Supporting Information

# Facile Preparation of 3-Substituted Benzisothiazoles from *o*-Mercaptoacylphenones

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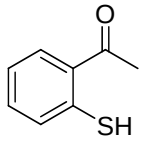
Contents

**Materials and Methods**: Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040 – 0.062mm). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Proton and carbon-13 NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are reported relative to chloroform (δ 7.26) for $^{1}$H NMR and chloroform (δ 77.0) $^{13}$C NMR.

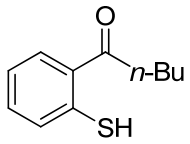
**Experimental Procedures and Compound Characterization Data**




**7a**

*o*-Mercaptoacylphenone compounds (**7a-7h**) were prepared according to a reported procedure[1]:

**7a**: $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J*= 8.4Hz, 1H), 7.32-7.30 (m, 3H), 4.45 (s, 1H); 2.62 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 198.8, 137.5, 132.6, 132.3, 131.7, 131.6, 124.6, 27.7; IR spectra ($cm^{-1}$) 3059.9, 2921.5, 2536.0, 1668.4, 1587.9, 1467.1, 1360.0, 1254.7, 756.2; mass spectrum (HRMS) m/z 153.0384, $[M+H]^+$ $C_8H_9OS$: calcd for : 153.0374.

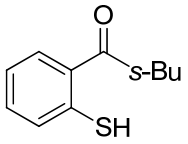



**7b**

**7b**: $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J*= 7.8Hz, 1H), 7.32-7.30 (m, 2H), 7.22-7.17 (m, 1H), 4.34 (s, 1H); 2.97 (t, *J*= 7.2Hz, 2H), 1.78-1.68 (m, 2H), 1.47-1.35 (m, 2H), 0.95 ( t, *J*= 7.2Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 201.4, 137.2, 132.9, 132.0, 131.8, 130.7, 124.7, 39.2, 26.5,

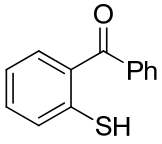
[1] Usachev, B. I.; Sosnovskikh, V. Ya.; Shafeev, M. A.; Röschenthaler, G-V. *Phosp. Sulfur and Silicon* **2005**, 180, 1315.

22.4, 13.9; IR spectra ($cm^{-1}$); 3073.1, 2958.0, , 2527.6, 1669.7, 1589.3, 1468.3, 1368.0, 1205.7, 999.5, 737.3; mass spectrum (HRMS) m/z 195.0866, $[M+H]^+$ $C_{11}H_{15}OS$: calcd for : 195.0844.



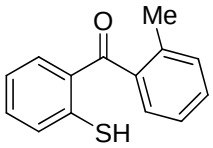

**7c**

**7c**: $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J*=7.8Hz, 1H), 7.34-7.27 (m, 2H), 7.23-7.17 (m, 1H), 4.23 (s, 1H), 3.37 (sext, *J*= 6.6Hz, 1H), 1.88-1.78 (m, 1H), 1.54-1.44 (m, 1H), 1.19 (dd, *J*= 2.1Hz, 6.9Hz, 3H), 0.89 (td, *J*= 1.5Hz, 7.2Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 205.5, 137.2, 133.2, 131.9, 131.8, 130.2, 124.7, 43.0, 26.7, 16.7, 11.8; IR spectra ($cm^{-1}$) 2966.5, 2874.5, 2539.3, 1668.1, 1587.8, 1464.0, 1373.9, 1216.3, 985.5, 741.0; mass spectrum (HRMS) m/z 195.0852, $[M+H]^+$ $C_{11}H_{15}OS$: calcd for 195.0844.




**7d**

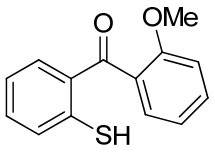
**7d**: white solid, m.p. 47.5-48.5 C; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.80-7.76 (m, 2H), 7.63-7.57 (m, 1H), 7.50-7.41 (m, 4H) 7.35 (td, *J*= 1.5Hz,7.2Hz, 1H), 7.19 (td, *J*= 1.2Hz, 7.5Hz 1H), 4.22 (s, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 196.8, 137.5, 135.4, 134.5, 132.9, 131.7, 131.5, 131.3, 130.2, 128.4, 124.5; IR spectra ($cm^{-1}$); 3058.9, 2554.9, 1650.0, 1595.9, 1264.8, 916.3, 742.9; mass spectrum (HRMS) m/z 215.0440, $[M+H]^+$ $C_{13}H_{11}OS$: calcd for : 215.0531.




**7e**

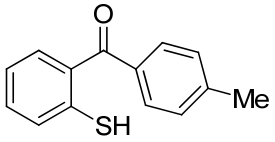
**7e**: white solid, m.p. 72.5-73.5 C; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.42-7.21 (m, 7H), 7.13-7.07 (m, 1H), 4.56 (s, 1H), 2.34 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 199.1, 138.6, 137.2, 137.1, 134.2, 133.6, 132.1, 131.5, 131.1, 130.5, 128.8, 125.3, 124.5, 20.1; IR spectra ($cm^{-1}$); 3059.9,

2558.5, 1654.5, 1585.9, 1380.7, 1307.2, 1258.1, 922.1, 742.5; mass spectrum (HRMS) m/z 229.0699, $[M+H]^+$ $C_{14}H_{13}OS$: calcd for : 229.0687.



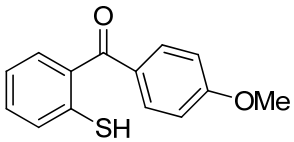

**7f**

**7f**: white crystals, m.p. 123.0-124.0; C $^1$H NMR (300 MHz, $CDCl_3$) δ 7.50-7.43 (m, 2H), 7.37-7.27 (m, 3H), 7.11-6.96 (m, 3H), 4.63 (s, 1H), 3.71 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 196.8, 157.3, 137.0, 134.5, 133.7, 132.2, 131.9, 131.2, 129.8, 128.8, 124.2, 120.5, 111.5, 55.6; IR spectra ($cm^{-1}$) 3058.9, 2937.6, 2553.0, 1649.7, 1598.8, 1462.6, 1316.3, 1257.0, 922.4, 751.8; mass spectrum (HRMS) m/z 245.0645, $[M+H]^+$ $C_{14}H_{13}O_2S$: calcd for : 245.0636.




**7g**

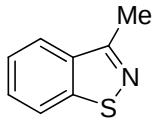
**7g**: white crystals, m.p. 81.0-82.0 C; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.69 (dt, *J*= 1.8Hz, 8.1Hz, 2H), 7.45-7.40 (m, 2H), 7.34 (td, *J*= 1.5Hz, 7.2Hz, 1H), 7.27 (d, *J*= 7.8Hz, 2H), 7.19 (td, *J*= 1.2Hz, 7.5Hz, 1H) 4.17 (s, 1H), 2.44 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 196.6, 144.0, 136.1, 134.8, 133.8, 131.4, 131.2, 131.0, 130.4, 129.1, 124.6, 21.7; IR spectra ($cm^{-1}$) 3058.8, 2557.5, 1649.7, 1604.1, 1311.9, 1264.8, 922.2, 746.8; mass spectrum (HRMS) m/z 229.0682, $[M+H]^+$ $C_{14}H_{13}OS$: calcd for : 229.0687.




