

# Enantioselective synthesis of C3-functionalized 2,1-benzothiazine 2,2-dioxides by N-heterocyclic carbene catalysis

Karina Mroczyńska, Liliana Dobrzańska, Zbigniew Rafiński

Faculty of Chemistry, Nicolaus Copernicus University in Toruń,  
7 Gagarin Street, 87-100 Toruń, Poland  
payudo@umk.pl

**SUPPORTING INFORMATION**

## Summary

<b>1</b>	<b>General Information</b>	<b>S3</b>
<b>2</b>	<b>General procedures</b>	<b>S4</b>
2.1	Procedure A - products <b>1</b> synthesis . . . . .	S4
2.2	Procedure B - products <b>3</b> synthesis . . . . .	S5
2.3	Procedure C - products <b>4</b> synthesis . . . . .	S6
2.3.1	Proposed mechanism . . . . .	S7
<b>3</b>	<b>X-Ray Crystallography Data</b>	<b>S8</b>
<b>4</b>	<b>Product Characterisation</b>	<b>S10</b>
<b>5</b>	<b>NMR Spectra</b>	<b>S41</b>
<b>6</b>	<b>HPLC Chromatograms</b>	<b>S126</b>
	<b>References</b>	<b>S165</b>



## 1 General Information

All syntheses were carried out in oven-dried glassware. Air- or moisture-sensitive reagents were kept under an inert argon atmosphere. Dry solvents were prepared in INERT PureSolv solvent purification system or by distillation and were kept under molecular sieves. Progress of reactions was monitored on TLC plates with a fluorescent indicator and a UV lamp (254 nm). Crude products were purified by column chromatography on silica gel using a CombiFlash Rf + Lumen system with UV Vis and ELSD detectors in *n*-hexane/ethyl acetate gradient. RediSepRf GOLD columns were used.

Given yields are for pure isolated products.

All  $\alpha,\beta$ -unsaturated aldehydes **2** are commercially available, except for (2*E*,4*E*)-5-[4-(dimethylamino)phenyl]penta-2,4-dienal<sup>1</sup>.

For known compounds NMR spectra and melting points were compared with literature data and only yields and <sup>1</sup>H NMR spectra are presented.

The structure of new (unknown) products was confirmed by <sup>1</sup>H, <sup>19</sup>F and <sup>13</sup>C NMR spectra recorded on Bruker AMX 400 (400 MHz) or AMX 700 (700 MHz) in CDCl<sub>3</sub>. FTIR ATR spectra were recorded on Bruker Alpha-P spectrophotometer. Mass spectra were recorded on an Agilent 6530 Q-TOF LC/MS system coupled with a 1290 Infinity II liquid chromatograph. Melting points were measured by Stuart SMP50 melting point apparatus.

The specific rotation of products was measured with Bellingham + Stanley ADP430 Polarimeter. The concentration is given in g/100mL.

The chiral HPLC chromatograms for compound **3a** and optimization process were prepared on ECOM Sapphire 600 HPLC apparatus with Phenomenex LUX 4.6 mm × 150 mm, 5 $\mu$ m Amylose-1 column in reverse phase with acetonitrile/water as a mobile phase and ChromaX software. The enantiomeric excess of chiral products **4** and **3m**, **3q** was determined by HPLC Agilent 1200 Infinity apparatus with Phenomenex LUX 4.6 mm × 250 mm, 3 $\mu$ m Amylose-1 (or 3 $\mu$ m Cellulose-1) column and *n*-hexane/*i*-propanol as a mobile phase.

## 2 General procedures

### 2.1 Procedure A - products 1 synthesis

The general procedure of obtaining substituted 2,1-benzothiazinones (Figure S1) was modified from known recipe<sup>2</sup> with additional step for anthranilic acid methyl esters synthesis (**step A1**).

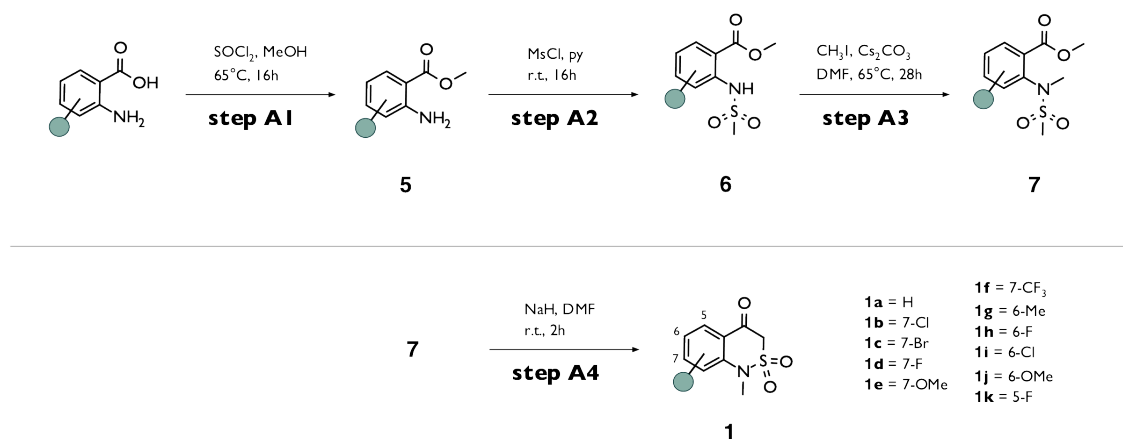


Figure S1: General procedure for obtaining substituted 2,1-benzothiazinones

**Step A1:** Proper anthranilic acid (30 mmol) was dissolved in dry methanol (48 mL) and cooled down to  $0^\circ\text{C}$ . Thionyl chloride (240 mmol, 17.5 mL) was added slowly and carefully (released gasses were quenched using Drechsler's gas washing bottle filled with 2M NaOH solution). The reaction was heated in an oil bath at  $65^\circ\text{C}$  for 16h. After completion methanol and excess of  $\text{SOCl}_2$  was removed under vacuum (with water vacuum pump). Precipitate was dissolved in chloroform and the remaining parts of thionyl chloride were quenched with saturated  $\text{NaHCO}_3$ . Extraction with chloroform gave pure anthranilic methyl ester **5** with 38 - 100% yields.

**Step A2:** Crude ester **5** (10 mmol) from the previous step was dissolved in pyridine (12 mL). Mesyl chloride (0.77 mL, 10 mmol) was added slowly at  $0^\circ\text{C}$ . After half an hour mixture was heated to room temperature and stirred for additional several hours (completion was monitored by TLC). After completion reaction was quenched with ice-cold water. Precipitate of a pure product **6** should occur during 15 minutes. If not - extraction with ethyl acetate was performed. Yields: 44 - 97%.

**Step A3:** To compound **6** (10 mmol) dissolved in DMF (20 mL) a  $\text{Cs}_2\text{CO}_3$  (4.9 g, 15 mmol) was added in one portion. Reaction was stirred for 12h. Afterwards,  $\text{CH}_3\text{I}$  (0.94 mL, 15 mmol) was added drop-wise, and mixture was stirred overnight at room temperature. Reaction was quenched with saturated  $\text{NH}_4\text{Cl}$  and extracted with ethyl acetate. Obtained product **7** was used in the next step without further purification. Yields: 64 - 100%.

**Step A4:** To a suspension of NaH (60% in oil, 0.28 g, 7 mmol) in dry DMF (3 mL) a solution of **7** (3.5 mmol) dissolved in dry DMF (12 mL) was added drop-wise by syringe and septum. Reaction was stirred at room temperature for 2h and quenched by pouring on cold 1M HCl (20 mL). Obtained precipitate was filtrated, washed with water, and dry under vacuum to give pure product **1** with 68 - 98% yields.

## 2.2 Procedure B - products **3** synthesis

Figure S2 presents the general procedure for obtaining the NHC-catalysed annulation products **3**.

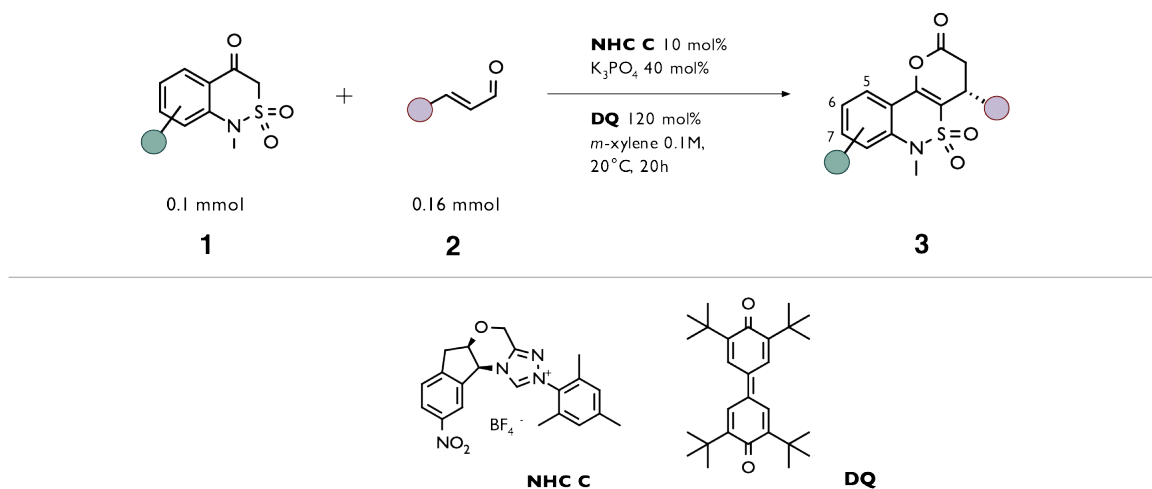


Figure S2: General procedure for N-heterocyclic carbene synthesis

To the oven-dried flask with pre-NHC catalyst (**C**; 4.7 mg, 10 mol%) an aldehyde (**2**) (0.16 mmol), benzothiazine (**1**) (0.1 mmol), oxidant (49mg, 0.12 mmol) and solvent (*m*-xylene; 1mL) was added and flask was filled with argon. Base ( $K_3PO_4$ ; 8.5 mg, 40 mol%) was added afterward in one portion. The reaction mixture was stirred at 20°C for 20h. After completion, solvent was evaporated and residue was purified by FLASH chromatography in *n*-hexane/ethyl acetate gradient.

## 2.3 Procedure C - products 4 synthesis

Final products was obtained in 3-step sequence (Figure S3).

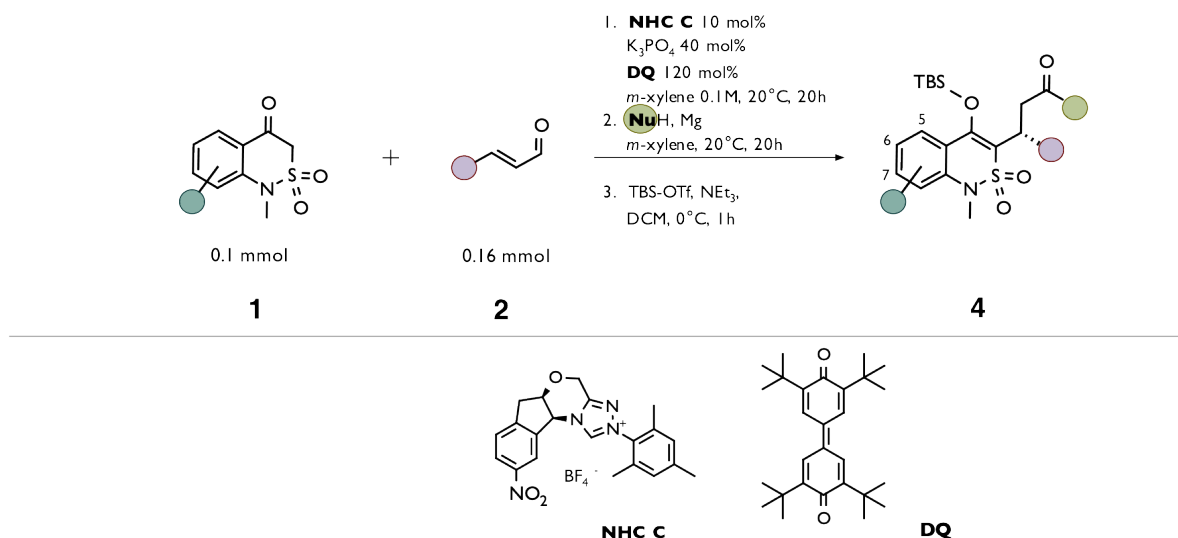


Figure S3: General procedure for obtaining product 4

To the oven-dried flask with pre-NHC catalyst (**C**; 4.7 mg, 10 mol%) an aldehyde (**2**) (0.16 mmol), benzothiazinone (**1**) (0.1 mmol), Kharasch oxidant (49mg, 0.12 mmol), and *m*-xylene (1mL) were added and the flask was filled with argon.  $K_3PO_4$  (8.5 mg, 40 mol%) was added afterward in one portion. The reaction mixture was stirred at 20°C for 20h. Afterwards, methanol (2 mL) and magnesium turnings (5 mg, 0.2 mmol) were added and reaction was stirred for an additional 20h. After this time mixture was evaporated to dryness. Residue was dissolved in ethyl acetate, filtrated through a PTFE syringe filter to a new oven-dry flask and evaporated once again. Last, third step was performed in dichloromethane (1 mL) in inert atmosphere. Triethyl amine (0.3 mmol, 42  $\mu$ L) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.2 mmol, 46  $\mu$ L) was added at 0°C. After 1h reaction was evaporated and the product **4** was purified by FLASH chromatography in *n*-hexane/ethyl acetate gradient. Yields: 36 - 96%.

For HPLC analysis and enantiomeric excess determination a racemic mixture of each product **4** was obtained by reaction in toluene with 1:1 molar ratio of **NHC-A** enantiomers (**NHC A** and **NHC ent-A** - Figure S4).

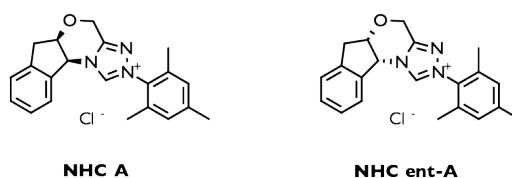


Figure S4: Two enantiomers of catalyst **NHC-A**

### 2.3.1 Proposed mechanism

Our proposed reaction pathway, illustrated in the Figure S5, begins with the reaction of an NHC catalyst with an enal to form the Breslow intermediate I. Under oxidative conditions, this intermediate is converted into the  $\alpha,\beta$ -unsaturated acyl azolium intermediate II. Subsequently, a Michael addition occurs with the tautomeric form of benzothiazinone 2,2-dioxide **1**, resulting in the formation of the Michael adduct III. This adduct then undergoes rapid hydrogen migration IV and intramolecular cyclization, yielding the fused dihydropyranone **3** and regenerating the NHC catalyst.

Following this, the opening of the lactone ring in the presence of an O- or HN-nucleophile leads to the formation of the corresponding ester or amide. When reacted with TBS triflate, the process results in the formation of a silyl ether **4**. This sequence highlights the versatility of the reaction, allowing for the introduction of various functional groups depending on the nucleophile employed.

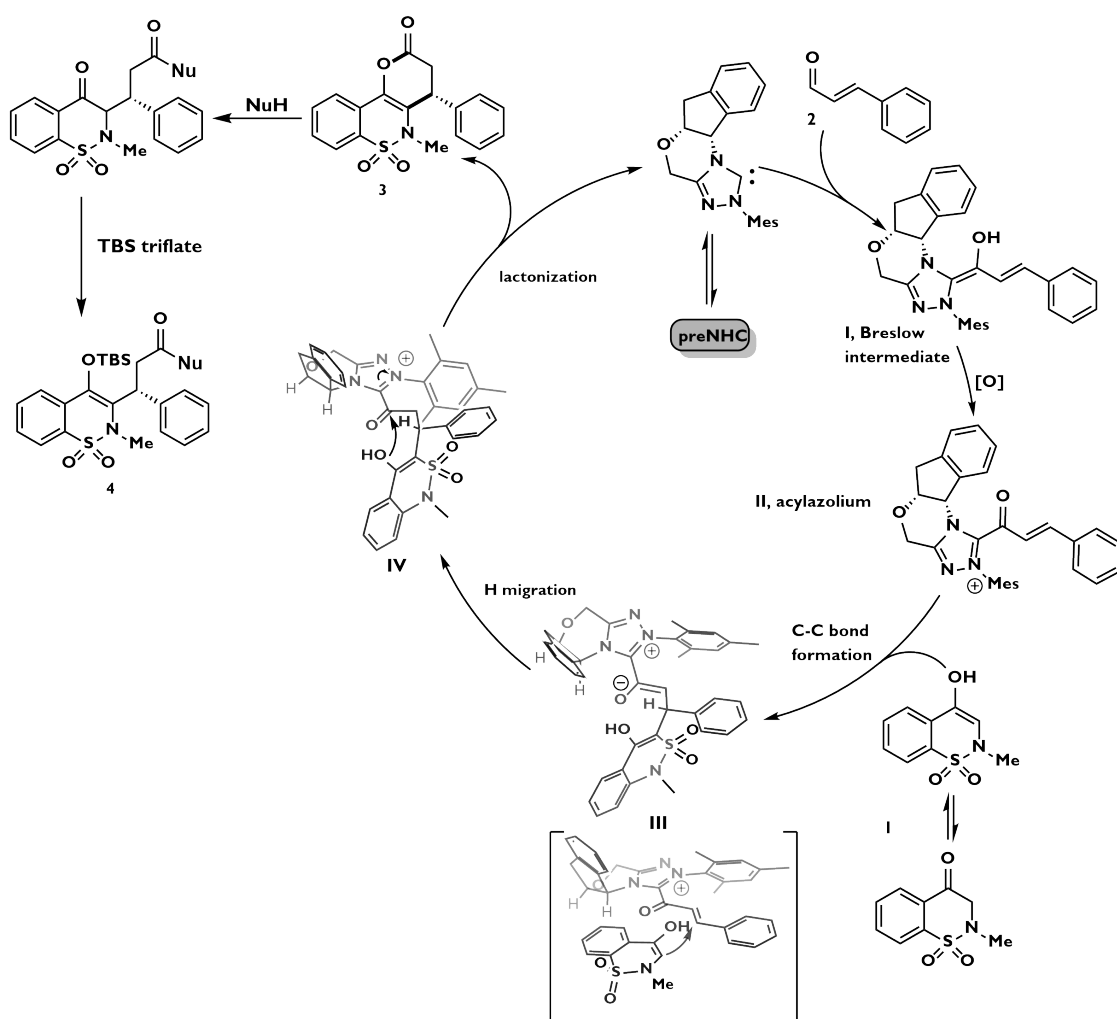


Figure S5: Proposed mechanism for the formation of products **4**

### 3 X-Ray Crystallography Data

Single-crystal X-ray diffraction data for **4g** were collected on an XtaLAB Synergy-S Dualflex diffractometer equipped with monochromated CuK $\alpha$  radiation ( $\lambda = 1.54184$  Å). The crystal was coated with Paratone-N oil and mounted on a loop. Data collection was carried out at 100(2) K to minimize solvent loss, possible structural disorder and thermal motion effects. Data frames were processed (unit cell determination, intensity data integration, correction for Lorentz and polarisation effects, and empirical absorption correction) by using the corresponding diffractometer's software package.<sup>3</sup> The structure was solved by using direct method with SHELXS-2018/3<sup>4</sup> and refined by using full-matrix least-squares method based on F<sup>2</sup> by using SHELXL-2018/3.<sup>5</sup> The programs Mercury<sup>6</sup> and POV-Ray<sup>7</sup> were both used to prepare molecular graphics. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were positioned geometrically with C-H = 0.95 Å (aromatic), 0.98 (methyl), 0.99 Å (methylene), 1.00 (methanetriyl) and refined as riding, with Uiso(H) = 1.2 Ueq (C) or 1.5 Ueq (C) for methyl groups. A summary of the data collection and structure refinement parameters are provided in Table S1.

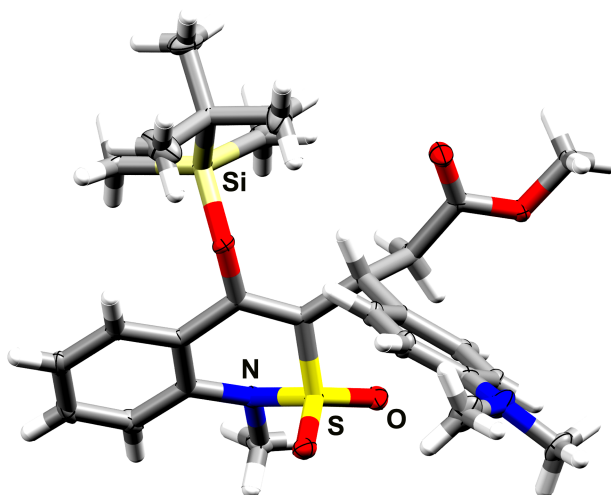


Figure S6: Molecular structure of **4g**, atomic displacement plot shown with 50% probability. CCDC No 2340332

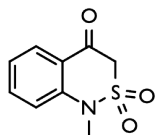
Compound reference	<b>4g</b>
Chemical formula	C <sub>27</sub> H <sub>38</sub> N <sub>2</sub> O <sub>5</sub> SSi
Formula Mass	530.74
Crystal system	monoclinic
Space group	P21
<i>a</i> /Å	8.9560(1)
<i>b</i> /Å	12.4093(1)
<i>c</i> /Å	12.9018(1)
$\alpha$ /°	90
$\beta$ /°	95.349(1)
$\gamma$ /°	90
Unit cell volume/Å <sup>3</sup>	1427.63(2)
Temperature/K	100(2)
No. of formula units per unit cell, Z	2
Radiation type	CuK $\alpha$
No. of reflections measured	42196
No. of independent reflections	5911
<i>R</i> <sub>int</sub>	0.0362
Final <i>R</i> <sub>1</sub> <sup><i>a</i></sup> values ( <i>I</i> > 2σ( <i>I</i> ))	0.0260
Final w <i>R</i> ( <i>F</i> <sup>2</sup> ) <sup><i>b</i></sup> values ( <i>I</i> > 2σ( <i>I</i> ))	0.0690
Final <i>R</i> <sub>1</sub> <sup><i>a</i></sup> values (all data)	0.0262
Final w <i>R</i> ( <i>F</i> <sup>2</sup> ) <sup><i>b</i></sup> values (all data)	0.0692
Goodness of fit on <i>F</i> <sup>2</sup>	1.067
Flack parameter	-0.007(5)

---


$$^a R_1 = \sum ||F_o - F_c|| / \sum F_o; ^b wR_2 = [\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]]^{1/2}$$

Table S1: Crystal data and details of the refinement parameters for **4g**

## 4 Product Characterisation

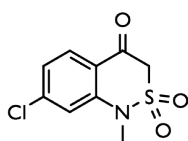


### 1-methyl-4-oxo-2λ<sup>6</sup>,1-benzothiazine-2,2(1*H*,2*H*,3*H*)-dione (1a)

white solid; scale: 37 mmol; yield: 86% (6.69 g)

Known compound - characterisation in agreement with literature.<sup>2</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 8.16 (ddd, *J* = 7.9, 1.7, 0.4 Hz, 1H), 7.69 (ddd, *J* = 8.3, 7.3, 1.7 Hz, 1H), 7.25 (ddd, *J* = 8.2, 7.3, 1.0 Hz, 1H), 7.17 (d, *J* = 7.7 Hz, 1H), 4.34 (s, 2H), 3.46 (s, 3H).



### 7-chloro-1-methyl-4-oxo-1,2,3,4-tetrahydro-2λ<sup>6</sup>,1-benzothiazine-2,2-dione (1b)

beige solid; scale: 3.8 mmol; yield: 83% (0.77 g);

mp: 178.5 - 180.8°C (2°/min)

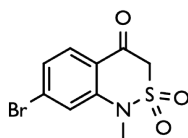
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 8.09 (d, *J* = 8.5 Hz, 1H), 7.22 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.15 (d, *J* = 1.8 Hz, 1H), 4.34 (s, 2H), 3.45 (s, 3H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 176 MHz) δ 182.8, 145.3, 143.3, 131.0, 124.2, 121.5,

117.5, 61.8, 30.9.

IR  $\nu_{max}$ : 3110, 2995, 2953, 2924, 2853, 1682, 1589, 1556, 1462, 1453, 1409, 1331, 1238, 1153, 1102, 1047, 1032, 903, 873, 821, 673, 662, 528 cm<sup>-1</sup>.

HRMS (ESI-TOF) calculated for C<sub>9</sub>H<sub>8</sub>ClNO<sub>3</sub>S, (*M* + *H*)<sup>+</sup> = 245.9992, found: 245.9996.



### 7-bromo-1-methyl-4-oxo-1,2,3,4-tetrahydro-2λ<sup>6</sup>,1-benzothiazine-2,2-dione (1c)

grey solid; scale: 1.9 mmol; yield: 70% (0.39 g);

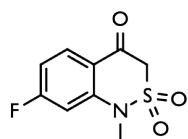
mp: 210.1 - 211.8°C (2°/min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.32 (d, *J* = 1.7 Hz, 1H), 4.33 (s, 2H), 3.44 (s, 3H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 176 MHz) δ 183.0, 145.1, 132.0, 130.9, 130.9, 127.2, 121.9, 120.5, 61.8, 31.0.

IR  $\nu_{max}$ : 3106, 3028, 2919, 2852, 1679, 1584, 1554, 1454, 1404, 1328, 1241, 1151, 1031, 886, 871, 821, 671, 659, 522 cm<sup>-1</sup>.

HRMS (ESI-TOF) calculated for C<sub>9</sub>H<sub>8</sub>BrNO<sub>3</sub>S, (*M* + *H*)<sup>+</sup> = 289.9487, found: 289.9490.



### 7-fluoro-1-methyl-4-oxo-1,2,3,4-tetrahydro-2λ<sup>6</sup>,1-benzothiazine-2,2-dione (1d)

yellow solid; scale: 3.4 mmol; yield: 89% (0.69 g);

mp: 125.5 - 127.8°C (2°/min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 8.19 (dd, *J* = 8.8, 6.4 Hz, 1H), 6.94 (ddd, *J* = 8.8, 7.5, 2.3 Hz, 1H), 6.84 (td, *J* = 10.1, 2.3 Hz, 1H), 4.33 (s,

2H), 3.43 (s, 3H).

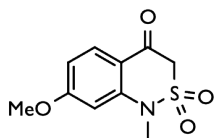


**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  182.3, 167.9 (d, J = 259.3 Hz), 146.7 (d, J = 11.5 Hz), 132.7 (d, J = 11.3 Hz), 119.7, 111.4 (d, J = 22.1 Hz), 104.6 (d, J = 26.5 Hz), 61.6, 30.8.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -98.37 (dt, J = 10.0, 7.3 Hz).

**IR**  $\nu_{max}$ : 3120, 3093, 3003, 2955, 2922, 2853, 1682, 1608, 1577, 1468, 1332, 1229, 1204, 1151, 1044, 1035, 962, 865, 832, 816, 802, 668, 534 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>9</sub>H<sub>8</sub>FNO<sub>3</sub>S, (M + H)<sup>+</sup> = 230.0287, found: 230.0291.



**7-methoxy-1-methyl-4-oxo-1,2,3,4-tetrahydro-2λ<sup>6</sup>,1-benzothiazine-2,2-dione (1e)**

yellow solid; scale: 3.1 mmol; yield: 89% (0.68 g);

**mp**: 157.7 - 160.1°C (2°/min)

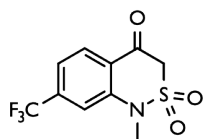
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  8.12 (d, J = 8.9 Hz, 1H), 6.75 (dd, J = 8.9, 2.3 Hz, 1H), 6.58 (d, J = 2.3 Hz, 1H), 4.28 (s, 2H), 3.92 (s, 3H),

3.42 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  182.4, 166.5, 146.5, 132.2, 117.0, 109.4, 103.1, 61.4, 56.0, 30.9.

**IR**  $\nu_{max}$ : 2987, 2953, 2923, 2851, 1671, 1592, 1560, 1457, 1445, 1331, 1283, 1122, 1052, 1037, 866, 838, 816, 798, 661, 529 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>10</sub>H<sub>11</sub>NO<sub>4</sub>S, (M + H)<sup>+</sup> = 242.0487, found: 242.0490.



**1-methyl-4-oxo-7-(trifluoromethyl)-2λ<sup>6</sup>,1-benzothiazine-2,2(1H,2H,3H)-dione (1f)**

beige solid; scale: 4.3 mmol; yield: 68% (0.82 g);

**mp**: 144.8 - 147.0°C (2°/min)

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.27 (ddd, J = 8.2, 0.9, 0.4 Hz, 1H), 7.49 (ddd, J = 8.2, 1.6, 0.6 Hz, 1H), 7.39 (s, 1H), 4.40 (s, 2H), 3.51 (s,

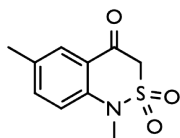
3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 101 MHz)  $\delta$  183.1, 144.6, 137.8 (q, J = 33.2 Hz), 130.6, 125.1 (d, J = 0.9 Hz), 123.0 (q, J = 273.4 Hz), 120.2 (q, J = 3.7 Hz), 114.3 (q, J = 3.9 Hz), 61.9, 31.1.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -64.58.

**IR**  $\nu_{max}$ : 3100, 3067, 3014, 2950, 1689, 1619, 1421, 1334, 1240, 1172, 1128, 1083, 909, 887, 844, 828, 785, 524 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NO<sub>3</sub>S, (M + H)<sup>+</sup> = 280.0255, found: 280.0257.



**1-methyl-6-methyl-4-oxo-2λ<sup>6</sup>,1-benzothiazine-2,2(1H,2H,3H)-dione (1g)**

yellow solid; scale: 3.1 mmol; yield: 73% (0.52 g);

**mp**: 119.3 - 120.1°C (2°/min)

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.94 (dd, J = 1.9, 0.8 Hz, 1H), 7.48 (ddd, J = 8.4, 2.2, 0.7 Hz, 1H), 7.06 (d, J = 8.3 Hz, 1H), 4.30 (s, 2H),

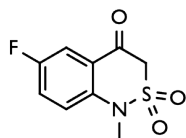
3.42 (s, 3H), 2.38 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  184.3, 142.4, 137.5, 133.9, 129.6, 123.2, 117.7, 77.3, 77.2, 77.0, 61.6, 31.5, 20.5.

**IR**  $\nu_{\text{max}}$ : 2993, 2953, 2922, 2853, 1680, 1609, 1491, 1461, 1334, 1235, 1146, 1118, 1042, 885, 832, 677, 626, 574, 524  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF) calculated for  $\text{C}_{10}\text{H}_{11}\text{NO}_3\text{S}$ ,  $(\text{M} + \text{H})^+ = 226.0538$ , found: 226.0543.

---



**6-fluoro-1-methyl-4-oxo-1,2,3,4-tetrahydro-2 $\lambda^6$ ,1-benzothiazine-2,2-dione (1h)**

green solid; scale: 3.4 mmol; yield: 75% (0.59 g);

**mp**: 143.4 - 145.7°C (2°/min)

**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.82 (ddd,  $J = 8.3, 3.1, 0.3$  Hz, 1H), 7.40 (ddd,  $J = 9.0, 7.2, 3.1$  Hz, 1H), 7.17 (dd,  $J = 9.0, 4.1$  Hz, 1H), 4.33 (s, 2H), 3.45 (s, 3H).

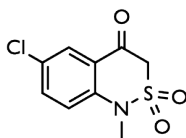
**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  183.3, 159.0 (d,  $J = 246.9$  Hz), 140.9 (d,  $J = 2.0$  Hz), 124.8 (d,  $J = 6.5$  Hz), 123.9 (d,  $J = 23.7$  Hz), 119.9 (d,  $J = 7.4$  Hz), 115.5 (d,  $J = 24.2$  Hz), 61.3, 32.1.

**$^{19}\text{F}$  NMR** ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -118.55 (td,  $J = 7.8, 4.0$  Hz).

**IR**  $\nu_{\text{max}}$ : 3066, 3004, 2955, 2927, 1691, 1610, 1490, 1465, 1425, 1338, 1286, 1190, 1146, 1058, 855, 841, 706, 687, 527, 508  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF) calculated for  $\text{C}_9\text{H}_8\text{FNO}_3\text{S}$ ,  $(\text{M} + \text{H})^+ = 230.0287$ , found: 230.0289.

---



**6-chloro-1-methyl-4-oxo-1,2,3,4-tetrahydro-2 $\lambda^6$ ,1-benzothiazine-2,2-dione (1i)**

yellow solid; scale: 3.8 mmol; yield: 85% (0.79 g);

**mp**: 114.3 - 116.6°C (2°/min)

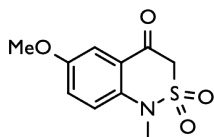
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  8.10 (dd,  $J = 2.6, 0.3$  Hz, 1H), 7.63 (dd,  $J = 8.8, 2.6$  Hz, 1H), 7.12 (d,  $J = 8.8$  Hz, 1H), 4.34 (s, 2H), 3.45 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  183.0, 143.0, 136.4, 130.1, 129.2, 124.3, 119.0, 61.6, 31.4.

**IR**  $\nu_{\text{max}}$ : 2988, 2976, 2955, 2920, 2853, 1687, 1596, 1475, 1462, 1410, 1334, 1286, 1149, 1057, 887, 870, 825, 800, 689, 664, 534  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF) calculated for  $\text{C}_9\text{H}_8\text{ClNO}_3\text{S}$ ,  $(\text{M} + \text{H})^+ = 245.9992$ , found: 245.9997.

---



**6-methoxy-1-methyl-4-oxo-1,2,3,4-tetrahydro-2 $\lambda^6$ ,1-benzothiazine-2,2-dione (1j)**

green solid; scale: 3.7 mmol; yield: 67% (0.60 g);

**mp**: 146.5 - 149.1°C (2°/min)

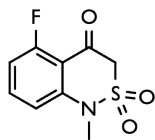
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.60 (d,  $J = 3.1$  Hz, 1H), 7.25 (dd,  $J = 8.9, 3.1$  Hz, 1H), 7.13 (d,  $J = 9.0$  Hz, 1H), 4.30 (s, 2H), 3.86 (s, 3H), 3.42 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  184.4, 156.2, 138.5, 124.8, 124.2, 119.9, 111.3, 61.1, 56.0, 32.5.

**IR**  $\nu_{max}$ : 3088, 3014, 2983, 2950, 2919, 2854, 2839, 1677, 1604, 1488, 1416, 1329, 1291, 1221, 1140, 1020, 847, 543  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF) calculated for  $\text{C}_{10}\text{H}_{11}\text{NO}_4\text{S}$ ,  $(\text{M} + \text{H})^+ = 242.0487$ , found: 242.0492.

---



**5-fluoro-1-methyl-4-oxo-1,2,3,4-tetrahydro-2 $\lambda^6$ ,1-benzothiazine-2,2-dione (1k)**

beige solid; scale: 8.1 mmol; yield: 82% (1.53 g);

**mp**: 141.6 - 143.0°C (2°/min)

**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.62 (td,  $J = 8.4, 5.7$  Hz, 1H), 6.97 (dt,  $J = 8.5, 1.0$  Hz, 1H), 6.96 (ddd,  $J = 10.7, 8.4, 1.0$  Hz, 1H), 4.33 (s, 2H),

3.45 (s, 3H).

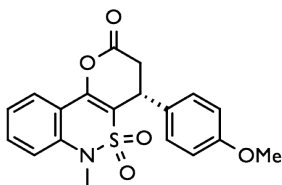
**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  181.5 (d,  $J = 2.1$  Hz), 163.3 (d,  $J = 269.2$  Hz), 145.2 (d,  $J = 2.7$  Hz), 136.8 (d,  $J = 12.2$  Hz), 113.1, 113.0 (d,  $J = 3.6$  Hz), 112.4 (d,  $J = 22.0$  Hz), 62.4, 31.7.

**$^{19}\text{F}$  NMR** ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -108.50 (dd,  $J = 10.3, 5.8$  Hz).

**IR**  $\nu_{max}$ : 3111, 2998, 2963, 2932, 1686, 1609, 1468, 1334, 1227, 1150, 1026, 954, 895, 799, 534  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF) calculated for  $\text{C}_9\text{H}_8\text{FNO}_3\text{S}$ ,  $(\text{M} + \text{H})^+ = 230.0287$ , found: 230.0292.

---



**(*R*)-1-(4-methoxyphenyl)-9-methyl-10,10-dioxo-1,2,9,10-tetrahydro-10H,10H,3H-4-oxa-10 $\lambda^6$ -thia-9-azaphenanthren-3-one (3a)**

orange oil; scale: 0.1 mmol; isolated yield 96% (35.5 mg);

*ee* 94% - 4.28 min (major), 4.79 min (minor); (Phenomenex Lux Amylose-1, 5  $\mu\text{m}$ ,  $\text{MeCN}:\text{H}_2\text{O}$  70:30, 0.7 mL/min)

**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.97 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.59 (ddd,  $J = 8.4, 7.4, 1.5$  Hz, 1H), 7.30 (ddd,  $J = 8.2, 7.3, 1.0$  Hz, 1H), 7.23 (d,  $J = 8.2$  Hz, 1H), 7.20 (d,  $J = 8.5$  Hz, 2H), 6.86 (d,  $J = 8.8$  Hz,

2H), 4.54 (dd,  $J = 7.4, 1.8$  Hz, 1H), 3.77 (s, 3H), 3.47 (s, 3H), 3.21 (dd,  $J = 15.8, 7.5$  Hz, 1H), 3.06 (dd,  $J = 15.8, 1.9$  Hz, 1H).

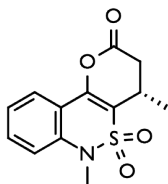
**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  164.3, 159.7, 150.1, 139.7, 132.5, 130.9, 128.1, 125.2, 123.4, 116.7, 116.6, 115.2, 115.0, 55.4, 37.6, 36.1, 31.0.

**IR**  $\nu_{max}$ : 3267, 3077, 3035, 2998, 2932, 2838, 1785, 1643, 1601, 1511, 1456, 1319, 1248, 1098, 1029, 829, 750, 543  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = -8.30$  ( $c = 1.45$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{19}\text{H}_{17}\text{NO}_5\text{S}$ ,  $(\text{M} + \text{H})^+ = 372.0906$ , found: 372.0909.

---



**(*S*)-1-methyl-9-methyl-10,10-dioxo-1,2,9,10-tetrahydro-3*H*,10*H*,10*H*-4-oxa-10 $\lambda^6$ -thia-9-azaphenanthren-3-one (3m)**

orange oil; scale: 0.1 mmol; isolated yield 51% (14.3 mg);

*ee* 89% - 10.88 min (major), 12.94 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 70:30, 1.0 mL/min)

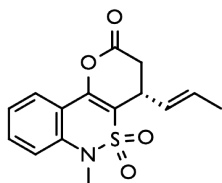
$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.89 (ddd,  $J$  = 8.1, 1.5, 0.4 Hz, 1H), 7.56 (ddd,  $J$  = 8.2, 7.4, 1.6 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.20 (dd,  $J$  = 8.4, 1.3 Hz, 1H), 3.51 (s, 3H), 3.48 – 3.44 (m, 1H), 2.99 (dd,  $J$  = 15.8, 6.7 Hz, 1H), 2.82 (dd,  $J$  = 16.0, 2.2 Hz, 1H), 1.44 (d,  $J$  = 7.0 Hz, 2H).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  164.9, 148.9, 139.2, 132.2, 124.9, 123.2, 116.8, 116.4, 116.3, 36.4, 30.7, 26.3, 20.6.

**IR**  $\nu_{\text{max}}$ : 3225, 3076, 3040, 2972, 2942, 2893, 1789, 1732, 1686, 1649, 1599, 1457, 1336, 1302, 1118, 865, 760, 528  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +12.35$  ( $c$  = 0.81,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{13}\text{H}_{13}\text{NO}_4\text{S}$ ,  $(\text{M} + \text{H})^+ = 280.0644$ , found: 280.0647.



**(*R*)-1-[(*E*)-prop-1-enyl]-9-methyl-10,10-dioxo-1,2,9,10-tetrahydro-3*H*,10*H*,10*H*-4-oxa-10 $\lambda^6$ -thia-9-azaphenanthren-3-one (3q)**

orange oil; scale: 0.1 mmol; isolated yield 81% (24.8 mg);

*ee* 88% - 27.80 min (major), 32.15 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 90:10, 1.0 mL/min)

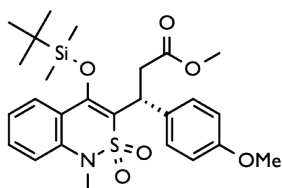
$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.90 (dd,  $J$  = 8.0, 1.5 Hz, 1H), 7.57 (ddd,  $J$  = 8.2, 7.4, 1.5 Hz, 1H), 7.31 – 7.22 (m, 1H), 7.21 (dd,  $J$  = 8.3, 1.2 Hz, 1H), 5.76 (ddd,  $J$  = 15.3, 6.5, 1.3 Hz, 1H), 5.55 (ddd,  $J$  = 15.3, 6.2, 1.6 Hz, 1H), 4.00 – 3.89 (m, 1H), 3.51 (s, 3H), 3.05 – 2.85 (m, 2H), 1.71 (dt,  $J$  = 6.5, 1.4 Hz, 3H).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  164.7, 149.5, 139.4, 136.3, 132.3, 129.2, 127.2, 125.0, 123.2, 116.4, 114.7, 35.0, 33.4, 30.8, 17.9.

**IR**  $\nu_{\text{max}}$ : 3287, 3037, 2919, 2856, 1708, 1681, 1599, 1457, 1337, 1303, 1139, 1058, 967, 870, 760  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +17.14$  ( $c$  = 0.88,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{15}\text{H}_{15}\text{NO}_4\text{S}$ ,  $(\text{M} + \text{H})^+ = 306.0800$ , found: 306.0803.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-methoxyphenyl)propionate (4a)**

yellow oil; scale: 0.1 mmol; isolated yield 83% (43.0 mg);

*ee* 92% - 19.89 min (major), 30.75 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.71 (dd,  $J$  = 8.0, 1.4 Hz, 1H), 7.43 (ddd,  $J$  = 8.7, 7.3, 1.5 Hz, 1H), 7.39 (d,  $J$  = 8.7 Hz, 2H), 7.17 (ddd,  $J$

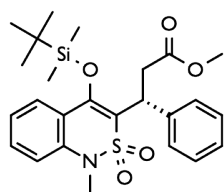
= 8.1, 7.3, 1.0 Hz, 1H), 7.12 (dd,  $J$  = 8.2, 1.1 Hz, 1H), 6.83 (d,  $J$  = 8.8 Hz, 2H), 5.14 (dd,  $J$  = 11.3, 4.3 Hz, 1H), 3.78 (dd,  $J$  = 16.8, 11.3 Hz, 1H), 3.75 (s, 3H), 3.63 (s, 3H), 3.37 (s, 3H), 2.93 (dd,  $J$  = 16.8, 4.3 Hz, 1H), 1.13 (s, 9H), 0.25 (s, 3H), 0.01 (s, 3H).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  172.4, 158.6, 150.6, 139.1, 131.9, 131.1, 129.0, 127.1, 125.5, 122.5, 121.8, 116.8, 114.0, 55.3, 51.8, 37.5, 37.1, 30.9, 26.1, 18.7, -2.9, -3.7..

IR  $\nu_{\text{max}}$ : 3071, 2999, 2931, 2899, 2859, 1736, 1605, 1592, 1561, 1512, 1463, 1321, 1287, 1249, 1164, 1086, 1035, 808, 753  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +67.26$  ( $c$  = 0.94,  $\text{CHCl}_3$ )

HRMS (ESI-TOF) calculated for  $\text{C}_{26}\text{H}_{35}\text{NO}_6\text{SSi}$ ,  $(\text{M} + \text{H})^+ = 518.2033$ , found: 518.2035.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-phenylpropionate (4b)**

yellow oil; scale: 0.1 mmol; isolated yield 36% (17.4 mg);

*ee* 95% - 11.80 min (major), 16.21 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu\text{m}$ , Hex:iPrOH 95:05, 1.0 mL/min)

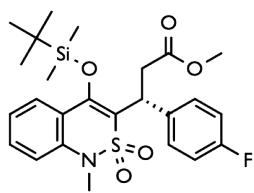
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.72 (dd,  $J$  = 8.0, 1.4 Hz, 1H), 7.46 (d,  $J$  = 7.3 Hz, 2H), 7.44 (ddd,  $J$  = 8.1, 7.3, 1.5 Hz, 1H), 7.29 (t,  $J$  = 7.8 Hz, 2H), 7.22 – 7.17 (m, 1H), 7.20 – 7.15 (m, 1H), 7.13 (dd,  $J$  = 8.2, 1.2 Hz, 1H), 5.19 (dd,  $J$  = 11.1, 4.5 Hz, 1H), 3.78 (dd,  $J$  = 16.8, 11.1 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.98 (dd,  $J$  = 16.9, 4.4 Hz, 1H), 1.12 (s, 9H), 0.25 (s, 3H), -0.01 (s, 3H).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  172.4, 151.0, 140.0, 139.2, 131.2, 128.6, 128.0, 127.2, 127.1, 125.3, 122.6, 121.8, 116.8, 51.9, 38.2, 37.0, 31.0, 26.1, 18.8, -2.9, -3.6.

IR  $\nu_{\text{max}}$ : 3030, 2953, 2931, 2898, 2859, 1736, 1604, 1592, 1561, 1453, 1435, 1320, 1287, 1259, 1164, 1149, 1085, 811, 755, 697  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +60.87$  ( $c$  = 1.38,  $\text{CHCl}_3$ )

HRMS (ESI-TOF) calculated for  $\text{C}_{25}\text{H}_{33}\text{NO}_5\text{SSi}$ ,  $(\text{M} + \text{H})^+ = 488.1927$ , found: 488.1930.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4c)**

yellow oil; scale: 0.1 mmol; isolated yield 96% (48.6 mg);

*ee* 95% - 12.29 min (major), 16.66 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu\text{m}$ , Hex:iPrOH 95:05, 1.0 mL/min)

scale 0.7 mmol - 86% (304.2 mg)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.71 (dd,  $J$  = 8.1, 1.3 Hz, 1H), 7.51 – 7.35 (m, 3H), 7.19 (ddd,  $J$  = 8.3, 7.3, 1.1 Hz, 1H), 7.14 (dd,  $J$  = 8.3, 1.2 Hz, 1H), 6.98 (t,  $J$  = 8.7 Hz, 2H), 5.16 (dd,  $J$  = 11.4, 4.3 Hz, 1H), 3.77 (dd,  $J$  = 16.9, 11.3 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.94 (dd,  $J$  = 16.9, 4.1 Hz, 1H), 1.13 (s, 9H), 0.25 (s, 3H), 0.00 (s, 3H).

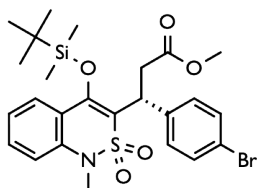
**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 101 MHz)  $\delta$  172.3, 162.0 (d,  $J$  = 245.3 Hz), 151.0, 139.1, 135.7 (d,  $J$  = 3.3 Hz), 131.3, 129.6 (d,  $J$  = 8.1 Hz), 127.1, 125.1, 122.6, 121.7, 116.8, 115.5 (d,  $J$  = 21.4 Hz), 51.9, 37.6, 37.1, 30.9, 26.0, 18.8, -2.9, -3.7.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -116.79 (tt,  $J$  = 8.5, 5.3 Hz).

**IR**  $\nu_{max}$ : 2954, 2932, 2888, 2860, 1736, 1604, 1593, 1561, 1509, 1319, 1287, 1260, 1223, 1161, 1087, 809, 756 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = +77.93 ( $c$  = 1.45, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>32</sub>FNO<sub>5</sub>SSi, ( $M + H$ )<sup>+</sup> = 506.1833, found: 506.1837.



**methyl (*R*)-3-(4-bromophenyl)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}propionate (4d)**

yellow oil; scale: 0.1 mmol; isolated yield 74% (41.9 mg);

*ee* 95% - 13.66 min (major), 20.63 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

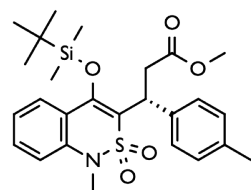
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.71 (dd,  $J$  = 8.0, 1.5 Hz, 1H), 7.45 (ddd,  $J$  = 8.2, 7.3, 1.6 Hz, 1H), 7.42 (d,  $J$  = 8.7 Hz, 2H), 7.34 (d,  $J$  = 8.2 Hz, 1H), 7.19 (ddd,  $J$  = 8.2, 7.3, 1.1 Hz, 1H), 7.14 (dd,  $J$  = 8.2, 1.2 Hz, 2H), 5.13 (dd,  $J$  = 11.3, 4.1 Hz, 1H), 3.76 (dd,  $J$  = 17.0, 11.3 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.94 (dd,  $J$  = 17.0, 4.1 Hz, 1H), 1.12 (s, 9H), 0.24 (s, 3H), 0.01 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 101 MHz)  $\delta$  172.2, 151.3, 139.1, 139.1, 131.8, 131.4, 129.8, 127.1, 124.7, 122.7, 121.7, 121.2, 116.8, 52.0, 37.8, 36.9, 31.0, 26.0, 18.8, -2.8, -3.6.

**IR**  $\nu_{max}$ : 2952, 2931, 2888, 2859, 1736, 1605, 1592, 1561, 1488, 1320, 1287, 1259, 1149, 1088, 808, 752 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = +89.47 ( $c$  = 0.95, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>32</sub>BrNO<sub>5</sub>SSi, ( $M + H$ )<sup>+</sup> = 566.1032, found: 566.1037.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-methylphenyl)propionate (4e)**

yellow oil; scale: 0.1 mmol; isolated yield 78% (39.1 mg);

*ee* 93% - 13.31 min (major), 18.01 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

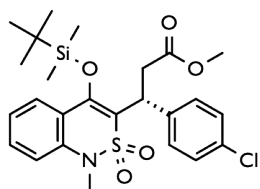
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.72 (dd,  $J$  = 8.0, 1.5 Hz, 1H), 7.43 (ddd,  $J$  = 8.2, 7.3, 1.6 Hz, 1H), 7.36 (d,  $J$  = 8.1 Hz, 2H), 7.18 (ddd,  $J$  = 8.2, 7.3, 1.2 Hz, 1H), 7.14 – 7.08 (m, 3H), 5.17 (dd,  $J$  = 11.1, 4.3 Hz, 1H), 3.79 (dd,  $J$  = 16.9, 11.2 Hz, 1H), 3.64 (s, 3H), 3.37 (s, 3H), 2.96 (dd,  $J$  = 16.9, 4.3 Hz, 1H), 2.28 (s, 3H), 1.13 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 101 MHz)  $\delta$  172.4, 150.8, 139.1, 136.8, 136.6, 131.1, 129.3, 127.8, 127.1, 125.5, 122.5, 121.9, 116.8, 51.8, 37.9, 37.0, 30.9, 26.1, 21.2, 18.8, -2.9, -3.7.

**IR**  $\nu_{max}$ : 3023, 2953, 2930, 2896, 2859, 1736, 1605, 1593, 1561, 1514, 1471, 1321, 1287, 1260, 1213, 1164, 1149, 1087, 808, 753  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +171.89$  ( $c = 0.94$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{26}\text{H}_{35}\text{NO}_5\text{Si}$ ,  $(\text{M} + \text{H})^+ = 502.2084$ , found: 502.2084.



methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-chlorophenyl)propionate (**4f**)

yellow oil; scale: 0.1 mmol; isolated yield 74% (38.4 mg);

*ee* 94% - 13.08 min (major), 18.86 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu\text{m}$ , Hex:iPrOH 95:05, 1.0 mL/min)

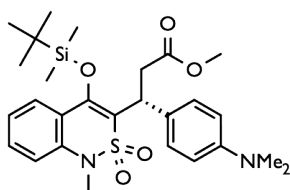
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.71 (dd,  $J = 8.0, 1.6$  Hz, 1H), 7.45 (ddd,  $J = 8.1, 7.3, 1.6$  Hz, 1H), 7.40 (dd,  $J = 8.8, 0.7$  Hz, 2H), 7.27 (d,  $J = 8.6$  Hz, 2H), 7.19 (ddd,  $J = 8.1, 7.3, 1.1$  Hz, 1H), 7.14 (dd,  $J = 8.2, 1.1$  Hz, 1H), 5.15 (dd,  $J = 11.2, 4.1$  Hz, 1H), 3.76 (dd,  $J = 17.0, 11.3$  Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.95 (dd,  $J = 17.0, 4.2$  Hz, 1H), 1.12 (s, 9H), 0.25 (s, 3H), 0.01 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  172.2, 151.3, 139.2, 138.6, 133.0, 131.4, 129.4, 128.8, 127.1, 124.8, 122.7, 121.7, 116.9, 52.0, 37.7, 37.0, 31.0, 26.1, 18.8, -2.8, -3.6.

**IR**  $\nu_{max}$ : 3025, 2953, 2931, 2889, 2859, 1736, 1605, 1592, 1561, 1492, 1320, 1287, 1259, 1150, 1089, 809, 752  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +62.77$  ( $c = 1.23$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{25}\text{H}_{32}\text{ClNO}_5\text{Si}$ ,  $(\text{M} + \text{H})^+ = 522.1537$ , found: 522.1542.



methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-[4-(dimethylamino)phenyl] propionate (**4g**)

yellow solid; scale: 0.1 mmol; isolated yield 66% (35.0 mg);

*ee* 86% - 11.18 min (major), 17.40 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu\text{m}$ , Hex:iPrOH 90:10, 1.0 mL/min)

**mp**: 172.2 - 173.6  $^{\circ}\text{C}$  ( $2^{\circ}/\text{min}$ )

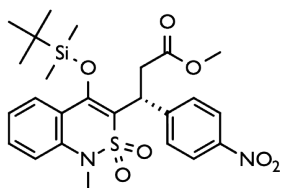
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.71 (dd,  $J = 8.0, 1.6$  Hz, 1H), 7.42 (ddd,  $J = 8.1, 7.3, 1.6$  Hz, 1H), 7.33 (d,  $J = 8.4$  Hz, 2H), 7.16 (ddd,  $J = 8.1, 7.3, 1.1$  Hz, 1H), 7.12 (dd,  $J = 8.2, 1.3$  Hz, 1H), 6.67 (d,  $J = 9.1$  Hz, 2H), 5.11 (dd,  $J = 11.3, 4.3$  Hz, 1H), 3.77 (dd,  $J = 16.7, 11.3$  Hz, 1H), 3.63 (s, 3H), 3.37 (s, 3H), 2.92 (dd,  $J = 16.8, 4.4$  Hz, 1H), 2.89 (s, 6H), 1.14 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  172.6, 150.3, 149.7, 139.1, 130.9, 128.6, 127.5, 127.1, 126.0, 122.4, 122.0, 116.7, 112.8, 51.8, 40.7, 37.5, 37.1, 30.9, 26.1, 18.8, -2.8, -3.7.

**IR**  $\nu_{max}$ : 2953, 2929, 2890, 2857, 2806, 1730, 1605, 1593, 1562, 1521, 1358, 1317, 1289, 1264, 1221, 1164, 1089, 904, 759  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +86.00$  ( $c = 1.00$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for C<sub>27</sub>H<sub>38</sub>N<sub>2</sub>O<sub>5</sub>SSi, (M + H)<sup>+</sup> = 531.2349, found: 531.2452.



**methyl (R)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-nitrophenyl)propionate (4h)**

yellow oil; scale: 0.1 mmol; isolated yield 68% (36.3 mg);

*ee* 94% - 19.74 min (major), 30.97 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

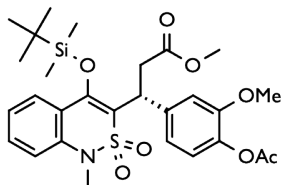
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 8.16 (d, *J* = 8.9 Hz, 2H), 7.73 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.48 (ddd, *J* = 8.2, 7.4, 1.5 Hz, 1H), 7.21 (ddd, *J* = 8.0, 7.3, 1.0 Hz, 1H), 7.15 (dd, *J* = 8.2, 1.2 Hz, 1H), 5.27 (dd, *J* = 11.4, 4.0 Hz, 1H), 3.84 (dd, *J* = 17.2, 11.4 Hz, 1H), 3.66 (s, 3H), 3.39 (s, 3H), 2.99 (dd, *J* = 17.3, 4.0 Hz, 1H), 1.13 (s, 9H), 0.25 (s, 3H), 0.03 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 171.9, 151.9, 147.7, 147.1, 139.1, 131.7, 129.0, 127.2, 123.9, 123.8, 122.8, 121.5, 116.9, 52.1, 38.1, 36.6, 31.0, 26.0, 18.8, -2.8, -3.6.

**IR** ν<sub>max</sub>: 2953, 2930, 2858, 1736, 1691, 1604, 1594, 1561, 1520, 1464, 1343, 1317, 1288, 1259, 1150, 1089, 810, 752 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>26</sup> = +55.43 (*c* = 1.34, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>32</sub>N<sub>2</sub>O<sub>7</sub>SSi, (M + H)<sup>+</sup> = 533.1778, found: 533.1782.



**methyl (R)-3-(4-acetoxy-3-methoxyphenyl)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl} propionate (4i)**

white solid; scale: 0.1 mmol; isolated yield 65% (37.4 mg);

*ee* 95% - 10.24 min (major), 16.32 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

**mp**: 77.4 - 78.9°C (2/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.70 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.45 (ddd, *J* = 8.2, 7.4, 1.5 Hz, 1H), 7.21 - 7.16 (m, 2H), 7.15 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.04 (ddd, *J* = 8.2, 2.1, 0.7 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 5.14 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.80 (s, 3H), 3.68 (dd, *J* = 14.0, 3.2 Hz, 1H), 3.64 (s, 3H), 3.39 (s, 3H), 3.02 (dd, *J* = 16.9, 4.7 Hz, 1H), 2.27 (s, 3H), 1.12 (s, 9H), 0.26 (s, 3H), -0.01 (s, 3H).

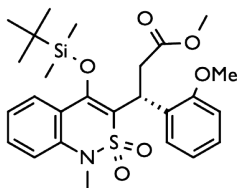
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.3, 169.1, 151.4, 151.0, 139.2, 139.1, 138.8, 131.3, 127.1, 124.9, 122.7, 122.7, 121.9, 120.4, 117.0, 112.7, 56.0, 51.9, 38.5, 37.7, 31.2, 26.1, 20.8, 18.8, -2.9, -3.5.

**IR** ν<sub>max</sub>: 3086, 3011, 2953, 2929, 2894, 2857, 1769, 1733, 1604, 1591, 1561, 1509, 1460, 1316, 1266, 1194, 1145, 1121, 1084, 1035, 894, 810, 757 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>25</sup> = +38.00 (*c* = 1.00, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>28</sub>H<sub>37</sub>NO<sub>8</sub>SSi, (M + H)<sup>+</sup> = 576.2087, found: 576.2090.





**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(2-methoxyphenyl)propionate (4j)**

yellow oil; scale: 0.1 mmol; isolated yield 79% (40.9 mg);

*ee* 92% - 11.36 min (major), 18.44 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

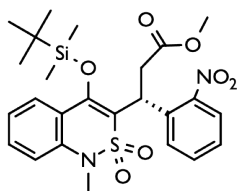
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.70 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.56 (ddd, *J* = 7.8, 1.6, 0.7 Hz, 1H), 7.42 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 7.24 – 7.14 (m, 2H), 7.12 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.92 (td, *J* = 7.6, 1.2 Hz, 1H), 6.82 (dd, *J* = 8.2, 1.2 Hz, 1H), 5.39 (dd, *J* = 9.8, 6.5 Hz, 1H), 3.81 (s, 3H), 3.68 (dd, *J* = 17.0, 9.4 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.99 (dd, *J* = 17.0, 6.5 Hz, 1H), 1.08 (s, 9H), 0.21 (s, 3H), -0.12 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.5, 157.5, 151.4, 139.1, 130.9, 128.4, 128.3, 128.1, 126.8, 124.1, 122.5, 122.3, 120.6, 116.7, 110.5, 55.3, 51.7, 36.5, 33.2, 30.8, 25.9, 18.7, -3.2, -3.4.

**IR**  $\nu_{max}$ : 2952, 2931, 2898, 2858, 1737, 1603, 1562, 1492, 1462, 1436, 1318, 1289, 1146, 1163, 1148, 1109, 1089, 825, 749 cm<sup>-1</sup>.

$[\alpha]_D^{26} = +15.98$  (*c* = 1.13, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>26</sub>H<sub>35</sub>NO<sub>6</sub>SSi, (*M* + *H*)<sup>+</sup> = 518.2033, found: 518.2027.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(2-nitrophenyl)propionate (4k)**

yellow oil; scale: 0.1 mmol; isolated yield 79% (40.9 mg);

*ee* 89% - 13.70 min (major), 15.71 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

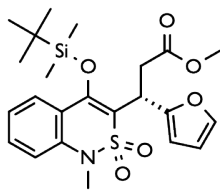
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.94 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.70 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 (td, *J* = 7.7, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.3, 7.3, 1.6 Hz, 1H), 7.37 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.18 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 7.15 (dd, *J* = 8.3, 1.2 Hz, 1H), 5.69 (dd, *J* = 8.8, 7.1 Hz, 1H), 3.66 (s, 3H), 3.54 (dd, *J* = 17.5, 8.7 Hz, 1H), 3.36 (s, 3H), 3.16 (dd, *J* = 17.5, 7.1 Hz, 1H), 1.05 (s, 9H), 0.23 (s, 3H), -0.14 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 176 MHz) δ 171.5, 152.8, 149.8, 138.9, 134.7, 133.0, 131.4, 130.5, 128.2, 127.1, 124.9, 123.0, 122.9, 122.4, 117.4, 52.0, 37.5, 34.7, 31.7, 26.1, 18.8, -3.1, -3.1.

**IR**  $\nu_{max}$ : 2953, 2931, 2897, 2859, 1738, 1606, 1593, 1560, 1526, 1317, 1289, 1257, 1148, 1091, 811, 751 cm<sup>-1</sup>.

$[\alpha]_D^{25} = +47.77$  (*c* = 0.88, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>32</sub>N<sub>2</sub>O<sub>7</sub>SSi, (*M* + *H*)<sup>+</sup> = 533.1778, found: 533.1784.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(fur-2-yl)propionate (4l)**

yellow oil; scale: 0.1 mmol; isolated yield 78% (37.3 mg);

*ee* 89% - 13.98 min (minor), 14.74 min (major); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

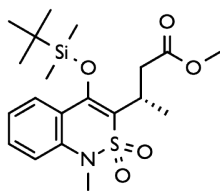
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.74 (dd,  $J$  = 8.1, 1.3 Hz, 1H), 7.46 (ddd,  $J$  = 8.2, 7.3, 1.6 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.19 (ddd,  $J$  = 8.1, 7.4, 1.2 Hz, 1H), 7.15 (dd,  $J$  = 8.2, 1.2 Hz, 1H), 6.30 (dd,  $J$  = 3.3, 1.8 Hz, 1H), 6.28 (dt,  $J$  = 3.2, 1.0 Hz, 1H), 5.22 – 5.03 (m, 1H), 3.69 (s, 3H), 3.53 (dd,  $J$  = 16.6, 10.1 Hz, 1H), 3.38 (s, 3H), 2.99 (dd,  $J$  = 16.7, 5.1 Hz, 1H), 1.10 (s, 9H), 0.16 (s, 3H), 0.07 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  171.9, 153.2, 152.1, 141.7, 139.2, 131.3, 127.0, 122.7, 121.9, 121.8, 117.0, 110.6, 106.9, 52.0, 36.8, 33.0, 31.2, 26.0, 18.8, -3.4, -3.5.

**IR**  $\nu_{\text{max}}$ : 2953, 2930, 2858, 1736, 1683, 1603, 1562, 1464, 1320, 1288, 1260, 1141, 1092, 810, 752  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +51.30$  ( $c$  = 0.90,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{23}\text{H}_{31}\text{NO}_6\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 478.1720, found: 478.1725.



**methyl (*S*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl} butyrate (4m)**

yellow oil; scale: 0.1 mmol; isolated yield 68% (29.0 mg);

*ee* 89% - based on a closed structure - lactone **3m**.

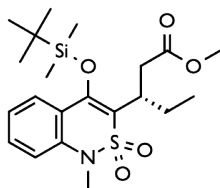
**$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 700 MHz)  $\delta$  7.68 (dd,  $J$  = 7.9, 1.5 Hz, 1H), 7.44 (ddd,  $J$  = 8.3, 7.3, 1.5 Hz, 1H), 7.17 (ddd,  $J$  = 8.0, 7.3, 1.1 Hz, 1H), 7.14 (dd,  $J$  = 8.3, 1.2 Hz, 1H), 3.92 – 3.85 (m, 1H), 3.69 (s, 3H), 3.41 (s, 3H), 3.01 (dd,  $J$  = 16.3, 10.6 Hz, 1H), 2.73 (dd,  $J$  = 16.4, 4.0 Hz, 1H), 1.44 (d,  $J$  = 6.9 Hz, 3H), 1.08 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H).

**$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 176 MHz)  $\delta$  172.8, 150.2, 138.9, 131.0, 126.8, 126.2, 122.5, 121.7, 116.7, 51.7, 39.4, 30.8, 28.6, 26.0, 19.3, 18.7, -3.2, -3.5.

**IR**  $\nu_{\text{max}}$ : 3072, 2951, 2934, 2890, 2860, 1733, 1693, 1608, 1564, 1467, 1313, 1285, 1265, 1164, 1108, 1009, 804, 787, 753  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +40.00$  ( $c$  = 0.85,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{20}\text{H}_{31}\text{NO}_5\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 426.1771, found: 426.1775.



methyl (*S*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl} valerate (**4n**)

yellow solid; scale: 0.1 mmol; isolated yield 89% (39.2 mg);

*ee* 96% - 12.19 min (major), 13.63 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 97:03, 0.7 mL/min)

**mp**: 93.7 - 96.3 (2°/min)

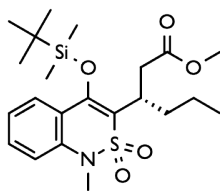
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.69 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.3, 7.3, 1.5 Hz, 1H), 7.18 (ddd, *J* = 8.3, 7.3, 1.1 Hz, 1H), 7.15 (dd, *J* = 8.3, 1.2 Hz, 1H), 3.69 (s, 3H), 3.68 – 3.65 (m, 1H), 3.40 (s, 3H), 3.13 (dd, *J* = 16.7, 10.7 Hz, 1H), 2.65 (dd, *J* = 16.6, 3.5 Hz, 1H), 1.89 – 1.75 (m, 2H), 1.09 (s, 9H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.17 (s, 3H), 0.03 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  173.3, 151.6, 139.0, 131.0, 126.8, 124.6, 122.5, 121.8, 116.7, 51.7, 38.2, 35.9, 30.9, 27.4, 26.0, 18.7, 12.2, -2.9, -4.0.

**IR**  $\nu_{max}$ : 2956, 2933, 2888, 2858, 1735, 1605, 1593, 1561, 1467, 1313, 1284, 1258, 1222, 1106, 1041, 803, 788, 752 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = -3.59 (*c* = 0.84, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>21</sub>H<sub>33</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 440.1927, found: 440.1929.



methyl (*S*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl} hexanoate (**4o**)

yellow oil; scale: 0.1 mmol; isolated yield 64% (29.0 mg);

*ee* 96% - 10.56 min (major), 11.70 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 97:03, 0.7 mL/min)

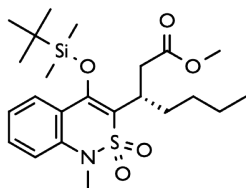
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.68 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.1, 7.3, 1.6 Hz, 1H), 7.17 (ddd, *J* = 8.3, 7.3, 1.1 Hz, 1H), 7.14 (dd, *J* = 8.1, 1.2 Hz, 1H), 3.76 (tdd, *J* = 10.5, 4.9, 3.3 Hz, 1H), 3.69 (s, 3H), 3.40 (s, 3H), 3.14 (dd, *J* = 16.7, 10.8 Hz, 1H), 2.64 (dd, *J* = 16.7, 3.3 Hz, 1H), 1.82 – 1.75 (m, 1H), 1.73 – 1.66 (m, 1H), 1.48 – 1.42 (m, 1H), 1.38 – 1.32 (m, 1H), 1.09 (s, 9H), 0.90 (t, *J* = 7.4 Hz, 3H), 0.17 (s, 3H), 0.01 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  173.2, 151.3, 139.0, 131.0, 126.9, 125.1, 122.5, 121.8, 116.7, 51.7, 38.3, 36.4, 34.0, 30.9, 26.0, 20.9, 18.7, 14.1, -2.9, -4.0.

**IR**  $\nu_{max}$ : 2955, 2932, 2899, 2860, 1736, 1606, 1596, 1563, 1464, 1318, 1287, 1257, 1103, 1041, 905, 808, 754 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = -3.24 (*c* = 0.93, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>22</sub>H<sub>35</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 454.2084, found: 454.2088.



**methyl (*S*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl} heptanoate (4p)**

yellow oil; scale: 0.1 mmol; isolated yield 33% (15.4 mg);

*ee* 95% - 5.42 min (major), 5.86 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

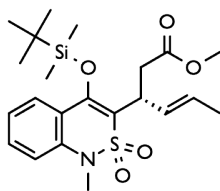
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.69 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.44 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 7.21 – 7.16 (m, 1H), 7.15 (dd, *J* = 8.4, 1.4 Hz, 1H), 3.80 – 3.68 (m, 1H), 3.69 (s, 3H), 3.40 (s, 3H), 3.14 (dd, *J* = 16.7, 10.6 Hz, 1H), 2.65 (dd, *J* = 16.6, 3.5 Hz, 1H), 1.85 – 1.67 (m, 2H), 1.44 – 1.27 (m, 4H), 1.09 (s, 9H), 0.86 (t, *J* = 7.1 Hz, 3H), 0.17 (s, 3H), 0.01 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 173.3, 151.3, 139.0, 131.0, 126.9, 125.1, 122.5, 121.8, 116.7, 51.7, 38.4, 34.1, 33.9, 30.9, 29.7, 26.0, 22.6, 18.7, 14.0, -2.9, -3.9.

**IR**  $\nu_{max}$ : 2954, 2931, 2860, 1736, 1606, 1596, 1563, 1464, 1318, 1287, 1258, 1153, 1105, 896, 809, 754 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = -9.57 (*c* = 0.94, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>23</sub>H<sub>37</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 468.2240, found: 468.2244.



**methyl (*R,E*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl} hex-4-enoate (4q)**

yellow oil; scale: 0.1 mmol; isolated yield 55% (25.0 mg);

*ee* 88% - based on a closed structure - lactone **3q**.

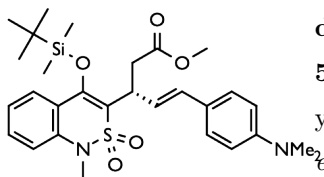
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.68 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.1, 7.3, 1.5 Hz, 1H), 7.17 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 7.14 (dd, *J* = 8.1, 1.2 Hz, 1H), 5.76 (ddd, *J* = 15.2, 7.7, 1.6 Hz, 1H), 5.66 (ddd, *J* = 15.2, 6.4, 1.0 Hz, 1H), 4.45 – 4.40 (m, 1H), 3.67 (s, 3H), 3.41 (s, 3H), 3.20 (dd, *J* = 16.0, 10.9 Hz, 1H), 2.70 (dd, *J* = 15.9, 3.9 Hz, 1H), 1.68 (ddd, *J* = 6.4, 1.7, 0.9 Hz, 3H), 1.10 (s, 9H), 0.17 (s, 3H), 0.09 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 176 MHz) δ 172.4, 150.6, 139.0, 131.0, 129.3, 128.1, 127.0, 124.4, 122.5, 121.8, 116.7, 51.7, 38.5, 36.8, 30.9, 26.1, 26.0, 18.8, 18.1, -2.9, -3.5.

**IR**  $\nu_{max}$ : 2952, 2932, 2888, 2859, 1737, 1606, 1594, 1562, 1472, 1319, 1287, 1258, 1151, 1093, 809, 754 cm<sup>-1</sup>.

$[\alpha]_D^{25}$  = +10.74 (*c* = 1.21, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>22</sub>H<sub>33</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 452.1927, found: 452.1930.



