

*Electronic Supplementary Information*

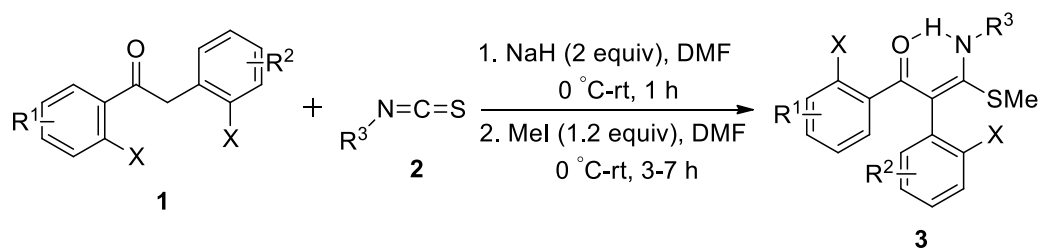
**Double Heteroannulation of *S,N*-Acetals: A Facile Access of Quinolone Derivatives**

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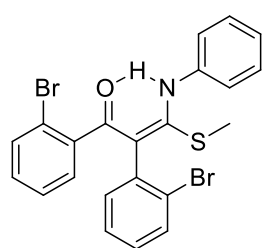
### General Procedure for the Synthesis of $\alpha$ -(2-Haloaroyl)- $\alpha$ -(2-haloaryl)-ketene *S,N*-acetals **3**



#### Scheme S1: Synthesis of $\alpha$ -(2-Haloaroyl)- $\alpha$ -(2-haloaryl)-ketene *S,N*-acetals **3**

To a stirring suspension of NaH (60% suspension in mineral oil) (0.240 g, 6.0 mmol) in DMF (4.0 mL) at 0 °C was added drop wise the corresponding deoxybenzoin **1** (3.0 mmol) in DMF (3.0 mL). After being further stirred for 1 h at room temperature, a solution of isothiocyanate **2** (3.0 mmol) in DMF (2.0 mL) was added to the reaction mixture at 0 °C and followed by further stirring for 1 h at room temperature. To this reaction mixture MeI (3.6 mmol) in DMF (1.0 mL) was added at 0 °C and further stirred for 2-6 h. After complete consumption of the starting materials (monitored by TLC), the reaction mixture was quenched with saturated  $NH_4Cl$  solution and extracted with EtOAc. The combined organic layer washed with water (3 x 20 mL) & brine (20 mL), dried over anhyd.  $Na_2SO_4$  and concentrated under reduced pressure. The crude products were purified by flash chromatography using EtOAc/hexanes as eluent.

#### 1,2-Bis(2-bromophenyl)-3-(methylthio)-3-(phenylamino)prop-2-en-1-one (**3a**)



Reaction time: 8 h

Yield: 93%, as a yellow colour solid.

Melting point: 116 – 118 °C

$R_f$ : 0.37 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3448, 3050, 3002, 2924, 2852, 1578, 1545, 1425, 1370, 1316, 1247, 1195, 1089, 1051, 1024, 976, 905, 850, 749, 734.

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  = 13.54 (s, 1H), 7.52 (d,  $J$  = 7.6 Hz, 2H), 7.47 (dd,  $J$  = 8.0, 1.2 Hz, 1H), 7.42 – 7.37 (m, 4H), 7.24 – 7.22 (m, 1H), 7.19 (dd,  $J$  = 7.6, 1.6 Hz, 1H), 7.08 (td,  $J$  = 7.6, 1.2 Hz, 1H), 7.05 – 6.94 (m, 3H), 1.91 (s, 3H).

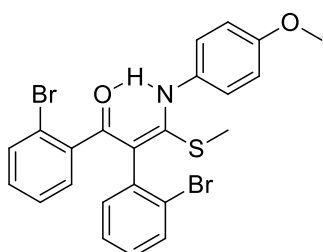
$^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  = 190.0, 165.5, 142.8, 139.8, 138.9, 134.0, 132.4, 132.2, 129.5, 129.4, 129.1, 128.7, 127.2, 126.9, 126.5, 125.8, 124.1, 119.2, 114.7, 17.2.

HR-MS (ESI): Calcd. for  $C_{22}H_{17}Br_2NOS$  [ $M+H$ ]: 501.9470, Found: 501.9491.

[M+H]: 503.9451, Found: 503.9474.

[M+H]: 505.9430, Found: 505.9450.

**1,2-Bis(2-bromophenyl)-3-((4-methoxyphenyl)amino)-3-(methylthio)prop-2-en-1-one (3b)**



Reaction time: 4 h

Yield: 64%, as a pale yellow colour solid.

Melting point: 128 – 130 °C

R<sub>f</sub>: 0.43 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3428, 3072, 2989, 2958, 2927, 2830, 1550, 1509, 1375, 1314, 1245, 1179, 1025, 871, 829, 763, 746.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.60 (s, 1H), 7.46 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.44 – 7.37 (m, 4H), 7.18 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.06 (td, *J* = 7.4, 1.2 Hz, 1H), 7.02 (td, *J* = 7.2, 1.2 Hz, 1H), 6.99 – 6.90 (m, 4H), 3.83 (s, 3H), 1.89 (s, 3H).

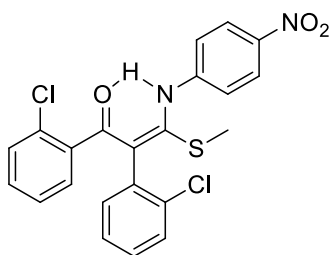
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 189.6, 166.2, 157.8, 142.9, 139.1, 134.1, 132.6, 132.4, 132.2, 129.3, 129.0, 128.9, 127.2, 126.9, 126.5, 125.8, 119.3, 114.6, 113.9, 55.6, 17.1.

HR-MS (ESI): Calcd. for C<sub>23</sub>H<sub>19</sub>Br<sub>2</sub>NO<sub>2</sub>S [M+H]: 531.9576, Found: 531.9538.

[M+H]: 533.9557, Found: 533.9526.

[M+H]: 535.9536, Found: 535.9512.

**1,2-Bis(2-chlorophenyl)-3-(methylthio)-3-((4-nitrophenyl)amino)prop-2-en-1-one (3c)**



Reaction time: 4 h

Yield: 71%, as a yellow colour solid.

Melting point: 122 – 124 °C

R<sub>f</sub>: 0.40 in 10% ethyl acetate in hexane

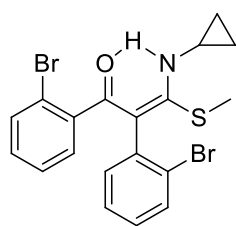
IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3447, 3050, 2925, 2843, 1587, 1560, 1514, 1423, 1364, 1338, 1312, 1266, 1250, 1112, 1091, 1062, 1032, 869, 854, 751.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.17 (s, 1H), 8.27 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 9.2 Hz, 2H), 7.33 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.15 – 7.06 (m, 4H), 7.02 – 6.98 (m, 1H), 2.02 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 191.6, 162.1, 146.2, 144.1, 140.1, 136.2, 136.0, 133.6, 130.1, 129.9, 129.6, 129.5, 129.2, 127.0, 126.7, 126.0, 125.4, 122.0, 116.4, 17.1.

HR-MS (ESI): Calcd. for C<sub>22</sub>H<sub>16</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>S [M+H]: 459.0331, Found: 459.0356.

### 1,2-Bis(2-bromophenyl)-3-(cyclopropylamino)-3-(methylthio)prop-2-en-1-one (3d)



Reaction time: 4 h

Yield: 70%, as a brown colour solid.

Melting point: 146 – 148 °C

R<sub>f</sub>: 0.28 in 5% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3431, 3063, 3046, 2993, 2925, 2848, 1542, 1559, 1423, 1390, 1280, 1251, 1155, 1050, 1024, 930, 805, 764, 751, 733.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 12.63 (s, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.29 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 7.02 – 6.90 (m, 4H), 3.14 – 3.09 (m, 1H), 2.32 (s, 3H), 0.99 – 0.95 (m, 4H).

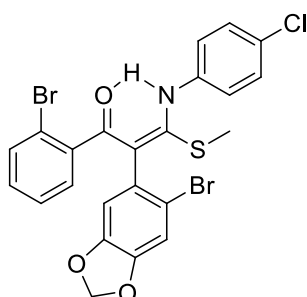
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 188.8, 169.7, 143.1, 139.6, 134.4, 132.3, 132.1, 129.1, 129.0, 128.6, 127.0, 126.9, 126.4, 119.4, 111.4, 28.6, 17.5, 9.2, 8.6.

HR-MS (ESI): Calcd. for C<sub>19</sub>H<sub>17</sub>Br<sub>2</sub>NOS [M+H]: 465.9470, Found: 465.9486.

[M+H]: 467.9450, Found: 467.9490.

[M+H]: 469.9430, Found: 469.9450.

### 2-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)-1-(2-bromophenyl)-3-((4-chlorophenyl)amino)-3-(methylthio)prop-2-en-1-one (3e)



Reaction time: 6 h

Yield: 59%, as a yellow colour solid.

Melting point: 155 – 157 °C

R<sub>f</sub>: 0.28 in 5% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3448, 3090, 3054, 2918, 2887, 1557, 1551, 1481, 1419, 1368, 1314, 1233, 1198, 1130, 1080, 1036, 935, 859,

819, 751, 732.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.37 (s, 1H), 7.44 – 7.41 (m, 3H), 7.37 – 7.34 (m, 2H), 7.22 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.09 (td, *J* = 7.6, 1.2 Hz, 1H), 7.03 (td, *J* = 7.6, 1.2 Hz, 1H), 6.92 (s, 1H), 6.88 (s, 1H), 5.89 (d, *J* = 7.6 Hz, 2H), 1.94 (s, 3H).

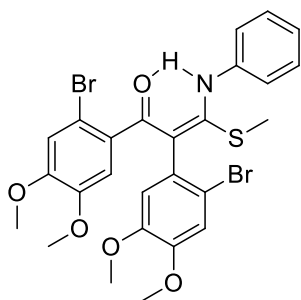
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 190.6, 165.5, 148.0, 147.1, 142.6, 138.5, 132.5, 131.6, 131.1, 129.6 (2C), 126.8, 126.7, 125.1, 119.4, 119.1, 115.1, 112.8, 112.2, 101.9, 17.1.

HR-MS (ESI): Calcd. for C<sub>23</sub>H<sub>16</sub>Br<sub>2</sub>ClNO<sub>3</sub>S [M+H]: 579.8979, Found: 579.8955.

[M+H]: 581.8958, Found: 581.8941.

[M+H]: 583.8938, Found: 583.8919.

**1,2-Bis(2-bromo-4,5-dimethoxyphenyl)-3-(methylthio)-3-(phenylamino)prop-2-en-1-one (3f)**



Reaction time: 8 h

Yield: 62%, as a yellow colour solid.

Melting point: 79 – 81 °C

R<sub>f</sub>: 0.38 in ethyl acetate/hexane (1:2)

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3448, 2997, 2929, 2838, 1594, 1542, 1507, 1459, 1381, 1356, 1327, 1256, 1206, 1168, 1098, 1026, 863, 831, 778.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.46 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.92 (s, 1H), 6.88 (s, 1H), 6.82 (s, 1H), 6.77 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H), 1.92 (s, 3H).

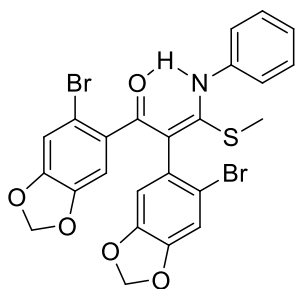
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 190.1, 165.9, 149.1, 148.9, 148.0, 147.5, 139.9, 135.4, 131.2, 129.5, 125.7, 123.9, 118.7, 116.0, 115.0, 114.6, 114.3, 110.1, 109.5, 56.10, 56.07, 56.065, 55.98, 17.1.

HR-MS (ESI): Calcd. for C<sub>26</sub>H<sub>25</sub>Br<sub>2</sub>NO<sub>5</sub>S [M+H]: 621.9916, Found: 621.9893.

[M+H]: 623.9874, Found: 623.9900.

[M+H]: 625.9853, Found: 625.9877.

**1,2-Bis(6-bromobenzo[*d*][1,3]dioxol-5-yl)-3-(methylthio)-3-(phenylamino)prop-2-en-1-one (3g)**



Reaction time: 6.5 h

Yield: 67%, as a yellow colour solid.

Melting point: 197 – 199 °C

R<sub>f</sub>: 0.40 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3428, 3081, 2923, 2848, 1563, 1540, 1497, 1476, 1410, 1391, 1360, 1340, 1311, 1241, 1117, 1069, 1033, 928, 881,

866, 765.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.43 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.96 (s, 1H), 6.92 (s, 1H), 6.86 (s, 1H), 6.76 (s, 1H), 5.94 (d, *J* = 6.8 Hz, 2H), 5.90 (d, *J* = 11.2 Hz, 2H), 1.90 (s, 3H).

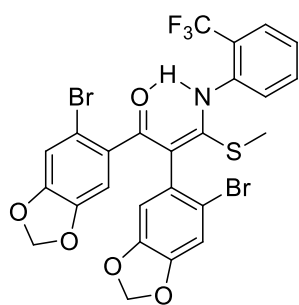
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 189.5, 166.1, 148.1, 148.0, 147.1, 146.6, 139.9, 136.5, 131.8, 129.5, 125.7, 124.0, 119.5, 114.4, 112.9, 112.7, 112.2, 110.3, 107.0, 101.9, 101.8, 17.1.

HR-MS (ESI): Calcd. for C<sub>24</sub>H<sub>17</sub>Br<sub>2</sub>NO<sub>5</sub>S [M+H]: 589.9267, Found: 589.9247.

[M+H]: 591.9248, Found: 591.9226.

[M+H]: 593.9227, Found: 593.9202.

**1,2-Bis(6-bromobenzo[d][1,3]dioxol-5-yl)-3-(methylthio)-3-((2-trifluoromethyl)phenyl)amino)prop-2-en-1-one (3h)**



Reaction time: 4.5 h

Yield: 63%, as a yellow colour solid.

Melting point: 106 – 108 °C

R<sub>f</sub>: 0.33 in 20% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3448, 3010, 2917, 2848, 1555, 1543, 1506, 1478, 1412, 1391, 1361, 1340, 1315, 1281, 1243, 1167, 1124, 1057, 1035,

931, 874, 841, 786, 765.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.28 (s, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 6.97 (s, 1H), 6.95 (s, 1H), 6.85 (s, 1H), 6.76 (s, 1H), 5.95 (dd, *J* = 7.4 Hz, 1.2 Hz, 2H), 5.91 (dd, *J* = 8.4 Hz, 1.2 Hz, 2H), 1.85 (s, 3H).

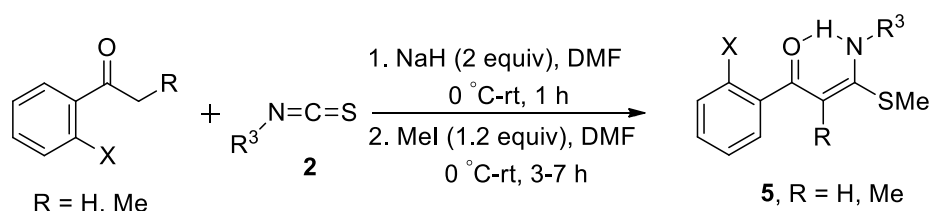
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 190.1, 165.1, 148.23, 148.18, 147.2, 146.7, 138.7 (d, *J* = 2 Hz), 136.0, 132.9, 131.3, 126.7 (q, *J* = 5.2 Hz), 125.8, 125.3, 123.8 (q, *J* = 271 Hz), 123.5 (q, *J* = 30 Hz), 119.1, 116.5, 112.7, 112.6, 112.3, 110.2, 107.0, 102.0, 101.9, 16.4.

HR-MS (ESI): Calcd. for C<sub>25</sub>H<sub>16</sub>Br<sub>2</sub>F<sub>3</sub>NO<sub>5</sub>S [M+H]: 657.9141, Found: 657.9176.

[M+H]: 659.9122, Found: 659.9151.

[M+H]: 661.9101, Found: 661.9135.

**General Procedure for the Synthesis of *S,N*-Acetals 5a-h**

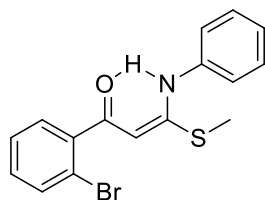


**Scheme S2:** Synthesis of *S,N*-Acetals **5a-h**

To a stirring suspension of NaH (60% suspension in mineral oil) (0.240 g, 6.0 mmol) in DMF (4.0 mL) at 0 °C was added drop wise the corresponding ketone (3.0 mmol) in DMF (3.0 mL). After being further stirred for 1 h at room temperature, a solution of isothiocyanate **2** (3.0 mmol) in DMF (2.0 mL) was added to the reaction mixture at 0 °C and followed by further stirring for 1 h at room temperature. To this reaction mixture MeI (3.6 mmol) in DMF (1.0 mL) was added at 0 °C and further stirred for 2-6 h. After complete consumption of the starting materials (monitored by TLC), the reaction mixture was quenched with saturated NH<sub>4</sub>Cl solution and extracted with EtOAc. The combined organic layer washed with water (3

x 20 mL) & brine (20 mL), dried over anhyd. Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude products were purified by flash chromatography using EtOAc/hexanes as eluent.

### 1-(2-Bromophenyl)-3-(methylthio)-3-(phenylamino)prop-2-en-1-one (5a)<sup>1</sup>



Reaction time: 6.5 h

Yield: 74%, as a yellow colour solid.

Melting point: 118 – 120 °C

R<sub>f</sub>: 0.30 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3437, 3054, 3005, 2923, 1594, 1565, 1476, 1429, 1301, 1246, 1157, 1023, 835, 748.

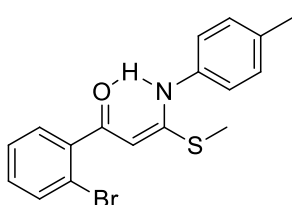
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.16 (s, 1H), 7.61 (dd,  $J$  = 8.0, 0.8 Hz, 1H), 7.51 (dd,  $J$  = 7.6, 1.6 Hz, 1H), 7.41 – 7.33 (m, 5H), 7.29 – 7.21 (m, 2H), 5.53 (s, 1H), 2.38 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 187.8, 168.1, 143.3, 138.0, 133.5, 130.4, 129.3, 129.2, 127.4, 126.8, 125.6, 119.6, 92.5, 14.9.

HR-MS (ESI): Calcd. for C<sub>16</sub>H<sub>14</sub>BrNOS [M+H]: 348.0052, Found: 348.0080.

[M+H]: 350.0032, Found: 350.0059.

### 1-(2-Bromophenyl)-3-(methylthio)-3-(*p*-tolylamino)prop-2-en-1-one (5b)



Reaction time: 4 h

Yield: 72%, as a yellow colour solid.

Melting point: 88 – 90 °C

R<sub>f</sub>: 0.35 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3449, 3032, 2998, 2905, 2848, 1591, 1551, 1476, 1456, 1432, 1289, 1222, 1152, 1095, 1023, 986, 817, 773, 752.

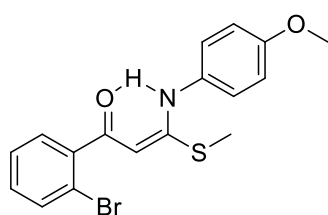
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.10 (s, 1H), 7.57 (d,  $J$  = 7.6 Hz, 1H), 7.49 (d,  $J$  = 7.6 Hz, 1H), 7.32 (t,  $J$  = 7.6 Hz, 1H), 7.21 – 7.15 (m, 5H), 5.49 (s, 1H), 2.34 (s, 3H), 2.31 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 187.3, 168.2, 143.1, 136.5, 135.0, 133.2, 130.1, 129.5, 129.1, 127.1, 125.2, 119.3, 91.9, 20.9, 14.5.

HR-MS (ESI): Calcd. for C<sub>17</sub>H<sub>16</sub>BrNOS [M+H]: 362.0209, Found: 362.0220.

[M+H]: 364.0189, Found: 364.0205.

### 1-(2-Bromophenyl)-3-((4-methoxyphenyl)amino)-3-(methylthio)prop-2-en-1-one (5c)



Reaction time: 4 h

Yield: 76%, as a brown colour solid.

Melting point: 80 – 82 °C

R<sub>f</sub>: 0.33 in 20% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3448, 3032, 3003, 2956, 2930, 2837, 1598, 1570, 1512, 1478, 1456, 1296, 1246, 1180, 1091, 1035, 1026, 843, 787, 746, 723.

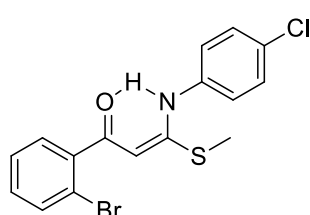
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 12.91 (s, 1H), 7.60 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.50 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.35 (td, *J* = 7.6, 0.8 Hz, 1H), 7.27 – 7.26 (m, 1H), 7.24 – 7.20 (m, 2H), 6.93 – 6.89 (m, 2H), 5.47 (s, 1H), 3.83 (s, 3H), 2.35 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 187.7, 169.2, 158.7, 143.5, 133.5, 130.7, 130.3, 129.3, 127.6, 127.4, 119.6, 114.4, 91.9, 55.6, 14.8.

HR-MS (ESI): Calcd. for C<sub>17</sub>H<sub>16</sub>BrNO<sub>2</sub>S [M+H]: 378.0158, Found: 378.0177.

[M+H]: 380.0138, Found: 380.0160.

### 1-(2-Bromophenyl)-3-((4-chlorophenyl)amino)-3-(methylthio)prop-2-en-1-one (5d)



Reaction time: 4.5 h

Yield: 74%, as a yellow colour solid.

Melting point: 130 – 132 °C

R<sub>f</sub>: 0.35 in 10% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3432, 3050, 2996, 2923, 1573, 1556, 1491, 1474, 1455, 1434, 1296, 1253, 1218, 1156, 1105, 1090, 1023, 1012, 984, 933, 845, 745.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 13.13 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.37 – 7.34 (m, 3H), 7.28 (d, *J* = 8.8 Hz, 2H), 7.26 – 7.22 (m, 1H), 5.54 (s, 1H), 2.39 (s, 3H).

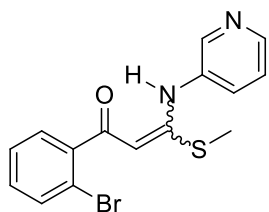
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 188.1, 167.9, 143.1, 136.6, 133.6, 132.4, 130.5, 129.38, 129.36, 127.4, 126.8, 119.6, 93.0, 14.9.

HR-MS (ESI): Calcd. for C<sub>16</sub>H<sub>13</sub>BrClNOS [M+H]: 381.9663, Found: 381.9614.

[M+H]: 383.9641, Found: 383.9592.



### 1-(2-Bromophenyl)-3-(methylthio)-3-(pyridin-3-ylamino)prop-2-en-1-one (5e)



Reaction time: 5 h

Yield: 72%, as a yellow colour solid.

R<sub>f</sub>: 0.33 in 50% ethyl acetate in hexane

Melting point: 98 – 100 °C

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3420, 2921, 1580, 1555, 1482, 1451, 1422, 1293, 1253, 1158, 1020, 746.

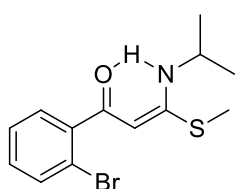
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) [obtained as a (7.7:1) inseparable mixture of E/Z isomers]  $\delta$  = 13.17 (s, 1H) [4.66 (s, 1H)], 8.66 (d, *J* = 2.4 Hz, 1H) [8.38 – 8.37 (m, 1H)], 8.51 – 8.50 (m, 1H) [8.34 – 8.32 (m, 1H)], 7.72 – 7.70 (m, 1H) [7.76 – 7.74 (m, 1H)], 7.61 (d, *J* = 7.6 Hz, 1H), 7.49 (dd, *J* = 7.4, 1.6 Hz, 1H) [7.56 – 7.54 (m, 2H)], 7.36 – 7.32 (m, 2H) [7.38 (br s, 2H)], 7.24 – 7.21 (m, 1H) [7.264 (br s, 1H)], 5.60 (s, 1H) [6.82 (s, 1H)], 2.41 (s, 3H) [2.38 (s, 3H)].

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 188.4 [199.6], 167.8 [170.0], 147.4 [145.1], 146.6 [144.5], 142.8 [140.5], 134.9 [134.2], 133.5 [132.1], 132.7 [131.8], 130.6 [131.5], 129.3 [130.0], 127.4 [127.5], 123.6 [123.83], 119.4 [123.79], 93.6 [118.6], 14.8 [16.6].

HR-MS (ESI): Calcd. for C<sub>15</sub>H<sub>13</sub>BrN<sub>2</sub>OS [M+H]: 349.0005, Found: 349.0000.

[M+H]: 350.9984, Found: 350.9985.

### 1-(2-Bromophenyl)-3-(isopropylamino)-3-(methylthio)prop-2-en-1-one (5f)



Reaction time: 4 h

Yield: 75%, as a pale yellow colour solid.

R<sub>f</sub>: 0.36 in 20% ethyl acetate in hexane

Melting point: 104 – 106 °C

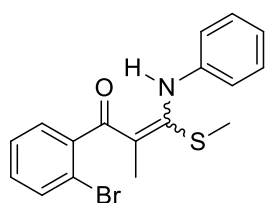
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 11.65 (s, 1H), 7.57 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.49 – 7.47 (m, 1H), 7.31 (td, *J* = 7.4, 0.8 Hz, 1H), 7.19 (td, *J* = 7.4, 1.6 Hz, 1H), 3.98 – 3.89 (m, 1H), 2.41 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 6H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 186.5, 168.4, 143.7, 133.3, 129.9, 129.3, 127.2, 119.5, 89.7, 46.4, 23.2, 14.4.

HR-MS (ESI): Calcd. for C<sub>13</sub>H<sub>16</sub>BrNOS [M+H]: 314.0209, Found: 314.0234.

[M+H]: 316.0188, Found: 316.0214.

### 1-(2-Bromophenyl)-2-methyl-3-(methylthio)-3-(phenylamino)prop-2-en-1-one (5g)



Reaction time: 4 h

Yield: 60%, as a yellow colour viscous liquid.

R<sub>f</sub>: 0.38 in 5% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3463, 3054, 2983, 2926, 1709, 1555, 1428, 1385,

1314, 1265, 1243, 1164, 1051, 1025, 993, 961, 902, 857, 761, 744.

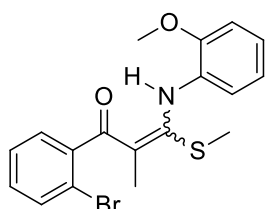
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) [obtained as a (2:1) inseparable mixture of E/Z isomers]  $\delta$  = 12.95 (s, 1H) [4.69 (s, 1H)], 7.57 (d, *J* = 8.0 Hz, 1H) [7.519 – 7.511 (m, 1H)], 7.37 – 7.34 (m, 4H) [7.39 – 7.38 (m, 1H), 7.323 – 7.321 (m, 1H), 7.31 – 7.29 (m, 2H)], 7.23 – 7.21 (m, 2H) [7.20 (br s, 1H), 7.18 – 7.16 (m, 1H)], 7.15 – 7.13 (m, 1H) [7.06 (t, *J* = 7.3 Hz, 1H)], 6.36 (m, 1H) [6.63 (br s, 1H)], 2.05 (s, 3H) [2.38 (s, 3H)], 1.90 (s, 3H) [1.48 (s, 3H)].

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 192.4 [200.3], 162.7 [167.6], 143.5 [150.0], 133.5 [128.7], 132.8 [140.7], 129.3 (2C) [129.7 (2C)], 127.60 [131.6], 127.56 [129.2], 124.9 [127.3], 123.3 [118.9], 119.7 [123.7], 106.9 [119.1], 16.8 [14.9], 16.5 [13.1].

HR-MS (ESI): Calcd. for C<sub>17</sub>H<sub>16</sub>BrNOS [M+H]: 362.0209, Found: 362.0235.

[M+H]: 364.0189, Found: 364.0213.

### 1-(2-Bromophenyl)-3-((2-methoxyphenyl)amino)-2-methyl-3-(methylthio)prop-2-en-1-one (5h)



Reaction time: 4.5 h

Yield: 60%, as a yellow colour solid.

Melting point: 88 – 90 °C

R<sub>f</sub>: 0.40 in 20% ethyl acetate in hexane

IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3447, 3002, 2962, 2933, 1592, 1582, 1553, 1495, 1458, 1383, 1312, 1254, 1177, 1112, 1026, 989, 862, 751.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) [obtained as a (2.7:1) inseparable mixture of E/Z isomers]  $\delta$  = 12.34 (s, 1H) [4.54 (br s, 1H)], 7.59 (d, *J* = 7.6 Hz, 1H) [7.48 – 7.46 (m, 1H)], 7.54 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H) [7.29 – 7.28 (m, 2H)], 7.24 – 7.21 (m, 1H) [7.16 – 7.15 (m, 1H)], 7.19 – 7.17 (m, 1H) [7.03 (t, *J* = 7.8 Hz, 1H)], 7.11 – 7.07 (m, 1H) [6.85 (d, *J* = 8.1, 1H)], 6.94 – 6.88 (m, 2H) [6.79 – 6.77 (m, 1H), 6.13 (br s, 1H)], 3.89 (s, 3H) [3.67 (s, 3H)], 2.09 (s, 3H) [2.41 (s, 3H)], 1.93 (s, 3H) [1.47 (s, 3H)].

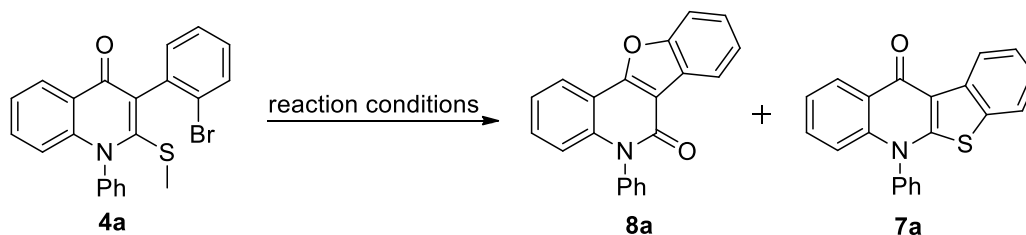
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 192.3 [200.7], 151.6 [161.4], 143.8 [148.7], 133.3 [140.9], 132.7 [128.9], 131.4 [138.6], 129.8, 129.6 [127.2 (2C)], 127.7 [124.7], 127.5 [122.4], 125.1

[121.4], 122.4 [121.6], 120.7 [121.1], 118.9 [111.5], 111.0 [108.0], 55.9 [55.5], 16.57 [14.3], 16.47 [13.2].

HR-MS (ESI): Calcd. for C<sub>18</sub>H<sub>18</sub>BrNO<sub>2</sub>S [M+H]: 392.0314, Found: 392.0319.