**7h**

**7h**: white crystals, m.p. 78.5-79.5 C; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.79 (dt, *J*= 3.0Hz, 9.9Hz, 2H), 7.41 (dd, , *J*= 1.5Hz, 7.8Hz, 2H), 7.36-7.30 (m, 1H), 7.22-7.16 (m, 1H), 6.95 (dt, , *J*= 2.7Hz, 9.6Hz, 2H), 4.09 (s, 1H), 3.88 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 195.5, 163.7, 136.7,

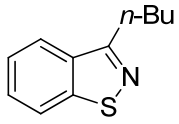
132.9, 132.7, 131.4, 130.7, 130.6, 130.0, 124.7, 113.7, 55.5; IR spectra ($cm^{-1}$) 2933.9, 2838.8, 2554.0, 1649.4, 1597.6, 1315.6, 1257.3, 922.3, 750.2; mass spectrum (HRMS) m/z 245.0628, $[M+H]^+$ $C_{14}H_{13}O_2S$: calcd for : 245.0636.




**5a**

**General procedure for the preparation of 3-substituted benzisothiazoles**

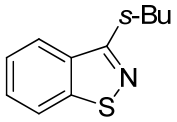
**3-methylbenzo[d]isothiazole (5a):** To a solution of compound **7a** (0.545 mmol, 82.9mg) in THF (2mL) was added *i*-pentylONO (1.64 mmol, 0.22 mL) at 0 C and in dark. Instantly, the reaction mixture turned deep red. The reaction was continued for 5 min at 0 C. Then, a solution of $EtPPh_2$ (1.14 mmol, 262 mg) in THF (1mL) was added quickly to the mixture. The reaction was allowed to stir for 10 min at 0 C and 50 min at room temperature. The reaction was diluted with water (10 mL) and was extracted with diethyl ether (10 mL, 3 times). The organic layers were combined and washed with 3 mL of 5% $H_2O_2$ solution (4 times) and 5 mL of 1M $Na_2S_2O_3$ (1 time). The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated in *vacuo*. Purification by flash chromatography (2% EtOAc/Hexanes) afforded **5a** in 85 % yield (69.4mg). $^1H$ NMR (300 MHz, $CDCl_3$) 7.95-7.90 (m, 2H), 7.55-7.49 (m, 1H), 7.56-7.40 (m, 1H), 2.76 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 162.8, 152.0, 135.0, 127.5, 124.4, 123.4, 119.8, 17.4; IR spectra ($cm^{-1}$) 3064.1, 2954.6, 1698.0, 1592.4, 1493.2, 1435.0, 1381.6, 1260.5, 758.8; mass spectrum (HRMS) m/z 150.0326, $[M+H]^+$ $C_8H_8NS$: calcd for : 150.0377.




**5b**

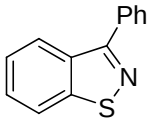
**5b** was prepared in an analogous method as **5a**. Isolated yield: 74%; $^1H$ NMR (300 MHz, $CDCl_3$) 7.97 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.92 (dt, *J*= 1.2Hz,8.1Hz, 1H), 7.54-7.49 (m, 1H), 7.45-7.40 (m, 1H), 3.12 (t, *J*= 7.5Hz, 2H) 1.92-1.82 (m, 2H), 1.46 (m, 2H), 0.98 (t, *J*= 7.2Hz, 3H) ; $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 166.9, 152.3, 134.7, 127.4, 124.3, 123.3, 119.9, 31.3, 30.3, 22.6, 13.9; IR

spectra ($cm^{-1}$) 3064.4, 2957.9, 1639.3, 1593.3, 1463.9, 1378.5, 1259.4, 1080.1, 758.9; mass spectrum (HRMS) m/z 192.0856, $[M+H]^+$ $C_{11}H_{14}NS$: calcd for : 192.0847.



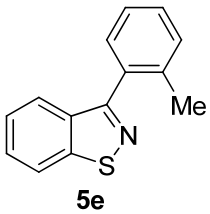

**5c**

**5c** was prepared in an analogous method as **5a**. Isolated yield: 64%; $^1H$ NMR (300 MHz, $CDCl_3$) 7.99 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.92 (dt, *J*= 0.9Hz,8.1Hz, 1H), 7.53-7.48 (m, 1H), 7.44-7.39 (m, 1H), 3.39 (m, 1H) 2.09-1.94 (m, 1H), 1.86-1.71 (m, 1H), 1.44 (d, *J*= 6.9Hz, 3H), 0.92 (t, *J*= 7.5Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ170.8, 152.6, 134.4, 127.4, 124.2, 123.3, 120.0, 37.7, 29.0, 19.2, 12.1 ; IR spectra ($cm^{-1}$) 3064.0, 2964.7, 1635.8, 1593.9, 1487.0, 1456.7, 1375.1, 1240.9, 736.8; mass spectrum (HRMS) m/z 192.0843, $[M+H]^+$ $C_{11}H_{14}NS$: calcd for : 192.0847.




**5d**

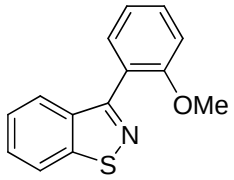
**5d** was prepared in an analogous method as **5a**. Isolated yield: 74%; $^1H$ NMR (300 MHz, $CDCl_3$) 8.19 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 8.00 (dt, *J*= 0.6Hz,8.4Hz, 1H), 7.90-7.87 (m, 2H), 7.59-7.51 (m, 4H), 7.49-7.44 (m, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 164.3, 153.4, 135.2, 133.7, 129.3, 128.8, 128.7, 127.5, 125.0, 124.8, 119.8; IR spectra ($cm^{-1}$) 3061.7, 2923.3, 1593.7, 1469.9, 1352.1, 960.5, 734.9; mass spectrum (HRMS) m/z 234.0349, $[M+Na]^+$ $C_{13}H_9NNaS$: calcd for : 234.0353.




**5e**

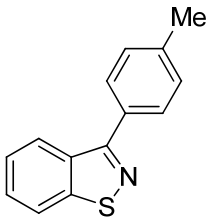
**5e** was prepared in an analogous method as **5a**. Isolated yield: 37%; $^1H$ NMR (300 MHz, $CDCl_3$) 8.01 (d, *J*= 8.1Hz, 1H), 7.77 (d, *J*= 8.1Hz, 1H), 7.58-7.52 (m, 1H), 7.44-7.30 (m, 5H), 2.27 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 165.3, 152.5, 137.3, 135.1, 134.3, 130.8, 129.7, 129.0, 127.5, 125.7, 124.9, 124.8, 119.7, 20.0; IR spectra 3059.4, 2923.6, 1635.9, 1558.1, 1473.4, 1457.2,

1347.7, 1319.3, 737.4; ($cm^{-1}$); mass spectrum (HRMS) m/z 242.0672, $[M+H]^+$ $C_{14}H_{12}NS$: calcd for : 242.0690.