**methyl (*R,E*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-5-[4-(dimethylamino)phenyl]pent-4-enoate (4r)**

yellow oil; scale: 0.1 mmol; isolated yield 39% (21.5 mg);  
*ee* 86% - 20.61 min (major), 34.50 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

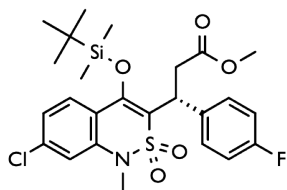
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.71 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.42 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.16 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H), 7.11 (dd, *J* = 8.3, 1.2 Hz, 2H), 6.83 – 6.61 (m, 3H), 5.11 (dd, *J* = 11.3, 4.3 Hz, 1H), 3.77 (dd, *J* = 16.7, 11.3 Hz, 1H), 3.63 (s, 3H), 3.37 (s, 3H), 3.00 – 2.91 (m, 1H), 2.89 (s, 6H), 1.13 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.6, 150.3, 139.2, 131.0, 128.7, 127.6, 127.1, 125.9, 122.5, 122.0, 116.7, 113.0, 51.8, 37.5, 37.1, 30.9, 29.8, 26.1, 18.8, -2.8, -3.7.

**IR**  $\nu_{max}$ : 3077, 2952, 2928, 2891, 2855, 2808, 1733, 1675, 1601, 1521, 1461, 1337, 1306, 1260, 1164, 1138, 875, 811, 754 cm<sup>-1</sup>.

$[\alpha]_D^{25} = +42.86$  (*c* = 1.12, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>29</sub>H<sub>40</sub>N<sub>2</sub>O<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 557.2506, found: 557.2509.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-7-chloro-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4s)**

yellow oil; scale: 0.1 mmol; isolated yield 65% (35.0 mg);  
*ee* 93% - 11.20 min (major), 12.41 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

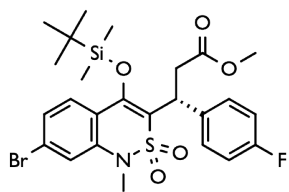
<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.64 (d, *J* = 8.5 Hz, 1H), 7.42 (dd, *J* = 8.9, 5.2 Hz, 2H), 7.16 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 5.14 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.76 (dd, *J* = 16.9, 11.3 Hz, 1H), 3.64 (s, 3H), 3.37 (s, 3H), 2.93 (dd, *J* = 16.9, 4.1 Hz, 1H), 1.13 (s, 9H), 0.25 (s, 3H), 0.01 (s, 3H).  
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 176 MHz) δ 172.1, 162.0 (d, *J* = 245.6 Hz), 150.4, 140.0, 137.2, 135.4 (d, *J* = 3.2 Hz), 129.6 (d, *J* = 8.2 Hz), 128.3, 125.3, 122.8, 120.0, 116.7, 115.6 (d, *J* = 21.4 Hz), 52.0, 37.6, 37.0, 30.5, 26.0, 18.7, -2.8, -3.7.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -116.52 (tt, *J* = 8.5, 5.3 Hz).

**IR**  $\nu_{max}$ : 2953, 2932, 2898, 2859, 1736, 1601, 1553, 1509, 1320, 1260, 1224, 1160, 1087, 915, 809, 753 cm<sup>-1</sup>.

$[\alpha]_D^{25} = +34.43$  (*c* = 1.22, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>31</sub>ClFNO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 540.1443, found: 540.1446.



**methyl (*R*)-3-{7-bromo-4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4t)**

yellow oil; scale: 0.1 mmol; isolated yield 68% (40.0 mg);

*ee* 93% - 11.97 min (major), 12.93 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.56 (d, *J* = 8.7 Hz, 1H), 7.42 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.31 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.28 (d, *J* = 1.8 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 5.14 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.75 (dd, *J* = 16.9, 11.3 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.92 (dd, *J* = 16.9, 4.1 Hz, 1H), 1.12 (s, 9H), 0.25 (s, 3H), 0.00 (s, 3H).

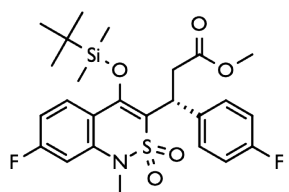
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 176 MHz) δ 172.1, 162.0 (d, *J* = 245.6 Hz), 150.5, 140.0, 135.3 (d, *J* = 3.2 Hz), 129.6 (d, *J* = 8.2 Hz), 128.4, 125.7, 125.5, 125.3, 120.5, 119.6, 115.6 (d, *J* = 21.4 Hz), 52.0, 37.6, 37.0, 30.6, 26.0, 18.7, -2.8, -3.7.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -116.50 (ddd, *J* = 14.1, 8.5, 5.0 Hz).

**IR** ν<sub>max</sub>: 2953, 2931, 2896, 2858, 1736, 1680, 1598, 1586, 1509, 1320, 1259, 1225, 1160, 1085, 905, 809, 753 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>25</sup> = +37.23 (*c* = 0.94, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>31</sub>BrFNO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 584.0938, found: 584.0940.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-7-fluoro-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4u)**

yellow oil; scale: 0.1 mmol; isolated yield 71% (37.0 mg);

*ee* 94% - 11.07 min (major), 13.78 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.70 (dd, *J* = 8.8, 6.2 Hz, 1H), 7.43 (dd, *J* = 8.3, 5.2 Hz, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.89 (ddd, *J* = 8.9, 7.9, 2.5 Hz, 1H), 6.83 (dd, *J* = 10.1, 2.4 Hz, 1H), 5.15 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.77 (dd, *J* = 16.9, 11.4 Hz, 1H), 3.64 (s, 3H), 3.36 (s, 3H), 2.93 (dd, *J* = 16.9, 4.1 Hz, 1H), 1.13 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

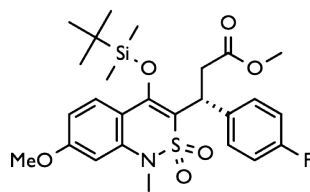
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.2, 165.4 (d, *J* = 252.4 Hz), 162.0 (d, *J* = 245.5 Hz), 150.6, 140.9 (d, *J* = 10.8 Hz), 135.5 (d, *J* = 3.1 Hz), 129.6 (d, *J* = 8.1 Hz), 129.3 (d, *J* = 10.0 Hz), 124.2, 117.8 (d, *J* = 2.9 Hz), 115.5 (d, *J* = 21.4 Hz), 109.9 (d, *J* = 22.3 Hz), 103.8 (d, *J* = 26.4 Hz), 52.0, 37.5, 37.0, 30.3, 26.0, 18.7, -2.9, -3.7.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -107.12 (ddd, *J* = 10.0, 7.8, 6.0 Hz), -116.60 (tt, *J* = 8.5, 5.3 Hz).

**IR** ν<sub>max</sub>: 3023, 2954, 2932, 2897, 2860, 1736, 1615, 1598, 1568, 1509, 1327, 1284, 1206, 1154, 1087, 964, 809, 752 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>26</sup> = +54.55 (*c* = 0.95, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>25</sub>H<sub>31</sub>F<sub>2</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 524.1739, found: 524.1744.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-7-methoxy-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4v)**

yellow oil; scale: 0.1 mmol; isolated yield 82% (44.0 mg);

*ee* 98% - 8.53 min (minor), 11.13 min (major); (Phenomenex Lux Cellulose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.62 (d, *J* = 8.8 Hz, 1H), 7.43 (dd, *J* = 8.4, 5.2 Hz, 2H), 6.97 (t, *J* = 8.8 Hz, 2H), 6.72 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 5.13 (dd, *J* = 11.5, 4.1 Hz, 1H), 3.85 (s, 3H), 3.77 (dd, *J* = 16.9, 11.4 Hz, 1H), 3.63 (s, 3H), 3.35 (s, 3H), 2.92 (dd, *J* = 16.9, 4.0 Hz, 1H), 1.12 (s, 9H), 0.25 (s, 3H), 0.02 (s, 3H).

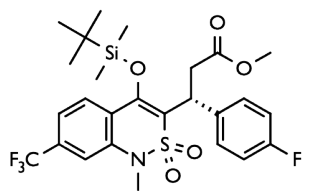
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 176 MHz) δ 172.3, 162.1, 161.9 (d, *J* = 247.0 Hz), 151.3, 140.8, 135.9, 129.6, 128.8, 122.3, 115.4 (d, *J* = 24.9 Hz), 114.8, 108.6, 102.2, 55.7, 51.9, 37.4, 37.2, 30.6, 26.0, 18.7, -2.8, -3.7.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -116.97 (tt, *J* = 8.5, 5.3 Hz).

**IR** ν<sub>max</sub>: 2953, 2932, 2896, 2859, 1736, 1609, 1595, 1555, 1508, 1328, 1297, 1259, 1224, 1160, 1087, 1046, 810 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>26</sup> = +39.93 (*c* = 0.93, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>26</sub>H<sub>34</sub>FNO<sub>6</sub>SSi, (*M* + *H*)<sup>+</sup> = 536.1938, found: 536.1941.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-7-(trifluoromethyl)-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4w)**

yellow oil; scale: 0.1 mmol; isolated yield 42% (24.0 mg);

*ee* 88% - 8.03 min (major), 8.73 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.84 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.45 - 7.36 (m, 4H), 6.99 (t, *J* = 8.7 Hz, 2H), 5.17 (dd, *J* = 11.4, 4.5 Hz, 1H), 3.75 (dd, *J* = 16.9, 11.2 Hz, 1H), 3.64 (s, 3H), 3.44 (s, 3H), 2.96 (dd, *J* = 16.9, 4.3 Hz, 1H), 1.13 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

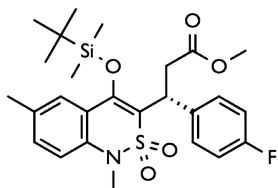
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.1, 162.1 (d, *J* = 245.8 Hz), 150.0, 139.3, 135.2 (d, *J* = 3.4 Hz), 132.9 (q, *J* = 33.1 Hz), 130.6 (d, *J* = 8.7 Hz), 129.6 (d, *J* = 8.1 Hz), 127.8, 125.9 (q, *J* = 286.7 Hz), 119.0 (q, *J* = 3.7 Hz), 116.5 (d, *J* = 22.3 Hz), 115.6 (d, *J* = 21.6 Hz), 113.7 (q, *J* = 4.2 Hz), 52.0, 37.8, 36.9, 30.8, 26.0, 18.8, -2.8, -3.6.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -64.66 (s), -114.04 (tt, *J* = 8.0, 5.0 Hz).

**IR** ν<sub>max</sub>: 2954, 2928, 2852, 1734, 1686, 1621, 1605, 1578, 1510, 1439, 1419, 1333, 1171, 1128, 1084, 915, 835 cm<sup>-1</sup>.

[α]<sub>D</sub><sup>25</sup> = +43.86 (*c* = 0.57, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>26</sub>H<sub>31</sub>F<sub>4</sub>NO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 574.1707, found: 574.1710.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-6-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4x)**

yellow oil; scale: 0.1 mmol; isolated yield 69% (36.0 mg);

*ee* 96% - 11.20 min (major), 18.82 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

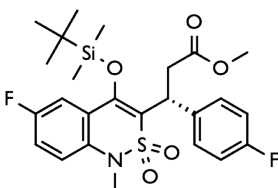
$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.52 (dd,  $J = 1.5, 0.7$  Hz, 1H), 7.43 (dd,  $J = 8.4, 5.3$  Hz, 2H), 7.24 (ddd,  $J = 8.3, 2.1, 0.8$  Hz, 1H), 7.04 (d,  $J = 8.4$  Hz, 1H), 6.97 (t,  $J = 8.7$  Hz, 2H), 5.15 (dd,  $J = 11.3, 4.4$  Hz, 1H), 3.74 (dd,  $J = 16.9, 11.3$  Hz, 1H), 3.64 (s, 3H), 3.34 (s, 3H), 2.95 (dd,  $J = 16.9, 4.4$  Hz, 1H), 2.36 (s, 3H), 1.13 (s, 9H), 0.25 (s, 3H), 0.01 (s, 3H).  
 $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  172.3, 161.9 (d,  $J = 245.1$  Hz), 151.1, 136.9, 135.8 (d,  $J = 3.3$  Hz), 132.3, 132.0, 129.6 (d,  $J = 7.9$  Hz), 127.4, 124.9, 121.7, 117.2, 115.4 (d,  $J = 21.4$  Hz), 51.9, 37.6, 37.1, 31.4, 26.1, 20.8, 18.8, -2.9, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.90 (tt,  $J = 8.5, 5.5$  Hz).

**IR**  $\nu_{\text{max}}$ : 3021, 2953, 2931, 2899, 2860, 1737, 1589, 1566, 1509, 1436, 1320, 1286, 1259, 1211, 1161, 1089, 825, 751  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +70.63$  ( $c = 1.26$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{26}\text{H}_{34}\text{FNO}_5\text{SSi}$ ,  $(\text{M} + \text{H})^+ = 520.1989$ , found: 520.1994.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-6-fluoro-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4y)**

yellow oil; scale: 0.1 mmol; isolated yield 84% (44.0 mg);

*ee* 93% - 11.61 min (major), 17.71 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.50 – 7.36 (m, 3H), 7.21 – 7.10 (m, 2H), 6.99 (t,  $J = 8.8$  Hz, 2H), 5.14 (dd,  $J = 11.4, 4.5$  Hz, 1H), 3.74 (dd,  $J = 16.9, 11.2$  Hz, 1H), 3.64 (s, 3H), 3.34 (s, 3H), 2.94 (dd,  $J = 16.9, 4.3$  Hz, 1H), 1.14 (s, 9H), 0.27 (s, 3H), 0.04 (s, 3H).

$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  172.1, 162.0 (d,  $J = 245.5$  Hz), 158.5 (d,  $J = 243.5$  Hz), 149.9 (d,  $J = 2.3$  Hz), 135.5 (d,  $J = 2.3$  Hz), 135.4 (d,  $J = 3.3$  Hz), 129.6 (d,  $J = 8.1$  Hz), 126.3, 123.7 (d,  $J = 7.7$  Hz), 119.4 (d,  $J = 7.9$  Hz), 118.3 (d,  $J = 23.3$  Hz), 115.6 (d,  $J = 21.4$  Hz), 113.4 (d,  $J = 25.0$  Hz), 52.0, 37.7, 36.9, 32.2, 26.0, 18.7, -2.9, -3.7.

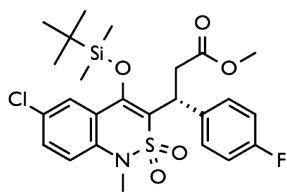
$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.52 (tt,  $J = 8.5, 5.5$  Hz), -119.61 (ddd,  $J = 9.5, 7.3, 4.8$  Hz).

**IR**  $\nu_{\text{max}}$ : 3022, 2954, 2932, 2899, 2860, 1737, 1601, 1567, 1509, 1488, 1325, 1284, 1260, 1198, 1160, 1082, 826, 752  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +63.85$  ( $c = 1.14$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{25}\text{H}_{31}\text{F}_2\text{NO}_5\text{SSi}$ ,  $(\text{M} + \text{H})^+ = 524.1739$ , found: 524.1744.





**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-6-chloro-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4z)**

yellow oil; scale: 0.1 mmol; isolated yield 63% (34.0 mg);

*ee* 91% - 11.46 min (major), 18.10 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.70 (d,  $J$  = 2.3 Hz, 1H), 7.46 – 7.38 (m, 3H), 7.08 (d,  $J$  = 8.8 Hz, 1H), 6.99 (t,  $J$  = 8.7 Hz, 2H), 5.14 (dd,  $J$  = 11.3, 4.5 Hz, 1H), 3.73 (dd,  $J$  = 16.9, 11.2 Hz, 1H), 3.64 (s, 3H), 3.36 (s, 3H), 2.95 (dd,  $J$  = 16.9, 4.4 Hz, 1H), 1.14 (s, 9H), 0.26 (s, 3H), 0.04 (s, 3H).

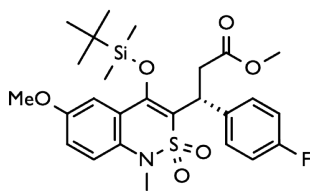
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  172.1, 162.0 (d,  $J$  = 245.6 Hz), 149.9, 137.5, 135.4 (d,  $J$  = 3.1 Hz), 131.0, 129.6 (d,  $J$  = 8.3 Hz), 128.5, 126.9, 126.1, 123.0, 118.3, 115.6 (d,  $J$  = 21.6 Hz), 52.0, 37.7, 37.0, 31.2, 26.0, 18.8, -3.0, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.49 (tt,  $J$  = 8.5, 5.3 Hz).

**IR**  $\nu_{\text{max}}$ : 2953, 2932, 2889, 2860, 1737, 1604, 1588, 1556, 1509, 1473, 1322, 1282, 1258, 1224, 1151, 1089, 810, 754  $\text{cm}^{-1}$ .

$[\alpha]_D^{25}$  = +77.31 ( $c$  = 1.19,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{25}\text{H}_{31}\text{ClFNO}_5\text{SSi}$ , ( $M + H$ ) $^+$  = 540.1443, found: 540.1447.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-6-methoxy-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4aa)**

yellow oil; scale: 0.1 mmol; isolated yield 85% (45.3 mg);

*ee* 96% - 18.80 min (major), 28.72 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.44 (dd,  $J$  = 8.4, 5.3 Hz, 2H), 7.20 (d,  $J$  = 2.9 Hz, 1H), 7.11 (d,  $J$  = 8.8 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.97 (d,  $J$  = 8.8 Hz, 1H), 5.13 (dd,  $J$  = 11.3, 4.4 Hz, 1H), 3.82 (s, 3H), 3.75 (dd,  $J$  = 16.9, 11.2 Hz, 1H), 3.64 (s, 3H), 3.29 (s, 3H), 2.94 (dd,  $J$  = 16.9, 4.3 Hz, 1H), 1.14 (s, 9H), 0.28 (s, 3H), 0.05 (s, 3H).

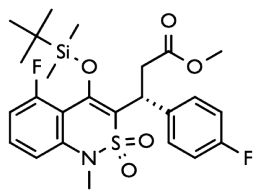
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  172.3, 161.9 (d,  $J$  = 245.3 Hz), 155.7, 150.6, 135.7 (d,  $J$  = 3.3 Hz), 133.0, 129.6 (d,  $J$  = 8.1 Hz), 125.5, 123.5, 119.9, 118.2, 115.5 (d,  $J$  = 21.4 Hz), 111.0, 55.8, 51.9, 37.7, 37.0, 33.0, 26.0, 18.7, -2.8, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.80 (tt,  $J$  = 8.5, 5.3 Hz).

**IR**  $\nu_{\text{max}}$ : 3004, 2953, 2931, 2859, 1737, 1591, 1563, 1509, 1492, 1321, 1284, 1218, 1160, 1086, 1032, 940, 825, 752  $\text{cm}^{-1}$ .

$[\alpha]_D^{25}$  = +73.39 ( $c$  = 0.97,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{26}\text{H}_{34}\text{FNO}_6\text{SSi}$ , ( $M + H$ ) $^+$  = 536.1938, found: 536.1940.



**methyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-5-fluoro-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4ab)**

yellow oil; scale: 0.1 mmol; isolated yield 89% (46.8 mg);

*ee* 95% - 10.06 min (major), 15.15 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.47 (ddd,  $J$  = 8.9, 5.3, 0.7 Hz, 2H), 7.39 (td,  $J$  = 8.3, 5.5 Hz, 1H), 7.00 (t,  $J$  = 8.8 Hz, 2H), 6.95 (d,  $J$  = 8.4 Hz, 1H), 6.87 (ddd,  $J$  = 11.3, 8.3, 1.1 Hz, 1H), 5.19 (dd,  $J$  = 11.7, 3.8 Hz, 1H), 3.80 (dd,  $J$  = 16.7, 11.7 Hz, 1H), 3.63 (s, 3H), 3.39 (s, 4H), 2.84 (dd,  $J$  = 16.9, 3.7 Hz, 1H), 1.10 (s, 9H), 0.14 (s, 3H), -0.07 (d,  $J$  = 2.5 Hz, 3H).

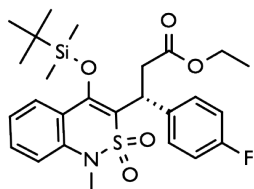
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  172.2, 162.0 (d,  $J$  = 245.5 Hz), 158.9 (d,  $J$  = 258.5 Hz), 149.1 (d,  $J$  = 1.9 Hz), 140.6 (d,  $J$  = 4.4 Hz), 135.4 (d,  $J$  = 3.3 Hz), 131.8 (d,  $J$  = 10.8 Hz), 129.7 (d,  $J$  = 8.1 Hz), 127.3, 115.6 (d,  $J$  = 21.4 Hz), 112.9 (d,  $J$  = 3.3 Hz), 111.8 (d,  $J$  = 10.8 Hz), 111.5 (d,  $J$  = 22.5 Hz), 51.9, 37.2, 31.6, 25.9, 25.8, 18.3, -4.2 (d,  $J$  = 5.1 Hz), -4.2.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -109.11 (dd,  $J$  = 11.0, 5.5 Hz), -116.58 (tt,  $J$  = 8.5, 5.0 Hz).

**IR**  $\nu_{\text{max}}$ : 2954, 2932, 2896, 2860, 1736, 1613, 1593, 1557, 1509, 1464, 1337, 1319, 1223, 1158, 1119, 1093, 956, 784, 721  $\text{cm}^{-1}$ .

$[\alpha]_D^{26}$  = +61.85 ( $c$  = 1.25,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{25}\text{H}_{31}\text{F}_2\text{NO}_5\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 524.1739, found: 524.1743.



**ethyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4ac)**

yellow oil; scale: 0.1 mmol; isolated yield 69% (36.0 mg);

*ee* 95% - 7.23 min (major), 10.38 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 90:10, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.71 (dd,  $J$  = 8.0, 1.4 Hz, 1H), 7.49 - 7.40 (m, 3H), 7.18 (ddd,  $J$  = 8.1, 7.3, 1.2 Hz, 1H), 7.13 (dd,  $J$  = 8.2, 1.2 Hz, 1H), 6.98 (t,  $J$  = 8.8 Hz, 2H), 5.16 (dd,  $J$  = 11.6, 4.1 Hz, 1H), 4.09 (q,  $J$  = 7.2 Hz, 2H), 3.78 (dd,  $J$  = 16.7, 11.6 Hz, 1H), 3.38 (s, 3H), 2.92 (dd,  $J$  = 16.8, 4.0 Hz, 1H), 1.17 (t,  $J$  = 7.2 Hz, 3H), 1.13 (s, 9H), 0.26 (s, 3H), 0.01 (s, 3H).

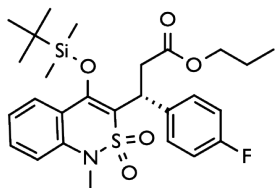
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  171.7, 161.9 (d,  $J$  = 245.3 Hz), 150.9, 139.1, 135.7 (d,  $J$  = 3.3 Hz), 131.3, 129.7 (d,  $J$  = 8.1 Hz), 127.1, 125.2, 122.6, 121.7, 116.8, 115.4 (d,  $J$  = 21.4 Hz), 60.7, 37.7, 37.3, 30.9, 26.1, 18.7, 14.3, -2.9, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.85 (tt,  $J$  = 8.5, 5.0 Hz).

**IR**  $\nu_{\text{max}}$ : 2955, 2931, 2903, 2859, 1732, 1604, 1593, 1561, 1509, 1471, 1320, 1287, 1260, 1124, 1160, 1087, 899, 809, 753  $\text{cm}^{-1}$ .

$[\alpha]_D^{25}$  = +67.18 ( $c$  = 1.31,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{26}\text{H}_{34}\text{FNO}_5\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 520.1989, found: 520.1992.



propyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (**4ad**)

yellow oil; scale: 0.1 mmol; isolated yield 53% (28.1 mg);

*ee* 95% - 11.64 min (major), 18.86 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.72 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.18 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H), 7.13 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.98 (t, *J* = 8.8 Hz, 2H), 5.16 (dd, *J* = 11.7, 4.1 Hz, 1H), 3.99 (t, *J* = 6.7 Hz, 2H), 3.81 (dd, *J* = 16.8, 11.7 Hz, 1H), 3.38 (s, 3H), 2.92 (dd, *J* = 16.9, 4.0 Hz, 1H), 1.56 (h, *J* = 7.4 Hz, 2H), 1.13 (s, 9H), 0.85 (t, *J* = 7.4 Hz, 3H), 0.26 (s, 3H), 0.01 (s, 3H).

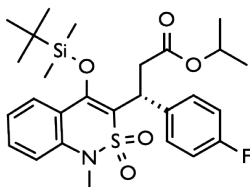
<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ 171.8, 162.0 (d, *J* = 245.1 Hz), 150.9, 139.1, 135.7 (d, *J* = 3.3 Hz), 131.3, 129.7 (d, *J* = 8.1 Hz), 127.1, 125.2, 122.6, 121.7, 116.8, 115.4 (d, *J* = 21.4 Hz), 66.4, 37.6, 37.3, 30.9, 26.1, 22.0, 18.7, 10.4, -2.9, -3.6.

<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ -116.85 (tt, *J* = 8.5, 5.0 Hz).

IR  $\nu_{max}$ : 2957, 2932, 2886, 2860, 1731, 1605, 1593, 1561, 1509, 1471, 1321, 1287, 1261, 1225, 1160, 1087, 895, 809, 754 cm<sup>-1</sup>.

[ $\alpha$ ]<sub>D</sub><sup>25</sup> = +71.82 (*c* = 1.10, CHCl<sub>3</sub>)

HRMS (ESI-TOF) calculated for C<sub>27</sub>H<sub>36</sub>FNO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 534.2146, found: 534.2149.



isopropyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (**4ae**)

yellow oil; scale: 0.1 mmol; isolated yield 41% (21.8 mg);

*ee* 94% - 10.45 min (major), 18.11 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.71 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.18 (ddd, *J* = 7.9, 7.3, 1.1 Hz, 1H), 7.13 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.97 (t, *J* = 8.8 Hz, 2H), 5.14 (dd, *J* = 12.0, 4.2 Hz, 1H), 4.95 (hept, *J* = 6.3 Hz, 1H), 3.78 (dd, *J* = 16.7, 11.8 Hz, 1H), 3.38 (s, 3H), 2.87 (dd, *J* = 16.6, 4.1 Hz, 1H), 1.13 (s, 9H), 1.12 (dd, *J* = 12.3, 6.2 Hz, 6H), 0.27 (s, 3H), 0.01 (s, 3H).

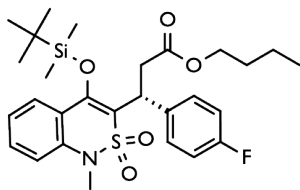
<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ 171.1, 161.9 (d, *J* = 245.1 Hz), 150.8, 139.1, 135.6 (d, *J* = 3.1 Hz), 131.3, 129.8 (d, *J* = 8.1 Hz), 127.1, 125.3, 122.6, 121.7, 116.8, 115.4 (d, *J* = 21.4 Hz), 68.0, 37.8, 37.6, 30.9, 26.1, 21.9, 21.8, 18.7, -2.8, -3.6.

<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ -116.90 (tt, *J* = 8.5, 5.0 Hz).

IR  $\nu_{max}$ : 2982, 2950, 2930, 2897, 2858, 1728, 1604, 1591, 1561, 1507, 1463, 1373, 1325, 1287, 1262, 1214, 1150, 1100, 841, 762 cm<sup>-1</sup>.

[ $\alpha$ ]<sub>D</sub><sup>25</sup> = +66.43 (*c* = 1.40, CHCl<sub>3</sub>)

HRMS (ESI-TOF) calculated for C<sub>27</sub>H<sub>36</sub>FNO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 534.2146, found: 534.2150.



**butyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionate (4af)**

yellow oil; scale: 0.1 mmol; isolated yield 66% (36.4 mg);

*ee* 95% - 6.91 min (major), 9.96 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 90:10, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.72 (dd,  $J = 8.0, 1.4$  Hz, 1H), 7.49 – 7.41 (m, 3H), 7.25 – 7.14 (m, 1H), 7.13 (dd,  $J = 8.2, 1.2$  Hz, 1H), 6.98 (t,  $J = 8.7$  Hz, 2H), 5.16 (dd,  $J = 11.7, 4.2$  Hz, 1H), 4.03 (t,  $J = 6.5$  Hz, 2H), 3.80 (dd,  $J = 16.8, 11.7$  Hz, 1H), 3.38 (s, 3H), 2.91 (dd,  $J = 16.7, 4.0$  Hz, 1H), 1.51 (p, 2H), 1.27 (h,  $J = 7.3$  Hz, 2H), 1.13 (s, 9H), 0.86 (t,  $J = 7.4$  Hz, 3H), 0.26 (s, 3H), 0.01 (s, 3H).

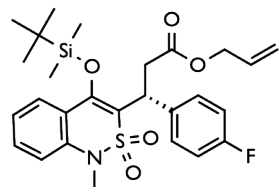
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  171.8, 162.0 (d,  $J = 245.3$  Hz), 150.9, 139.1, 135.7 (d,  $J = 3.3$  Hz), 131.3, 129.7 (d,  $J = 8.1$  Hz), 127.1, 125.2, 122.6, 121.7, 116.8, 115.4 (d,  $J = 21.4$  Hz), 64.6, 37.7, 37.3, 30.9, 30.7, 26.1, 19.1, 18.7, 13.7, -2.8, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.86 (tt,  $J = 8.5, 5.3$  Hz).

**IR**  $\nu_{\text{max}}$ : 2957, 2932, 2899, 2860, 1731, 1604, 1593, 1561, 1509, 1465, 1321, 1287, 1260, 1227, 1160, 1087, 809, 753  $\text{cm}^{-1}$ .

$[\alpha]_D^{25} = +48.31$  ( $c = 1.18$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{28}\text{H}_{38}\text{FNO}_5\text{SSi}$ , ( $M + H$ ) $^+ = 548.2302$ , found: 548.2308.



**prop-2-enyl (*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl) propionate (4ag)**

yellow oil; scale: 0.1 mmol; isolated yield 84% (44.4 mg);

*ee* 95% - 8.12 min (major), 11.79 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 90:10, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.72 (dd,  $J = 8.0, 1.5$  Hz, 1H), 7.49 – 7.41 (m, 3H), 7.19 (ddd,  $J = 8.4, 7.3, 1.2$  Hz, 1H), 7.14 (dd,  $J = 8.2, 1.2$  Hz, 1H), 6.98 (t,  $J = 8.8$  Hz, 2H), 5.82 (ddt,  $J = 17.3, 10.4, 5.7$  Hz, 1H), 5.22 (dq,  $J = 17.2, 1.5$  Hz, 1H), 5.19 – 5.08 (m, 2H), 4.54 (dt,  $J = 5.6, 1.4$  Hz, 2H), 3.82 (dd,  $J = 16.9, 11.4$  Hz, 1H), 3.38 (s, 3H), 2.97 (dd,  $J = 16.9, 4.0$  Hz, 1H), 1.13 (s, 9H), 0.25 (s, 3H), 0.01 (s, 3H).

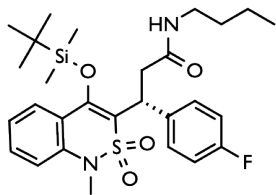
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  171.4, 162.0 (d,  $J = 245.3$  Hz), 151.0, 139.1, 135.6 (d,  $J = 3.1$  Hz), 132.1, 131.3, 129.7 (d,  $J = 8.1$  Hz), 127.1, 125.1, 122.6, 121.7, 118.3, 116.8, 115.5 (d,  $J = 21.4$  Hz), 30.9, 26.1, 18.7, -2.9, -3.6.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -116.78 (tt,  $J = 8.5, 5.0$  Hz).

**IR**  $\nu_{\text{max}}$ : 2954, 2931, 2888, 2860, 1735, 1604, 1593, 1561, 1509, 1472, 1320, 1288, 1261, 1226, 1160, 1087, 897, 809, 754  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +58.68$  ( $c = 1.06$ ,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{27}\text{H}_{34}\text{FNO}_5\text{SSi}$ , ( $M + H$ ) $^+ = 532.1989$ , found: 532.1995.



***N*-butyl-(*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionamide (4ah)**

yellow oil; scale: 0.1 mmol; isolated yield 57% (31.0 mg);

*ee* 94% - 13.93 min (major), 17.44 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.72 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.52 – 7.40 (m, 3H), 7.19 (ddd, *J* = 7.9, 7.3, 1.1 Hz, 1H), 7.16 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.97 (t, *J* = 8.7 Hz, 2H), 5.78 (t, *J* = 5.6 Hz, 1H), 5.19 (dd, *J* = 9.4, 6.3 Hz, 1H), 3.41 (s, 3H), 3.29 (dd, *J* = 14.5, 8.9 Hz, 1H), 3.21 – 3.11 (m, 2H), 3.03 – 2.84 (m, 1H), 1.37 – 1.28 (m, 1H), 1.22 – 1.15 (m, 1H), 1.09 (s, 9H), 0.81 (t, *J* = 7.3 Hz, 3H), 0.24 (s, 3H), -0.05 (s, 3H).

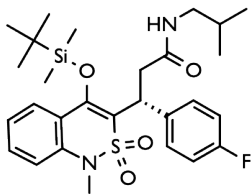
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 170.5, 161.8 (d, *J* = 245.1 Hz), 152.1, 139.0, 136.3 (d, *J* = 3.1 Hz), 131.3, 129.6 (d, *J* = 7.9 Hz), 127.2, 124.5, 122.7, 121.8, 116.7, 115.3 (d, *J* = 21.2 Hz), 40.5, 39.4, 38.5, 31.7, 30.9, 26.1, 20.0, 18.8, 13.8, -3.0, -3.2.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -117.18 (tt, *J* = 8.5, 5.3 Hz).

**IR**  $\nu_{max}$ : 3389, 3309, 3078, 2956, 2930, 2859, 1649, 1603, 1549, 1509, 1464, 1315, 1288, 1259, 1225, 1141, 1057, 1042, 809, 756 cm<sup>-1</sup>.

$[\alpha]_D^{26} = +24.54$  (*c* = 1.63, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>28</sub>H<sub>39</sub>FN<sub>2</sub>O<sub>4</sub>SSi, (*M* + *H*)<sup>+</sup> = 547.2462, found: 547.2463.



***N*-isobutyl-(*R*)-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionamide (4ai)**

yellow oil; scale: 0.1 mmol; isolated yield 64% (35.0 mg);

*ee* 96% - 13.20 min (major), 16.67 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 90:10, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.71 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.19 (ddd, *J* = 8.1, 7.3, 1.0 Hz, 1H), 7.16 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.97 (t, *J* = 8.7 Hz, 2H), 5.80 (t, *J* = 5.9 Hz, 1H), 5.20 (dd, *J* = 9.0, 6.7 Hz, 1H), 3.41 (s, 3H), 3.31 (dd, *J* = 14.7, 9.1 Hz, 1H), 3.10 – 2.92 (m, 3H), 1.62 (hept, *J* = 6.7 Hz, 1H), 1.09 (s, 9H), 0.77 (dd, *J* = 6.7, 4.0 Hz, 6H), 0.25 (s, 3H), -0.06 (s, 3H).

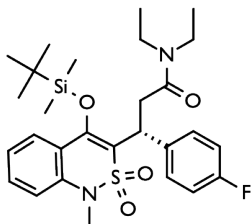
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 170.6, 161.9 (d, *J* = 245.3 Hz), 152.0, 139.0, 136.4 (d, *J* = 3.3 Hz), 131.3, 129.7 (d, *J* = 8.1 Hz), 127.2, 124.6, 122.7, 121.8, 116.7, 115.3 (d, *J* = 21.4 Hz), 47.1, 40.6, 38.5, 30.9, 28.5, 26.1, 20.0, 18.8, -3.0, -3.2.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -117.17 (tt, *J* = 8.5, 5.5 Hz).

**IR**  $\nu_{max}$ : 3390, 3311, 3077, 2956, 2930, 2859, 1650, 1604, 1545, 1509, 1465, 1316, 1288, 1259, 1226, 1149, 1086, 895, 809, 755 cm<sup>-1</sup>.

$[\alpha]_D^{26} = +29.41$  (*c* = 1.02, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>28</sub>H<sub>39</sub>FN<sub>2</sub>O<sub>4</sub>SSi, (*M* + *H*)<sup>+</sup> = 547.2462, found: 547.2464.



***N,N*-diethyl-*(R)*-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionamide (4aj)**

yellow oil; scale: 0.1 mmol; isolated yield 56% (30.4 mg);

*ee* 95% - 15.62 min (major), 28.36 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 95:05, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.72 (dd,  $J$  = 8.1, 1.5 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.18 (ddd,  $J$  = 8.1, 7.3, 1.1 Hz, 1H), 7.14 (dd,  $J$  = 8.2, 1.2 Hz, 1H), 6.94 (t,  $J$  = 8.8 Hz, 2H), 5.34 (dd,  $J$  = 10.8, 4.0 Hz, 1H), 3.68 (dd,  $J$  = 16.4, 10.5 Hz, 1H), 3.41 (s, 3H), 3.38 – 3.30 (m, 4H), 2.86 (dd,  $J$  = 16.3, 4.0 Hz, 1H), 1.16 (t,  $J$  = 7.1 Hz, 3H), 1.08 (s, 9H), 1.02 (t,  $J$  = 7.1 Hz, 3H), 0.24 (s, 3H), -0.06 (s, 3H).

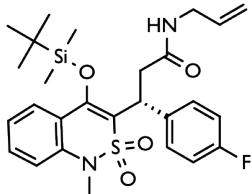
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  169.6, 161.7 (d,  $J$  = 244.5 Hz), 151.4, 139.0, 137.2 (d,  $J$  = 3.3 Hz), 131.1, 129.8 (d,  $J$  = 7.9 Hz), 127.1, 125.5, 122.6, 122.0, 116.7, 115.1 (d,  $J$  = 21.4 Hz), 42.1, 40.5, 38.1, 36.3, 31.0, 29.8, 26.1, 18.8, 14.5, 13.2, -3.0, -3.3.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -117.71 (tt,  $J$  = 8.5, 5.3 Hz).

**IR**  $\nu_{\text{max}}$ : 3364, 3072, 2957, 2932, 2897, 2859, 1639, 1604, 1561, 1509, 1461, 1316, 1288, 1264, 1222, 1152, 1086, 810, 757  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +13.85$  ( $c$  = 1.30,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{28}\text{H}_{39}\text{FN}_2\text{O}_4\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 547.2462, found: 547.2466.



***N*-(prop-2-enyl)-*(R)*-3-{4-[(*tert*-butyl)bis(methyl)siloxy]-1-methyl-2,2-dioxo-1,2-dihydro-2*H*,2*H*-2 $\lambda^6$ ,1-benzothiazin-3-yl}-3-(4-fluorophenyl)propionamide (4ak)**

yellow oil; scale: 0.1 mmol; isolated yield 66% (35.0 mg);

*ee* 96% - 15.50 min (major), 17.33 min (minor); (Phenomenex Lux Amylose-1, 3  $\mu$ m, Hex:iPrOH 90:10, 1.0 mL/min)

$^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.72 (dd,  $J$  = 8.0, 1.4 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.19 (ddd,  $J$  = 8.1, 7.3, 1.2 Hz, 1H), 7.16 (dd,  $J$  = 8.2, 1.2 Hz, 1H), 6.97 (t,  $J$  = 8.7 Hz, 2H), 5.85 (t,  $J$  = 5.5 Hz, 1H), 5.69 (ddt,  $J$  = 17.3, 10.0, 5.5 Hz, 1H), 5.21 (dd,  $J$  = 8.8, 6.5 Hz, 1H), 5.07 – 4.95 (m, 2H), 3.90 – 3.76 (m, 2H), 3.41 (s, 3H), 3.33 (dd,  $J$  = 14.7, 9.0 Hz, 1H), 3.01 (dd,  $J$  = 14.7, 6.2 Hz, 1H), 1.10 (s, 9H), 0.25 (s, 3H), -0.05 (s, 3H).

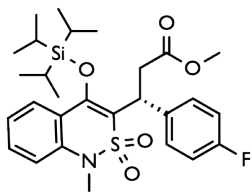
$^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 101 MHz)  $\delta$  170.5, 161.9 (d,  $J$  = 245.3 Hz), 152.1, 139.0, 136.3 (d,  $J$  = 3.1 Hz), 134.2, 131.3, 129.7 (d,  $J$  = 8.1 Hz), 127.2, 124.5, 122.7, 121.8, 116.7, 116.1, 115.4 (d,  $J$  = 21.2 Hz), 42.0, 40.3, 38.4, 30.9, 26.1, 18.8, -3.0, -3.3.

$^{19}\text{F NMR}$  ( $\text{CDCl}_3$ , 376 MHz)  $\delta$  -117.06 (tt,  $J$  = 8.5, 5.0 Hz).

**IR**  $\nu_{\text{max}}$ : 3381, 3305, 3079, 2954, 2930, 2858, 1656, 1645, 1603, 1538, 1509, 1470, 1315, 1288, 1259, 1225, 1149, 1086, 809, 756  $\text{cm}^{-1}$ .

$[\alpha]_D^{26} = +40.20$  ( $c$  = 1.02,  $\text{CHCl}_3$ )

**HRMS** (ESI-TOF) calculated for  $\text{C}_{27}\text{H}_{35}\text{FN}_2\text{O}_4\text{SSi}$ , ( $\text{M} + \text{H}$ ) $^+$  = 531.2149, found: 531.2154.



**methyl (*R*)-3-(4-fluorophenyl)-3-{1-methyl-2,2-dioxo-4-[tris(isopropyl)siloxy]-1,2-dihydro-2*H*,2*H*-2λ<sup>6</sup>,1-benzothiazin-3-yl}propionate (4al)**

yellow oil; scale: 0.1 mmol; isolated yield 75% (41.0 mg);

*ee* 95% - 10.05 min (major), 13.71 min (minor); (Phenomenex Lux Amylose-1, 3 μm, Hex:iPrOH 95:05, 1.0 mL/min)

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.73 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.53 – 7.41 (m, 3H), 7.21 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H), 7.15 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.98 (t, *J* = 8.8 Hz, 2H), 5.19 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.76 (dd, *J* = 16.9, 11.3 Hz, 1H), 3.64 (s, 3H), 3.38 (s, 3H), 2.97 (dd, *J* = 16.7, 4.0 Hz, 1H), 1.31 – 1.24 (m, 3H), 1.12 (d, *J* = 7.3 Hz, 9H), 1.06 (d, *J* = 7.3 Hz, 9H).

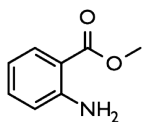
<sup>13</sup>**C NMR** (CDCl<sub>3</sub>, 101 MHz) δ 172.2, 161.9 (d, *J* = 245.3 Hz), 152.3, 139.1, 135.7 (d, *J* = 3.3 Hz), 131.3, 129.6 (d, *J* = 8.1 Hz), 126.5, 124.3, 123.0, 122.5, 117.0, 115.4 (d, *J* = 21.4 Hz), 51.9, 37.6, 37.2, 31.1, 18.0, 18.0, 14.2.

<sup>19</sup>**F NMR** (CDCl<sub>3</sub>, 376 MHz) δ -116.91 (tt, *J* = 8.5, 5.3 Hz).

**IR**  $\nu_{max}$ : 2948, 2893, 2869, 1737, 1605, 1592, 1560, 1509, 1463, 1320, 1288, 1224, 1160, 1093, 883, 837, 754, 721, 684 cm<sup>-1</sup>.

$[\alpha]_D^{25} = +106.32$  (*c* = 0.95, CHCl<sub>3</sub>)

**HRMS** (ESI-TOF) calculated for C<sub>28</sub>H<sub>38</sub>FNO<sub>5</sub>SSi, (*M* + *H*)<sup>+</sup> = 548.2302, found: 548.2306.

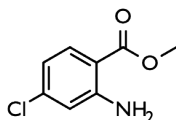


**methyl anthranilate (5a)**

dark orange liquid; scale: 43.8 mmol; yield: 72% (4.76g);

Known compound - characterisation in agreement with literature.<sup>2</sup>

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.86 (ddd, *J* = 7.9, 1.6, 0.6 Hz, 1H), 7.26 (ddd, *J* = 8.2, 7.0, 1.6 Hz, 1H), 6.68 – 6.61 (m, 2H), 5.62 (bs, 2H), 3.87 (s, 3H).

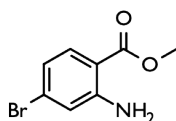


**methyl 2-amino-4-chlorobenzoate (5b)**

light beige solid; scale: 20 mmol; yield: 88% (3.26 g);

Known compound - characterisation in agreement with literature.<sup>8</sup>

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 400 MHz) δ 7.78 (d, *J* = 8.6 Hz, 1H), 6.68 (d, *J* = 2.0, 1H), 6.61 (dd, *J* = 8.6, 2.0 Hz, 1H), 3.86 (s, 3H)

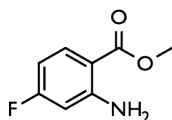


**methyl 2-amino-4-bromobenzoate (5c)**

beige solid; scale: 30 mmol; yield: 38% (2.62 g);

Known compound - characterisation in agreement with literature.<sup>9,10</sup>

<sup>1</sup>**H NMR** (CDCl<sub>3</sub>, 700 MHz) δ 7.70 (d, *J* = 8.6 Hz, 1H), 6.86 (s, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 3.86 (s, 3H).

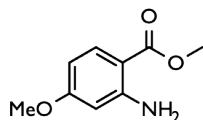


**methyl 2-amino-4-fluorobenzoate (5d)**

beige solid; scale: 30 mmol; yield: 76% (3.83 g);

Known compound - characterisation in agreement with literature.<sup>10</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.91 – 7.82 (m, 1H), 6.41 – 6.31 (m, 2H), 3.86 (s, 3H).

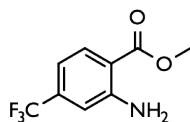


**methyl 2-amino-4-anisate (5e)**

brown solid; scale: 30 mmol; yield: 60% (3.29 g);

Known compound - characterisation in agreement with literature.<sup>10,11</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.78 (d, J = 8.9 Hz, 1H), 6.23 (dd, J = 8.9, 2.5 Hz, 1H), 6.11 (d, J = 2.4 Hz, 1H), 5.82 (s, 2H), 3.83 (s, 2H), 3.79 (s, 3H).

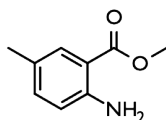


**methyl 2-amino-4-(trifluoromethyl)benzoate (5f)**

orange solid; scale: 30 mmol; yield: 88% (5.78 g);

Known compound - characterisation in agreement with literature.<sup>12</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.95 (dd, J = 8.4, 0.4 Hz, 1H), 6.90 (dd, J = 1.2, 0.6 Hz, 1H), 6.85 (ddd, J = 8.3, 1.7, 0.5 Hz, 1H), 3.90 (s, 3H).

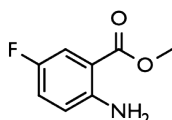


**methyl 2-amino-5-methylbenzoate (5g)**

dark orange liquid; scale: 30 mmol; yield: 100% (4.96 g);

Known compound - characterisation in agreement with literature.<sup>8</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.68 – 7.65 (m, 1H), 7.10 (ddd, J = 8.2, 2.2, 0.5 Hz, 1H), 6.63 (d, J = 8.2 Hz, 1H), 5.54 (bs, 2H), 3.87 (s, 3H), 2.23 (s, 3H).

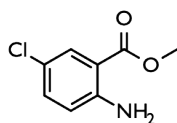


**methyl 2-amino-5-fluorobenzoate (5h)**

brown liquid; scale: 30 mmol; yield: 81% (4.09 g);

Known compound - characterisation in agreement with literature.<sup>8</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.54 (ddd, J = 9.7, 3.1, 0.4 Hz, 1H), 7.04 (ddd, J = 9.0, 7.7, 3.1 Hz, 1H), 6.65 (ddd, J = 9.0, 4.5, 0.4 Hz, 1H), 5.64 (bs, 2H), 3.88 (s, 3H).



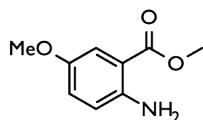
**methyl 2-amino-5-chlorobenzoate (5i)**

brown solid; scale: 30 mmol; yield: 83% (4.61 g);

Known compound - characterisation in agreement with literature.<sup>8</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.84 (d, J = 2.5 Hz, 1H), 7.24 (dd, J = 8.8, 2.6 Hz, 1H), 6.70 (d, J = 8.7 Hz, 1H), 3.88 (s, 3H).



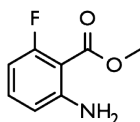


#### methyl 2-amino-5-anisate (5j)

dark brown liquid; scale: 30 mmol; yield: 87% (4.73 g);

Known compound - characterisation in agreement with literature.<sup>10,13</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 00 MHz)  $\delta$  7.35 (d, J = 3.0 Hz, 1H), 6.95 (dd, J = 8.9, 3.1 Hz, 1H), 6.63 (dd, J = 8.9, 0.4 Hz, 1H), 5.41 (s, 1H), 3.88 (s, 4H), 3.76 (s, 3H).

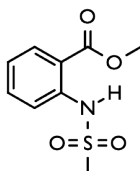


#### methyl 2-amino-6-fluorobenzoate (5k)

brown solid; scale: 30 mmol; yield: 70% (3.55 g);

Known compound - characterisation in agreement with literature.<sup>11</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.14 (td, J = 8.2, 5.8 Hz, 1H), 6.43 (dt, J = 8.4, 1.0 Hz, 1H), 6.35 (ddd, J = 11.5, 8.1, 1.1 Hz, 1H), 5.74 (bs, 2H), 3.90 (s, 3H).

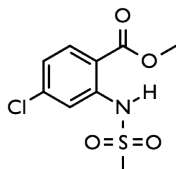


#### methyl 2-(mesylamino)benzoate (6a)

white solid; scale: 132,3 mmol; yield: 59% (17.93 g);

Known compound - characterisation in agreement with literature.<sup>2</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.46 (s, 1H), 8.06 (ddd, J = 8.0, 1.7, 0.4 Hz, 1H), 7.75 (ddd, J = 8.4, 1.1, 0.4 Hz, 1H), 7.56 (dddd, J = 8.4, 7.3, 1.7, 0.4 Hz, 1H), 7.13 (ddd, J = 8.0, 7.3, 1.1 Hz, 1H), 3.94 (s, 3H), 3.06 (s, 3H)..

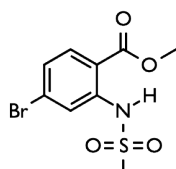


#### methyl 4-chloro-2-(mesylamino)benzoate (6b)

light orange solid; scale: 16.4 mmol, yield: 91% (3.96 g);

Known compound - characterisation in agreement with literature.<sup>14</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.55 (s, 1H), 7.99 (dd, J = 8.6, 0.4 Hz, 1H), 7.77 (dd, J = 2.0, 0.4 Hz, 1H), 7.09 (dd, J = 8.6, 2.0 Hz, 1H), 3.94 (s, 3H), 3.10 (s, 3H).

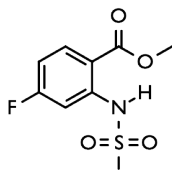


#### methyl 4-bromo-2-(mesylamino)benzoate (6c)

orange solid; scale: 10.9 mmol; yield: 44% (1.47 g);

Known compound - characterisation in agreement with literature.<sup>15</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.53 (s, 1H), 7.93 (d, J = 1.8 Hz, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.26 (dd, J = 8.6, 1.9 Hz, 2H), 3.94 (s, 3H), 3.10 (s, 3H).

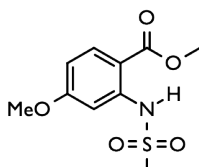


#### methyl 4-fluoro-2-(mesylamino)benzoate (6d)

pink solid; scale: 5.8 mmol; yield: 81% (1.16 g);

Known compound - characterisation in agreement with literature.<sup>16</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.68 (s, 1H), 8.08 (dd, J = 8.9, 6.4 Hz, 1H), 7.50 (dd, J = 10.9, 2.5 Hz, 1H), 6.81 (ddd, J = 8.9, 7.5, 2.5 Hz, 1H), 3.93 (s, 3H), 3.10 (s, 3H).



#### methyl 2-(mesylamino)-4-anisate (6e)

peach solid; scale: 16.9 mmol; yield: 80% (3.52 g);

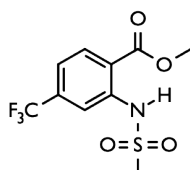
mp: 92.6 - 94.8°C (2°/min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.61 (s, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.28 (d, J = 2.5 Hz, 1H), 6.63 (dd, J = 8.9, 2.5 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.05 (s, 3H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 176 MHz)  $\delta$  168.4, 164.9, 143.1, 133.2, 109.5, 108.4, 103.1, 55.8, 52.3, 40.0.

IR  $\nu_{max}$ : 3150, 3012, 2962, 2840, 1687, 1614, 1576, 1510, 1428, 1398, 1323, 1264, 1143, 1094, 1038, 969, 860, 768, 614 cm<sup>-1</sup>.

HRMS (ESI-TOF) calculated for C<sub>10</sub>H<sub>13</sub>NO<sub>5</sub>S, (M + H)<sup>+</sup> = 260.0593, found: 260.0595.



#### methyl 2-(mesylamino)-4-(trifluoromethyl)benzoate (6f)

yellow solid; scale: 25 mmol; yield: 93% (6.90 g);

mp: 86.7 - 89.7°C (2°/min)

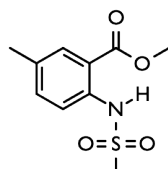
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.56 (s, 1H), 8.18 (d, J = 8.3 Hz, 1H), 8.03 - 8.00 (m, 1H), 7.36 (dd, J = 8.4, 1.1 Hz, 1H), 3.98 (s, 3H), 3.11 (s, 3H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz)  $\delta$  167.6, 141.4, 136.4 (q, J = 33.0 Hz), 132.5, 124.5 (q, J = 273.3 Hz), 119.3 (q, J = 3.7 Hz), 118.0, 114.9 (q, J = 3.9 Hz), 53.2, 40.6.

<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -64.56.

IR  $\nu_{max}$ : 3168, 3099, 3032, 2960, 2852, 1698, 1583, 1508, 1437, 1402, 1324, 1248, 1160, 1124, 1093, 973, 943, 889, 783, 760, 703, 516, 498 cm<sup>-1</sup>.

HRMS (ESI-TOF) calculated for C<sub>10</sub>H<sub>10</sub>F<sub>3</sub>NO<sub>4</sub>S, (M + H)<sup>+</sup> = 298.0361, found: 298.0364.

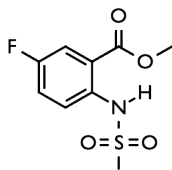


#### methyl 2-(mesylamino)-5-methylbenzoate (6g)

brown solid; scale: 22.4 mmol; yield: 85% (4.67 g);

Known compound - characterisation in agreement with literature.<sup>17</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.22 (s, 1H), 7.88 - 7.84 (m, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.37 (ddt, J = 8.5, 2.2, 0.6 Hz, 1H), 3.93 (s, 3H), 3.01 (s, 3H), 2.34 (s, 3H).



**methyl 5-fluoro-2-(mesylamino)benzoate (6h)**

brown solid; scale: 15.8 mmol; yield: 88% (3.45 g);

**mp:** 93.0 - 94.7°C (2°/min)

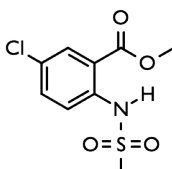
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.77 - 7.73 (m, 2H), 7.29 (dddd, J = 9.1, 7.4, 3.1, 0.3 Hz, 1H), 3.96 (s, 3H), 3.02 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  167.5, 158.2 (d, J = 244.5 Hz), 137.2 (d, J = 2.9 Hz), 122.3 (d, J = 22.8 Hz), 121.1 (d, J = 7.4 Hz), 117.8 (d, J = 24.4 Hz), 117.4 (d, J = 7.3 Hz), 53.0, 40.1.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -119.33 (ddd, J = 9.5, 7.3, 4.5 Hz).

**IR**  $\nu_{max}$ : 3151, 3094, 3019, 2957, 2936, 1689, 1493, 1442, 1391, 1314, 1226, 1151, 1134, 1072, 975, 837, 759 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>9</sub>H<sub>10</sub>FN<sub>2</sub>O<sub>4</sub>S, (M + H)<sup>+</sup> = 248.0393, found: 248.0396.

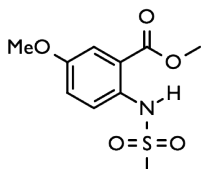


**methyl 5-chloro-2-(mesylamino)benzoate (6i)**

yellow solid; scale: 16.2 mmol; yield: 94% (3.99 g);

Known compound - characterisation in agreement with literature.<sup>18</sup>

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.34 (s, 1H), 8.04 (dd, J = 2.6, 0.3 Hz, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.52 (ddd, J = 9.0, 2.6, 0.3 Hz, 1H), 3.95 (s, 3H), 3.06 (s, 3H).



**methyl 2-(mesylamino)-5-anisate (6j)**

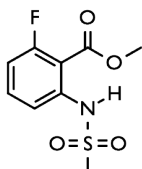
dark brown liquid; scale: 20 mmol; yield: 79% (4.02 g);

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  9.88 (s, 1H), 7.68 (d, J = 9.0 Hz, 1H), 7.54 (d, J = 3.1 Hz, 1H), 7.13 (dd, J = 9.0, 3.1 Hz, 1H), 3.95 (s, 3H), 3.83 (s, 3H), 2.96 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  168.1, 155.8, 134.1, 121.8, 121.6, 117.7, 115.5, 55.9, 52.8, 39.7.

**IR**  $\nu_{max}$ : 3209, 3012, 2955, 2933, 2840, 1687, 1612, 1586, 1497, 1436, 1394, 1330, 1228, 1145, 1078, 1035, 964, 774 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>10</sub>H<sub>13</sub>NO<sub>5</sub>S, (M + H)<sup>+</sup> = 260.0593, found: 260.0598.



**methyl 2-fluoro-6-(mesylamino)benzoate (6k)**

yellow solid; scale: 18 mmol; yield: 79% (3.51 g);

**mp:** 95.7 - 98.4°C (2°/min)

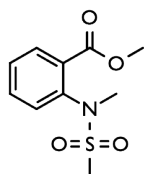
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  10.06 (s, 1H), 7.53 (dt, J = 8.5, 1.0 Hz, 1H), 7.49 (td, J = 8.3, 5.6 Hz, 1H), 6.88 (ddd, J = 10.7, 8.2, 1.2 Hz, 1H), 3.98 (s, 3H), 3.07 (s, 3H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 176 MHz) δ 167.2 (d, J = 4.0 Hz), 162.9 (d, J = 261.4 Hz), 141.6 (d, J = 3.8 Hz), 135.0 (d, J = 11.4 Hz), 114.4 (d, J = 3.3 Hz), 111.7 (d, J = 23.8 Hz), 106.9 (d, J = 13.6 Hz), 53.1, 40.3.

<sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz) δ -103.96 (dd, J = 10.8, 5.3 Hz).

IR ν<sub>max</sub>: 3182, 3058, 2961, 2940, 2857, 1685, 1616, 1578, 1469, 1397, 1326, 1307, 1256, 1242, 1156, 1033, 966, 878, 804 cm<sup>-1</sup>.

HRMS (ESI-TOF) calculated for C<sub>9</sub>H<sub>10</sub>FNO<sub>4</sub>S, (M + H)<sup>+</sup> = 248.0393, found: 248.0396.

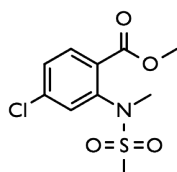


**methyl 2-(*N*-mesyl-*N*-methylamino)benzoate (7a)**

beige solid; scale: 43.6 mmol; yield: 64% (6.83 g).

Known compound - characterisation in agreement with literature.<sup>2</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 7.91 (ddd, J = 7.8, 1.7, 0.4 Hz, 1H), 7.56 (td, J = 7.4, 1.7 Hz, 1H), 7.45 (ddd, J = 8.0, 1.3, 0.4 Hz, 1H), 7.41 (ddd, J = 7.8, 7.4, 1.3 Hz, 1H), 3.92 (s, 3H), 3.31 (s, 3H), 2.97 (s, 3H).

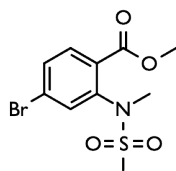


**methyl 2-(*N*-mesyl-*N*-methylamino)-4-chlorobenzoate (7b)**

orange liquid; scale: 3.8 mmol; yield: 100% (1.05 g)

Known compound - characterisation in agreement with literature.<sup>19</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.87 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 7.39 (dd, J = 8.4, 2.1 Hz, 1H), 3.92 (s, 3H), 3.29 (s, 3H), 2.99 (s, 3H).

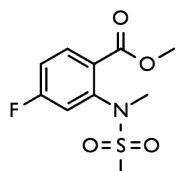


**methyl 2-(*N*-mesyl-*N*-methylamino)-4-bromobenzoate (7c)**

orange liquid; scale: 2 mmol; yield: 95% (0.62 g);

Known compound - characterisation in agreement with literature.<sup>20</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 7.79 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 1.9 Hz, 1H), 7.55 (dd, J = 8.4, 1.9 Hz, 1H), 3.91 (s, 3H), 3.29 (s, 3H), 2.99 (s, 3H).

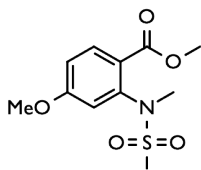


**methyl 2-(*N*-mesyl-*N*-methylamino)-4-fluorobenzoate (7d)**

orange solid; scale: 4 mmol; yield: 97% (1.03 g);

Known compound - characterisation in agreement with literature.<sup>20</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 700 MHz) δ 7.96 (dd, J = 8.8, 6.4 Hz, 1H), 7.19 (dd, J = 9.2, 2.6 Hz, 1H), 7.11 (ddd, J = 8.8, 7.4, 2.6 Hz, 1H), 3.91 (s, 3H), 3.29 (s, 3H), 2.99 (s, 3H).



**methyl 2-(*N*-mesyl-*N*-methylamino)-4-anisate (7e)**

dark orange solid; scale: 3.9 mmol; yield: 94% (1.00 g);

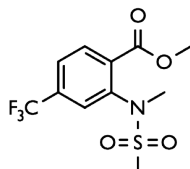
**mp:** 77.6 - 81.4°C (2°/min)

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.94 (d, *J* = 8.8 Hz, 1H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.90 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.29 (s, 3H), 2.99 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  165.8, 163.3, 142.9, 133.5, 121.6, 117.4, 114.0, 55.9, 52.2, 39.2, 38.9.

**IR**  $\nu_{max}$ : 3065, 3013, 2965, 2937, 2843, 1718, 1682, 1602, 1435, 1331, 1254, 1221, 1138, 1103, 1029, 969, 942, 845, 755 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>11</sub>H<sub>15</sub>NO<sub>5</sub>S, (*M* + *H*)<sup>+</sup> = 274.0749, found: 274.0751.

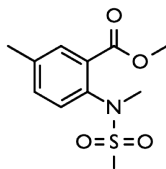


**methyl 2-(*N*-mesyl-*N*-methylamino)-4-(trifluoromethyl)benzoate (7f)**

orange liquid; scale: 5 mmol; yield: 91% (1.42 g);

Known compound - characterisation in agreement with literature.<sup>14</sup>

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  8.00 (ddd, *J* = 8.1, 0.8, 0.4 Hz, 1H), 7.69 (dd, *J* = 1.2, 0.6 Hz, 1H), 7.66 (ddd, *J* = 8.1, 1.8, 0.7 Hz, 1H), 3.96 (s, 3H), 3.33 (s, 3H), 3.00 (s, 3H).

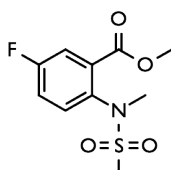


**methyl 2-(*N*-mesyl-*N*-methylamino)-5-methylbenzoate (7g)**

dark orange solid; scale: 4.1 mmol; yield: 99% (1.05 g);

Known compound - characterisation in agreement with literature.<sup>17</sup>

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.71 (dt, *J* = 2.1, 0.7 Hz, 1H), 7.35 (ddd, *J* = 8.1, 2.2, 0.7 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 3.91 (s, 3H), 3.29 (s, 3H), 2.95 (s, 3H), 2.39 (s, 3H).



**methyl 2-(*N*-mesyl-*N*-methylamino)-5-fluorobenzoate (7h)**

dark orange solid; scale: 4 mmol; yield: 98% (1.04 g);

**mp:** 65.1 - 66.7°C (2°/min)

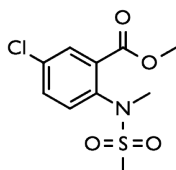
**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.61 (dd, *J* = 8.6, 3.0 Hz, 1H), 7.44 (dd, *J* = 8.7, 5.0 Hz, 1H), 7.25 (ddd, *J* = 8.8, 7.4, 3.2 Hz, 1H), 3.93 (s, 3H), 3.29 (s, 3H), 2.97 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  165.4, 161.8 (d, *J* = 251.0 Hz), 137.0 (d, *J* = 3.7 Hz), 133.4 (d, *J* = 8.7 Hz), 132.3 (d, *J* = 8.2 Hz), 120.2 (d, *J* = 22.4 Hz), 118.7 (d, *J* = 24.6 Hz), 53.0, 39.2, 39.2.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -112.37 - -112.49 (m).

**IR**  $\nu_{max}$ : 3082, 3024, 3002, 2951, 2848, 1729, 1492, 1442, 1330, 1252, 1202, 1143, 1060, 978, 888, 768 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>10</sub>H<sub>12</sub>FNO<sub>4</sub>S, (M + H)<sup>+</sup> = 262.0549, found: 262.0555.

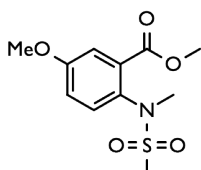


**methyl 2-(*N*-mesyl-*N*-methylamino)-5-chlorobenzoate (7i)**

dark orange solid; scale: 4.5 mmol; yield: 98% (1.21 g);

Known compound - characterisation in agreement with literature.<sup>14</sup>

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.89 (dd, *J* = 2.6, 0.3 Hz, 1H), 7.51 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.40 (dd, *J* = 8.5, 0.3 Hz, 1H), 3.93 (s, 3H), 3.28 (s, 3H), 2.97 (s, 3H).



**methyl 2-(*N*-mesyl-*N*-methylamino)-5-anisate (7j)**

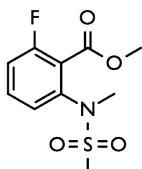
dark orange liquid; scale: 3.8 mmol; yield: 96% (1.0 g);

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.39 (d, *J* = 3.1 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.06 (dd, *J* = 8.8, 3.1 Hz, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 3.28 (s, 3H), 2.94 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  166.3, 159.1, 133.0, 132.2, 131.4, 118.7, 116.1, 55.8, 52.6, 39.0, 38.6.

**IR**  $\nu_{max}$ : 3012, 2951, 2841, 1725, 1604, 1572, 1498, 1435, 1322, 1287, 1222, 1140, 1092, 1059, 1029, 960, 866, 760 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>11</sub>H<sub>15</sub>NO<sub>5</sub>S, (M + H)<sup>+</sup> = 274.0749, found: 274.0754.



**methyl 2-(*N*-mesyl-*N*-methylamino)-6-fluorobenzoate (7k)**

orange solid; scale: 10 mmol; yield: 95% (2.49 g);

**mp**: 97.3 - 99.0°C (2°/min)

**<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 700 MHz)  $\delta$  7.46 (td, *J* = 8.3, 6.1 Hz, 1H), 7.27 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.15 (td, *J* = 8.7, 0.9 Hz, 1H), 3.96 (s, 3H), 3.27 (s, 3H), 2.97 (s, 3H).

**<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 176 MHz)  $\delta$  164.4, 160.3 (d, *J* = 254.2 Hz), 140.8 (d, *J* = 4.6 Hz), 132.1 (d, *J* = 9.8 Hz), 125.5 (d, *J* = 3.6 Hz), 122.6 (d, *J* = 16.6 Hz), 116.4 (d, *J* = 21.5 Hz), 53.0, 39.1, 38.5.

**<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz)  $\delta$  -112.41 (dd, *J* = 8.8, 6.3 Hz).

**IR**  $\nu_{max}$ : 3021, 2986, 2962, 2941, 2890, 1732, 1611, 1581, 1467, 1328, 1292, 1146, 962, 819, 759, 728, 574 cm<sup>-1</sup>.

**HRMS** (ESI-TOF) calculated for C<sub>10</sub>H<sub>12</sub>FNO<sub>4</sub>S, (M + H)<sup>+</sup> = 262.0549, found: 262.0549.

