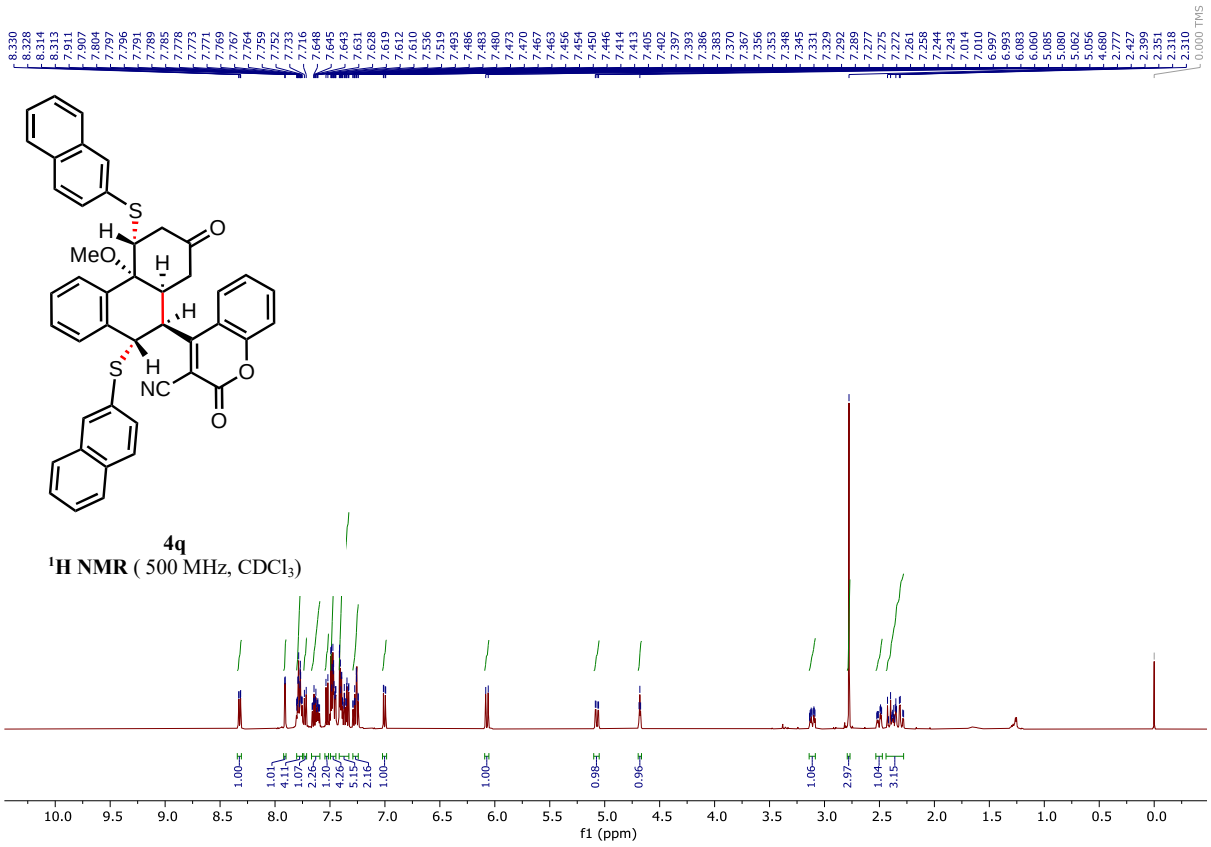
4p

^{13}C{^{1}H}{^{19}F} NMR (125 MHz, $CDCl_3$)