[M+H]: 394.0294, Found: 394.0298.

**Table S1: Controlled Experiments<sup>c</sup>**

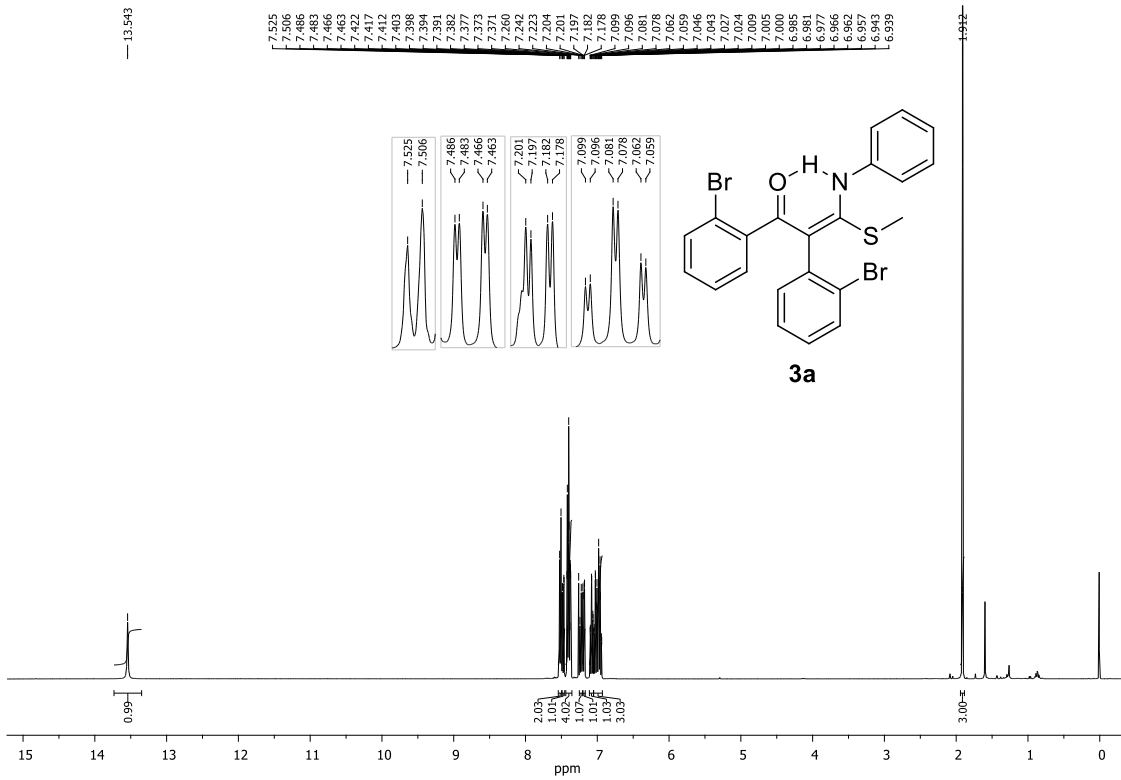


Entry	Metal salt	Ligand	Base	Solvent	Additive	<b>8a</b> (Yield)	<b>7a</b> (Yield)
1	CuI	1,10-phen	KO <sup>t</sup> Bu	DMF	-	no reaction	
2	CuI	1,10-phen	KO <sup>t</sup> Bu	DMF	benzylamine	45% <sup>b</sup>	5% <sup>b</sup>
3	CuI	1,10-phen	KO <sup>t</sup> Bu	DMF	benzylamine/ H <sub>2</sub> O	no reaction	

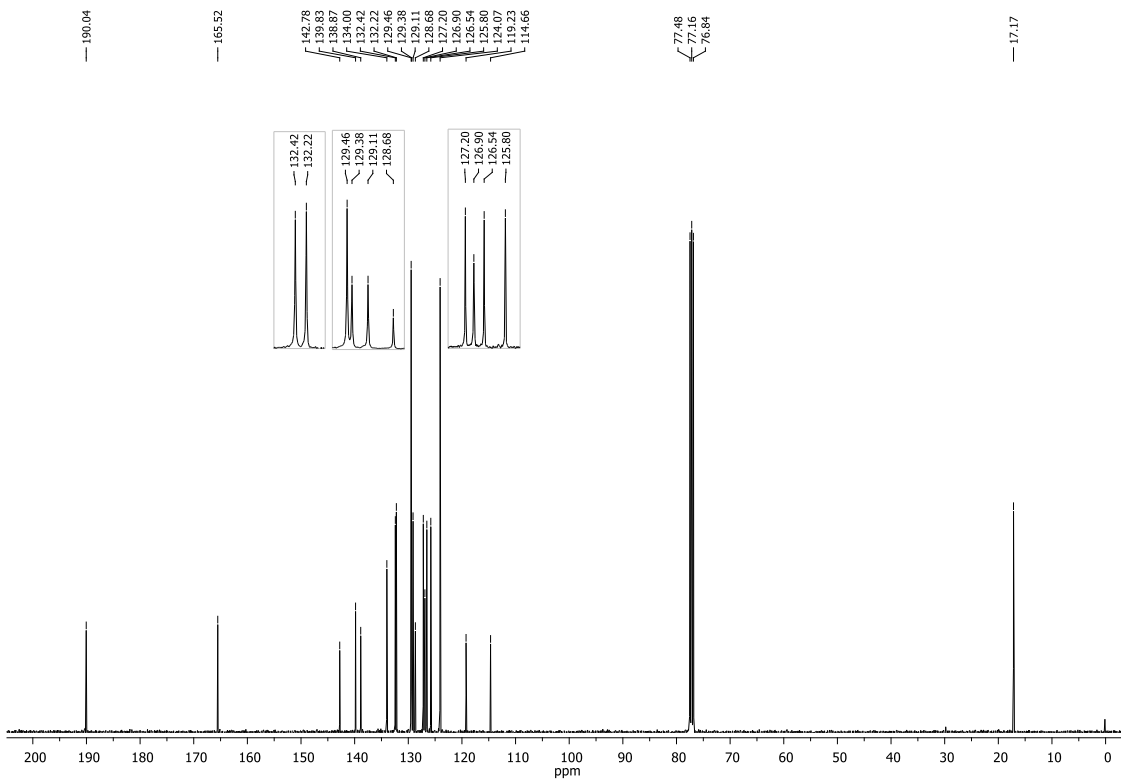
a) Reaction conditions: **4a** (10 mol %), **1**, 10-phen (12 mol%), KO<sup>t</sup>Bu (3 equiv), BnNH<sub>2</sub> (1.5 equiv), DMF (2.0 mL). b) Isolated yield. c) Standard vial technique

## References:

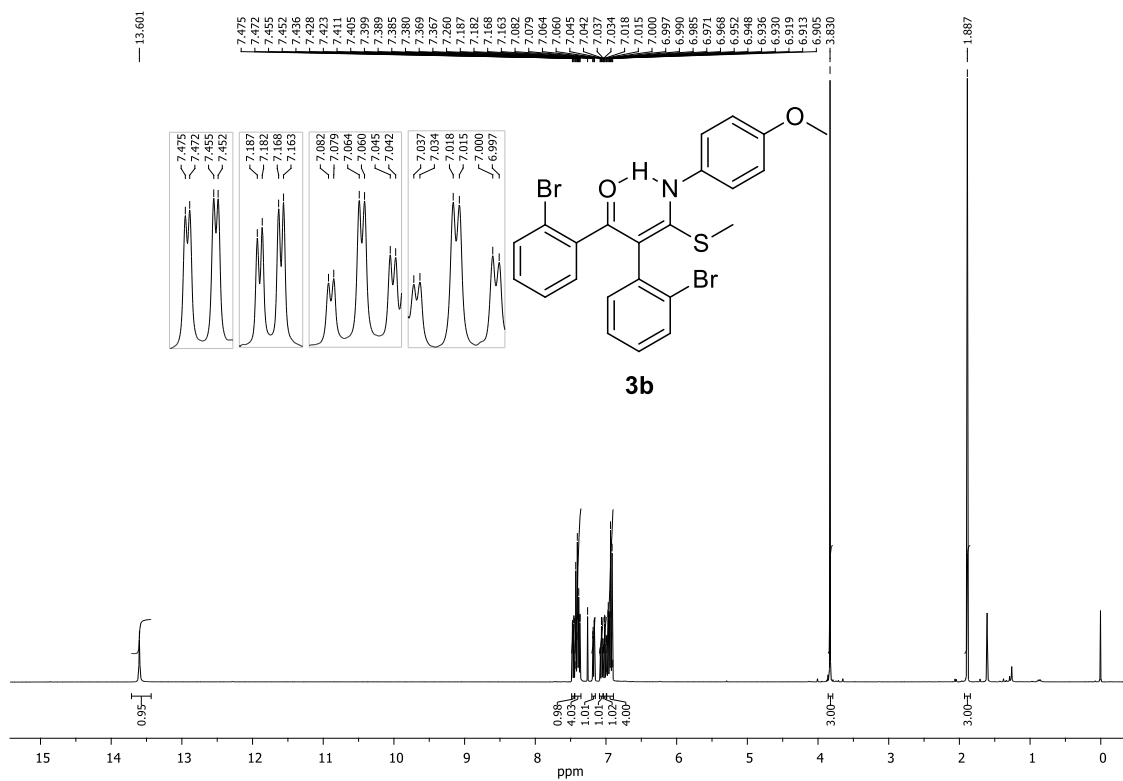
1. W. D. Rudolf, A. Schierhorn and M. Augustin, *Tetrahedron*, **1979**, 35, 551.