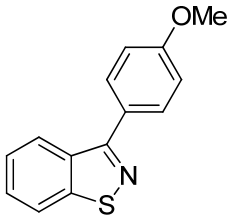

**5f**

**5f:** was prepared in an analogous method as **5a**. Isolated yield: 81%; $^1H$ NMR (300 MHz, $CDCl_3$) 7.97 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.82 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.55-7.46 (m, 3H), 7.41-7.36 (m, 1H), 7.14-7.07 (m, 2H), 3.78 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 163.0, 157.2, 152.3, 135.0, 131.5, 130.7, 127.3, 125.4, 124.4, 124.2, 120.8, 119.5, 111.3, 55.5; IR spectra ($cm^{-1}$) 3061.7, 2934.9, 1599.9, 1464.2, 1352.2, 1246.7, 754.7; mass spectrum (HRMS) m/z 242.0648, $[M+H]^+$ $C_{14}H_{12}NOS$: calcd for : 242.0640.



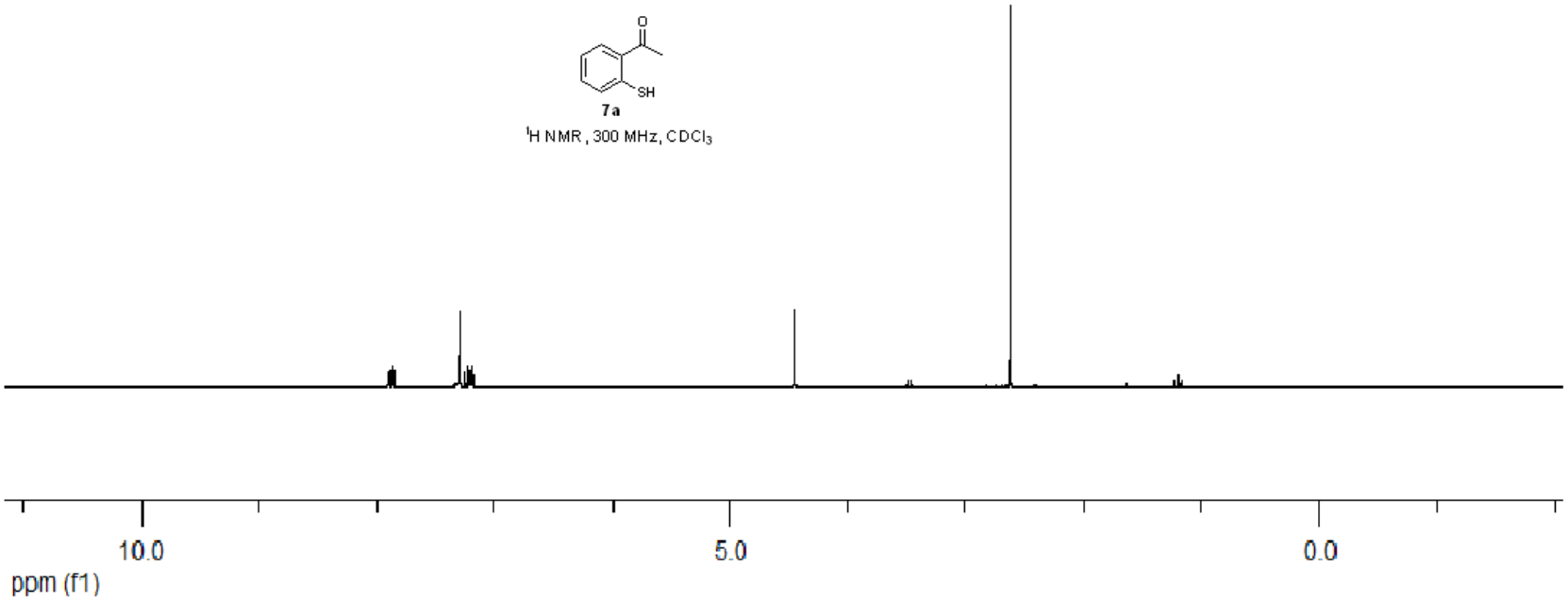

**5g**

**5g** was prepared in an analogous method as **5a**. Isolated yield: 75%; $^1H$ NMR (300 MHz, $CDCl_3$) 8.19 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.99 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.78 (dt, *J*= 1.8Hz, 8.1Hz, 2H), 7.58-7.52 (m, 1H), 7.48-7.43 (m, 1H), 7.36 (d, *J*= 7.8Hz, 2H), 2.46 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 164.4, 153.4, 139.3, 133.8, 132.4, 129.5, 128.5, 127.4, 124.9, 119.9, 21.4; IR spectra ($cm^{-1}$) 3058.9, 2919.0, 1612.6, 1592.1, 1467.0, 1349.7, 829.3, 736.0; mass spectrum (HRMS) m/z 226.0619, $[M+H]^+$ $C_{14}H_{12}NS$: calcd for : 226.0690.