## 5 NMR Spectra

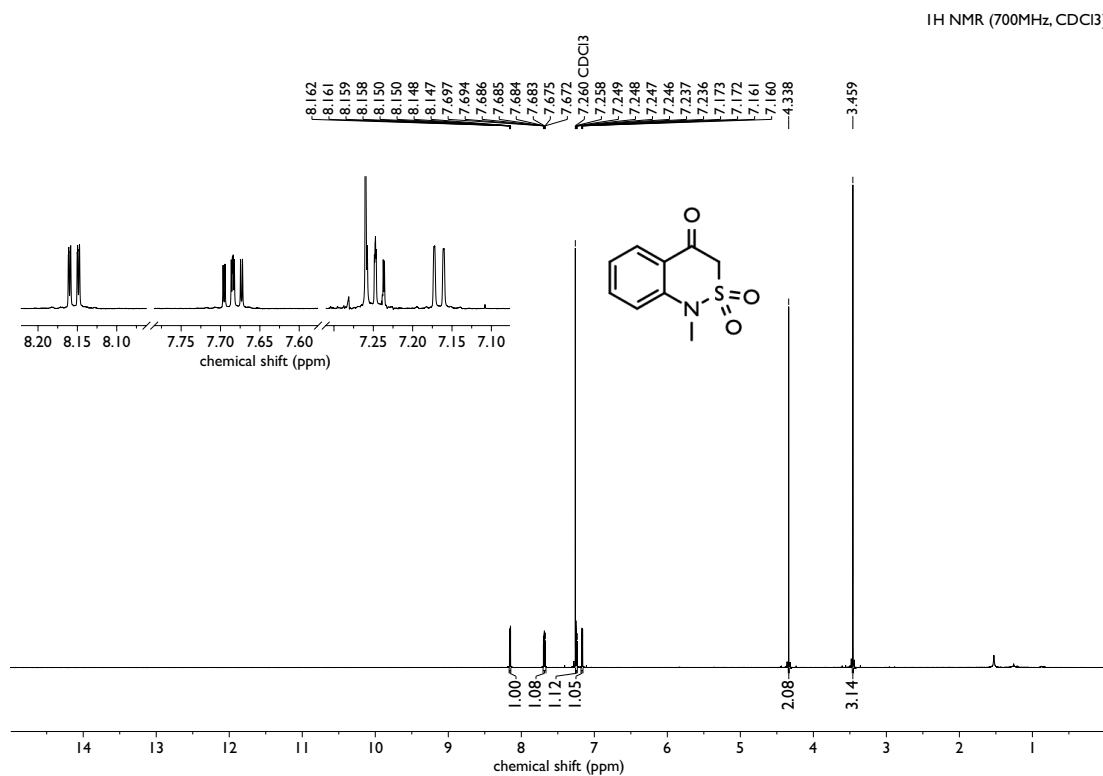


Figure S7: <sup>1</sup>H spectra of compound 1a

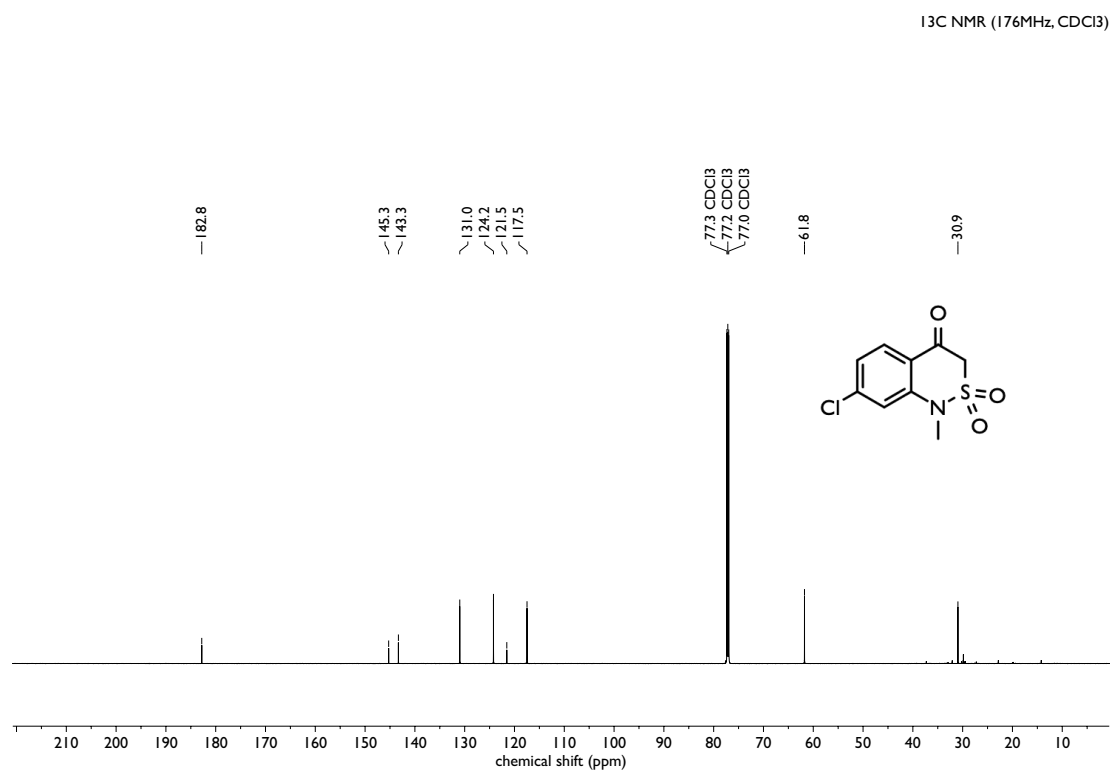


Figure S8: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1b**



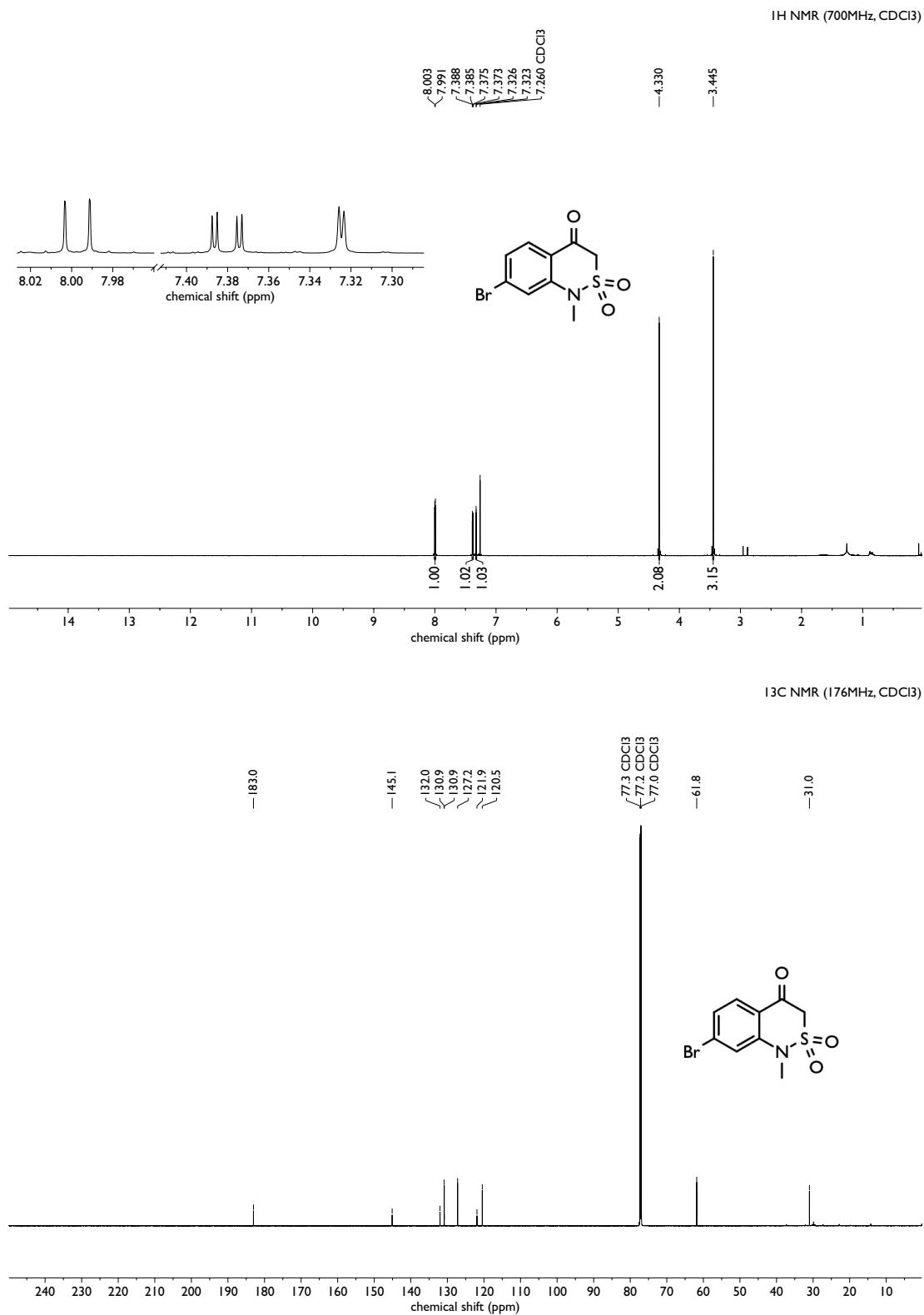


Figure S9: <sup>1</sup>H and <sup>13</sup>C spectra of compound 1c

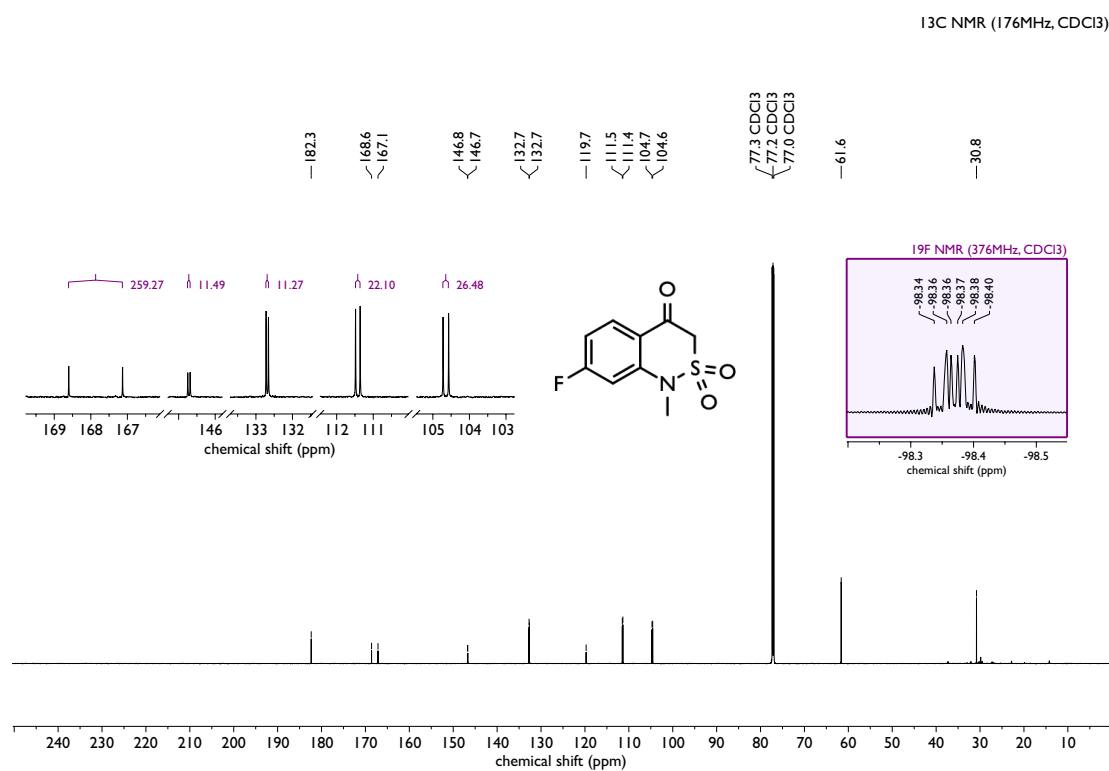
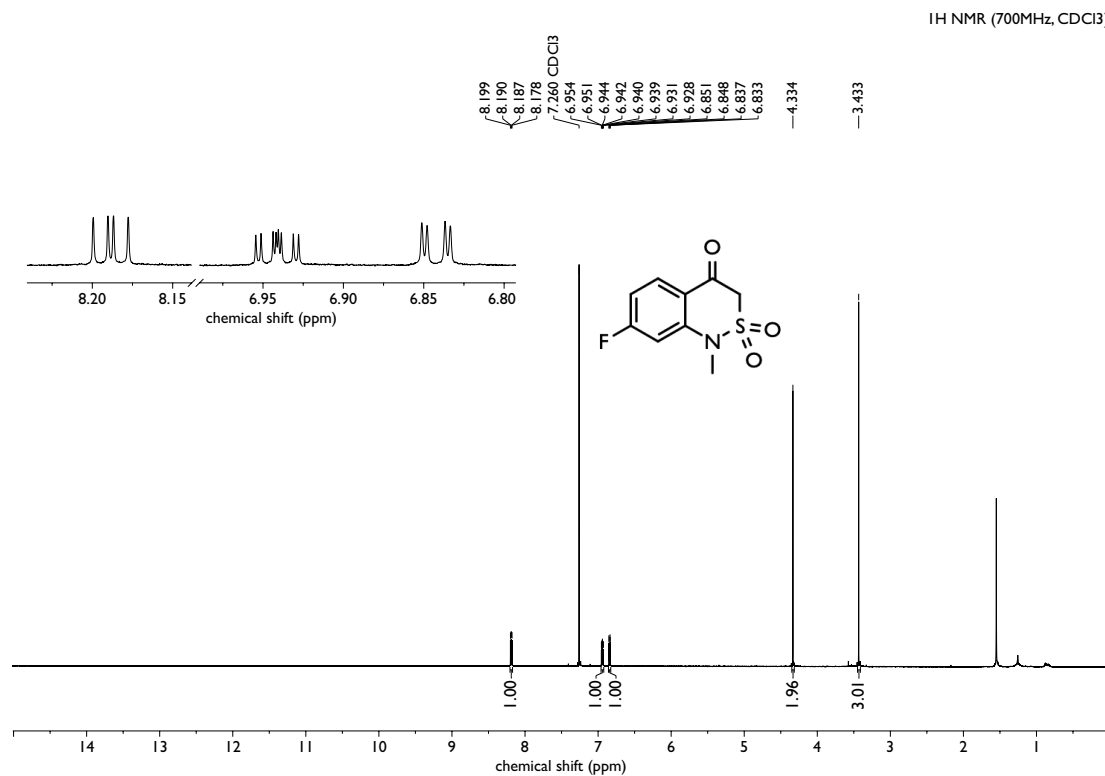


Figure S10: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1d**

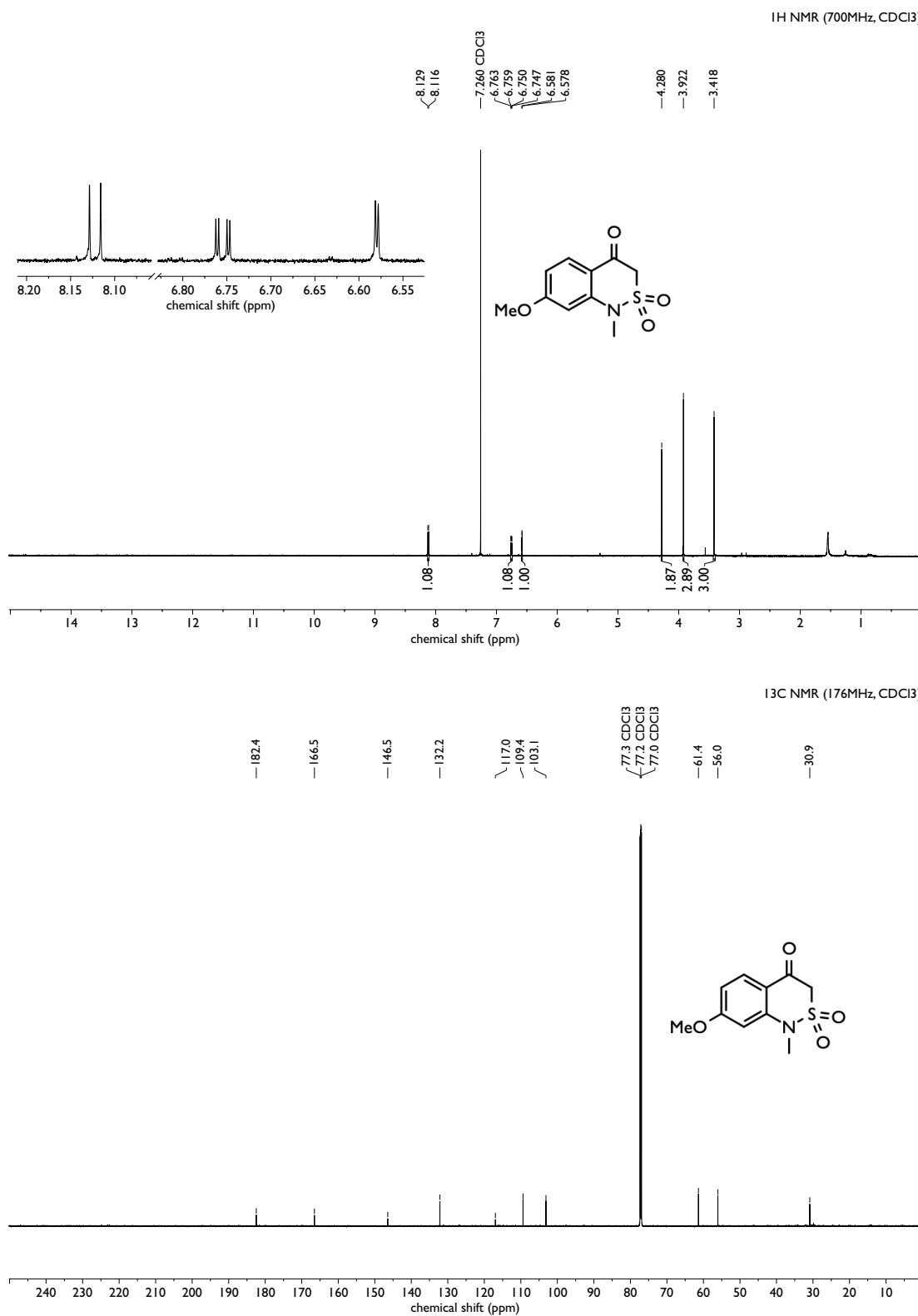


Figure S11: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1e**

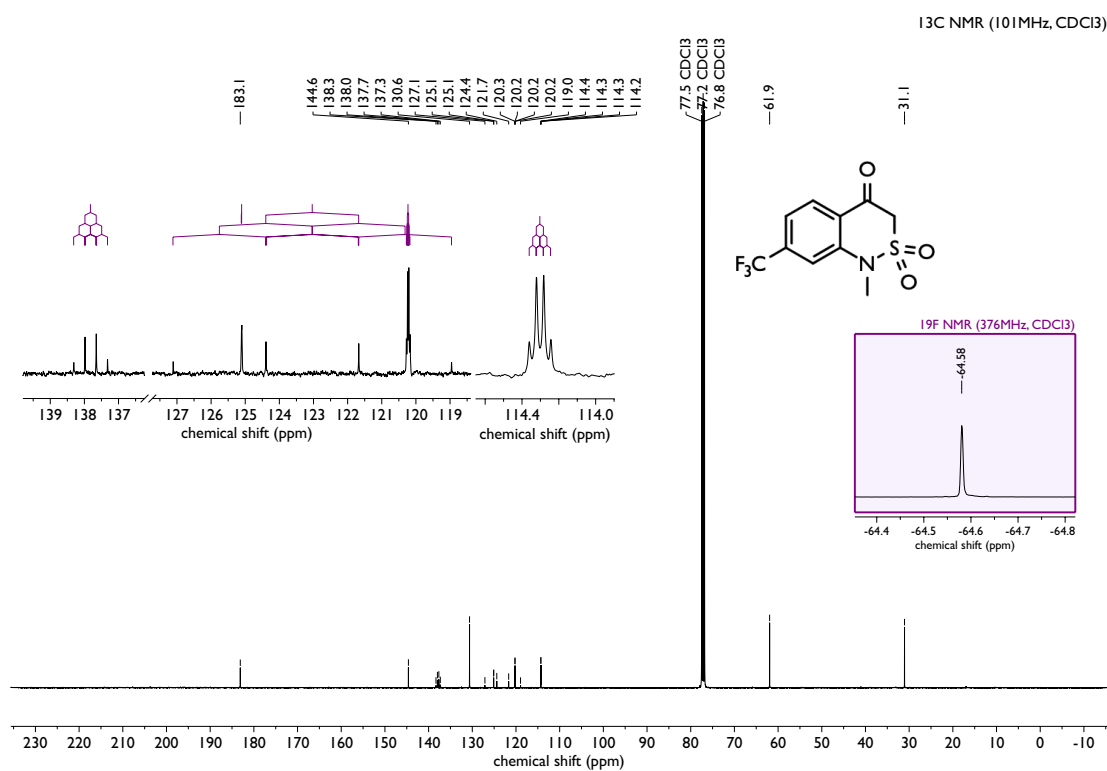
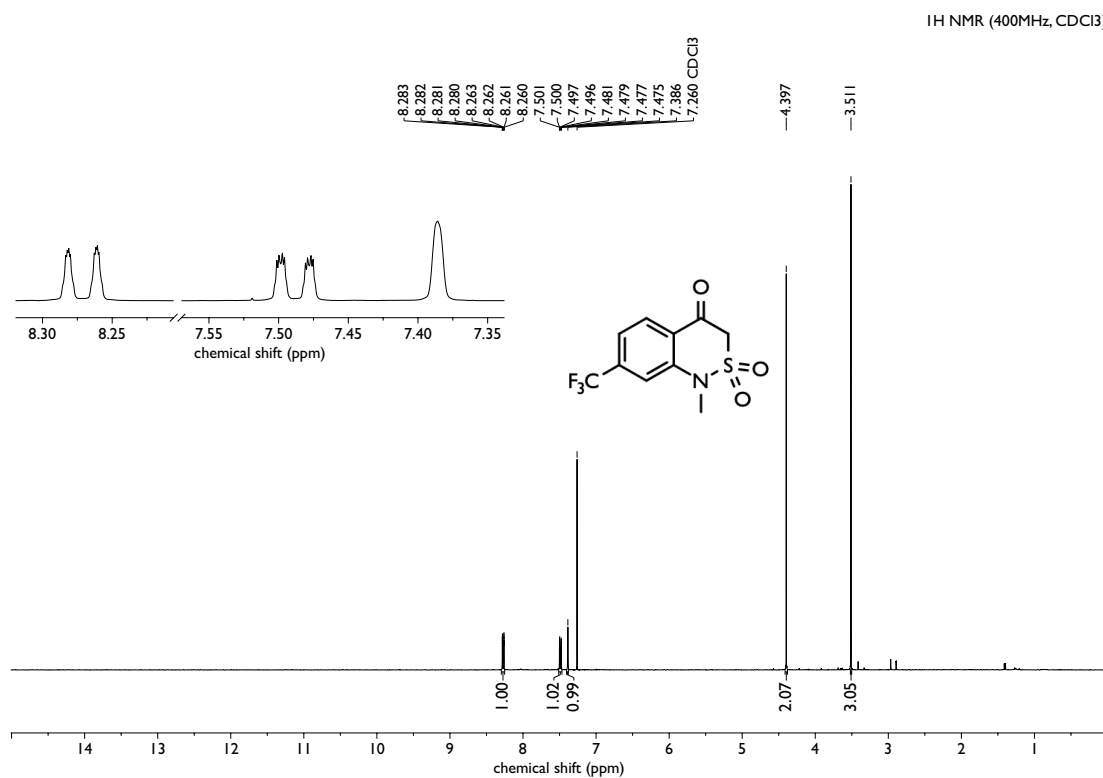


Figure S12: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1f**

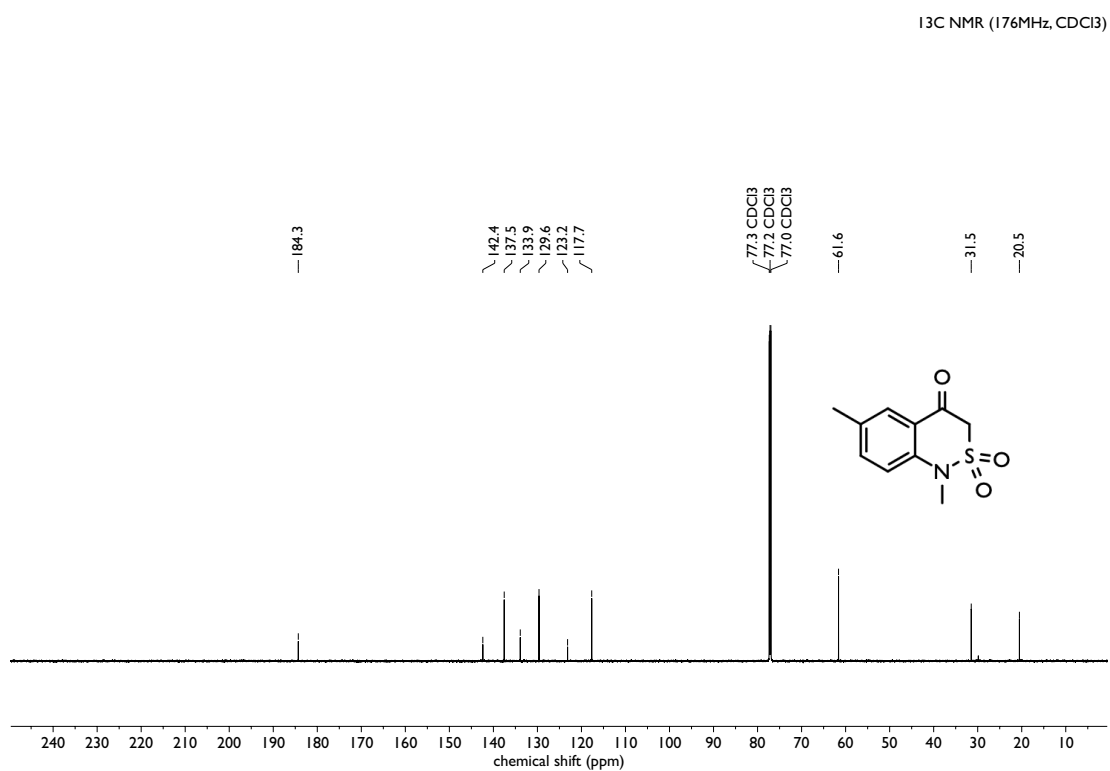
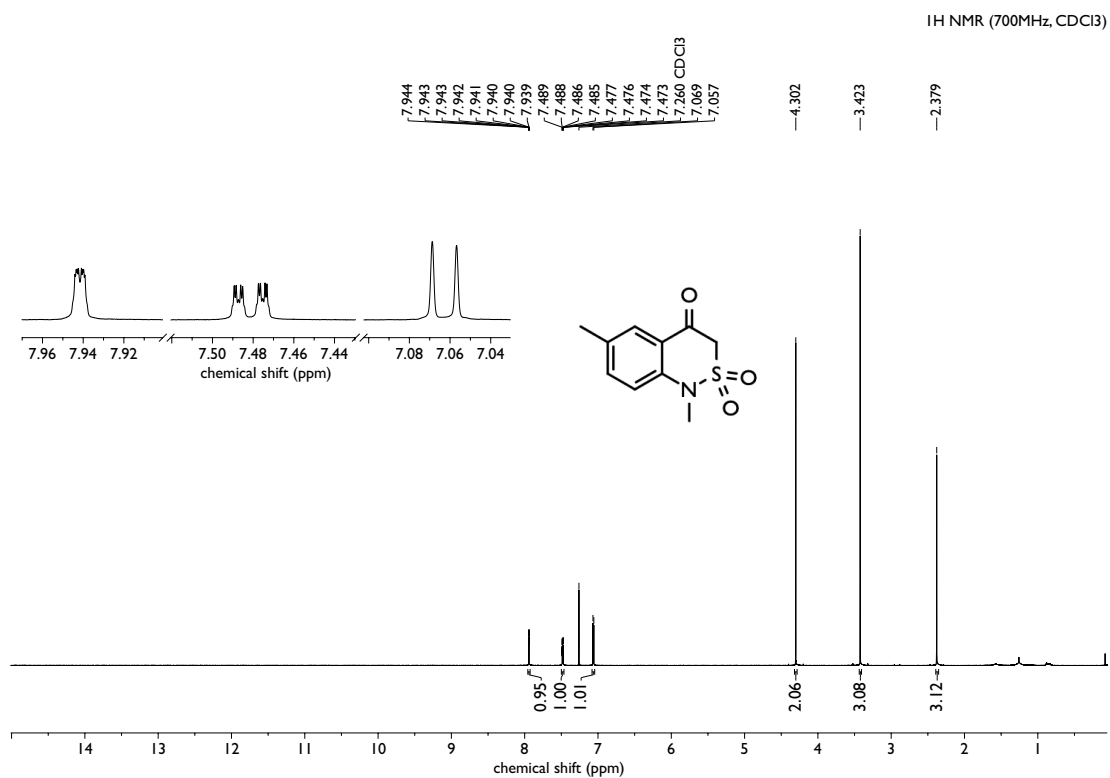


Figure S13: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1g**

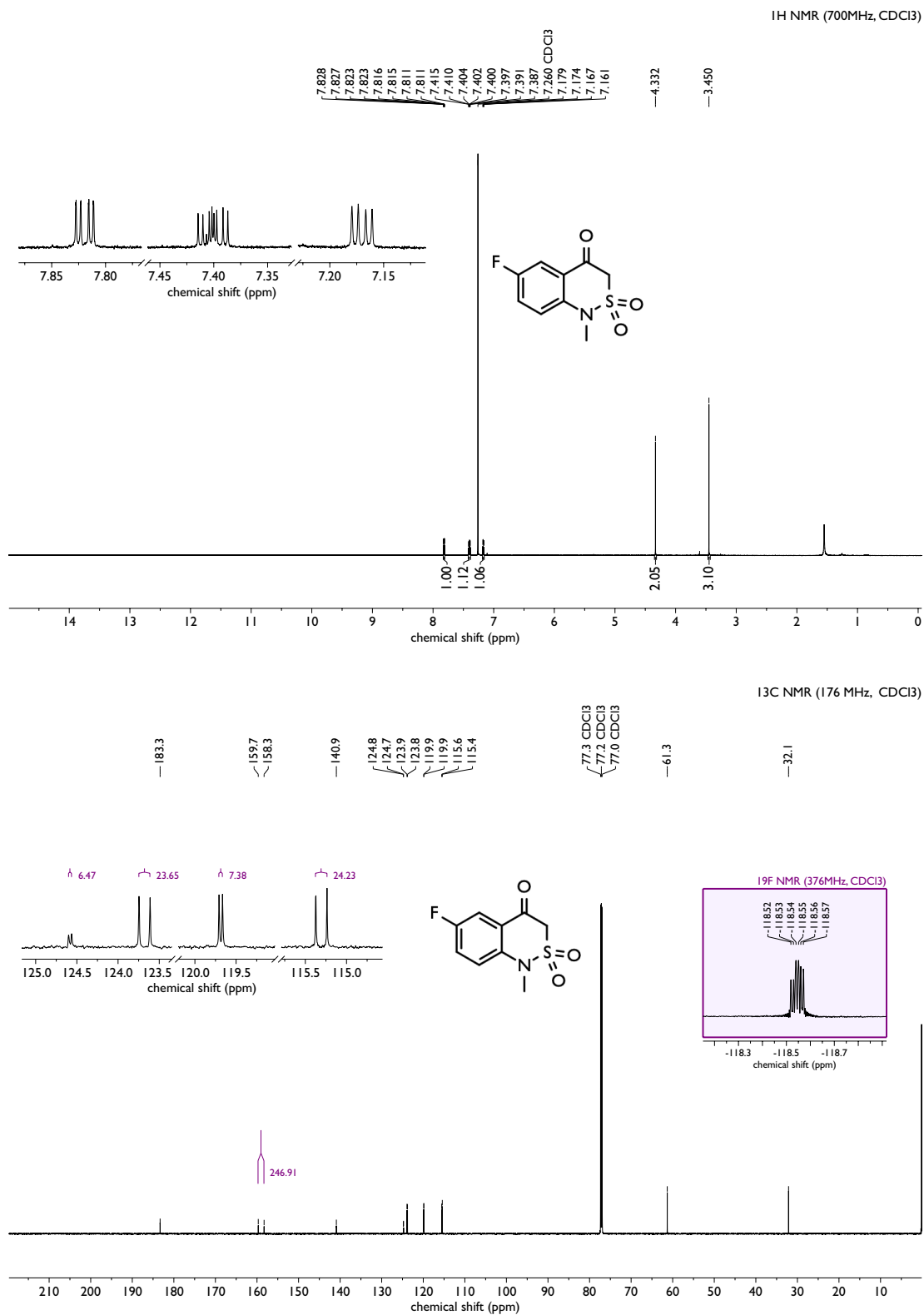


Figure S14: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1h**

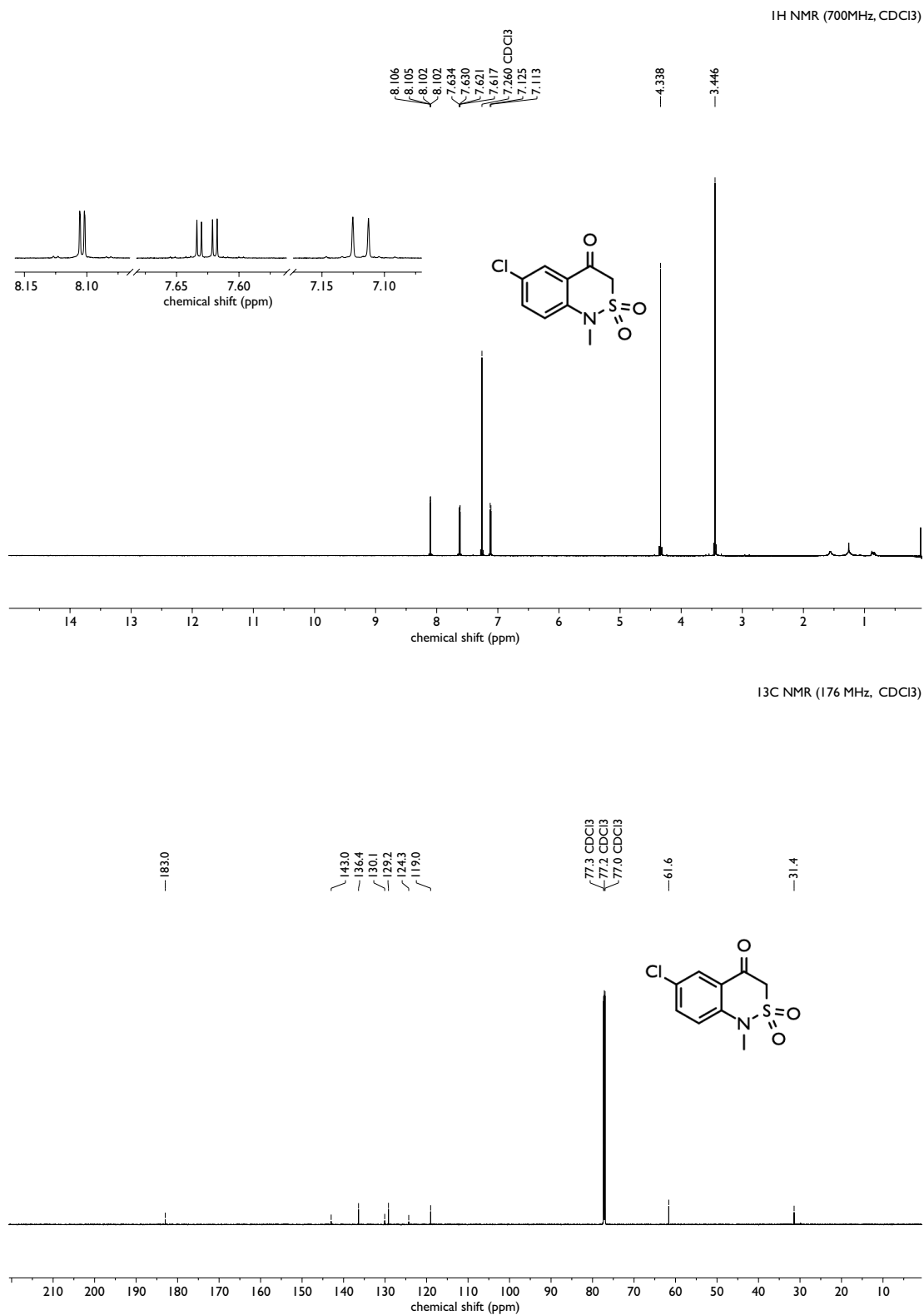


Figure S15: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1i**

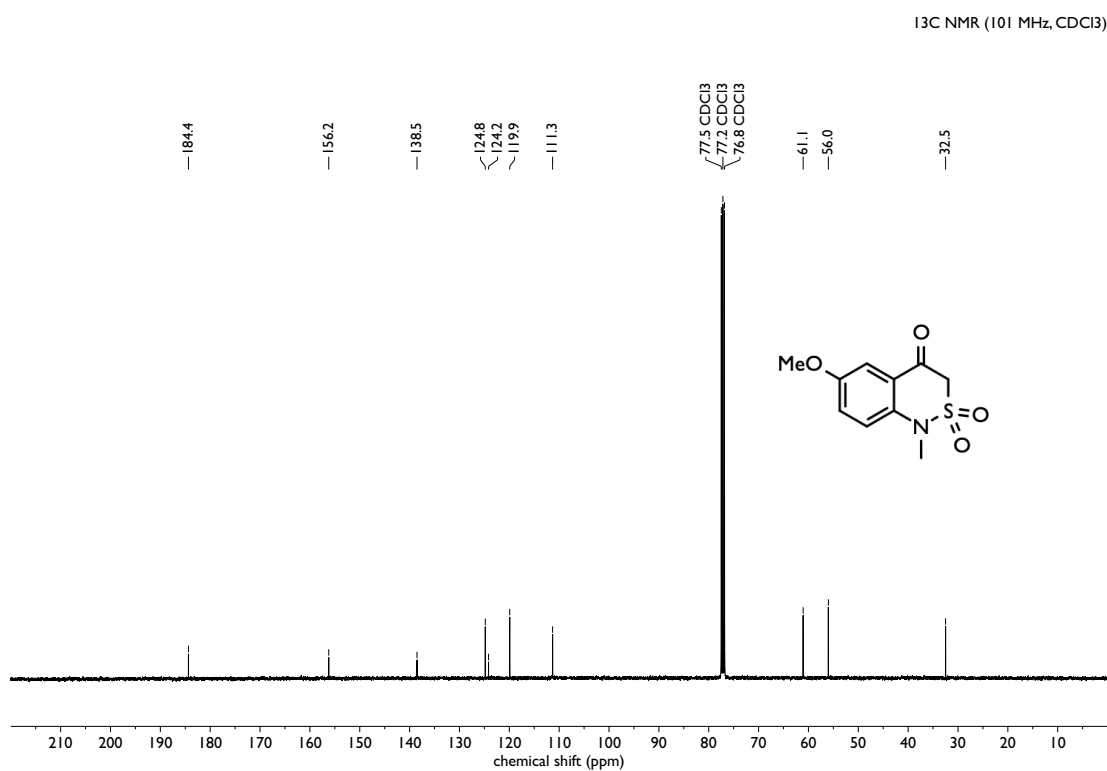
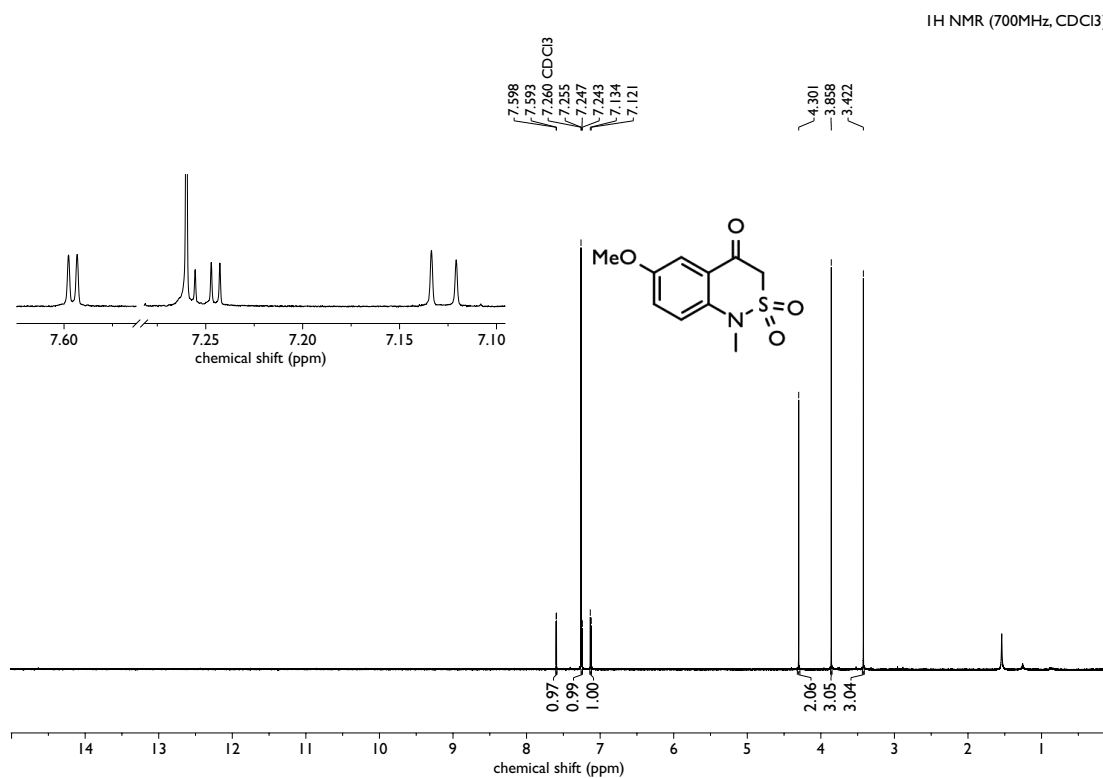


Figure S16: <sup>1</sup>H and <sup>13</sup>C spectra of compound **1j**



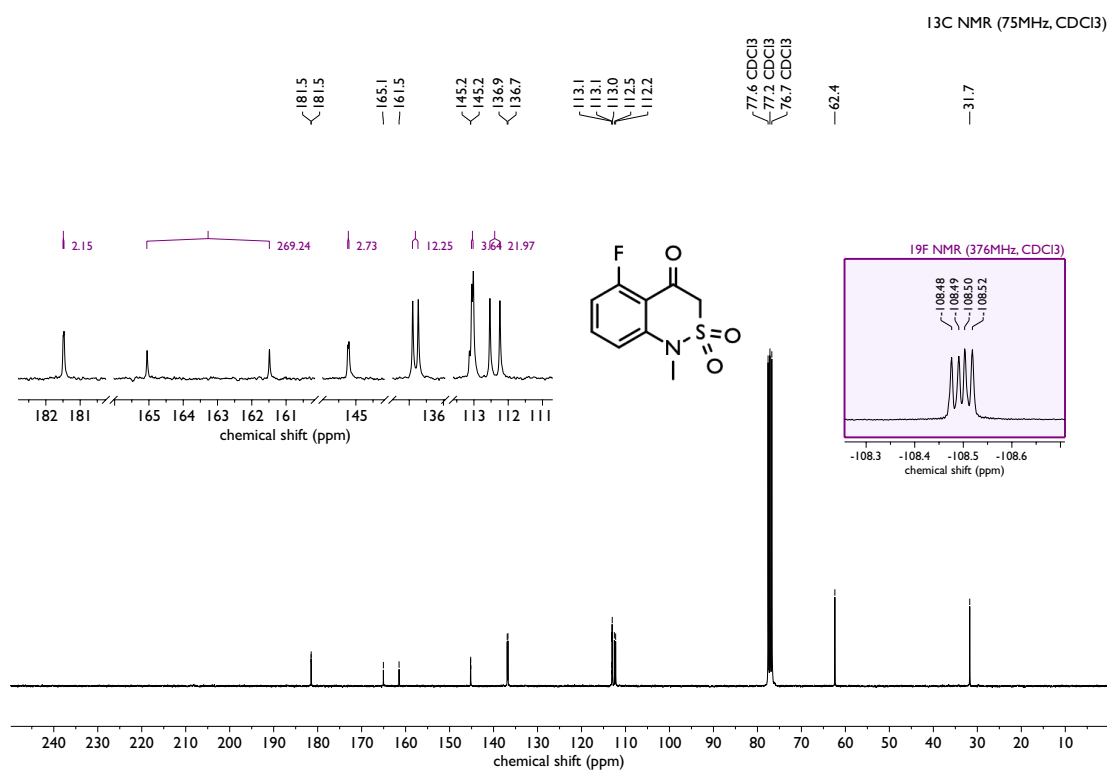
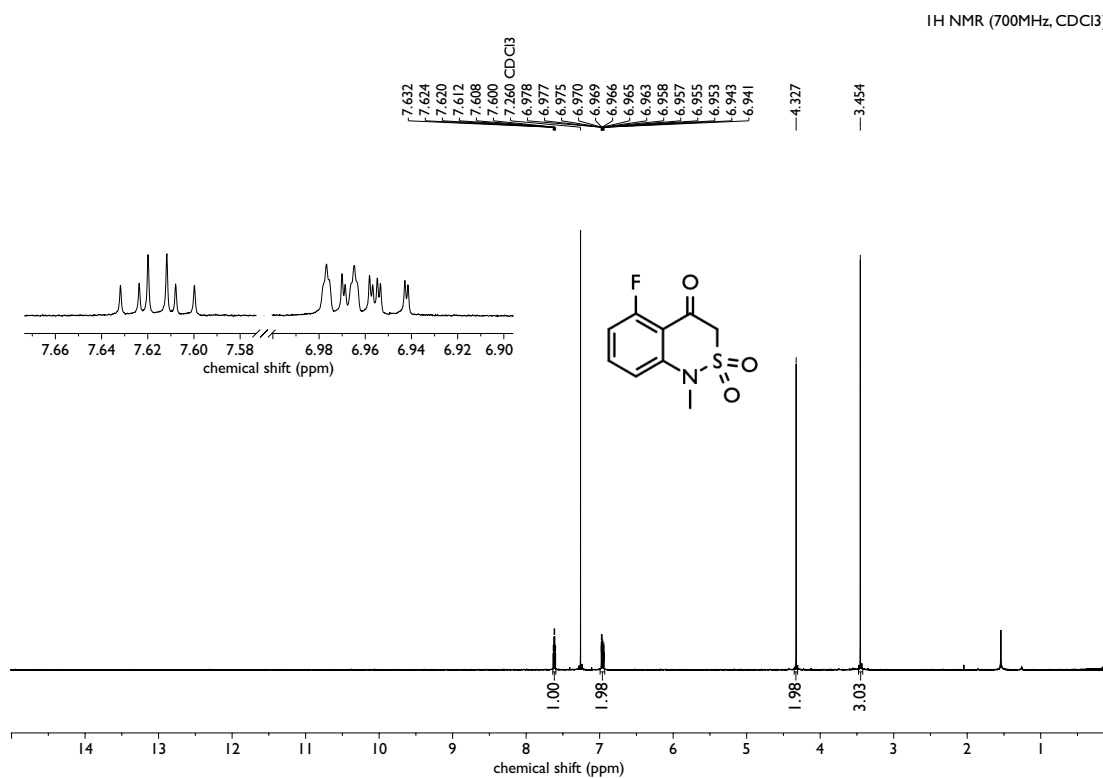


Figure S17: <sup>1</sup>H and <sup>13</sup>C spectra of compound 1k



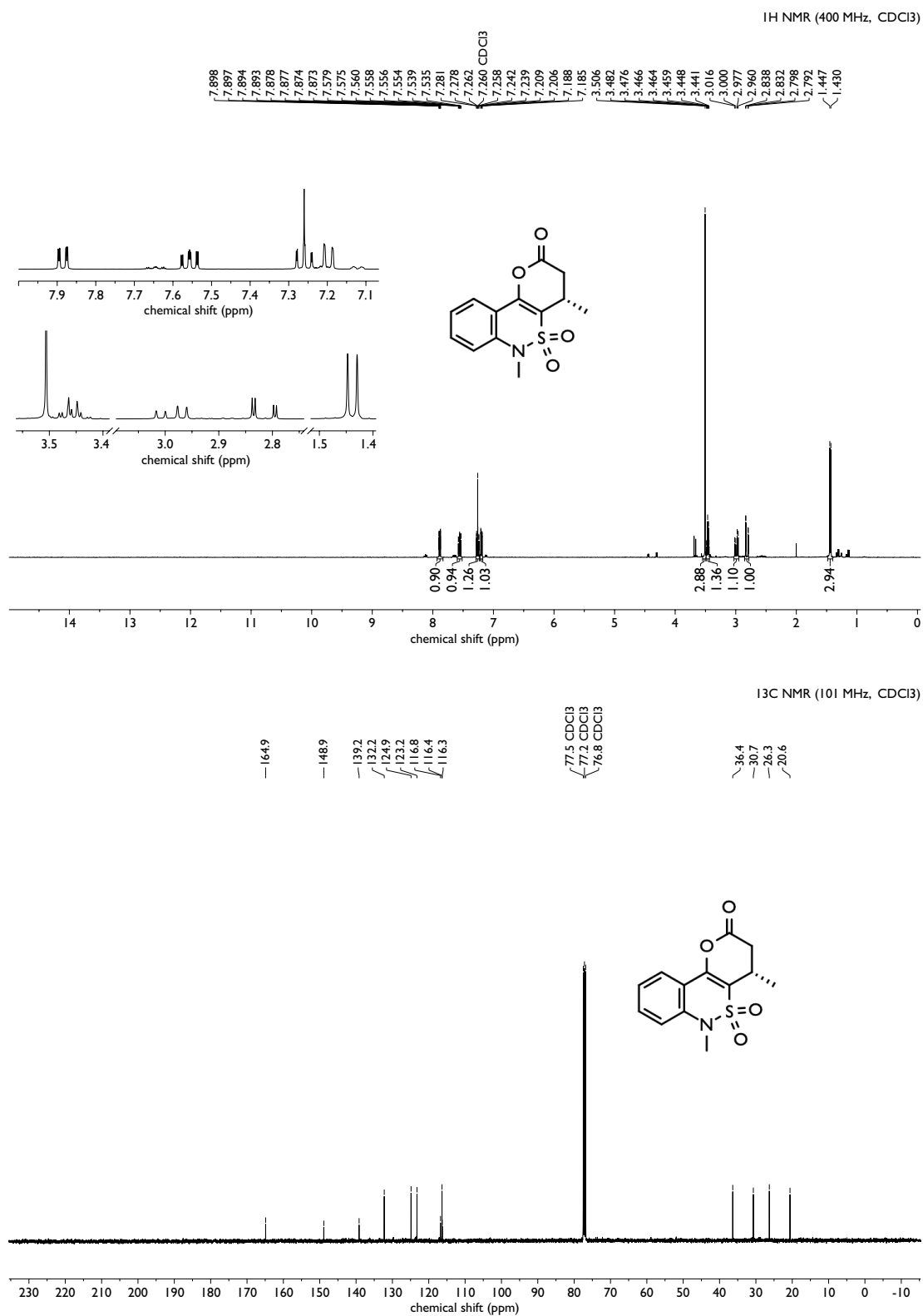


Figure S19: <sup>1</sup>H and <sup>13</sup>C spectra of compound **3m**

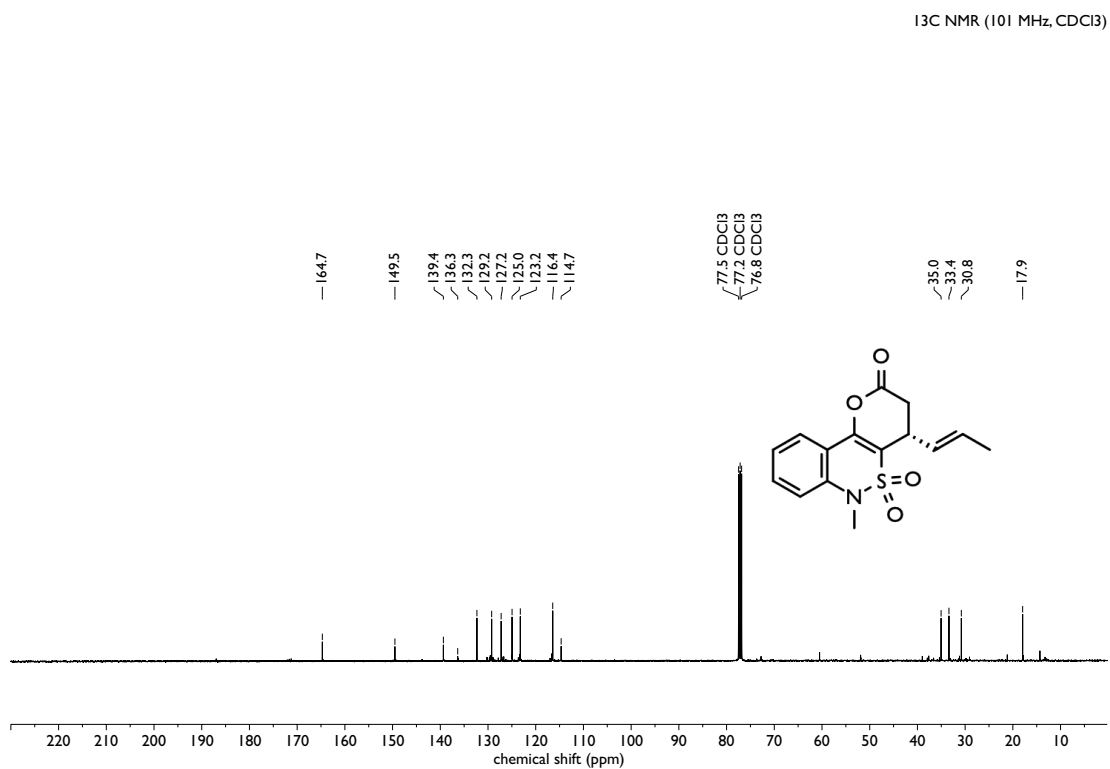
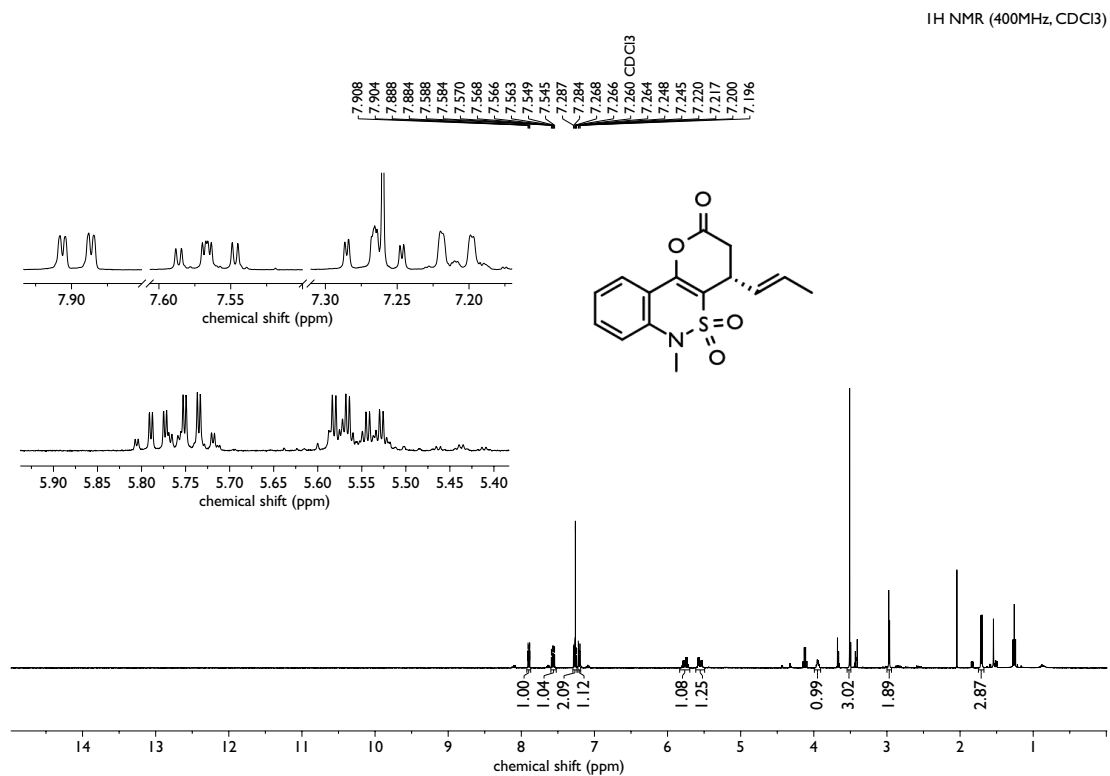


Figure S20: <sup>1</sup>H and <sup>13</sup>C spectra of compound **3q**

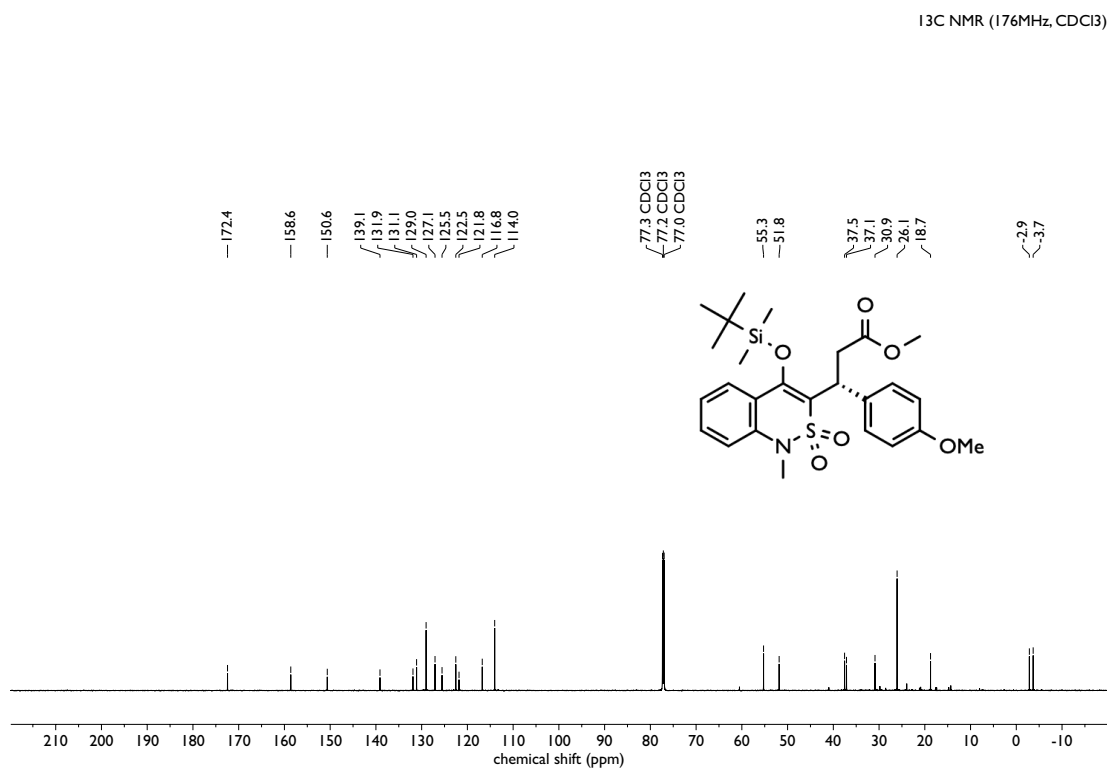
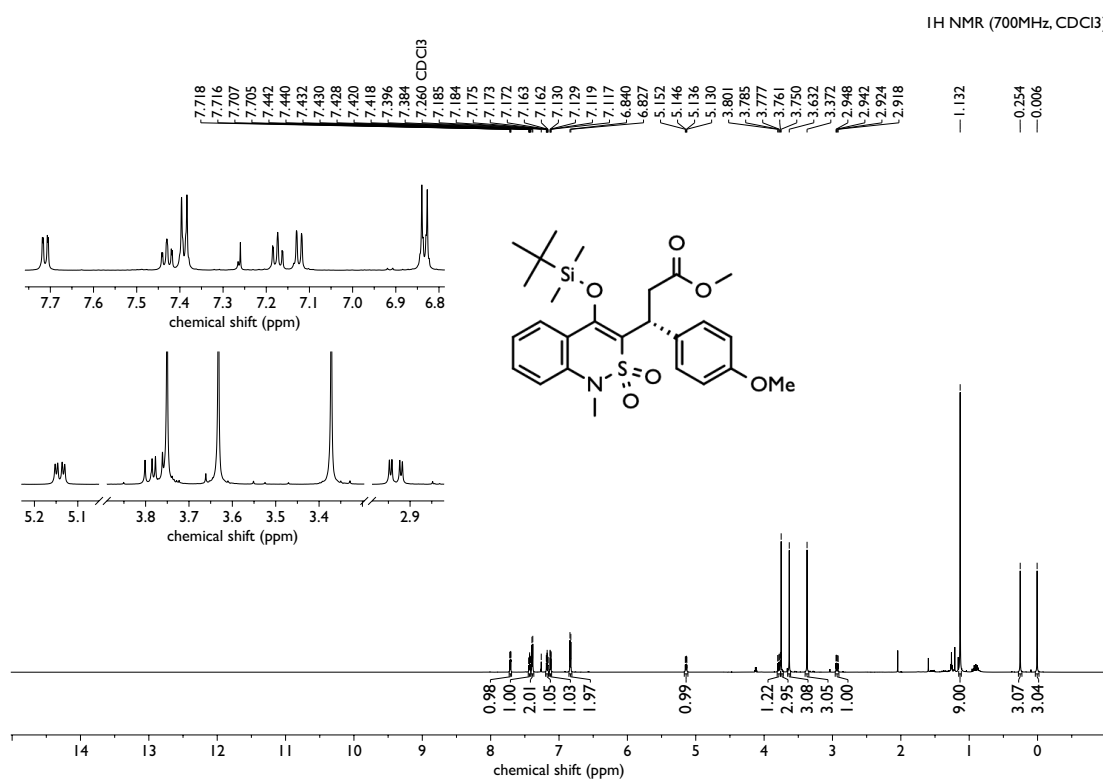


Figure S21: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4a

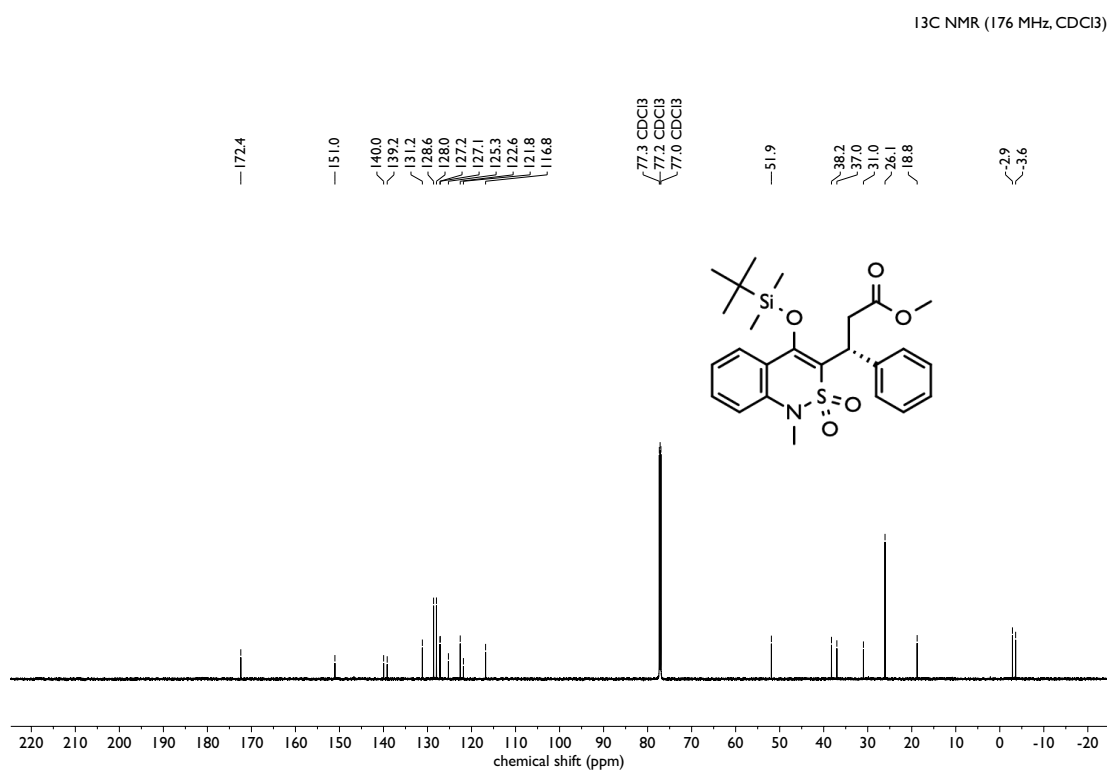
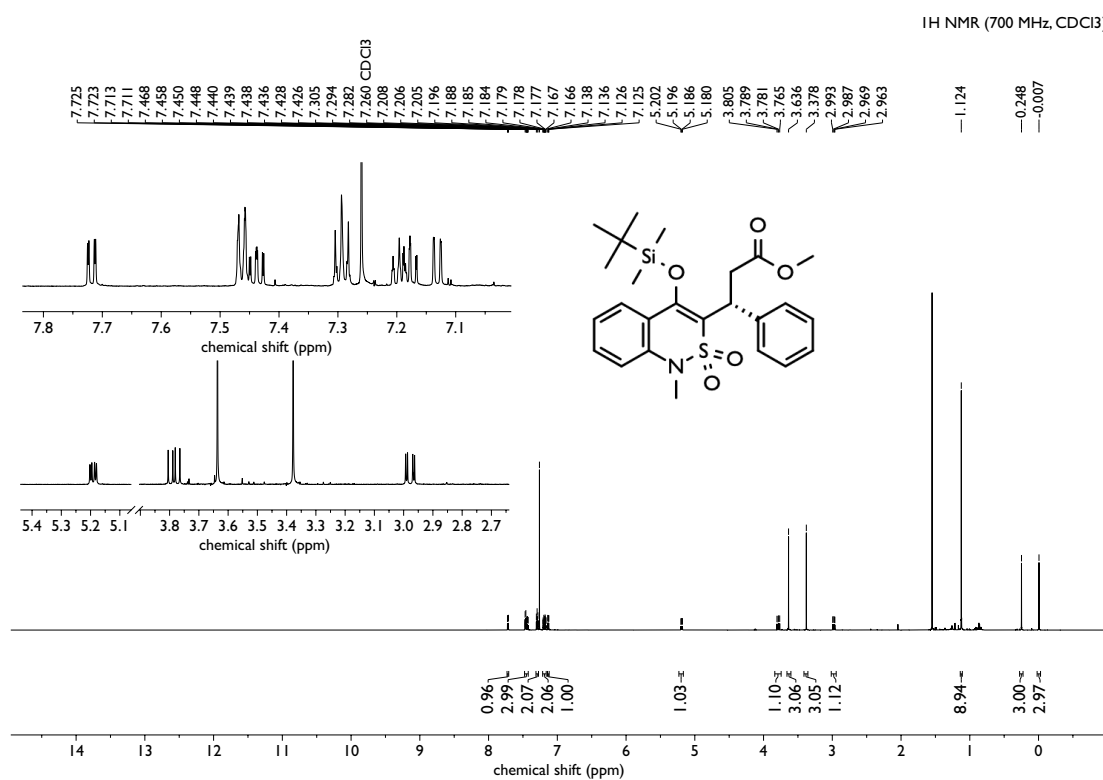


Figure S22: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4b**

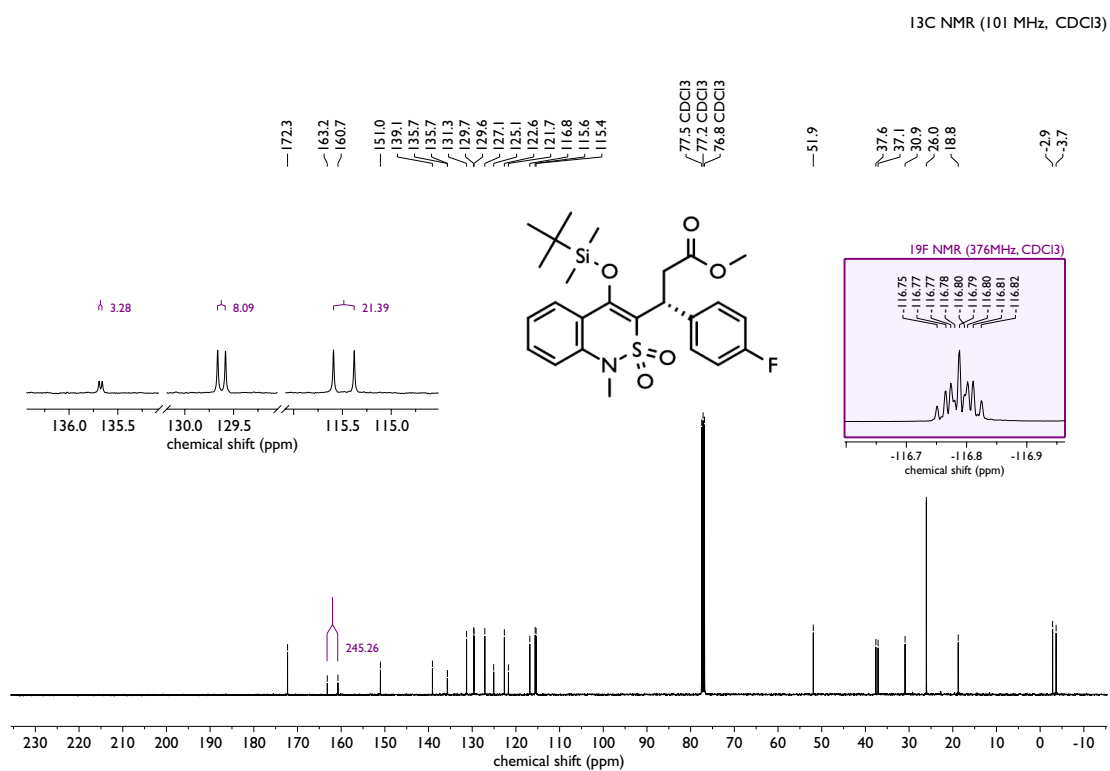
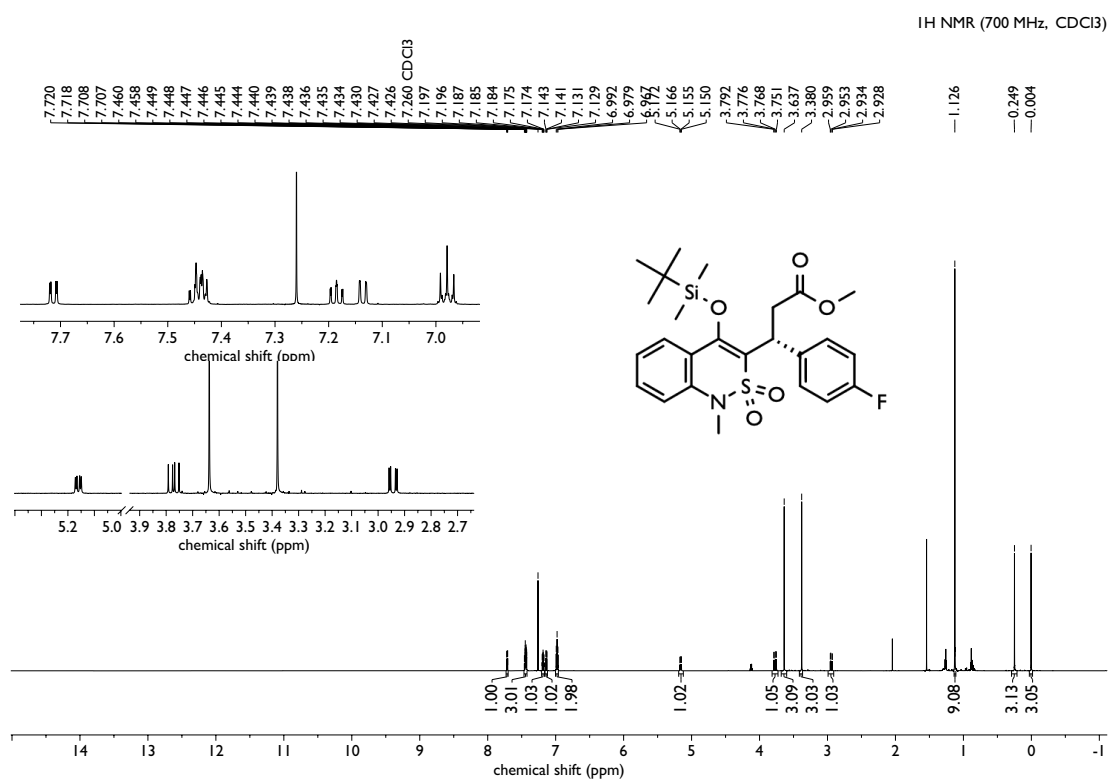


Figure S23: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4c**





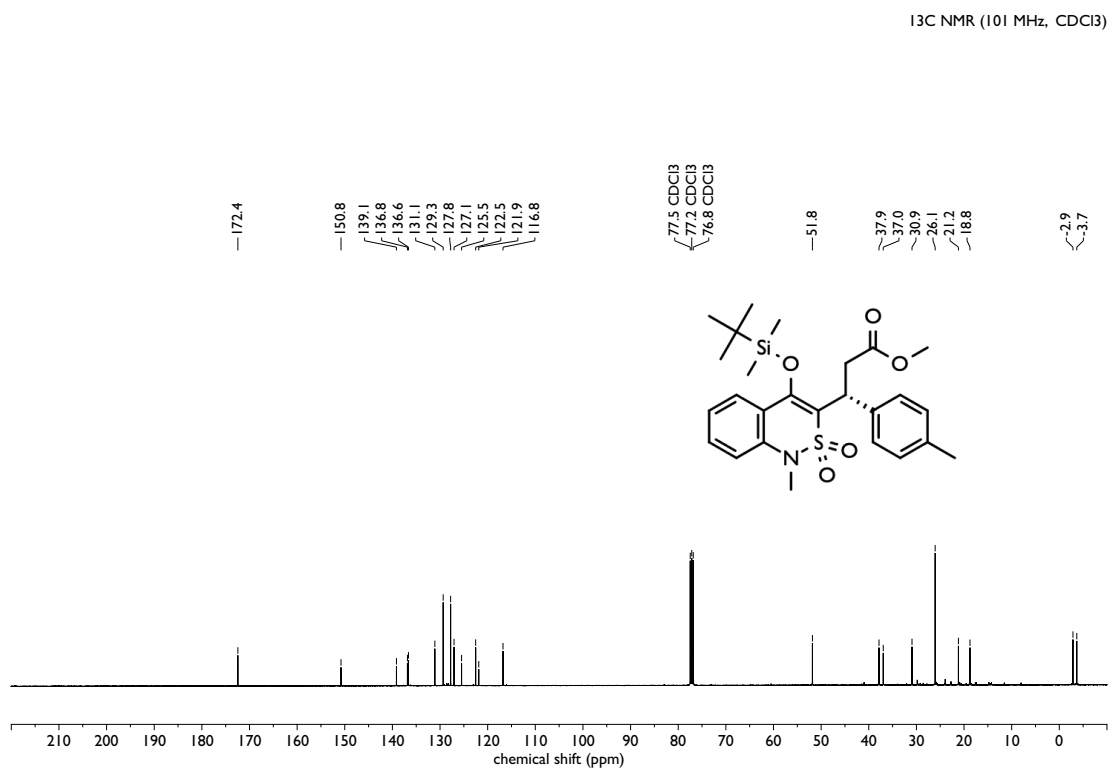
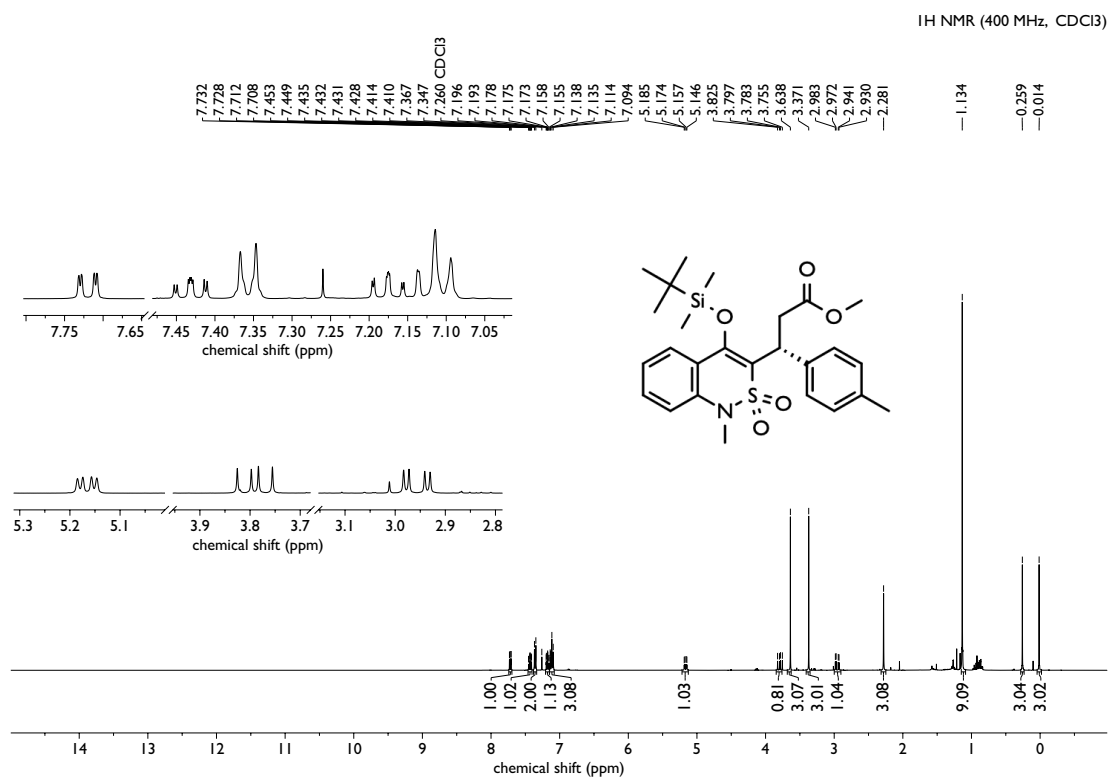