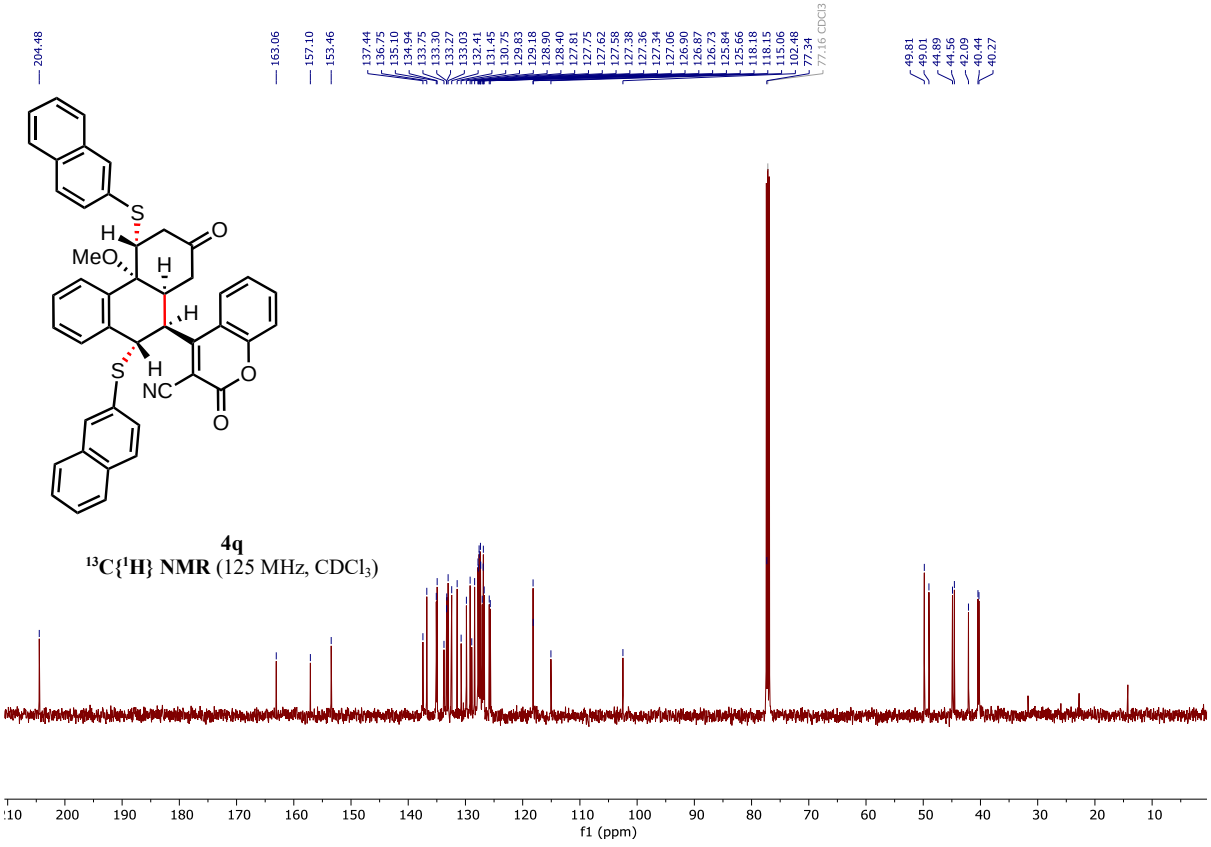
4p

^{19}F NMR (471 MHz, $CDCl_3$)



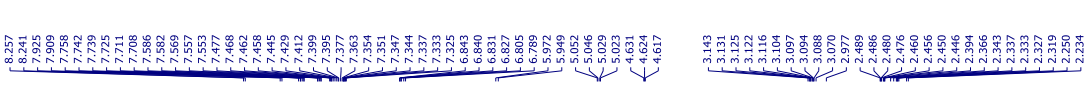
4q

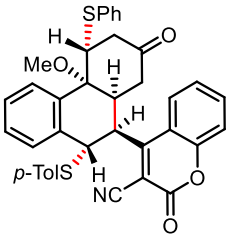
^{1}H NMR (500 MHz, $CDCl_3$)



4q

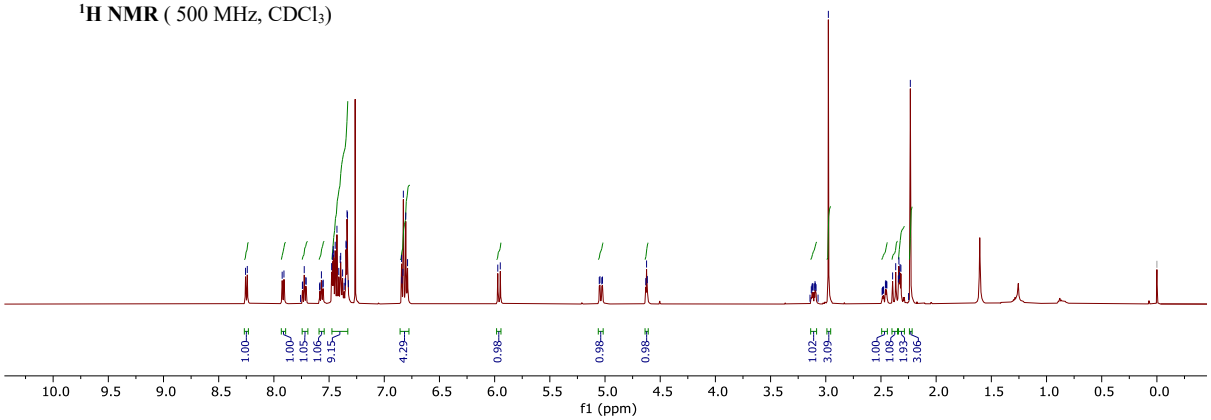
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