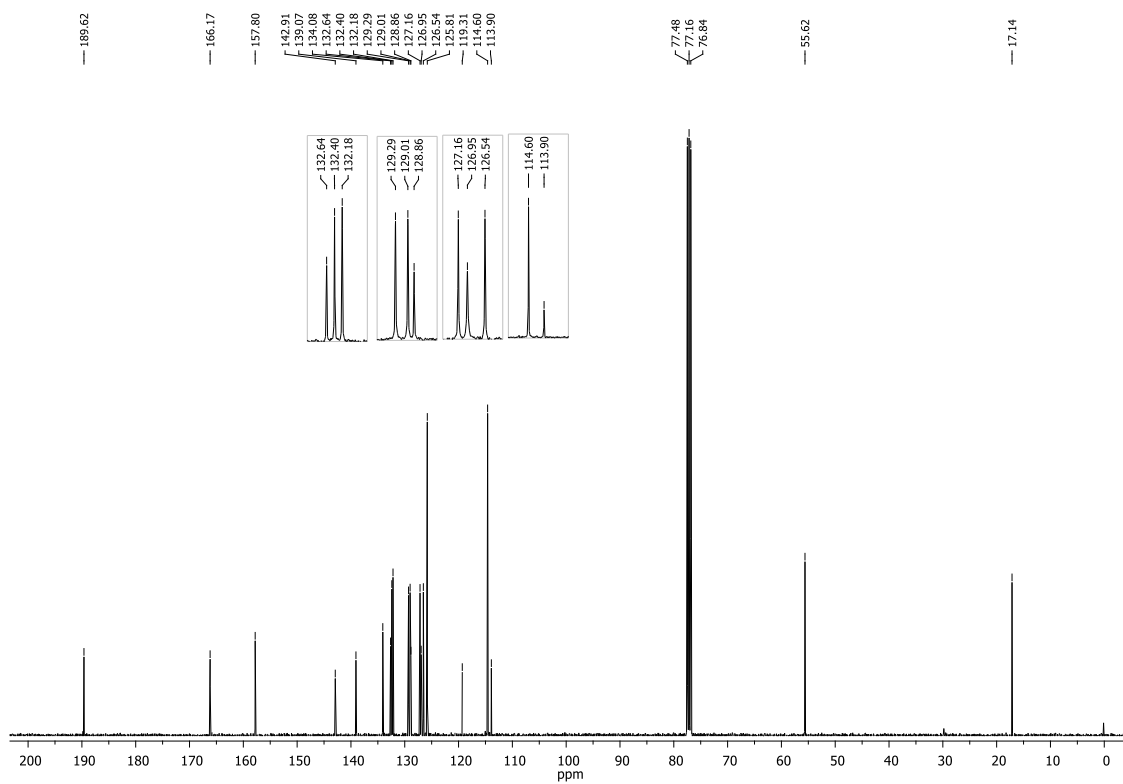
<sup>1</sup>H NMR Spectra of **3a**



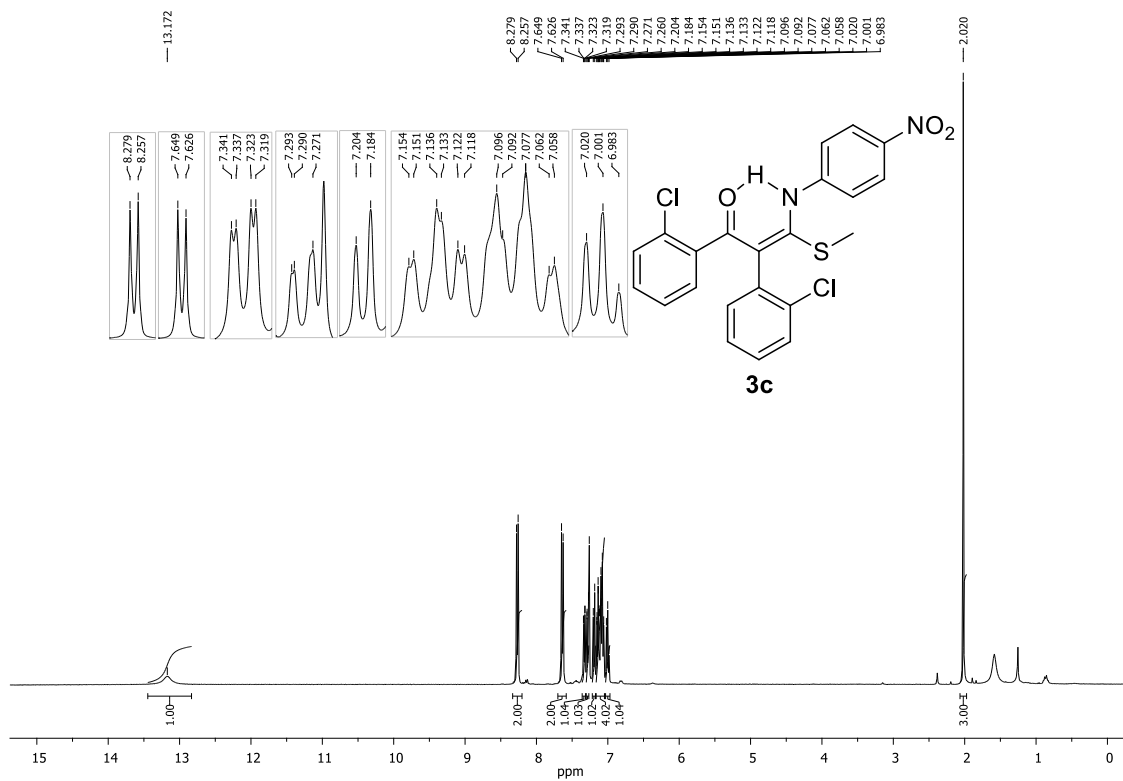
<sup>13</sup>C NMR Spectra of **3a**



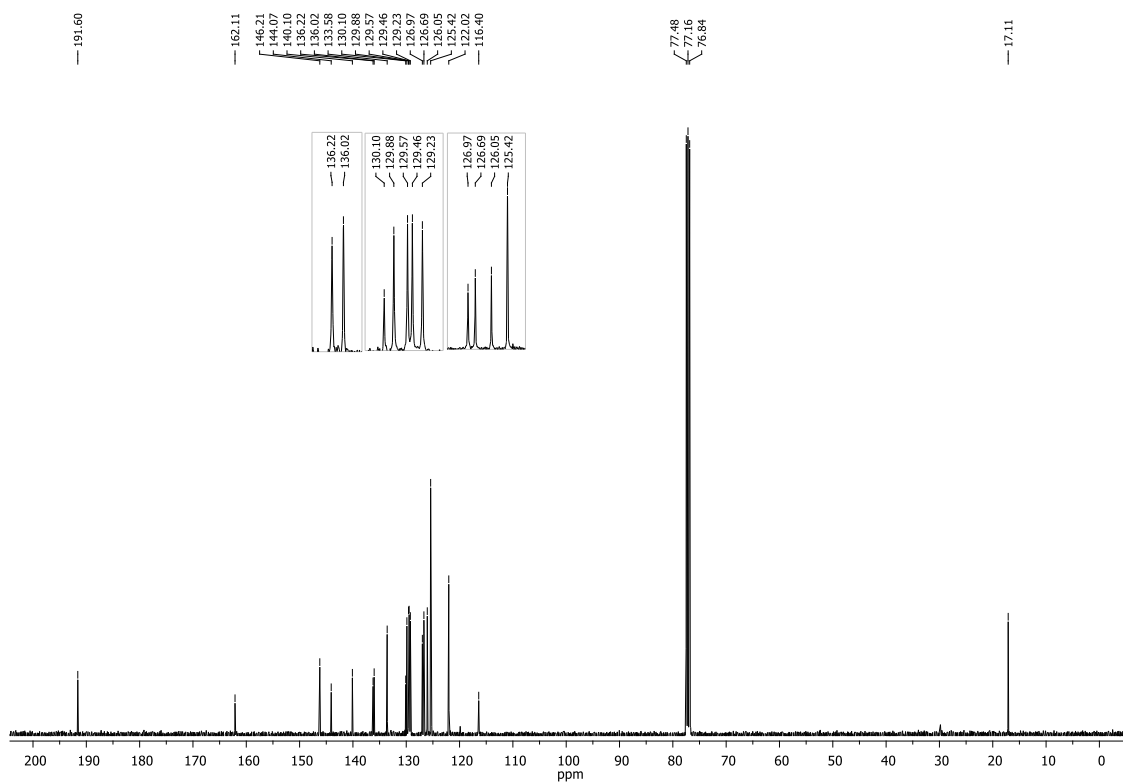
<sup>1</sup>H NMR Spectra of **3b**



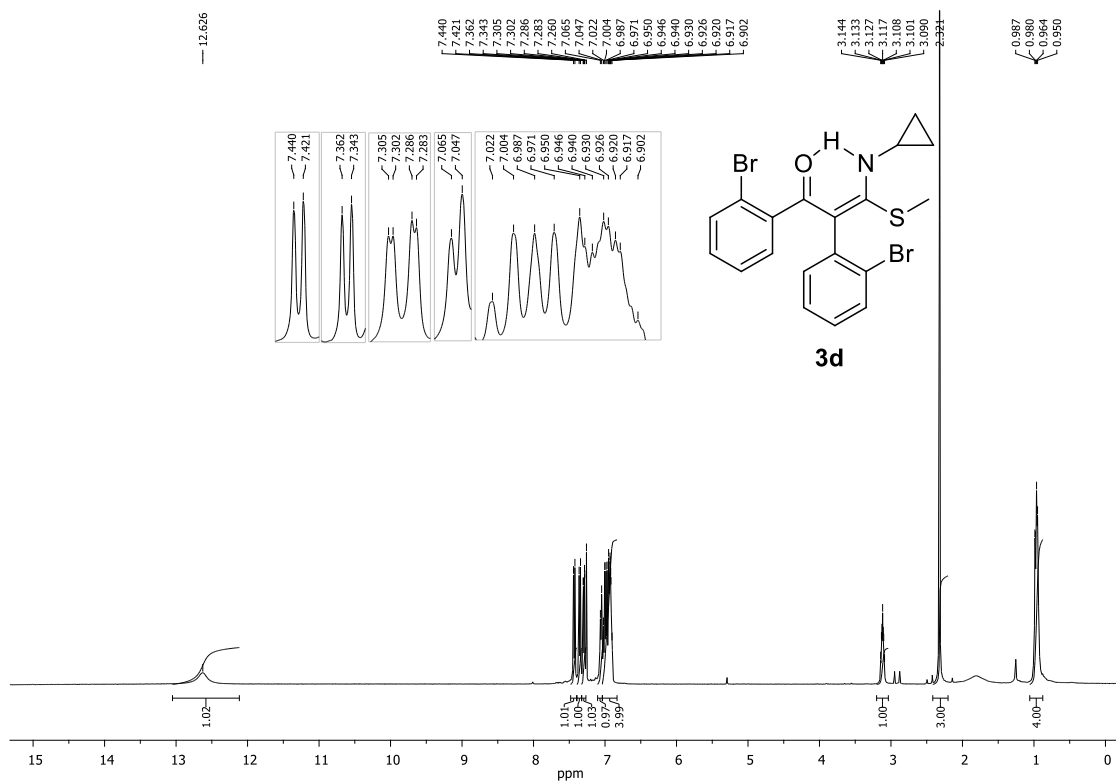
<sup>13</sup>C NMR Spectra of **3b**



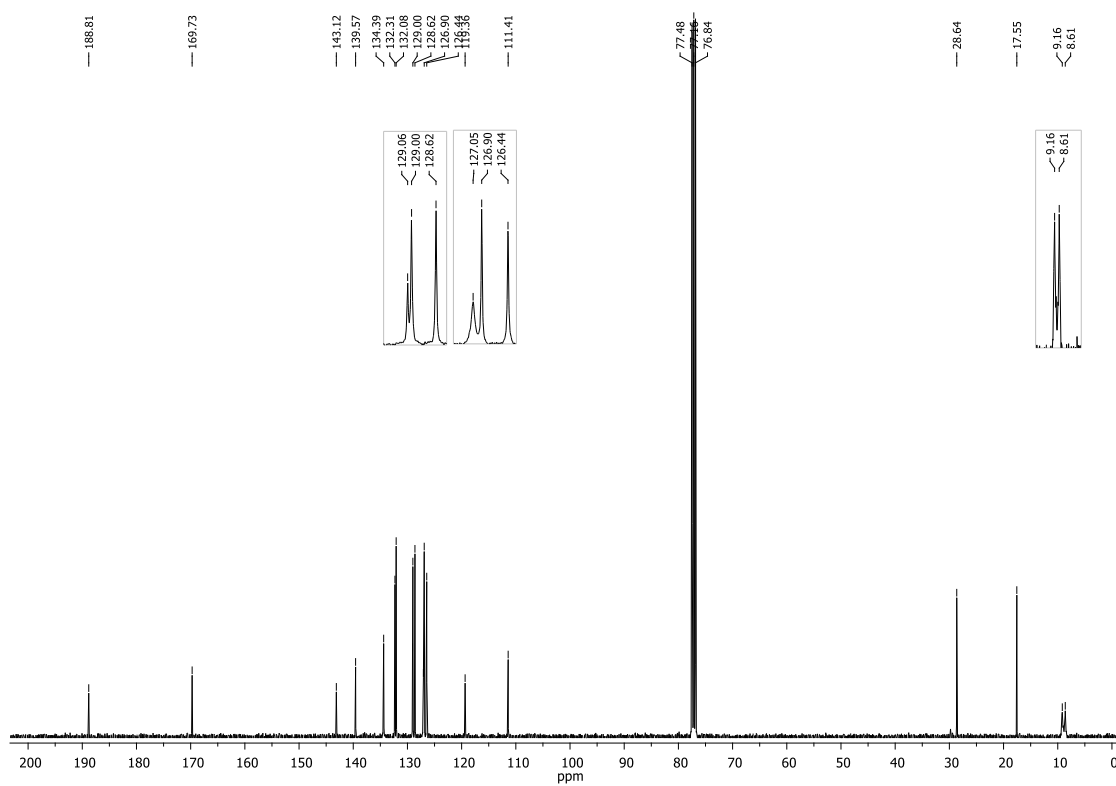
<sup>1</sup>H NMR Spectra of **3c**



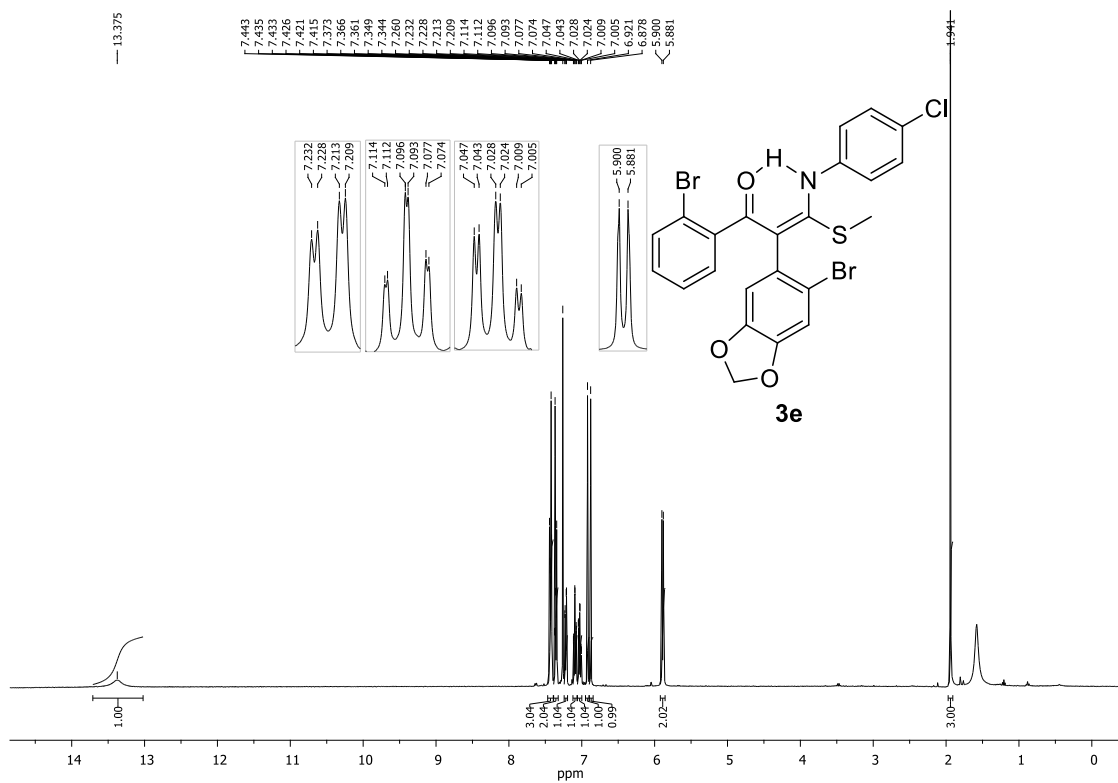
<sup>13</sup>C NMR Spectra of **3c**



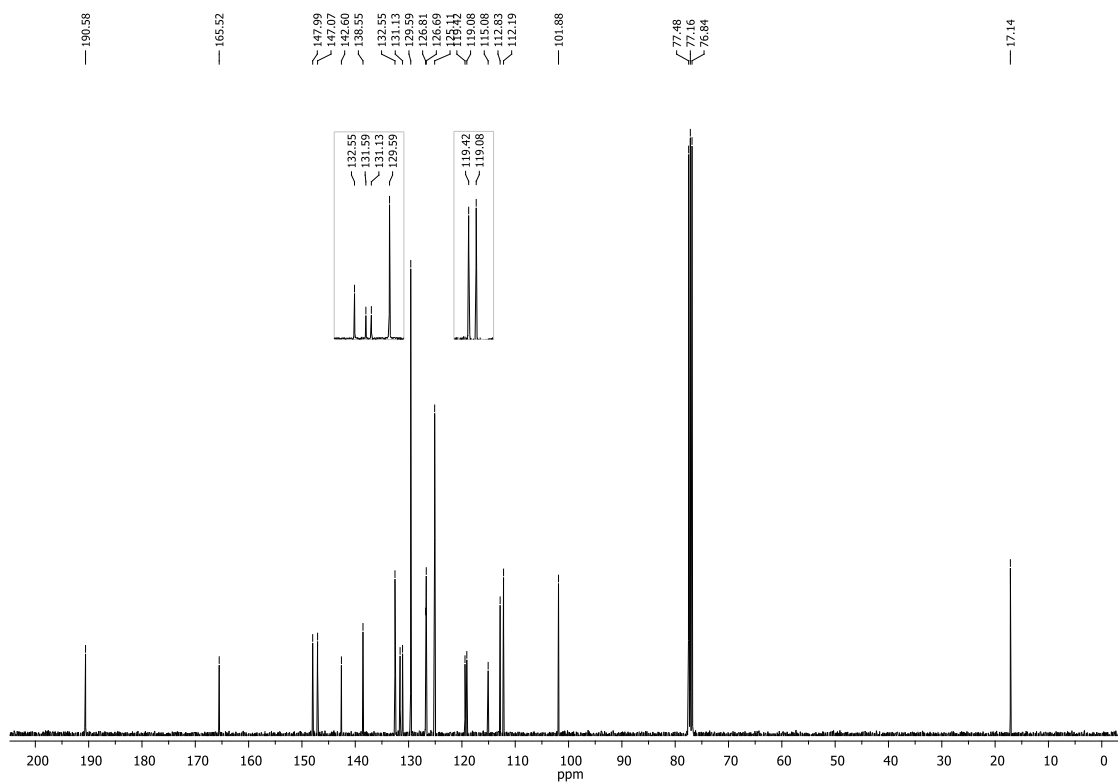
<sup>1</sup>H NMR Spectra of 3d



<sup>13</sup>C NMR Spectra of 3d

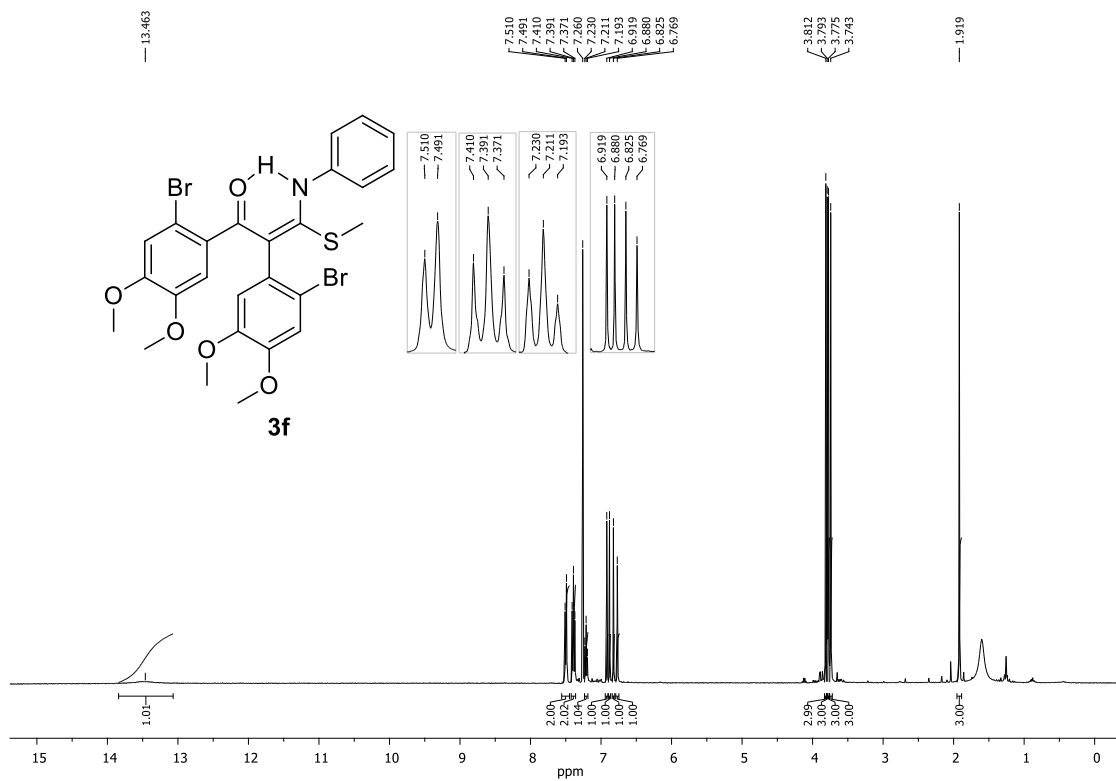


<sup>1</sup>H NMR Spectra of 3e

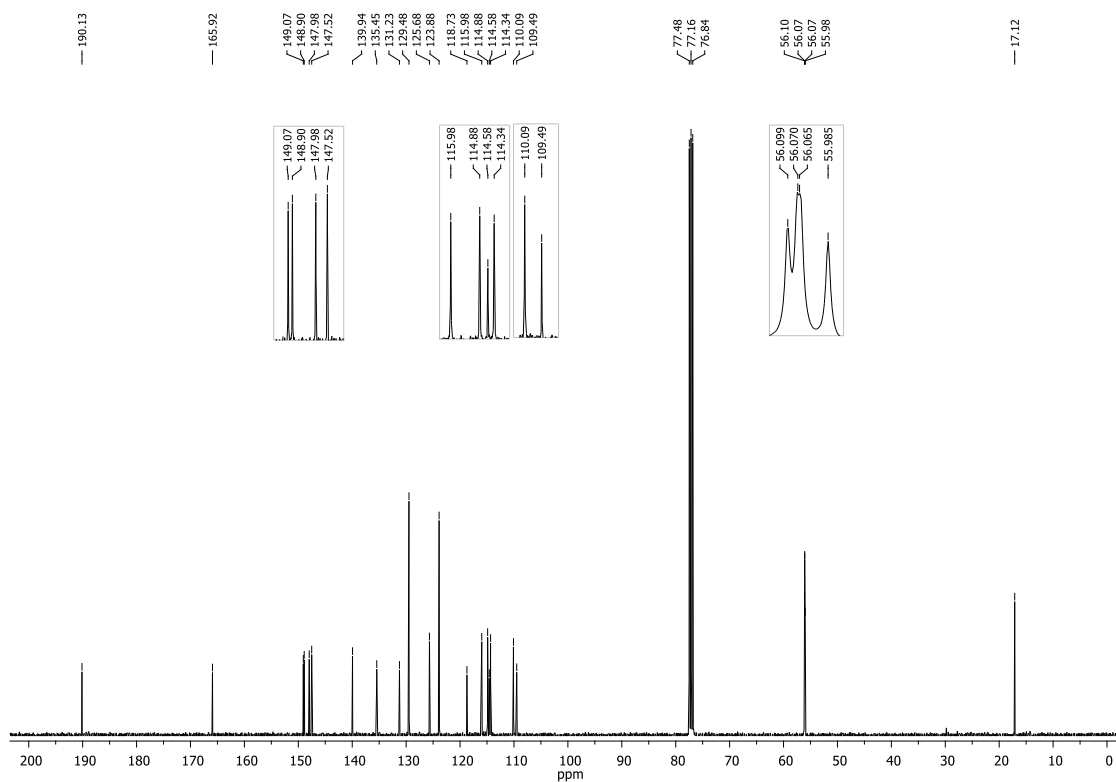


<sup>13</sup>C NMR Spectra of 3e

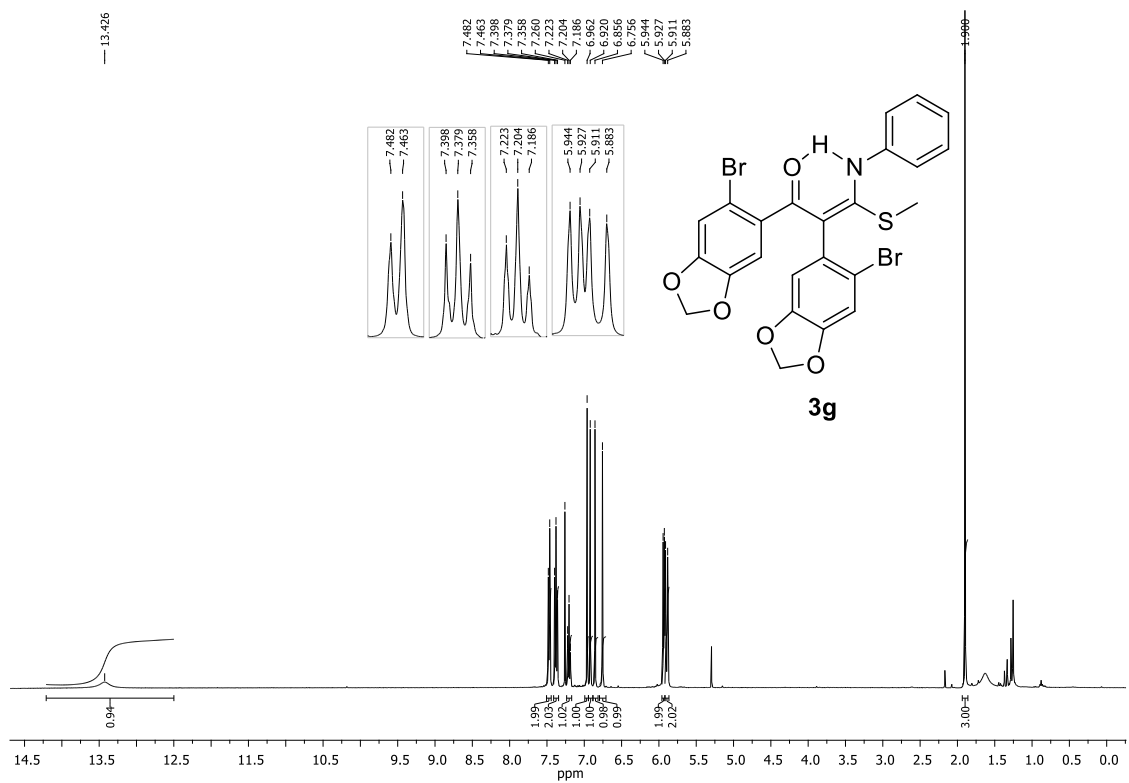




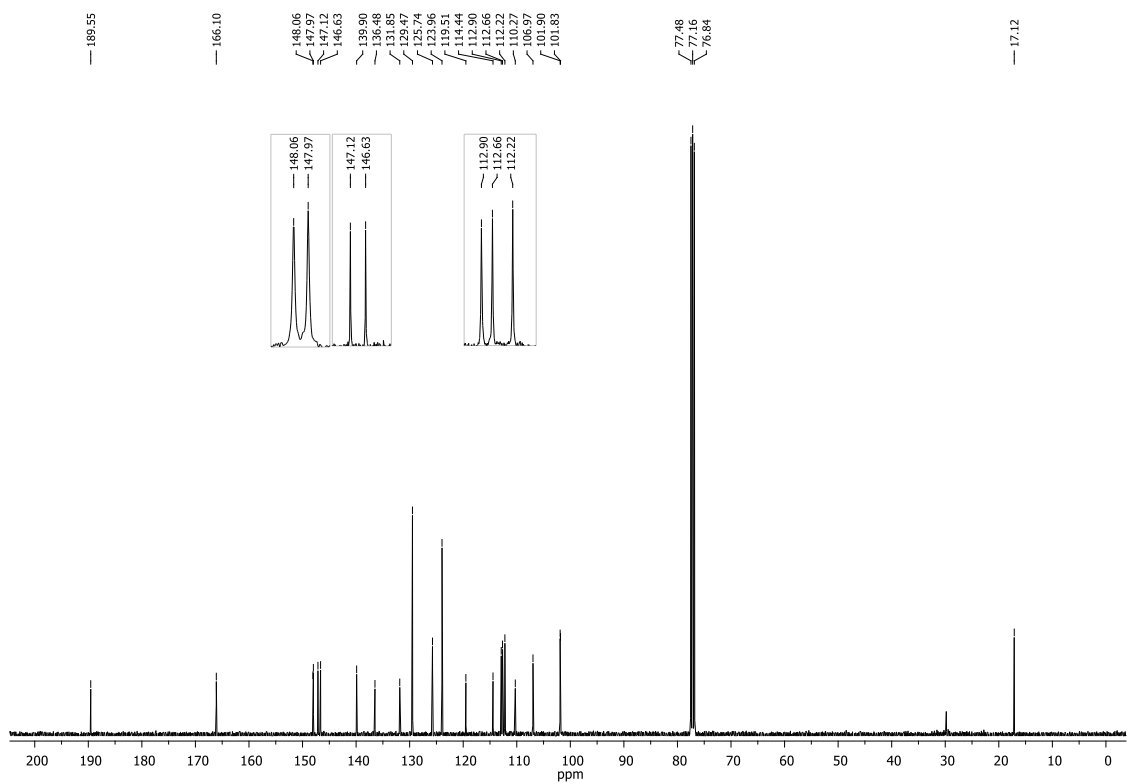
<sup>1</sup>H NMR Spectra of **3f**



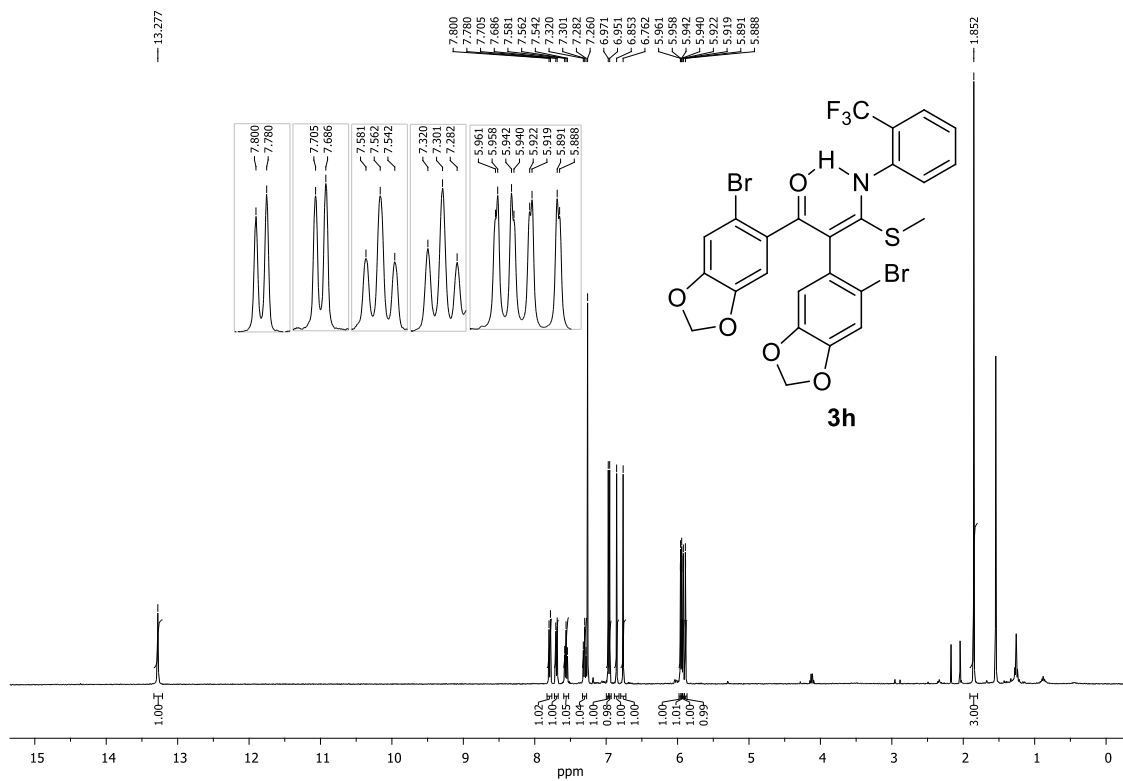
<sup>13</sup>C NMR Spectra of **3f**