Figure S25: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4e



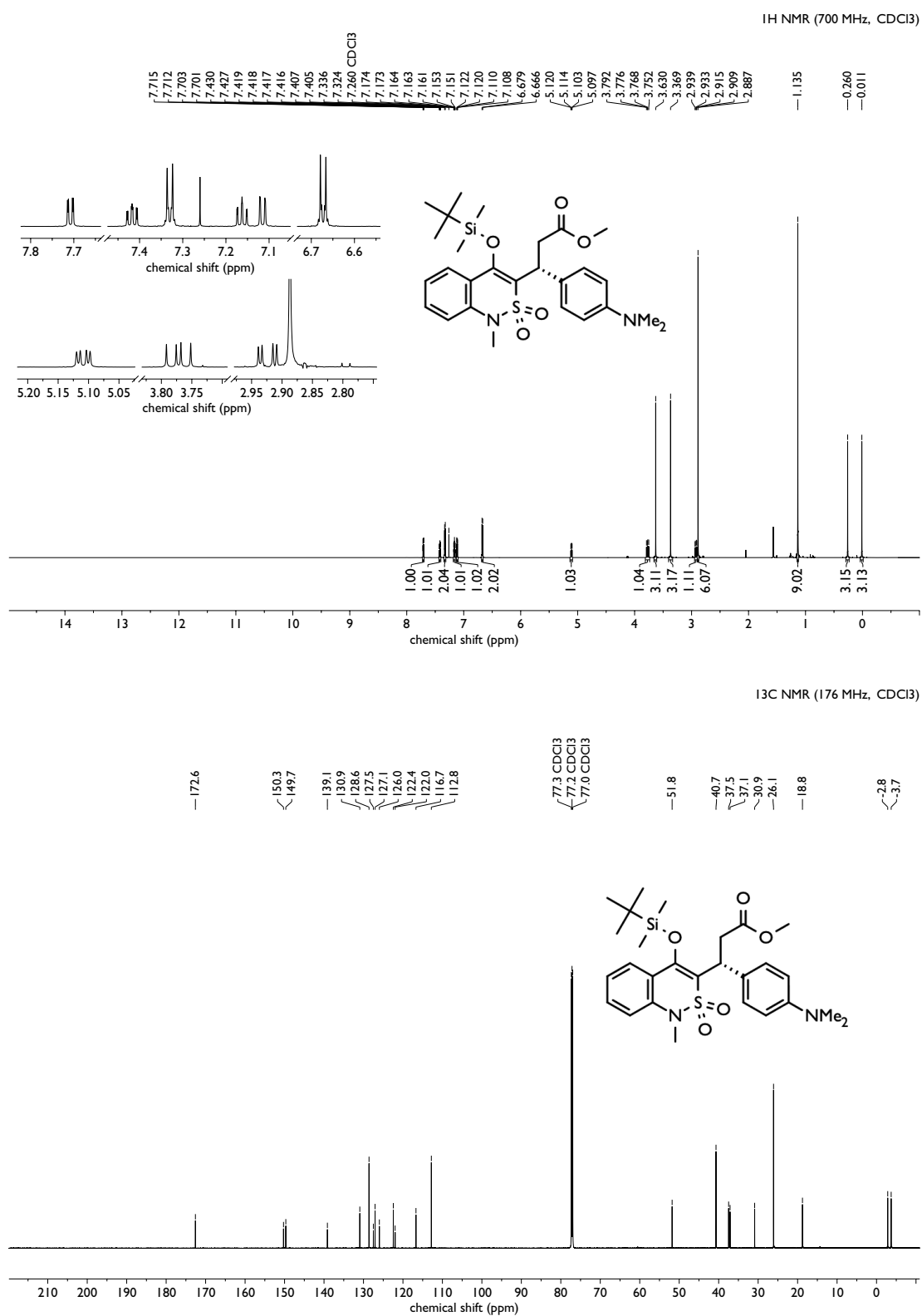


Figure S27: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4g**

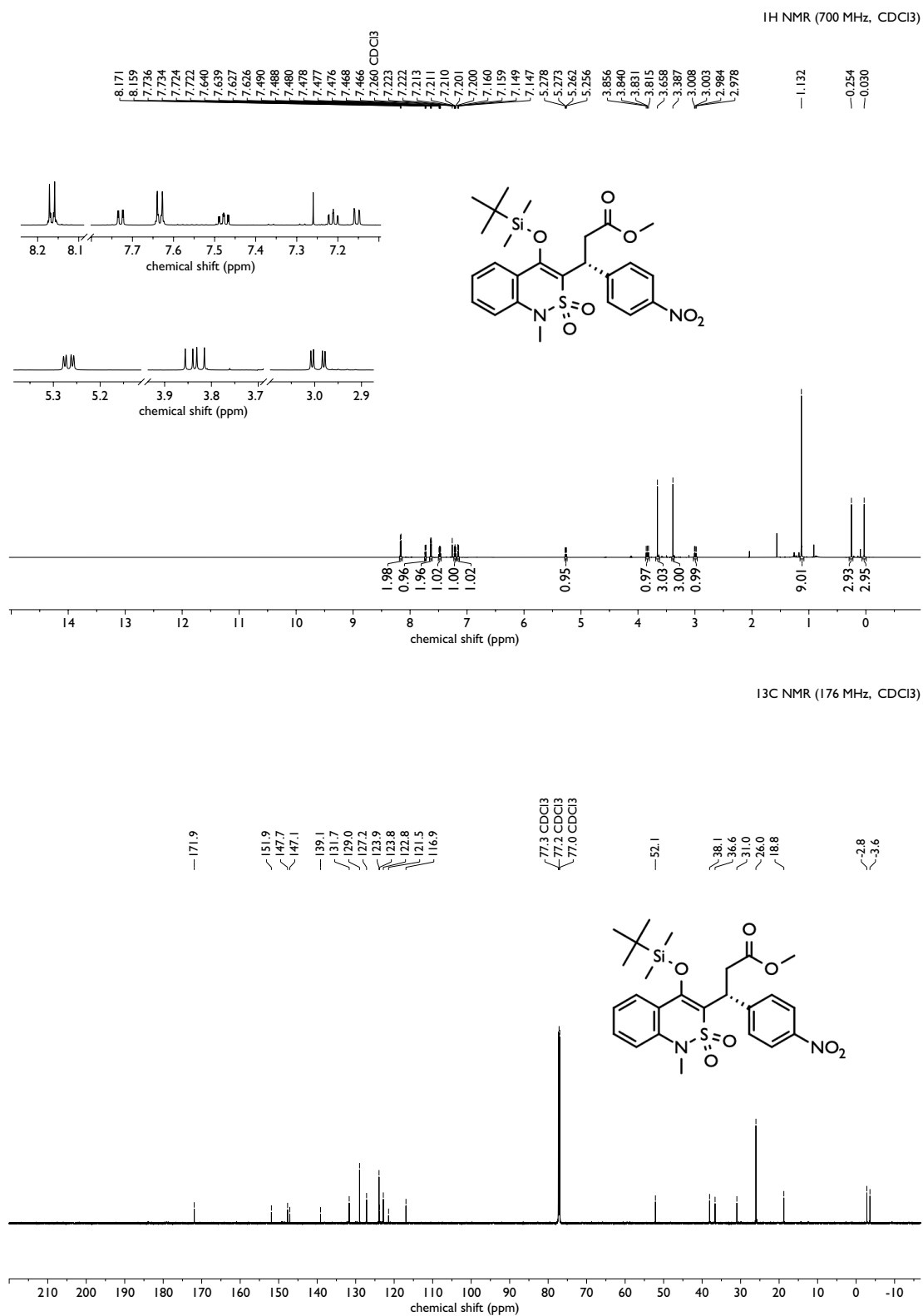


Figure S28: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4h**

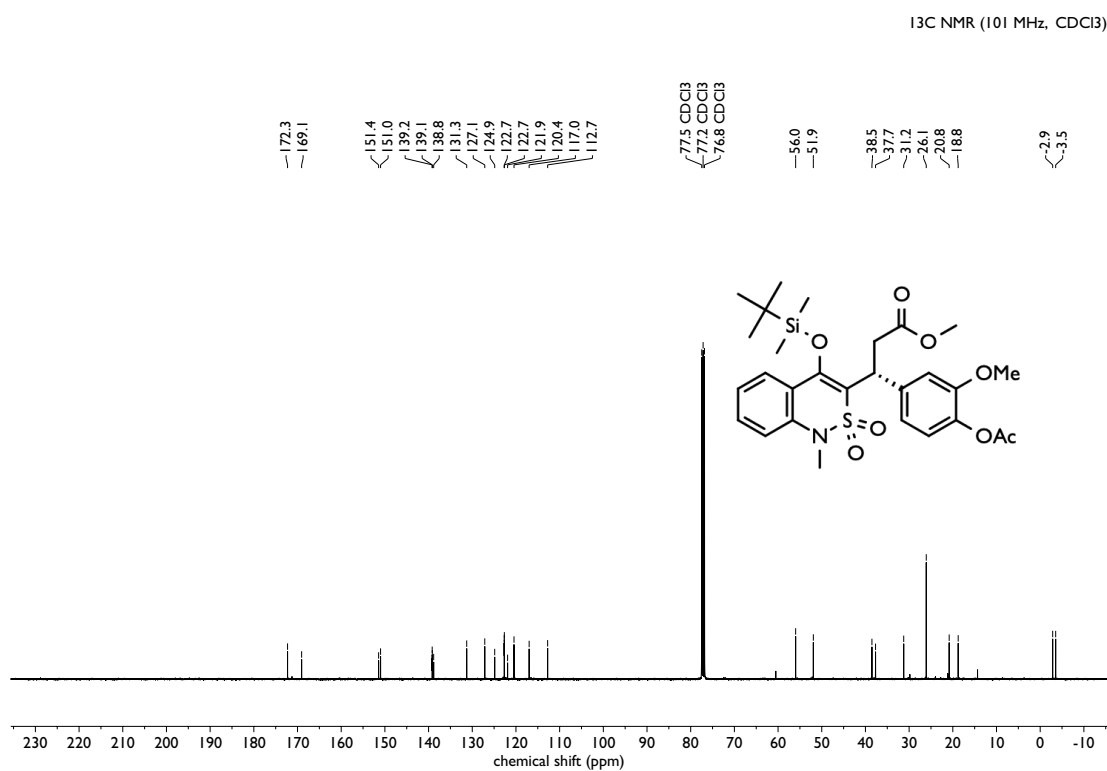
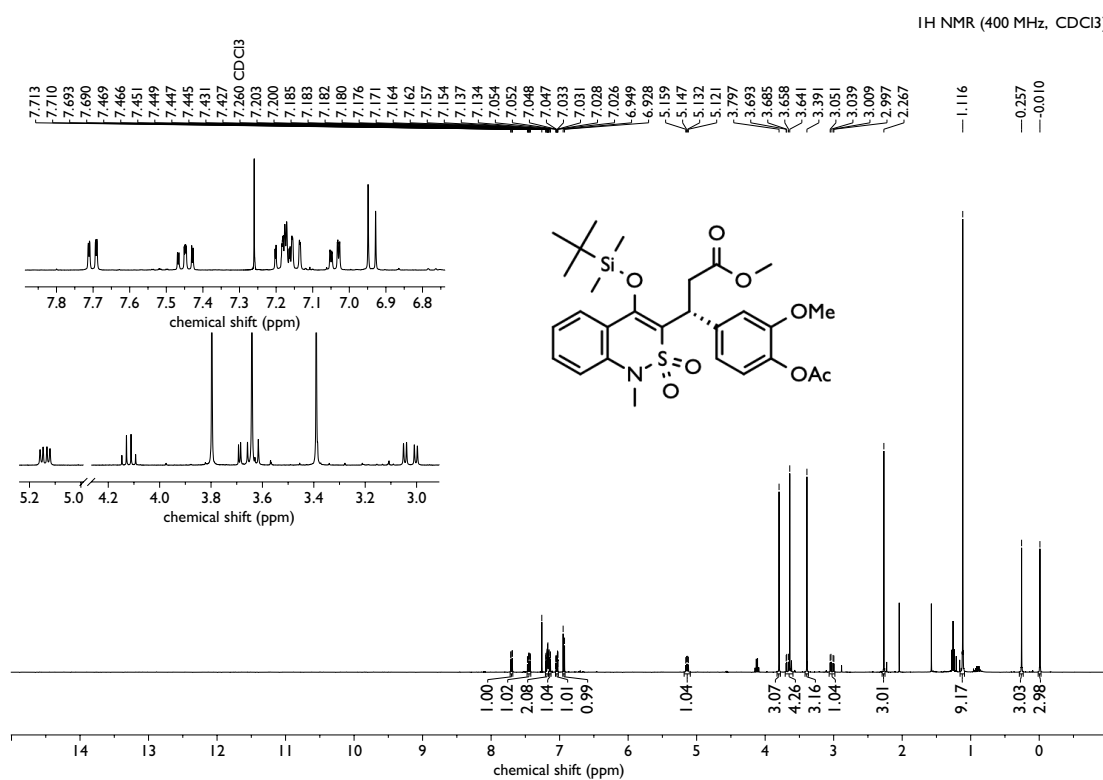


Figure S29: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4i**

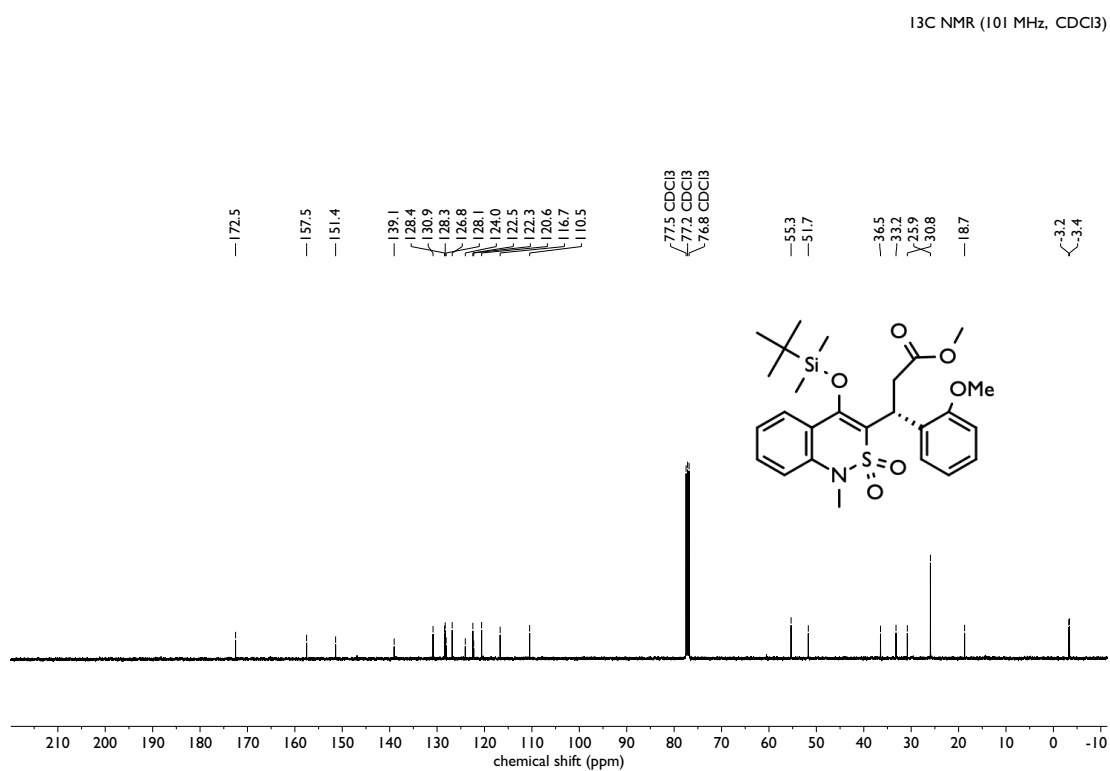
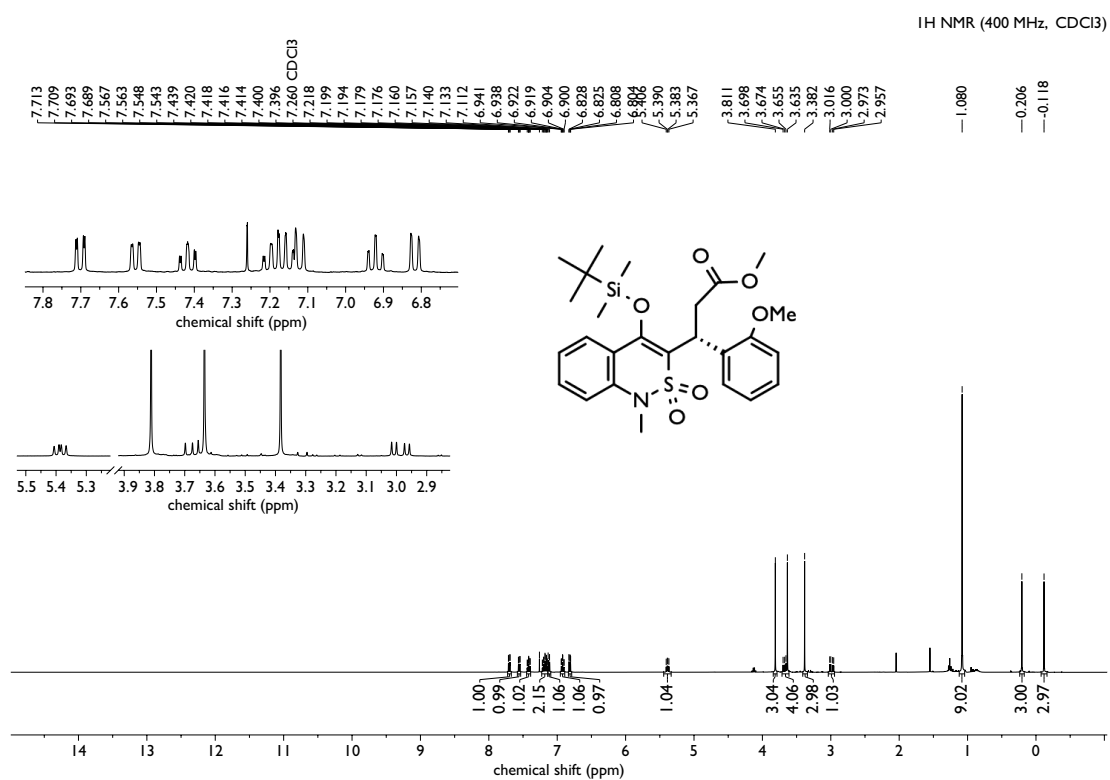


Figure S30: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4j

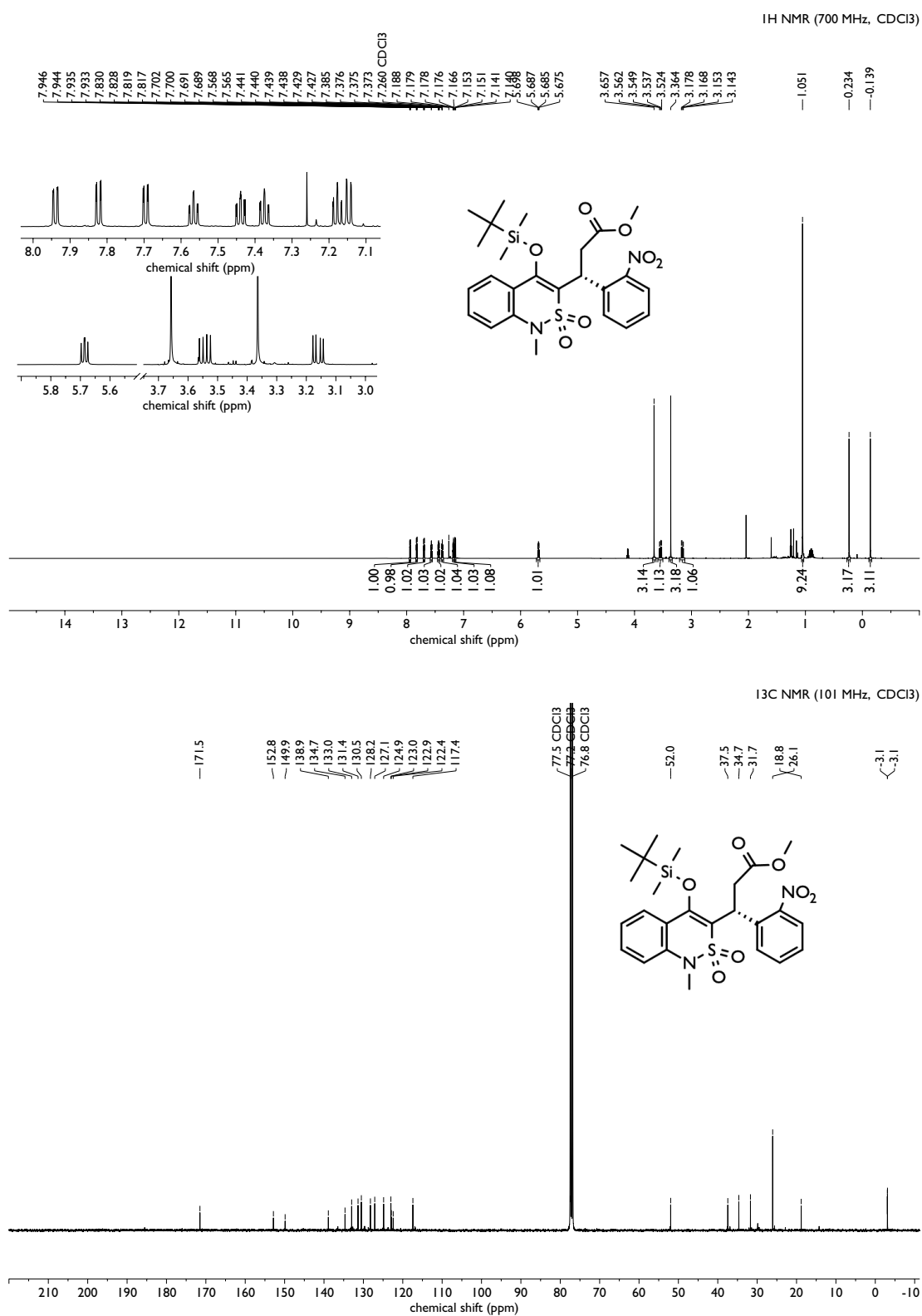


Figure S31: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4k**

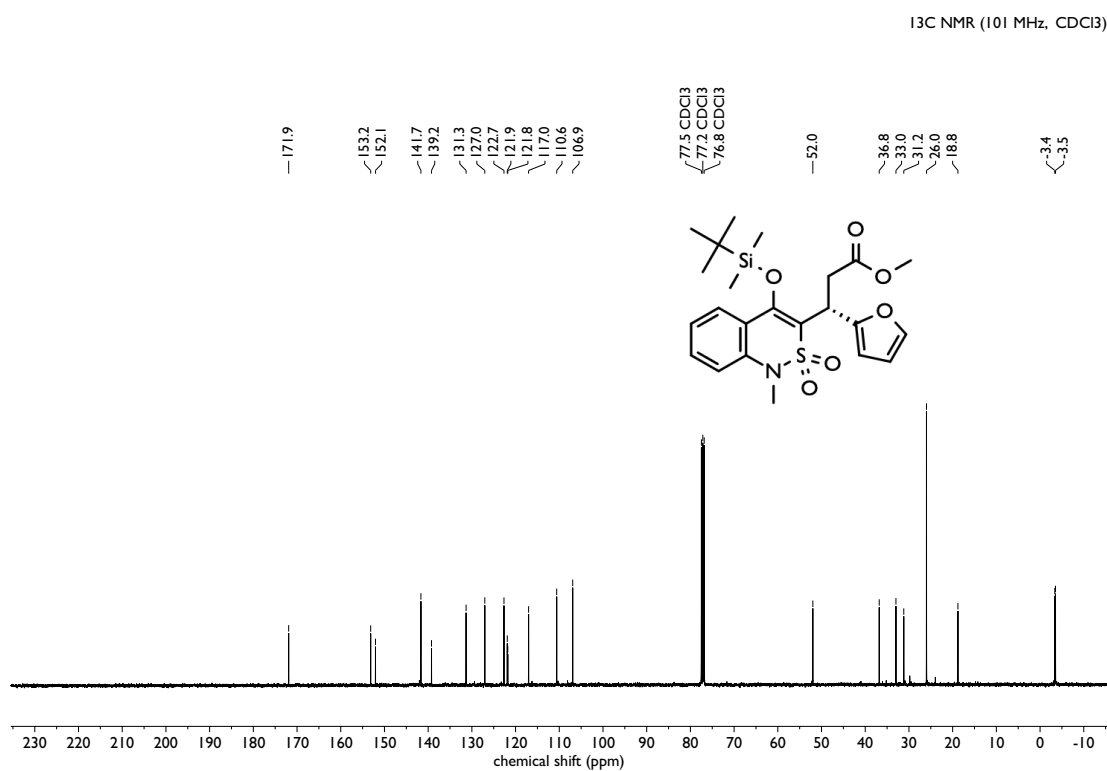
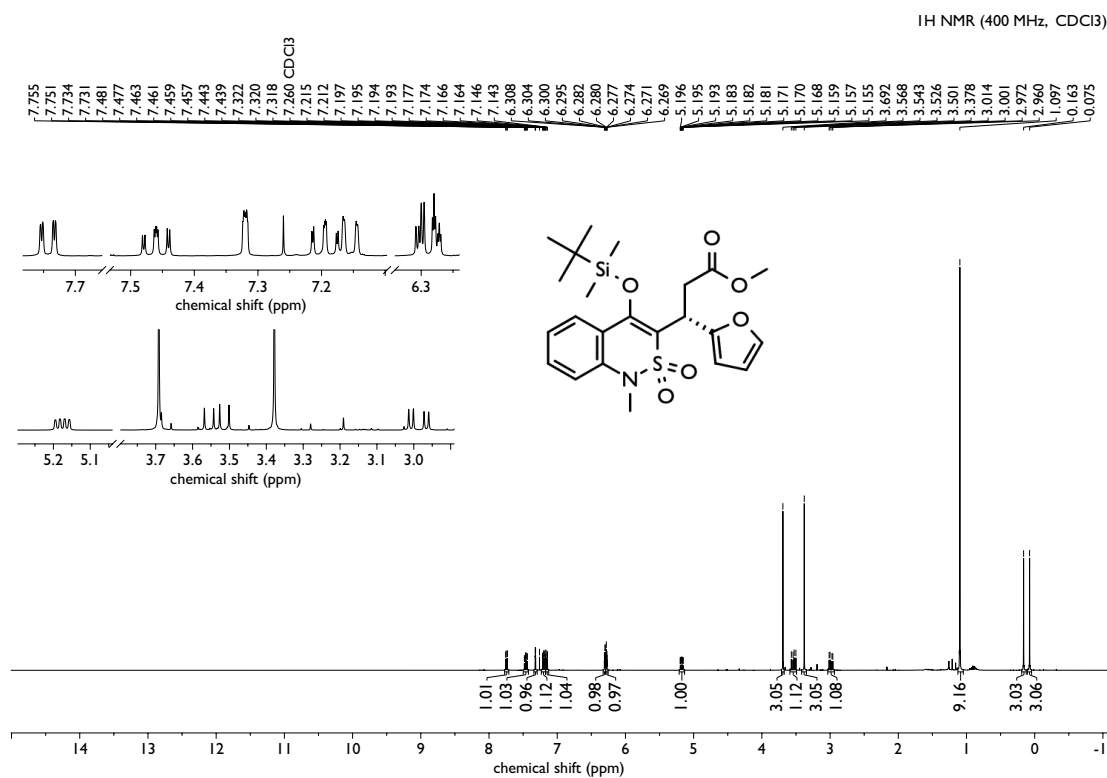


Figure S32: <sup>1</sup>H and <sup>13</sup>C spectra of compound 41



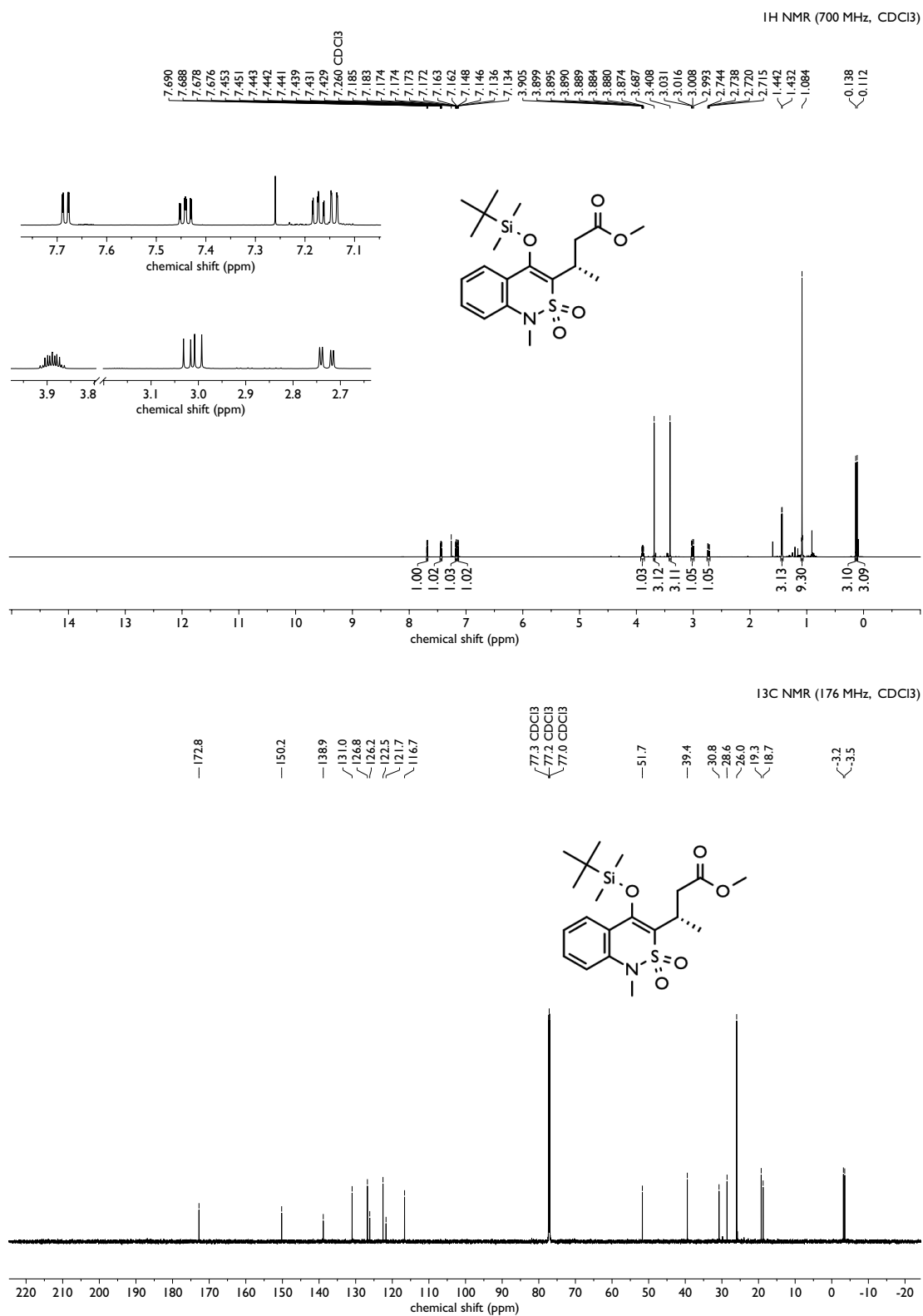


Figure S33: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4m**







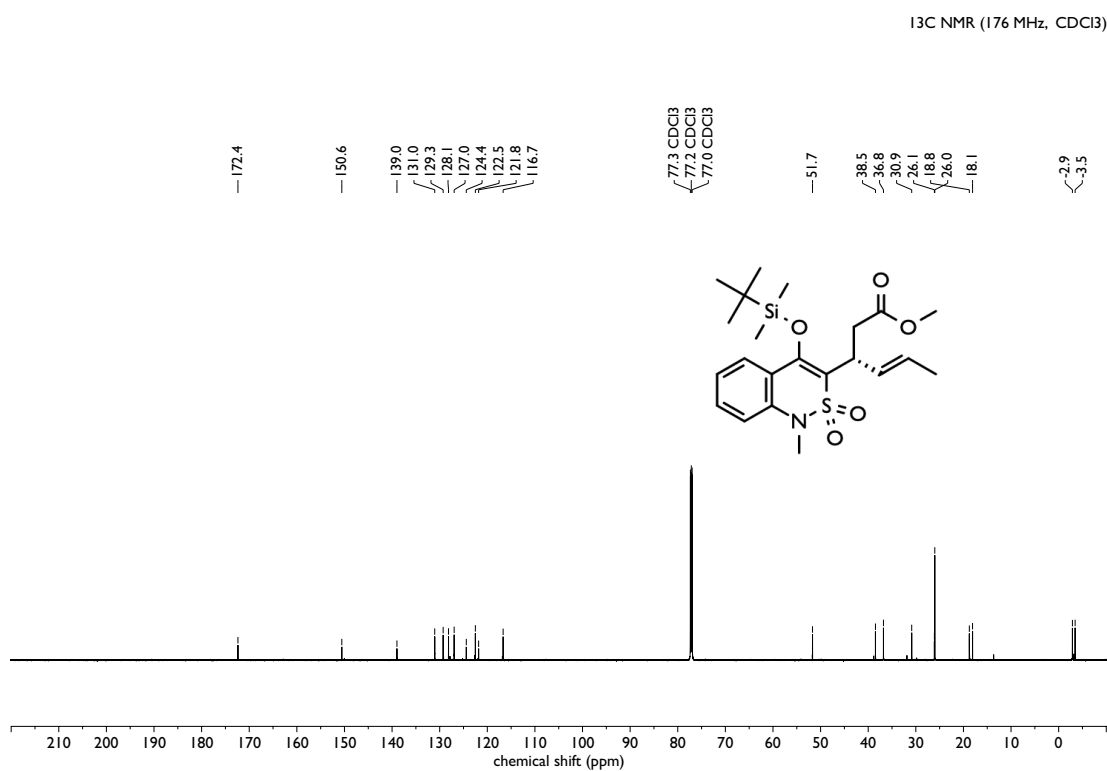
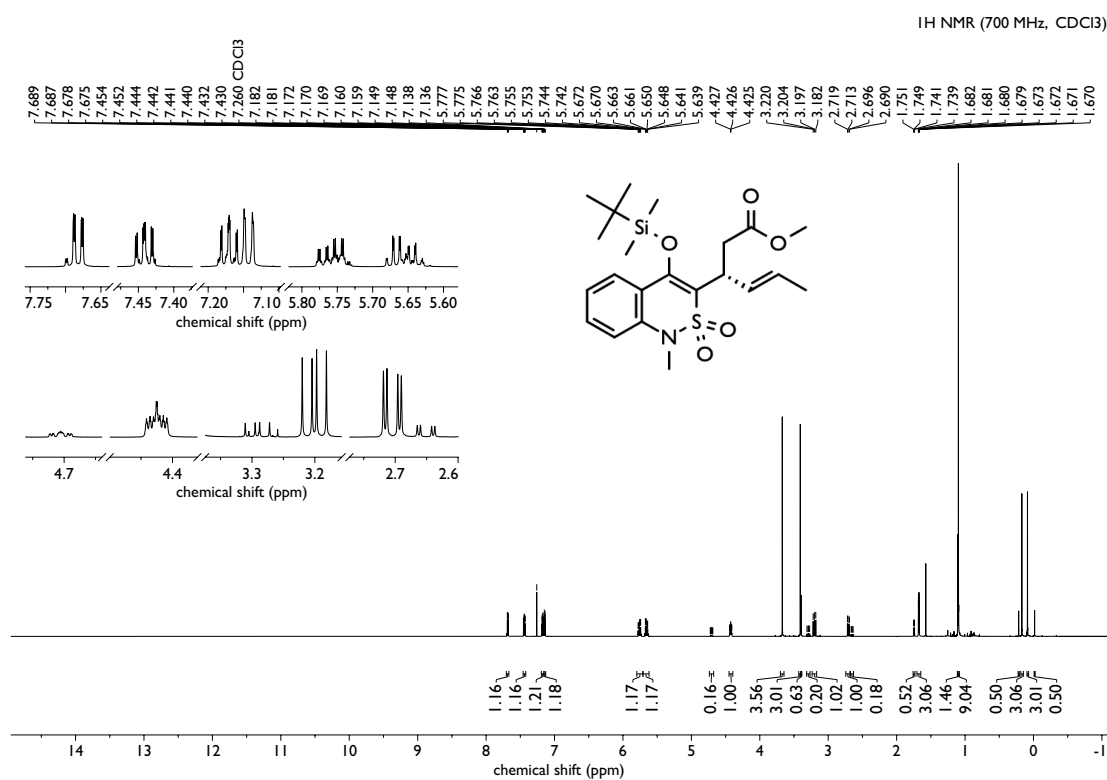


Figure S37: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4q**

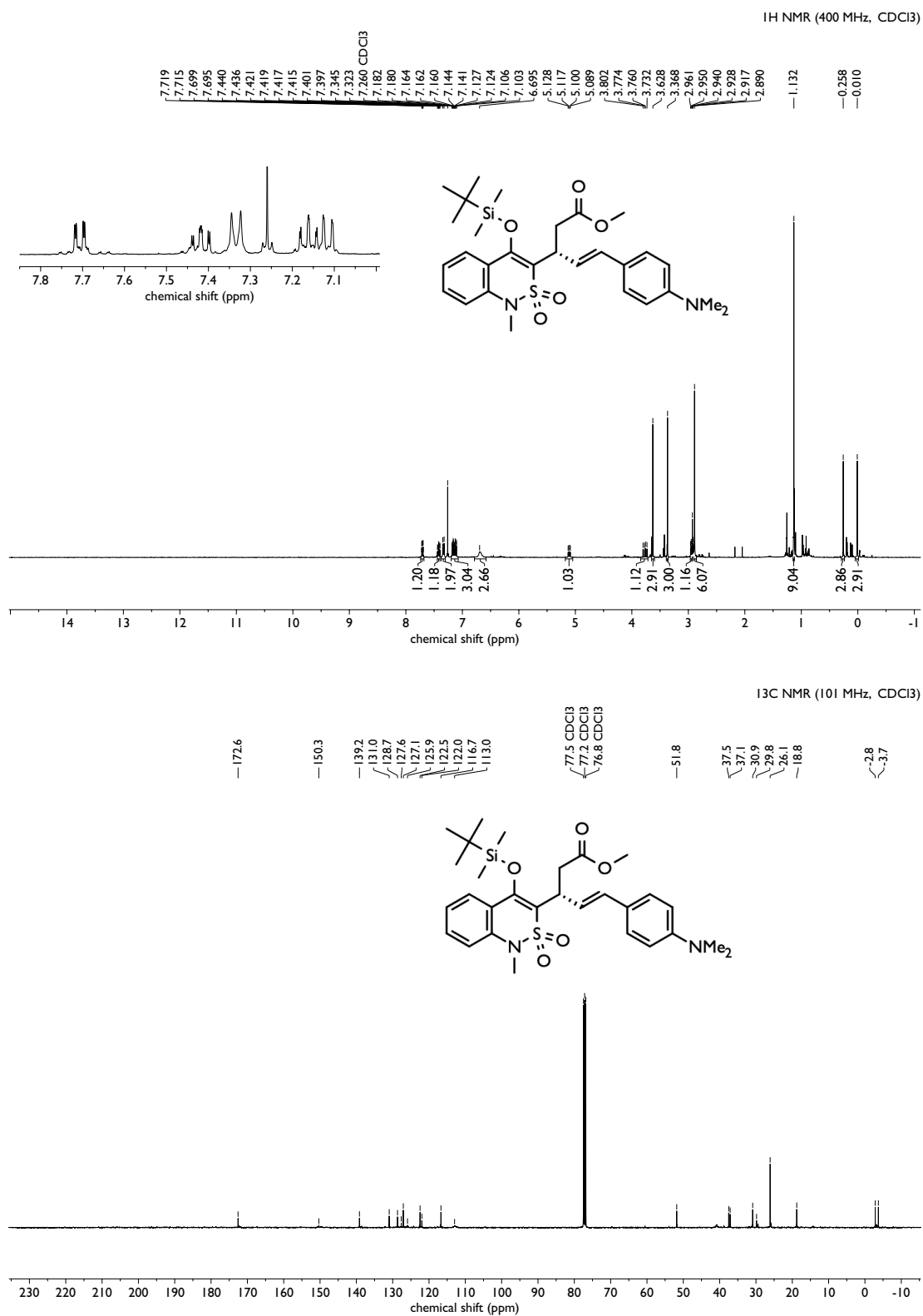


Figure S38: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4r**

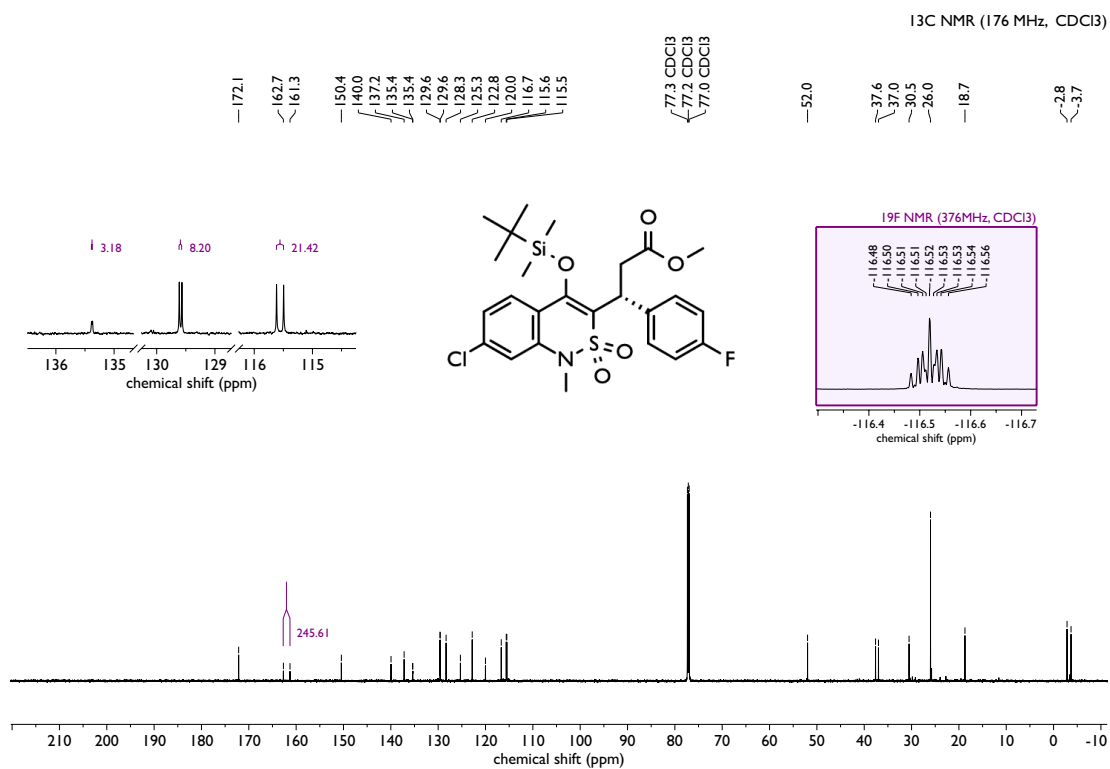
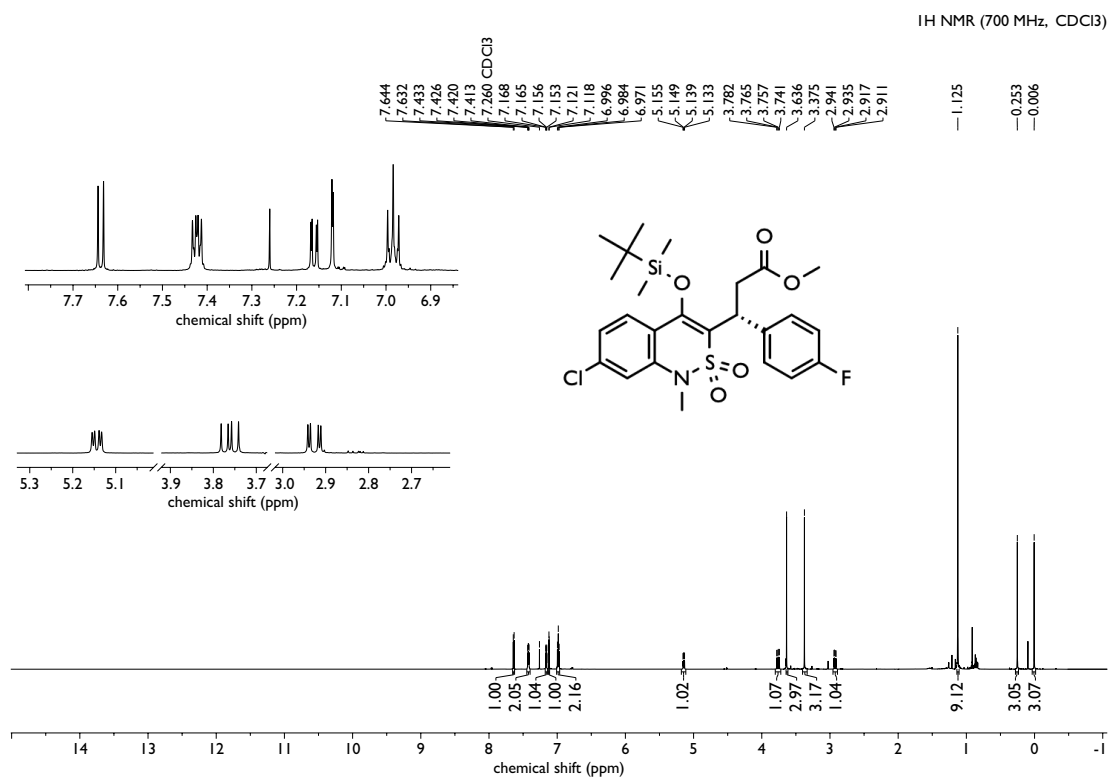


Figure S39: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4s





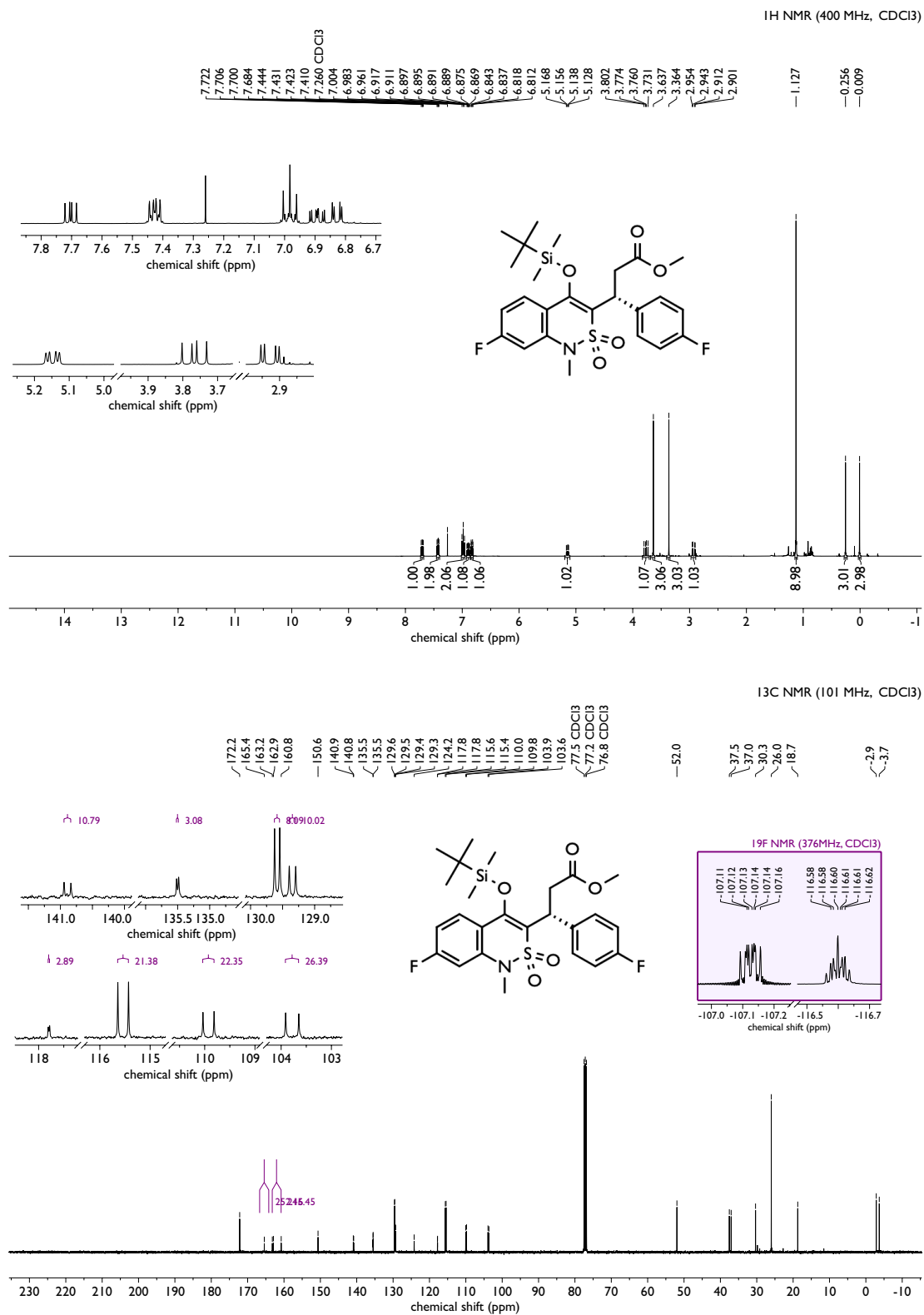


Figure S41: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4u**

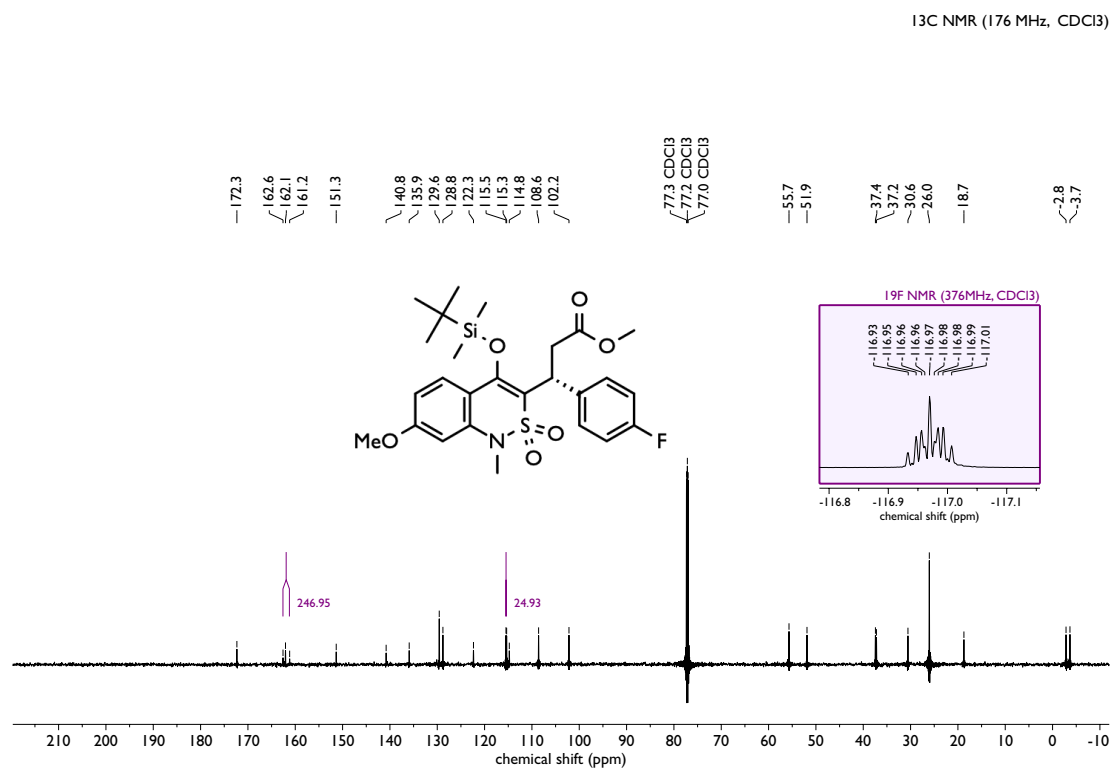
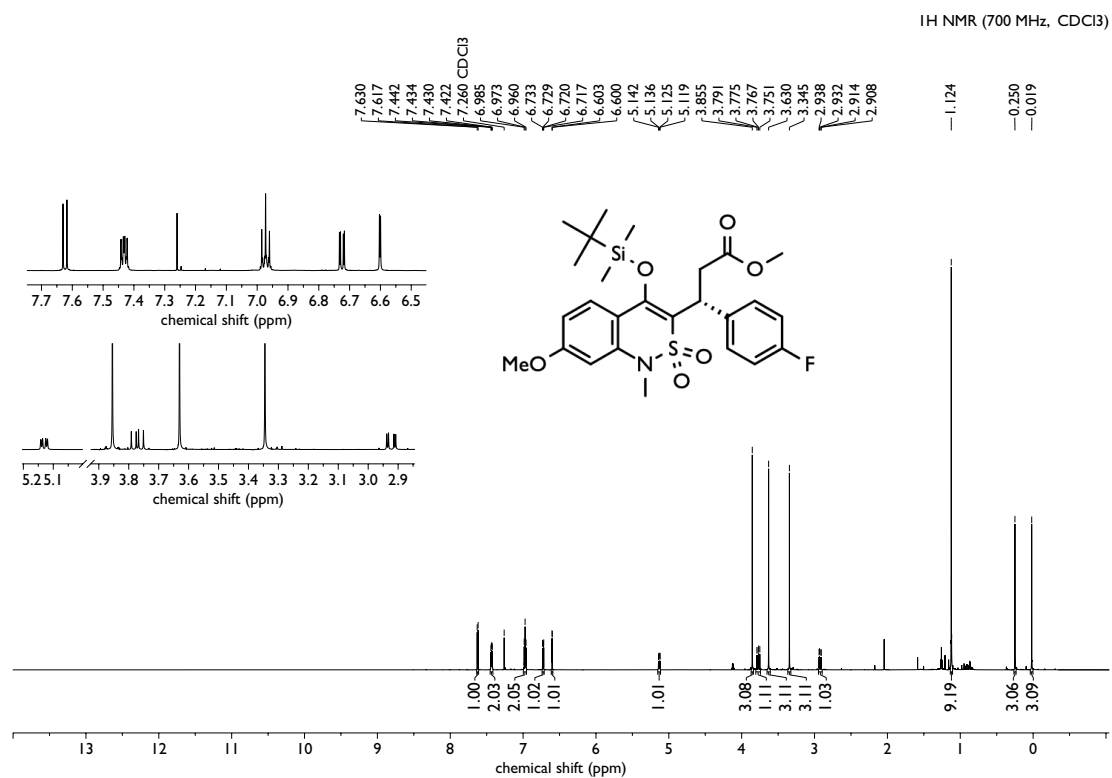


Figure S42: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4v

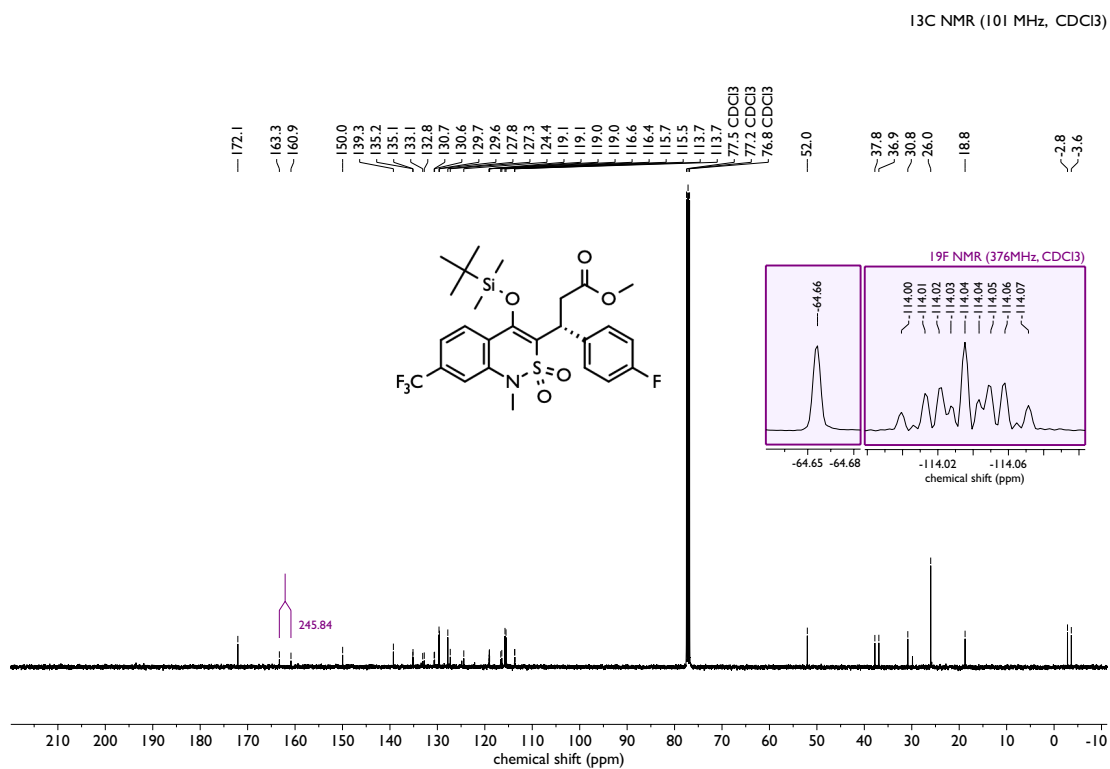
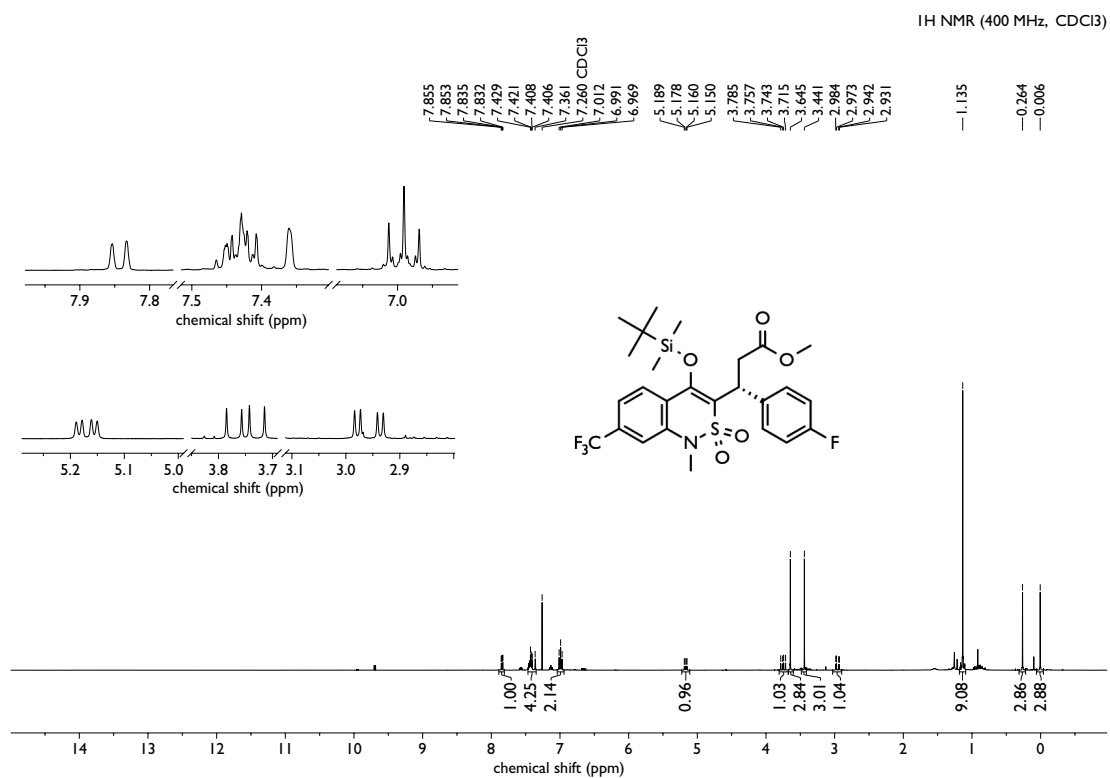


Figure S43: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4w

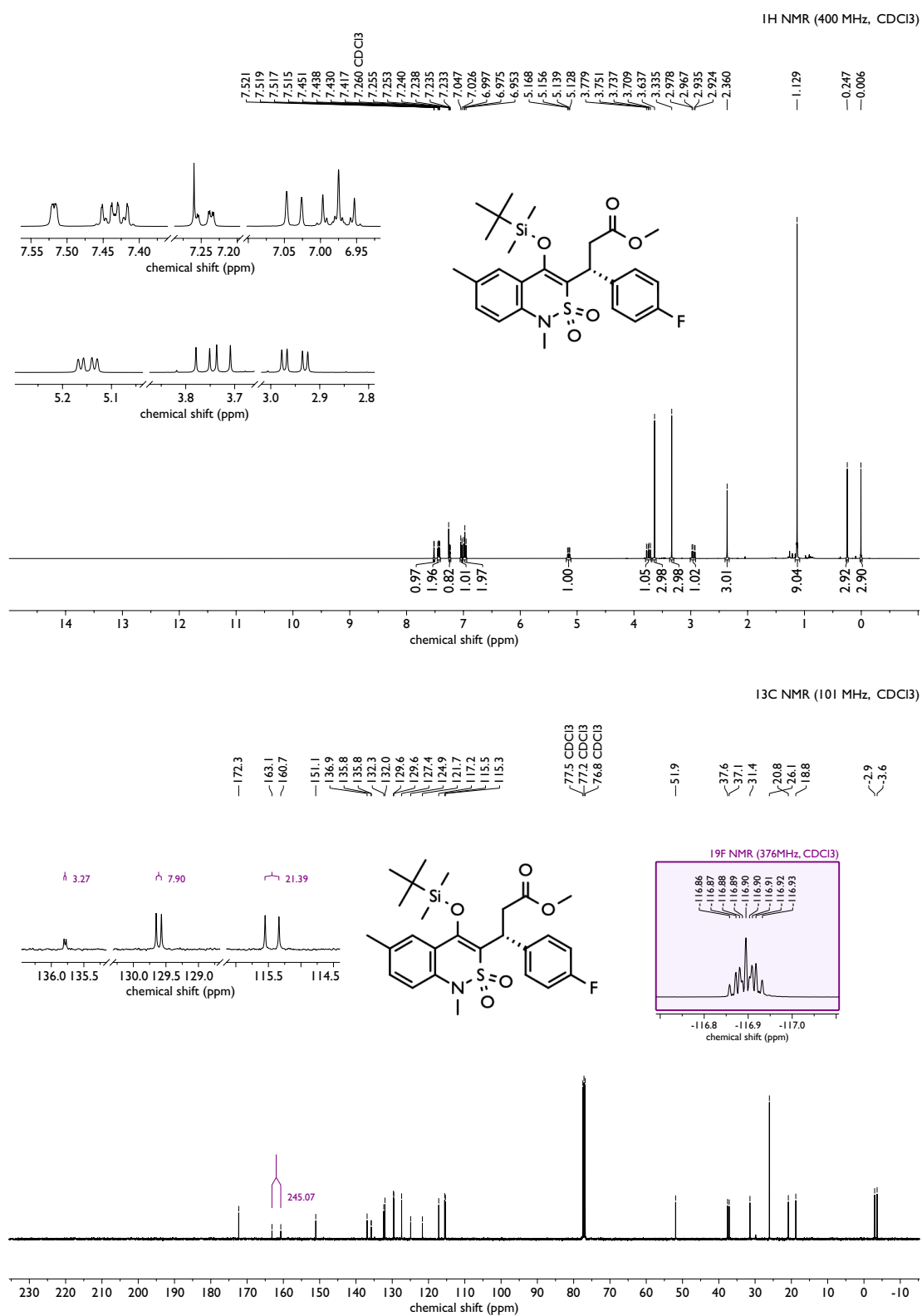


Figure S44: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4x

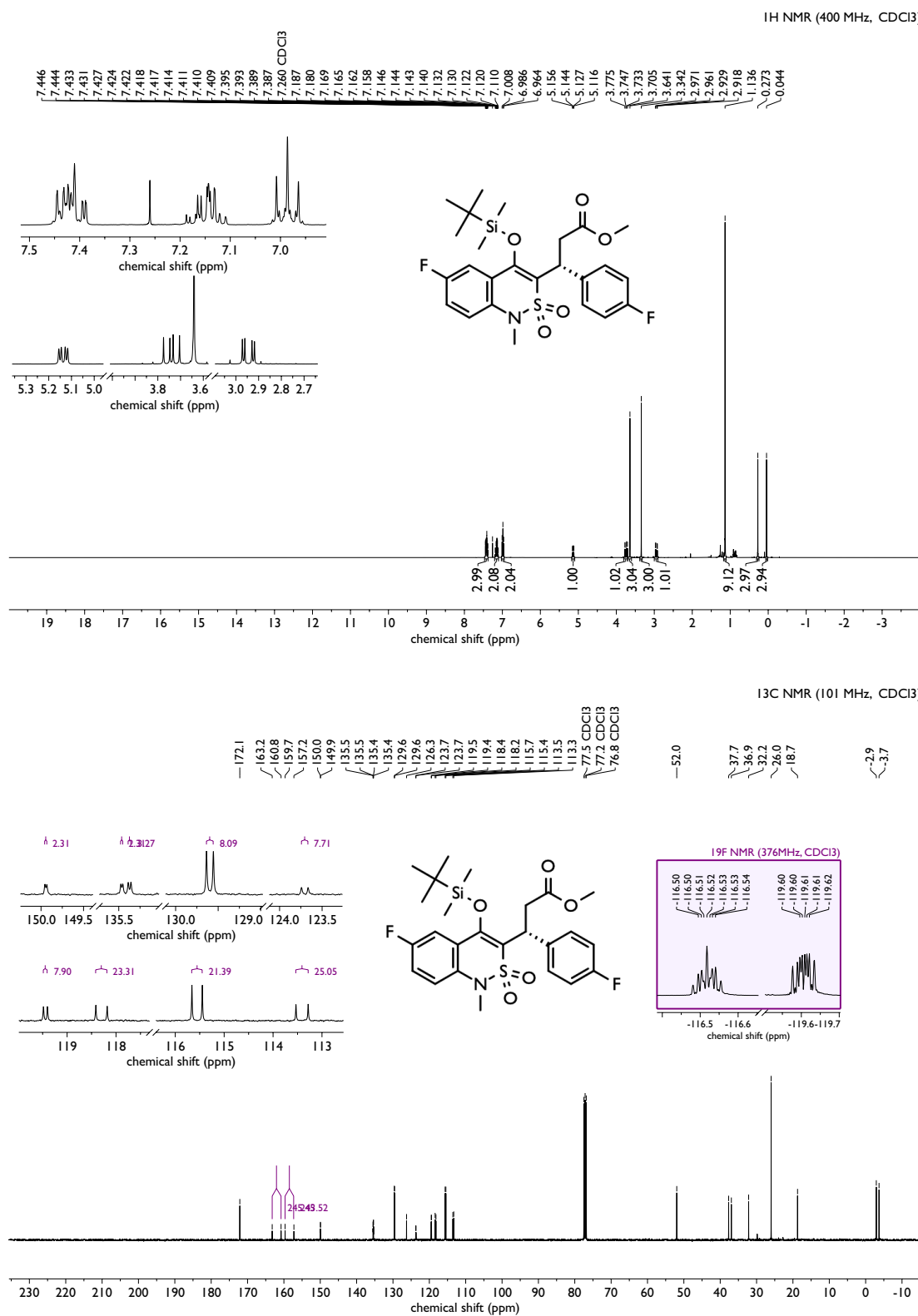


Figure S45: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4y

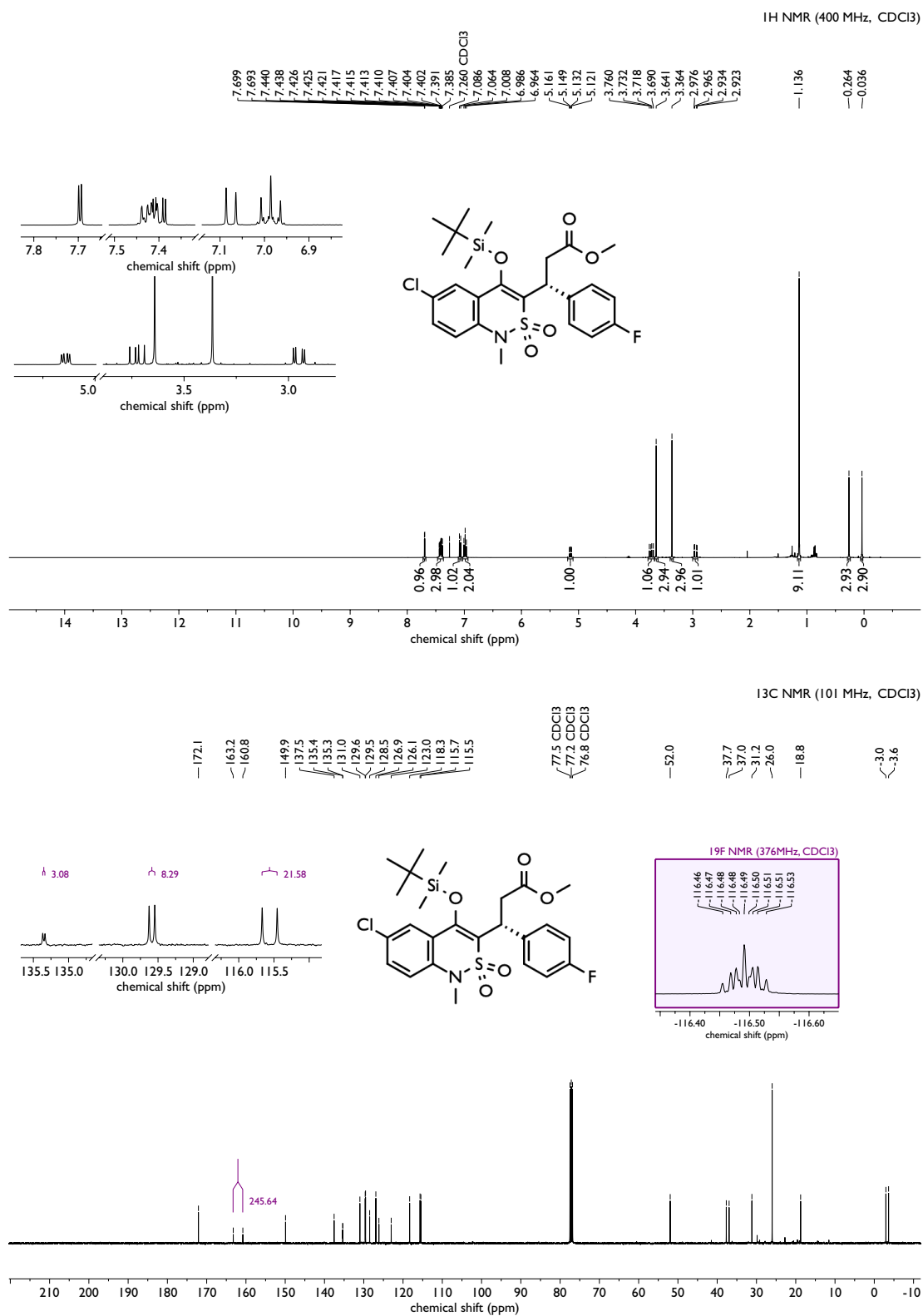


Figure S46: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4z**

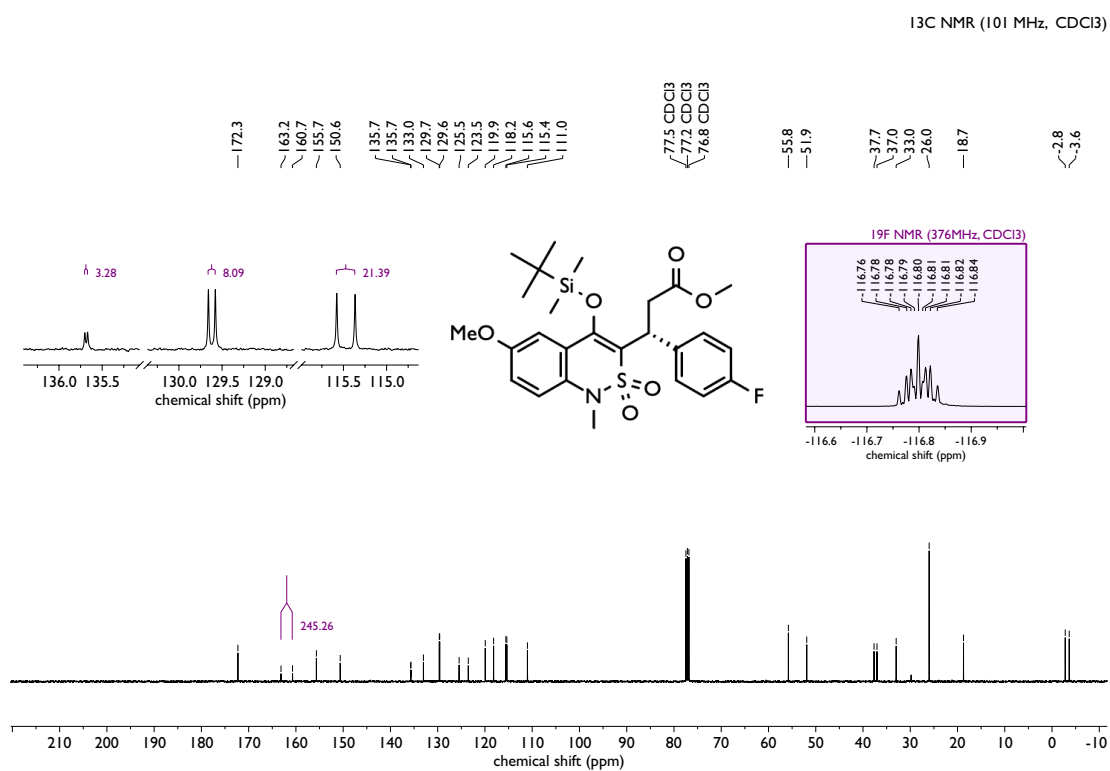
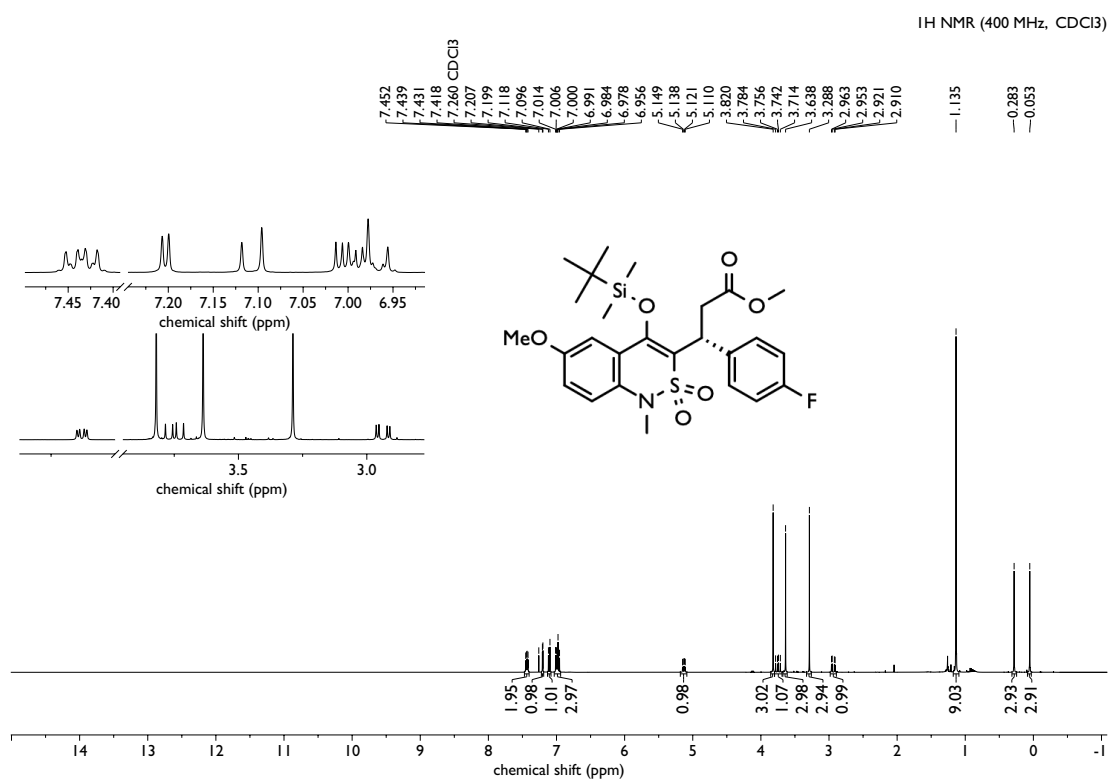