**5h**

**5h:** was prepared in an analogous method as **5a**. Isolated yield: 77%; $^{1}$H NMR (300 MHz, $CDCl_3$) 8.18 (dt, *J*= 1.2Hz, 8.4Hz, 1H), 7.98 (dt, *J*= 0.9Hz, 8.1Hz, 1H), 7.84 (dt, *J*= 3.0Hz, 9.6Hz, 2H), 7.57-7.52 (m, 1H), 7.48-7.43 (m, 1H), 7.07 (dt, *J*= 2.7Hz, 9.6Hz, 2H), 3.90 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 164.0, 160.4, 153.4, 133.7, 130.0, 127.9, 127.4, 124.9, 124.8, 119.9, 114.2, 55.4; IR spectra ($cm^{-1}$) 3060.5, 2957.6, 1609.3, 1519.4, 1466.0, 1352.2, 1251.4, 838.4, 737.6; mass spectrum (HRMS) m/z 242.0672, $[M+H]^+$ $C_{14}H_{12}NOS$: calcd for : 242.0640.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SH
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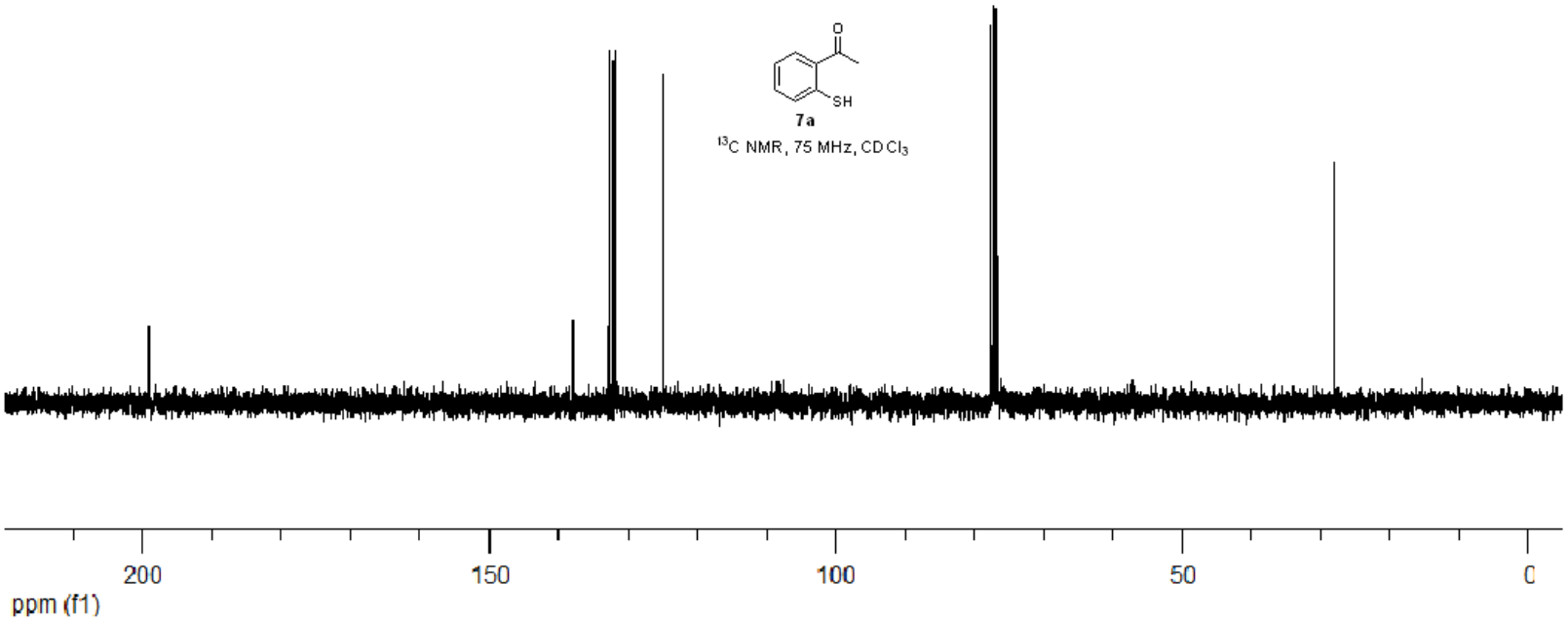
0.0
ppm (f1)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SH
7a
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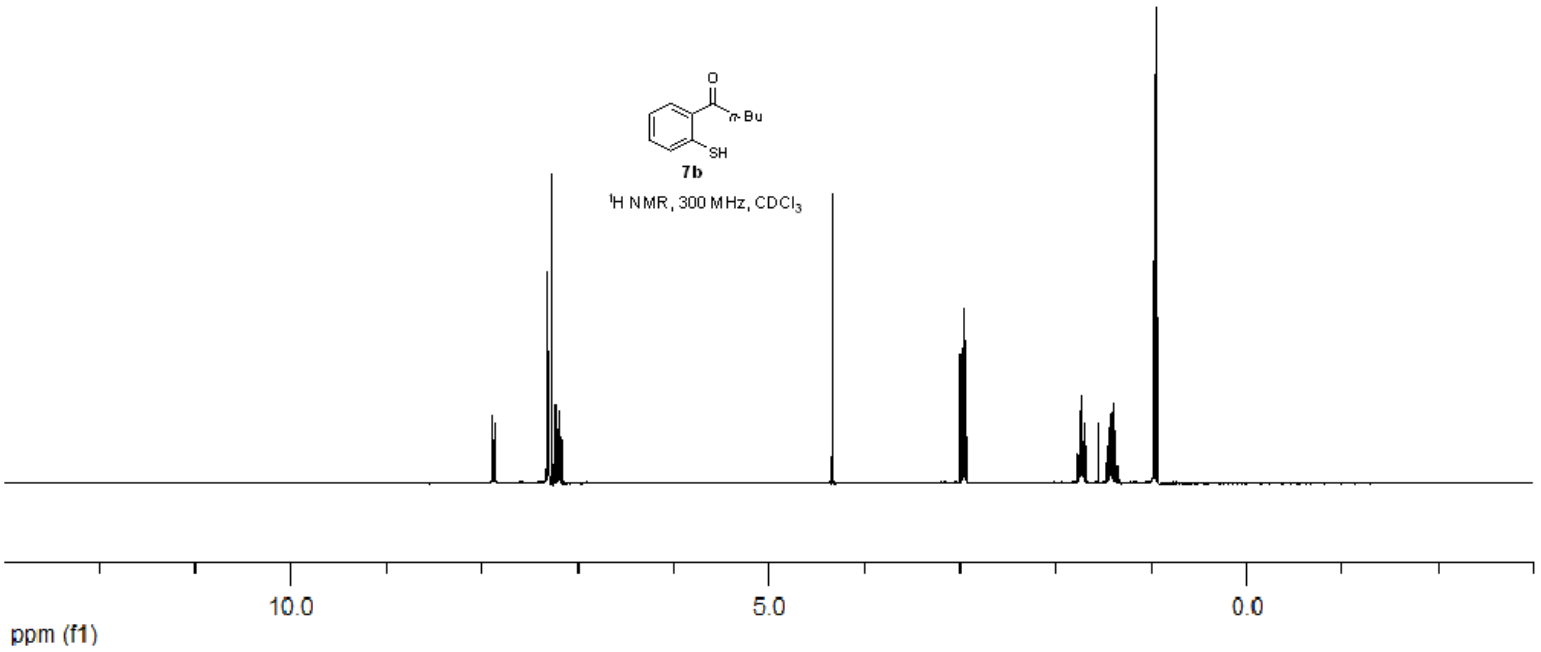
200
150
100
50
0
ppm (f1)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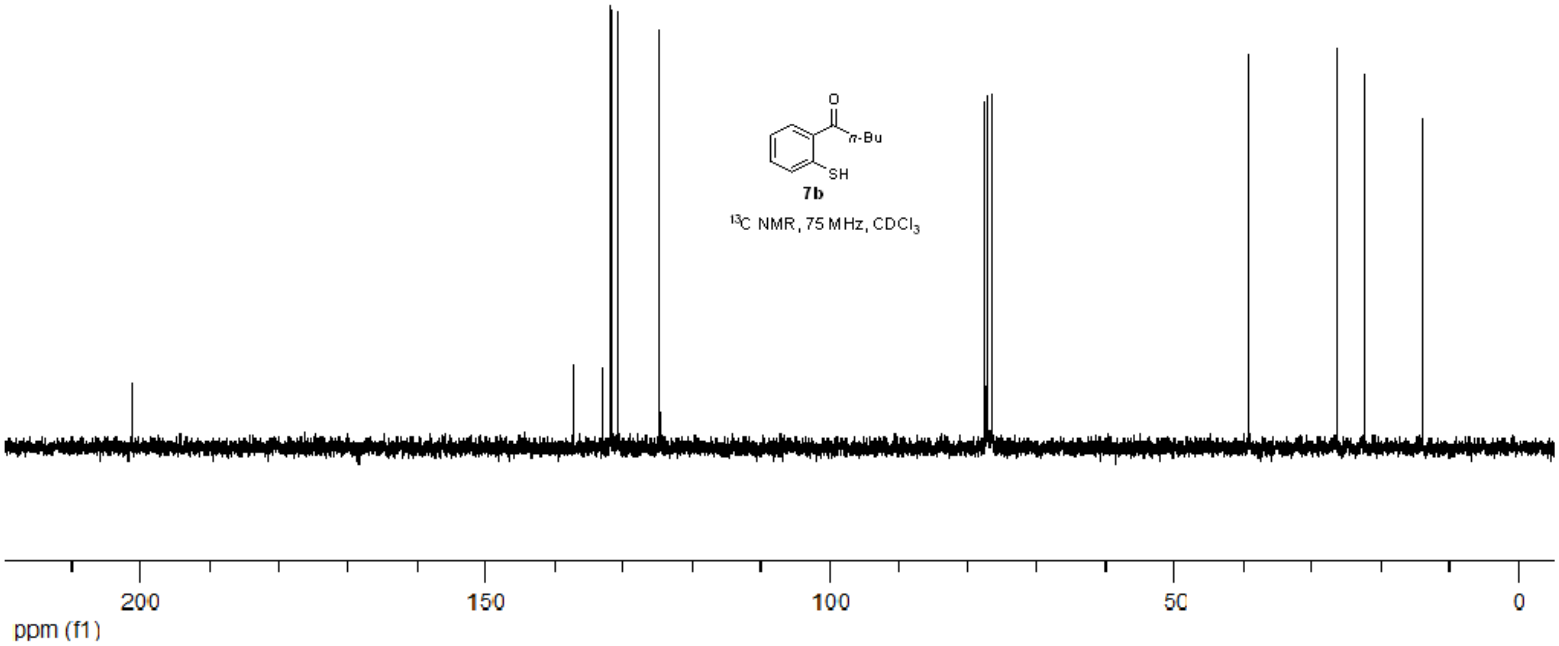
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SH
7b
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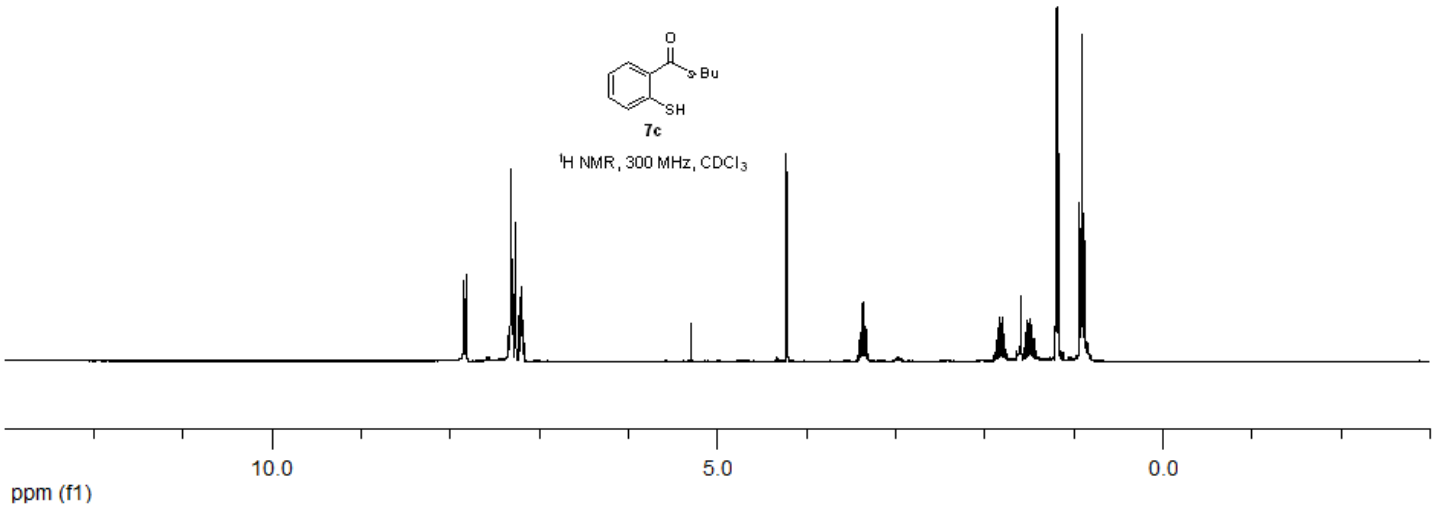
200
150
100
50
0
ppm (f1)