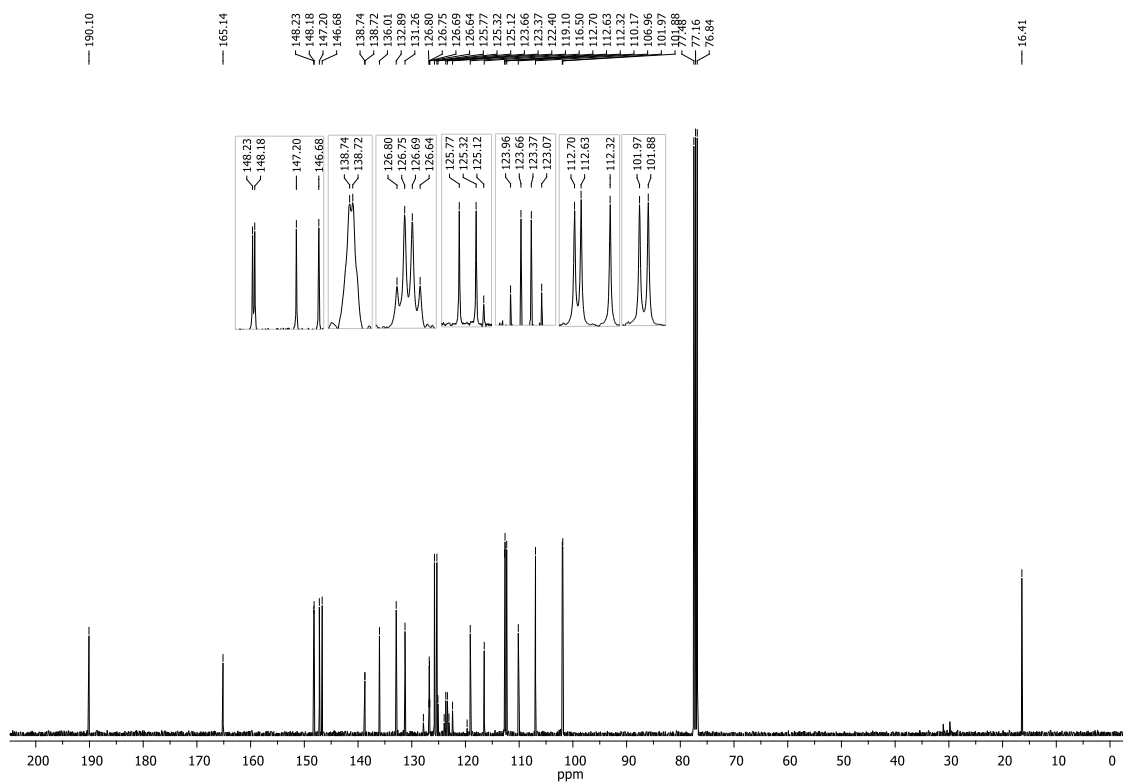
<sup>1</sup>H NMR Spectra of **3g**



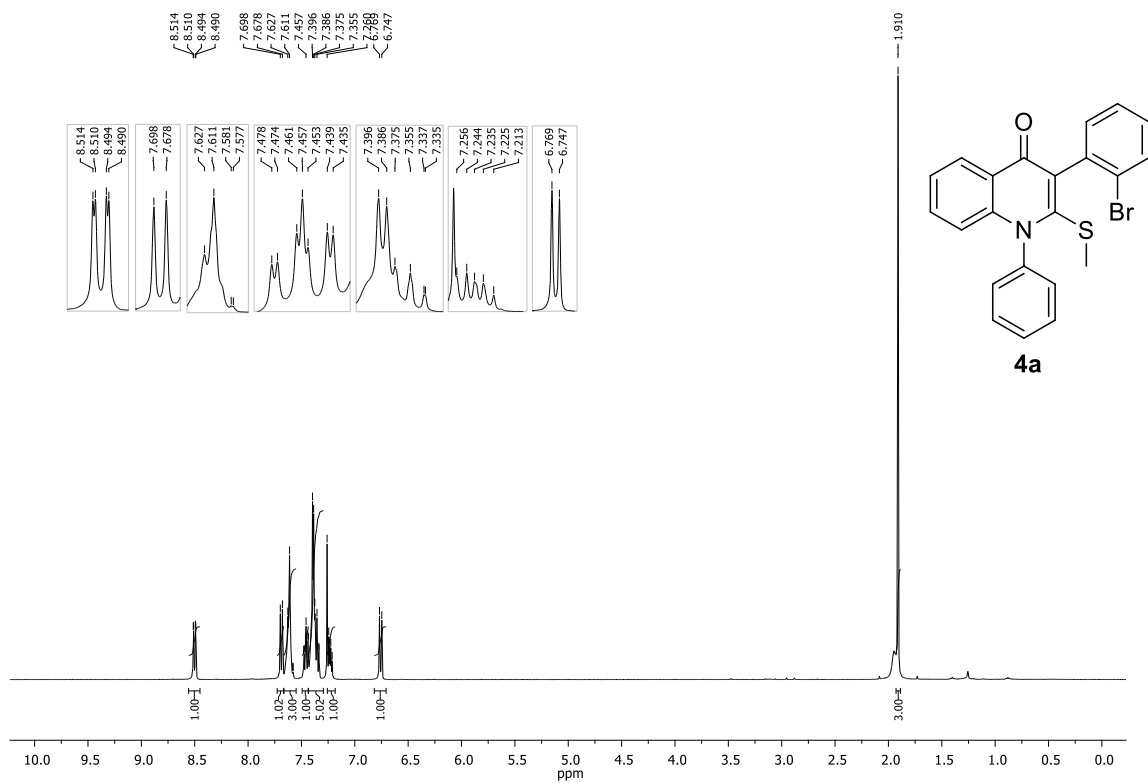
<sup>13</sup>C NMR Spectra of **3g**



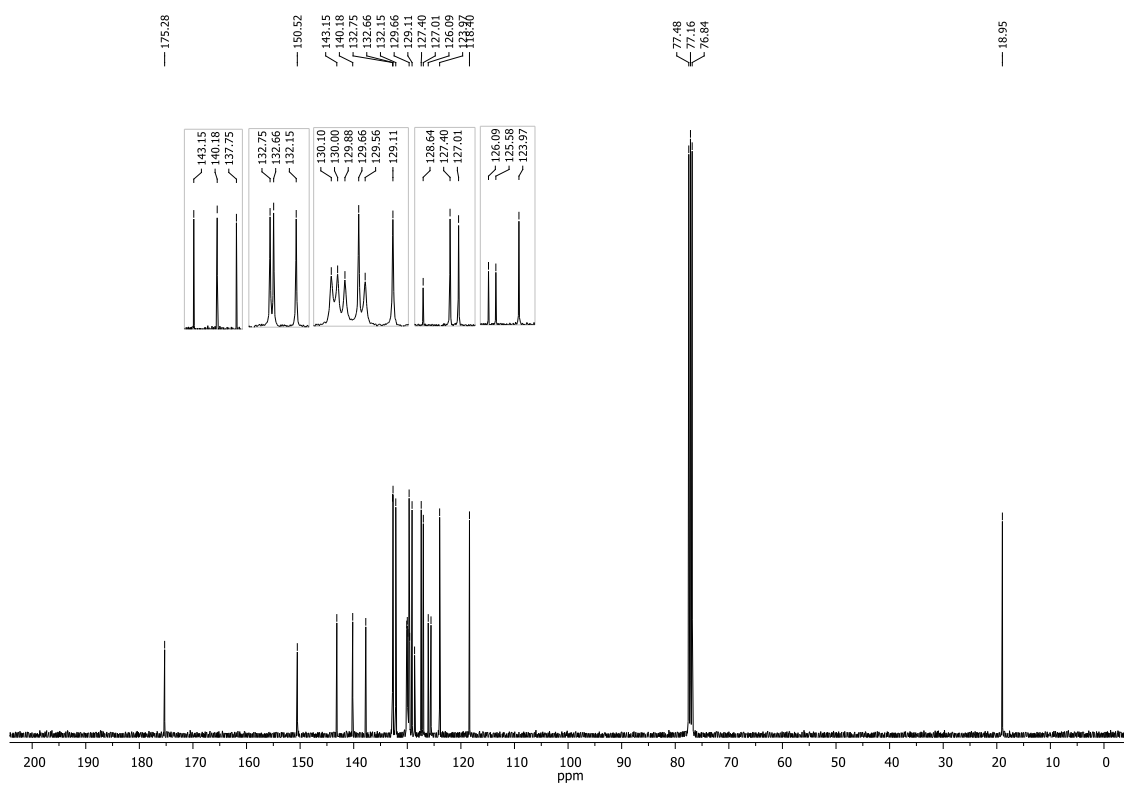
<sup>1</sup>H NMR Spectra of **3h**



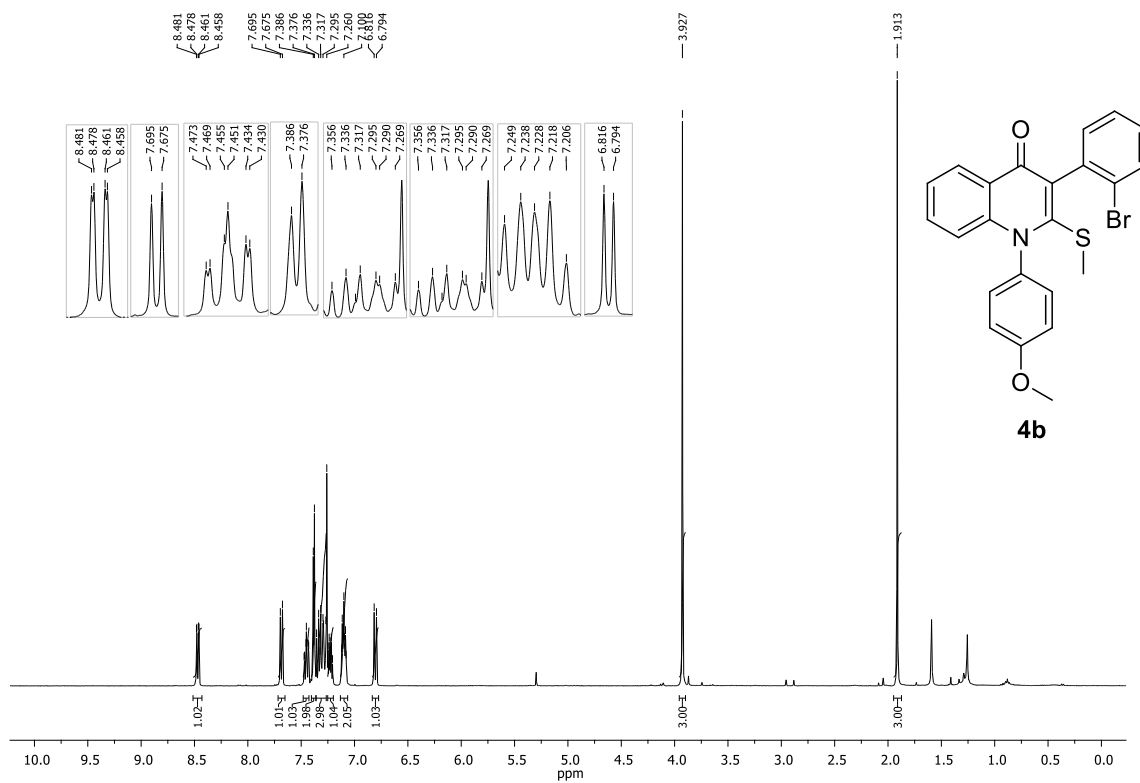
<sup>13</sup>C NMR Spectra of **3h**



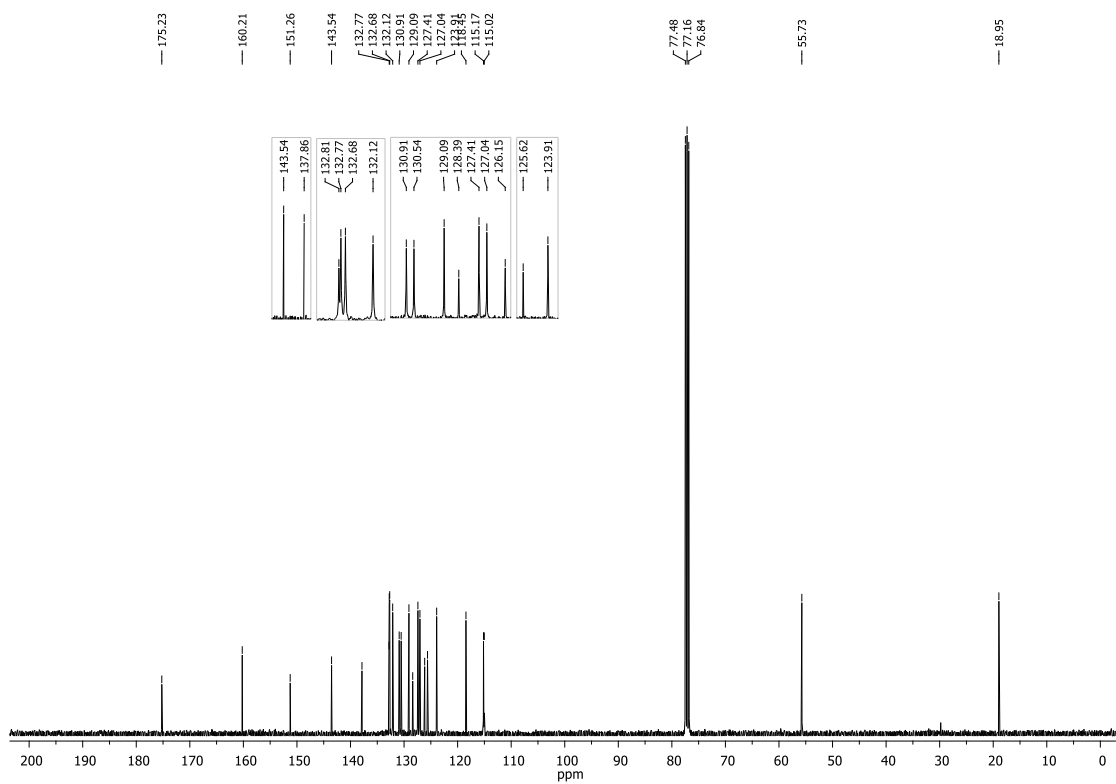
<sup>1</sup>H NMR Spectra of **4a**



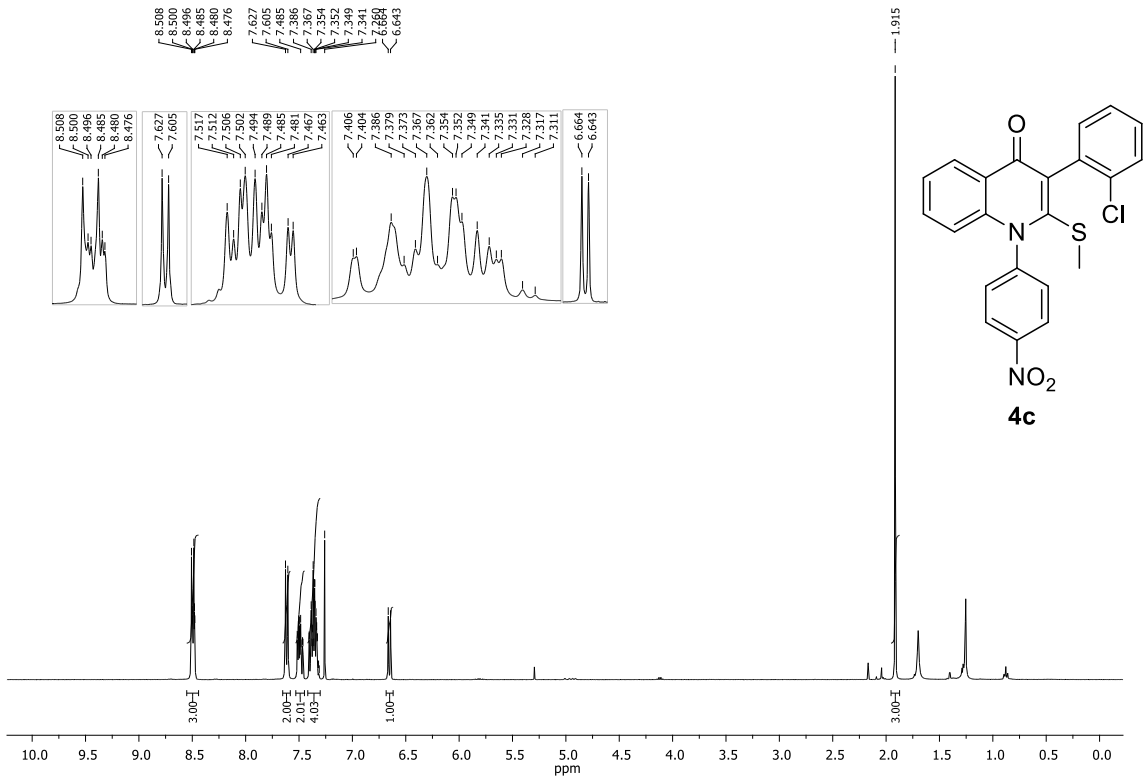
<sup>13</sup>C NMR Spectra of **4a**



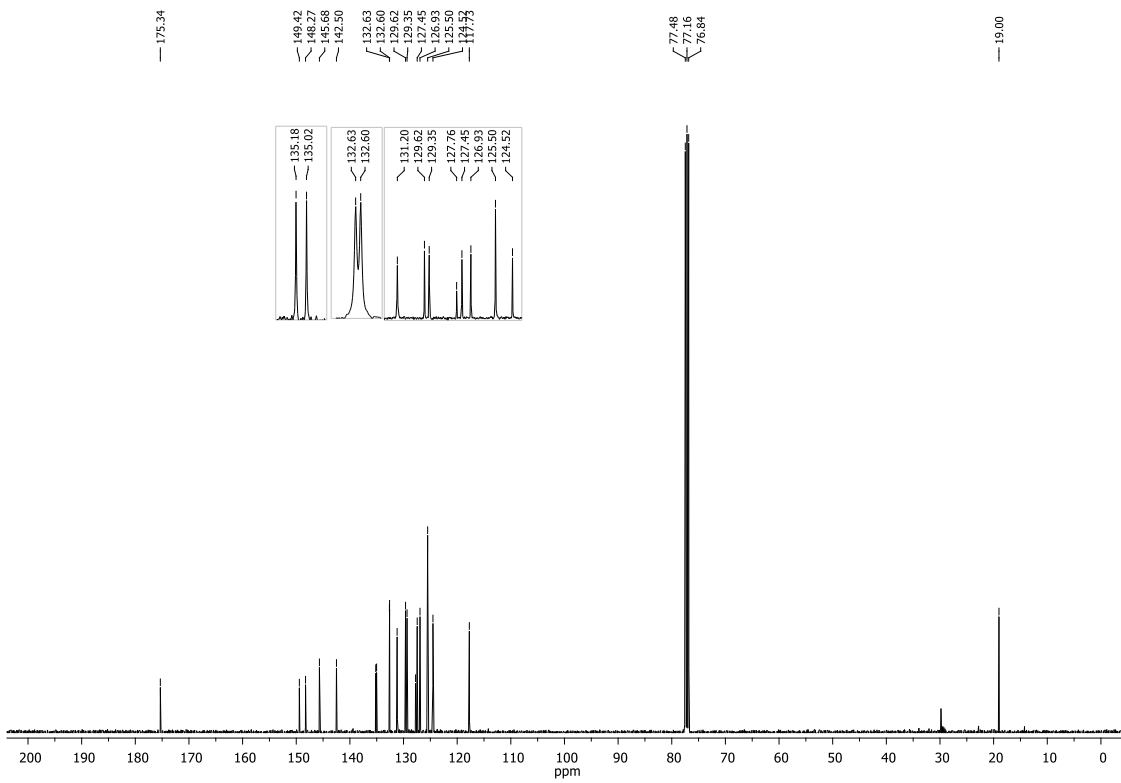
<sup>1</sup>H NMR Spectra of **4b**



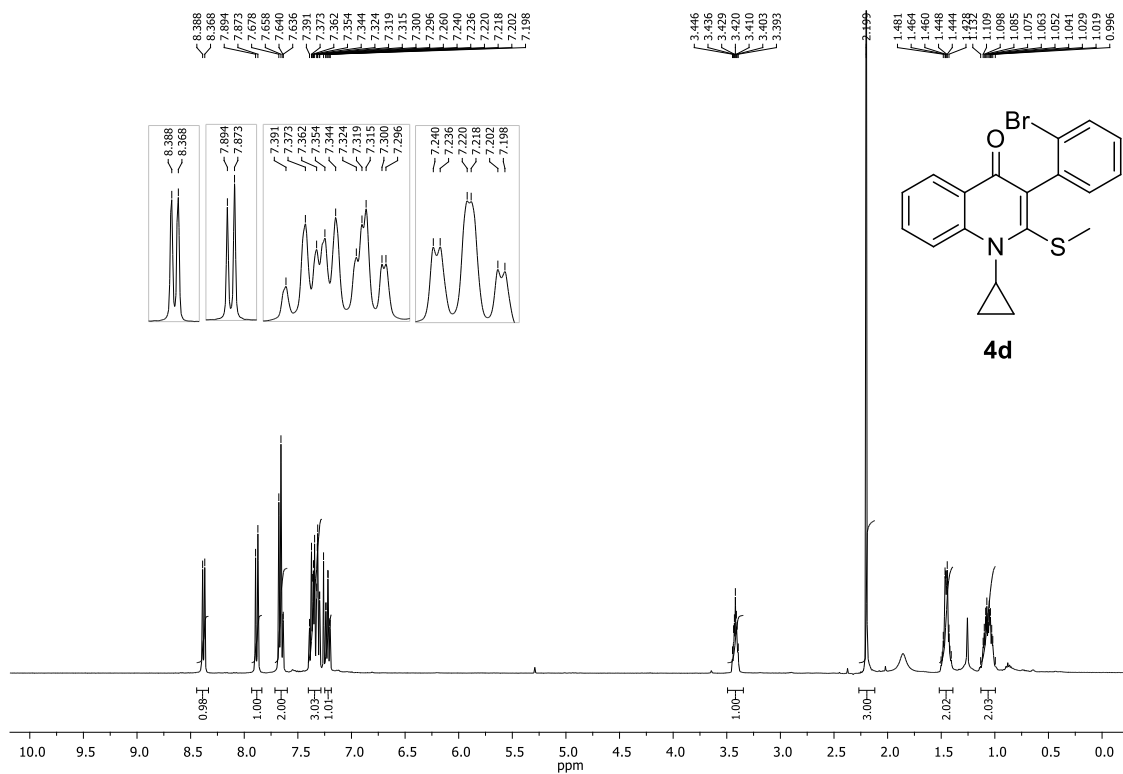
<sup>13</sup>C NMR Spectra of **4b**



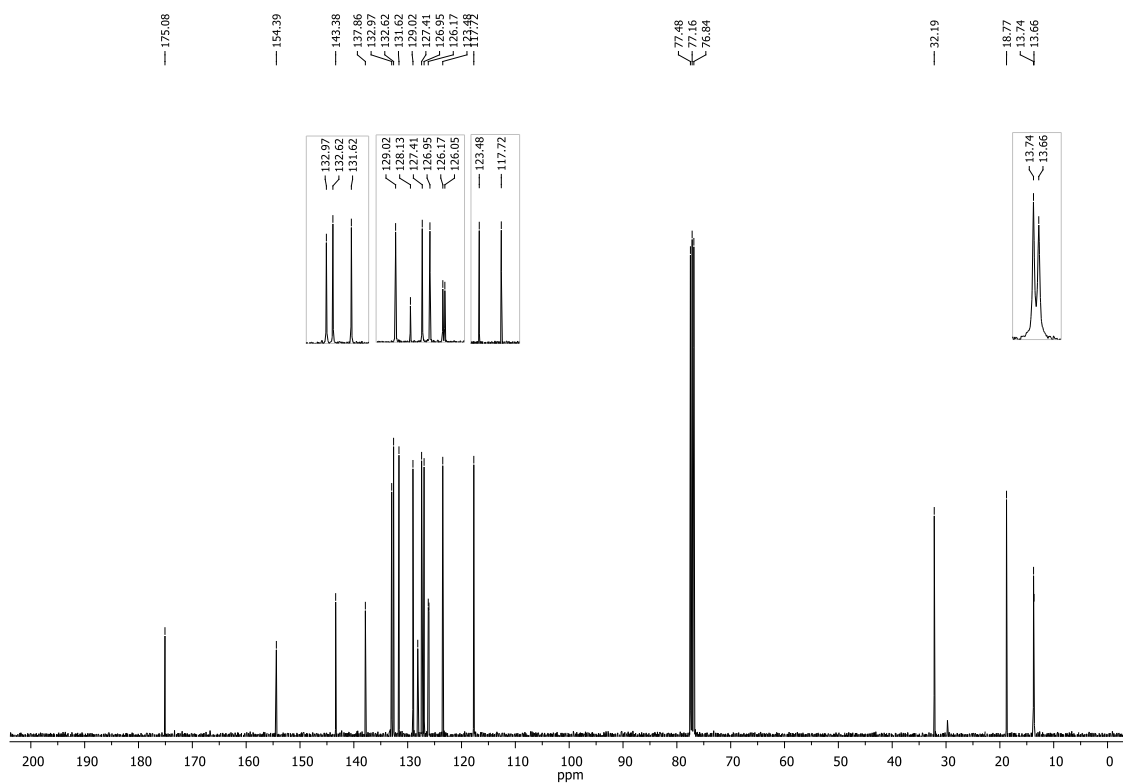
<sup>1</sup>H NMR Spectra of 4c



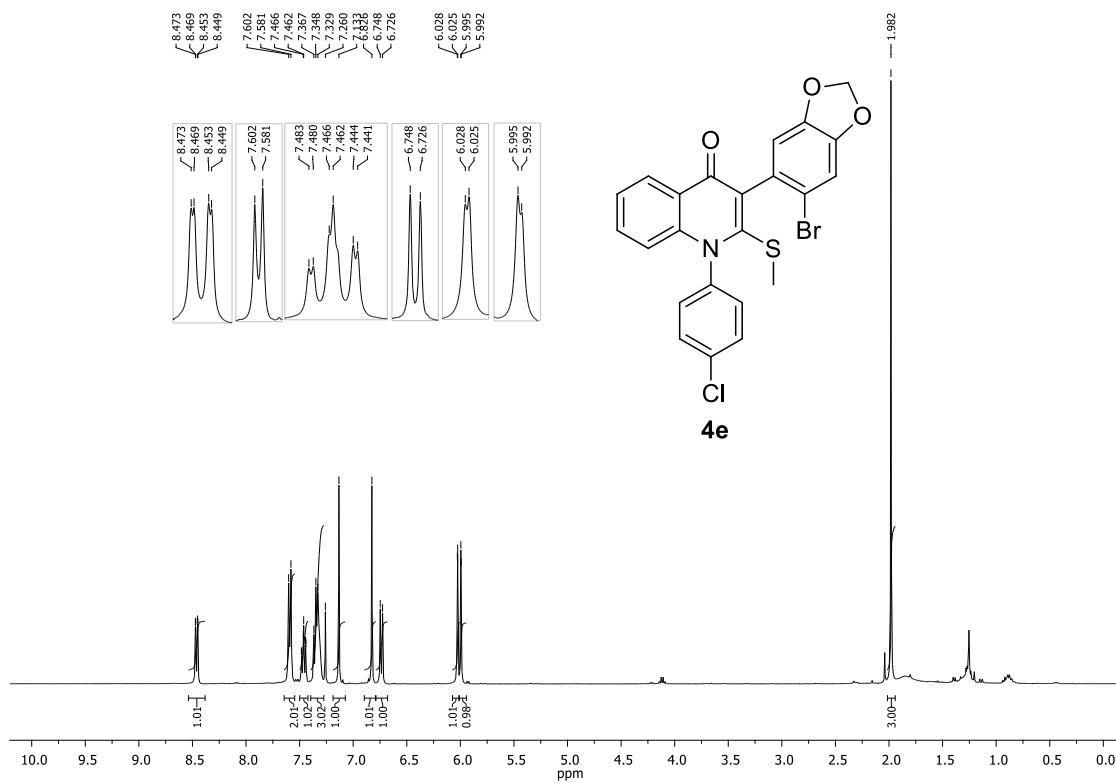
<sup>13</sup>C NMR Spectra of 4c



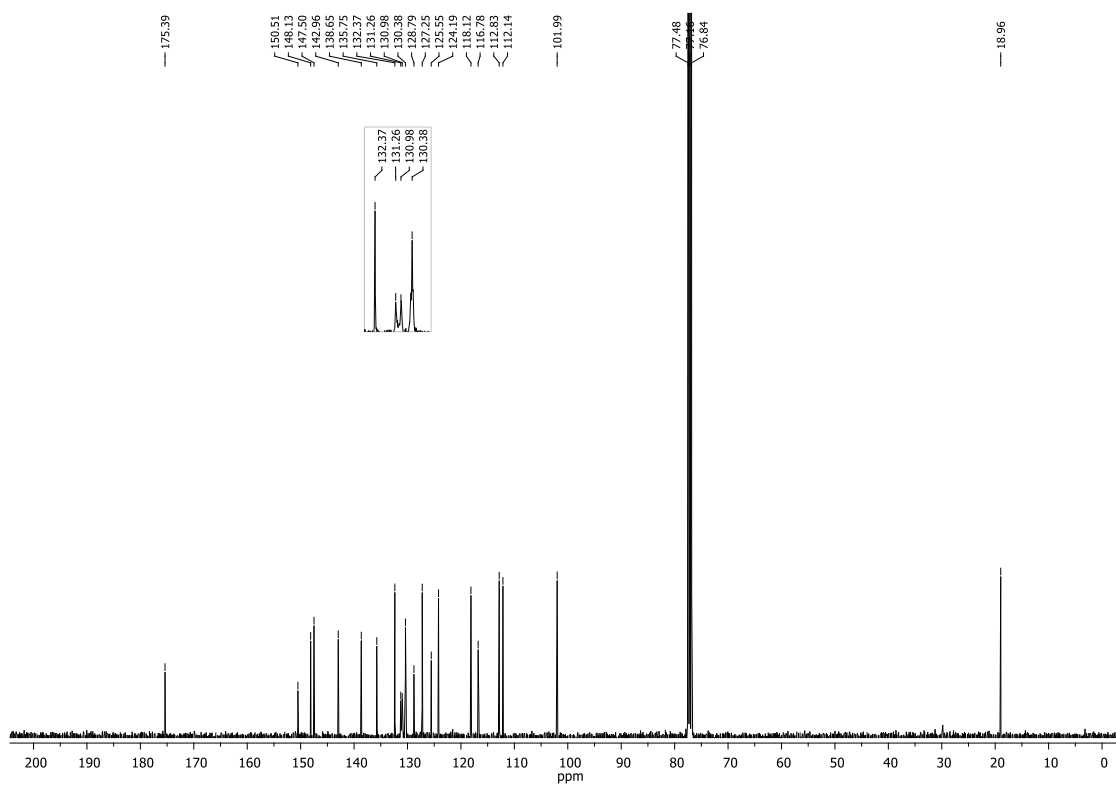
<sup>1</sup>H NMR Spectra of **4d**



<sup>13</sup>C NMR Spectra of **4d**

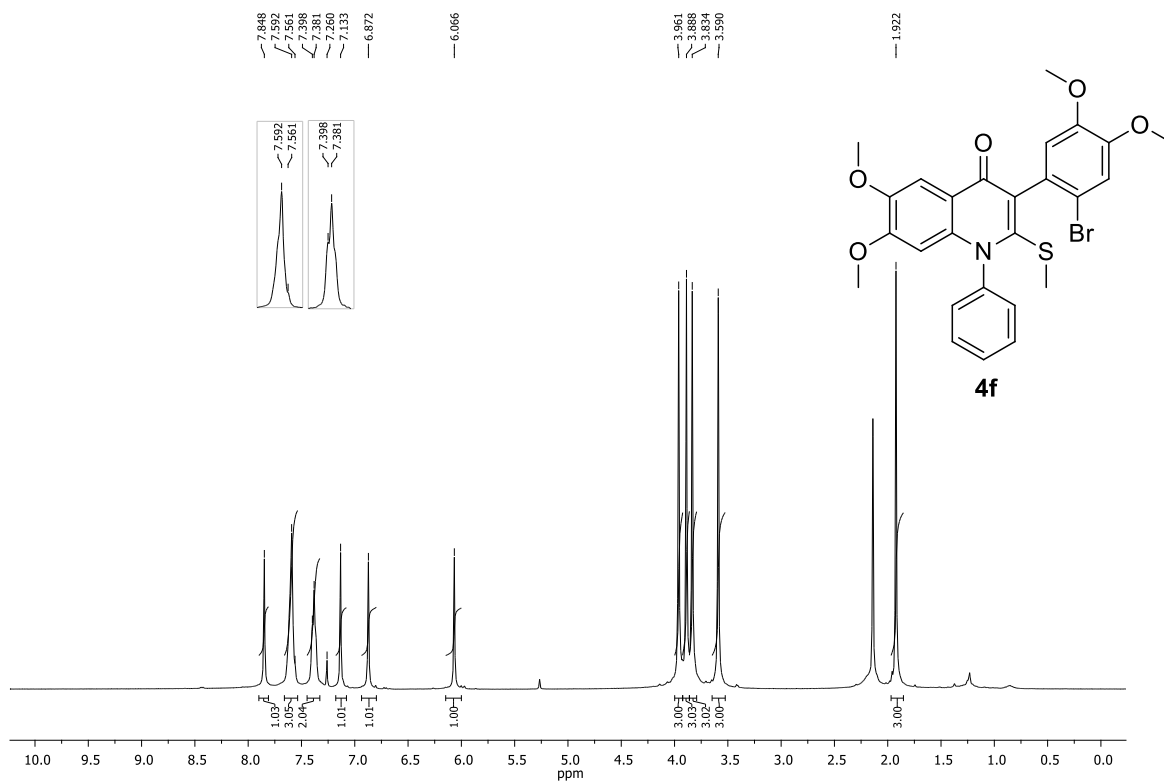