Figure S47: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4aa

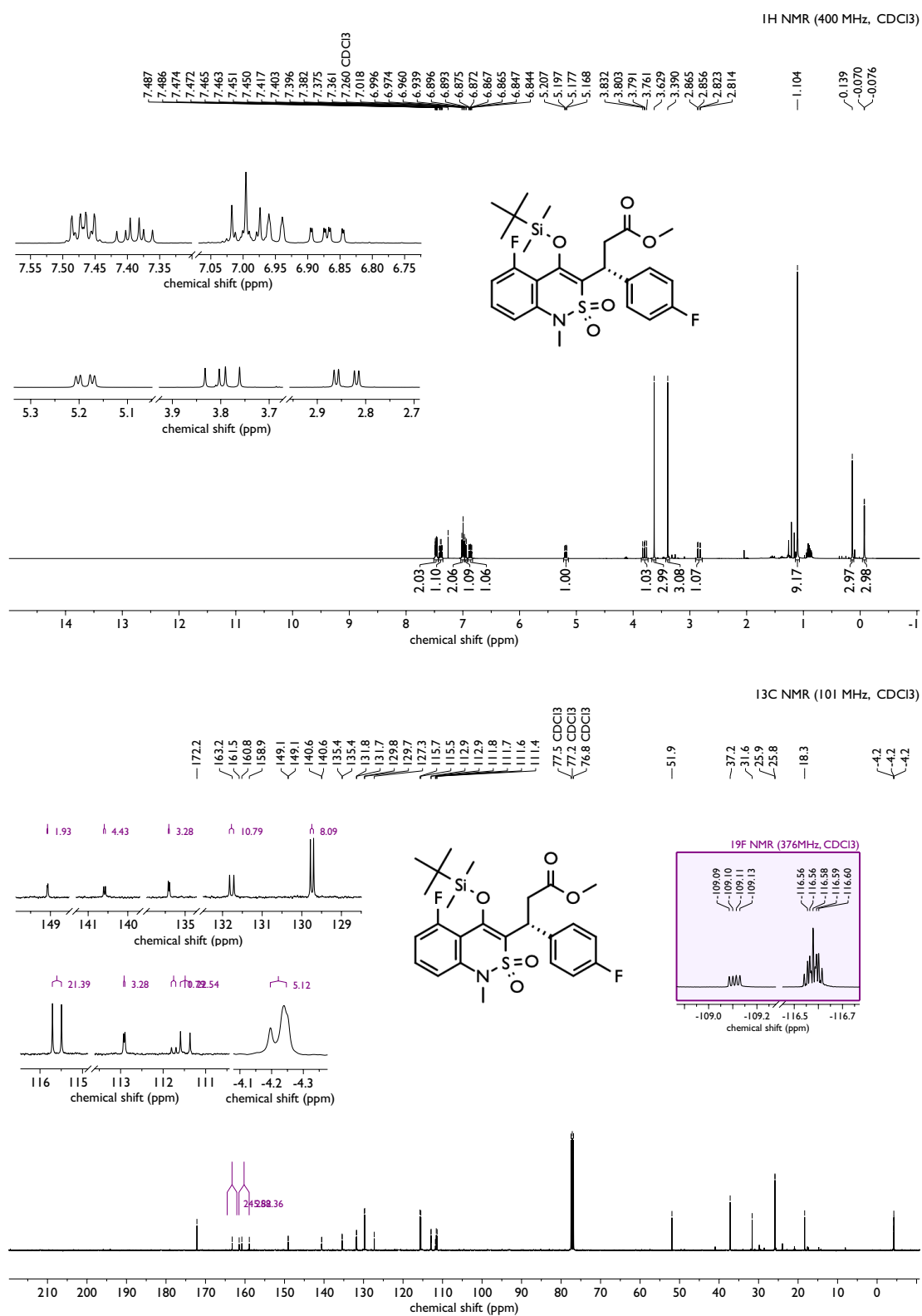


Figure S48: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ab**



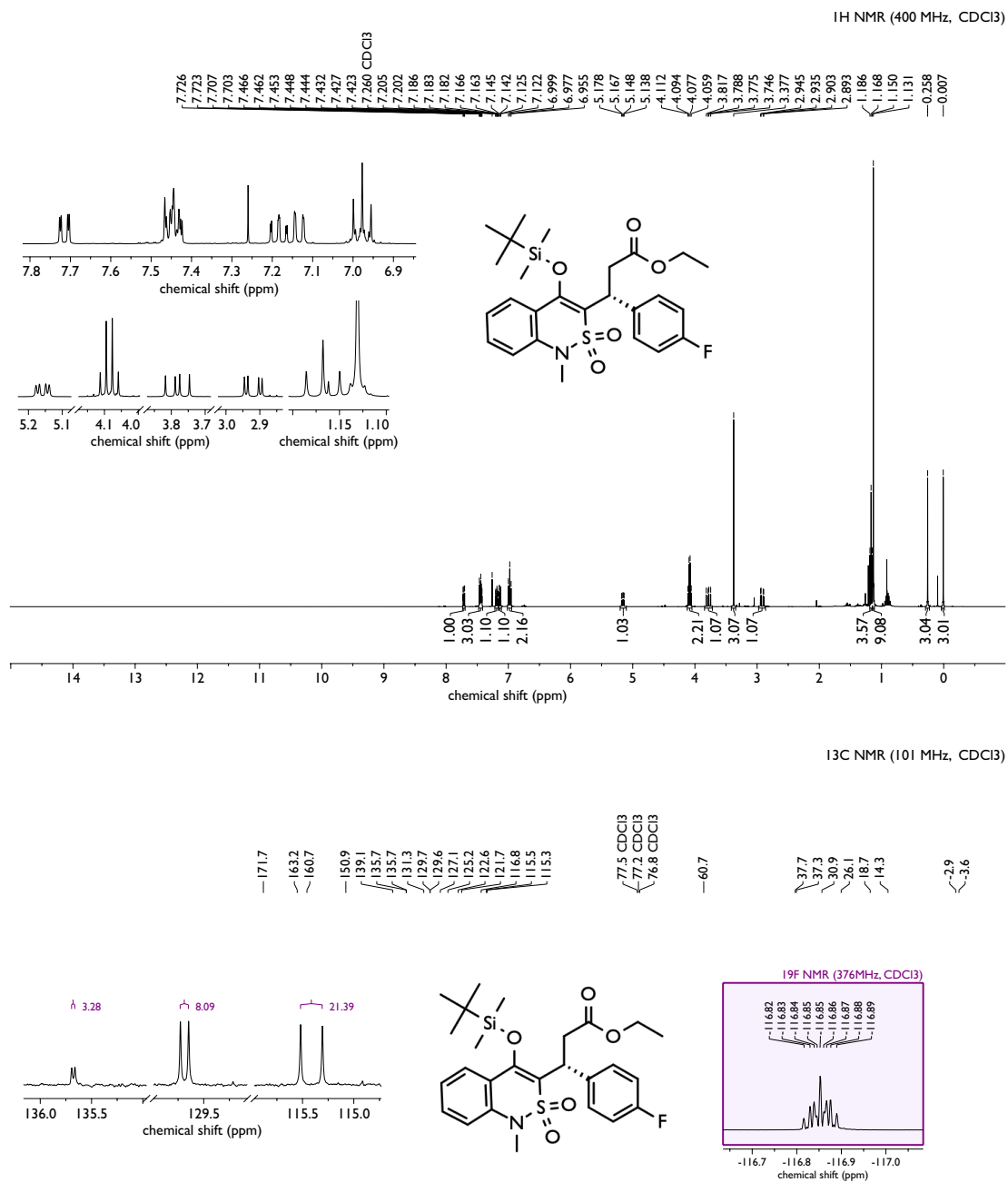


Figure S49: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ac**

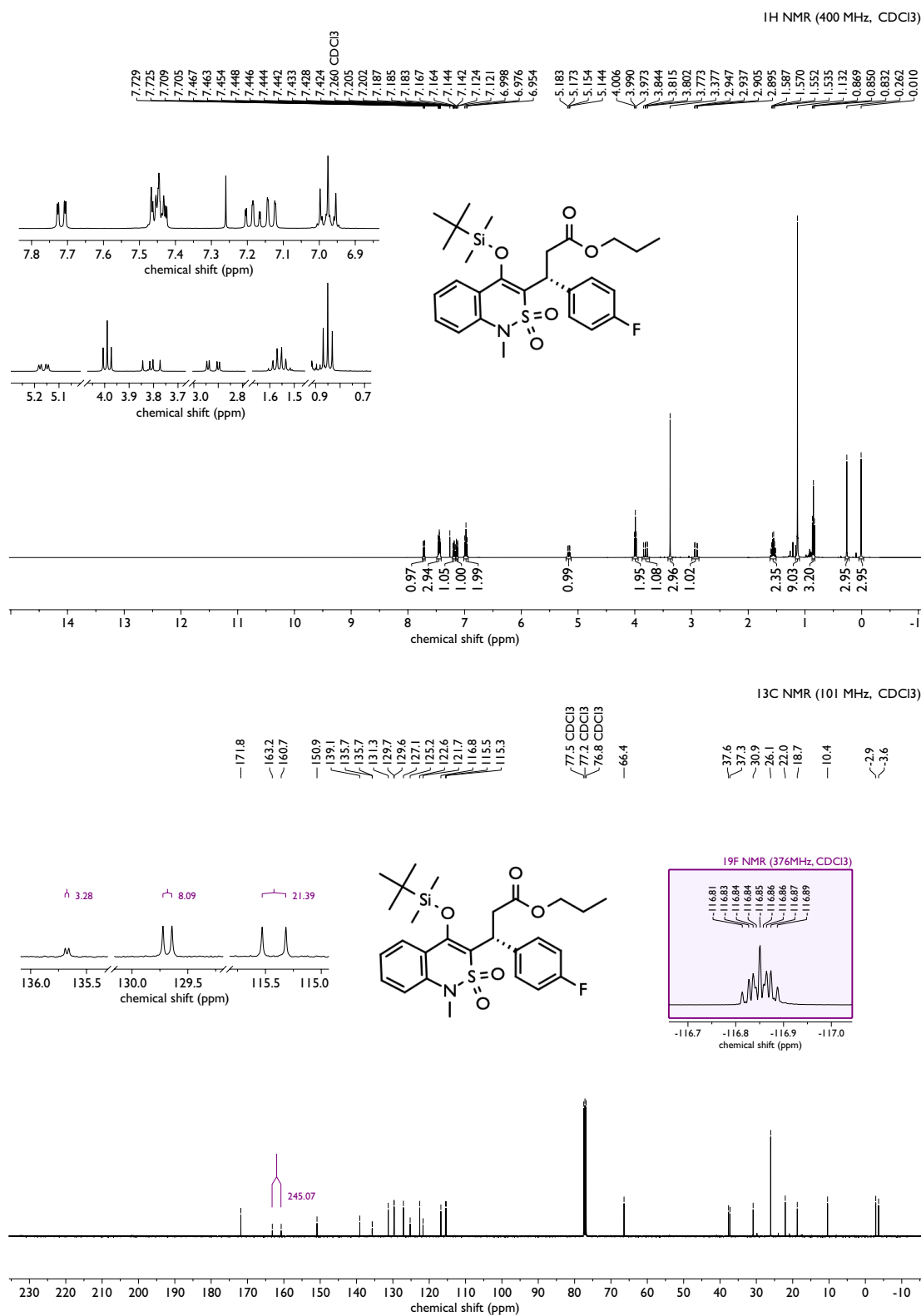


Figure S50: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ad**

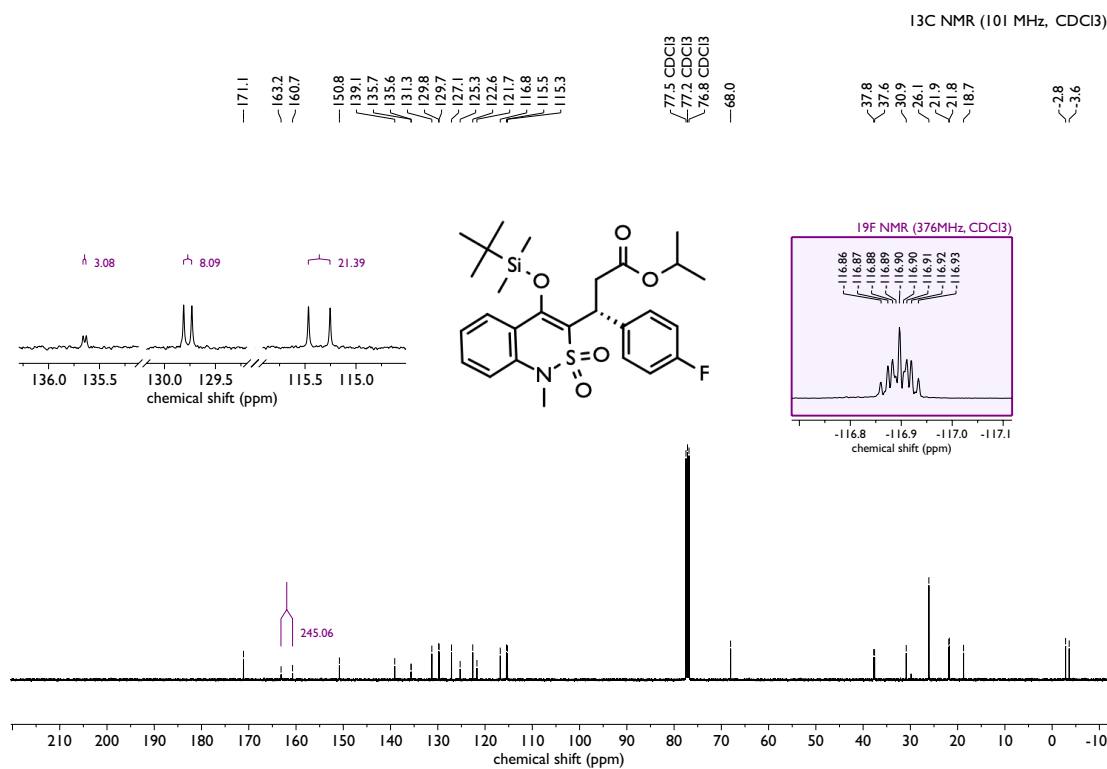
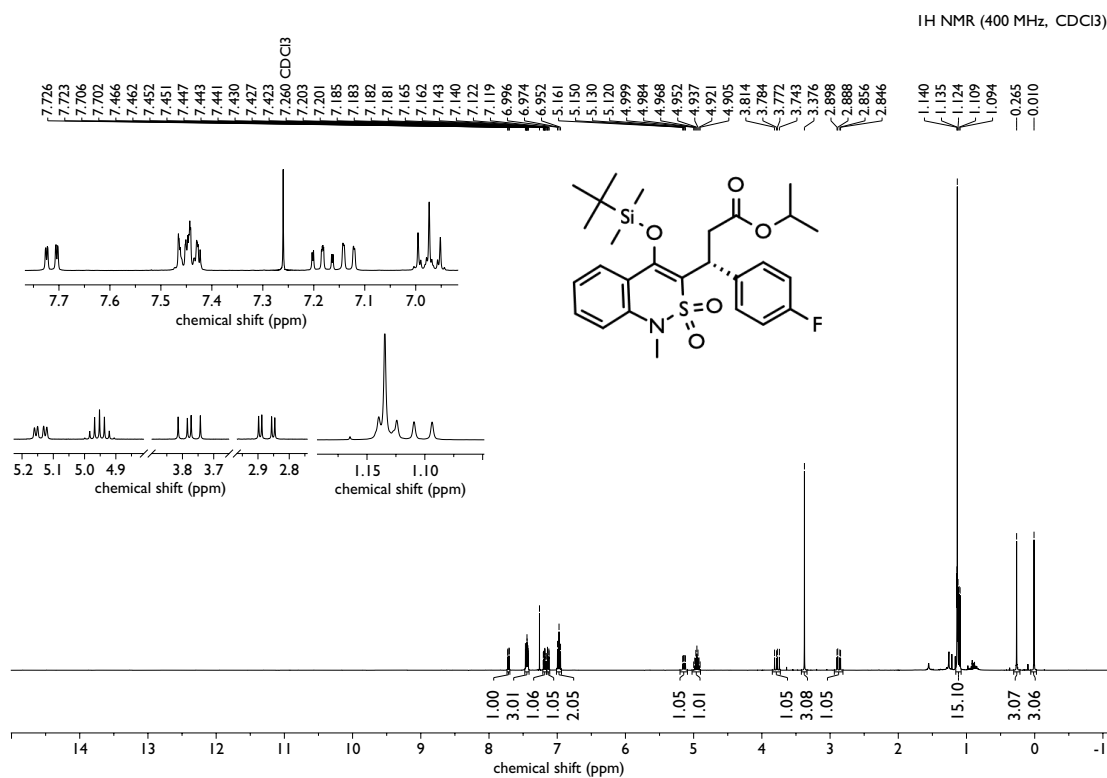


Figure S51: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4ae

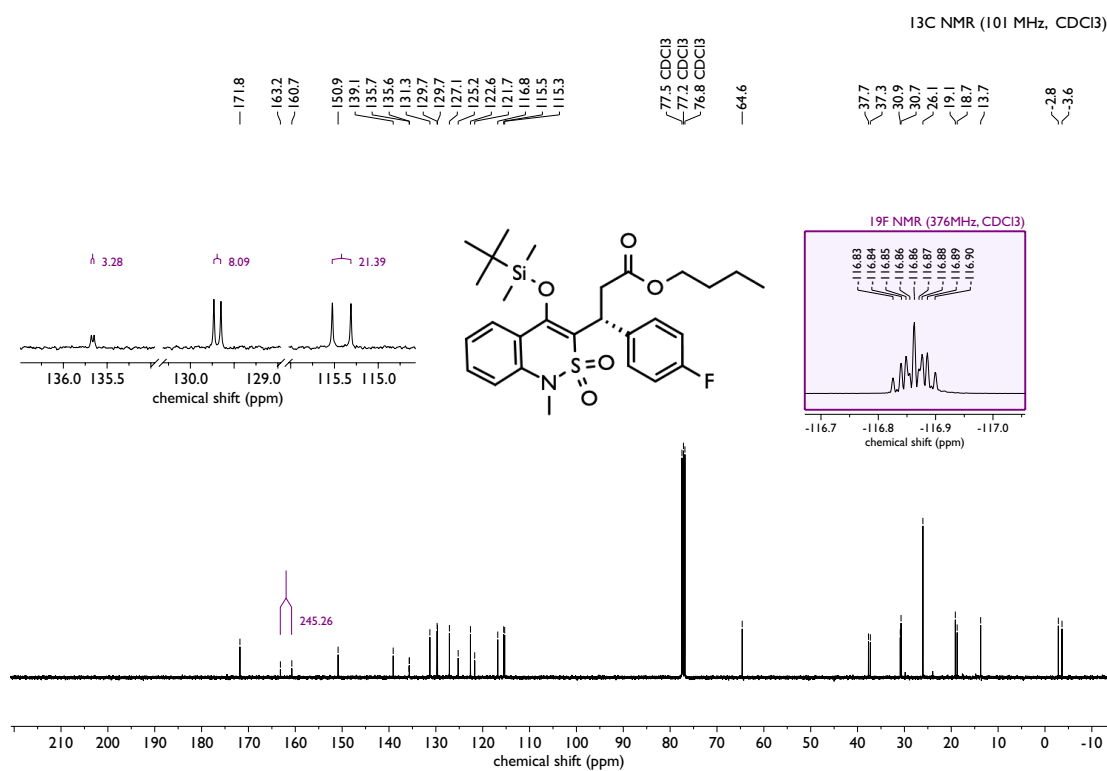
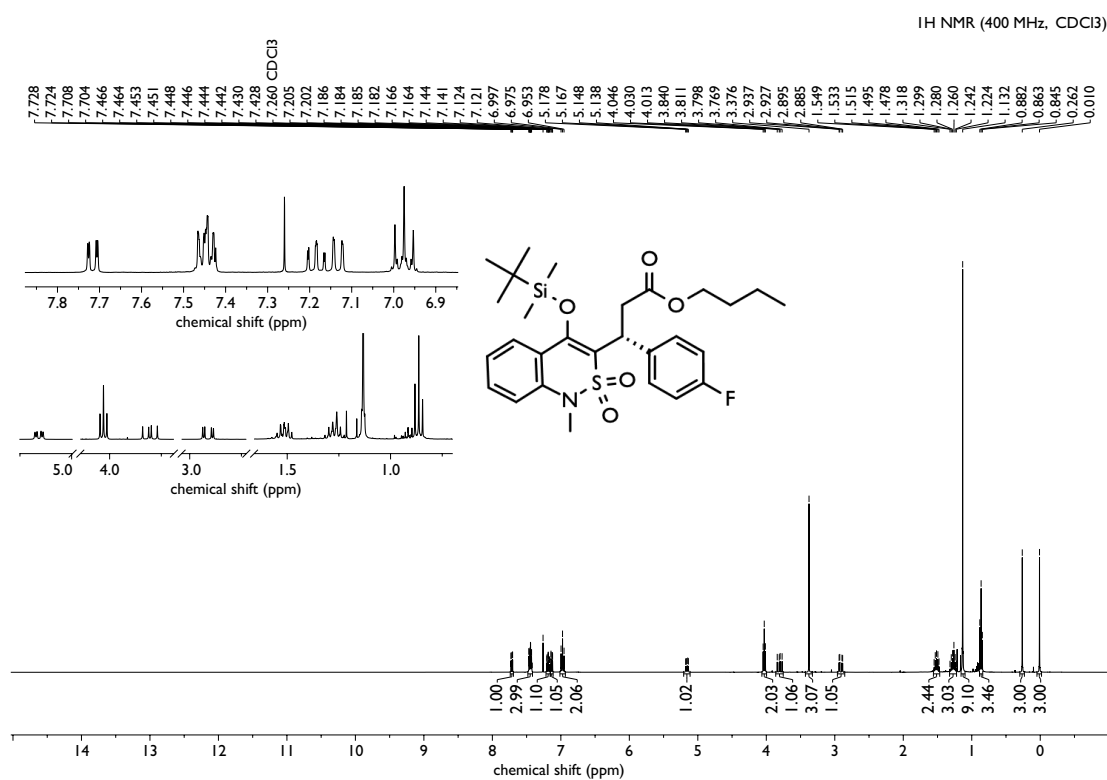


Figure S52: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4af

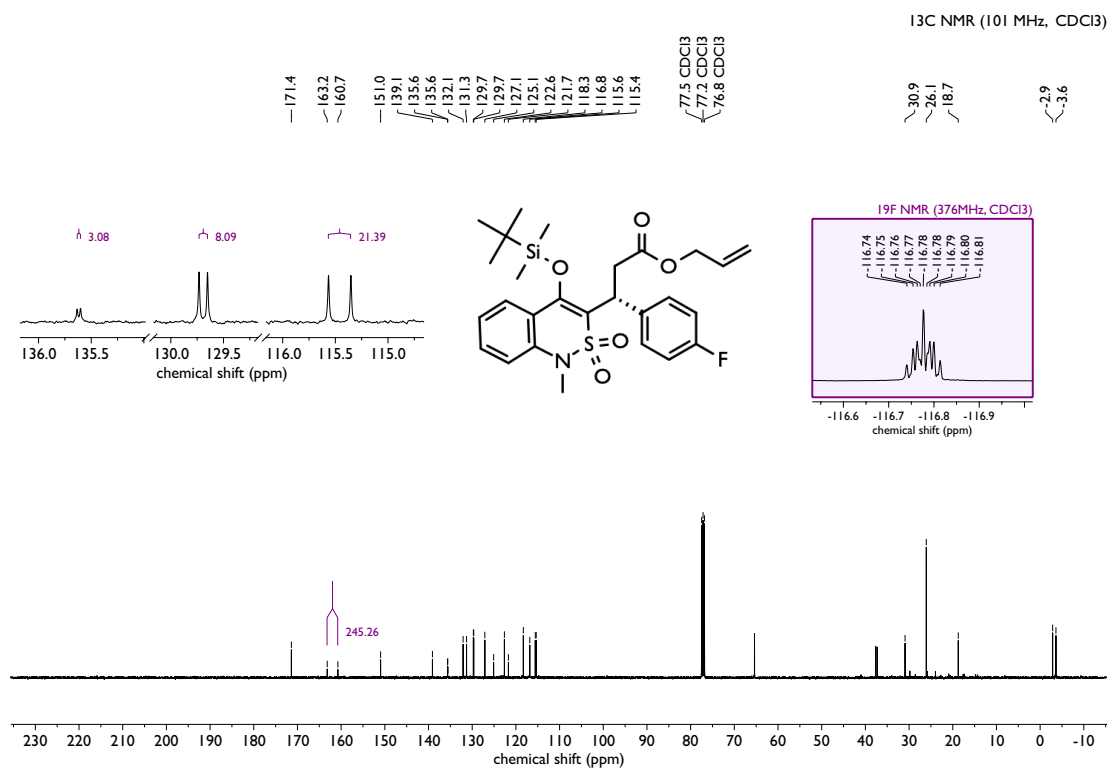
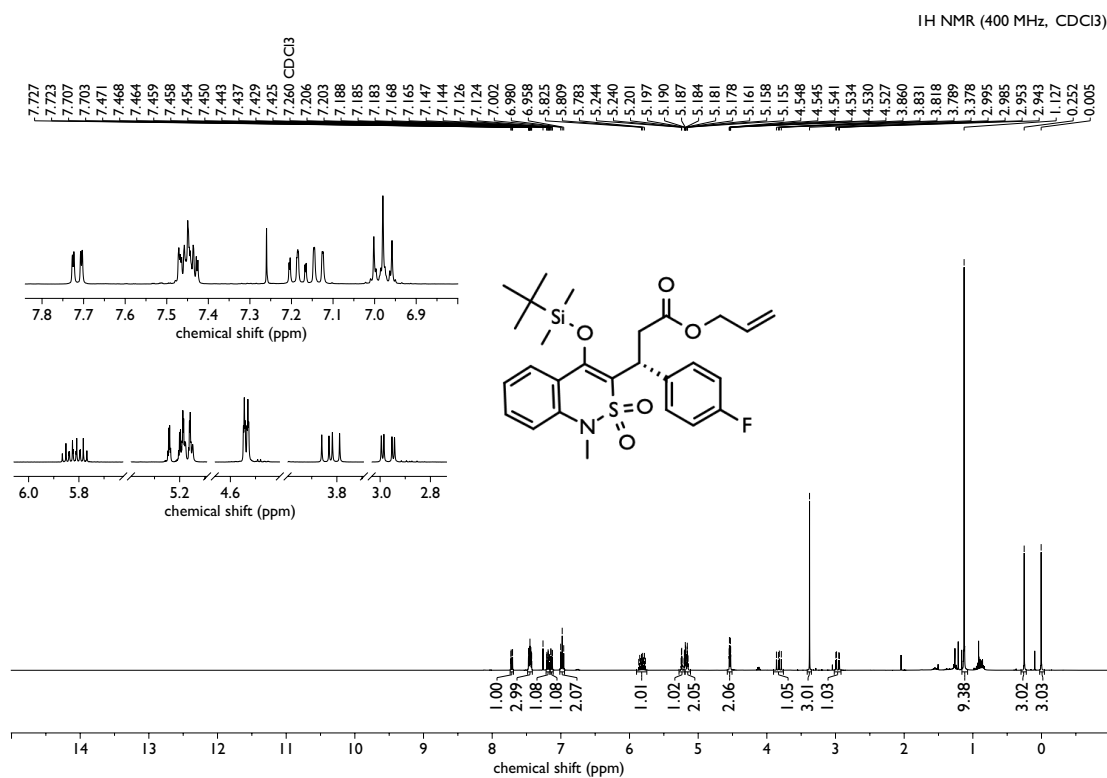


Figure S53: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ag**

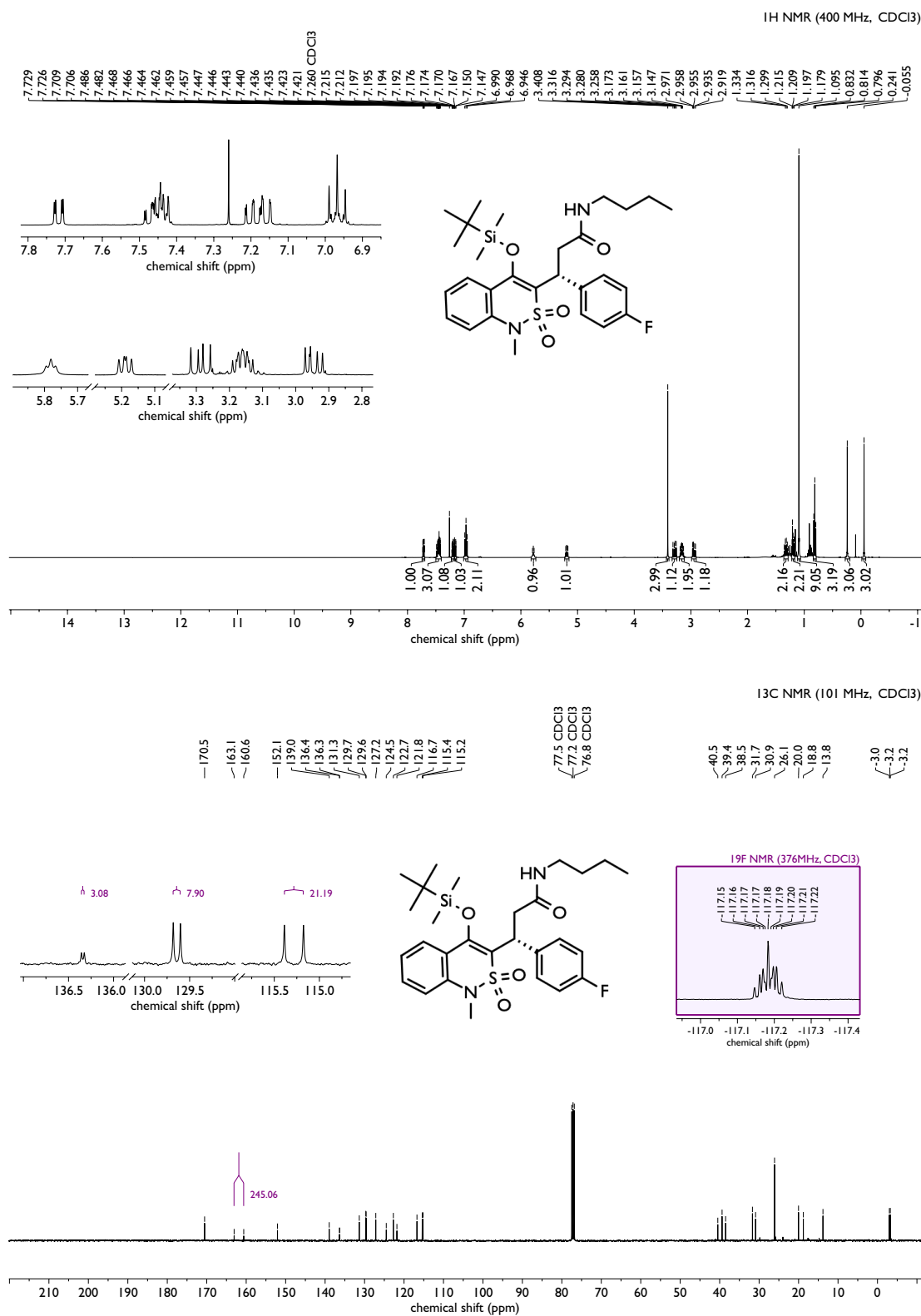


Figure S54: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ah**

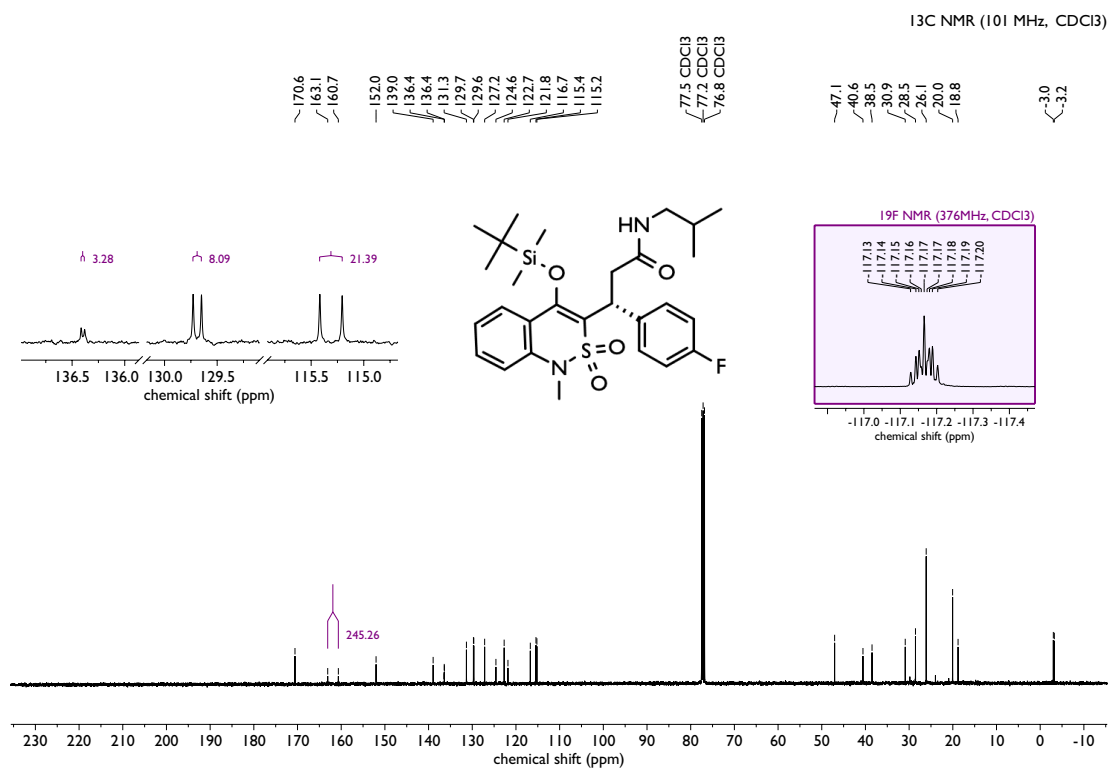
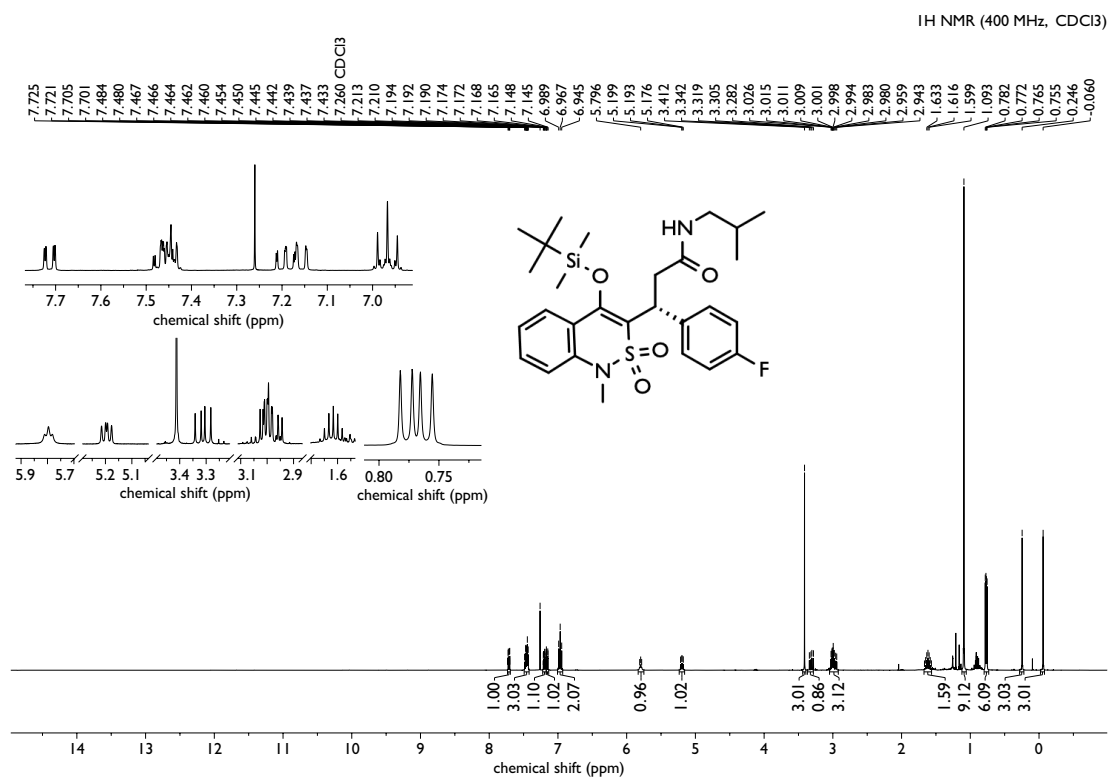


Figure S55: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4ai

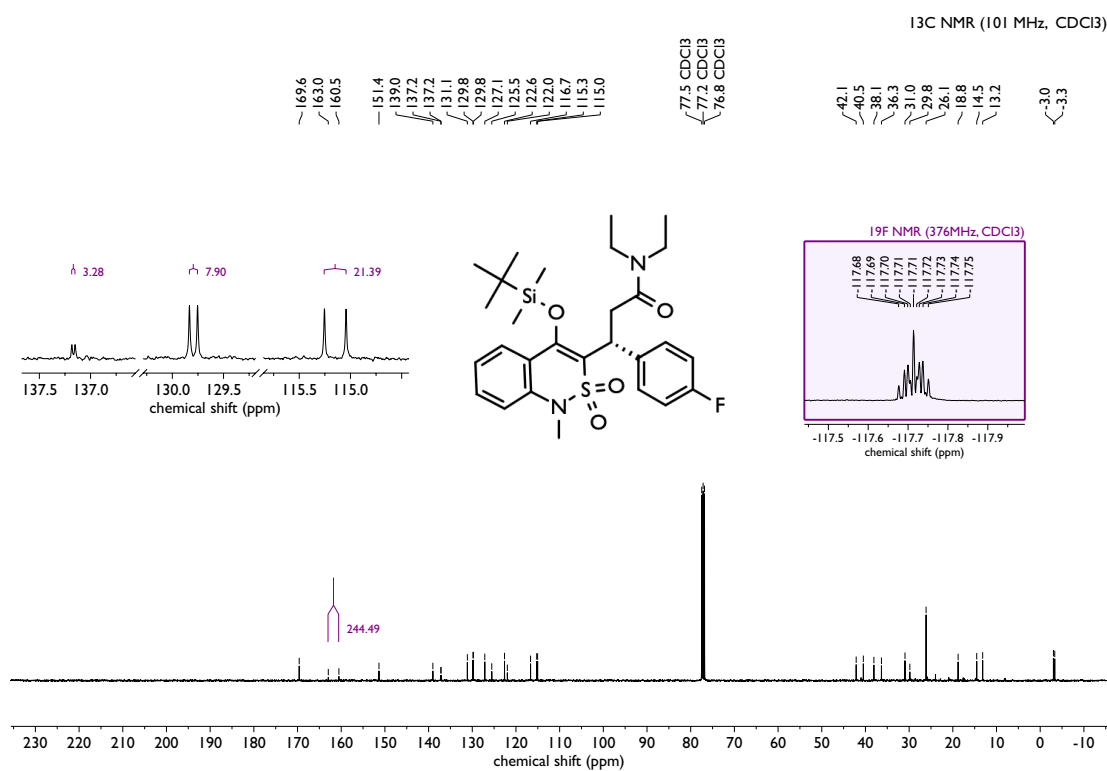
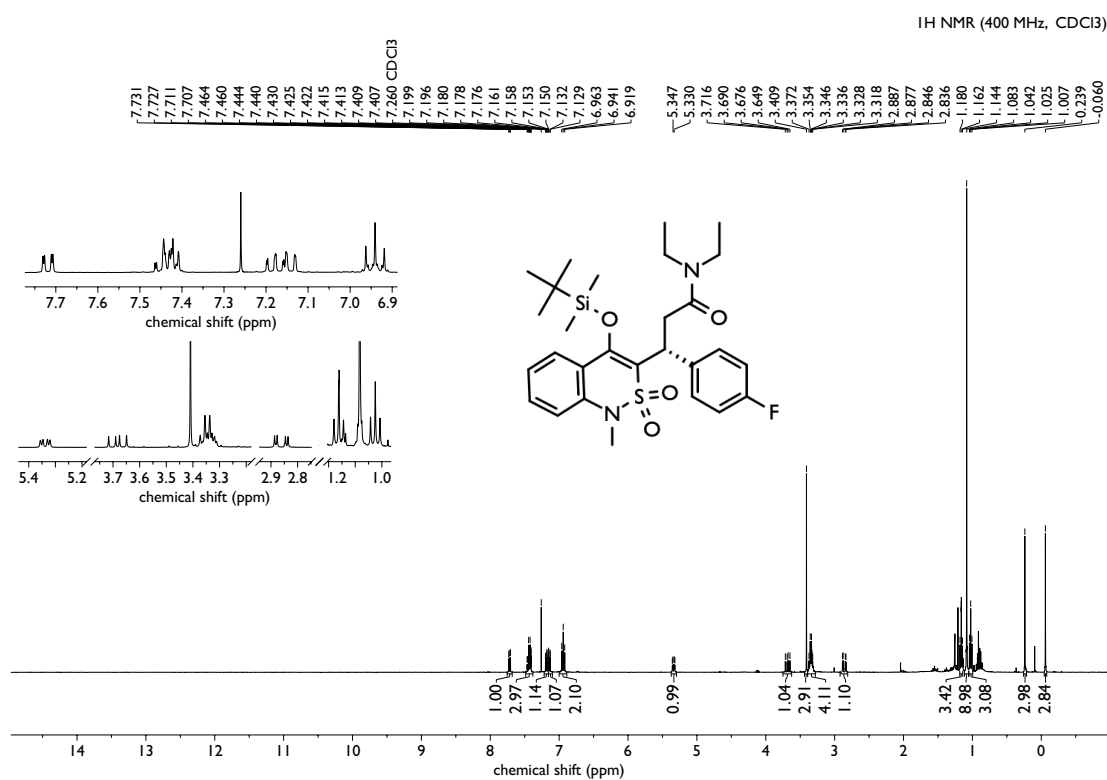