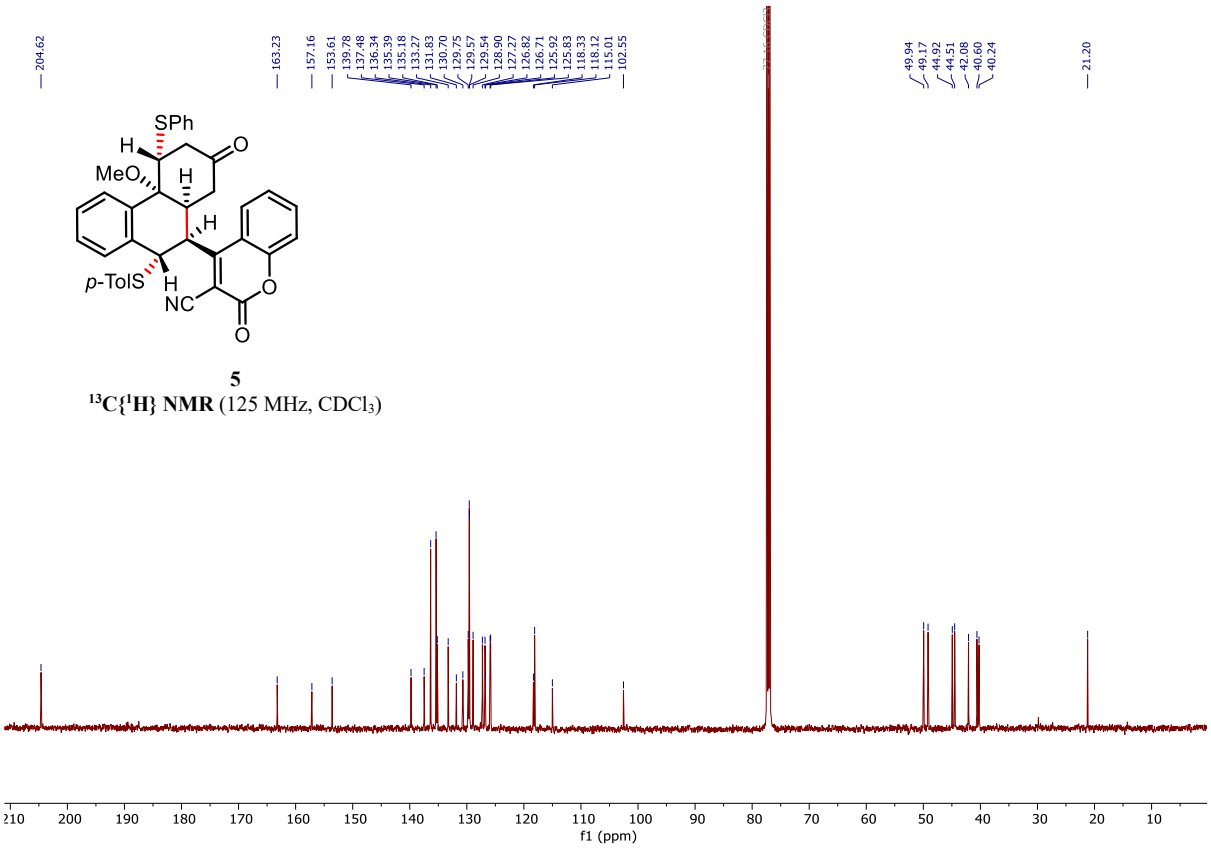




5

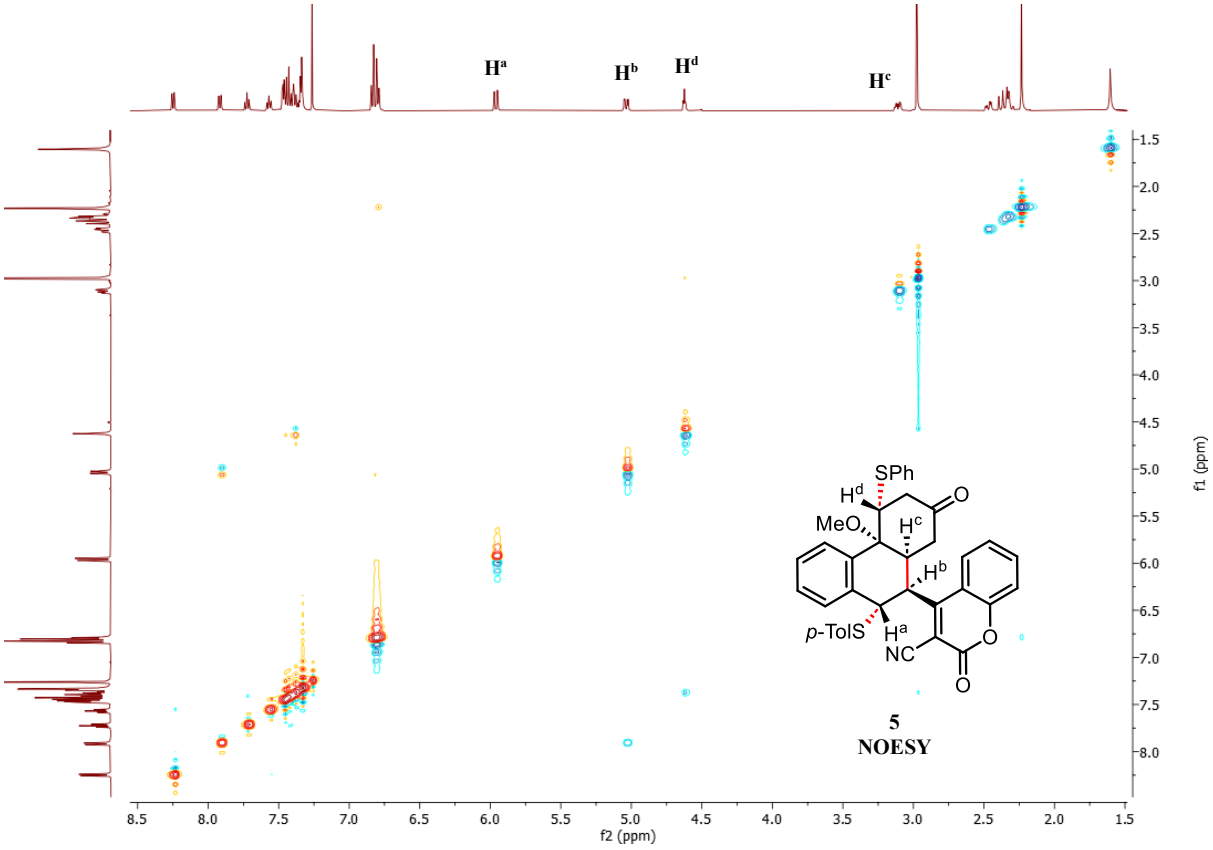
^{1}H NMR (500 MHz, $CDCl_3$)