O
s-Bu
SH
7c
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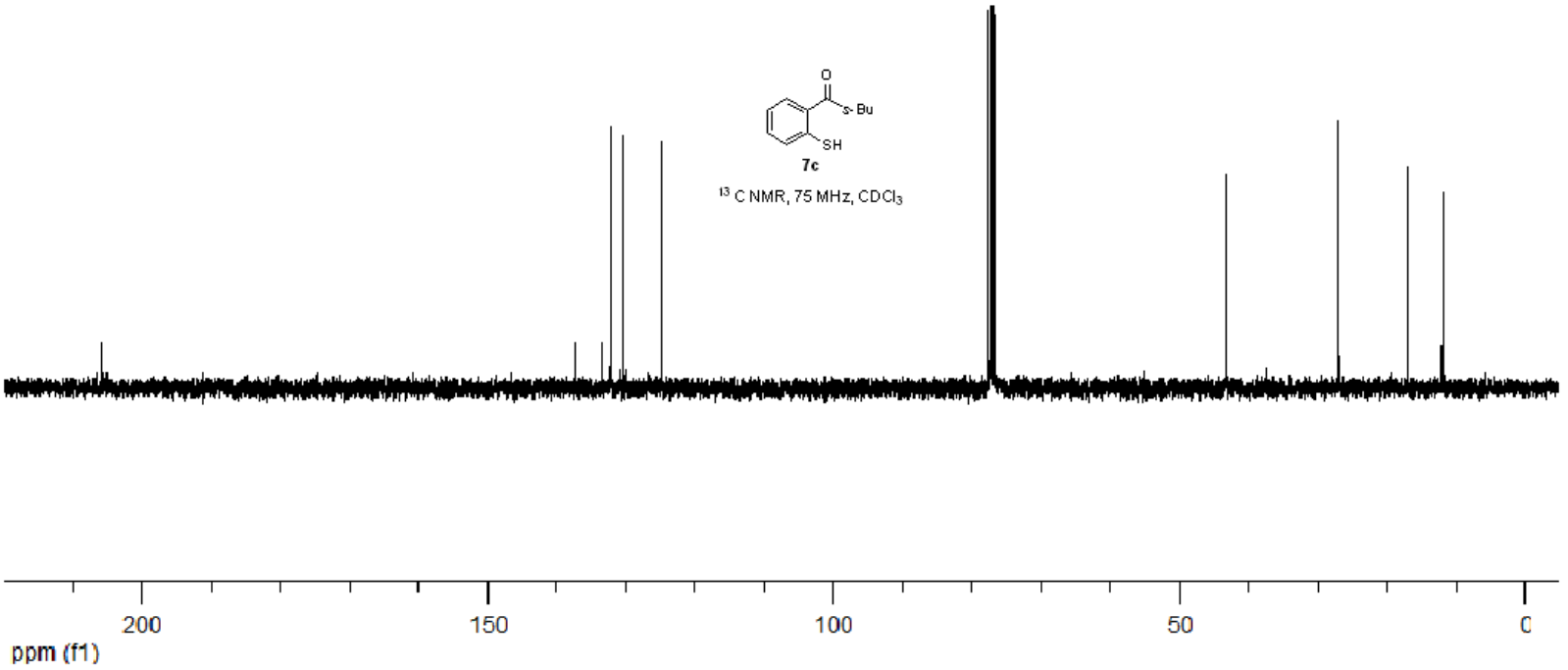
5.0
0.0
ppm (f1)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s-Bu
SH
7c
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150
100
50
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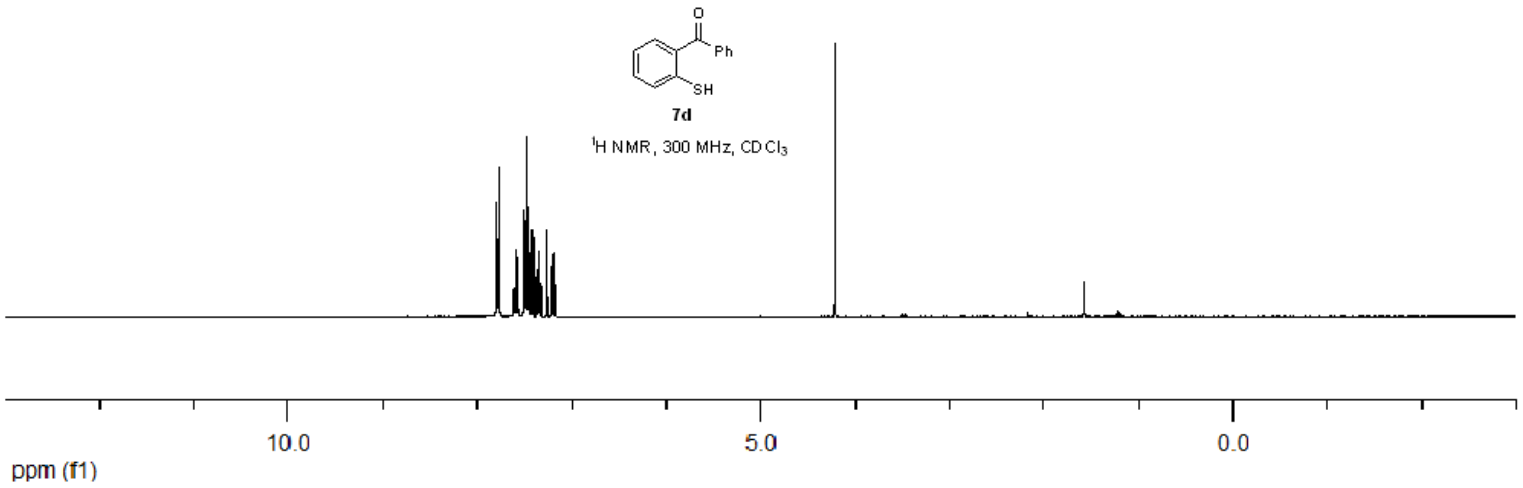
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Ph
SH
7d
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5.0