<sup>1</sup>H NMR Spectra of **4e**

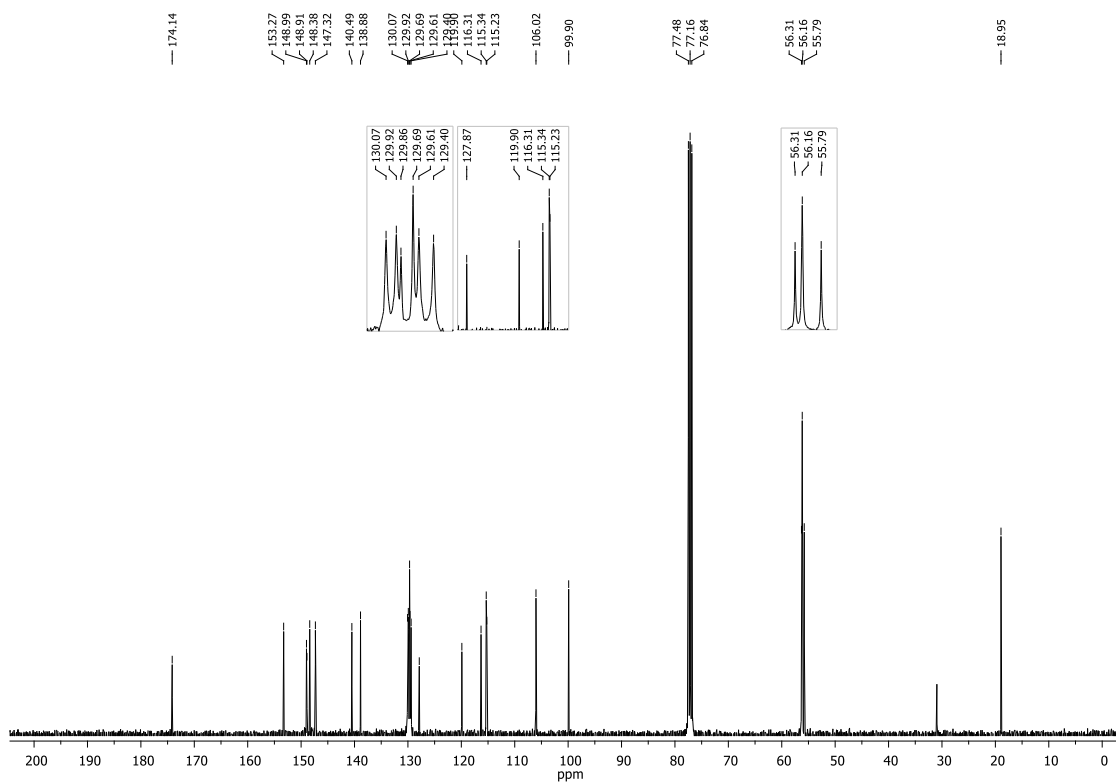


<sup>13</sup>C NMR Spectra of **4e**

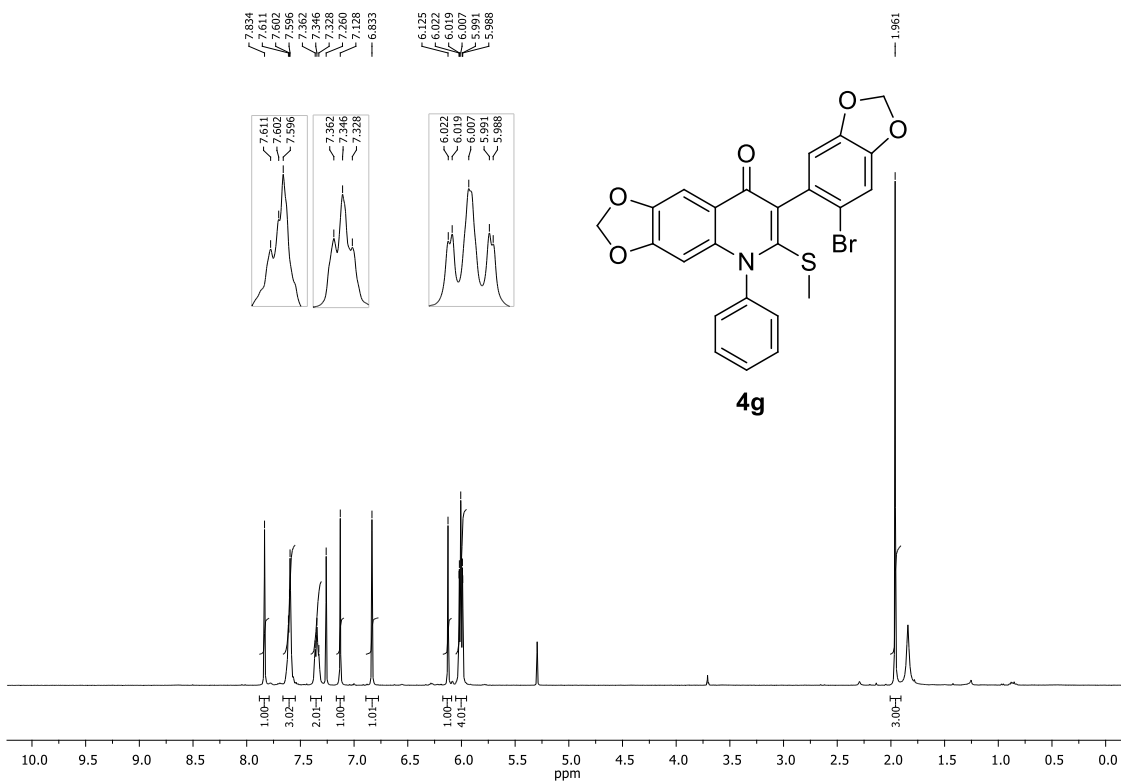




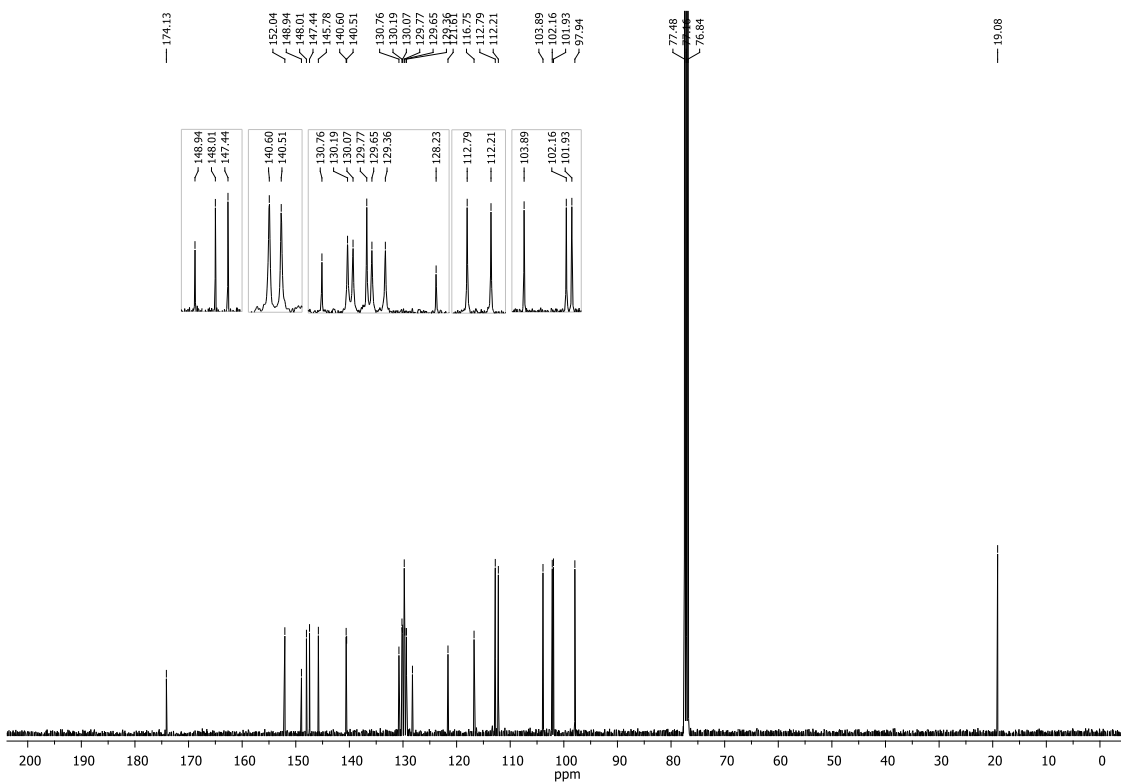
<sup>1</sup>H NMR Spectra of **4f**



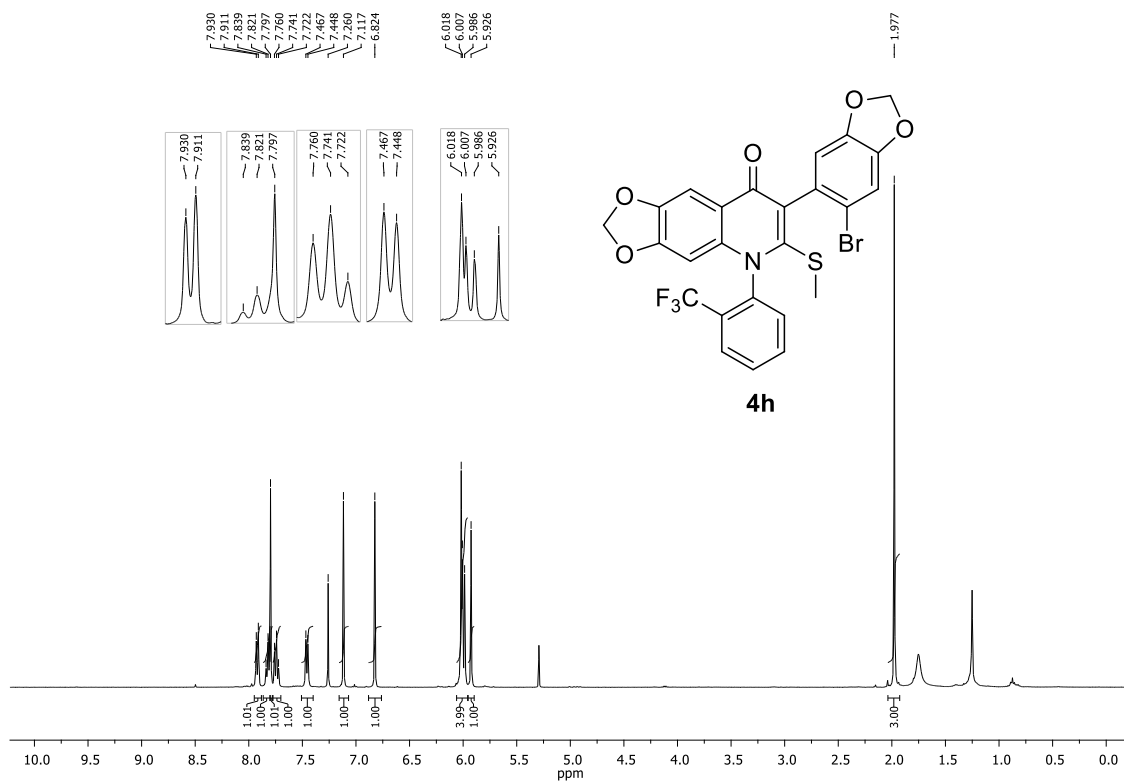
<sup>13</sup>C NMR Spectra of **4f**



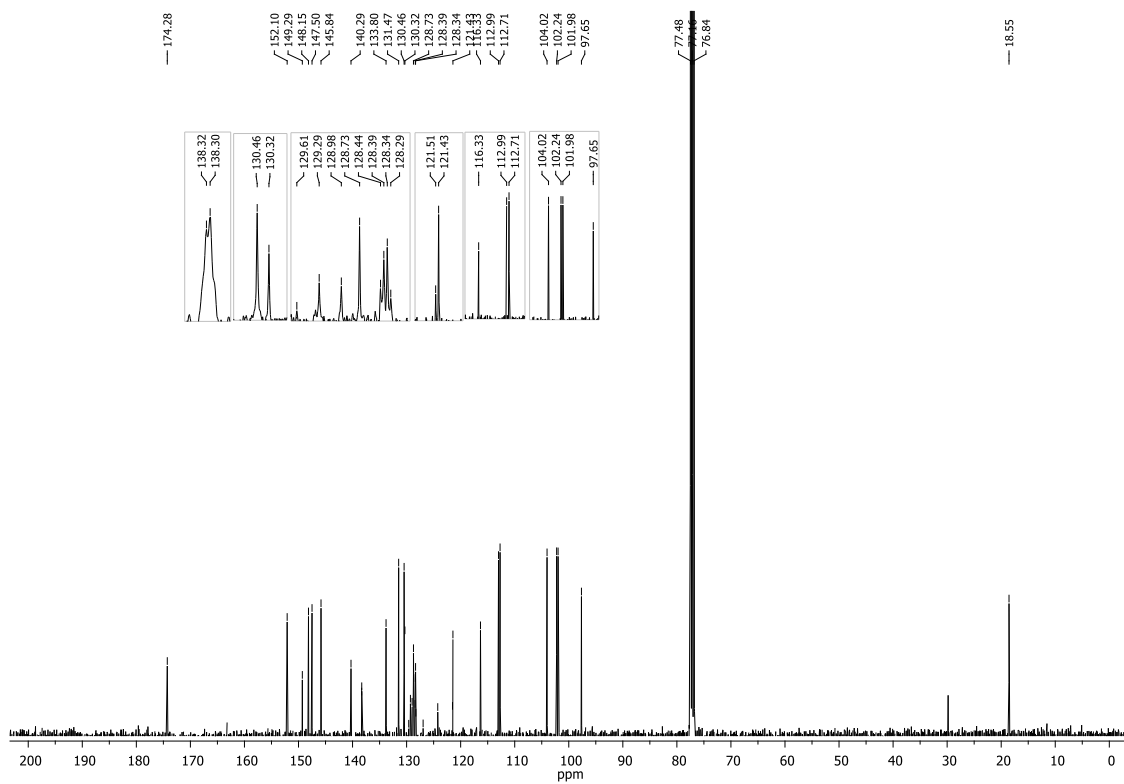
**<sup>1</sup>H NMR Spectra of 4g**



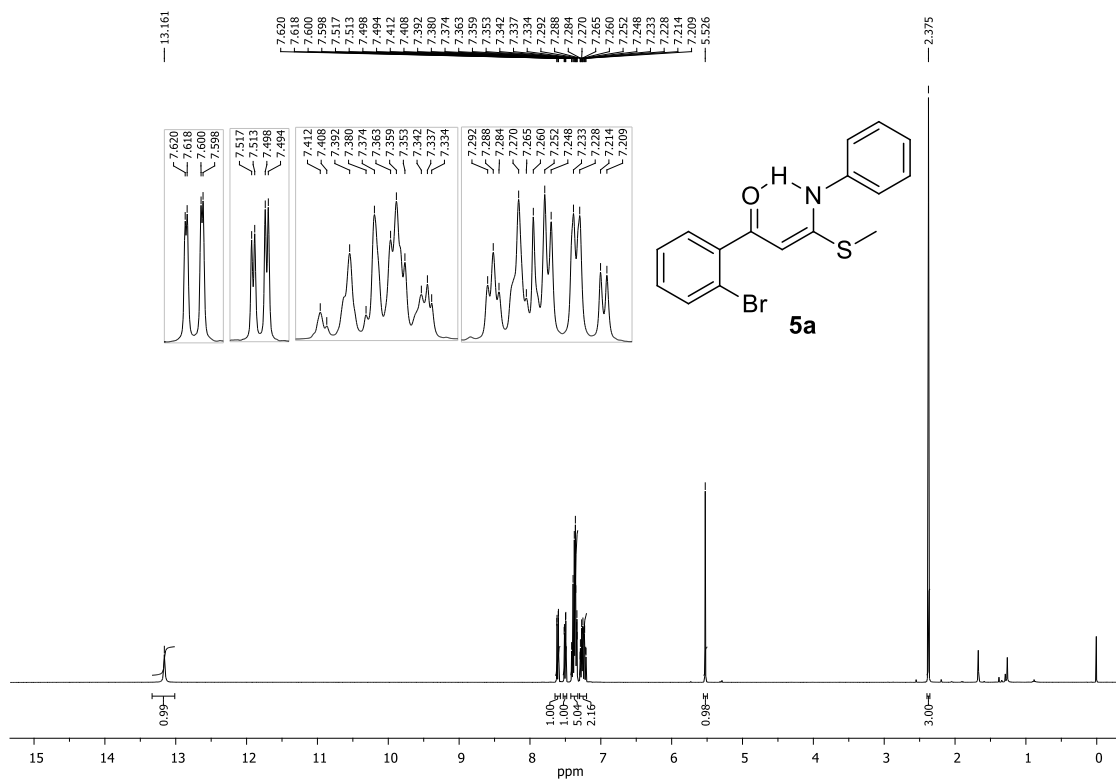
**<sup>13</sup>C NMR Spectra of 4g**



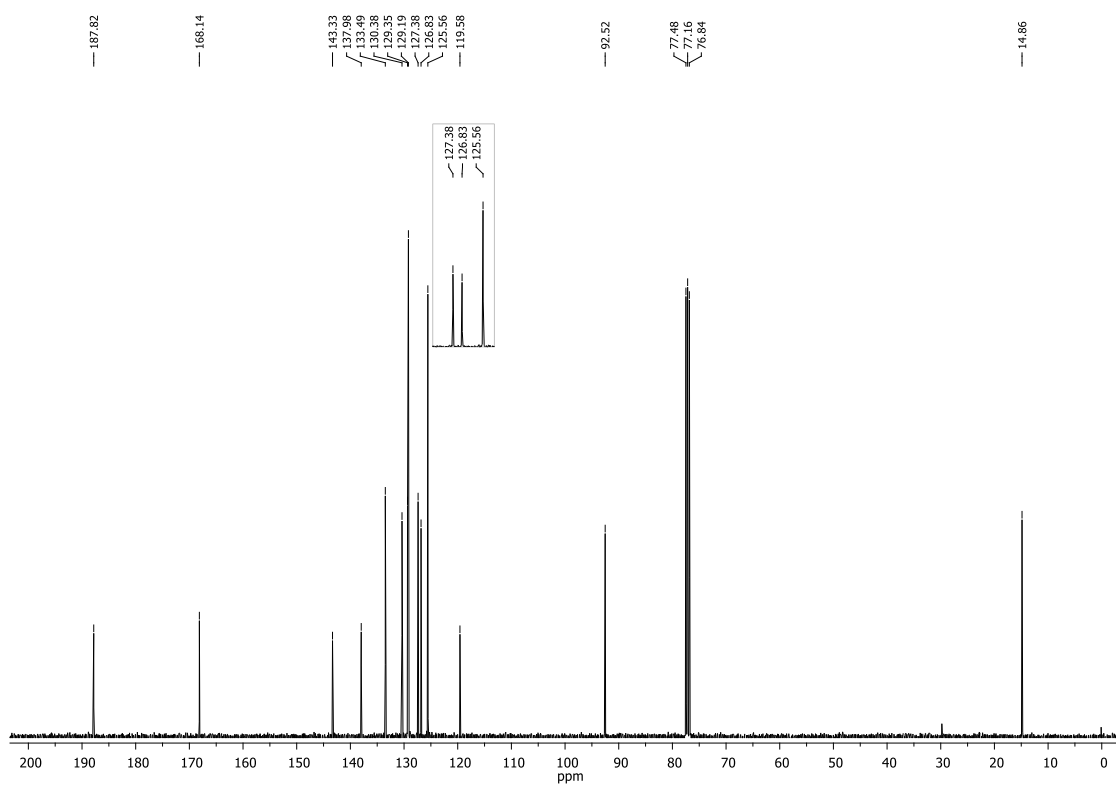
**<sup>1</sup>H NMR Spectra of 4h**



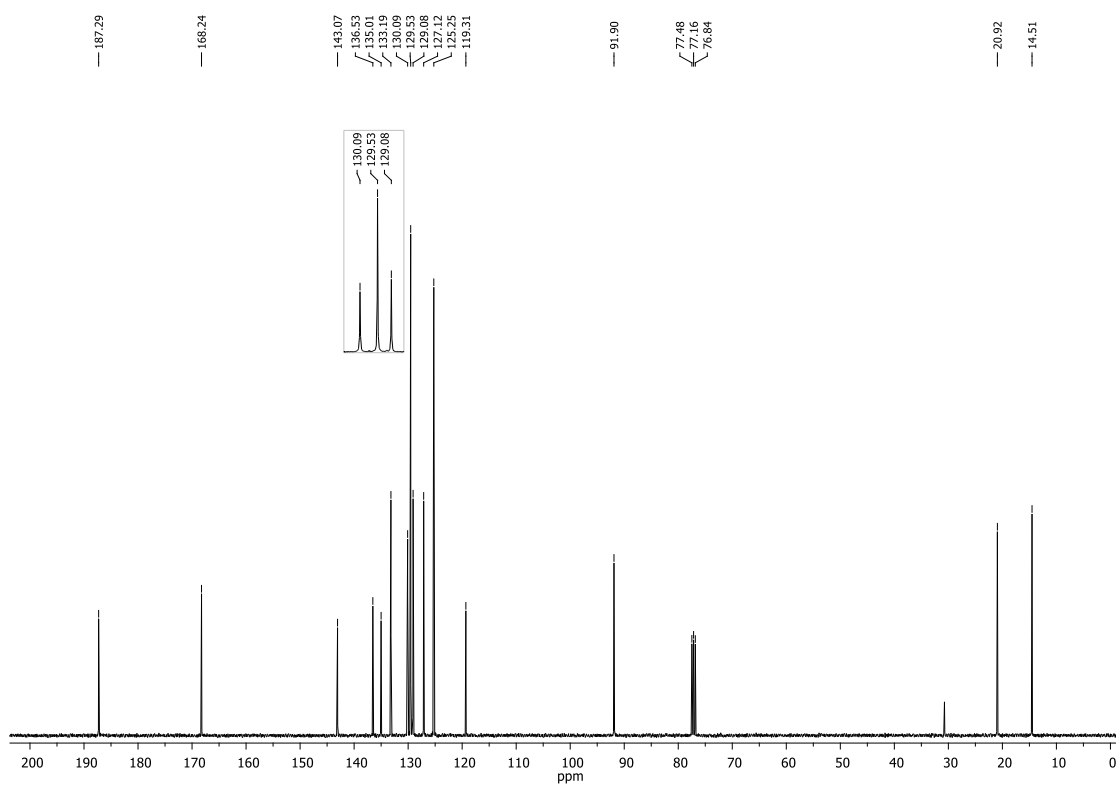
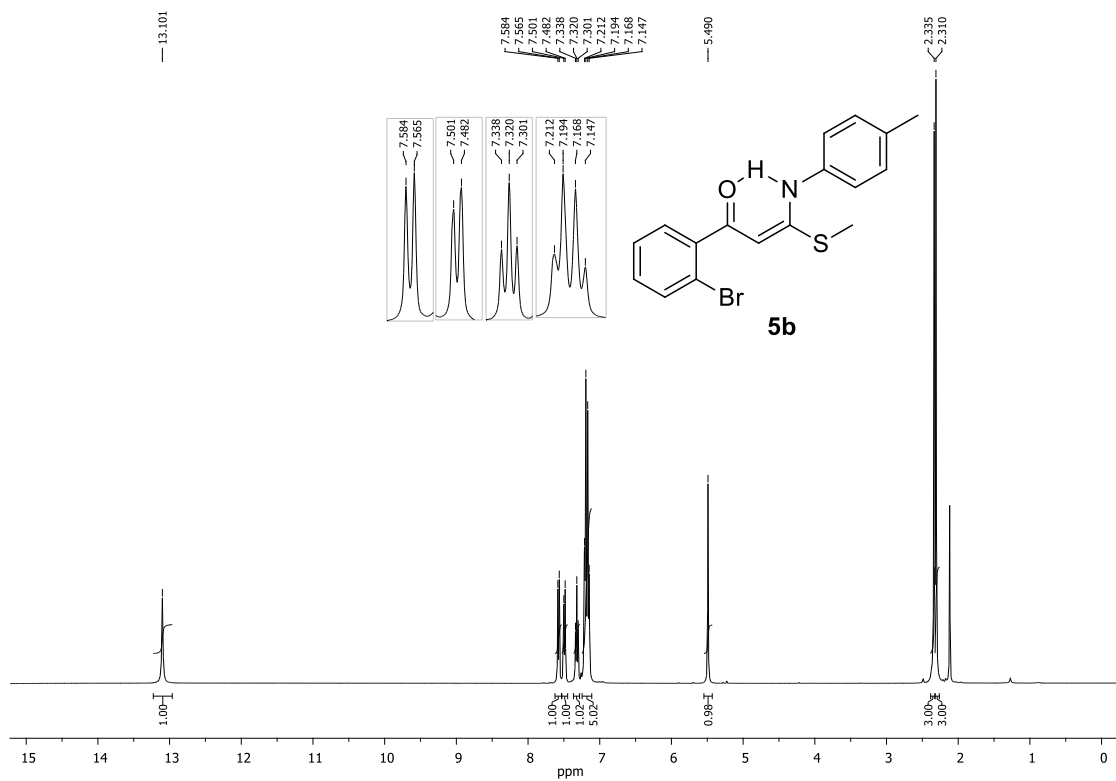
**<sup>13</sup>C NMR Spectra of 4h**

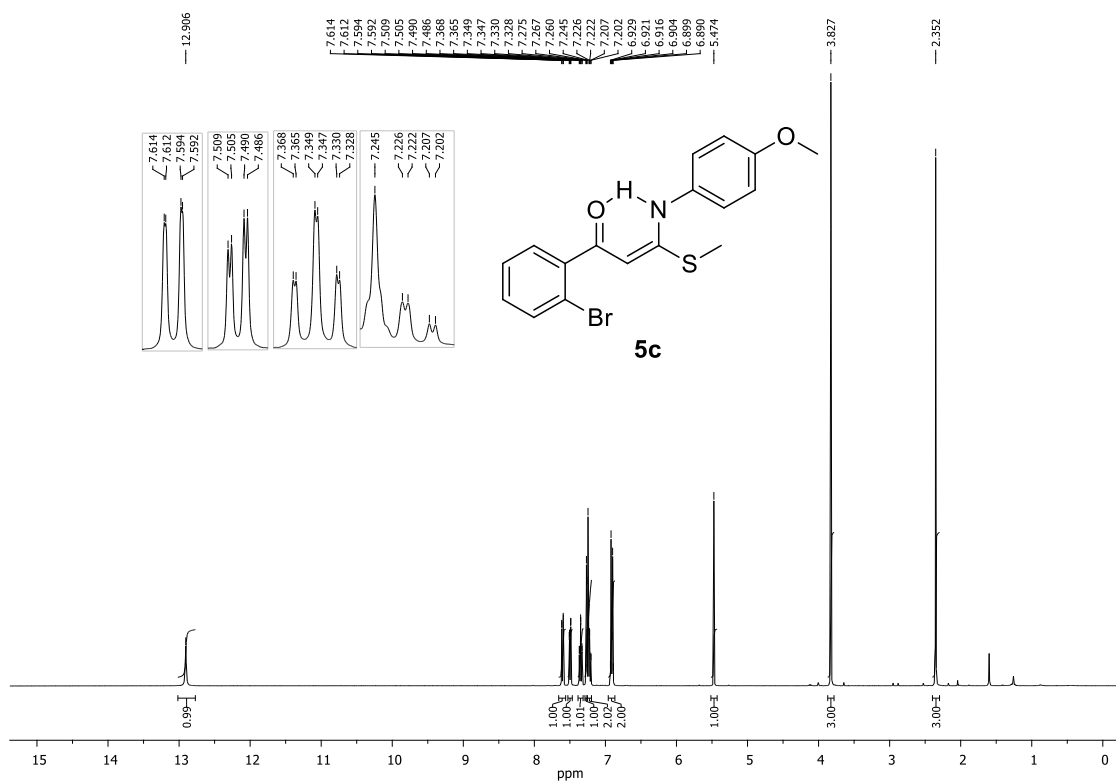


<sup>1</sup>H NMR Spectra of **5a**

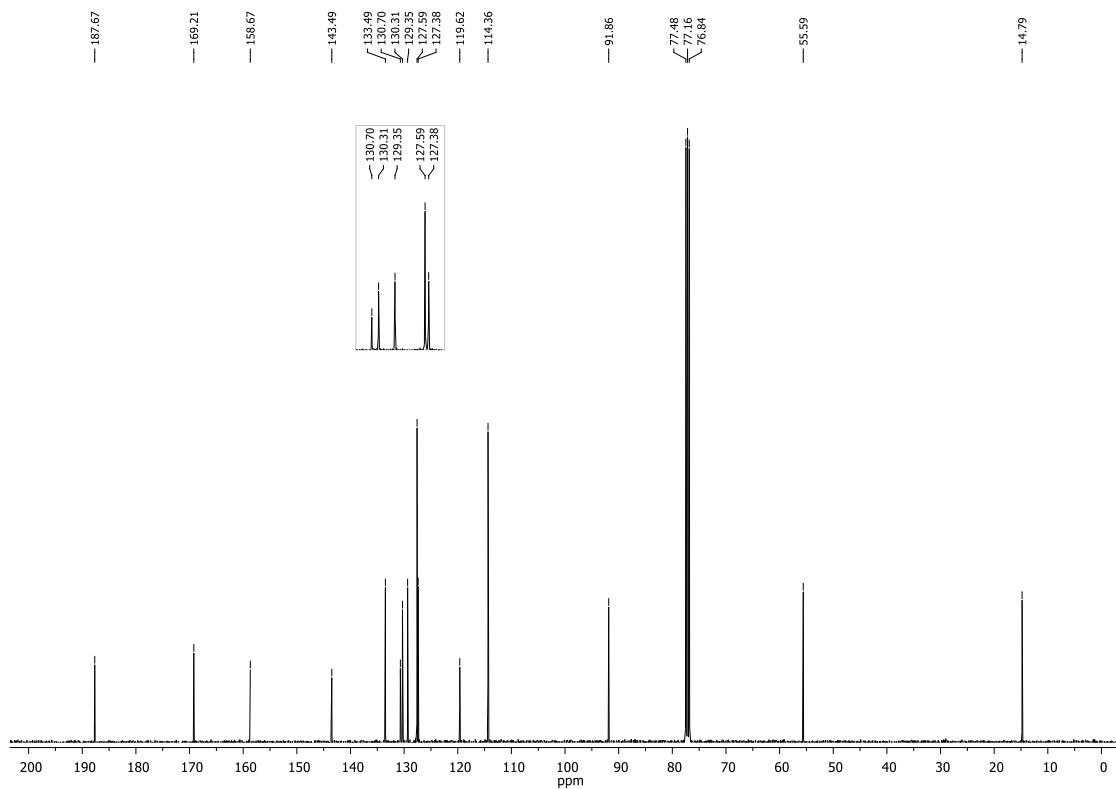


<sup>13</sup>C NMR Spectra of **5a**

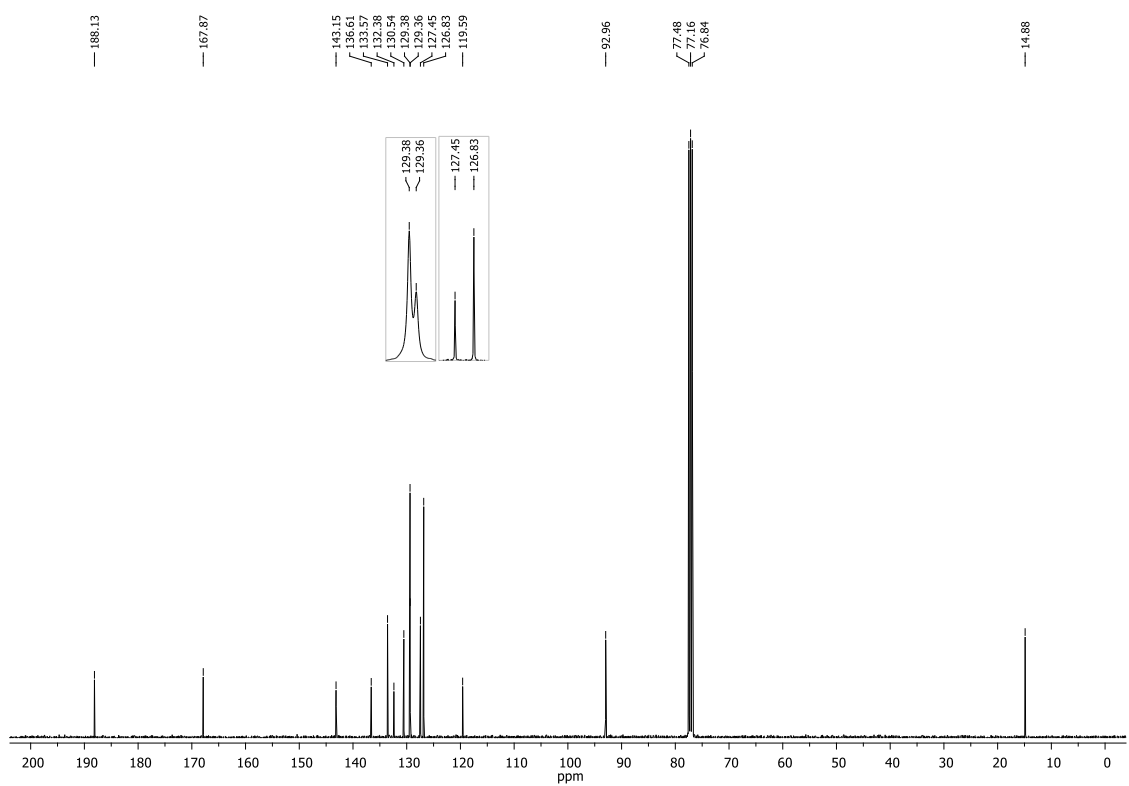
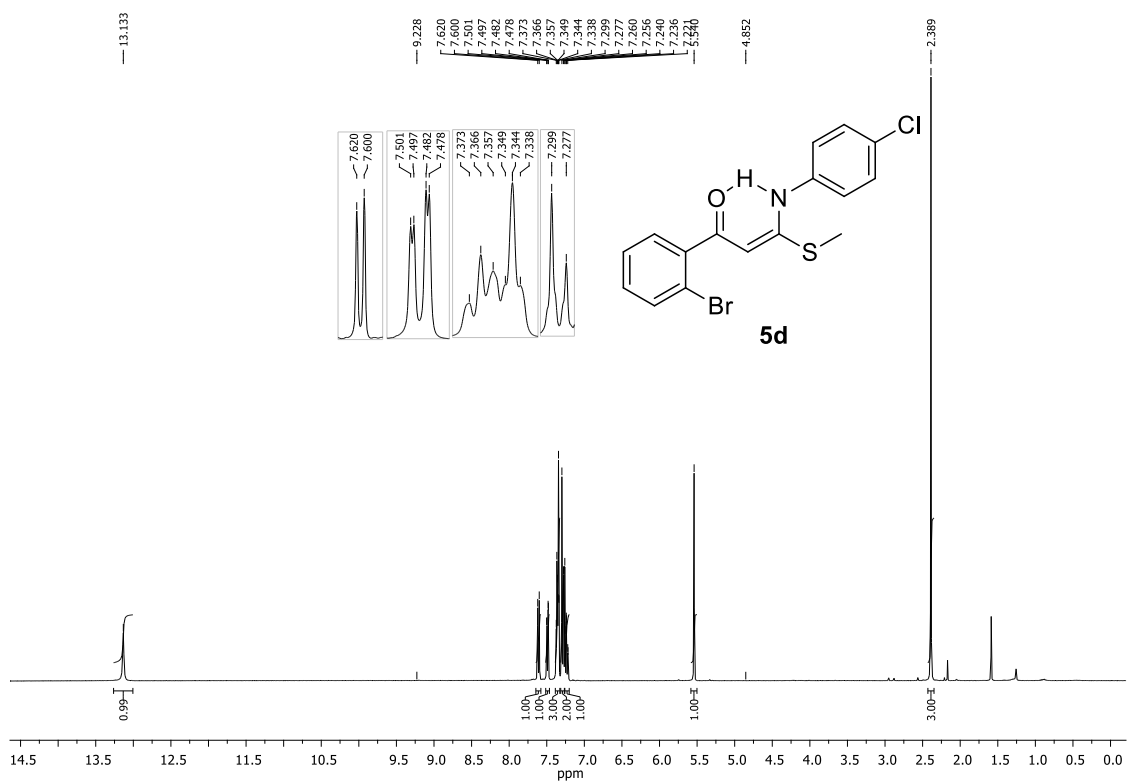