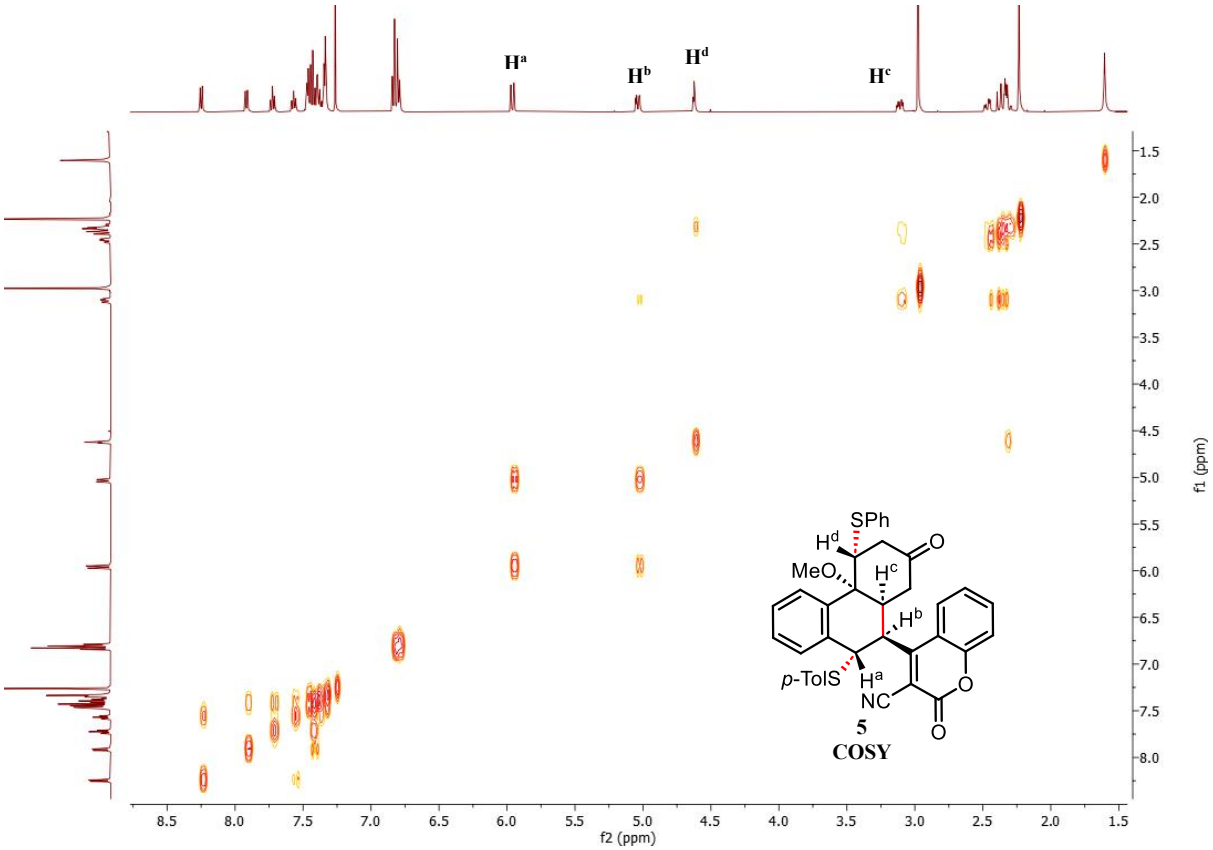


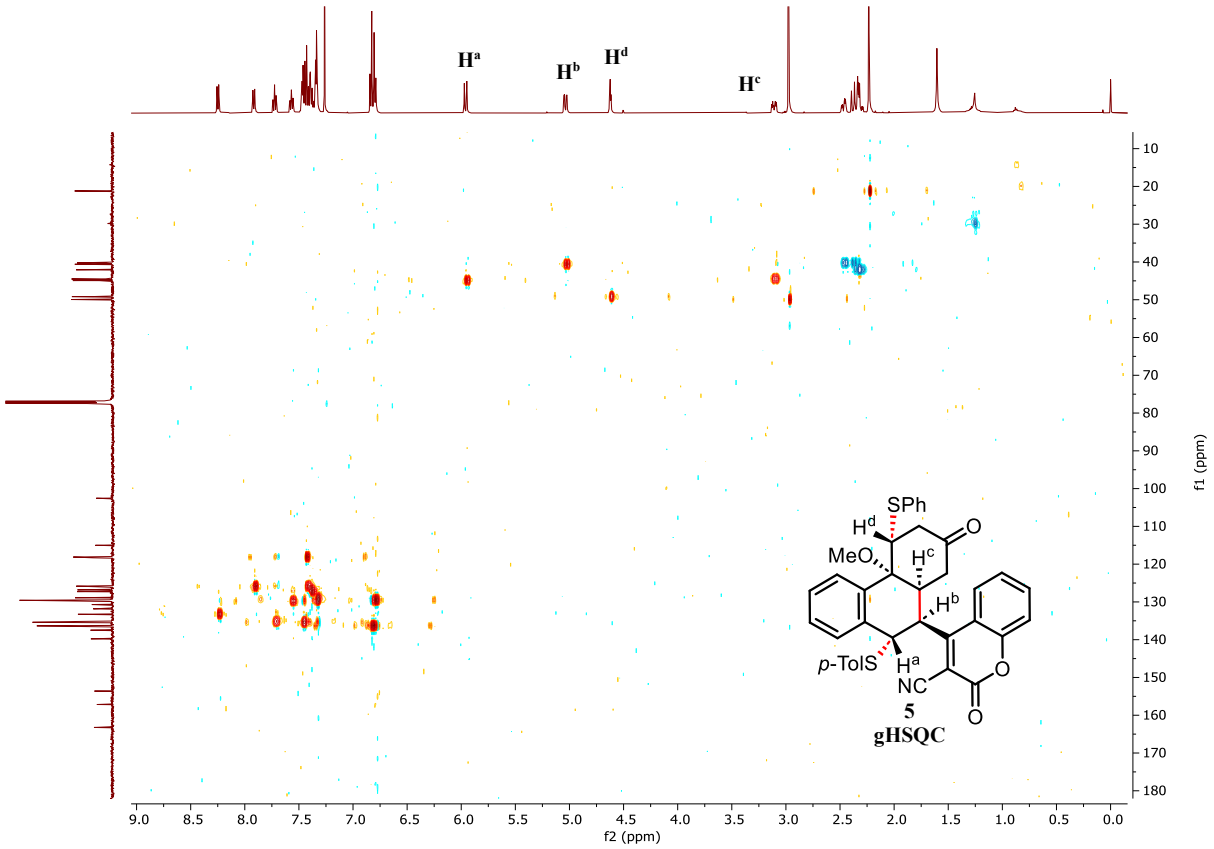


5

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)