Figure S56: <sup>1</sup>H and <sup>13</sup>C spectra of compound 4aj



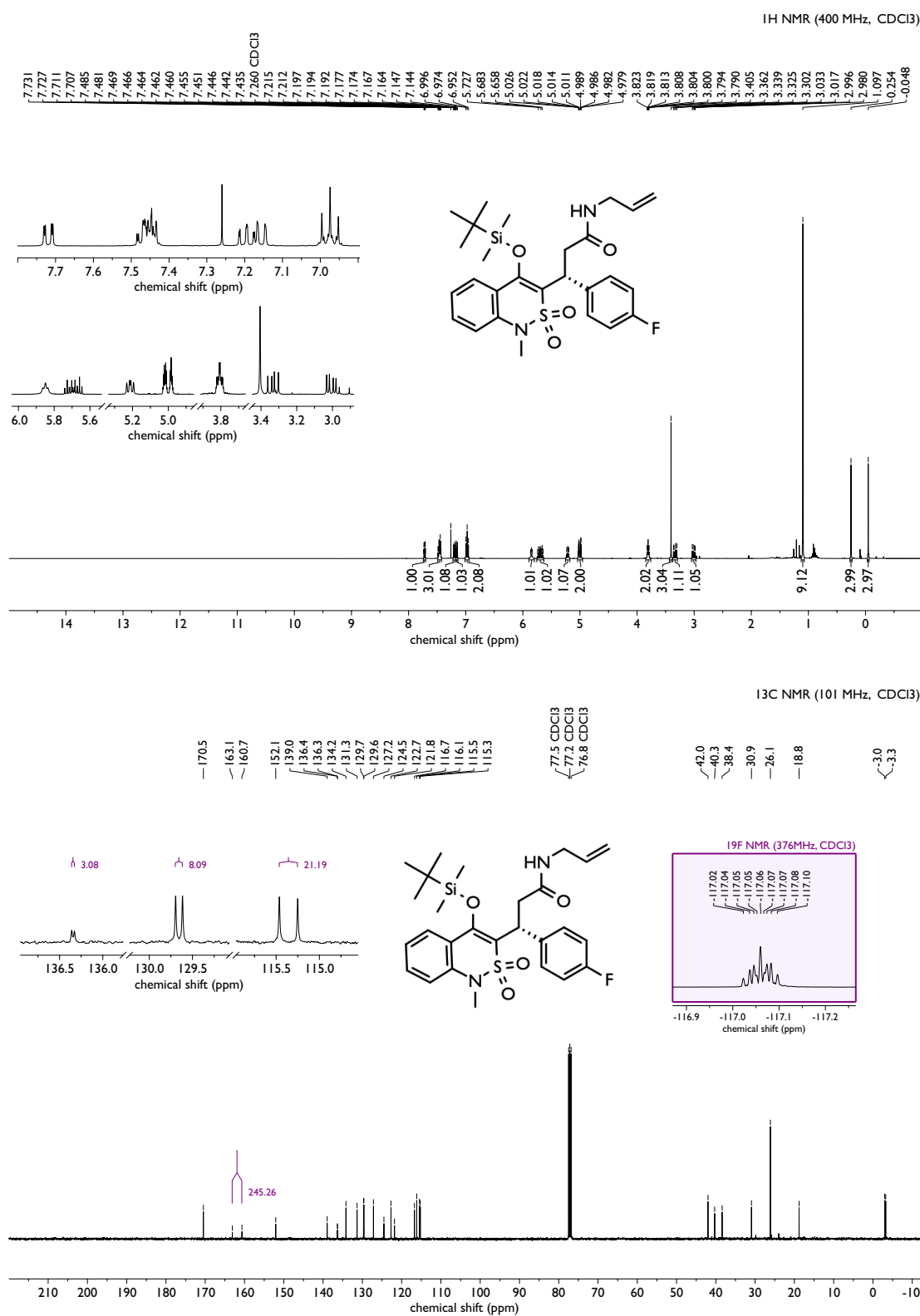


Figure S57: <sup>1</sup>H and <sup>13</sup>C spectra of compound **4ak**



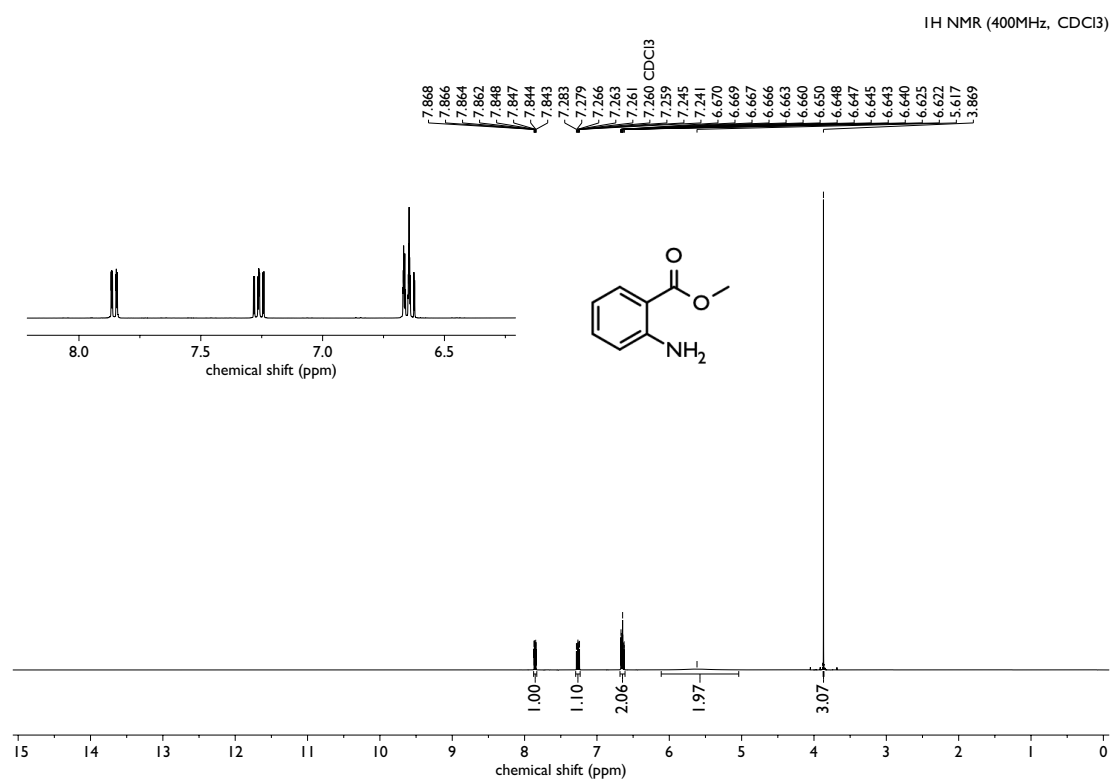


Figure S59:  $^1\text{H}$  spectra of compound **5a**

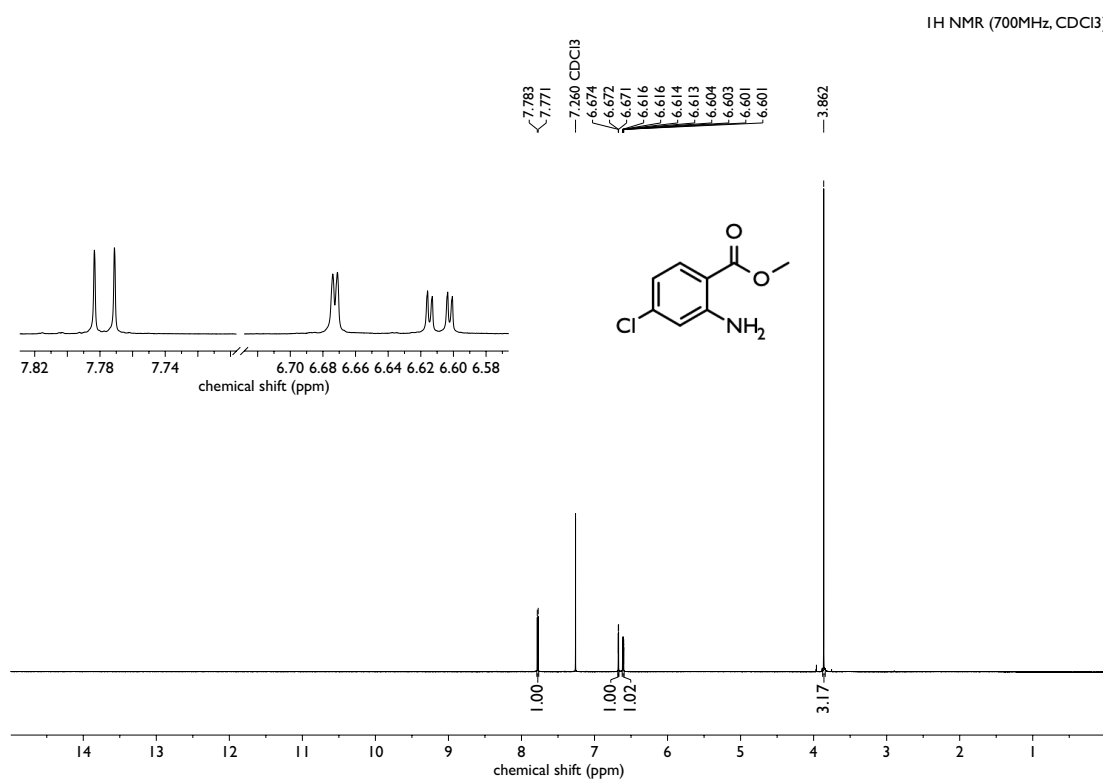


Figure S60:  $^1\text{H}$  spectra of compound **5b**

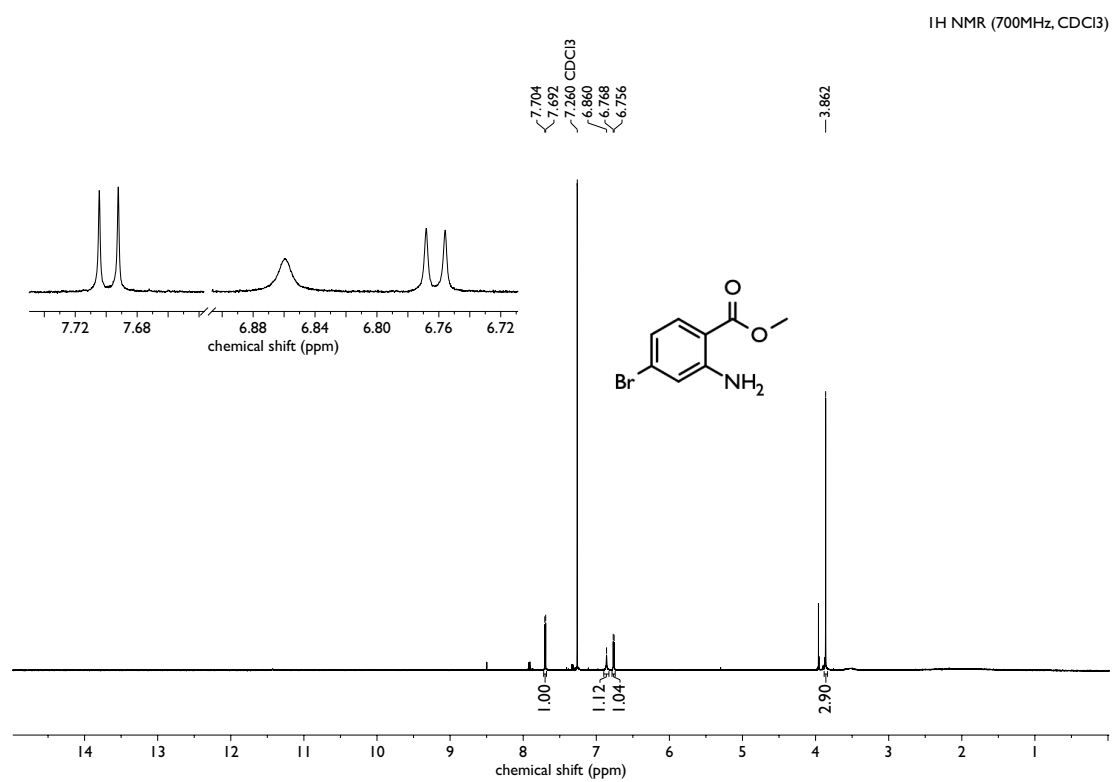


Figure S61:  $^1\text{H}$  spectra of compound **5c**

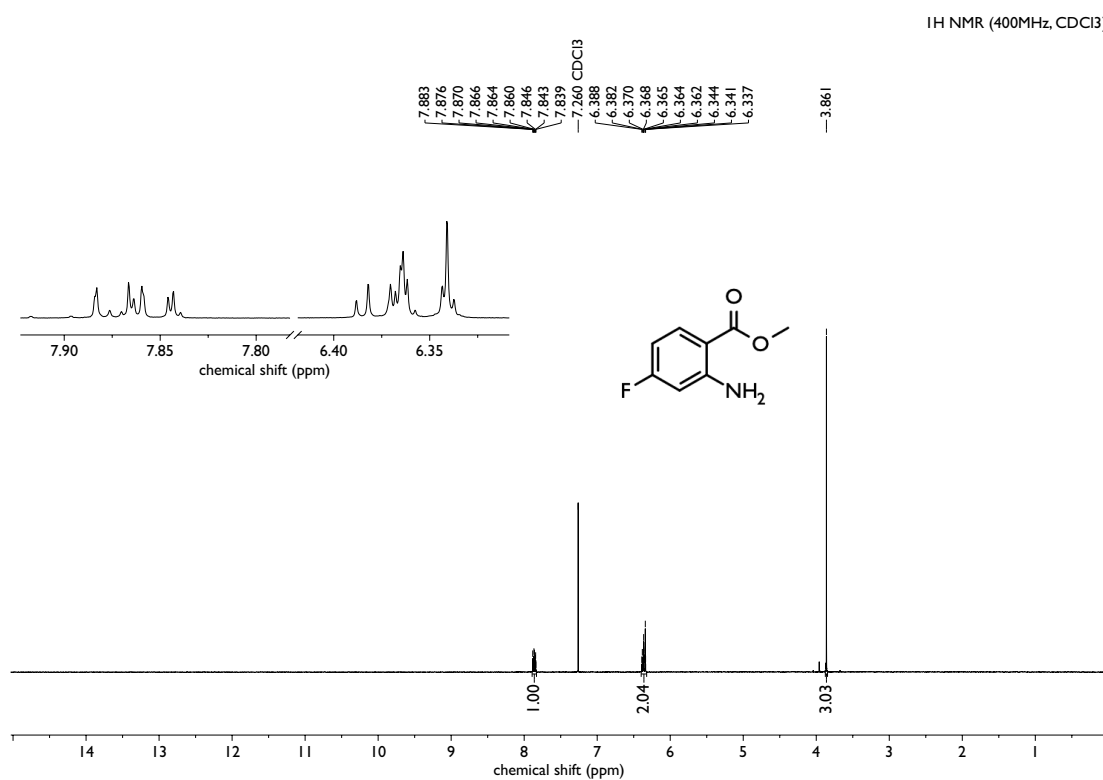


Figure S62: <sup>1</sup>H spectra of compound **5d**

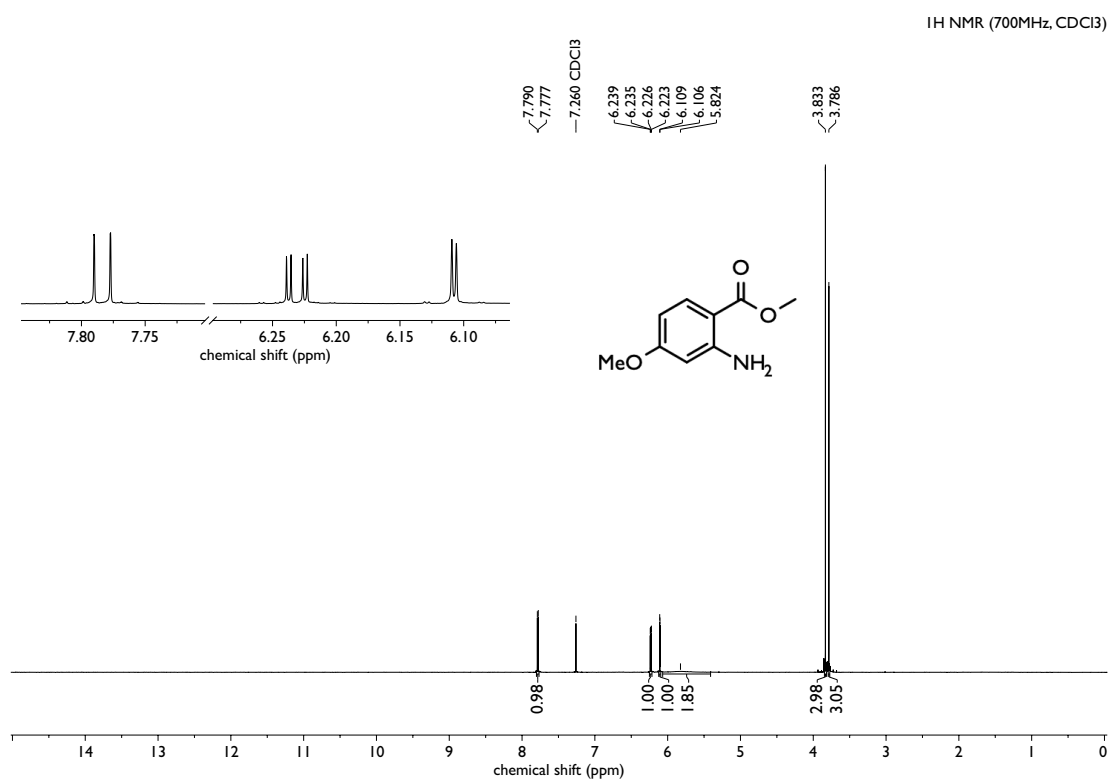


Figure S63: <sup>1</sup>H spectra of compound **5e**

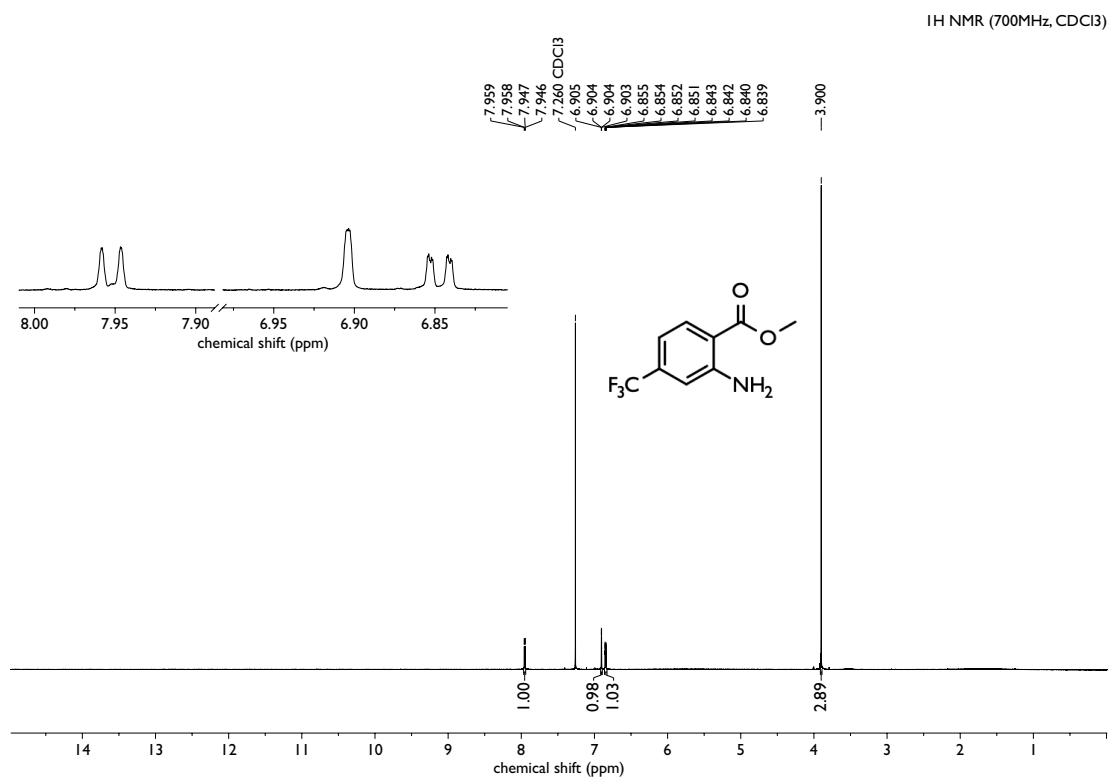


Figure S64: <sup>1</sup>H spectra of compound **5f**



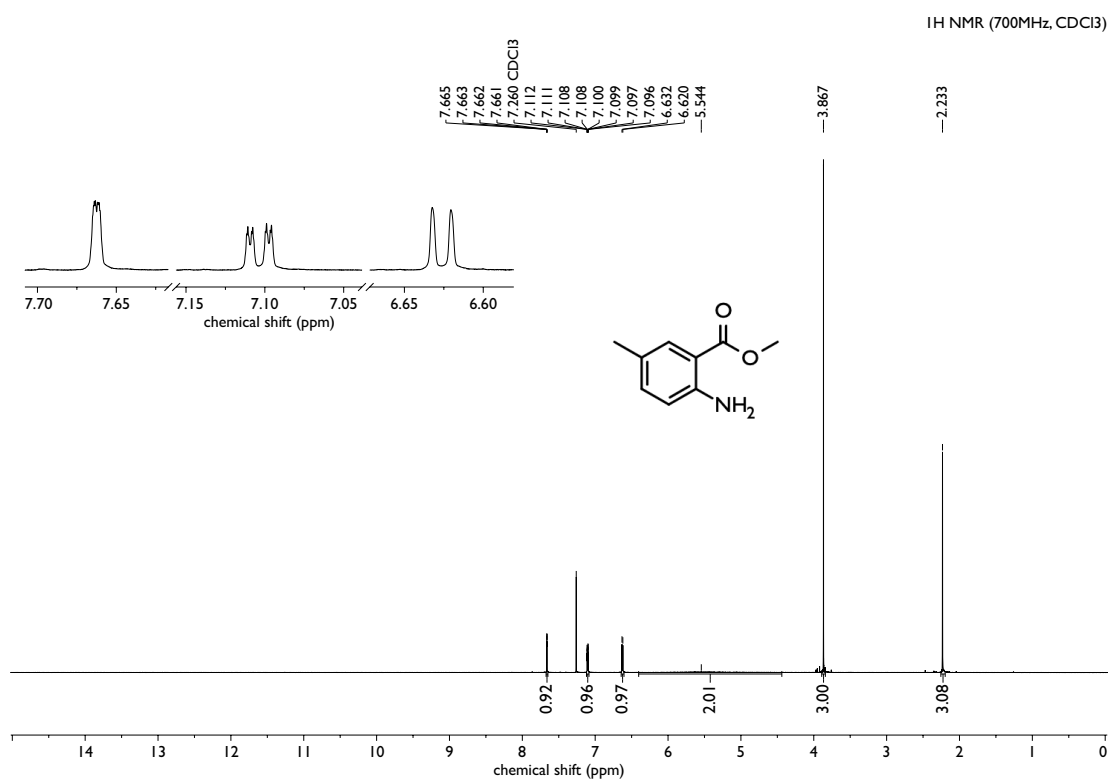


Figure S65: <sup>1</sup>H spectra of compound **5g**

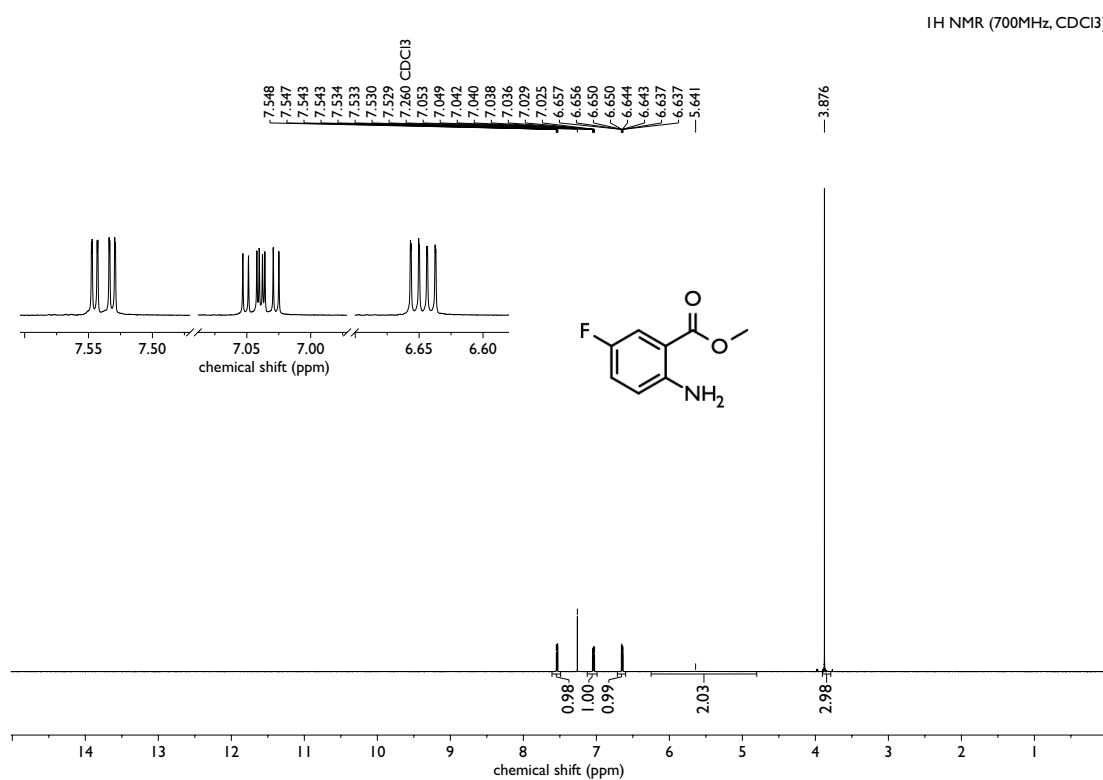


Figure S66: <sup>1</sup>H spectra of compound **5h**

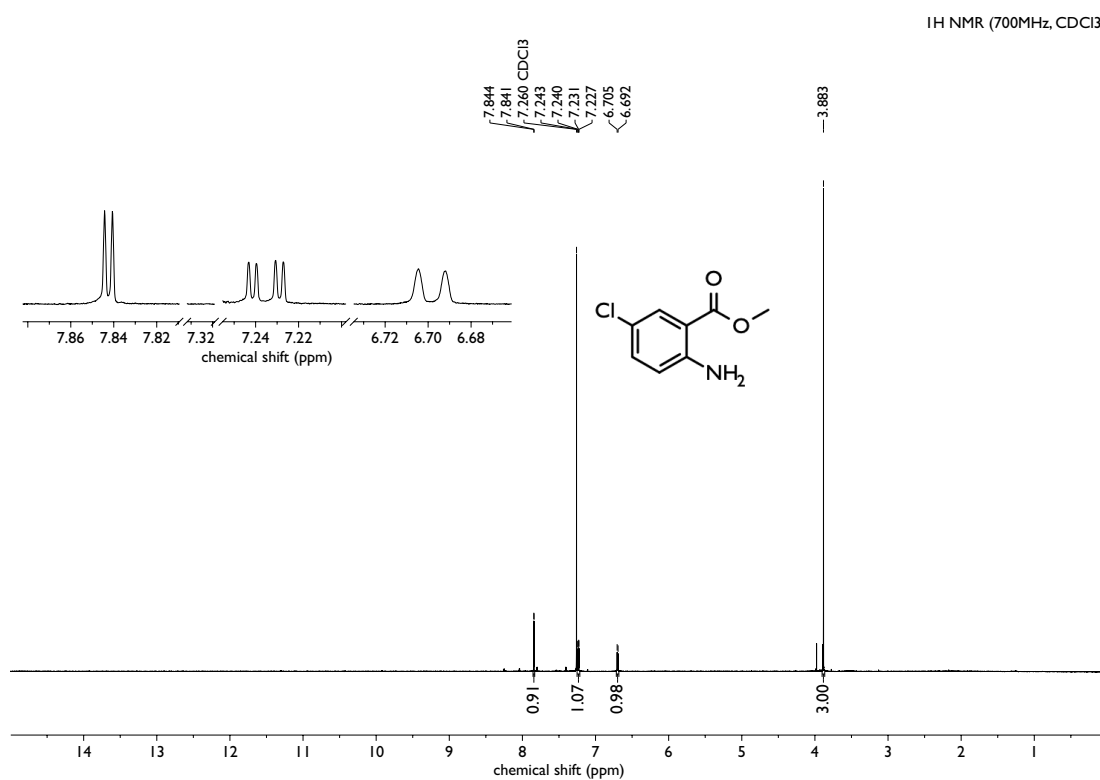


Figure S67:  $^1\text{H}$  spectra of compound **5i**

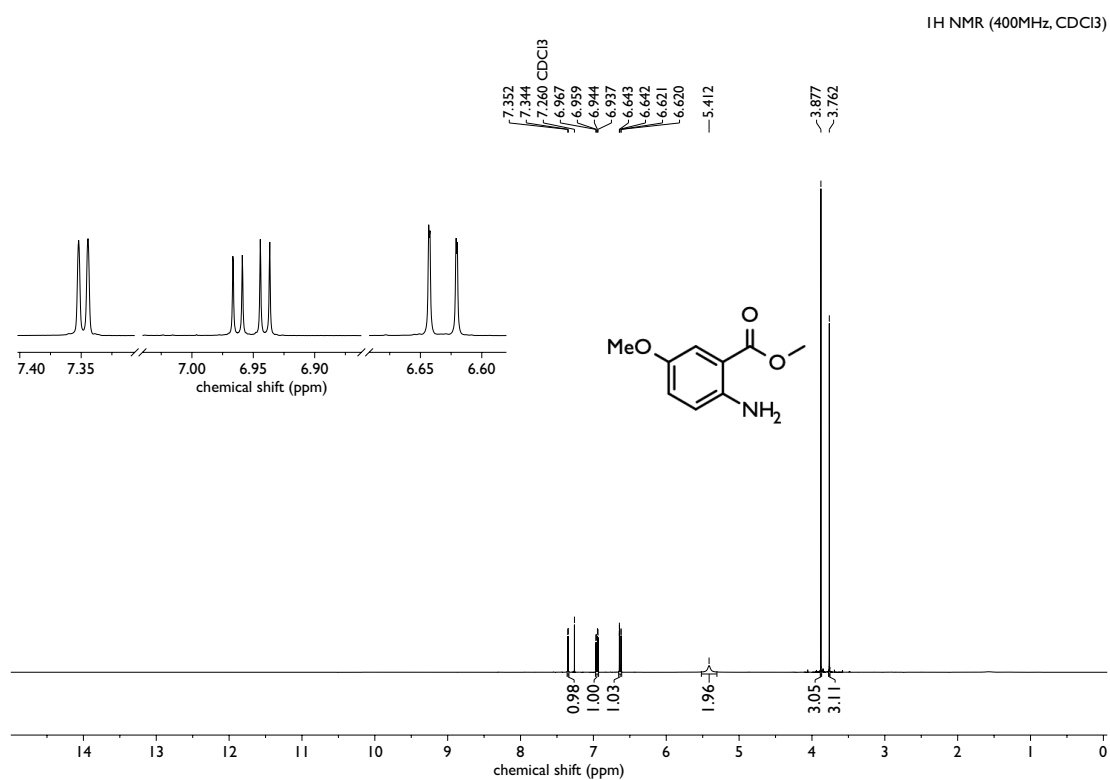


Figure S68: <sup>1</sup>H spectra of compound **5j**

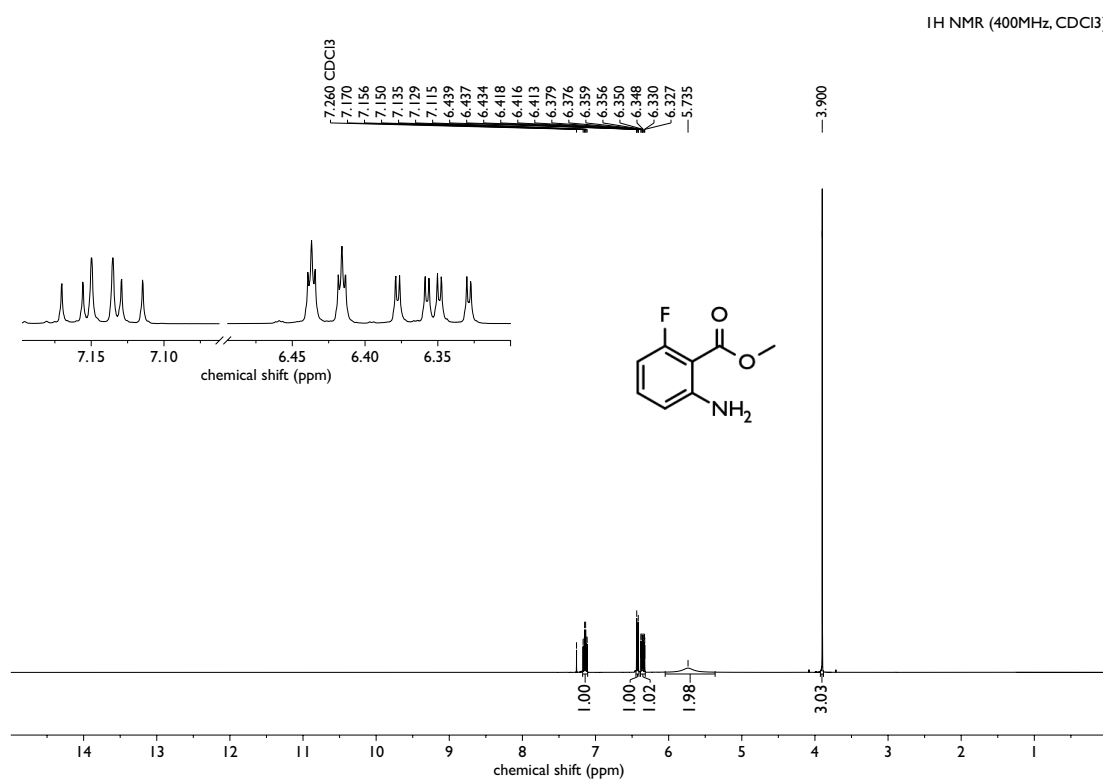


Figure S69: <sup>1</sup>H spectra of compound **5k**

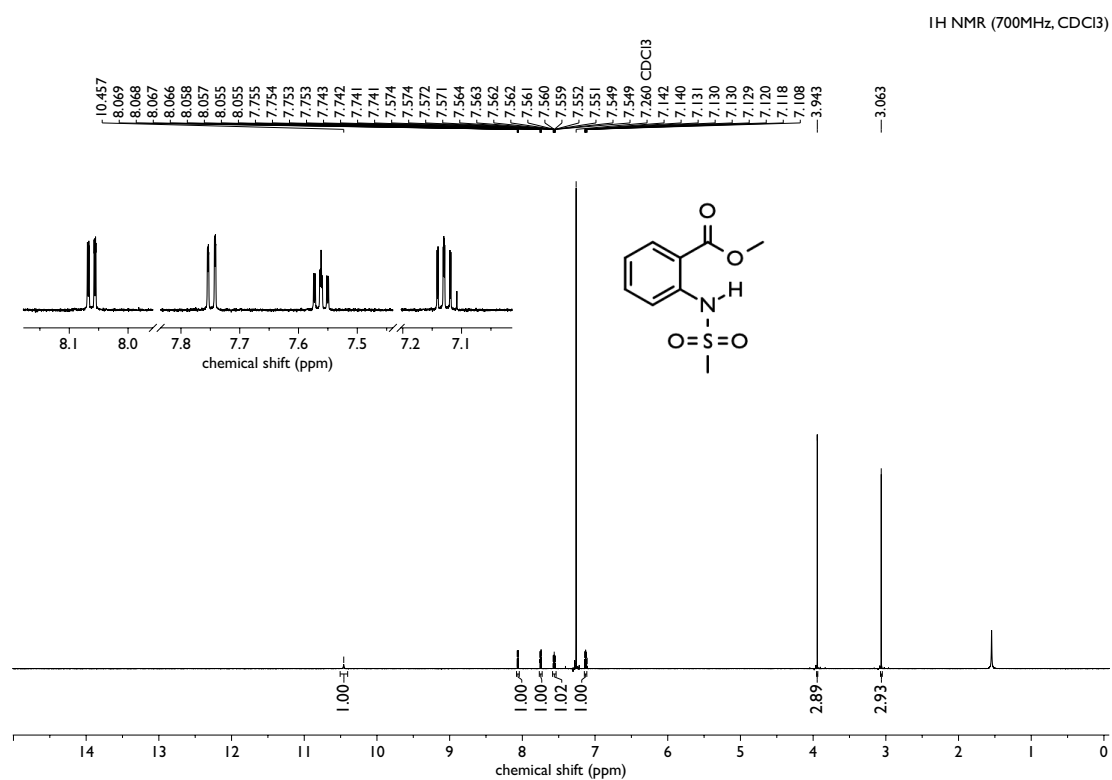


Figure S70: <sup>1</sup>H spectra of compound **6a**

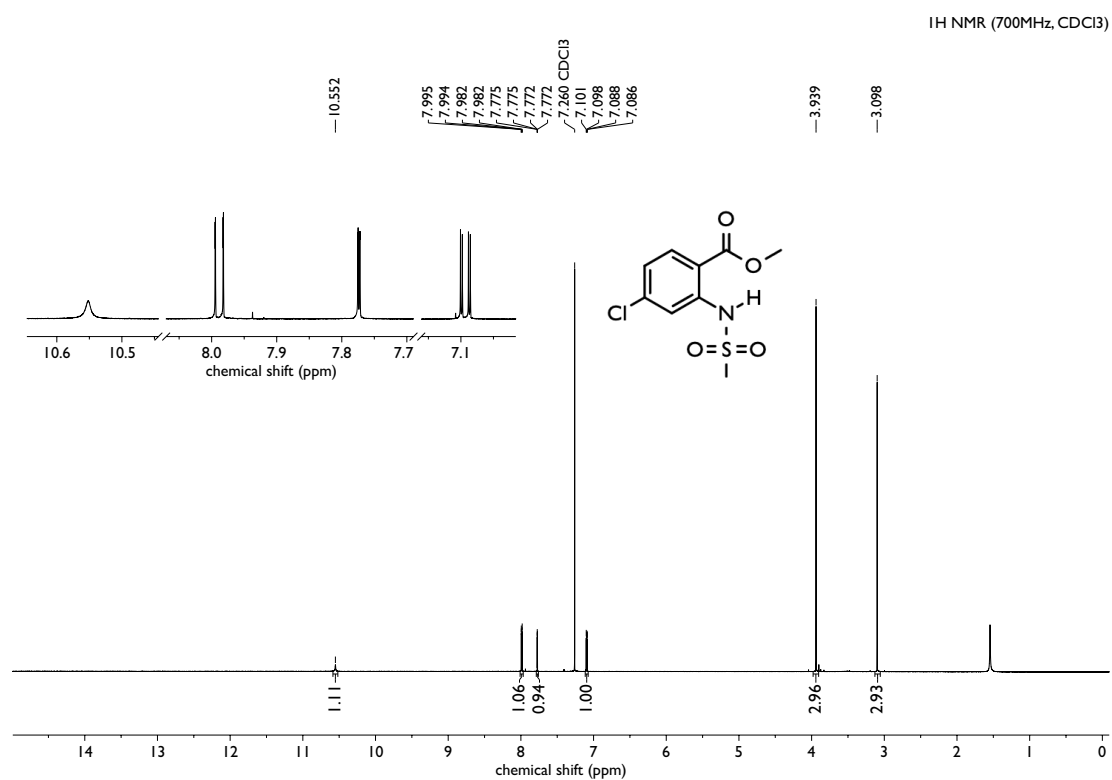


Figure S71: <sup>1</sup>H spectra of compound **6b**

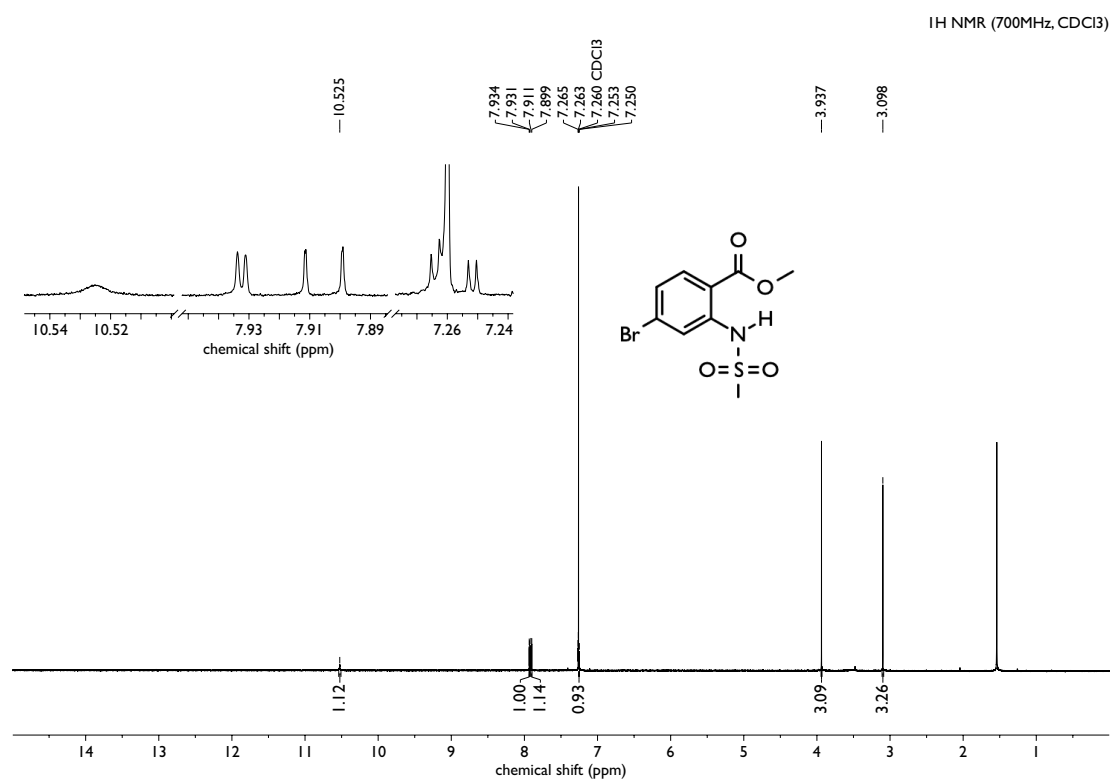


Figure S72:  $^1\text{H}$  spectra of compound **6c**



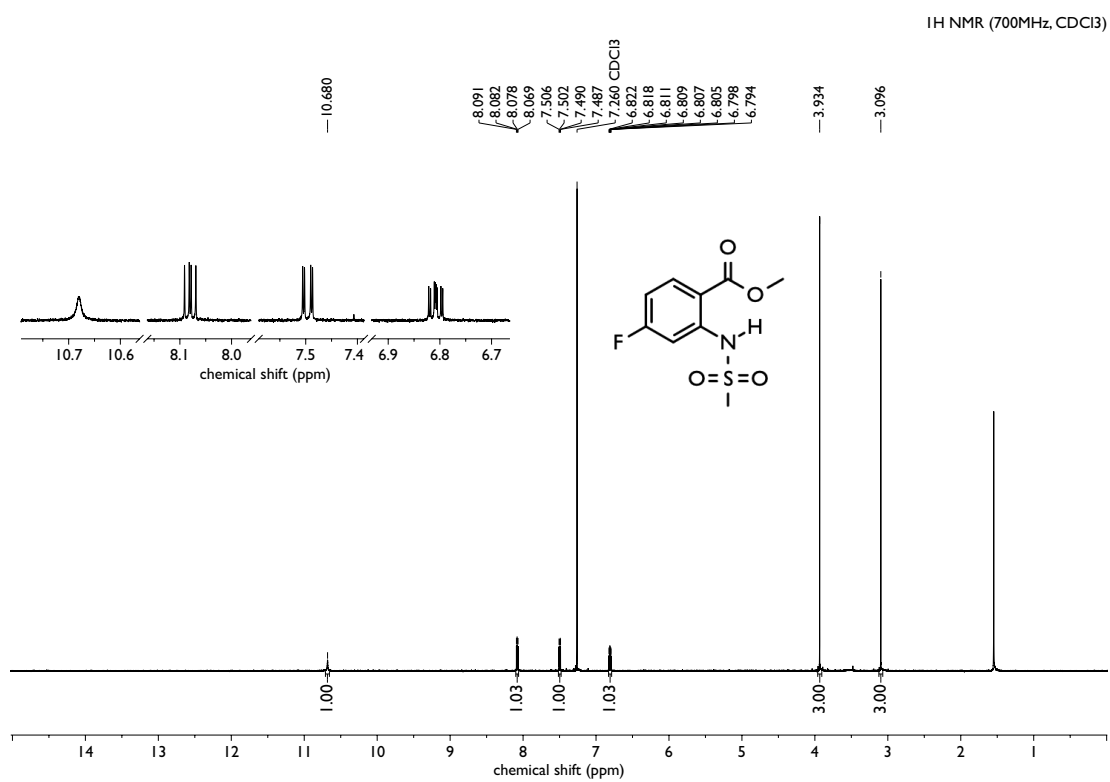


Figure S73: <sup>1</sup>H spectra of compound **6d**

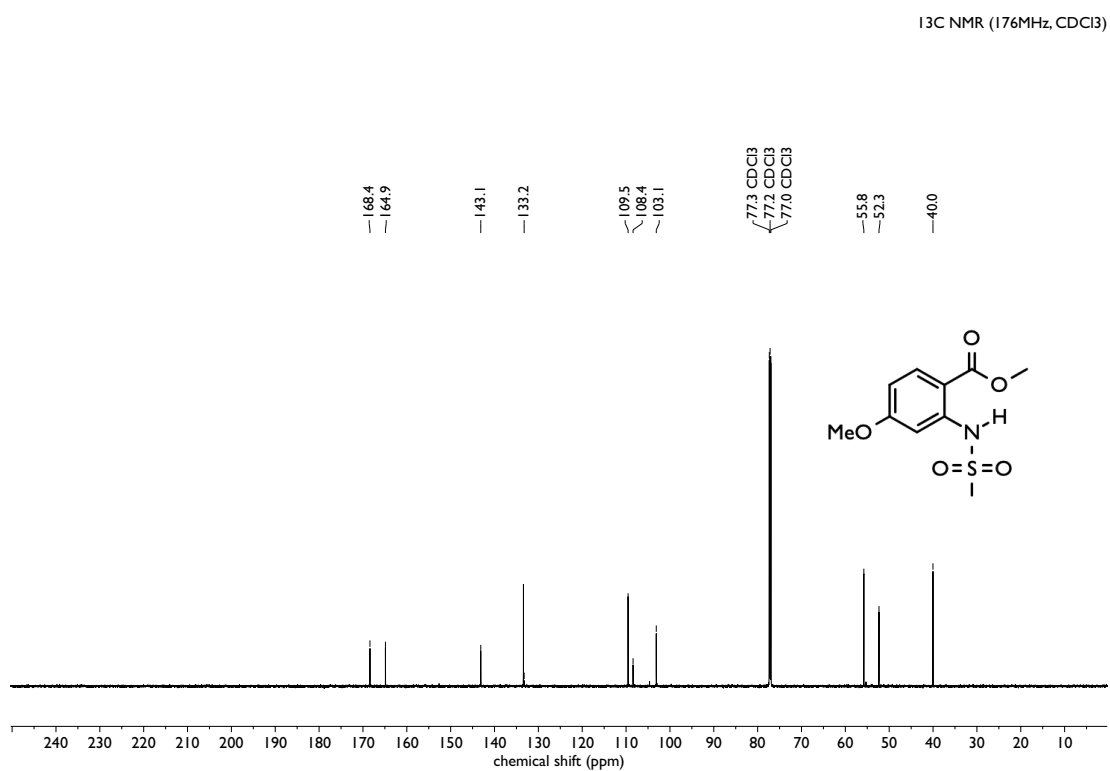
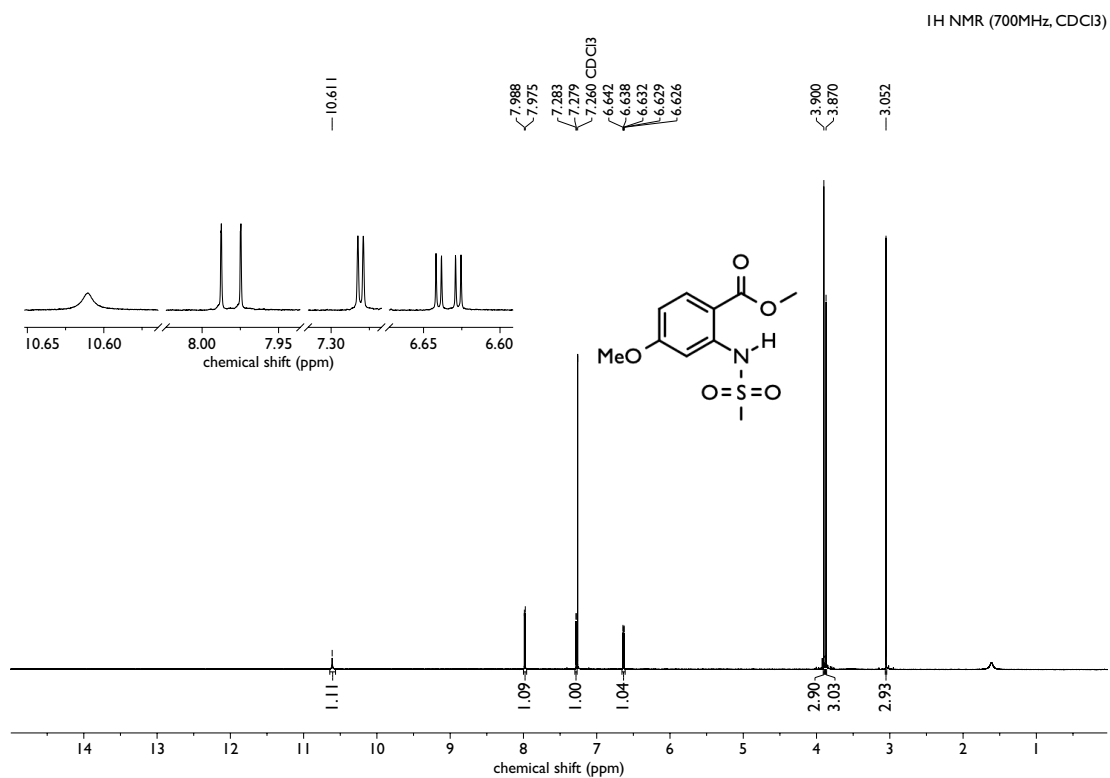


Figure S74: <sup>1</sup>H and <sup>13</sup>C spectra of compound **6e**

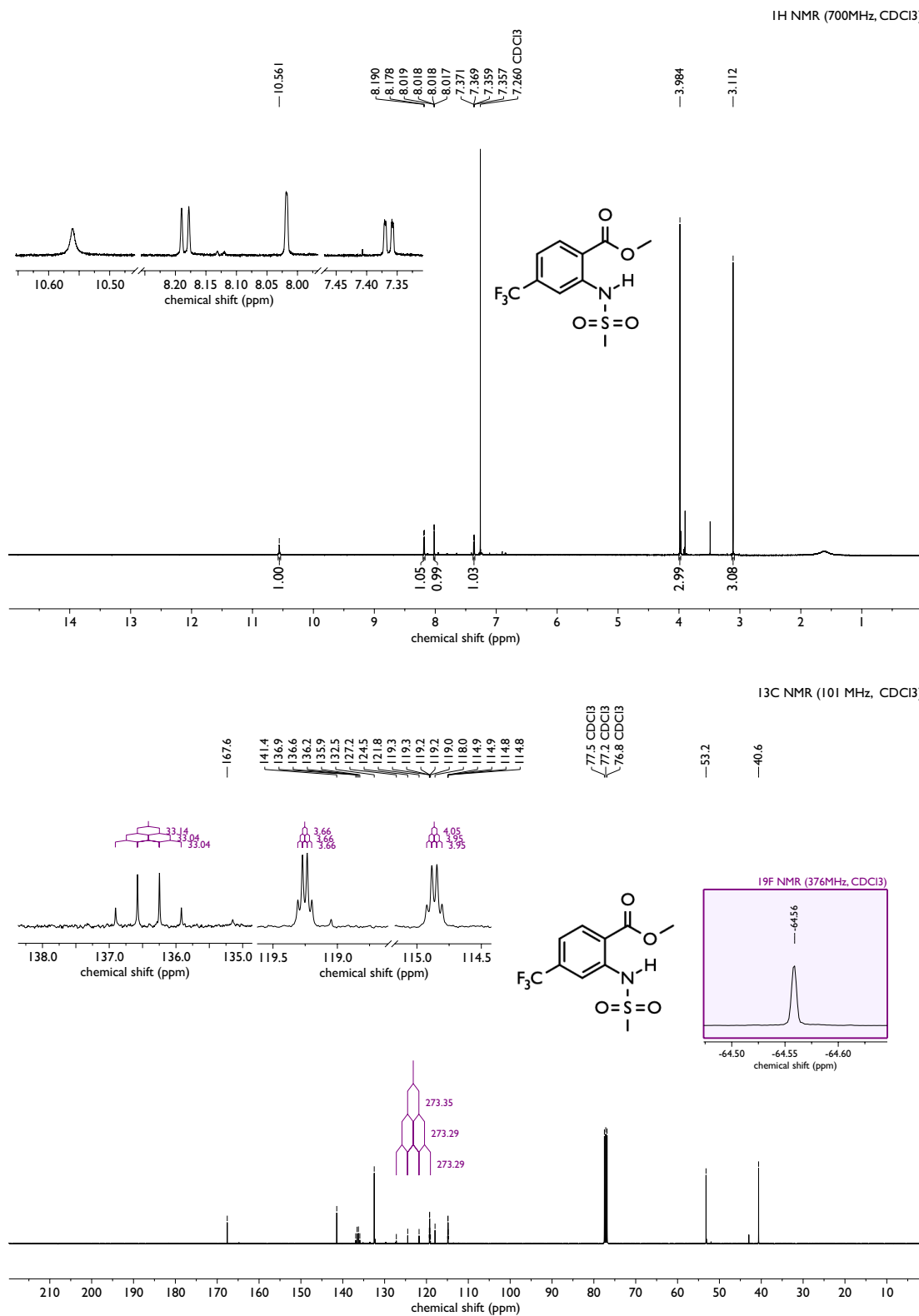


Figure S75: <sup>1</sup>H spectra of compound **6f**

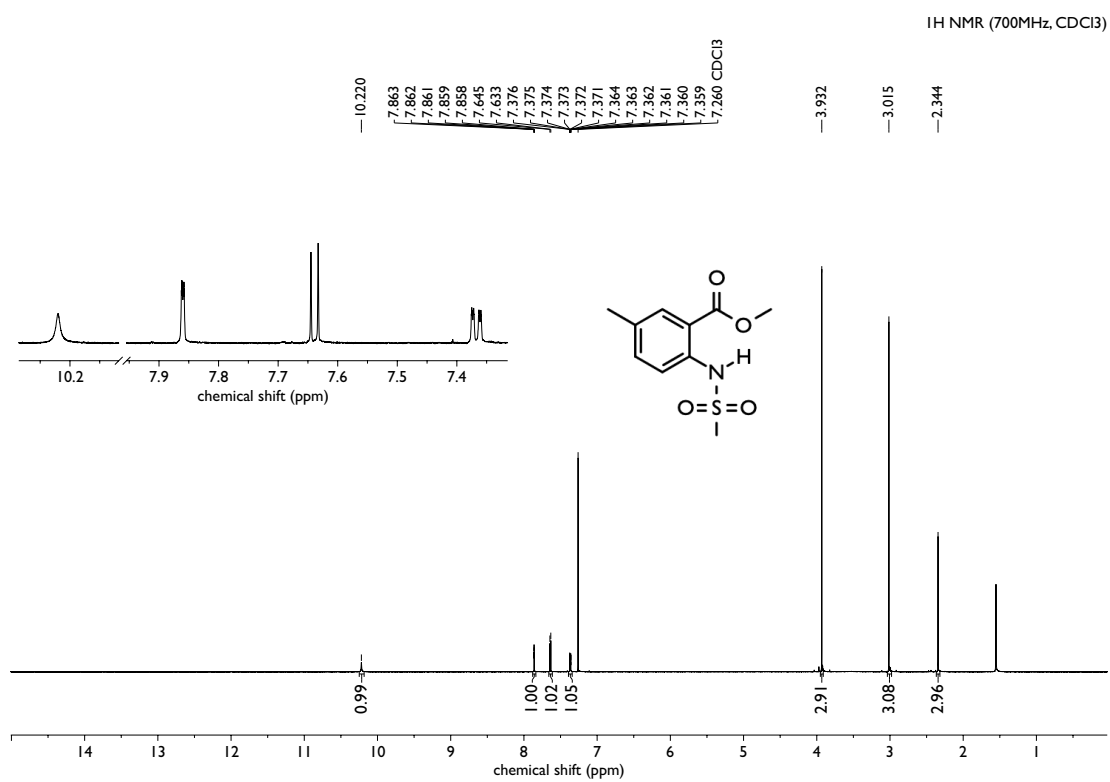


Figure S76:  $^1\text{H}$  spectra of compound **6g**

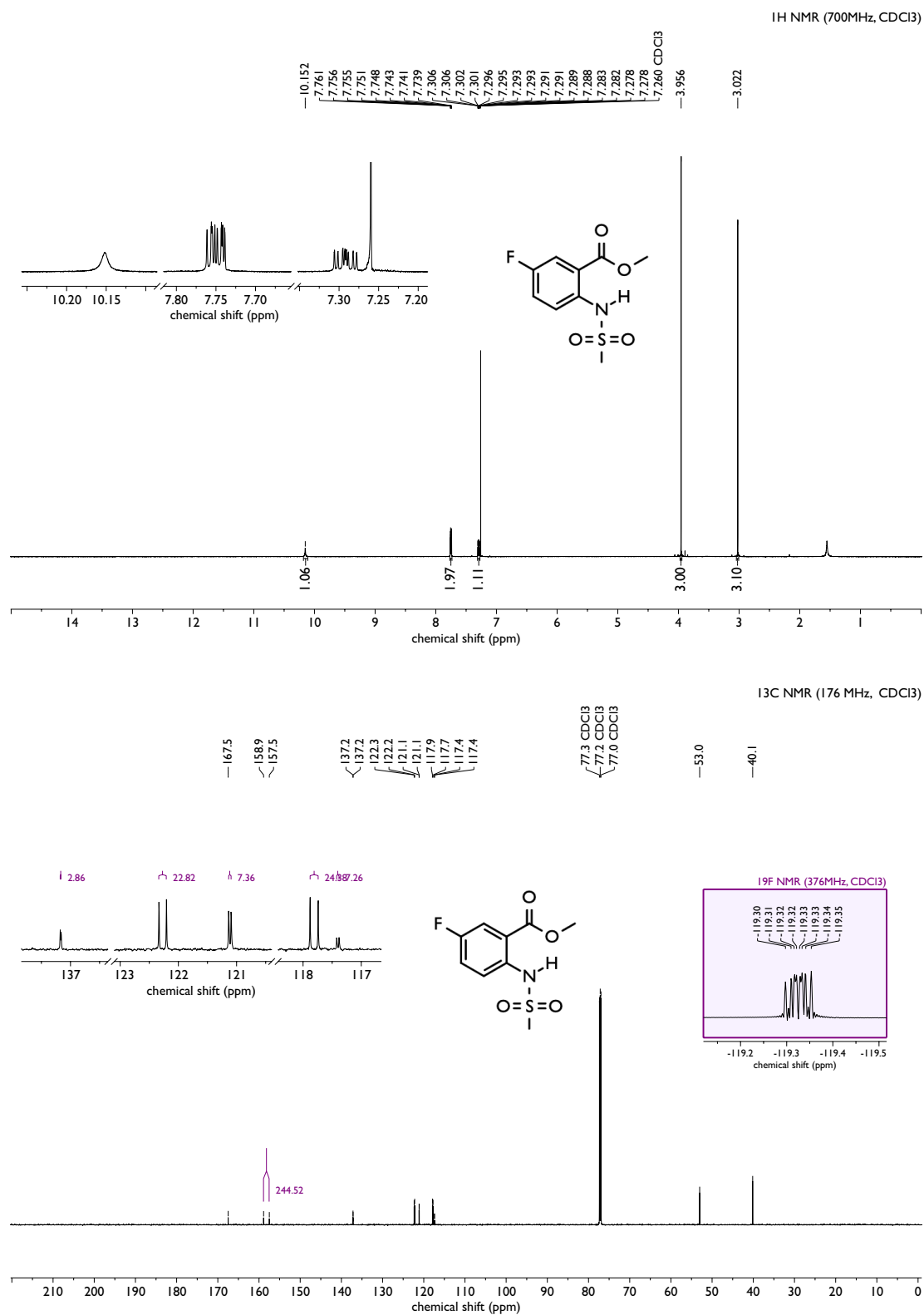


Figure S77: <sup>1</sup>H and <sup>13</sup>C spectra of compound **6h**

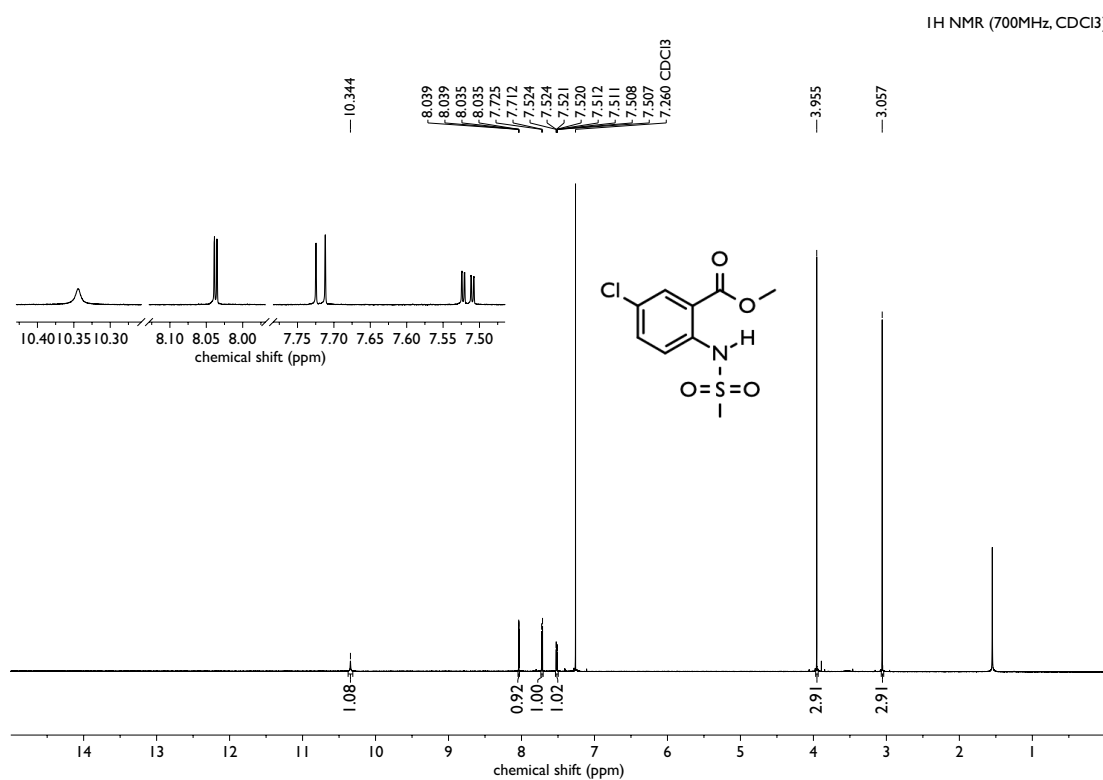


Figure S78: <sup>1</sup>H spectra of compound **6i**

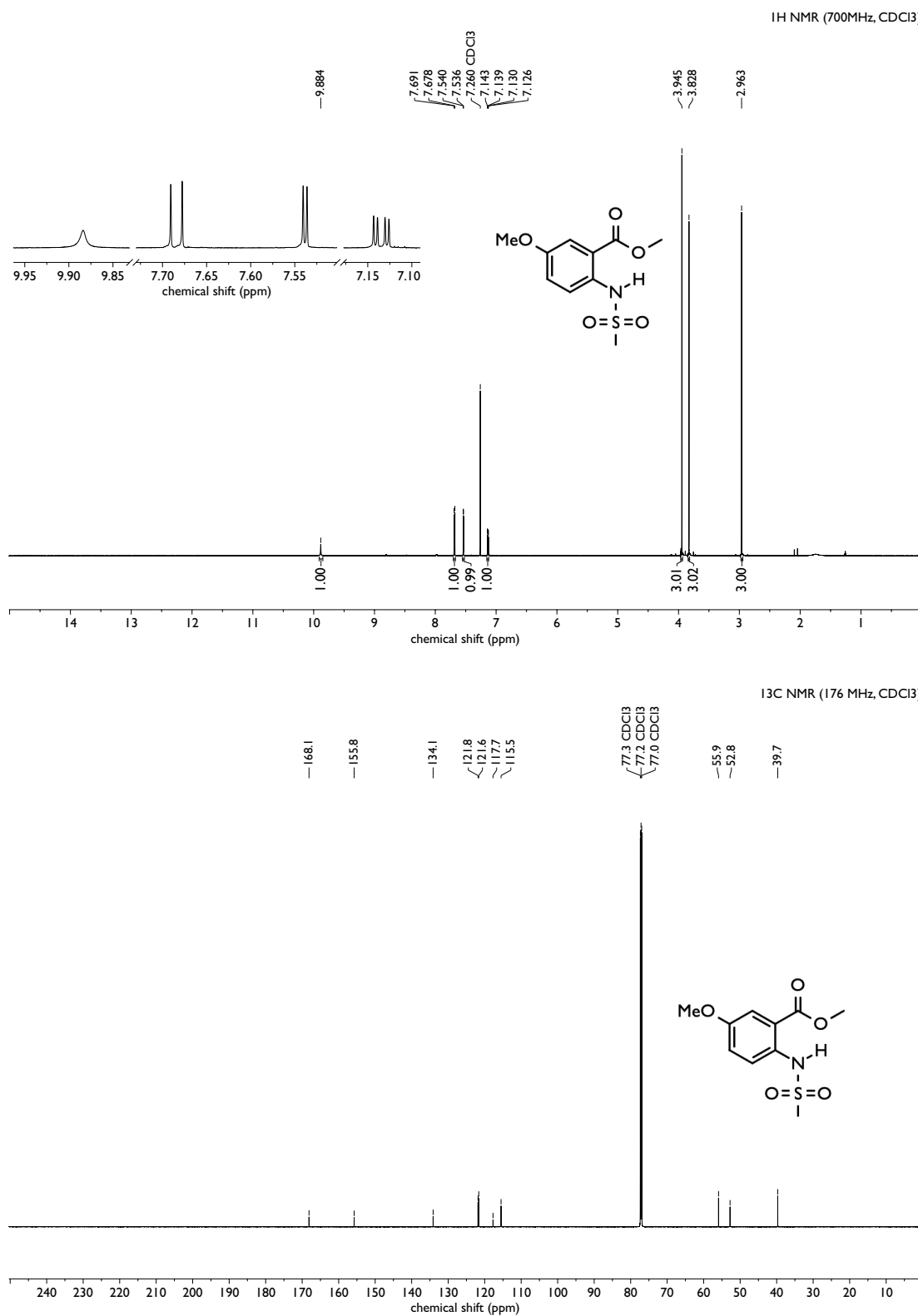


Figure S79: <sup>1</sup>H and <sup>13</sup>C spectra of compound **6j**

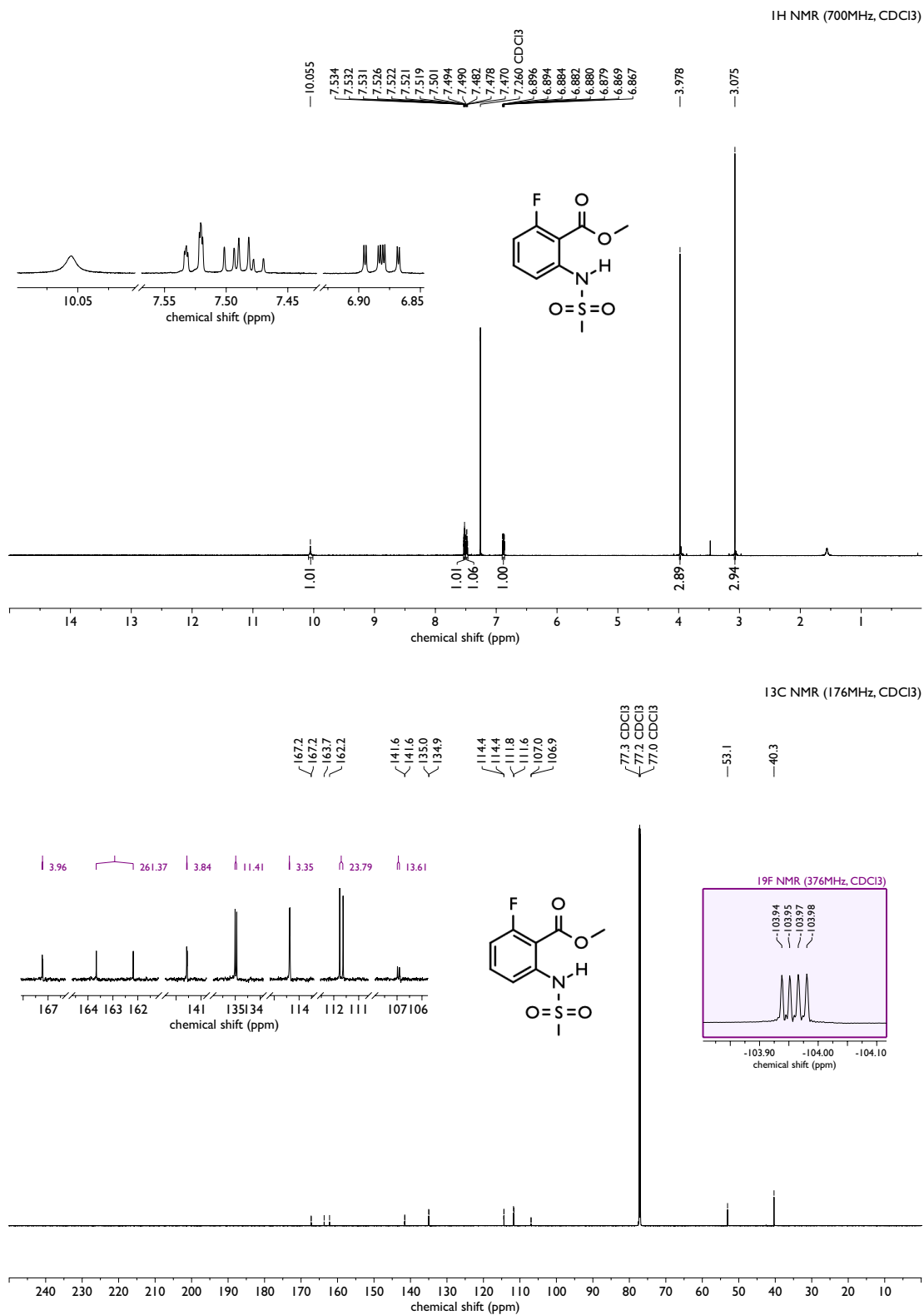


Figure S80: <sup>1</sup>H and <sup>13</sup>C spectra of compound **6k**



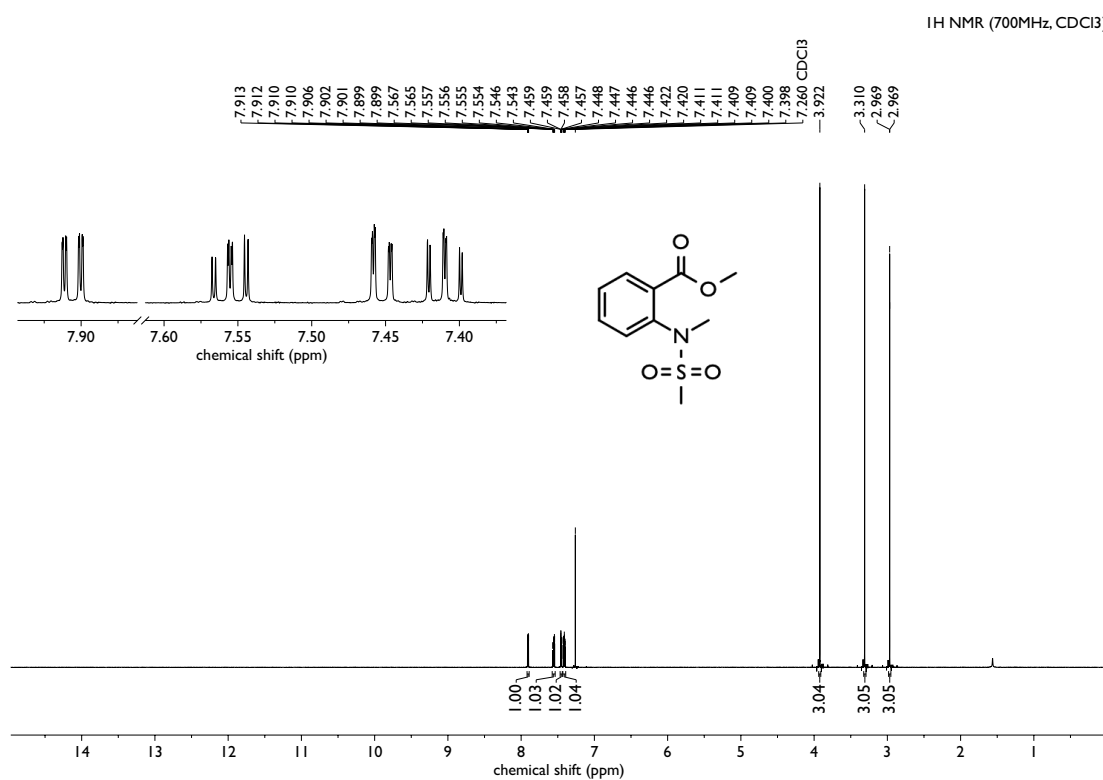


Figure S81:  $^1\text{H}$  spectra of compound **7a**

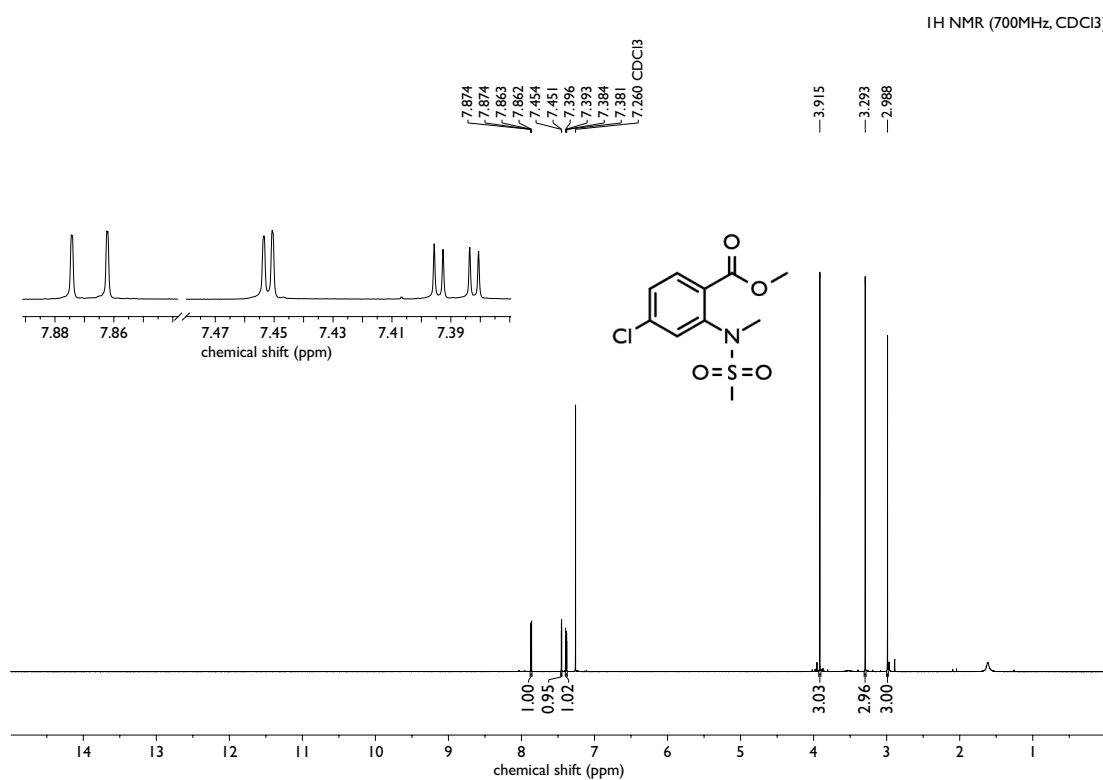


Figure S82:  $^1\text{H}$  spectra of compound **7b**

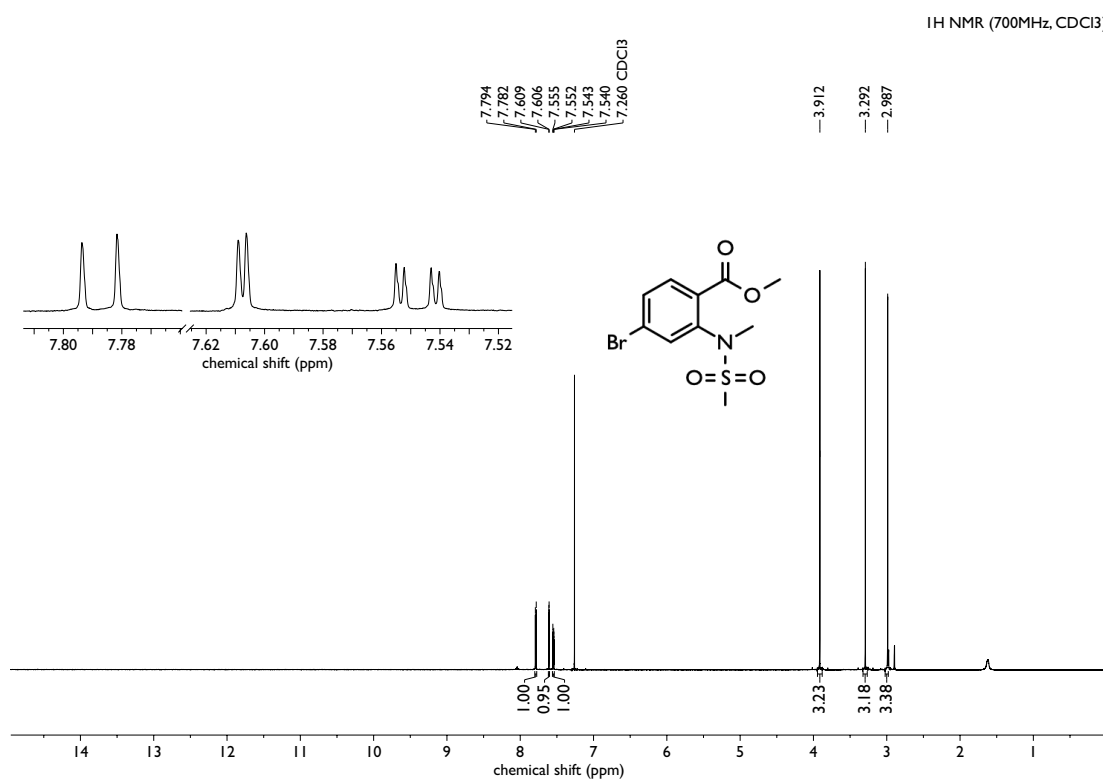


Figure S83: <sup>1</sup>H spectra of compound **7c**

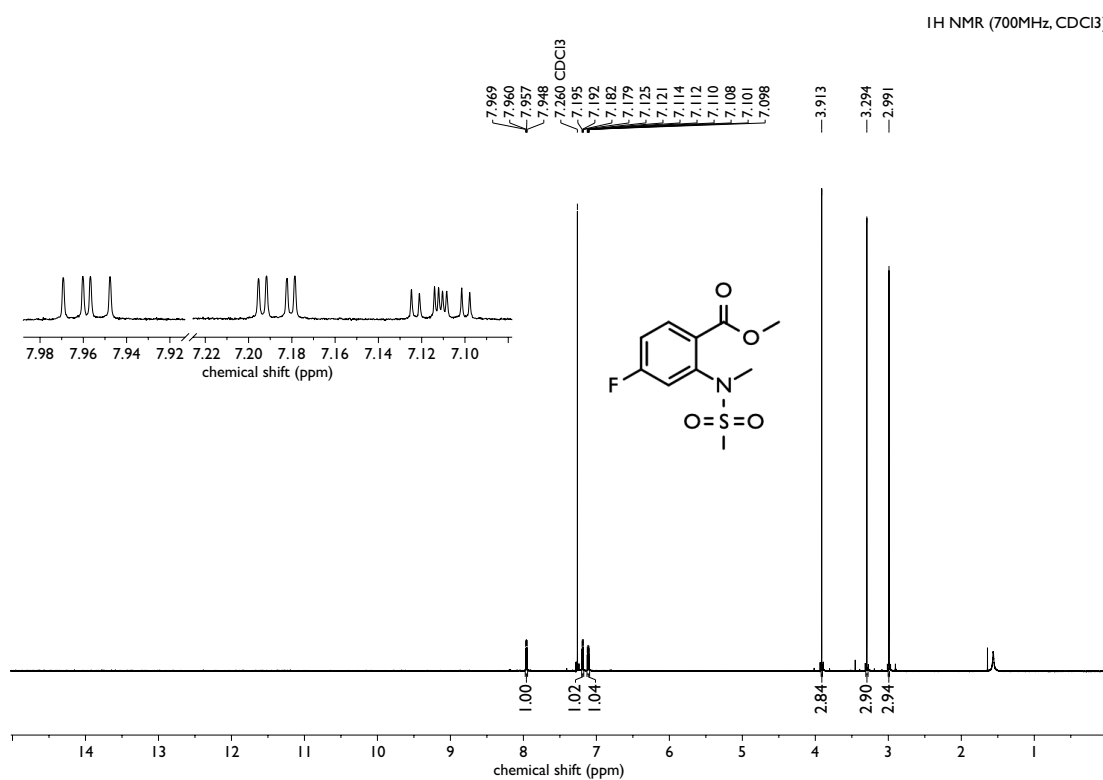


Figure S84:  $^1\text{H}$  spectra of compound **7d**

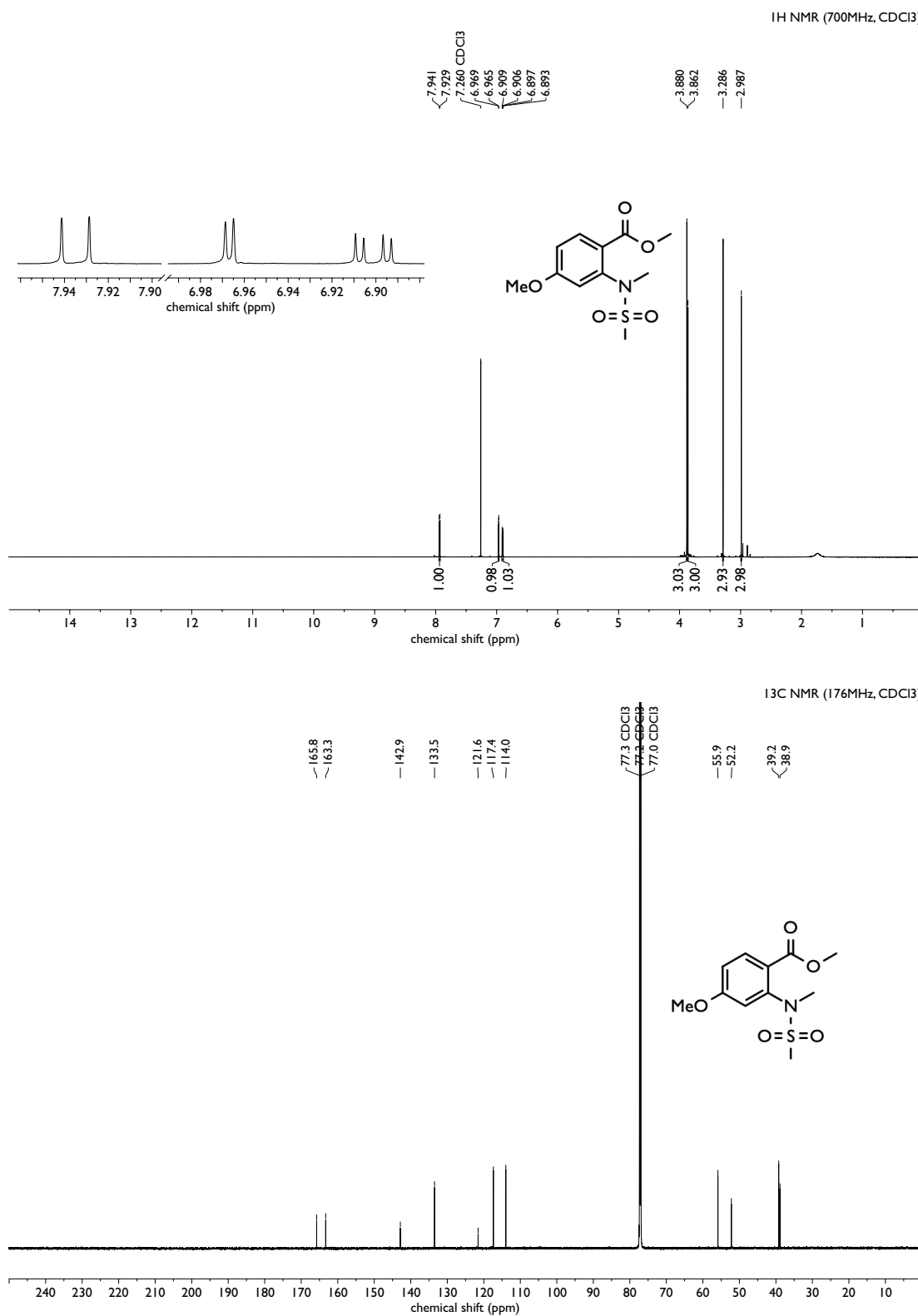


Figure S85: <sup>1</sup>H and <sup>13</sup>C spectra of compound **7e**

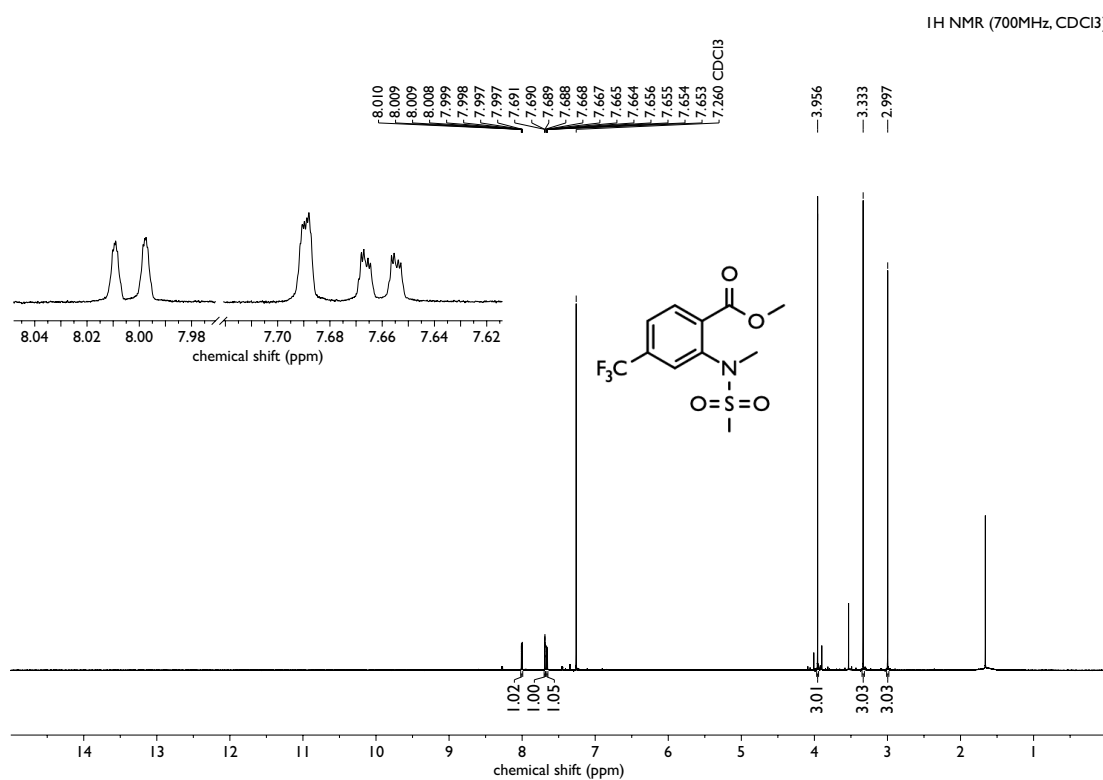


Figure S86:  $^1\text{H}$  spectra of compound **7f**

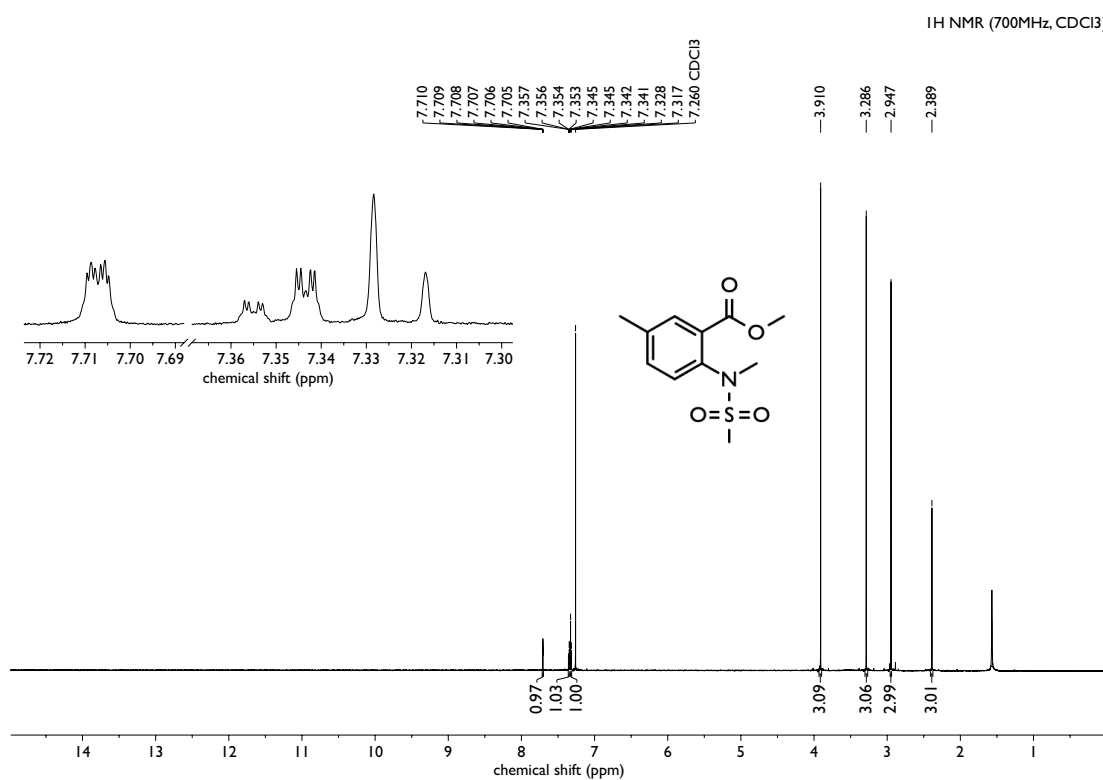


Figure S87: <sup>1</sup>H spectra of compound **7g**

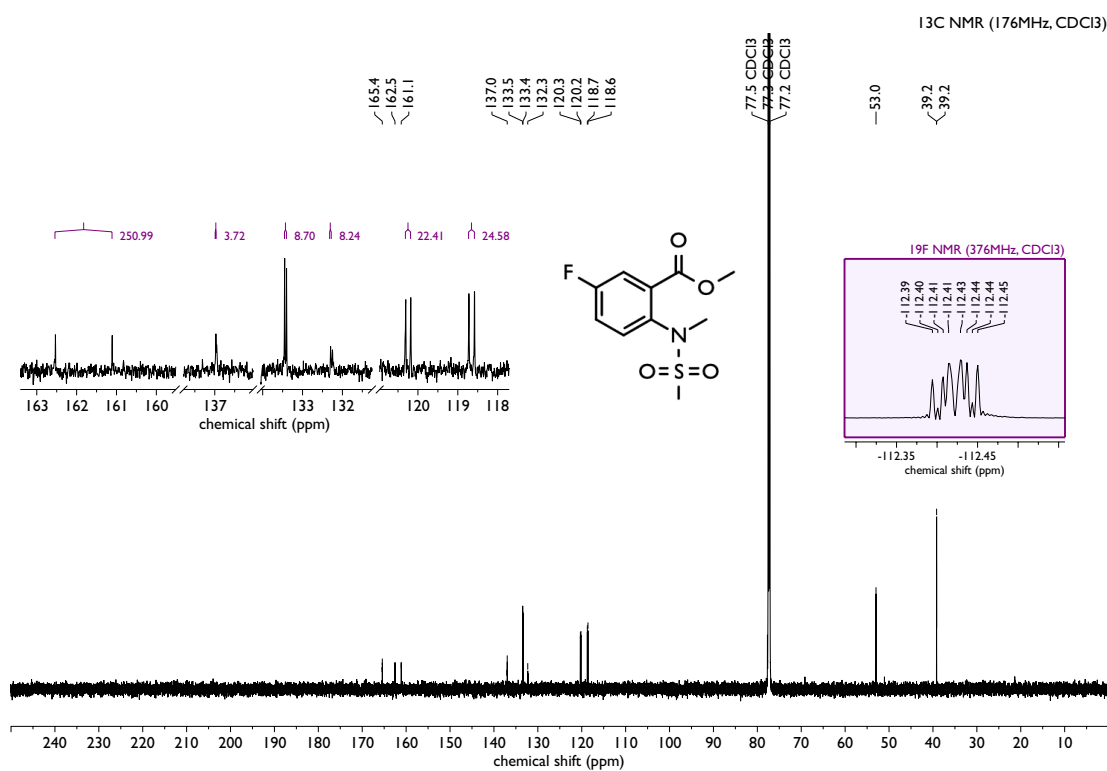
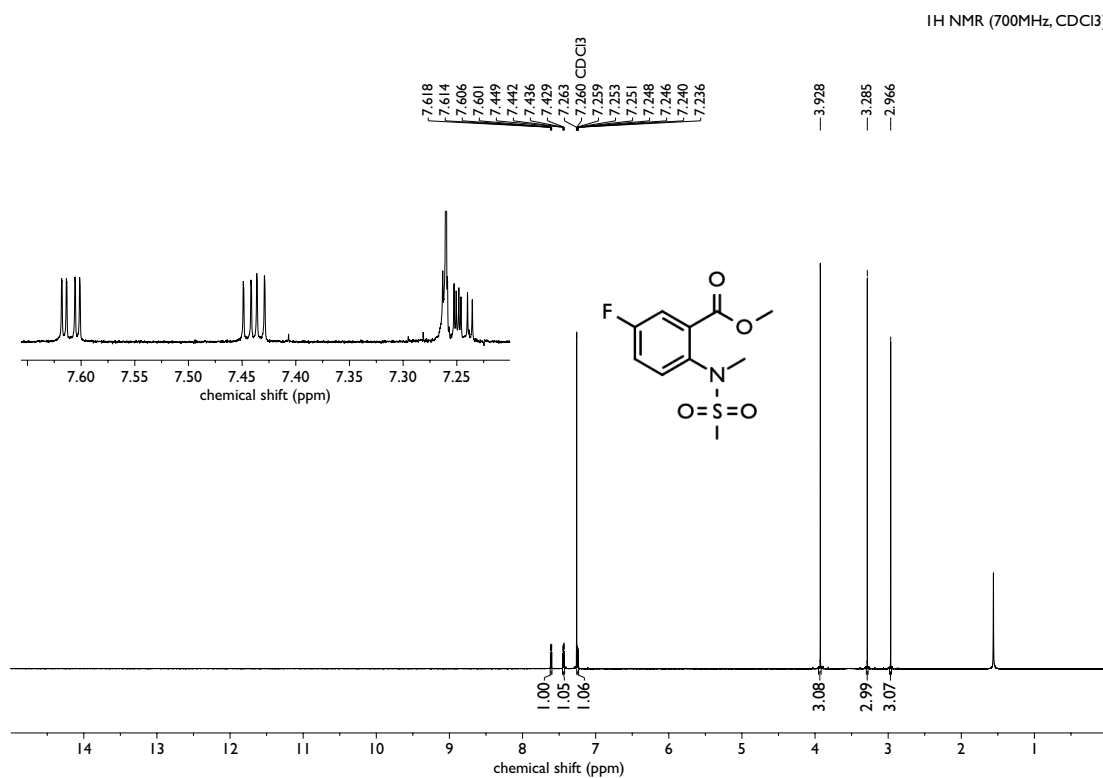