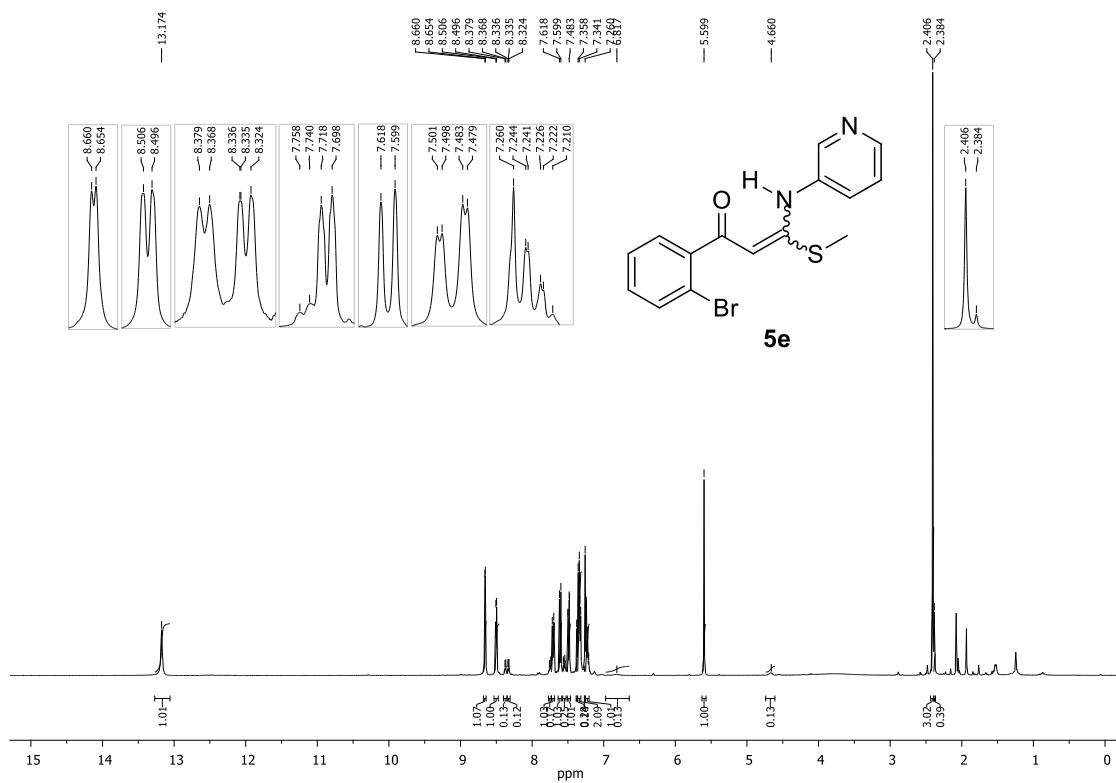


<sup>1</sup>H NMR Spectra of **5c**

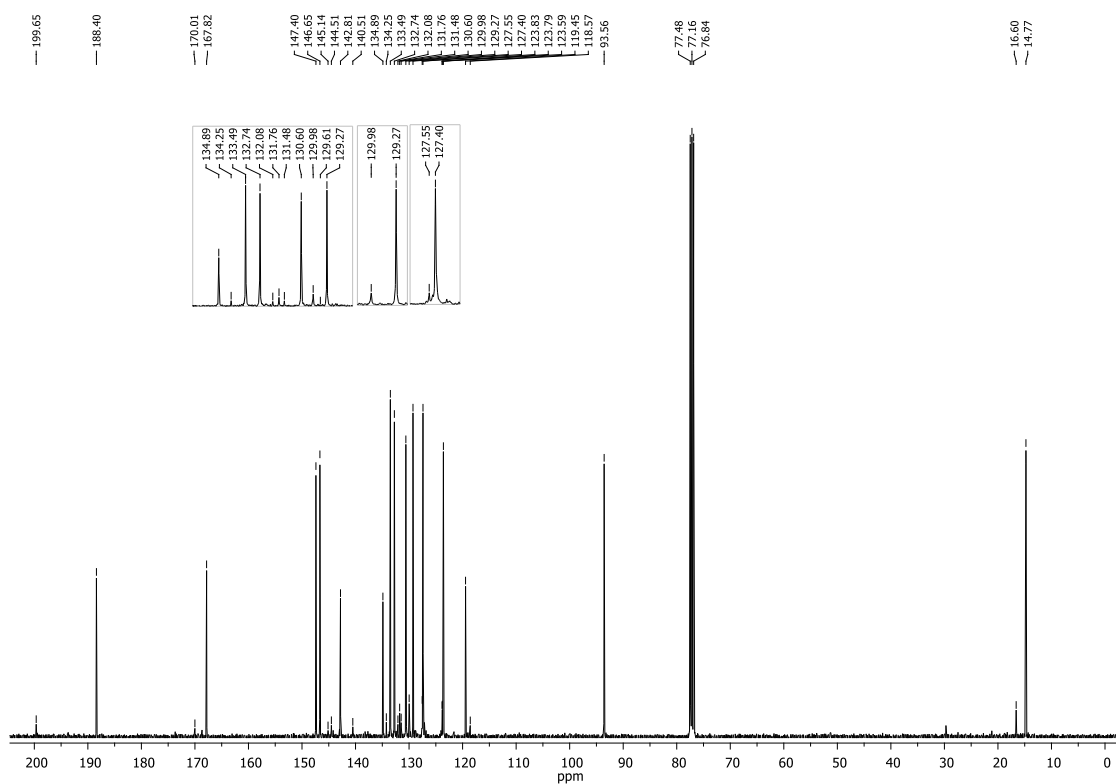


<sup>13</sup>C NMR Spectra of **5c**



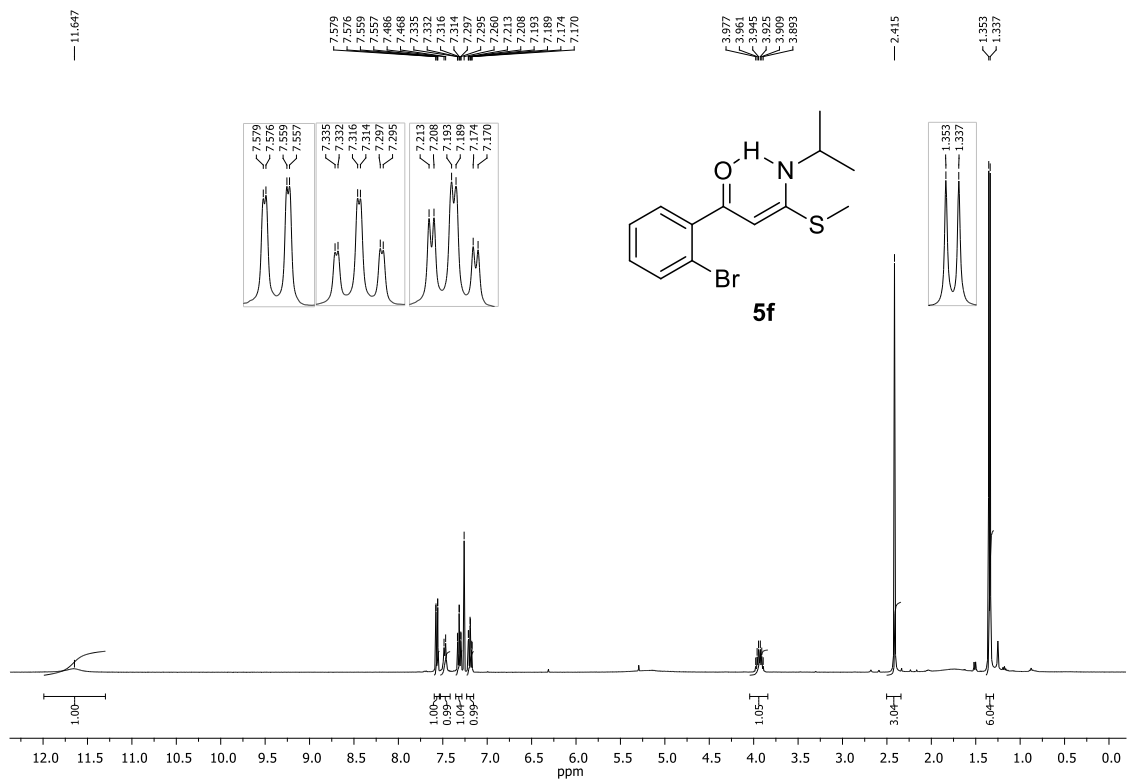


<sup>1</sup>H NMR Spectra of 5e

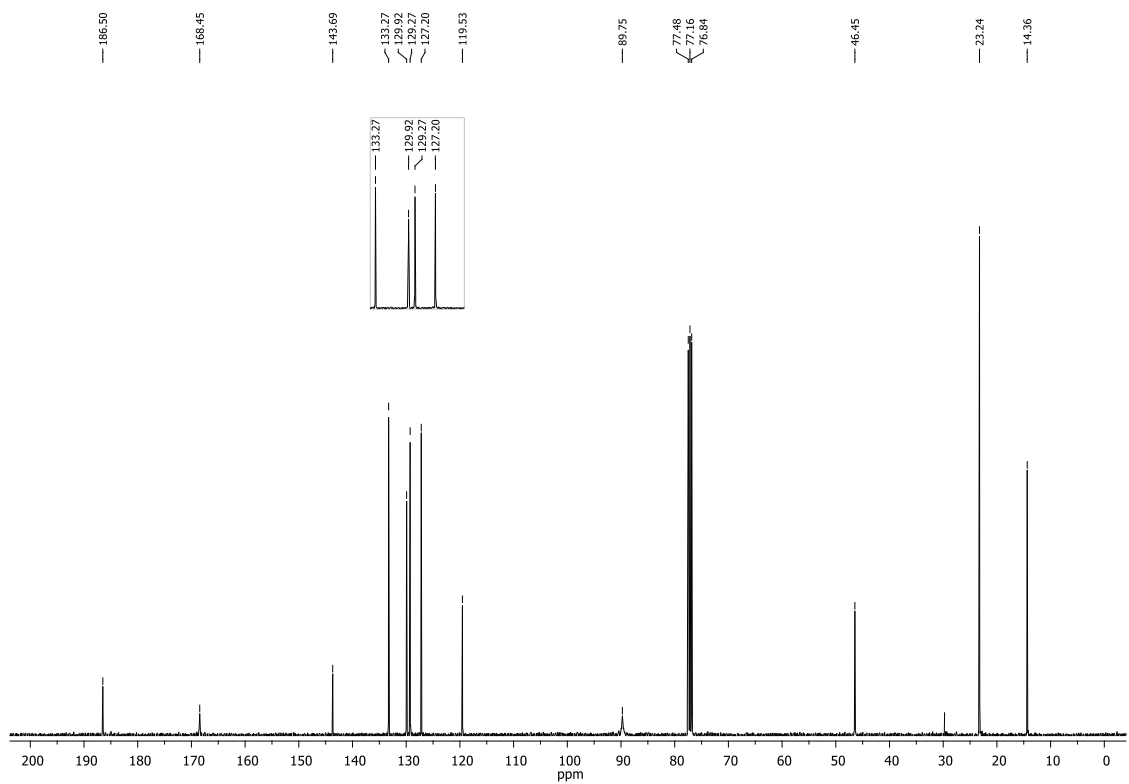


<sup>13</sup>C NMR Spectra of 5e

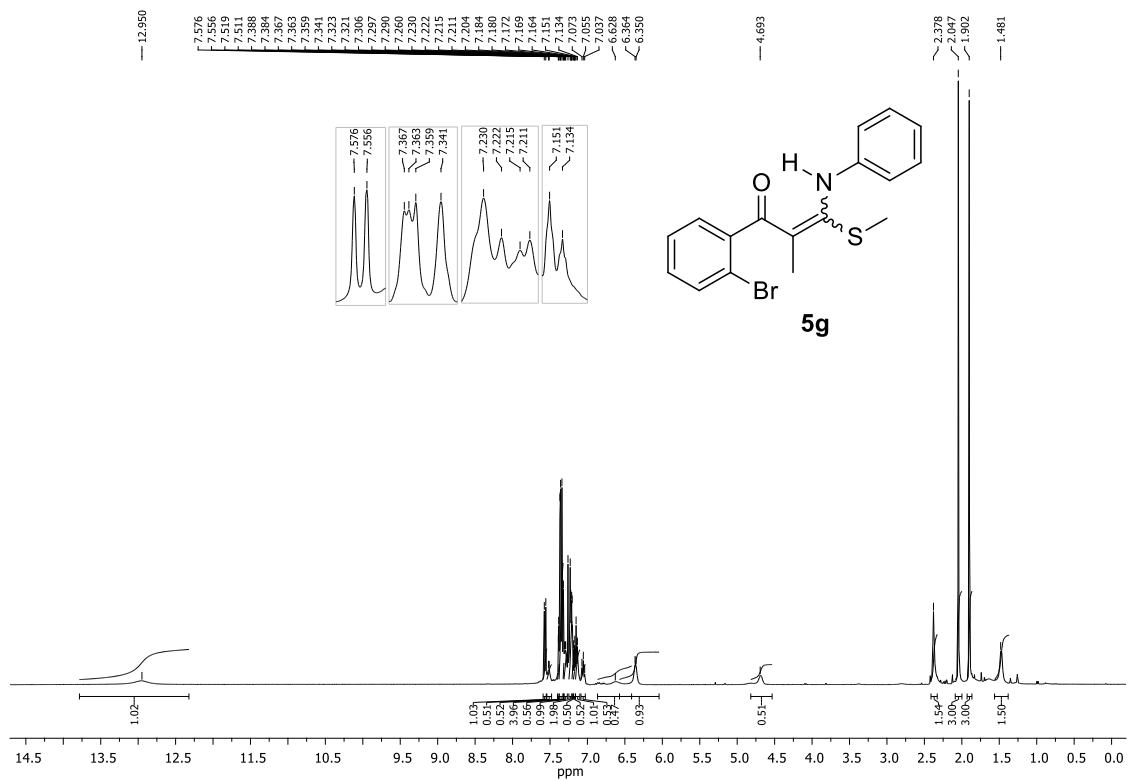




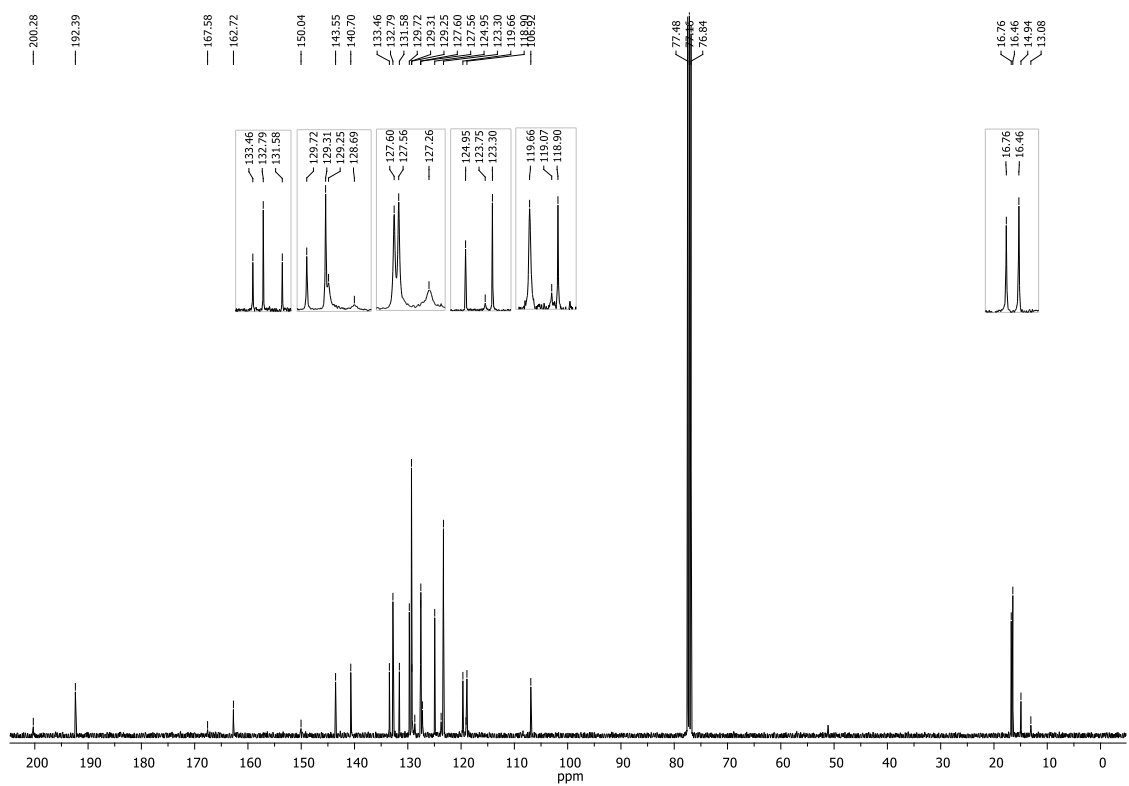
<sup>1</sup>H NMR Spectra of **5f**



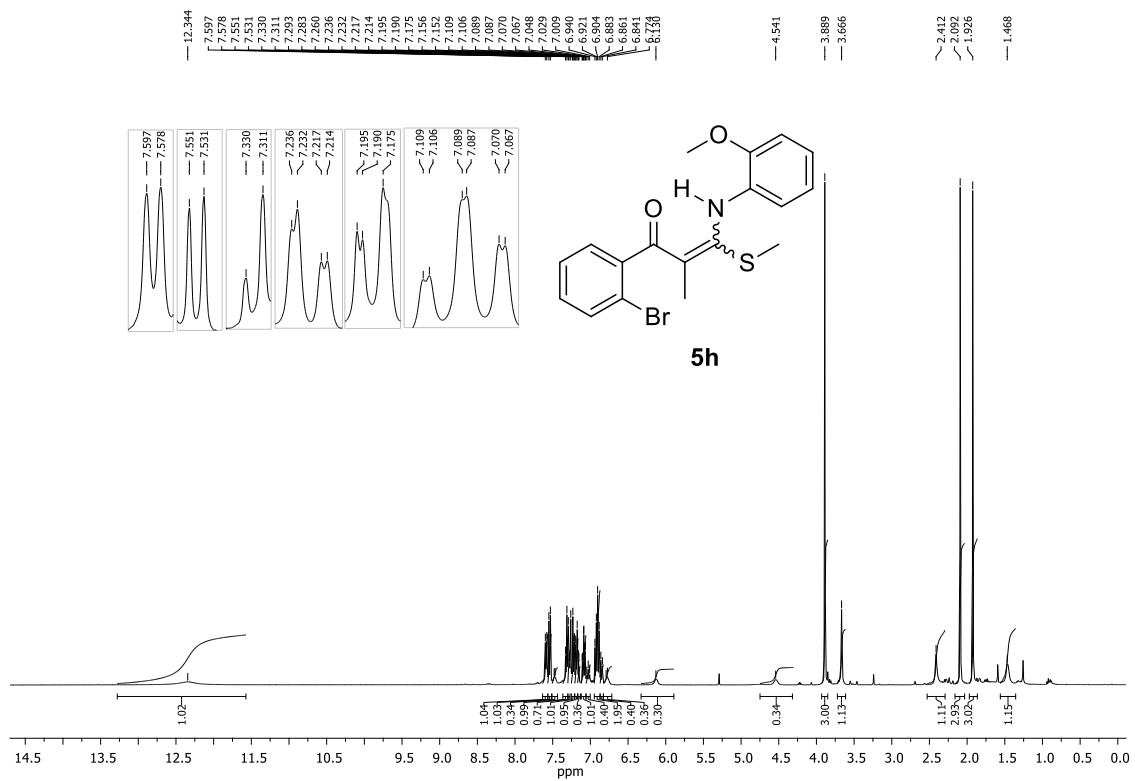
<sup>13</sup>C NMR Spectra of **5f**



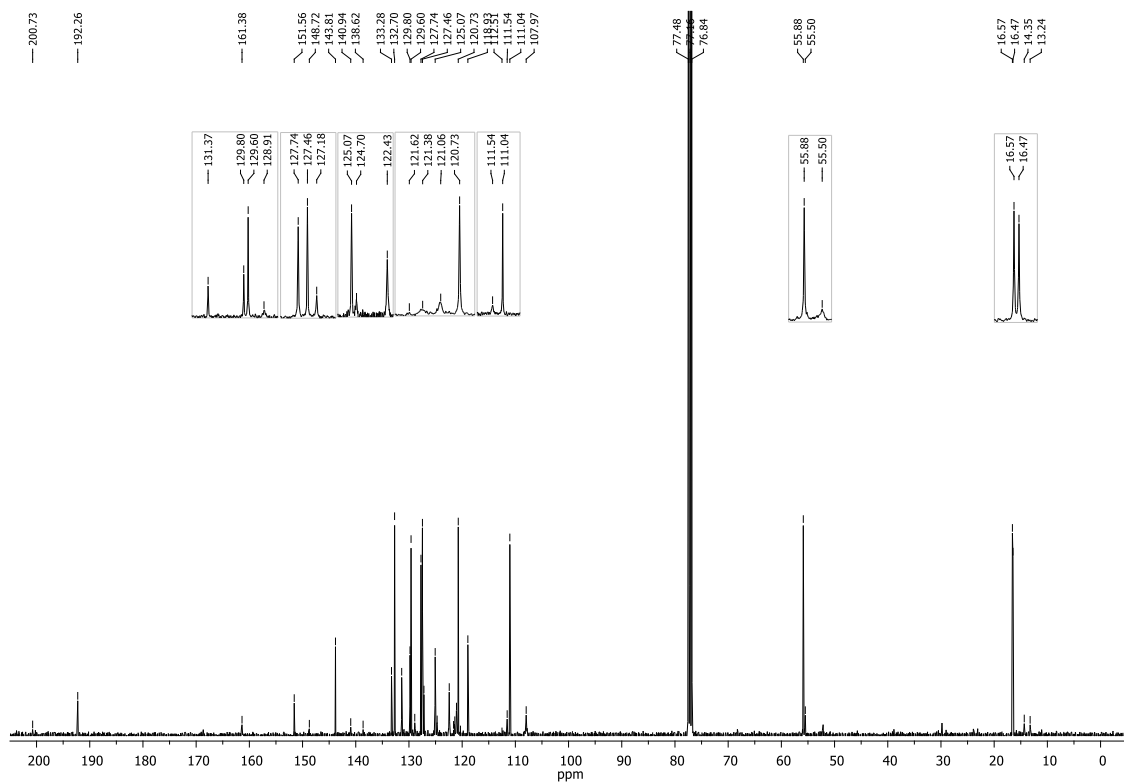
**<sup>1</sup>H NMR Spectra of 5g**



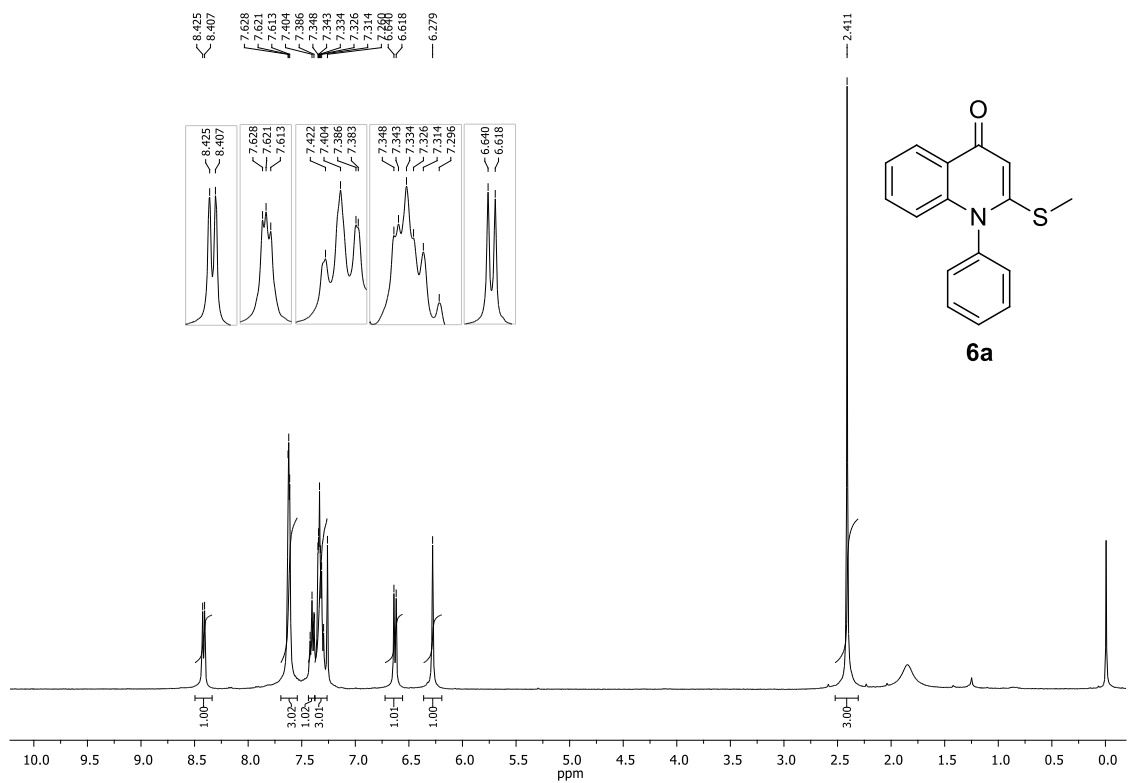
**<sup>13</sup>C NMR Spectra of 5g**



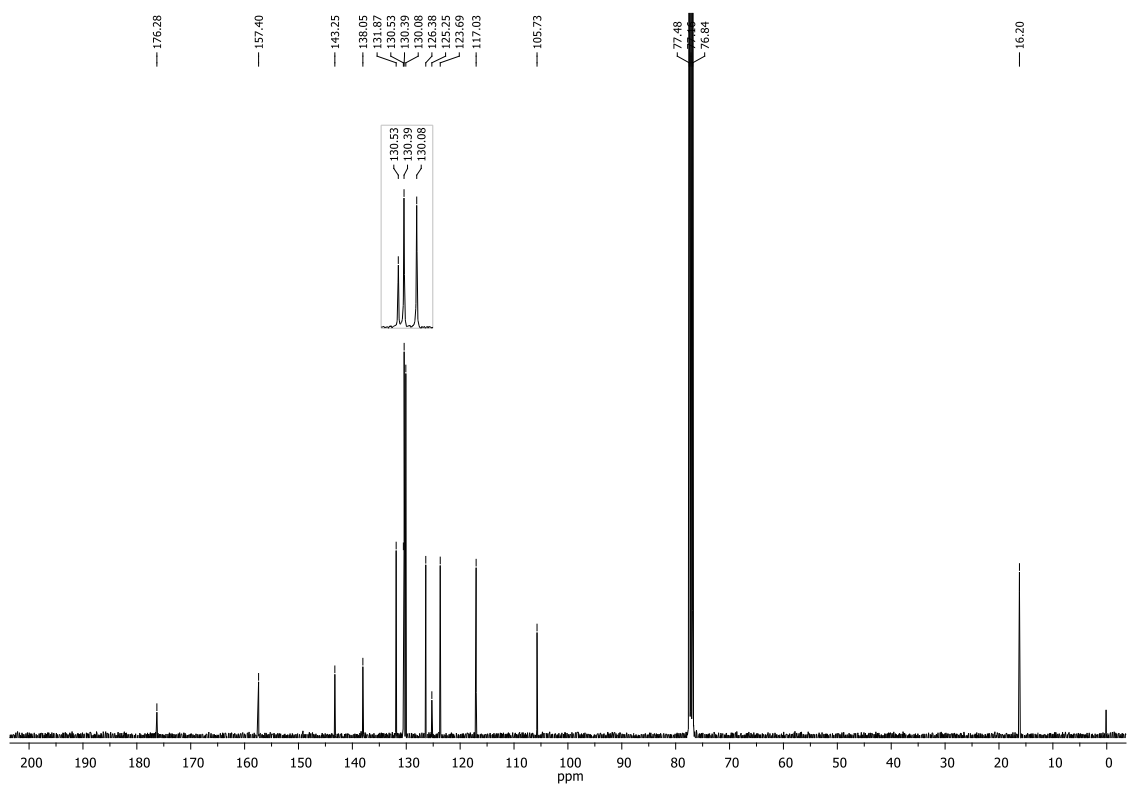
<sup>1</sup>H NMR Spectra of 5h



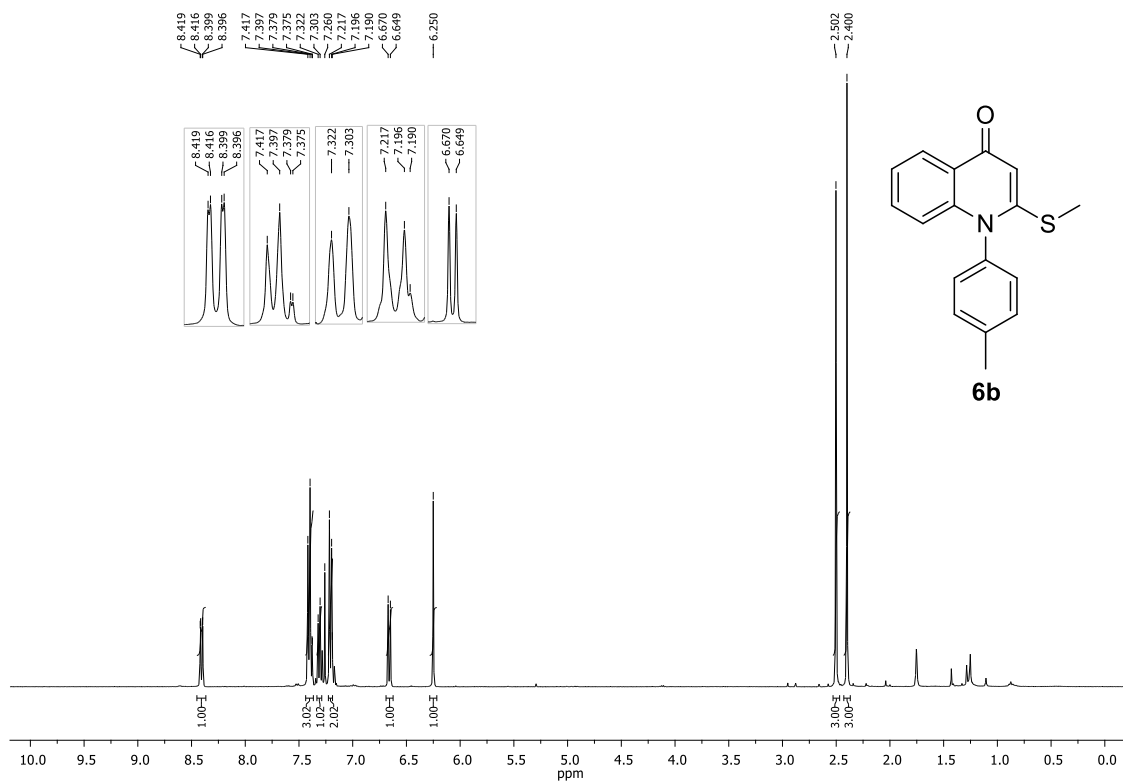
<sup>13</sup>C NMR Spectra of 5h



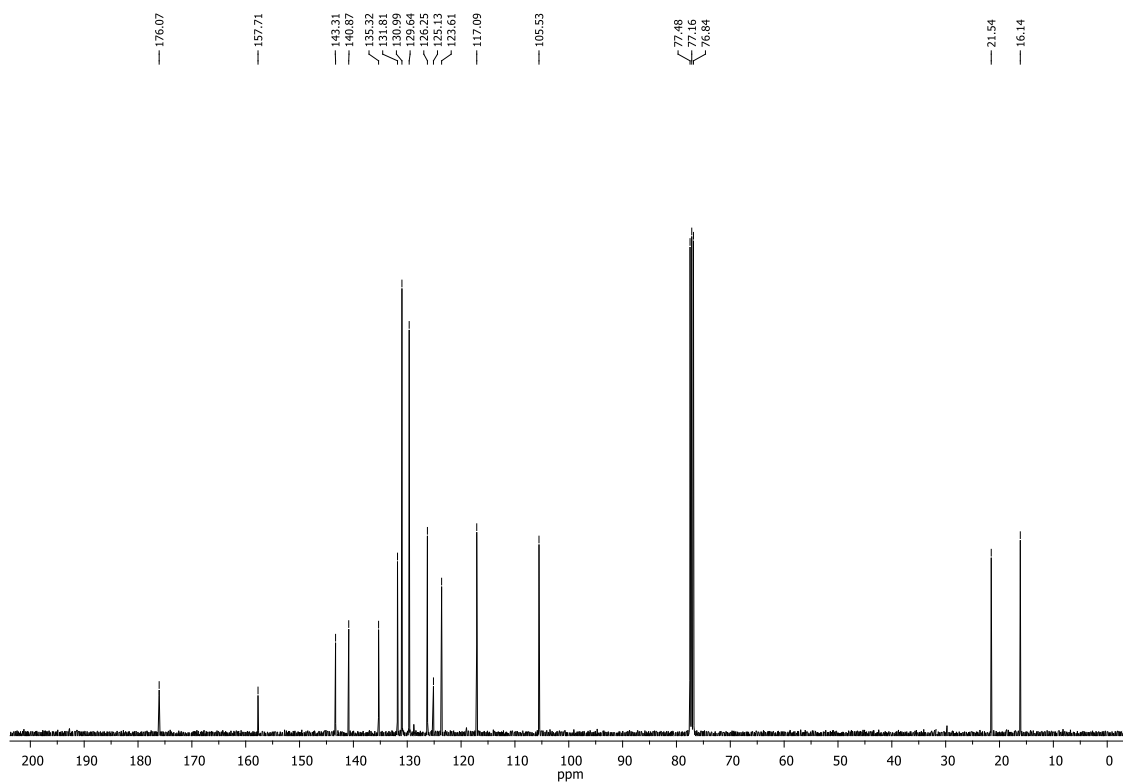
<sup>1</sup>H NMR Spectra of **6a**