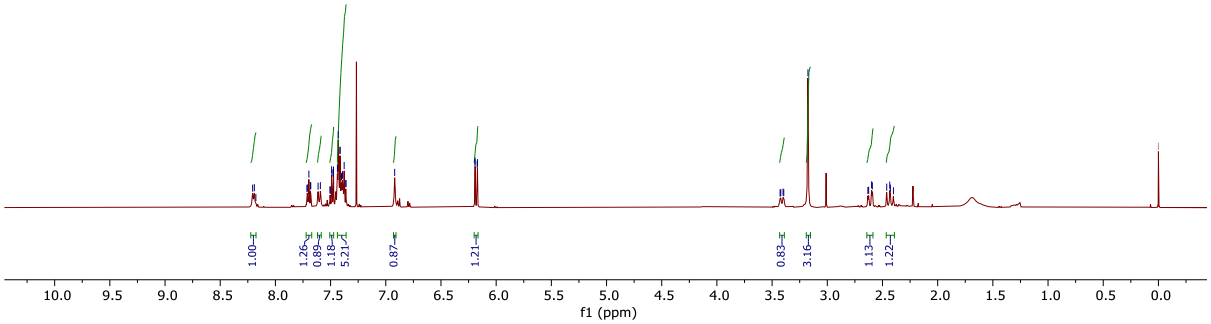

Ha
Hb
Hd
Hc
SPh
Hd
MeO
Hc
Hb
p-TolS
Ha
NC
O
O
O
5
NOESY
f2 (ppm)
f1 (ppm)