Figure S88: <sup>1</sup>H and <sup>13</sup>C spectra of compound **7h**



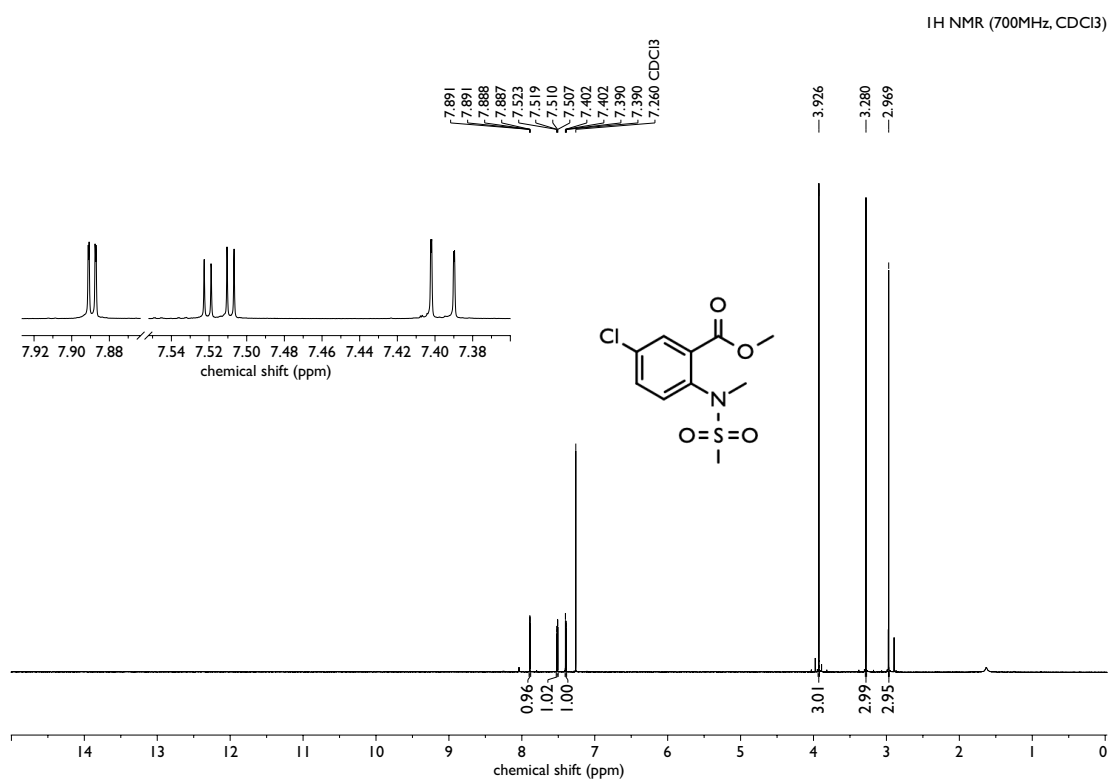


Figure S89: <sup>1</sup>H spectra of compound **7i**

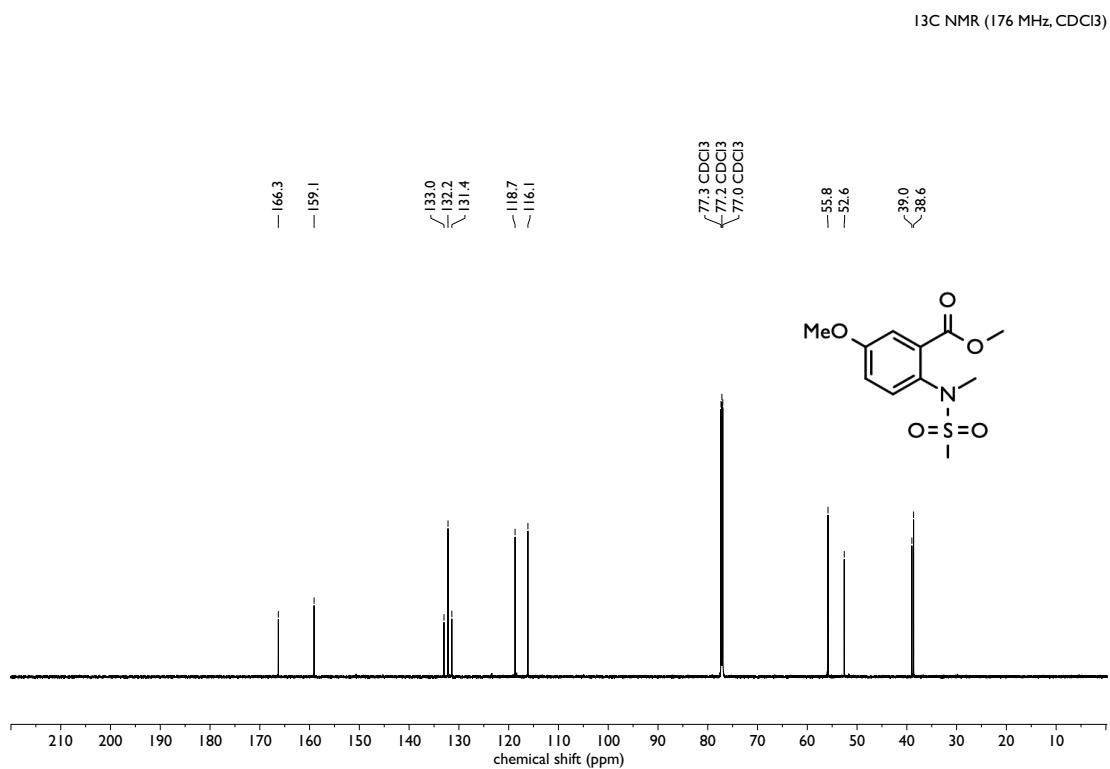
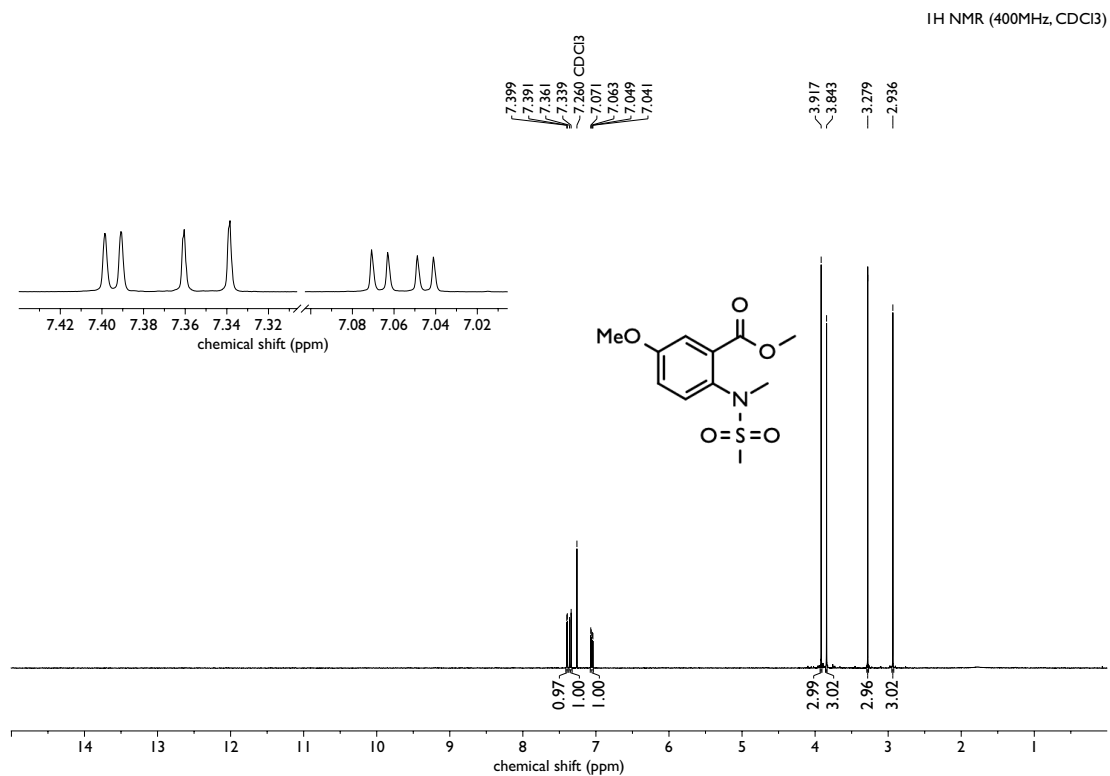


Figure S90: <sup>1</sup>H and <sup>13</sup>C spectra of compound **7j**

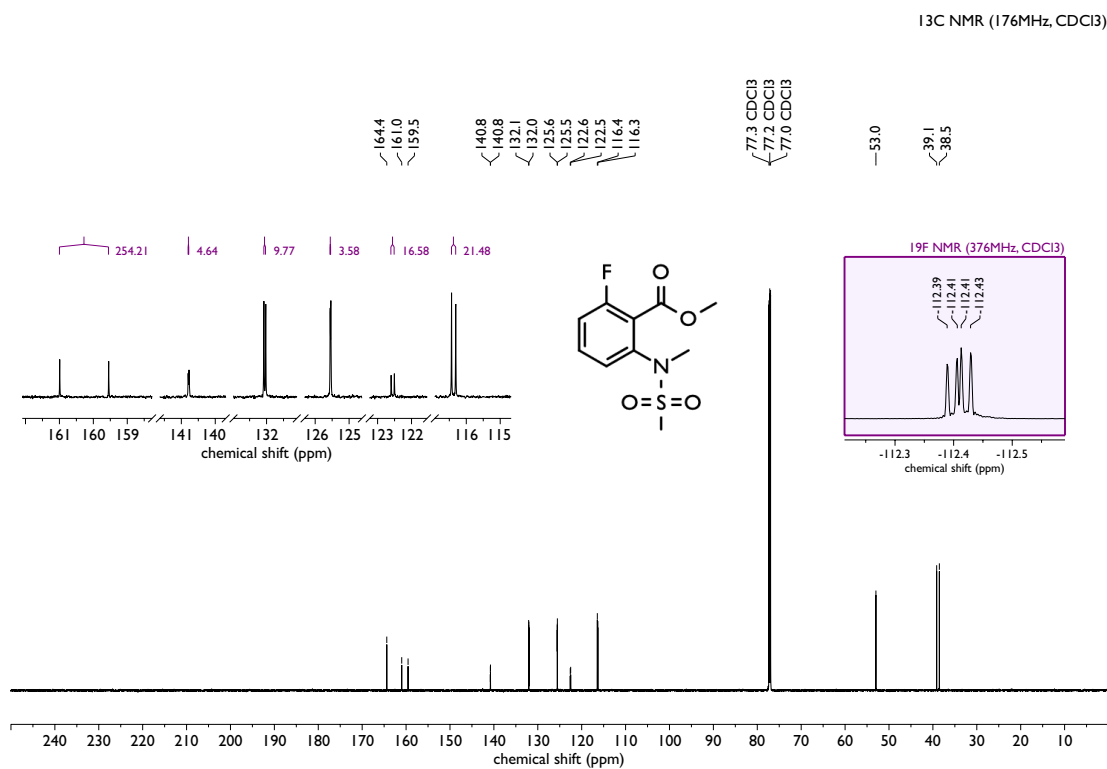
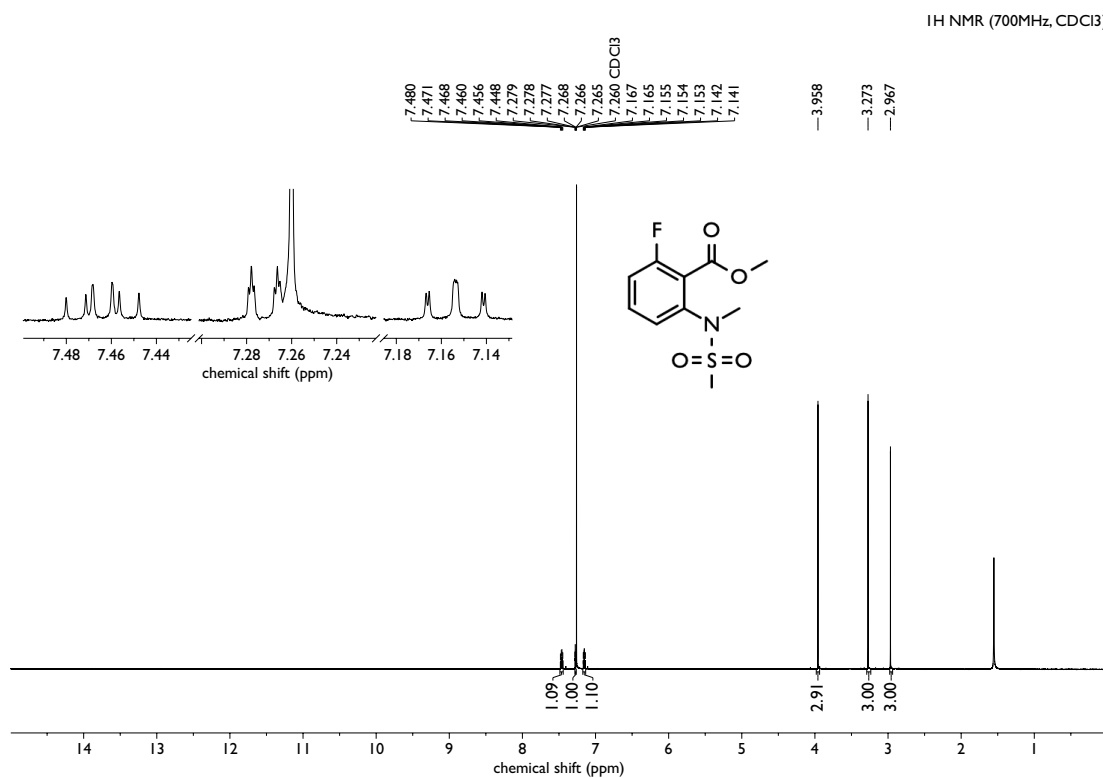
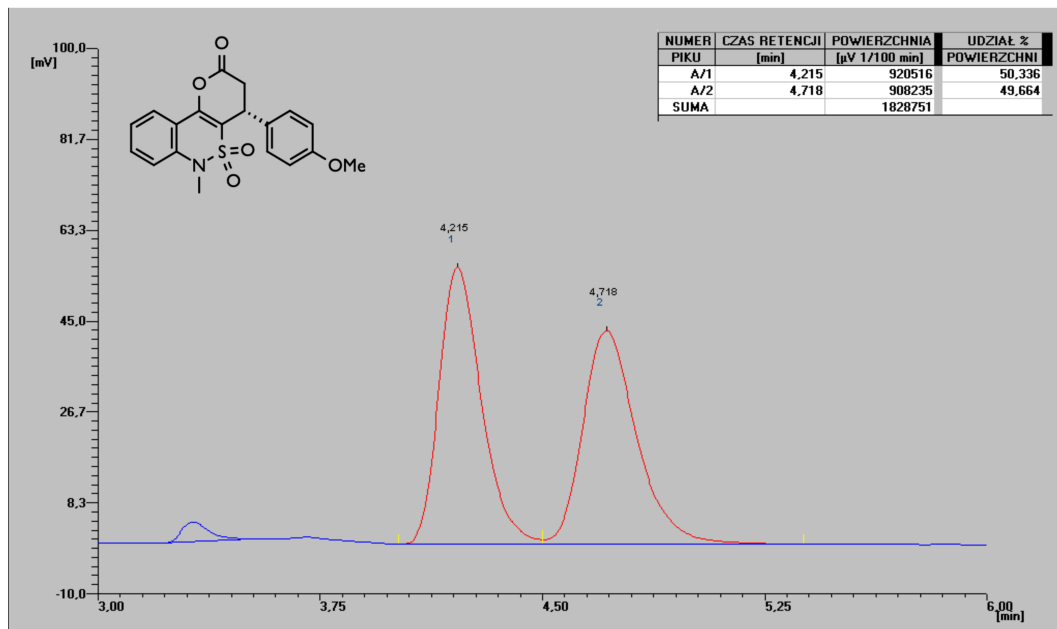


Figure S91: <sup>1</sup>H and <sup>13</sup>C spectra of compound **7k**

## 6 HPLC Chromatograms

KM221A (4uL)  
Phenomenex-Lux Amylose-1, 5 $\mu$ m  
MeCN:H<sub>2</sub>O 70:30, 0.7mL/min., 26°C



KM223b1s3 (m-xylene) (4uL)  
Phenomenex-Lux Amylose-1, 5 $\mu$ m  
MeCN:H<sub>2</sub>O 70:30, 0.7mL/min., 26°C

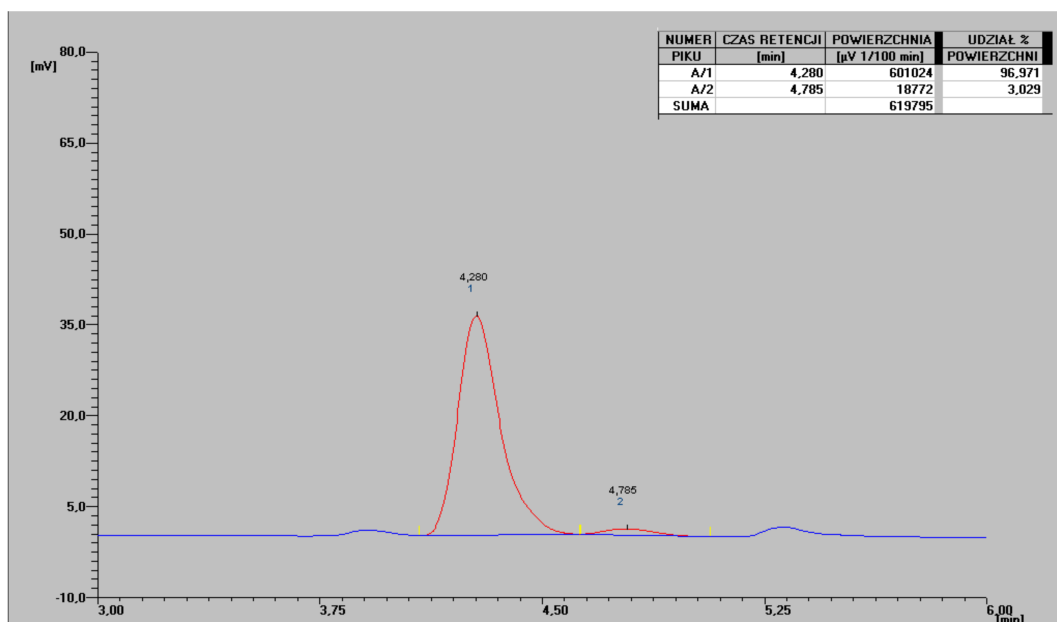


Figure S92: HPLC chromatograms of compound **3a**

Phenomenex Lux Amylose-1, 3µm, 70:30, 1.0 mL/min, p = 127bar, T = 25°C

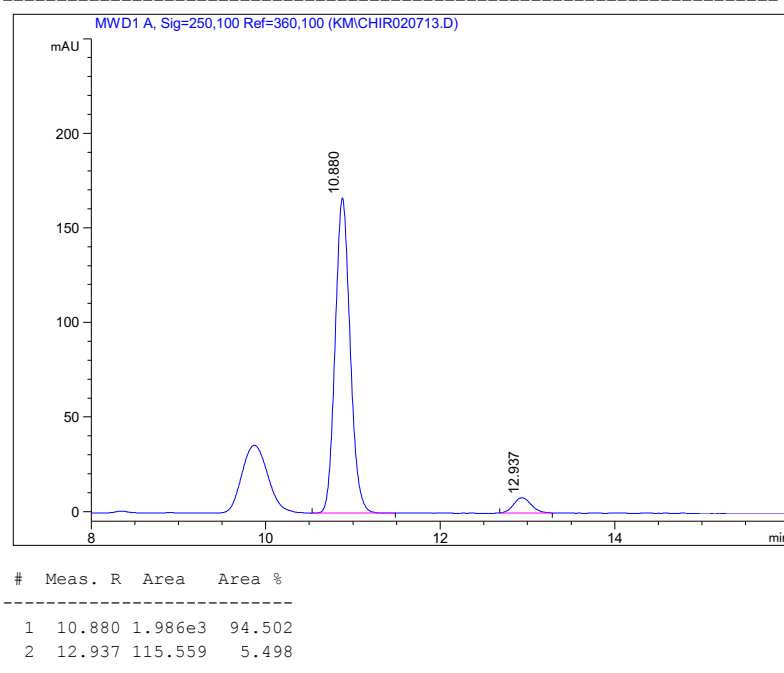
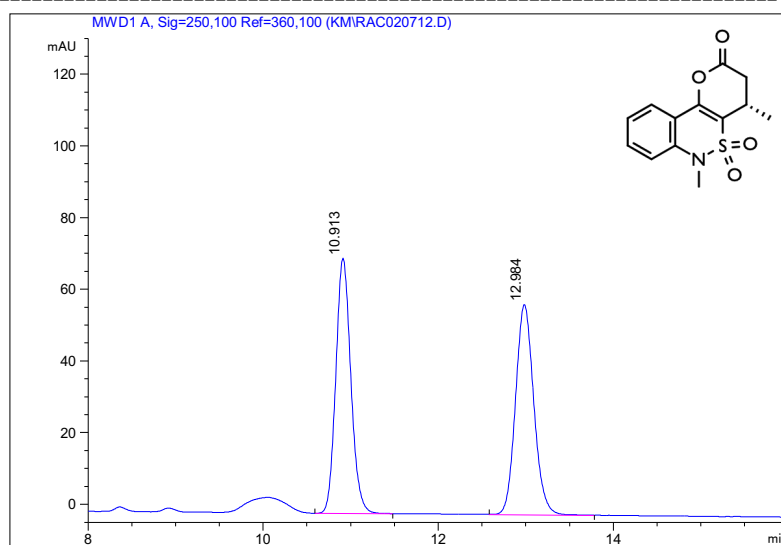


Figure S93: HPLC chromatograms of compound **3m**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 97bar, T = 25°C

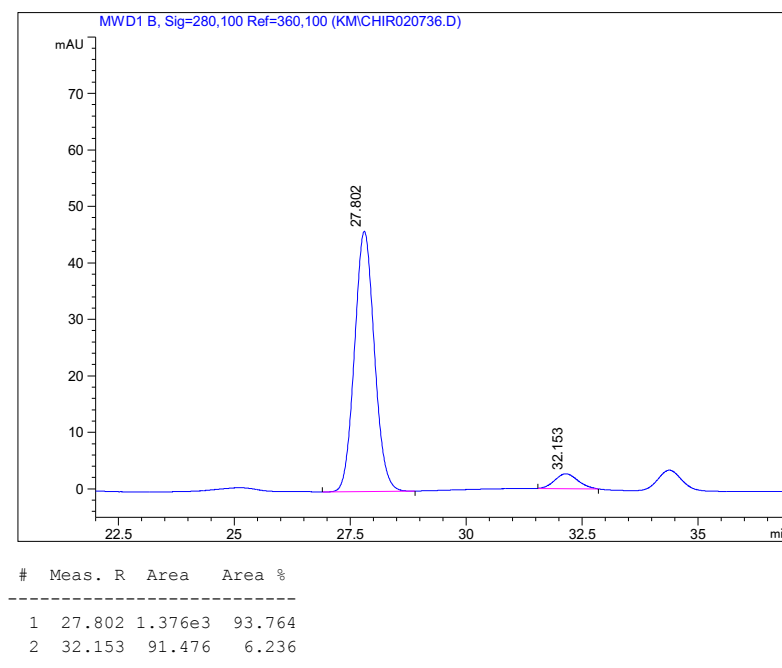
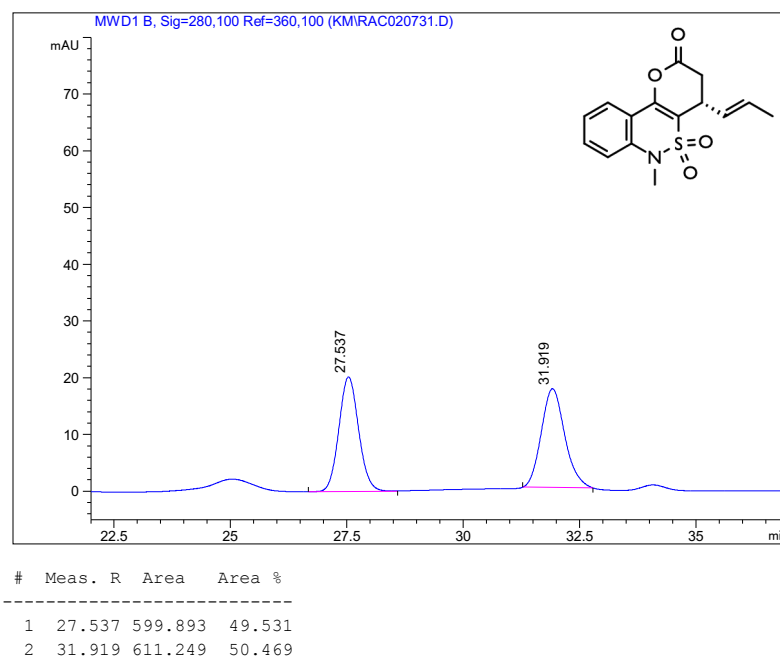
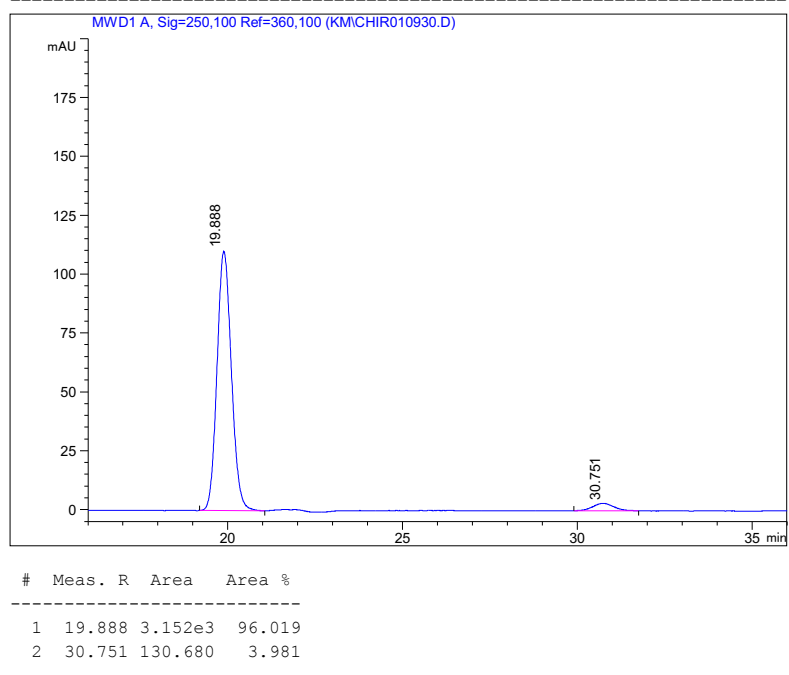


Figure S94: HPLC chromatograms of compound **3q**

MWD1 A, Sig=250,100 Ref=360,100 (KMIRAC010924.D)

Chemical structure: COc1ccc(cc1)[C@H](COC(=O)C)C2=C(C(=C3C=CC=CC=C3N(C)C2=O)C4(C)(C)C(C)(C)C4)OC5(C)C(C)(C)C(C)(C)C5

#	Meas. R	Area	Area %
1	19.934	221.004	50.087
2	30.780	220.236	49.913



S129

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

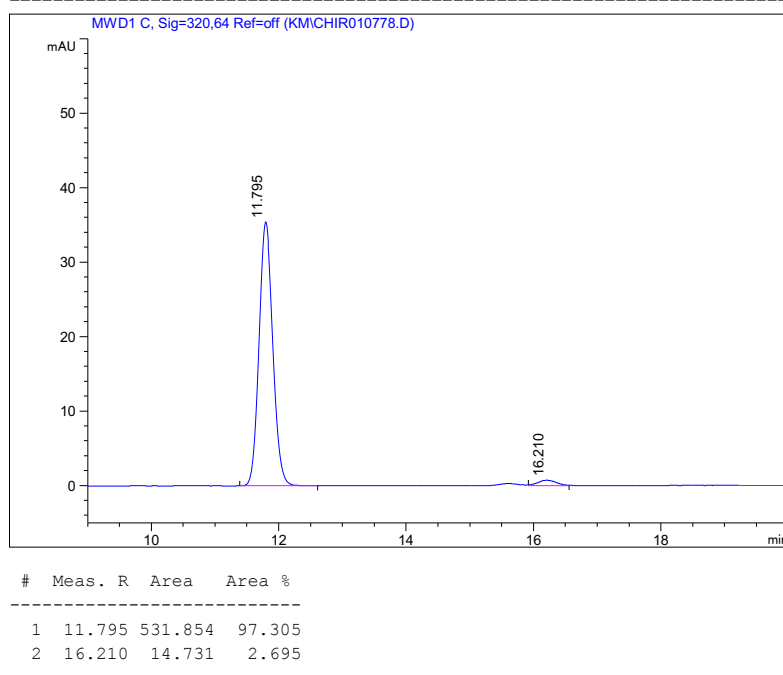
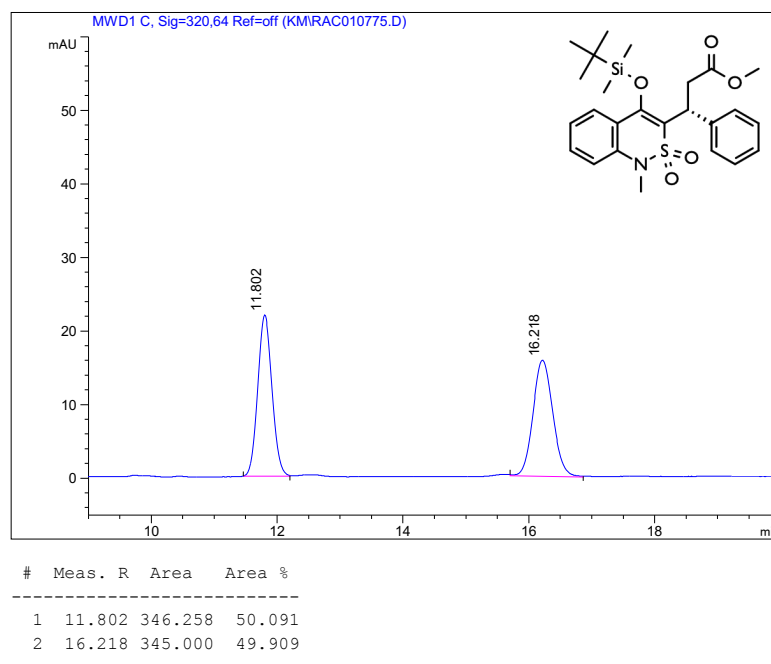


Figure S96: HPLC chromatograms of compound **4b**



Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

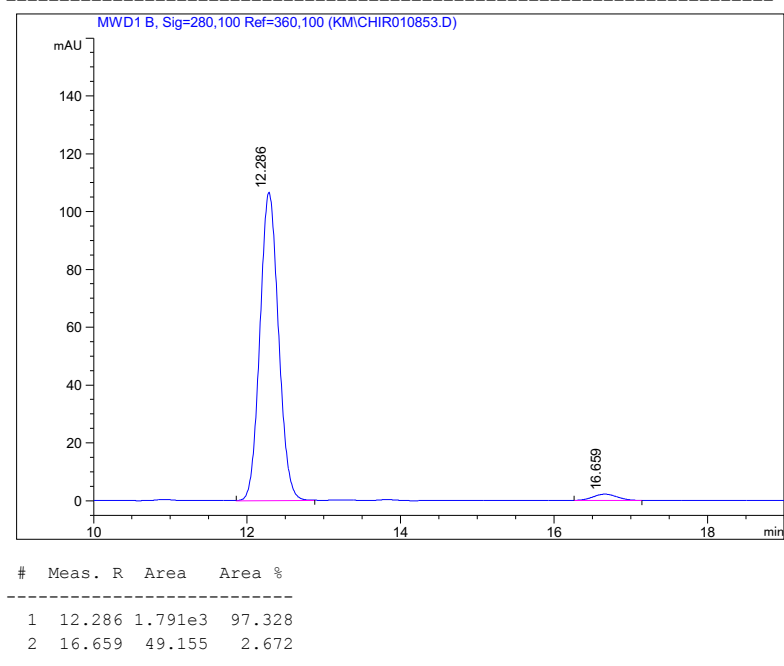
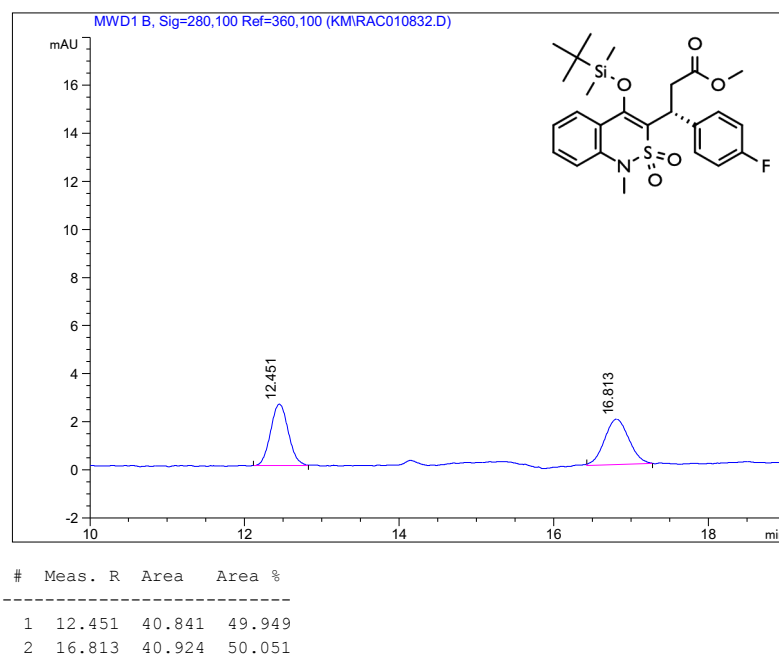


Figure S97: HPLC chromatograms of compound **4c**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

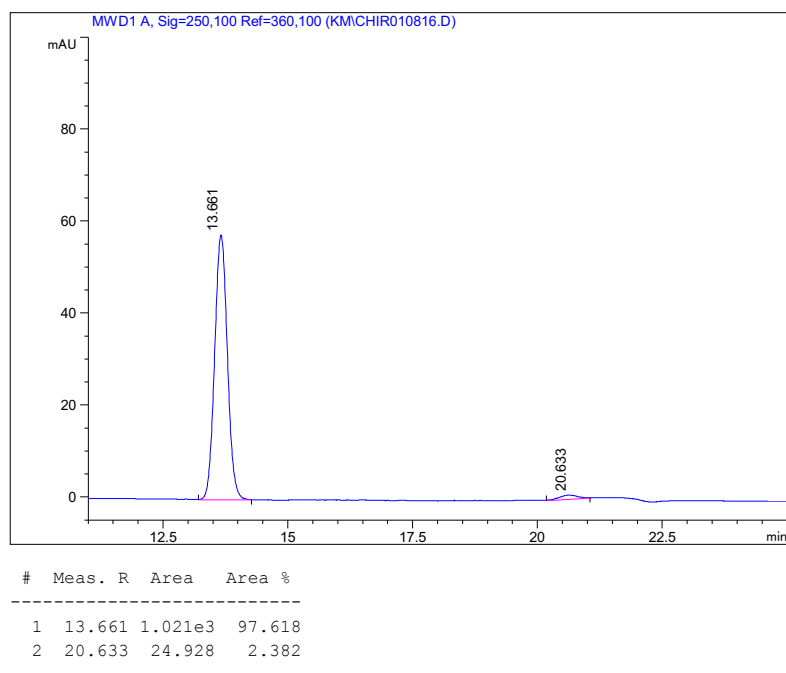
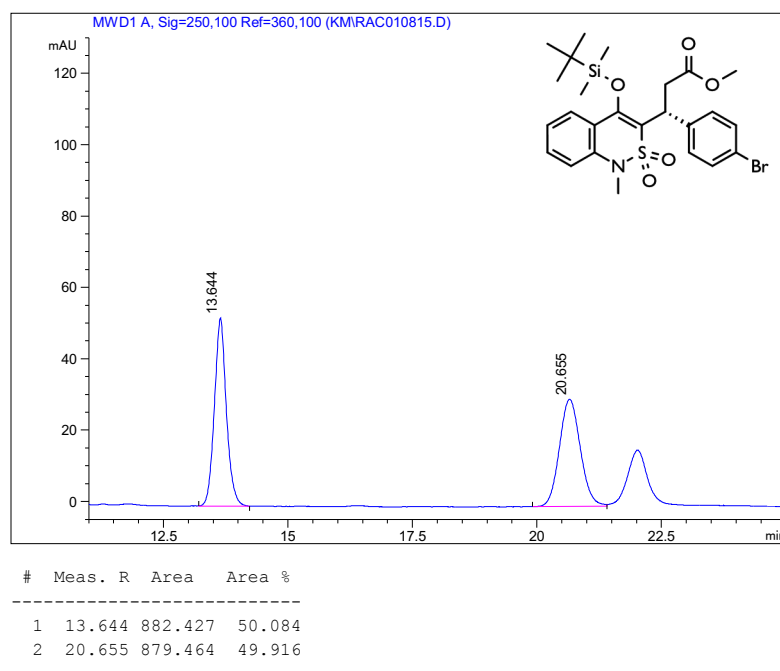


Figure S98: HPLC chromatograms of compound **4d**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

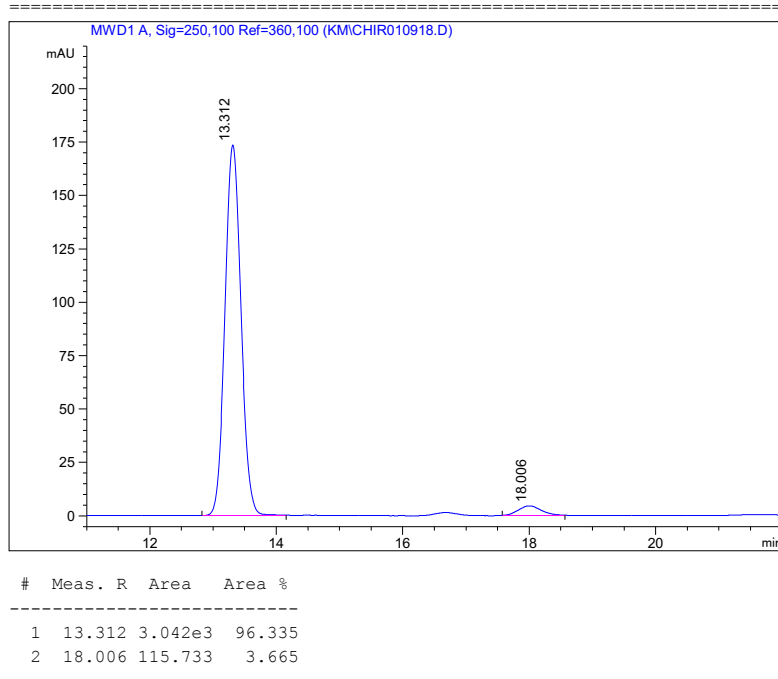
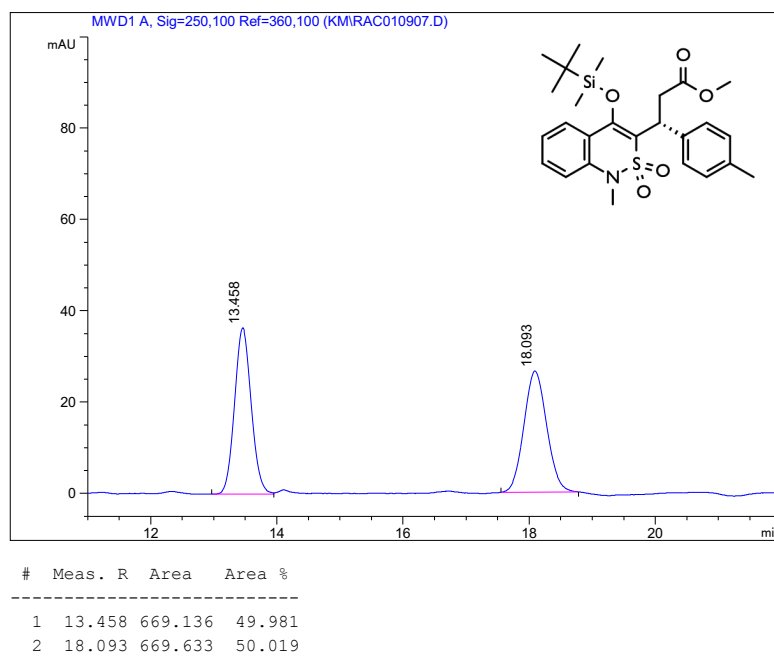


Figure S99: HPLC chromatograms of compound **4e**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

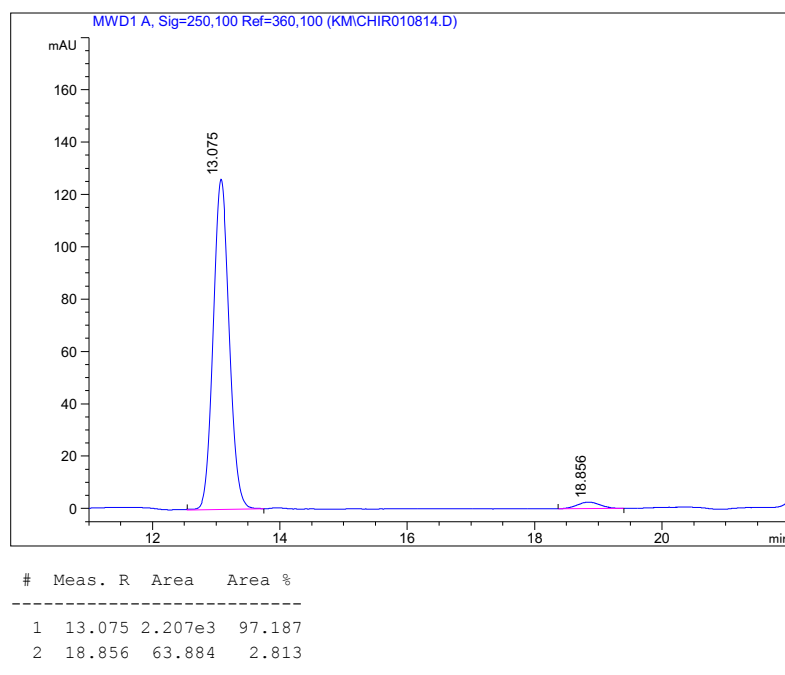
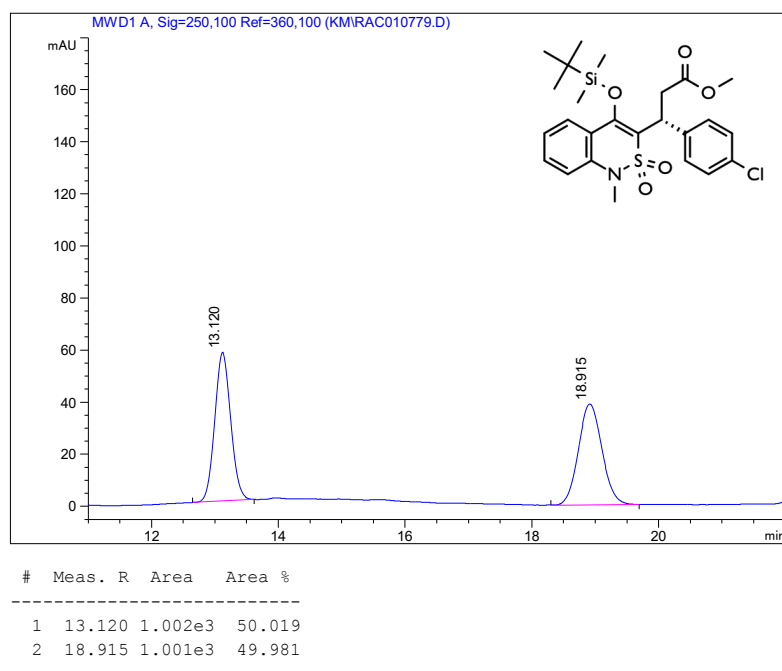


Figure S100: HPLC chromatograms of compound 4f

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 93bar, T = 25°C

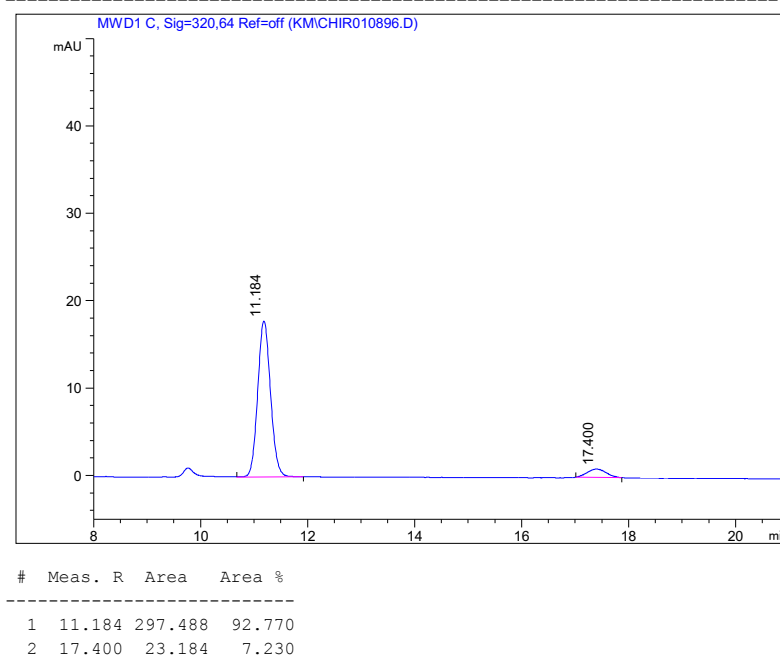
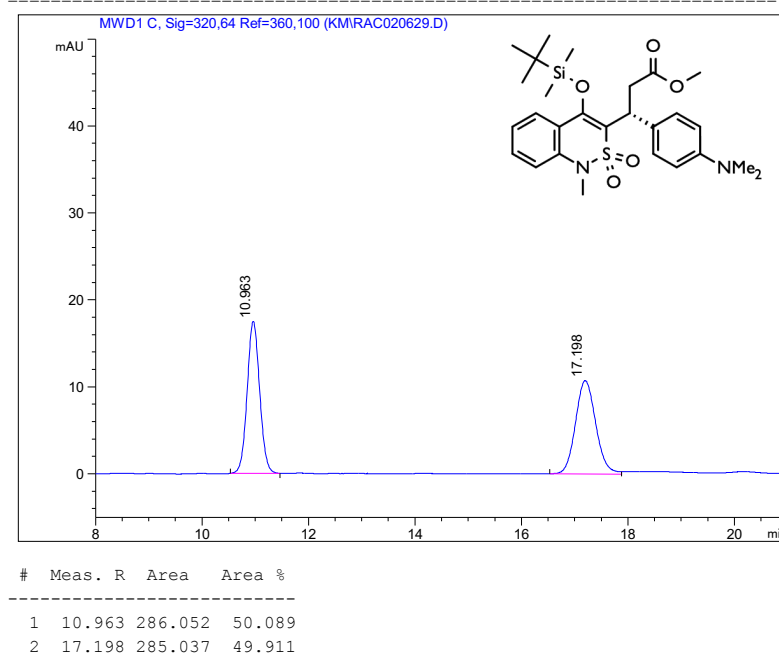


Figure S101: HPLC chromatograms of compound **4g**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

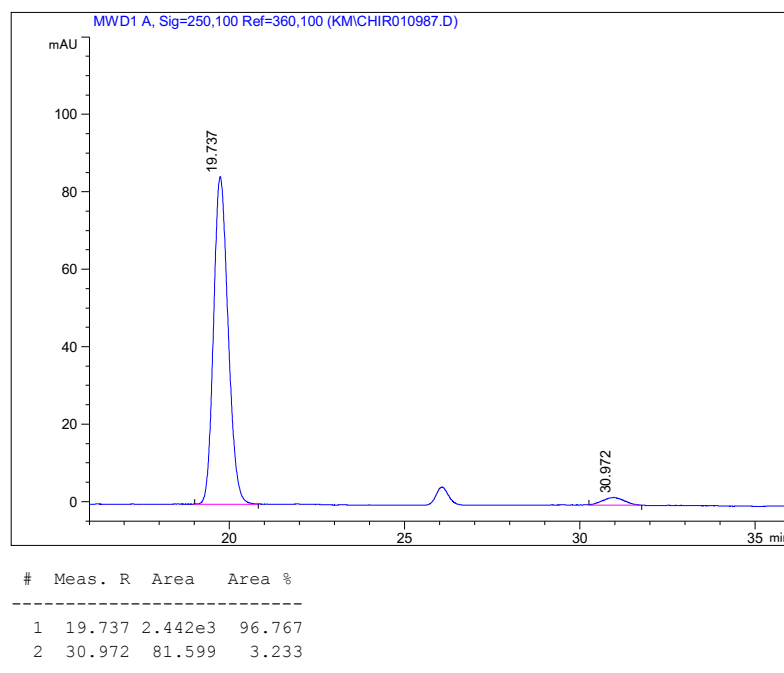
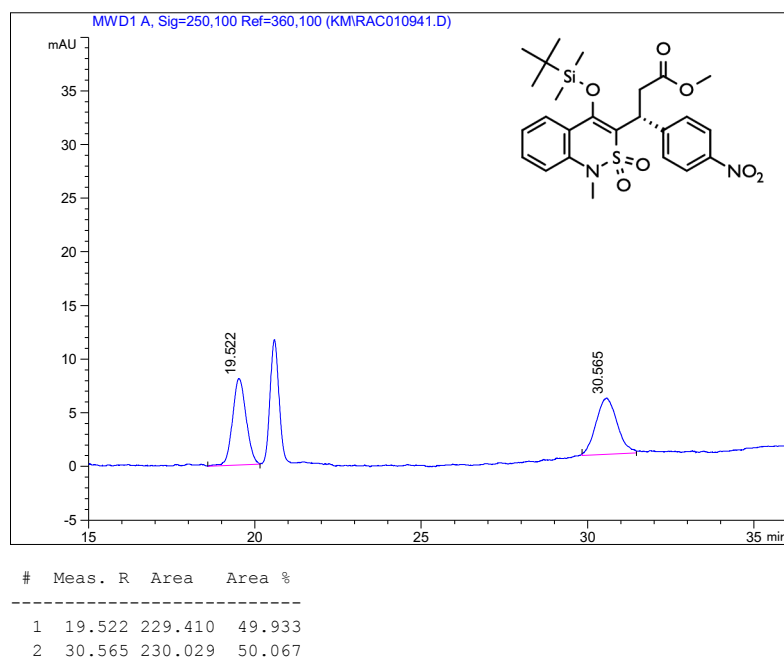


Figure S102: HPLC chromatograms of compound **4h**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

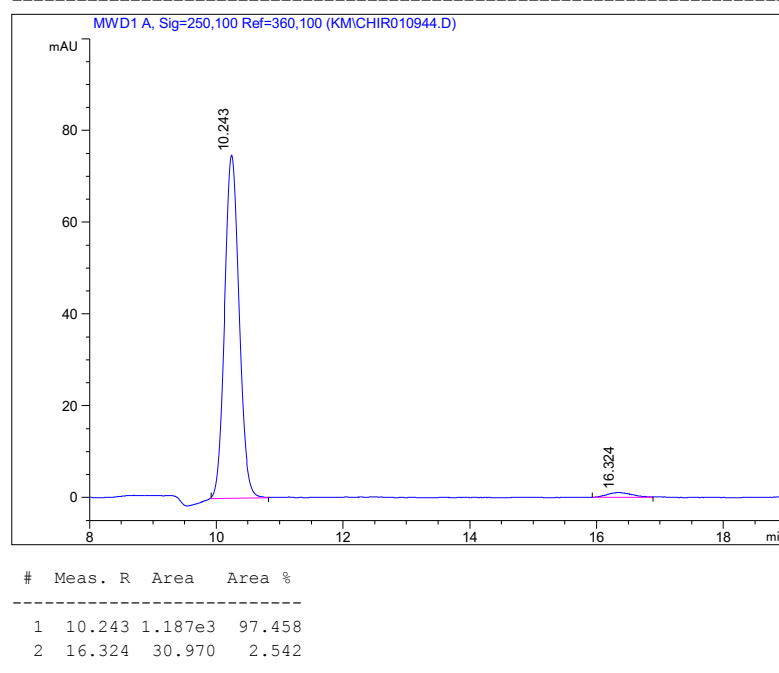
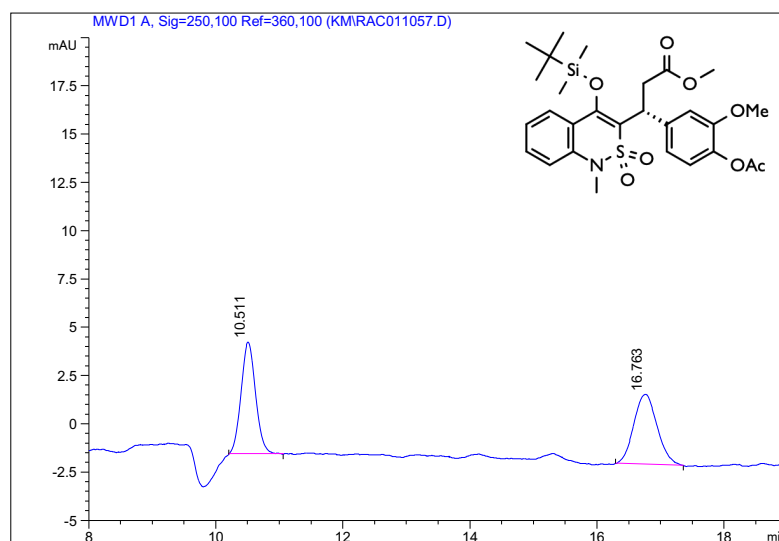


Figure S103: HPLC chromatograms of compound 4i

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

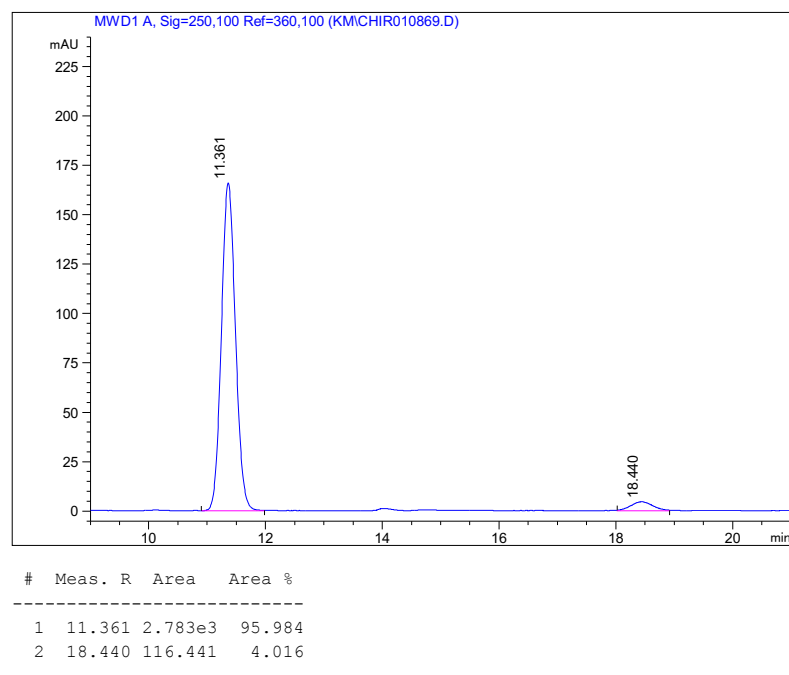
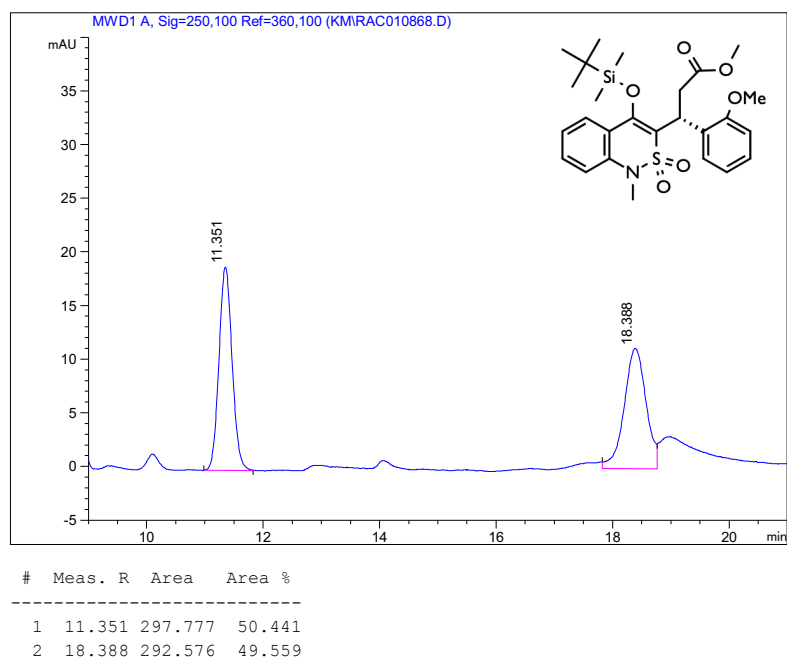


Figure S104: HPLC chromatograms of compound 4j



Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

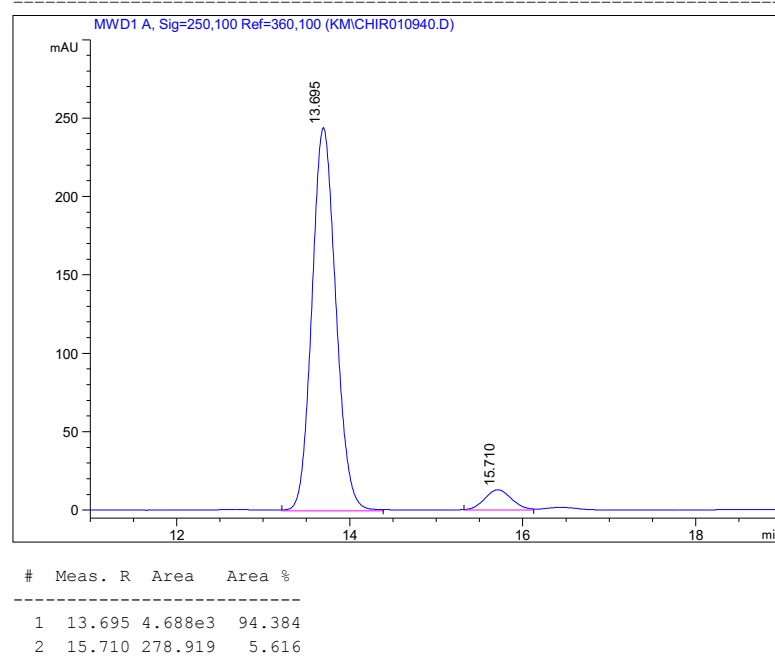
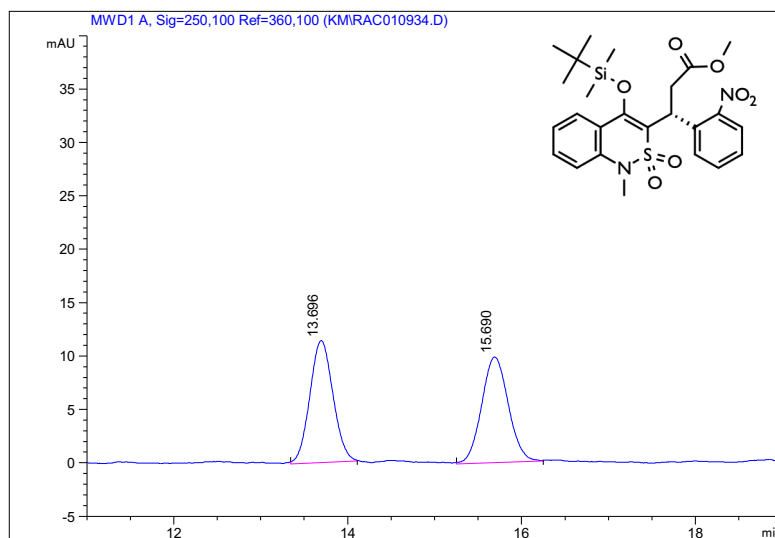


Figure S105: HPLC chromatograms of compound **4k**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

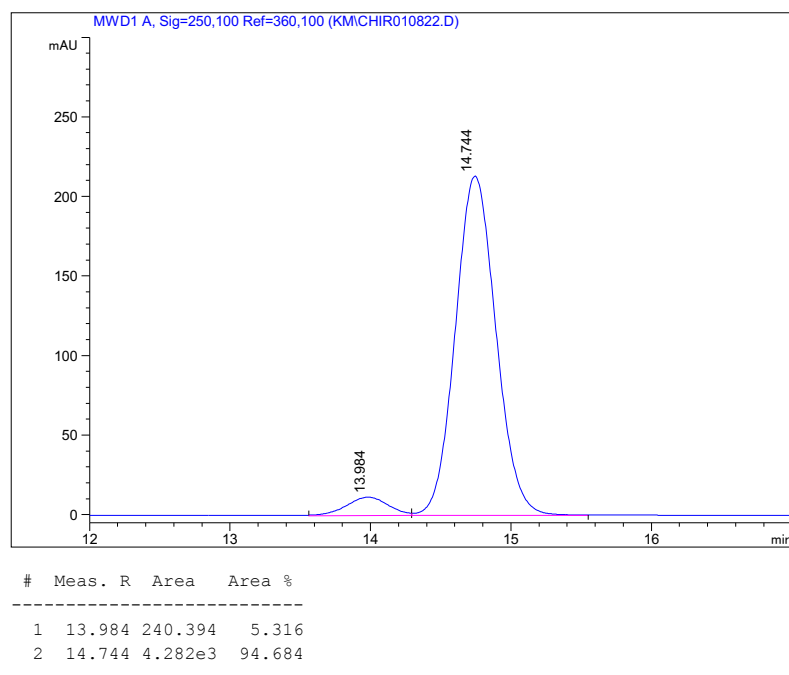
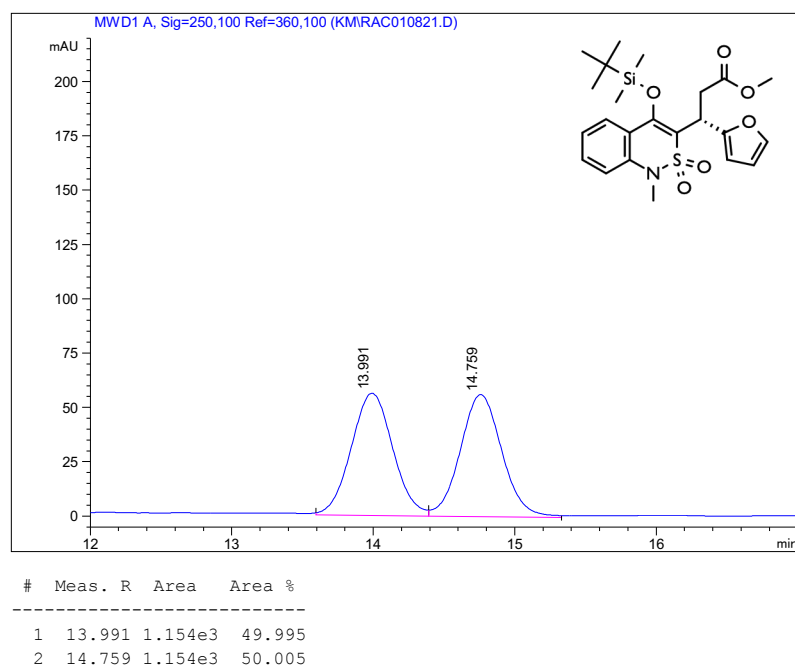


Figure S106: HPLC chromatograms of compound 41

Phenomenex Lux Amylose-1, 3 $\mu$ m, 97:3, 0.7 mL/min, p = 60bar, T = 25°C

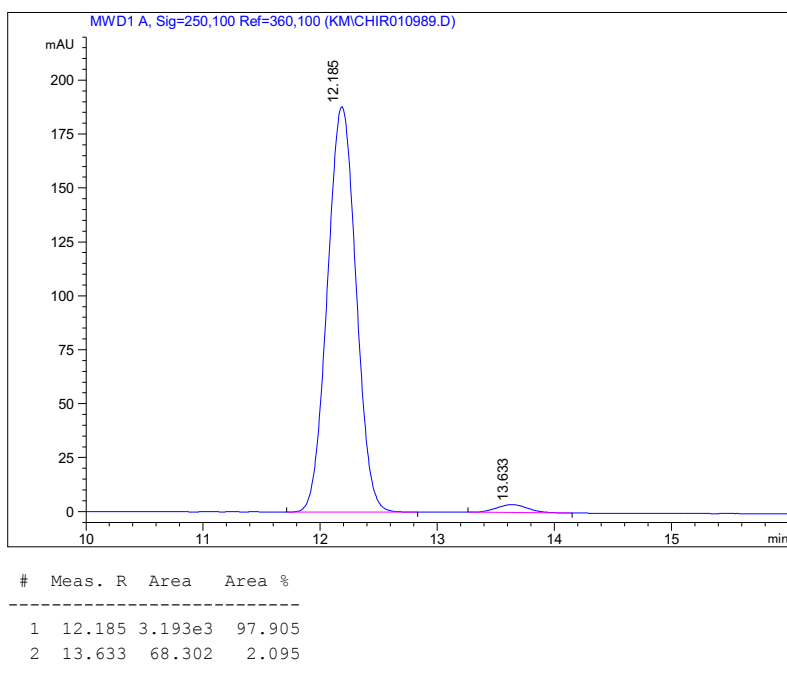
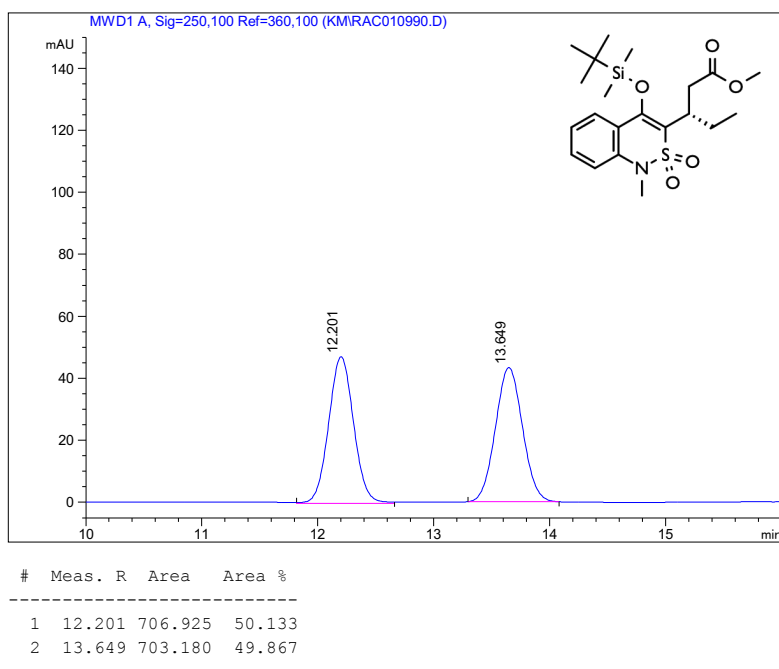


Figure S107: HPLC chromatograms of compound **4n**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 97:3, 0.7 mL/min, p = 60bar, T = 25°C

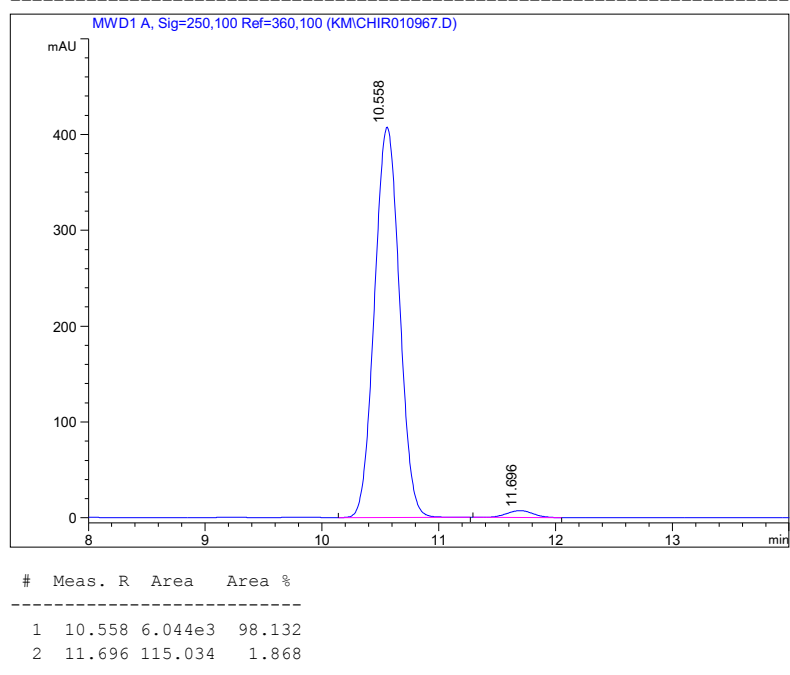
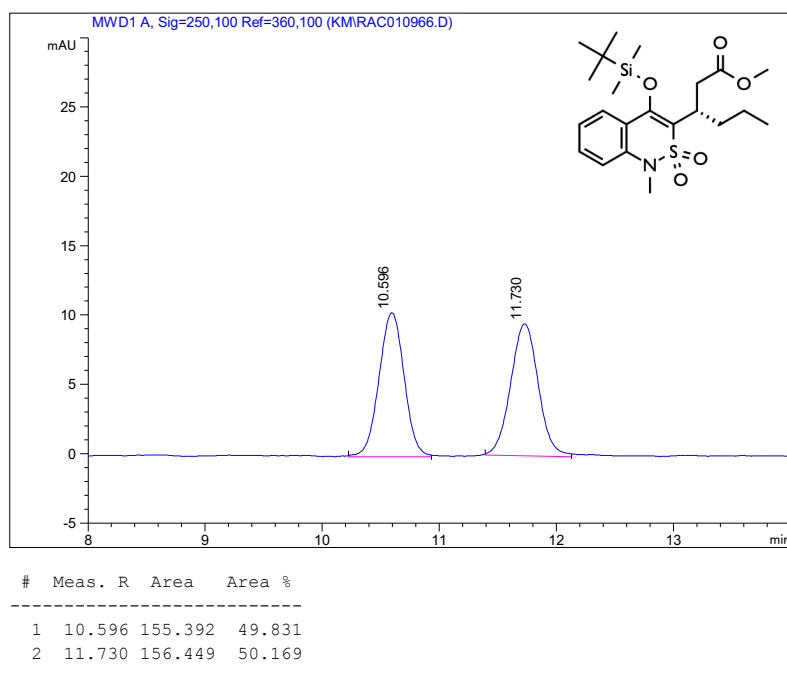


Figure S108: HPLC chromatograms of compound **4o**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