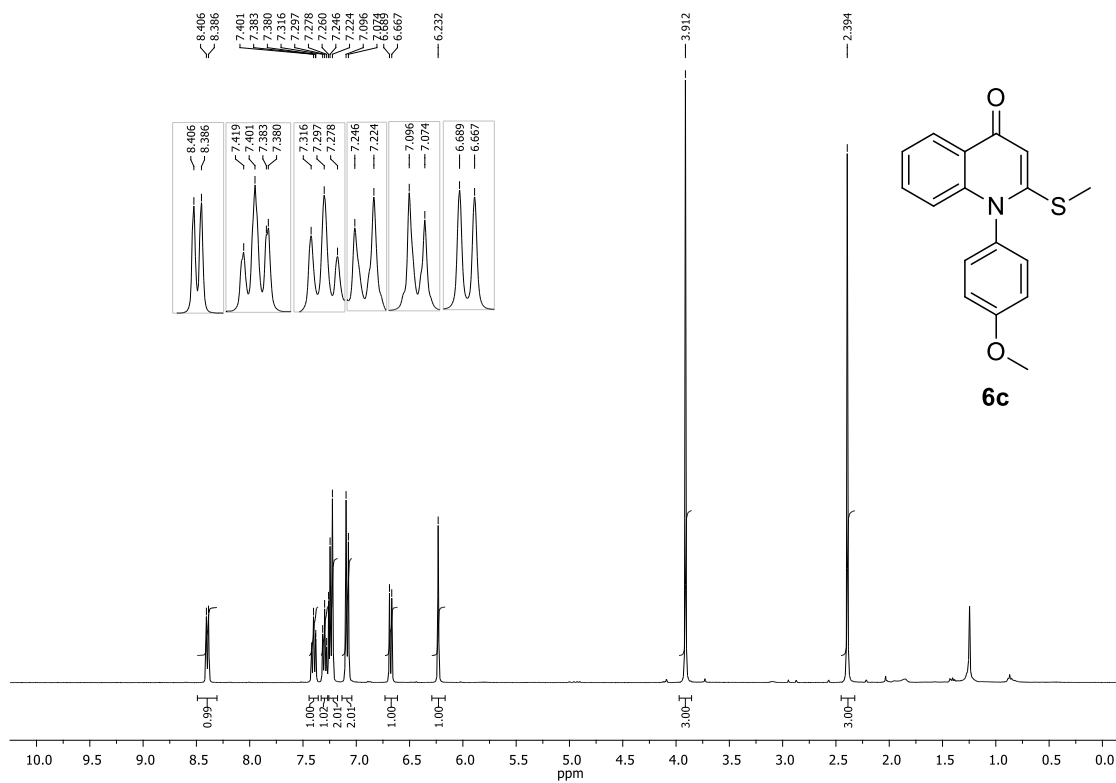
<sup>13</sup>C NMR Spectra of **6a**



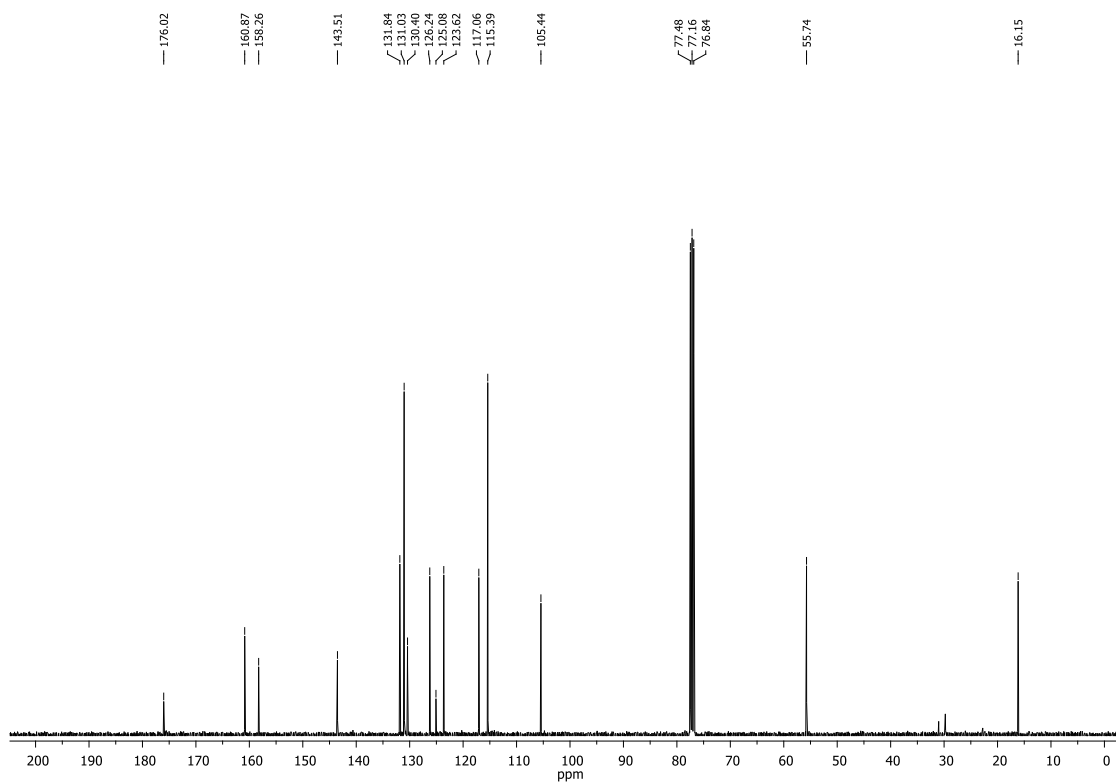
<sup>1</sup>H NMR Spectra of **6b**



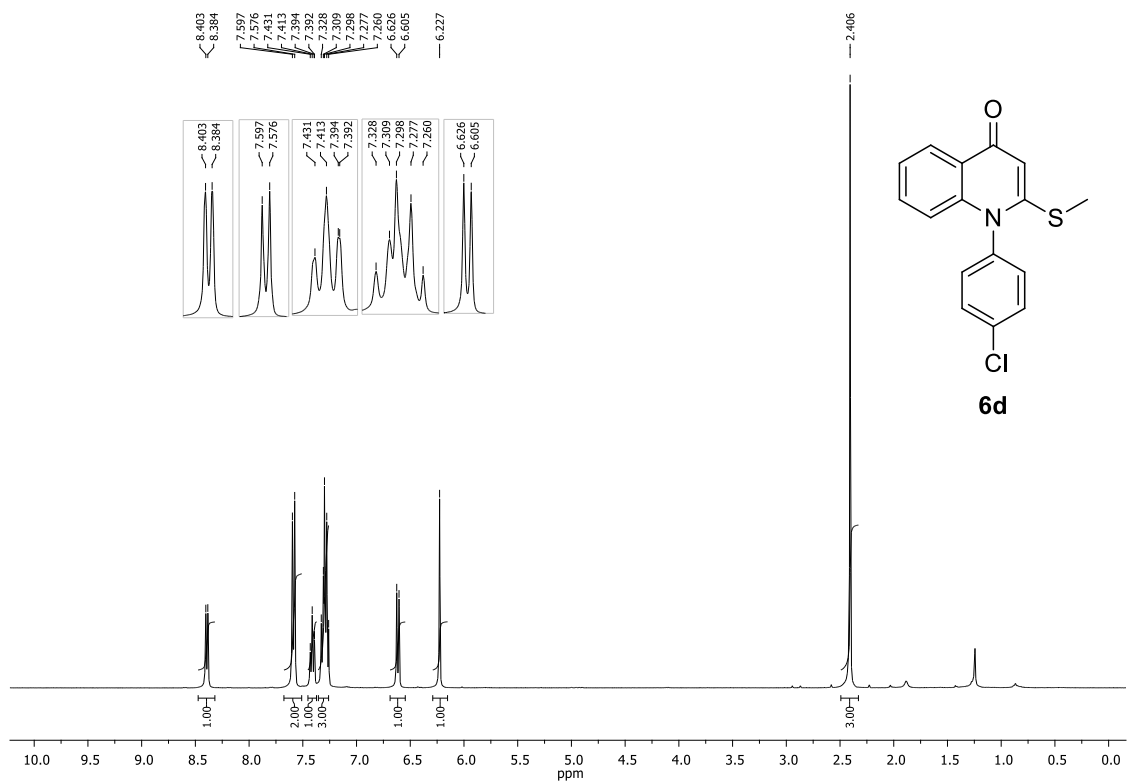
<sup>13</sup>C NMR Spectra of **6b**



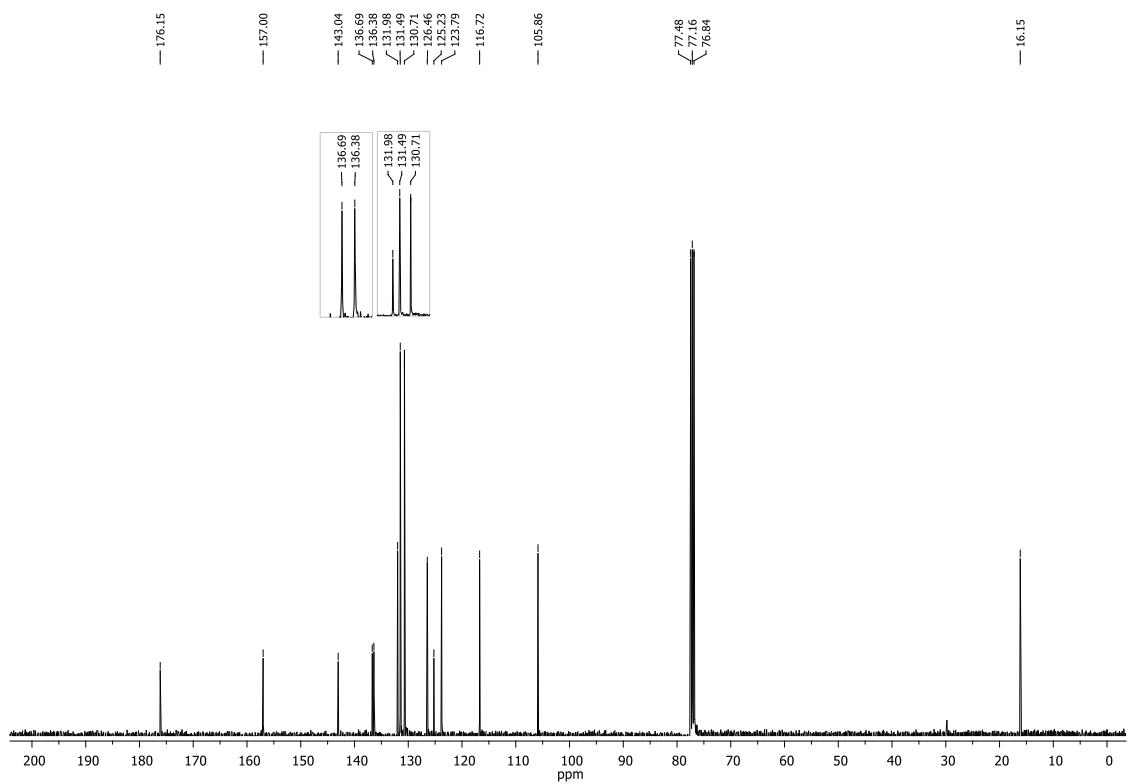
<sup>1</sup>H NMR Spectra of **6c**



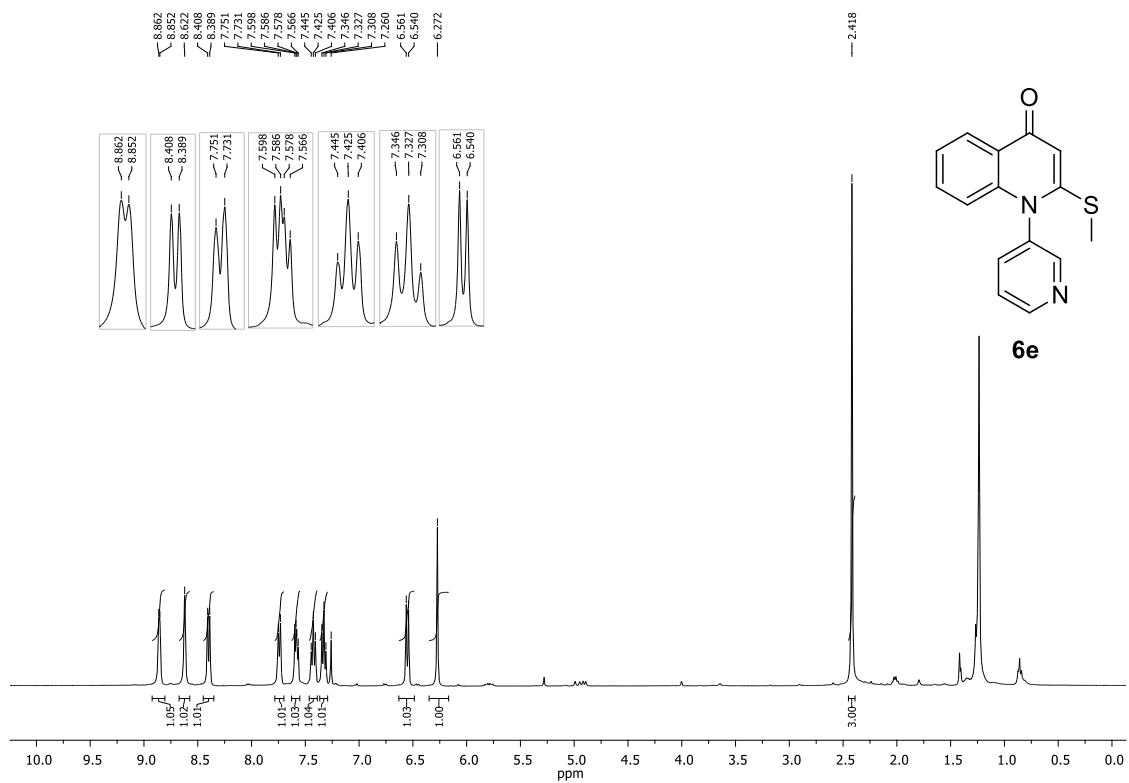
<sup>13</sup>C NMR Spectra of **6c**



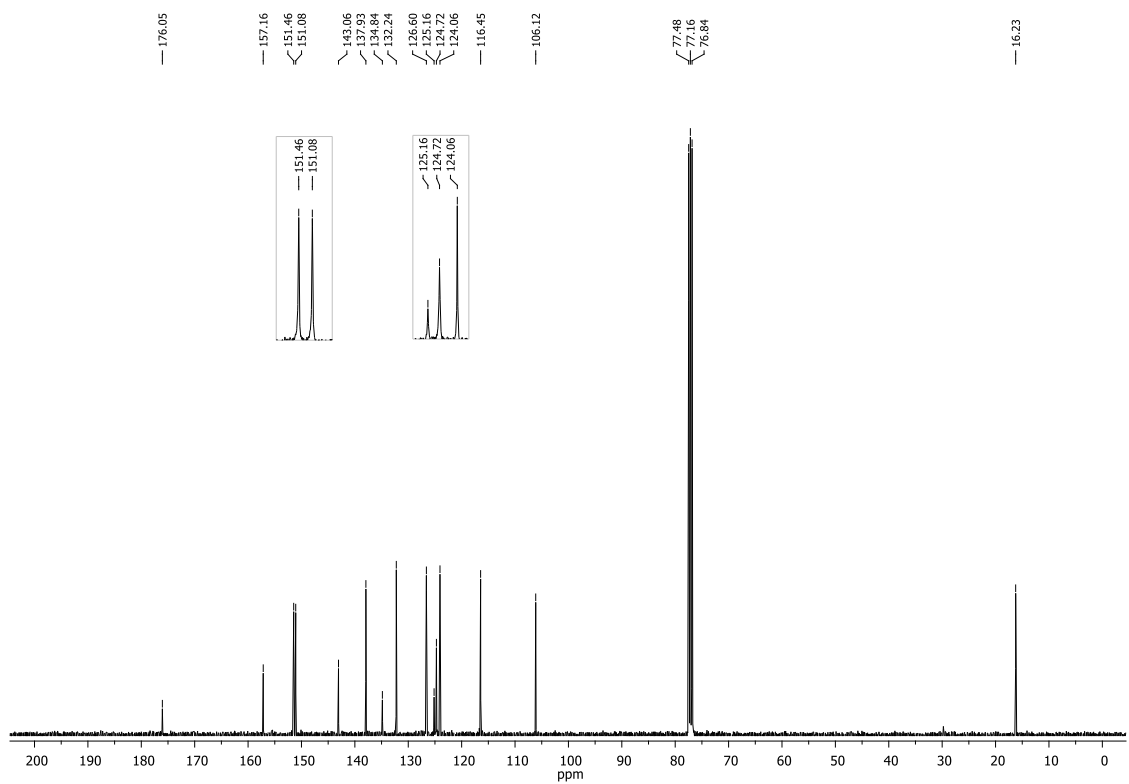
<sup>1</sup>H NMR Spectra of **6d**



<sup>13</sup>C NMR Spectra of **6d**

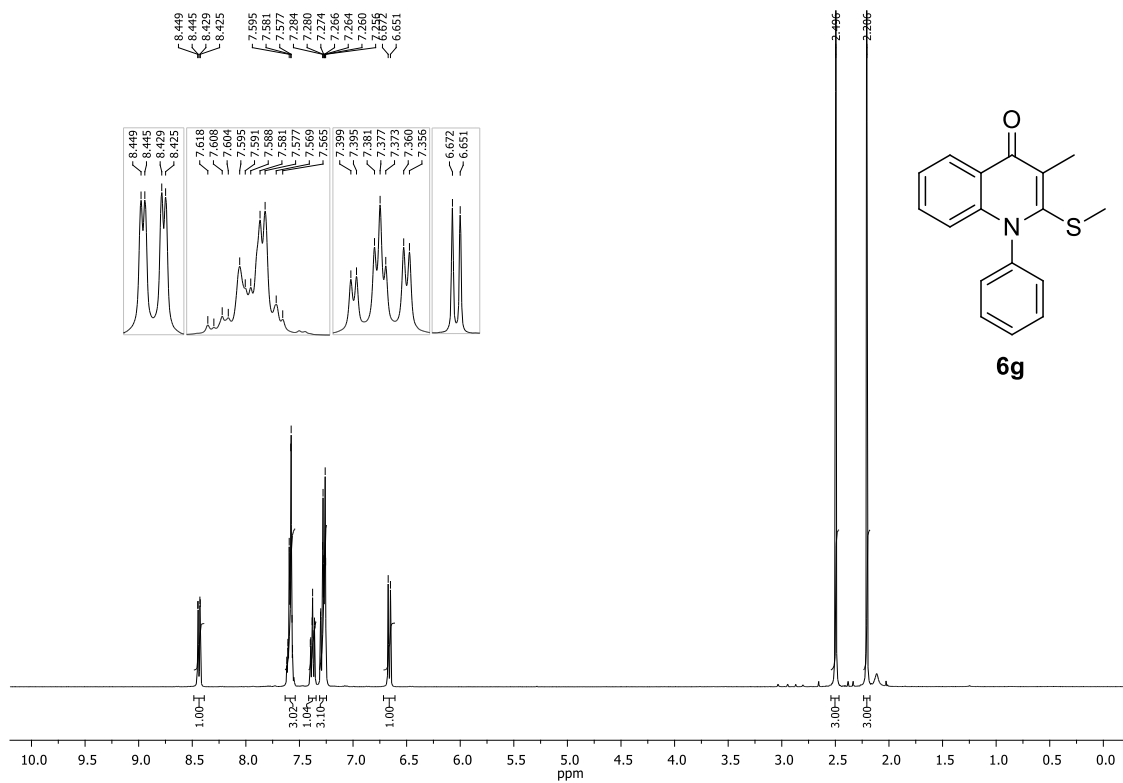


<sup>1</sup>H NMR Spectra of **6e**

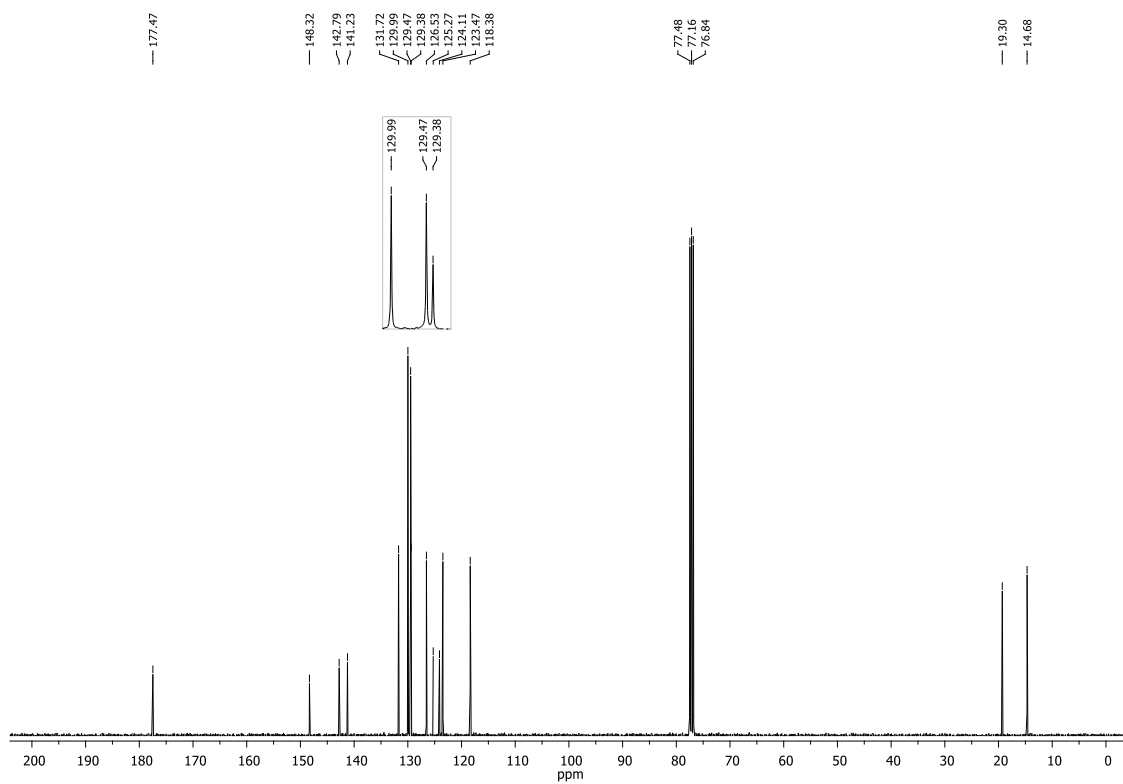


<sup>13</sup>C NMR Spectra of **6e**

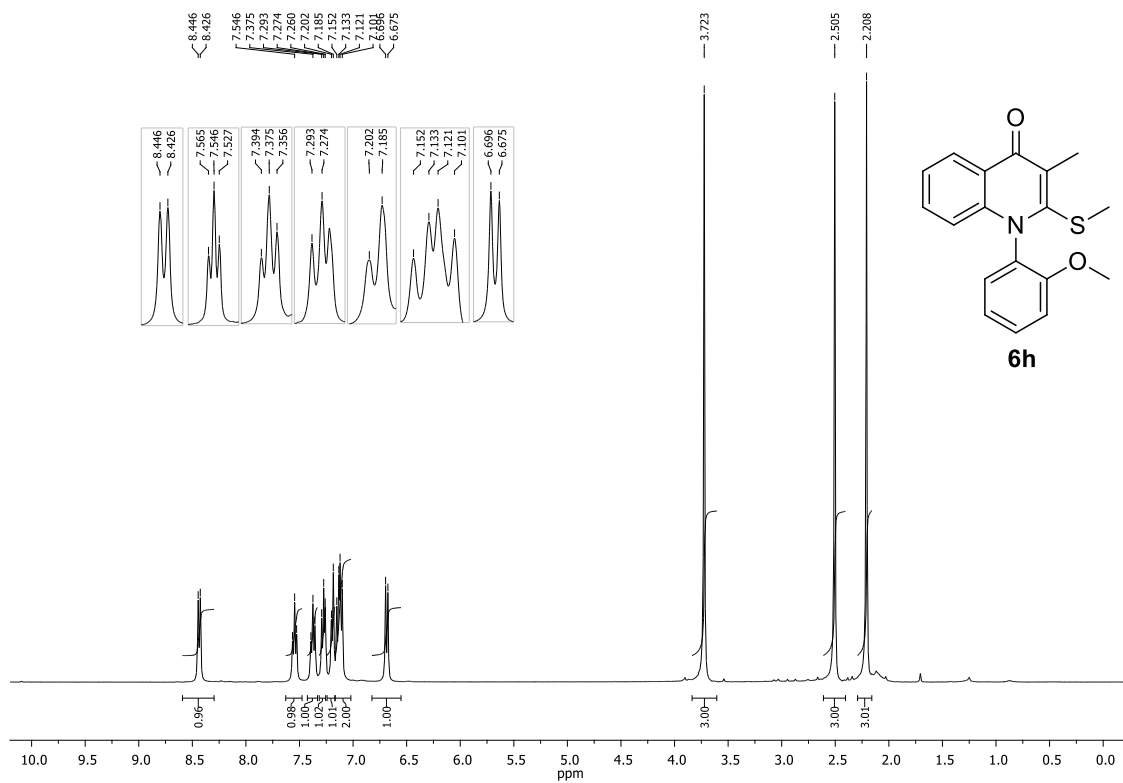




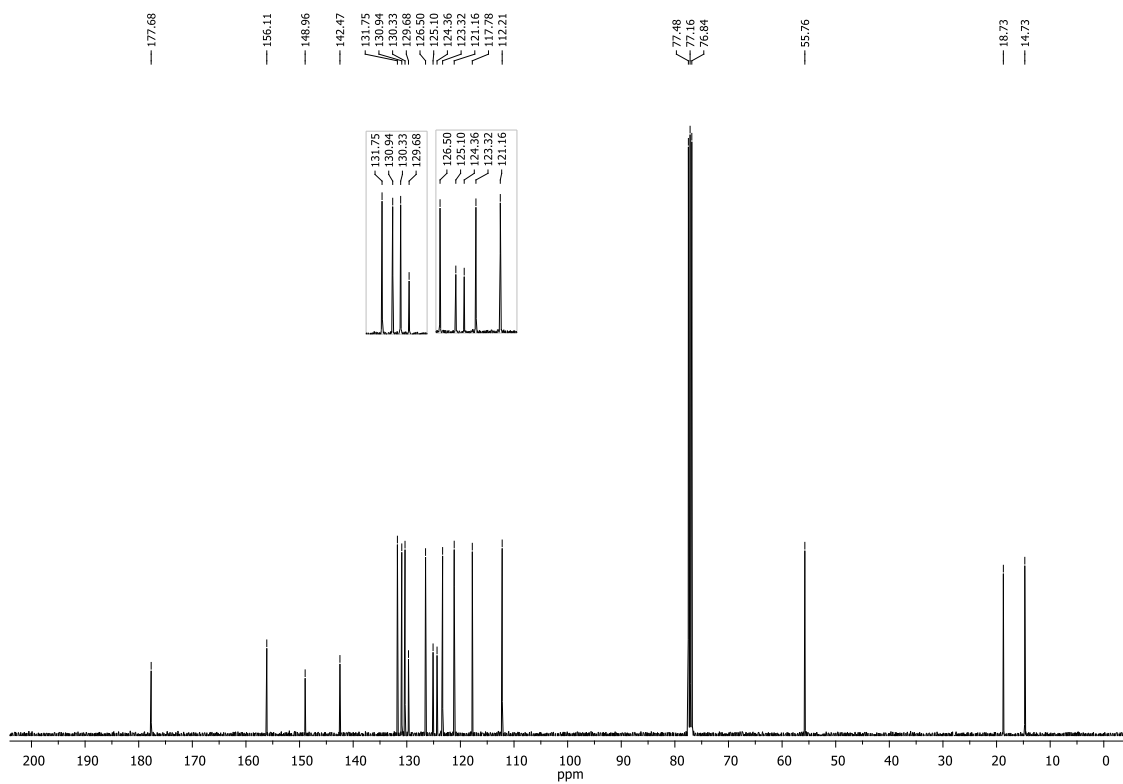
<sup>1</sup>H NMR Spectra of **6g**



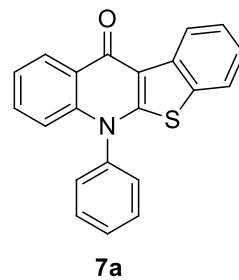
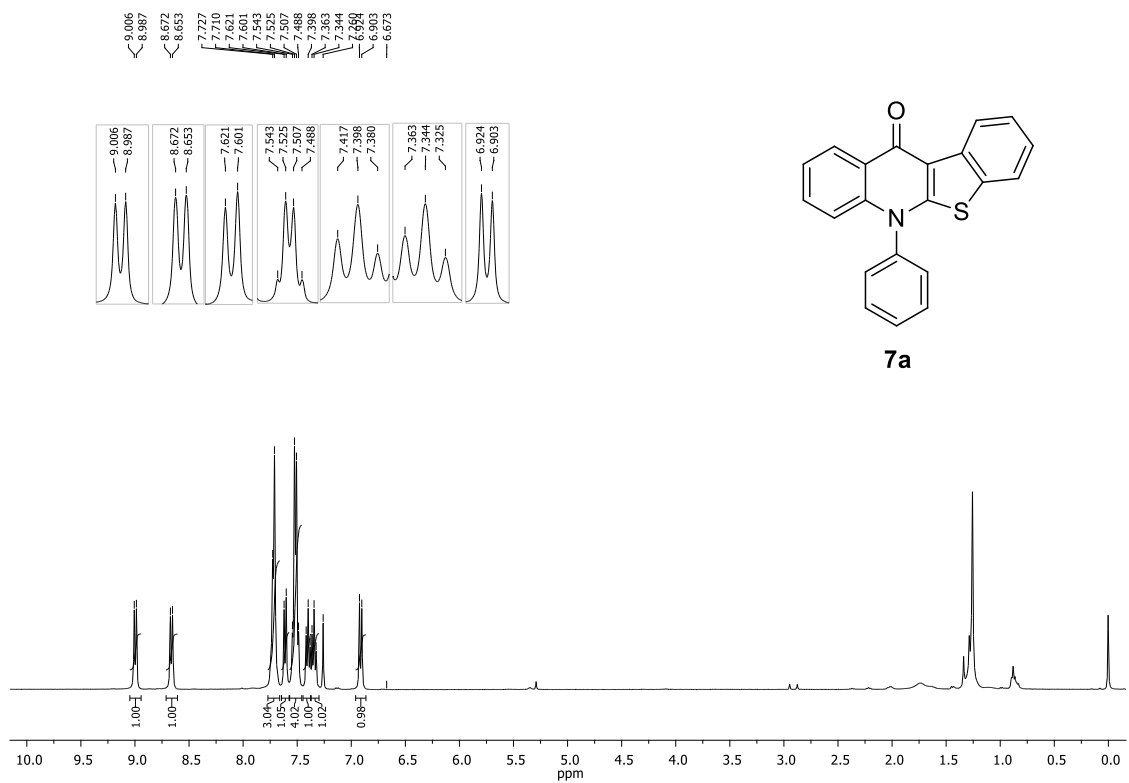
<sup>13</sup>C NMR Spectra of **6g**