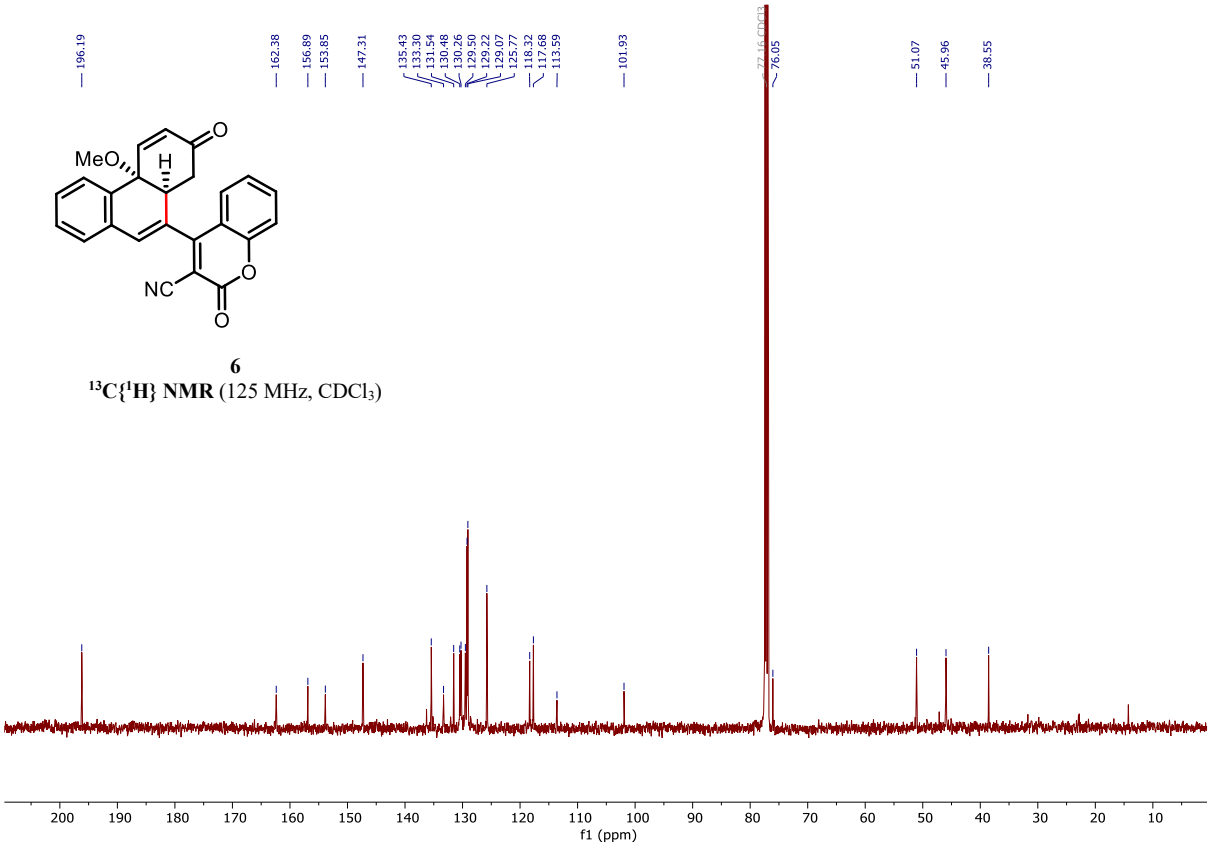

Ha
Hb
Hd
Hc
SPh
Hd
MeO
Hc
Hb
p-TolS
Ha
NC
O
O
O
5
COSY
f2 (ppm)
f1 (ppm)


H^a
H^b
H^d
H^c
f2 (ppm)