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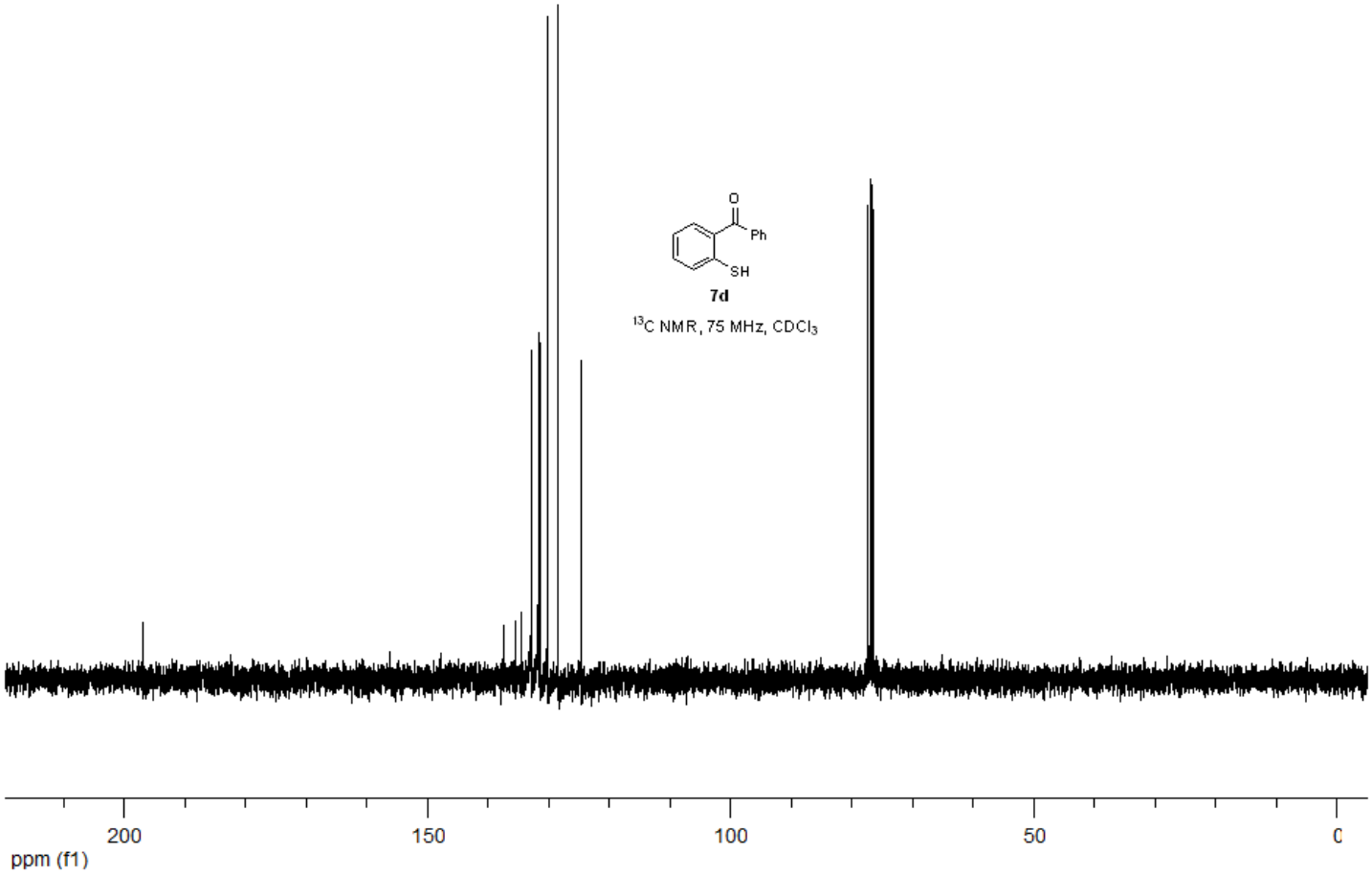
ppm (f1)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Ph
SH
7d
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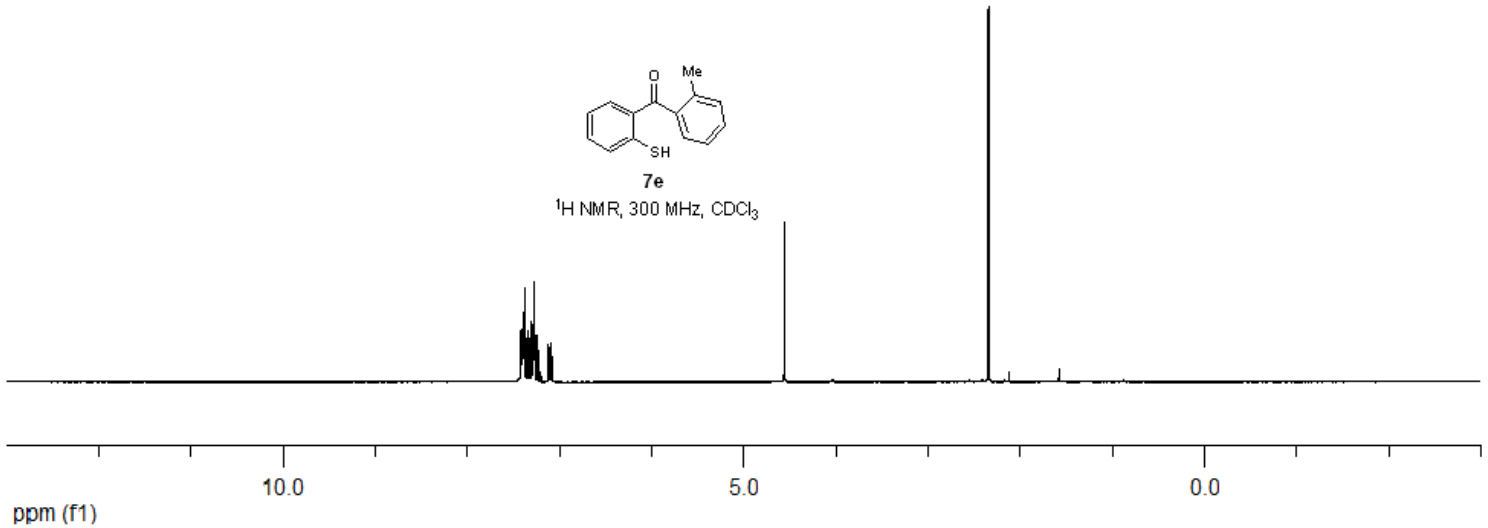
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Me
SH
7e
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10.0
5.0
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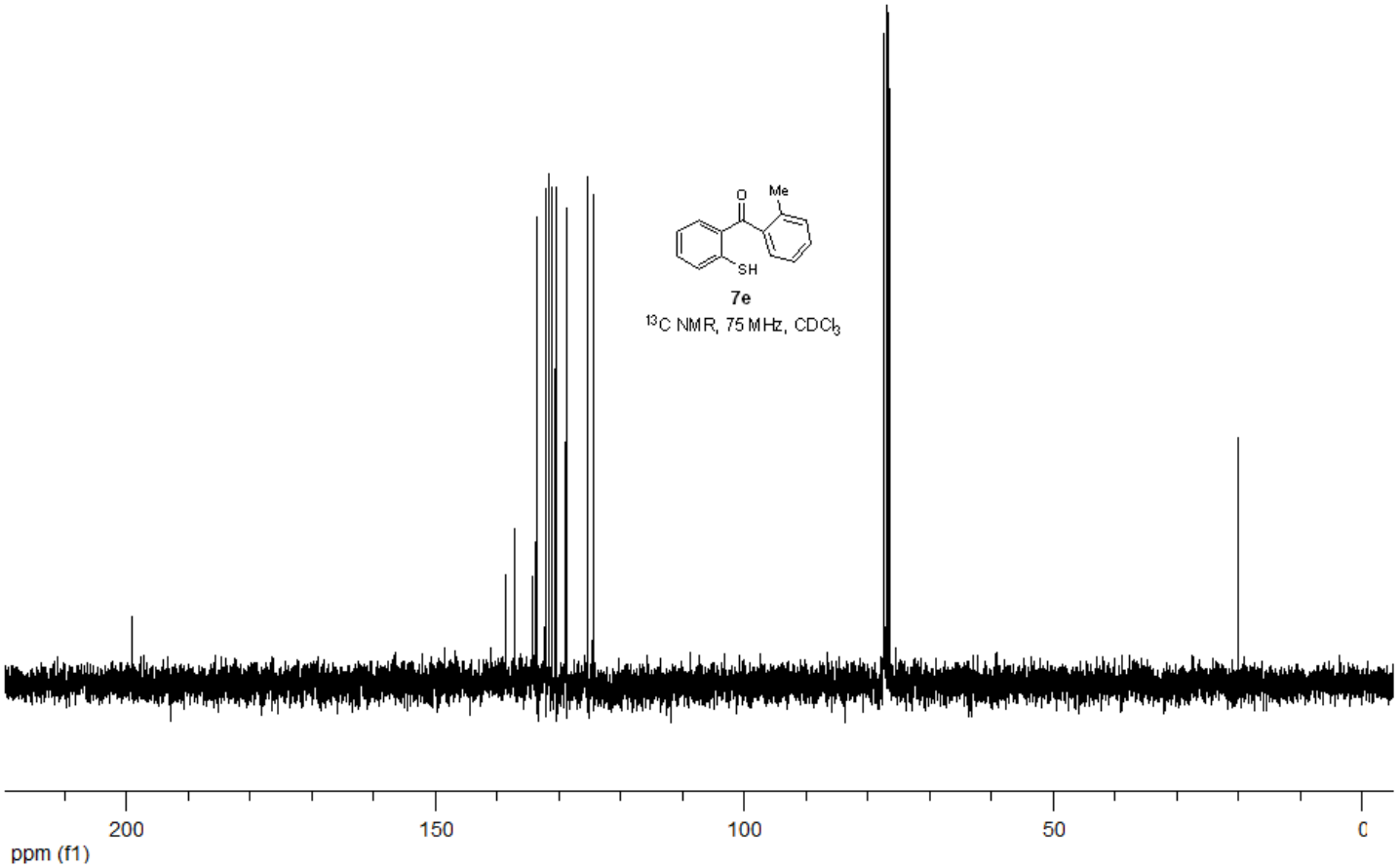