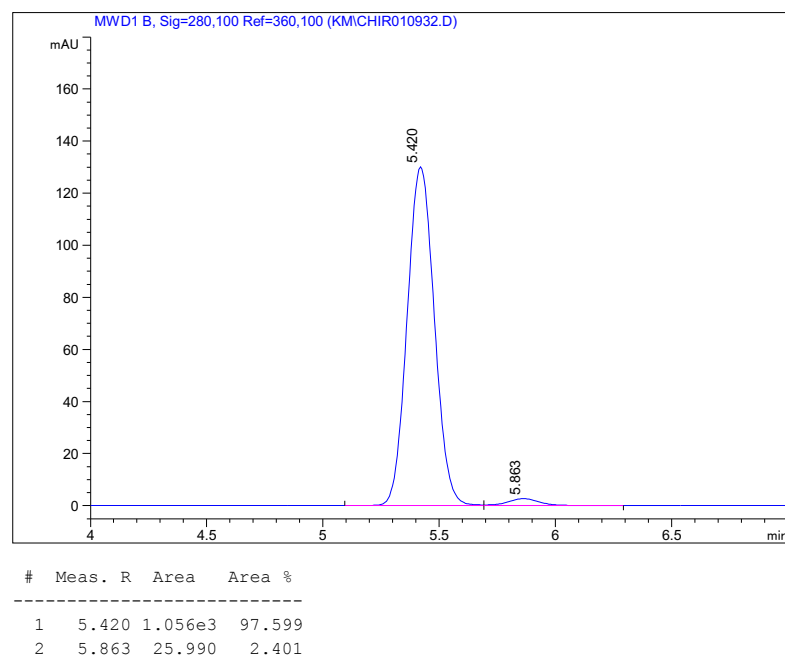
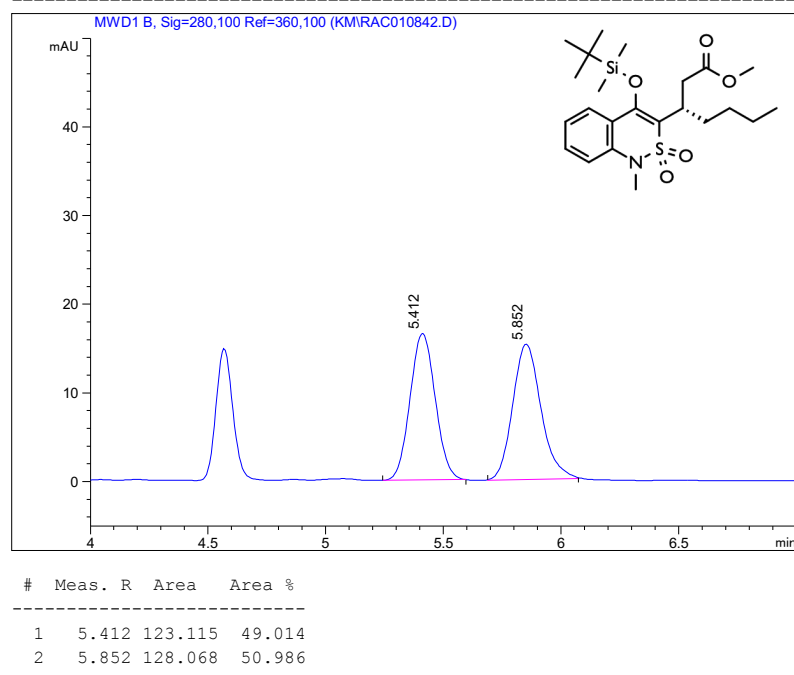


Figure S109: HPLC chromatograms of compound **4p**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

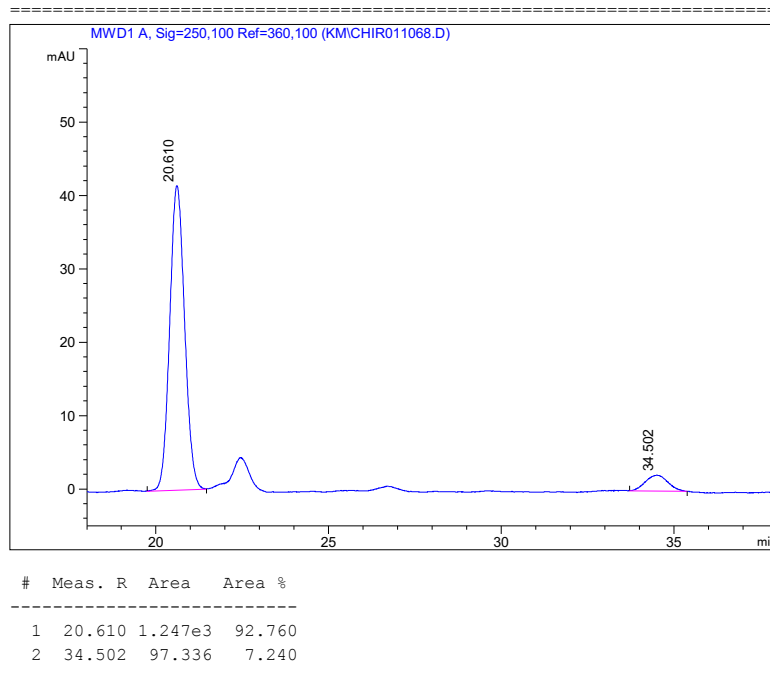
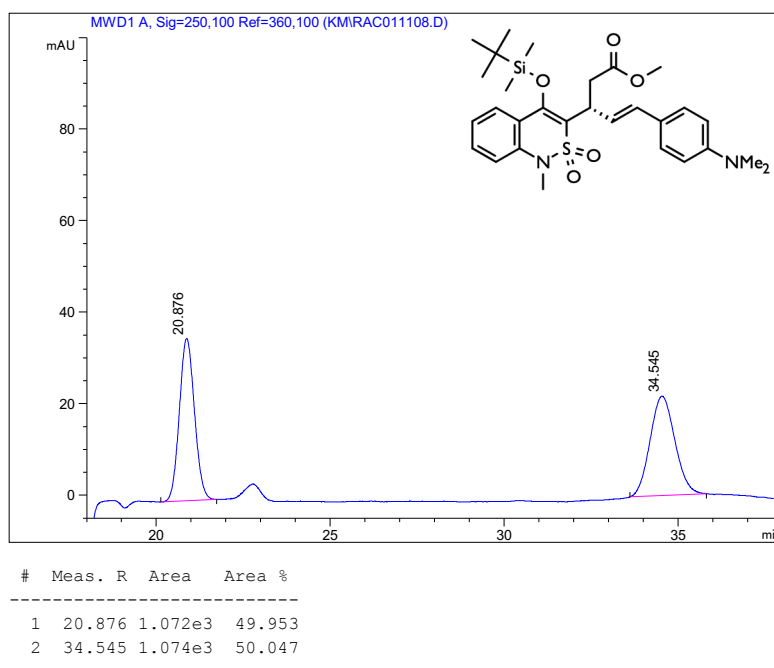


Figure S110: HPLC chromatograms of compound 4r

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

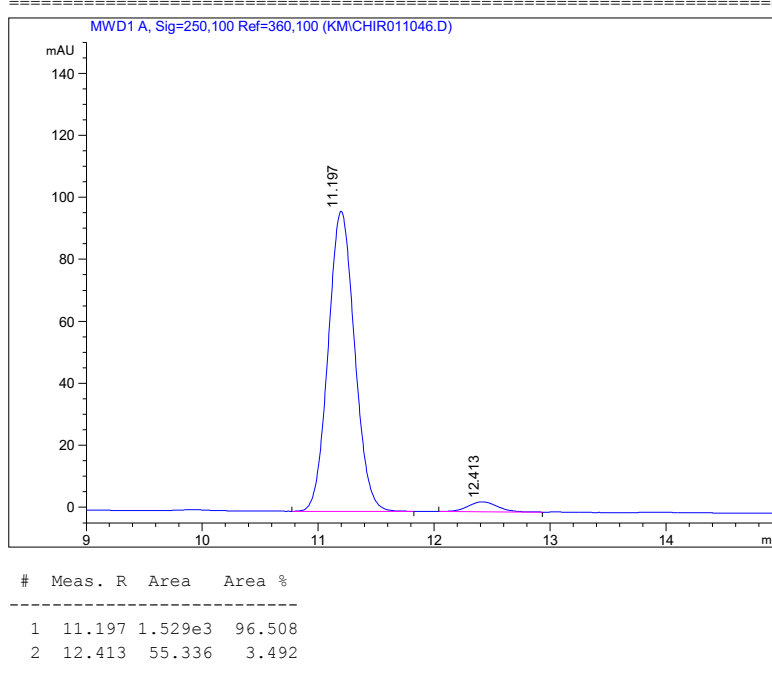
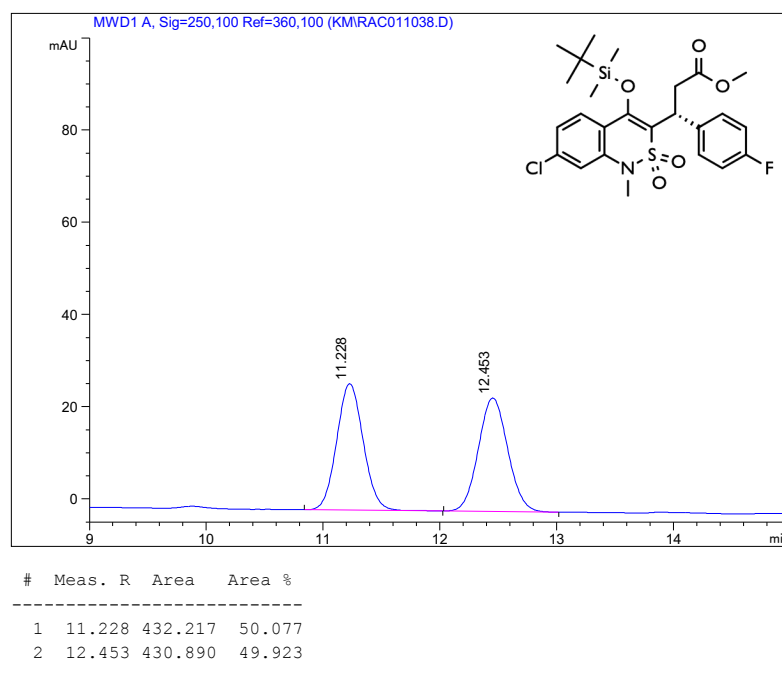


Figure S111: HPLC chromatograms of compound 4s

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

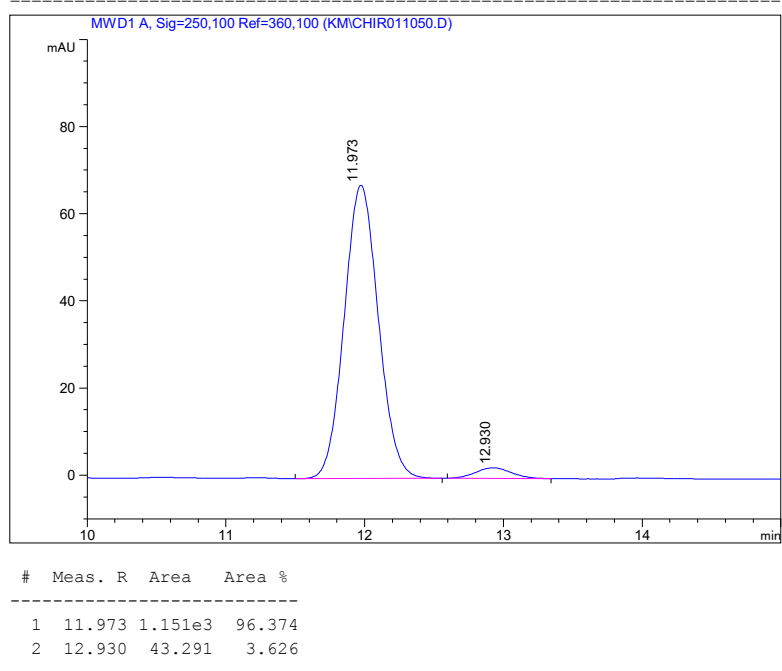
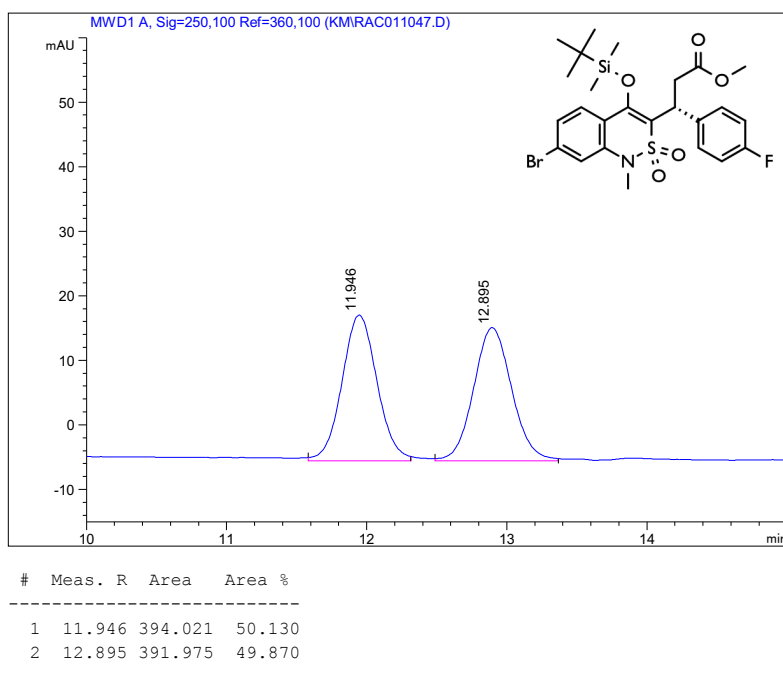


Figure S112: HPLC chromatograms of compound 4t



Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

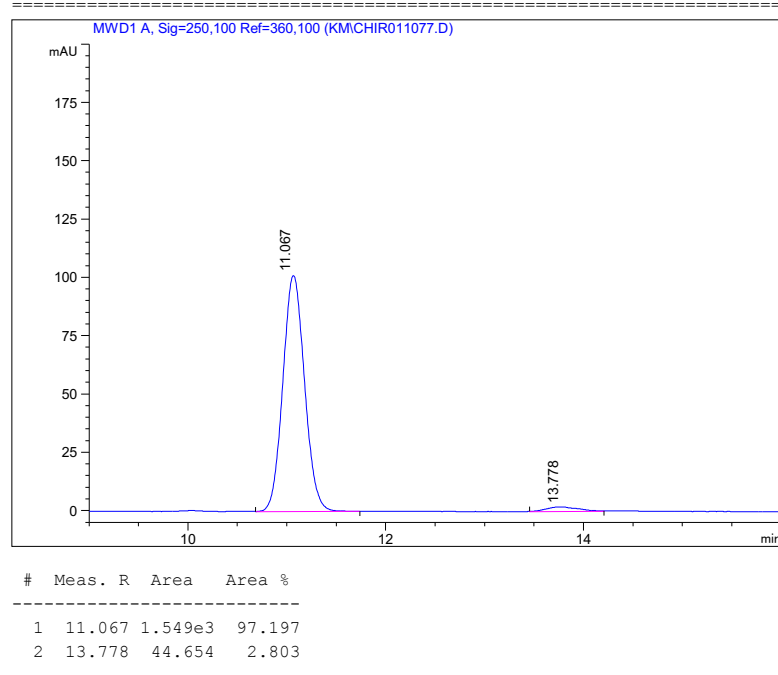
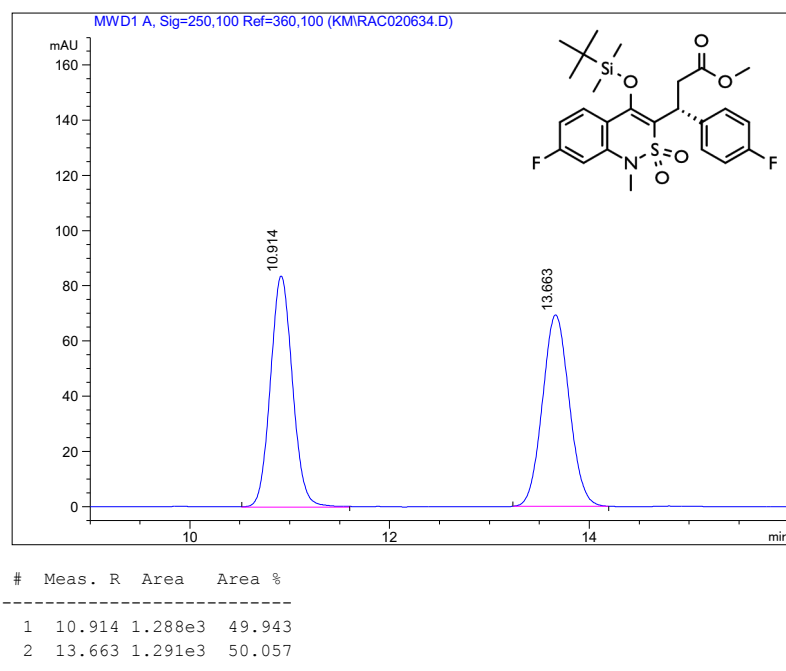
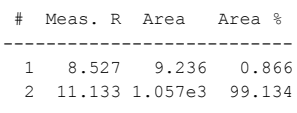
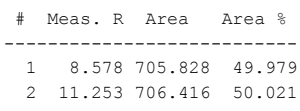


Figure S113: HPLC chromatograms of compound **4u**



S148

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

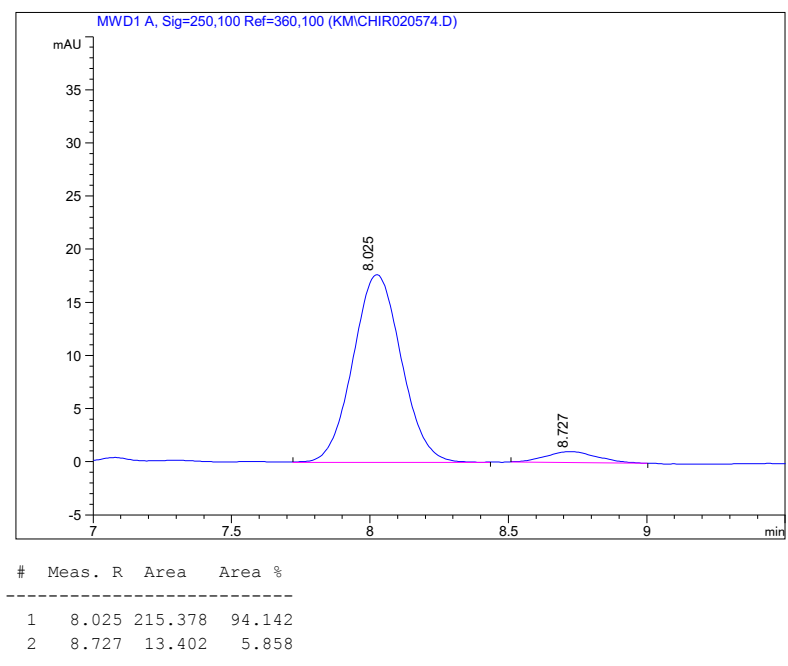
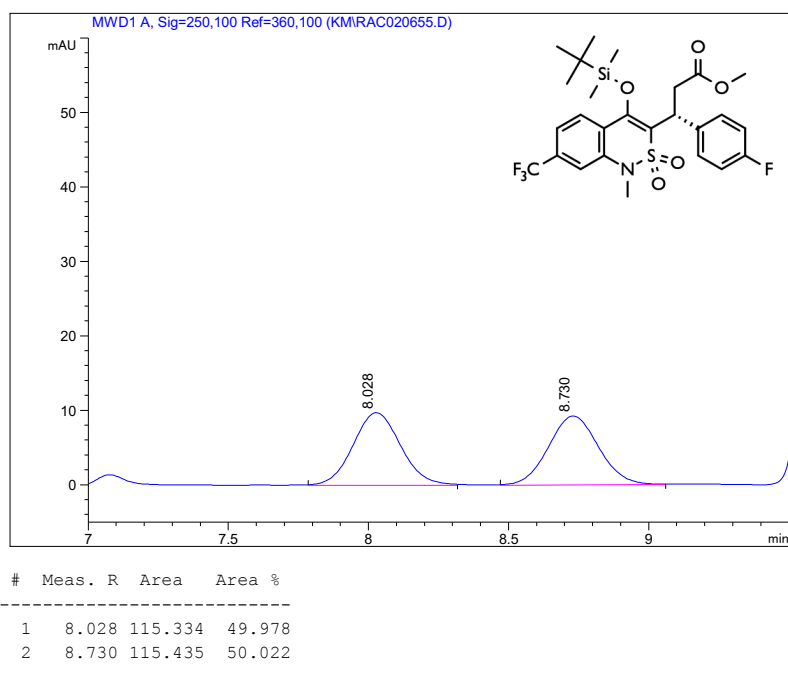


Figure S115: HPLC chromatograms of compound **4w**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

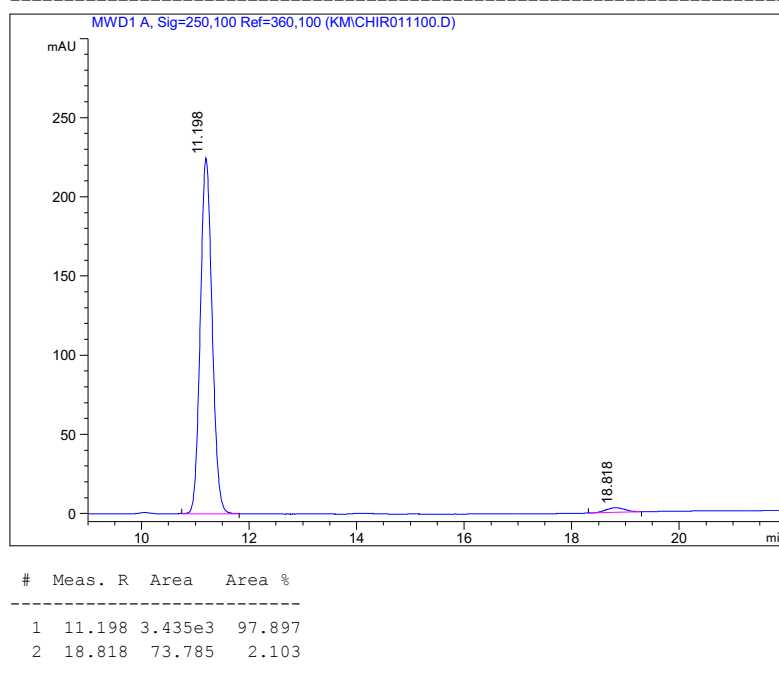
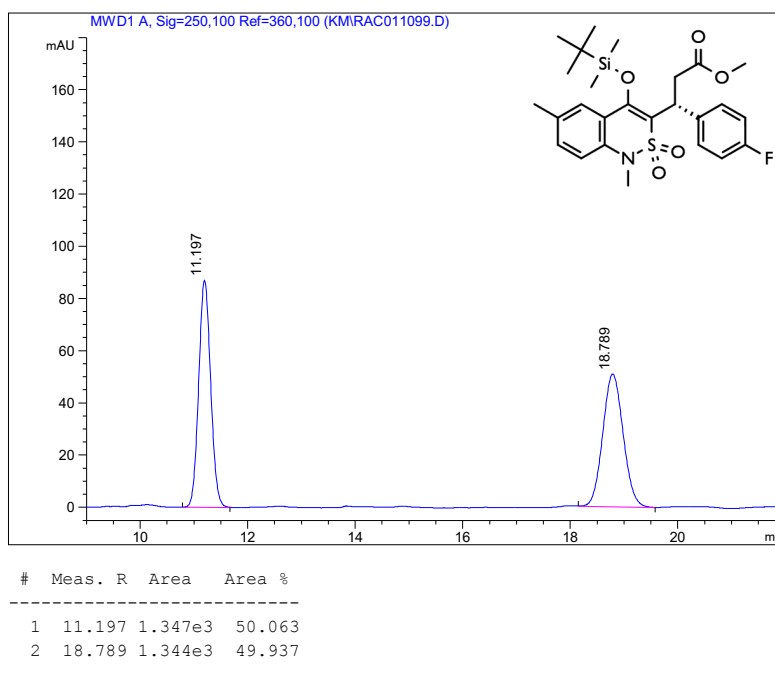


Figure S116: HPLC chromatograms of compound 4x

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

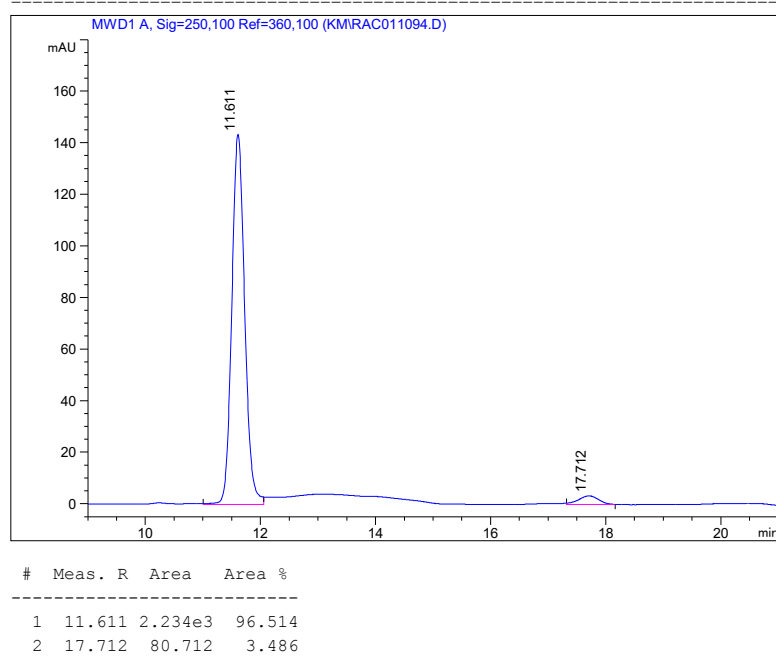
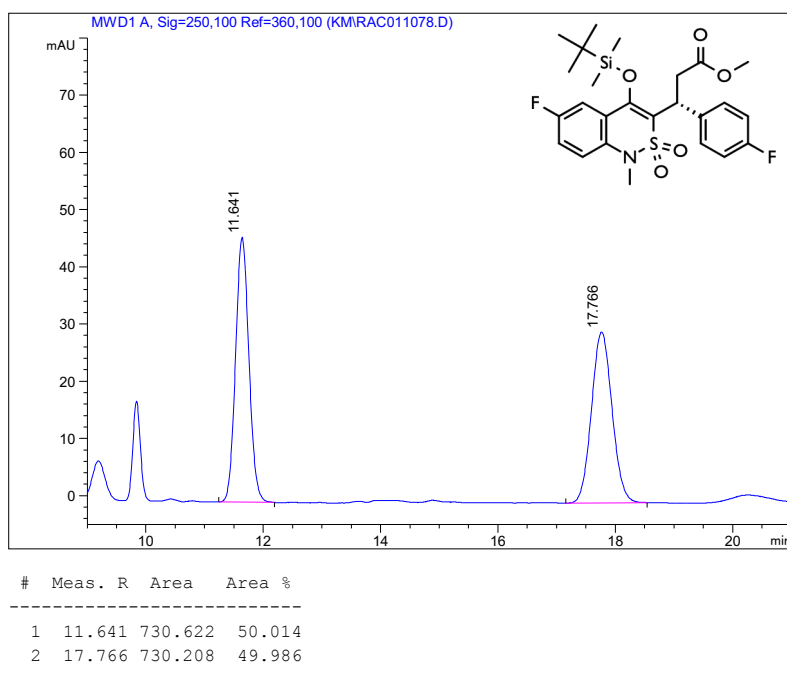


Figure S117: HPLC chromatograms of compound 4y

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

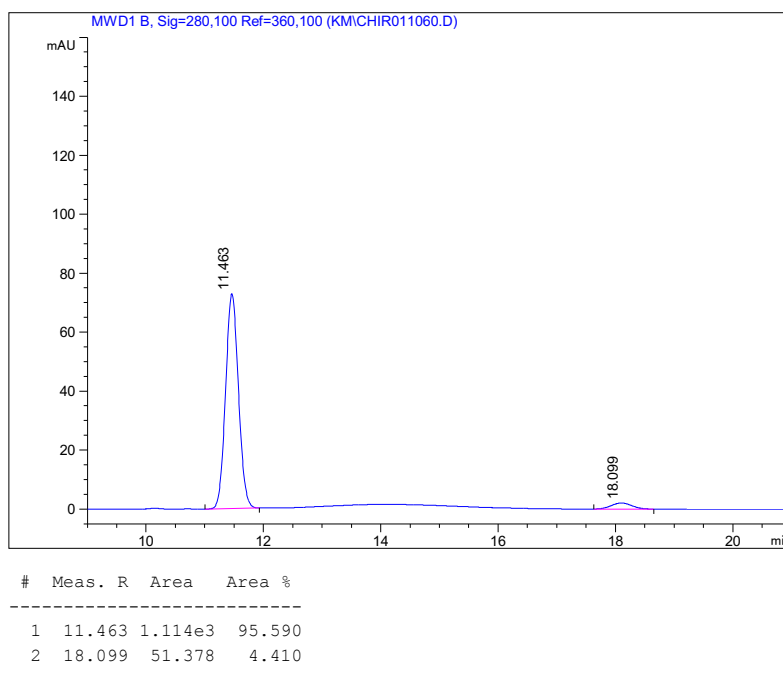
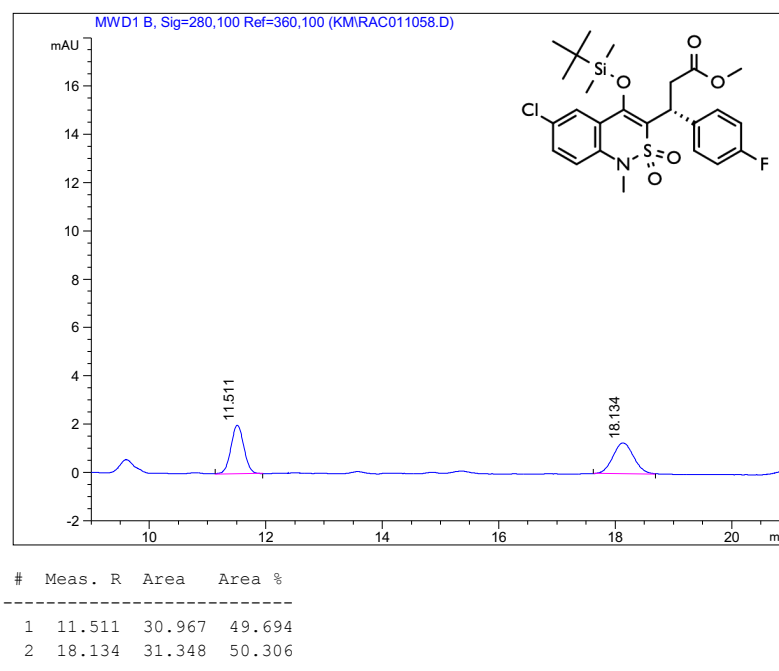


Figure S118: HPLC chromatograms of compound **4z**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

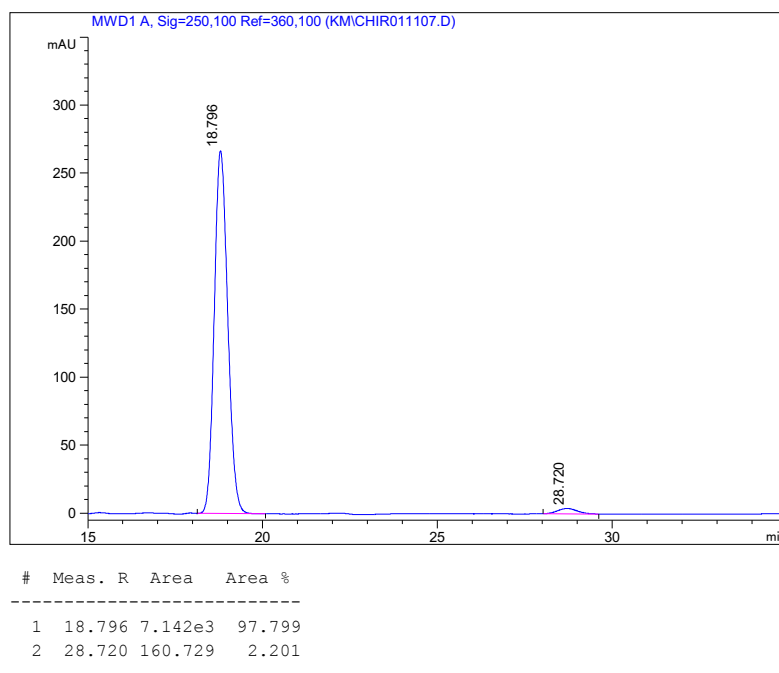
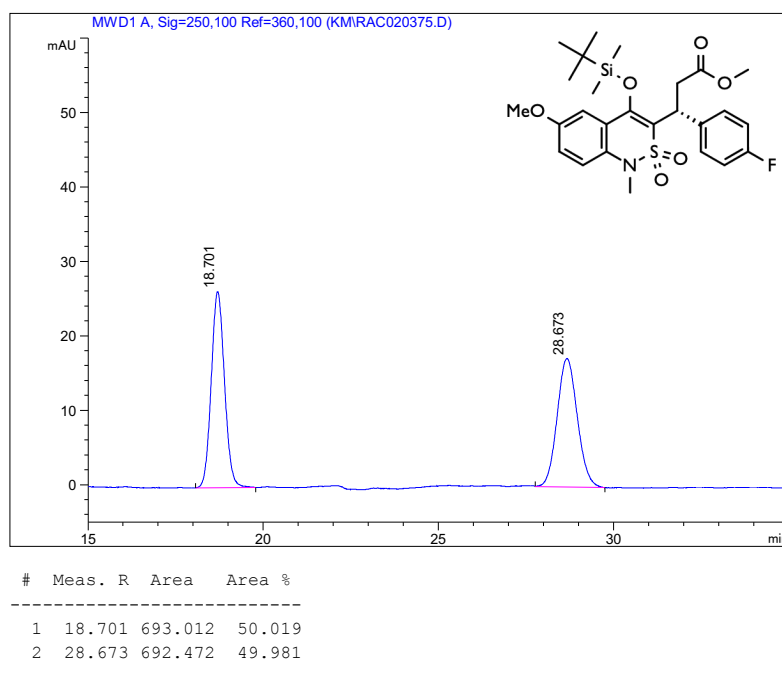


Figure S119: HPLC chromatograms of compound **4aa**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

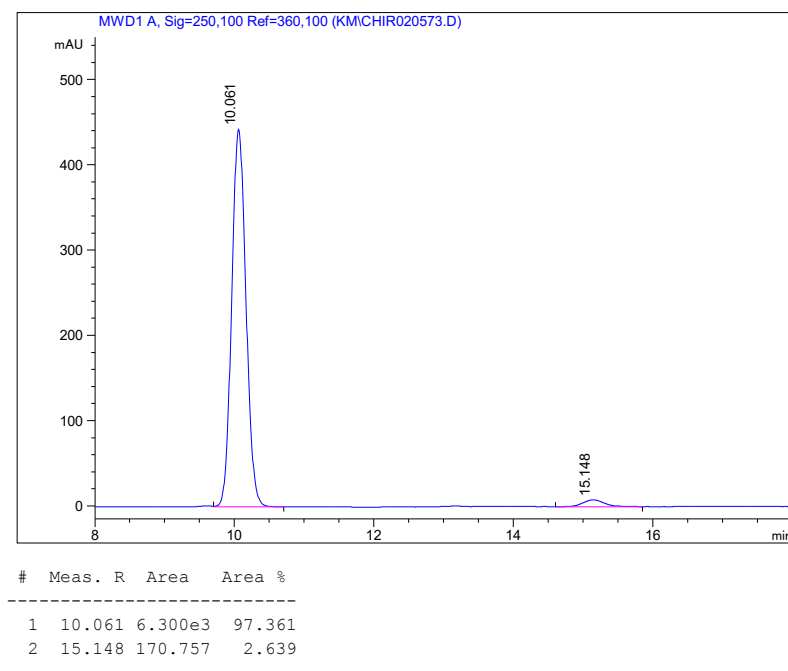
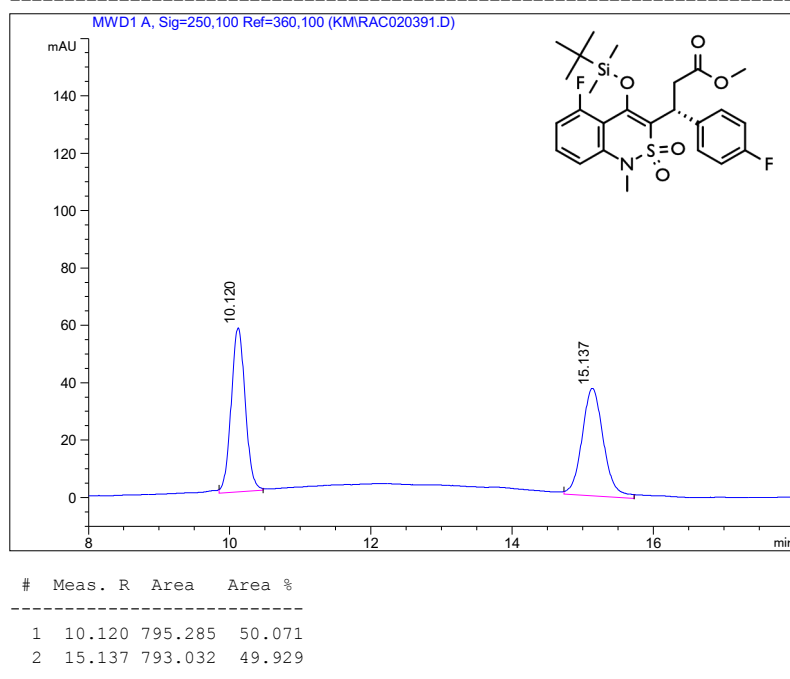


Figure S120: HPLC chromatograms of compound **4ab**



Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

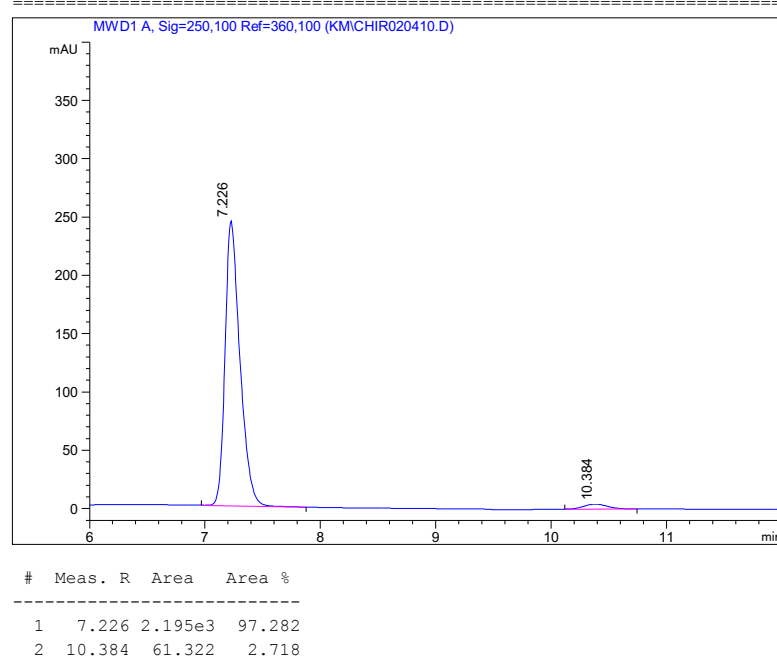
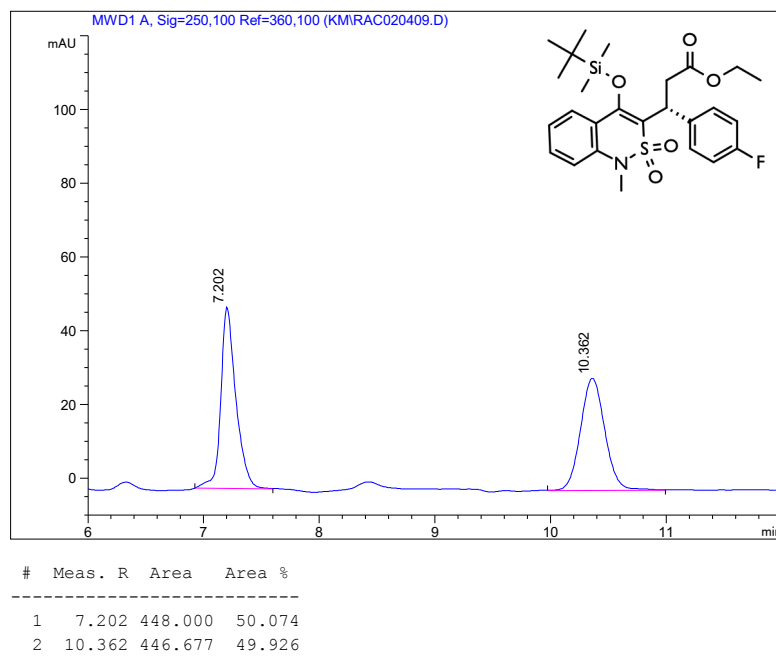


Figure S121: HPLC chromatograms of compound **4ac**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

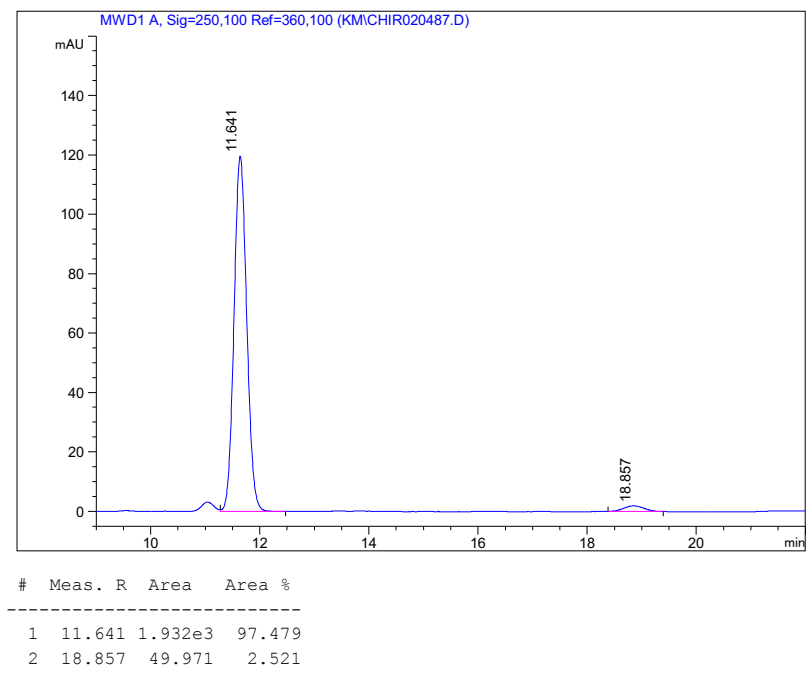
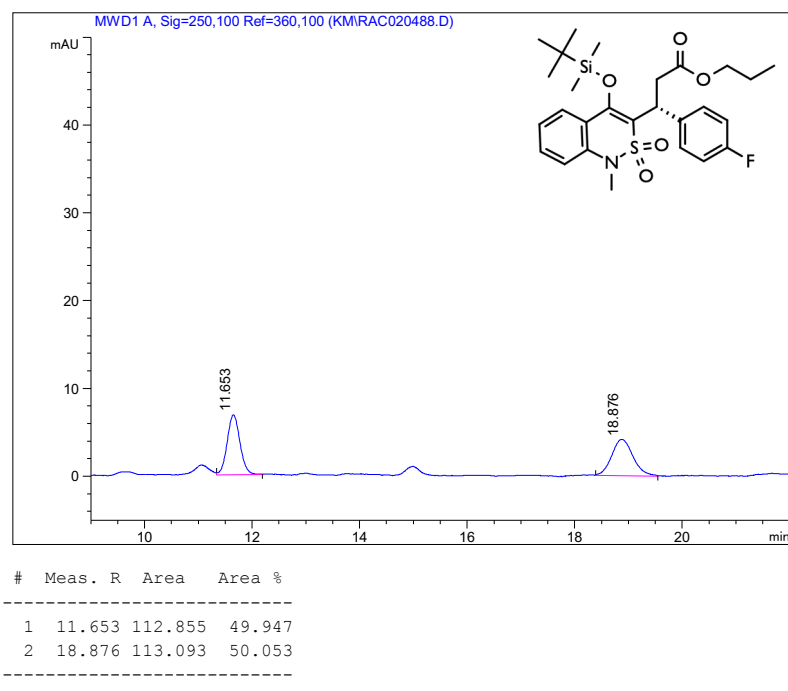


Figure S122: HPLC chromatograms of compound **4ad**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 92bar, T = 25°C

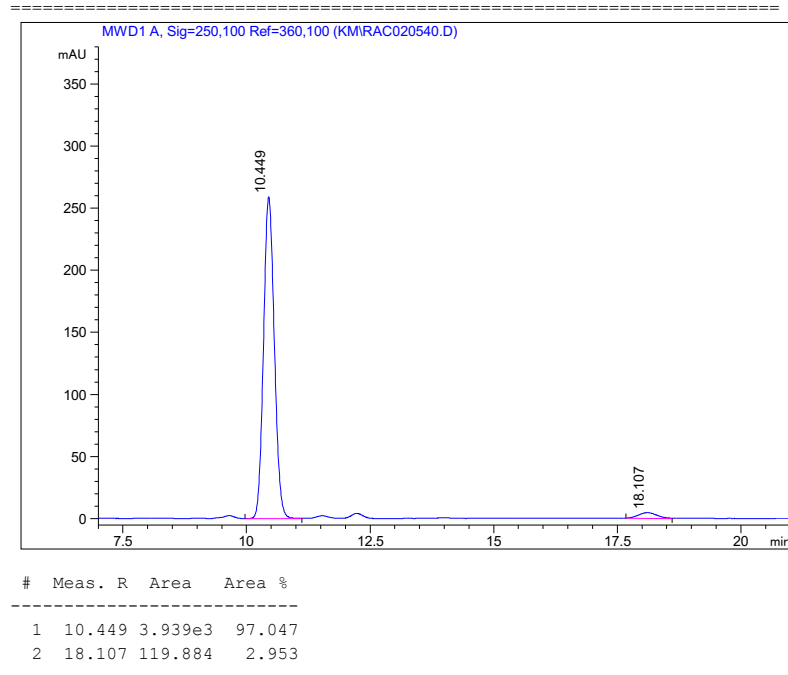
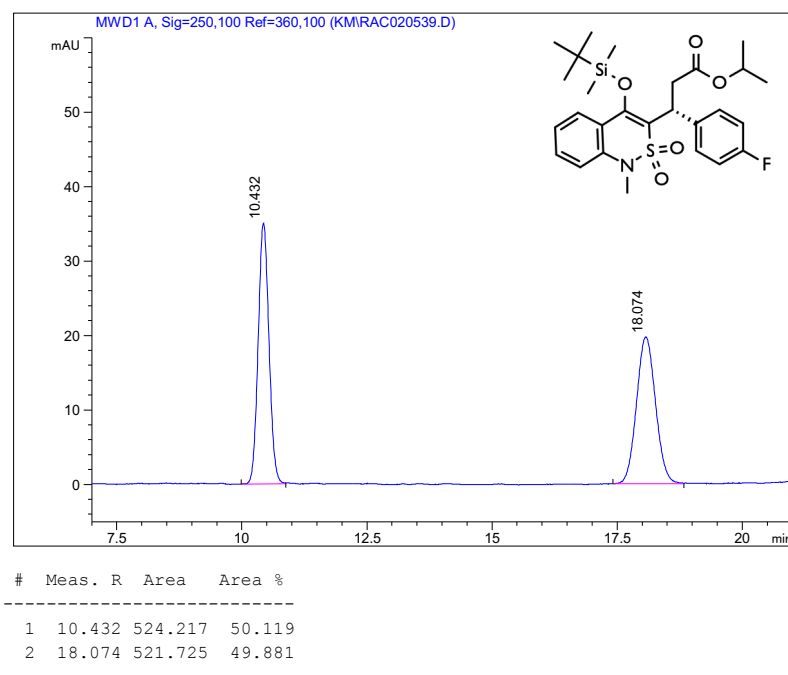


Figure S123: HPLC chromatograms of compound 4ae

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

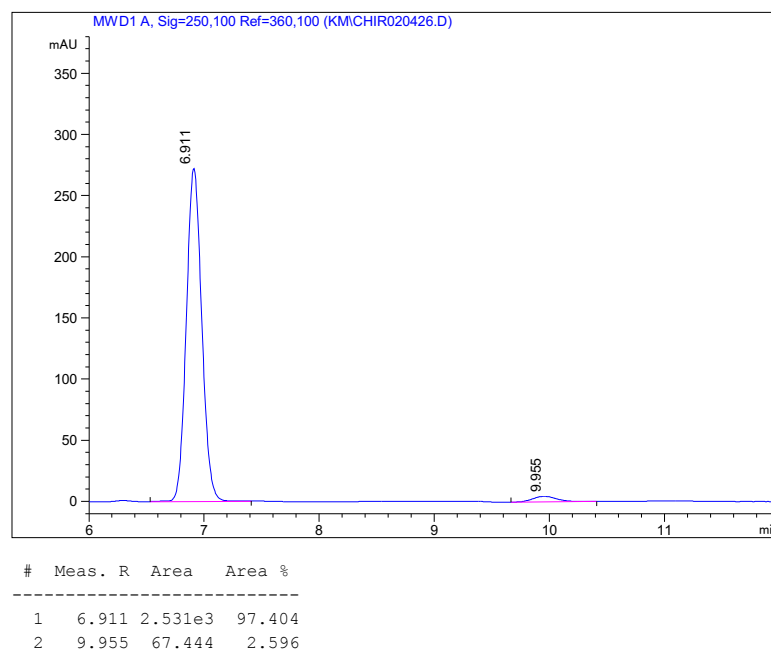
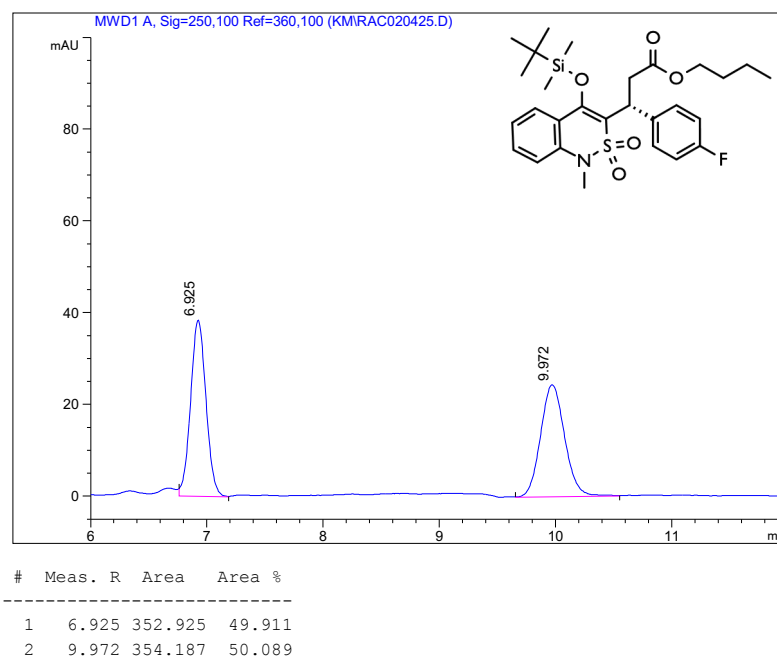


Figure S124: HPLC chromatograms of compound **4af**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

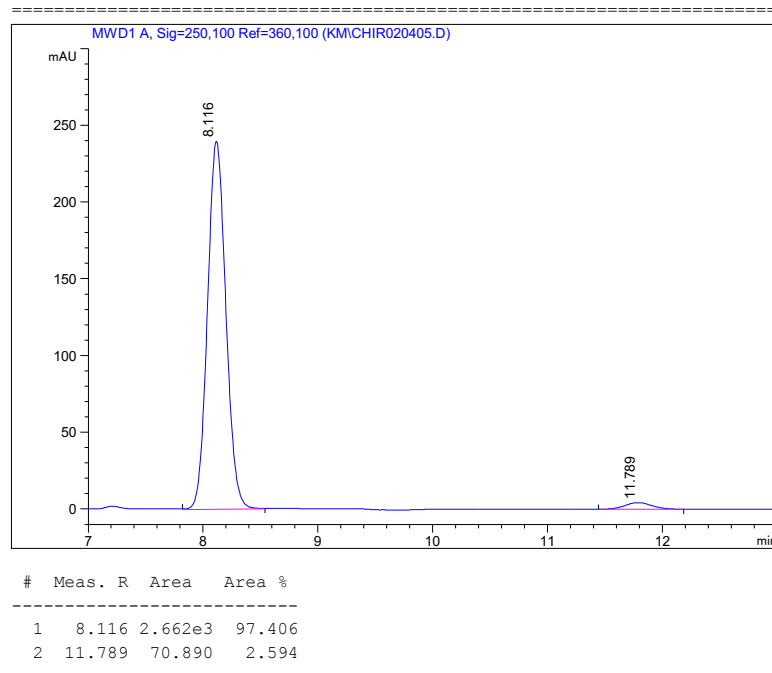
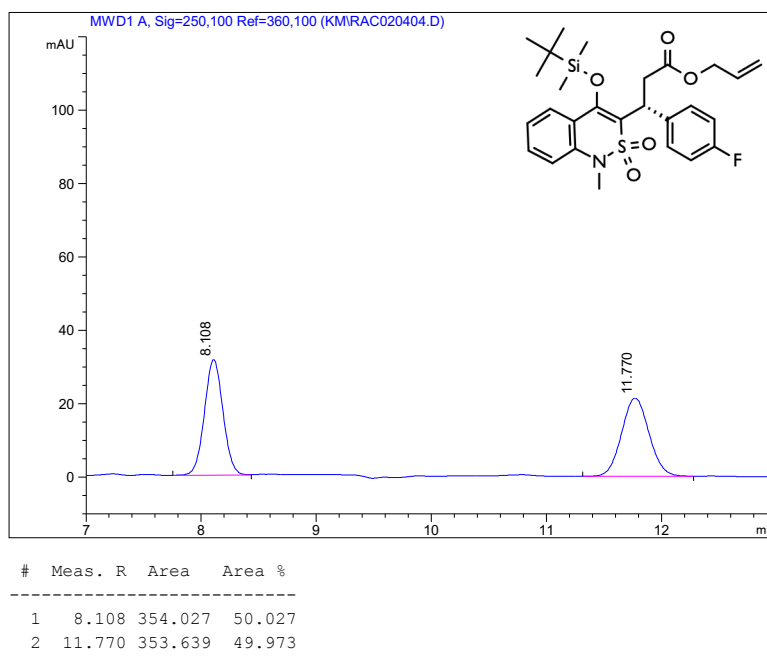


Figure S125: HPLC chromatograms of compound 4ag

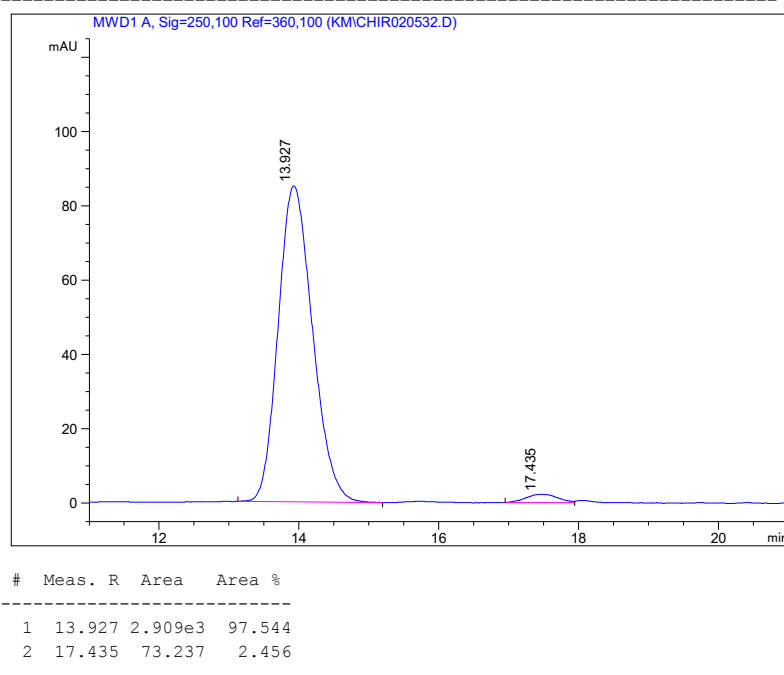
MWD1 A, Sig=250,100 Ref=360,100 (KMIRAC020605.D)

Chemical structure of the compound (likely a sulfonamide derivative):

CCCCNC(=O)C[C@H](c1ccc(F)cc1)S(=O)(=O)N2C(=C3C(=C(C=C3)Si(C)(C)C)OC2=CC=C3)C

Chromatogram Data:

#	Meas. R	Area	Area %
1	14.190	591.988	49.828
2	17.683	596.064	50.172

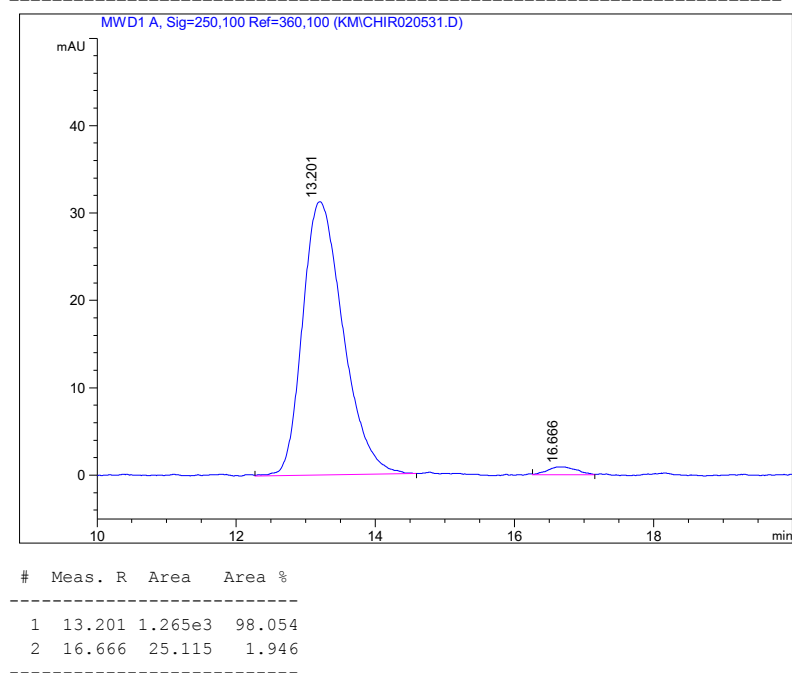


S160

MWD1 A, Sig=250,100 Ref=360,100 (KMIRAC020625.D)

Chemical structure: CC(C)NC(=O)C[C@H](c1ccc(F)cc1)C2=C(C(=C3C=CC=CC=C3N2C(=O)S(=O)(=O)C4=CC=CC=C4)OC5(C)(C)C(C)C5)C6=CC=CC=C6

#	Meas. R	Area	Area %
1	13.384	1.834e3	50.049
2	16.852	1.830e3	49.951



S161

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

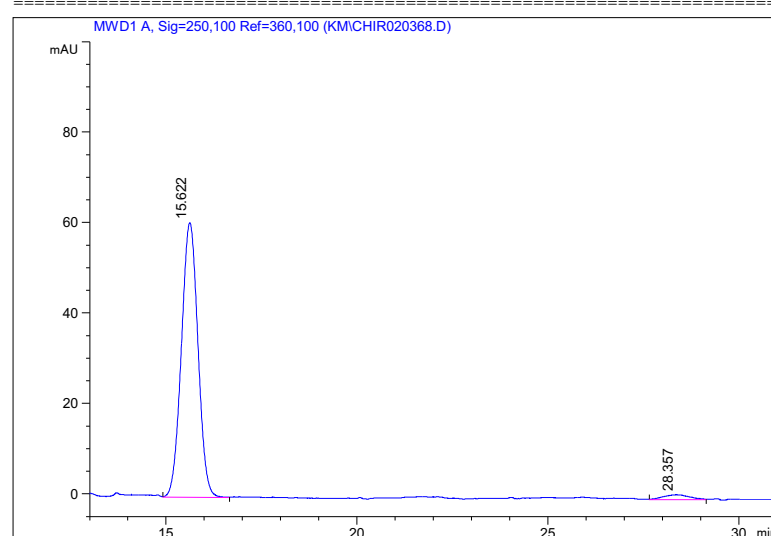
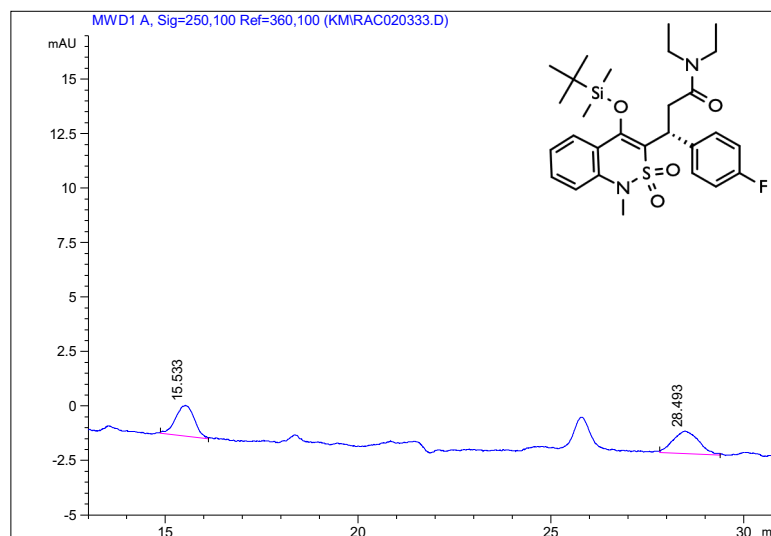


Figure S128: HPLC chromatograms of compound 4aj



Phenomenex Lux Amylose-1, 3 $\mu$ m, 90:10, 1.0 mL/min, p = 92bar, T = 25°C

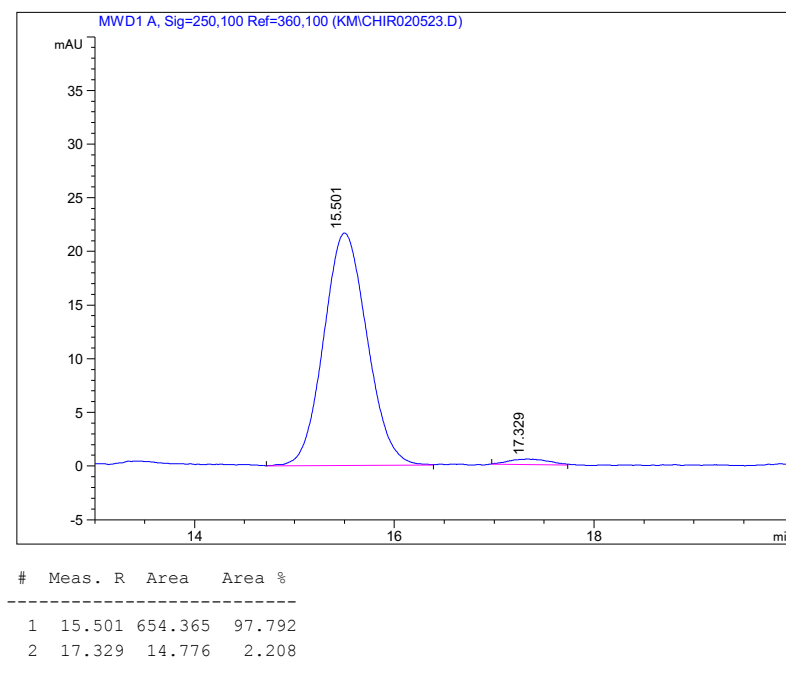
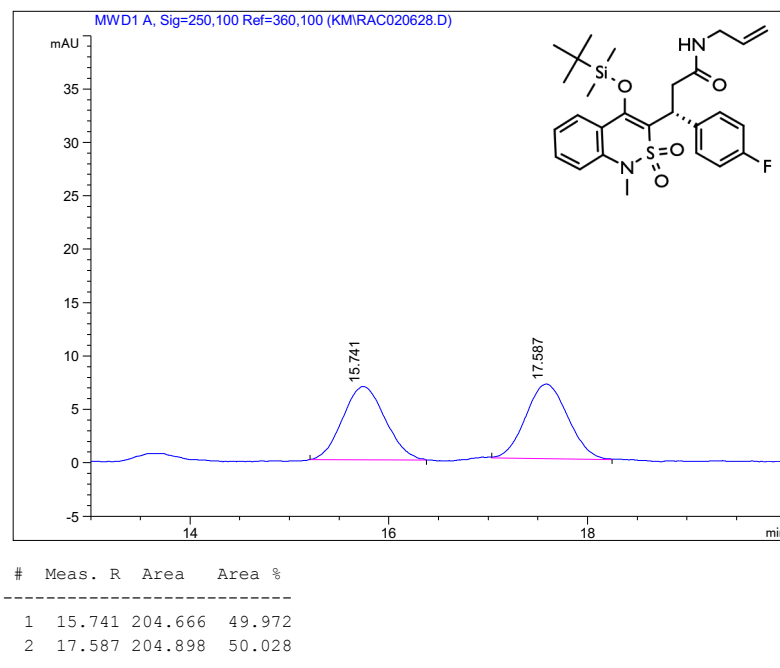


Figure S129: HPLC chromatograms of compound **4ak**

Phenomenex Lux Amylose-1, 3 $\mu$ m, 95:5, 1.0 mL/min, p = 88bar, T = 25°C

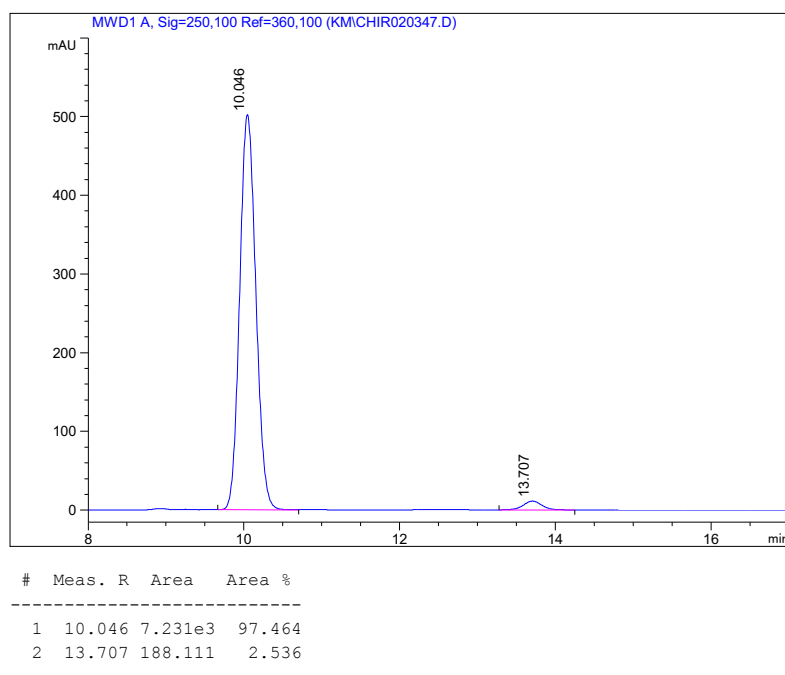
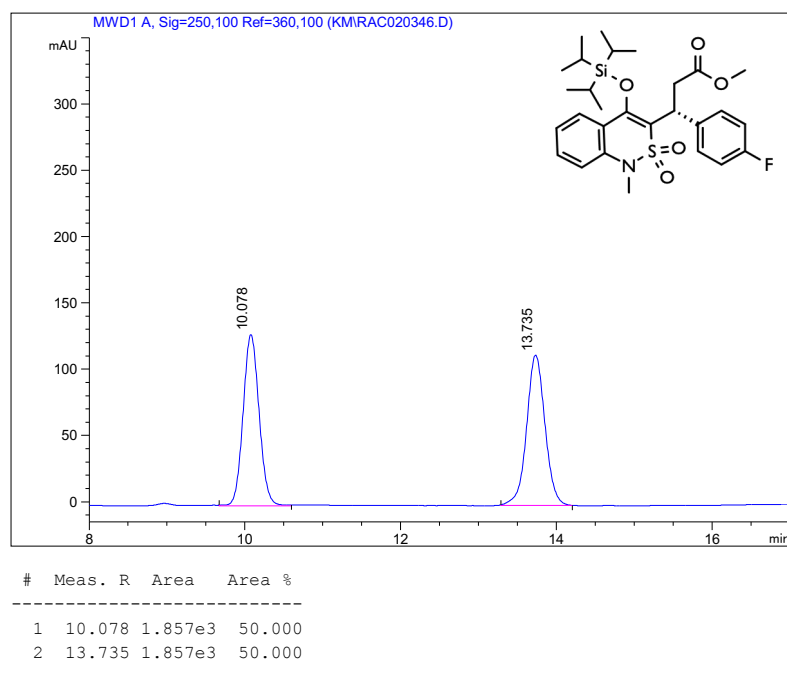


Figure S130: HPLC chromatograms of compound 4aI

## References

- [1] A. K. A. H. Damian Plažuk, Izabela Janowska and J. Zakrzewski, *Synth. Commun.*, 2003, **33**, 381–385.
- [2] K. Lei, X.-W. Hua, Y.-Y. Tao, Y. Liu, N. Liu, Y. Ma, Y.-H. Li, X.-H. Xu and C.-H. Kong, *Bioorg. Med. Chem.*, 2016, **24**, 92–103.
- [3] *CrysAlis Red and CrysAlis CCD*, 2000, <https://www.rigaku.com/products/crystallography/crystalis>.
- [4] G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112–122.
- [5] G. Sheldrick, *Acta Crystallogr.*, 2015, **C71**, 3–8.
- [6] C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. Van De Streek and P. A. Wood, *J. Appl. Cryst.*, 2008, **41**, 466–470.
- [7] <http://www.povray.org>.
- [8] P. Qian, J. Liu, Y. Zhang and Z. Wang, *J. Org. Chem.*, 2021, **86**, 16008–16015.
- [9] K. T. Hylland, S. Øien Ødegaard and M. Tilset, *Eur. J. Org. Chem.*, 2020, **2020**, 4208–4226.
- [10] S. Hinsberger, K. Hüsecken, M. Groh, M. Negri, J. Hauptenthal and R. W. Hartmann, *J. Med. Chem.*, 2013, **56**, 8332–8338.
- [11] P. Levesque and P.-A. Fournier, *J. Org. Chem.*, 2010, **75**, 7033–7036.
- [12] D. Roell, T. W. Rösler, W. Hessenkemper, F. Kraft, M. Hauschild, S. Bartsch, T. E. Abraham, A. B. Houtsmuller, R. Matusch, M. E. van Royen and A. Baniahmad, *J. Steroid Biochem.*, 2019, **188**, 59–70.
- [13] C. Granchi, G. Bononi, R. Ferrisi, E. Gori, G. Mantini, S. Glasmacher, G. Poli, S. Palazzolo, I. Caligiuri, F. Rizzolio, V. Canzonieri, T. Perin, J. Gertsch, A. Sodi, E. Giovannetti, M. Macchia, F. Minutolo, T. Tuccinardi and A. Chicca, *Eur. J. Med. Chem.*, 2021, **209**, 112857.
- [14] *Current Patent Assignee: RHONE-POULENC AGRICULTURE LIMITED - US6323155, 2001, B1.*
- [15] H. Chen, Z. Chen, Z. Zhang, Y. Li, S. Zhang, F. Jiang, J. Wei, P. Ding, H. Zhou, Q. Gu and J. Xu, *European Journal of Medicinal Chemistry*, 2020, **194**, 112240.
- [16] *Current Patent Assignee: ORSOBIO - US2019/359565, 2019, A1.*
- [17] *Current Patent Assignee: ASANA BIOSCIENCES - WO2015/38417, 2015, A1.*
- [18] *Current Patent Assignee: PELOTON THERAPEUTICS - WO2023/64058, 2023, A1.*

- [19] *Current Patent Assignee: RHONE-POULENC AGRICULTURE LIMITED - US5804532, 1998, A.*
- [20] *Current Patent Assignee: RHONE-POULENC AGRICULTURE LIMITED - US2002/45551, 2002, A1.*