f1 (ppm)
SPh
H^d
MeO
H^c
H^b
p-TolS
H^a
NC
O
O
O
5
gHSQC

6

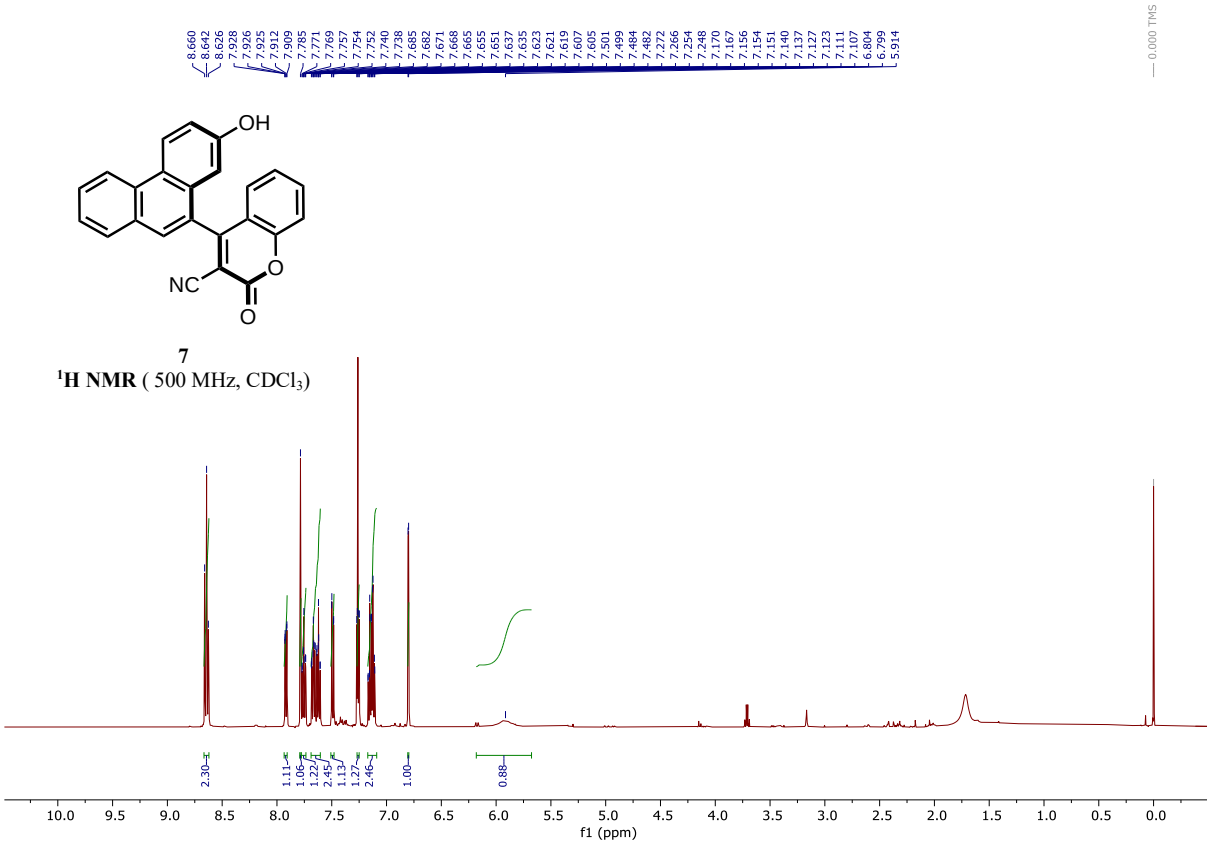
^{1}H NMR (500 MHz, $CDCl_3$)