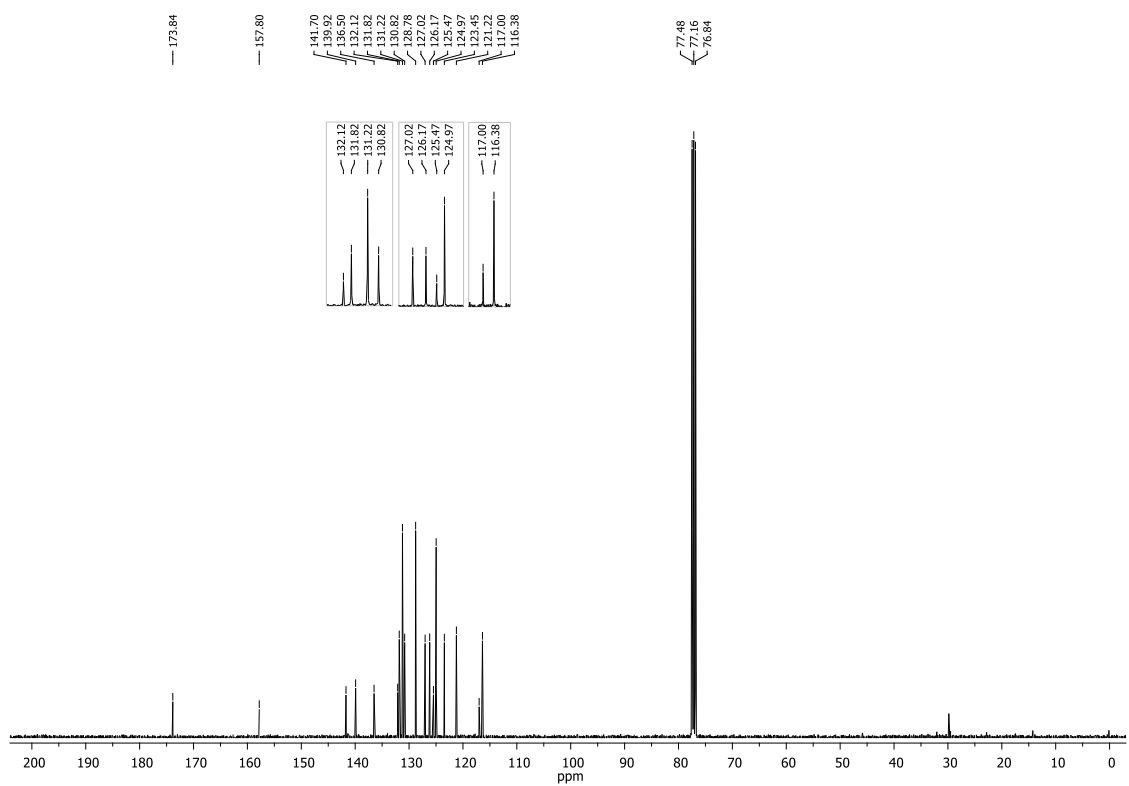
<sup>1</sup>H NMR Spectra of **6h**



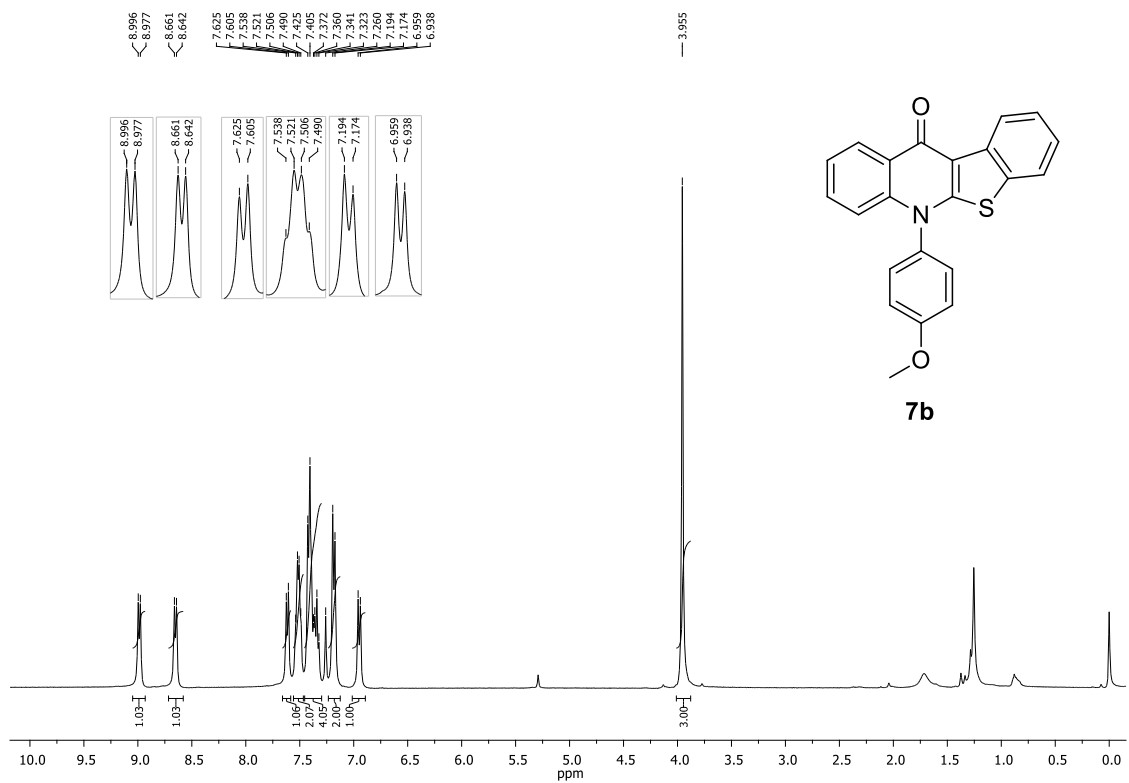
<sup>13</sup>C NMR Spectra of **6h**



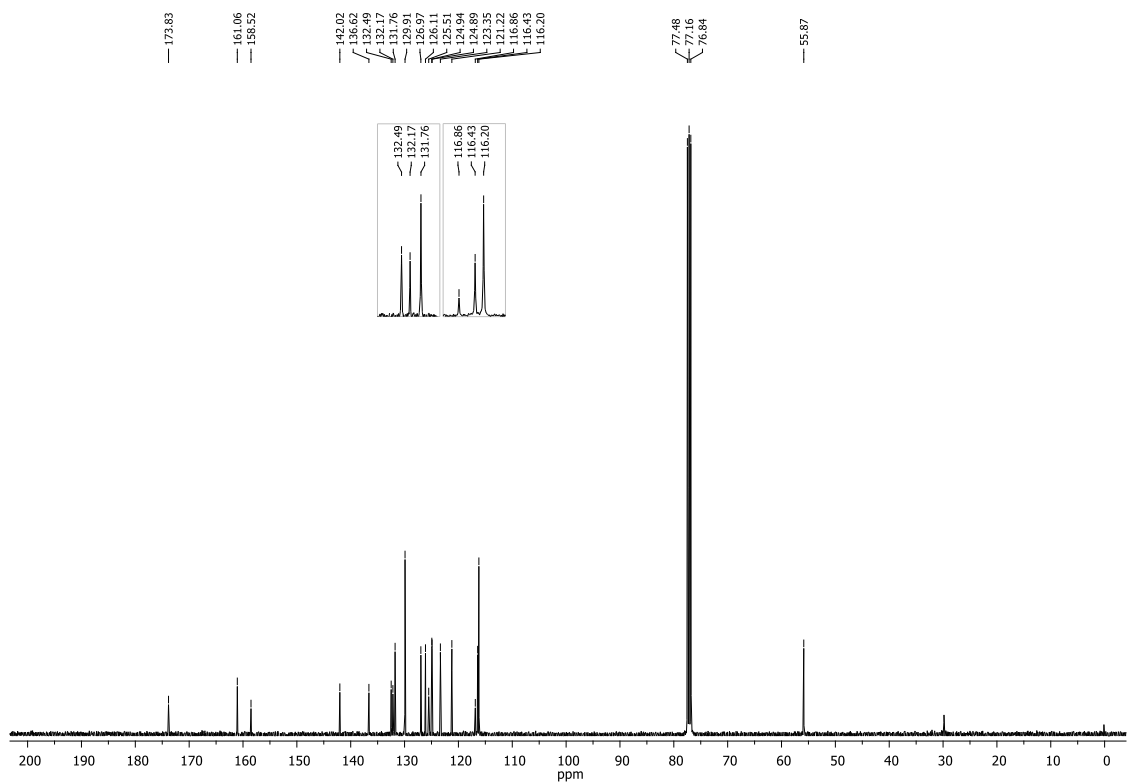
<sup>1</sup>H NMR Spectra of **7a**



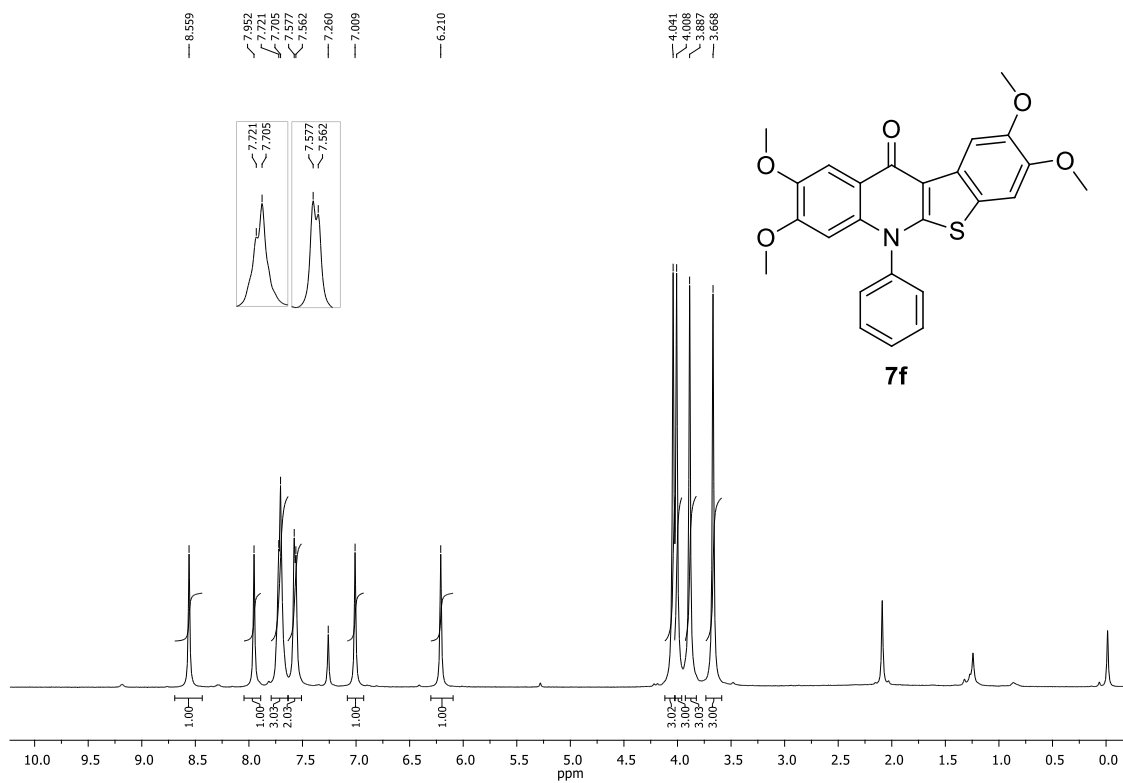
<sup>13</sup>C NMR Spectra of **7a**



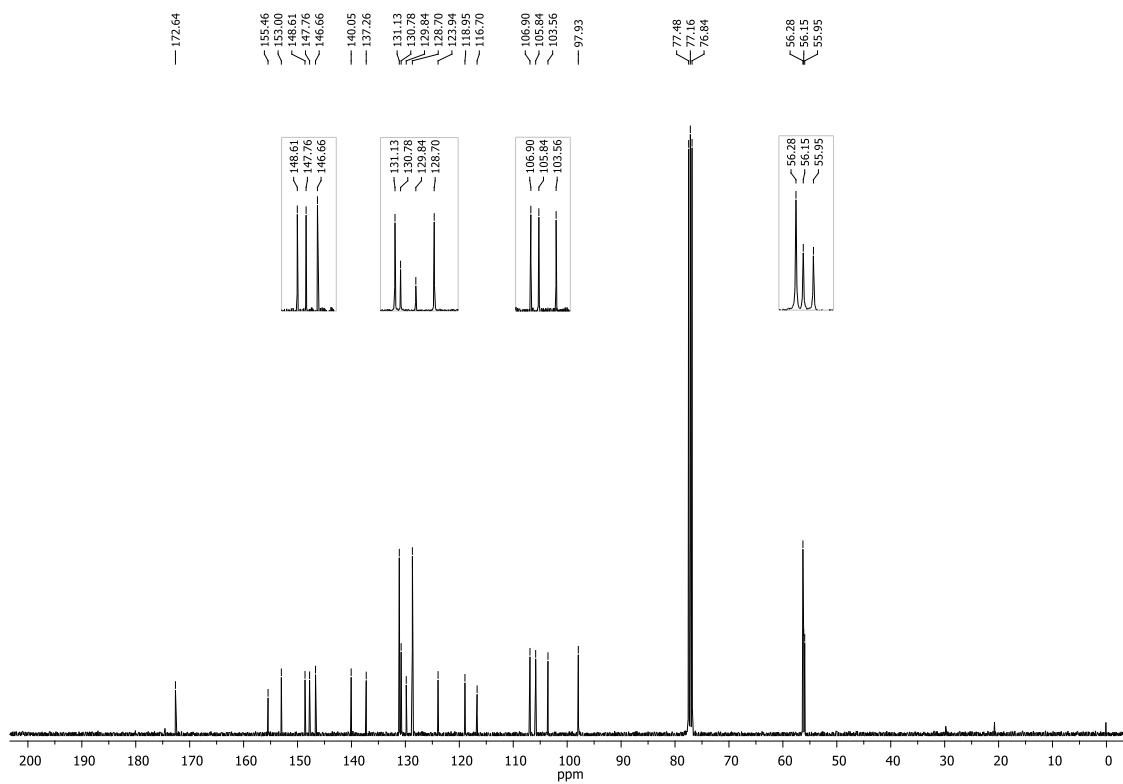
<sup>1</sup>H NMR Spectra of **7b**



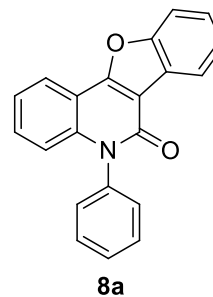
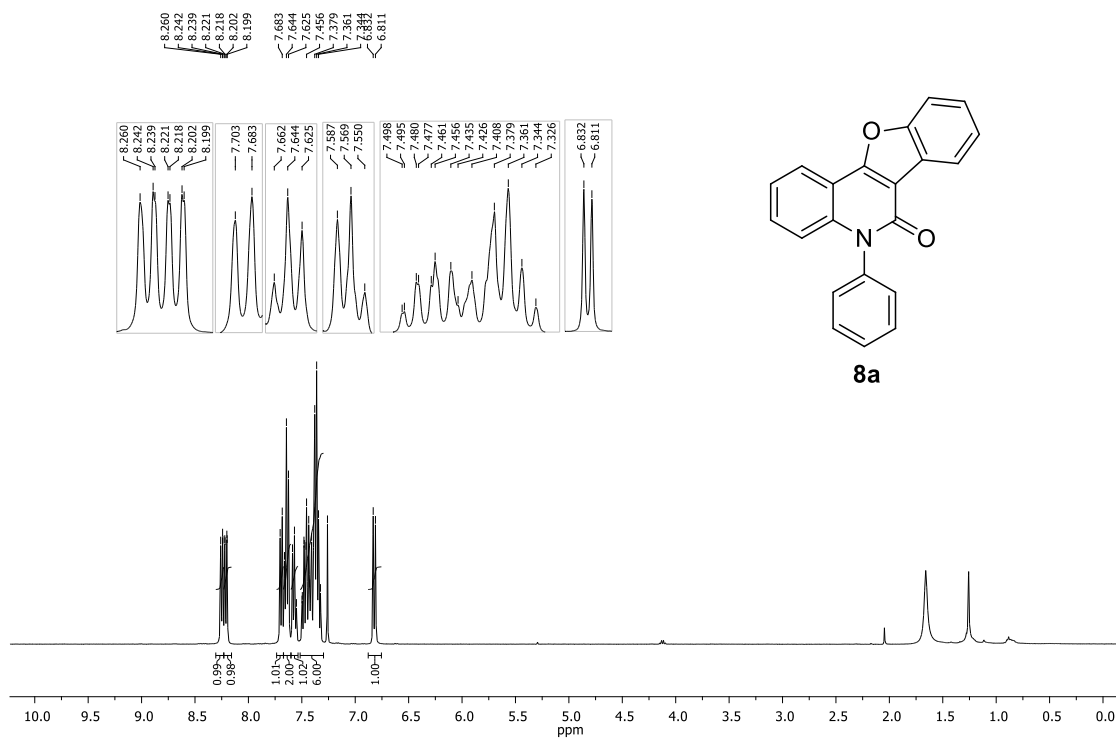
<sup>13</sup>C NMR Spectra of **7b**



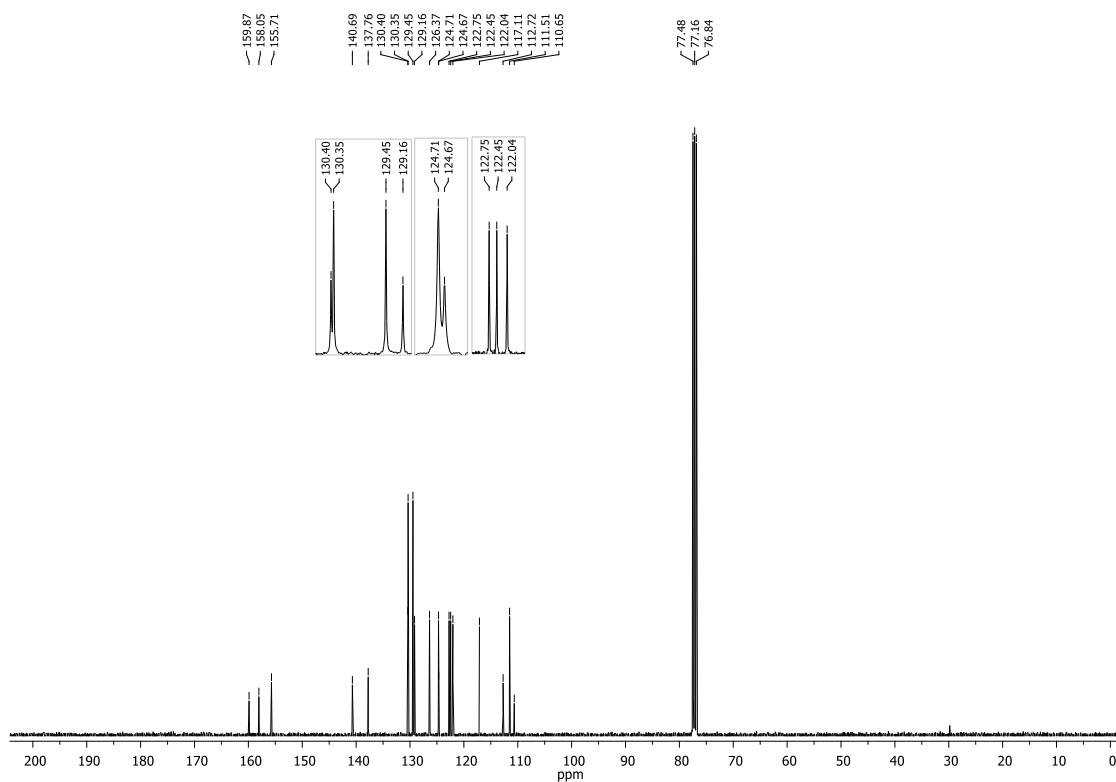
<sup>1</sup>H NMR Spectra of **7f**



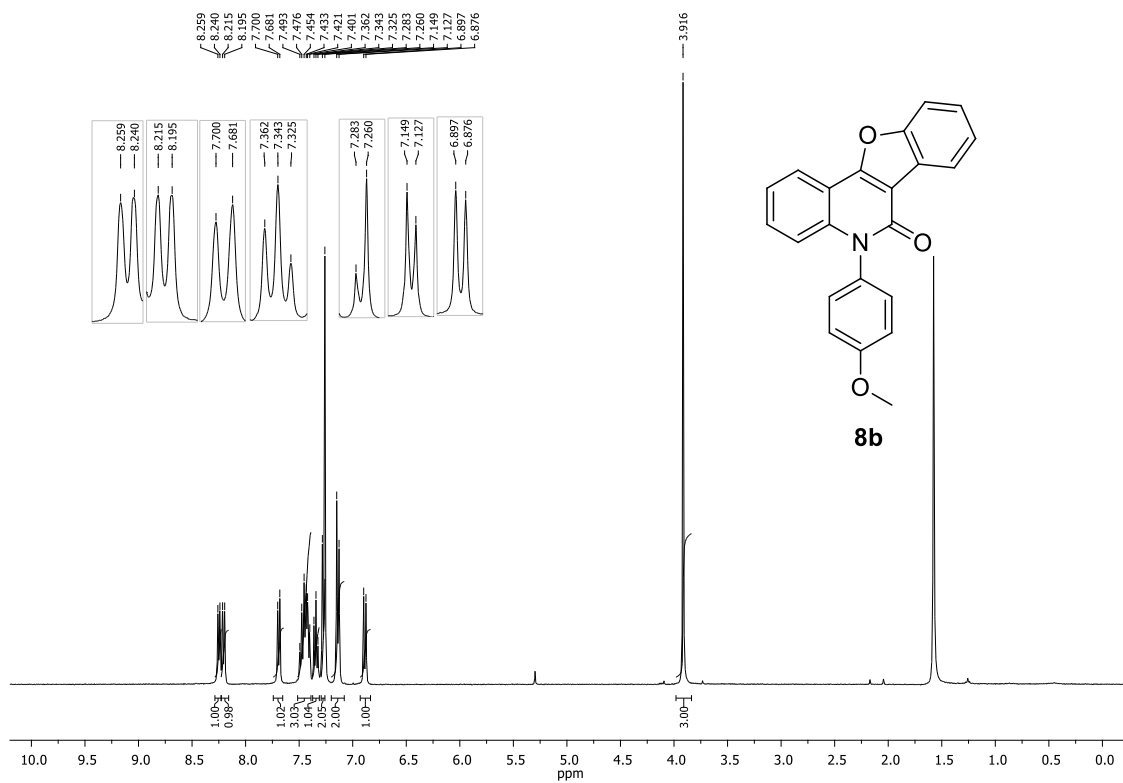
<sup>13</sup>C NMR Spectra of **7f**



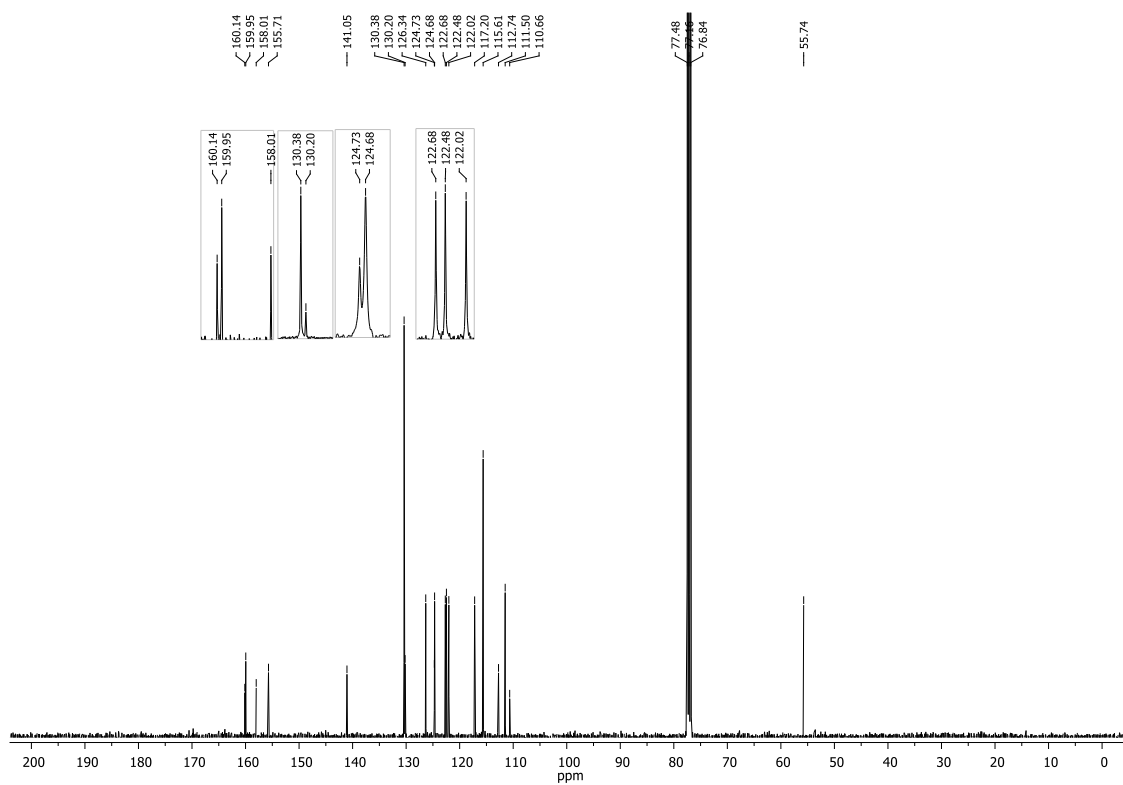
<sup>1</sup>H NMR Spectra of **8a**



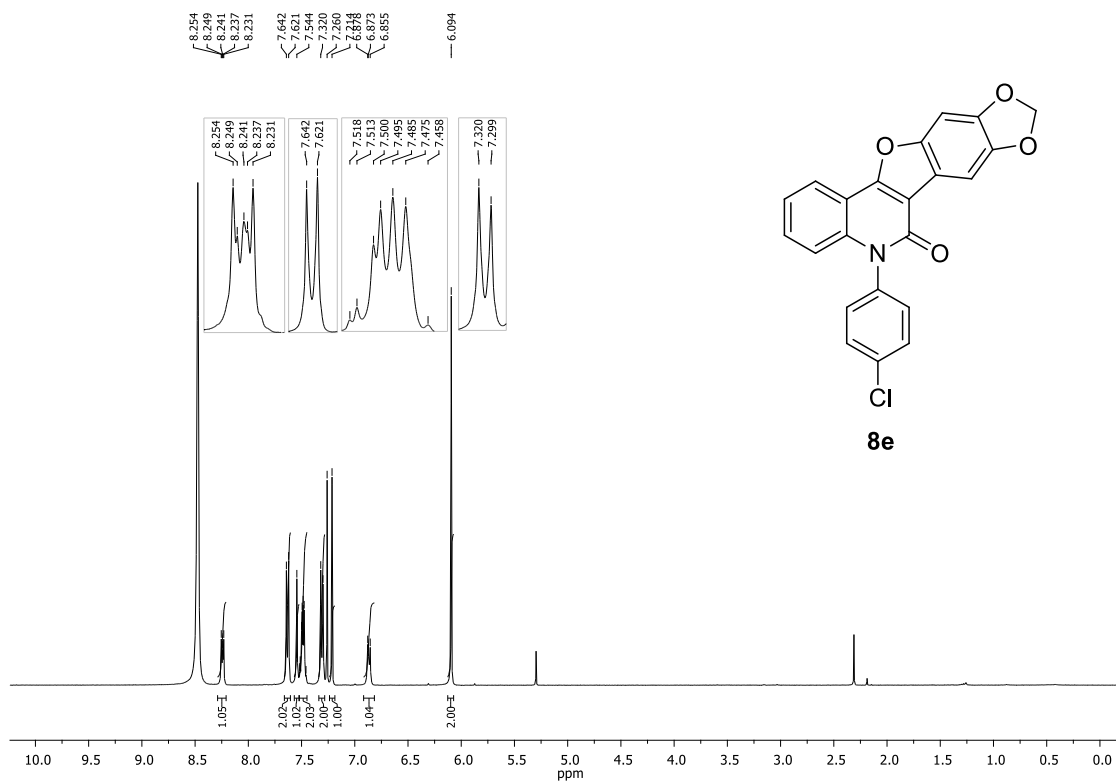
<sup>13</sup>C NMR Spectra of **8a**



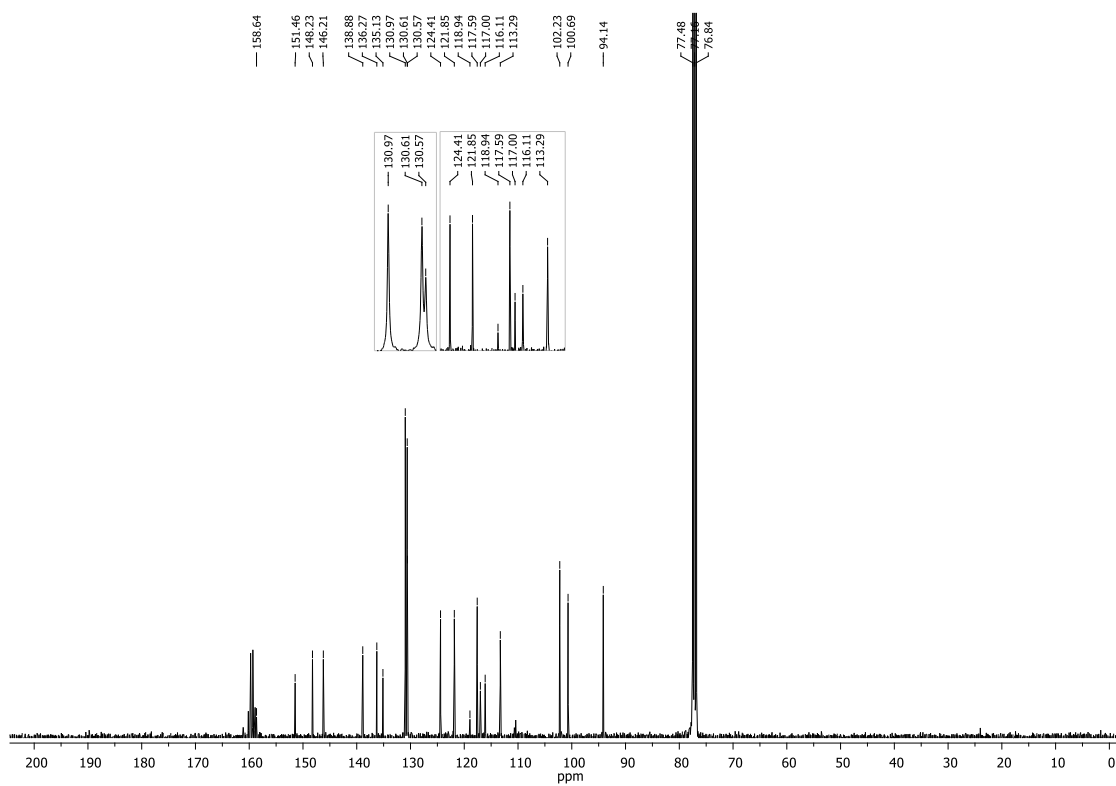
<sup>1</sup>H NMR Spectra of **8b**



<sup>13</sup>C NMR Spectra of **8b**

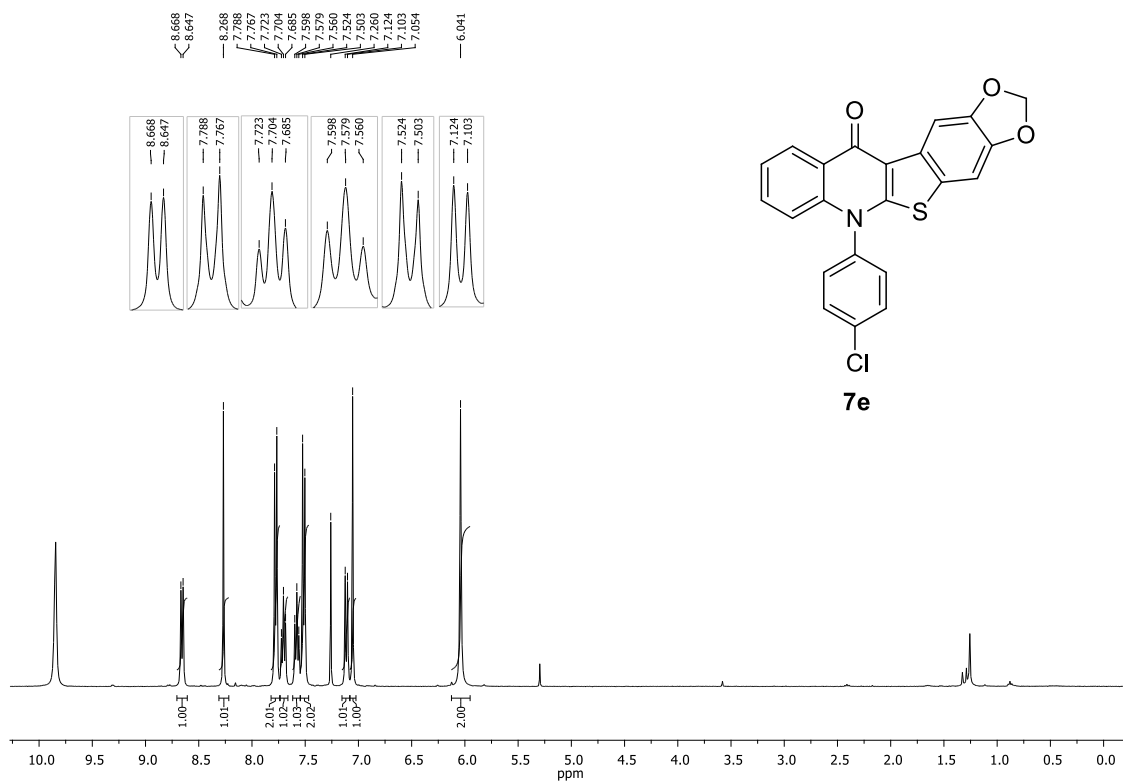


<sup>1</sup>H NMR Spectra of **8e**

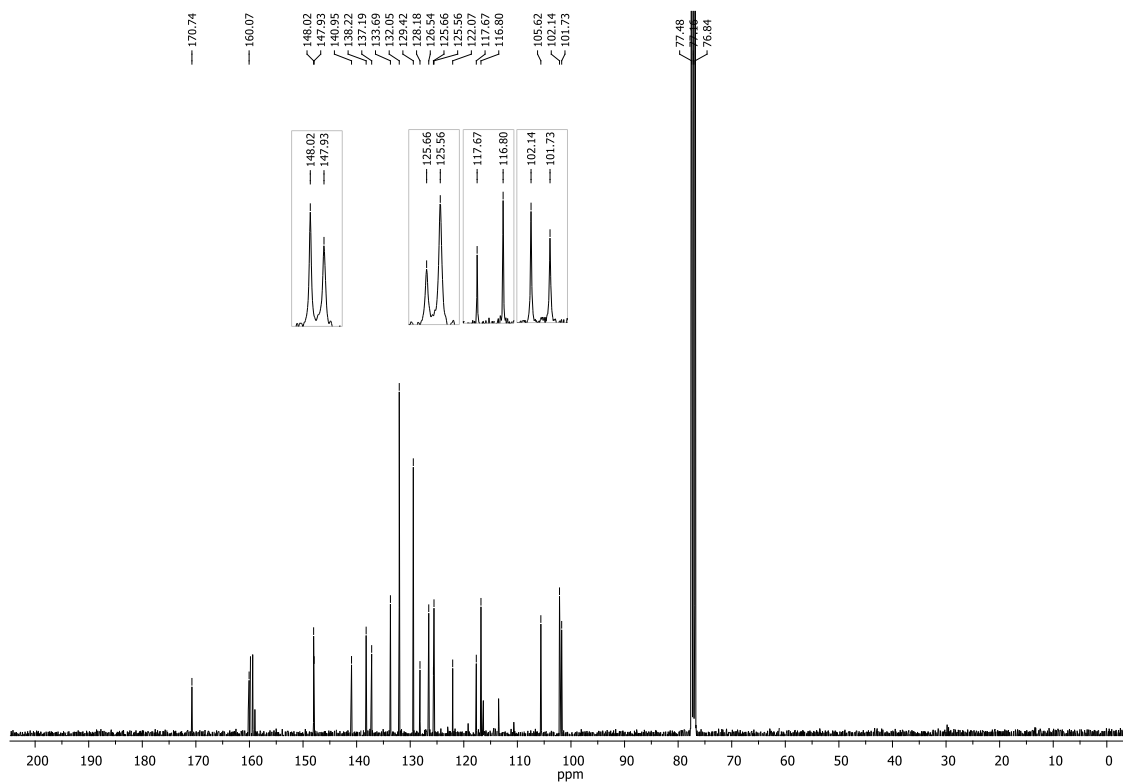


<sup>13</sup>C NMR Spectra of **8e**





<sup>1</sup>H NMR Spectra of **7e**



<sup>13</sup>C NMR Spectra of **7e**