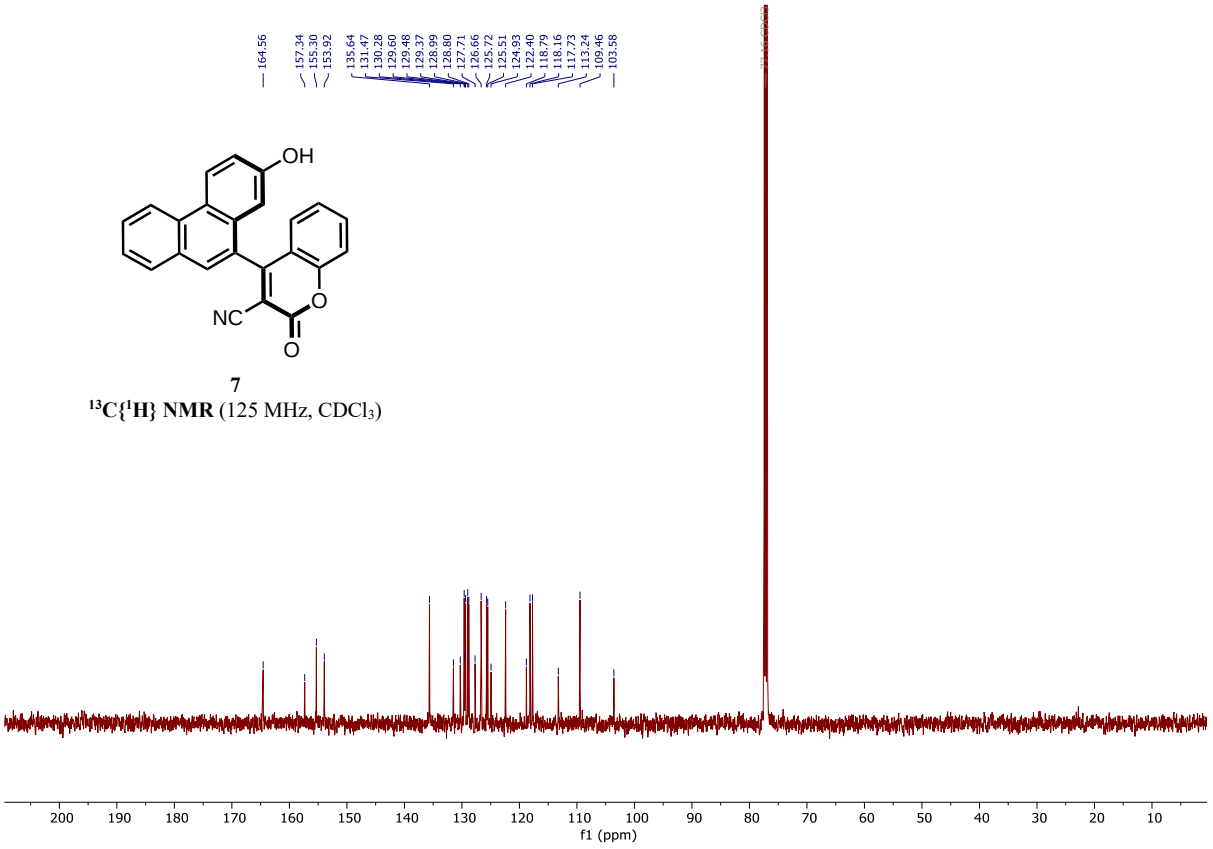
6

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



7

^{1}H NMR (500 MHz, $CDCl_3$)



7

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)