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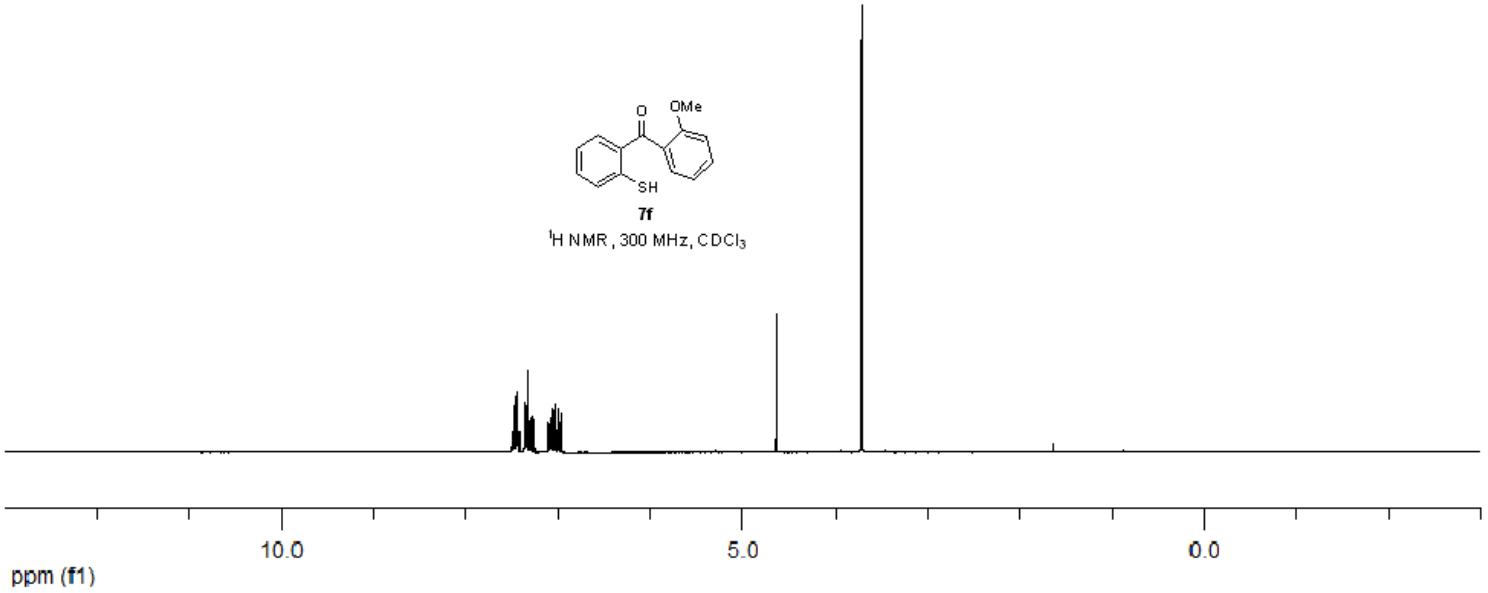
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OMe
SH
7f
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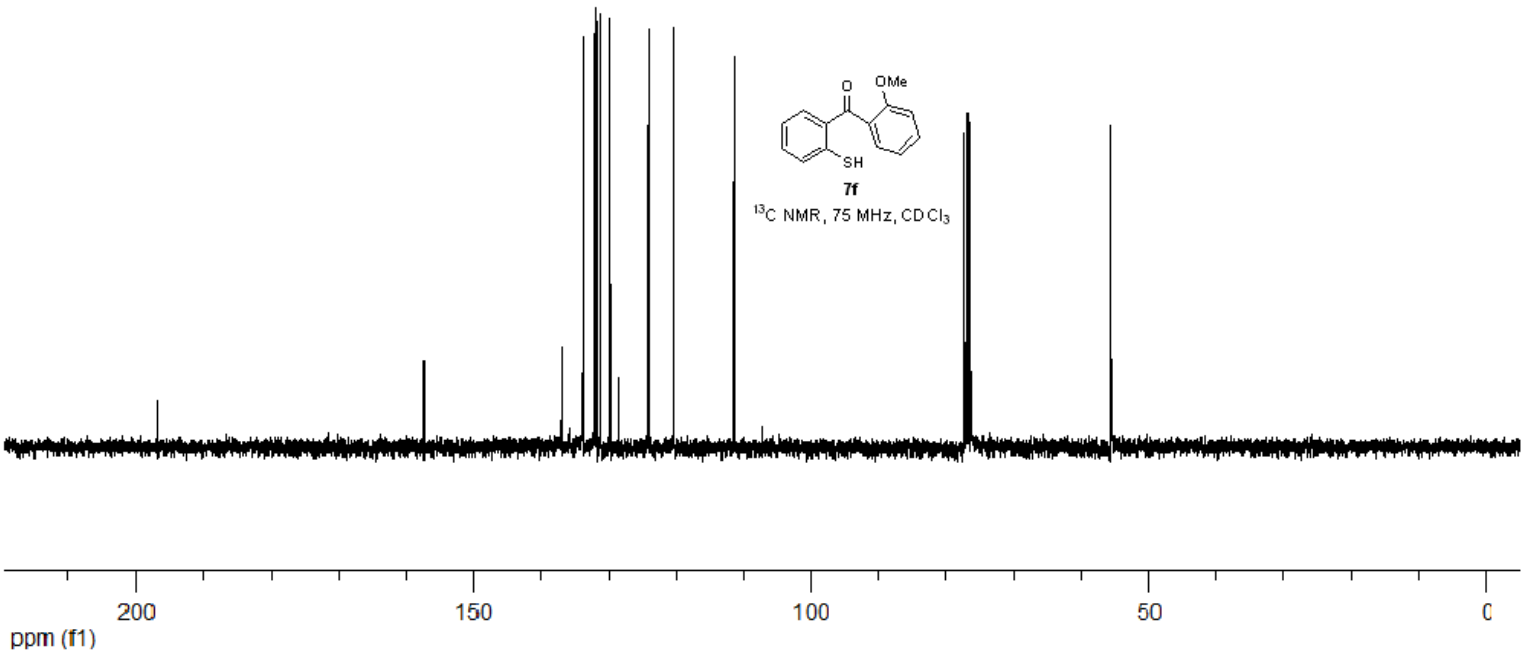
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OMe
SH
7f
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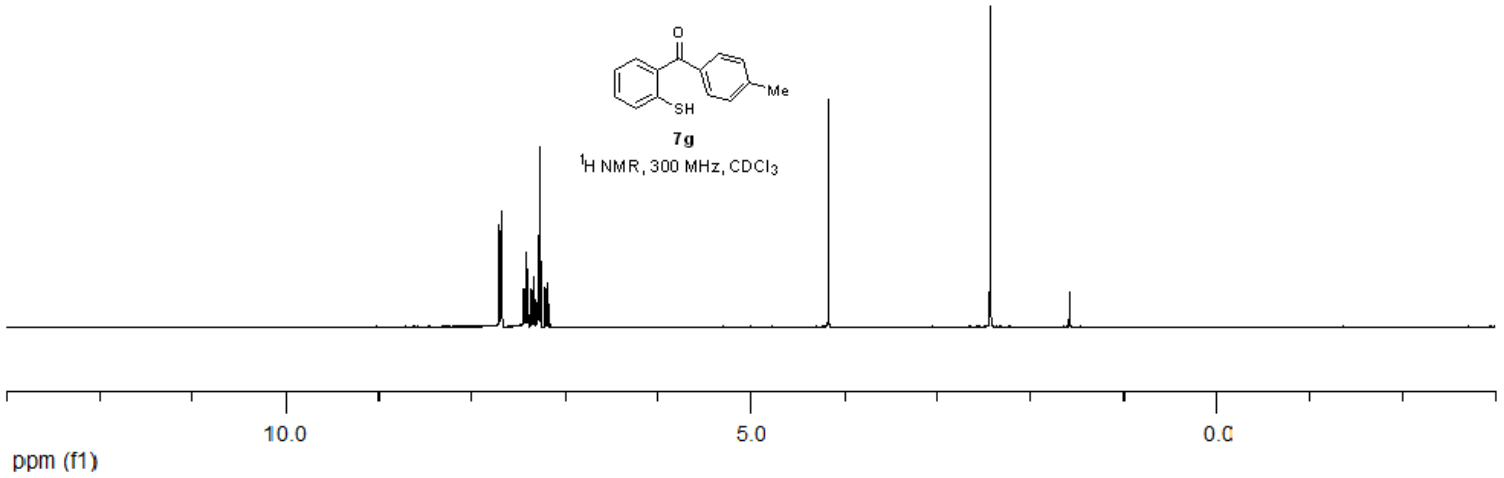
ppm (f1)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SH
Me
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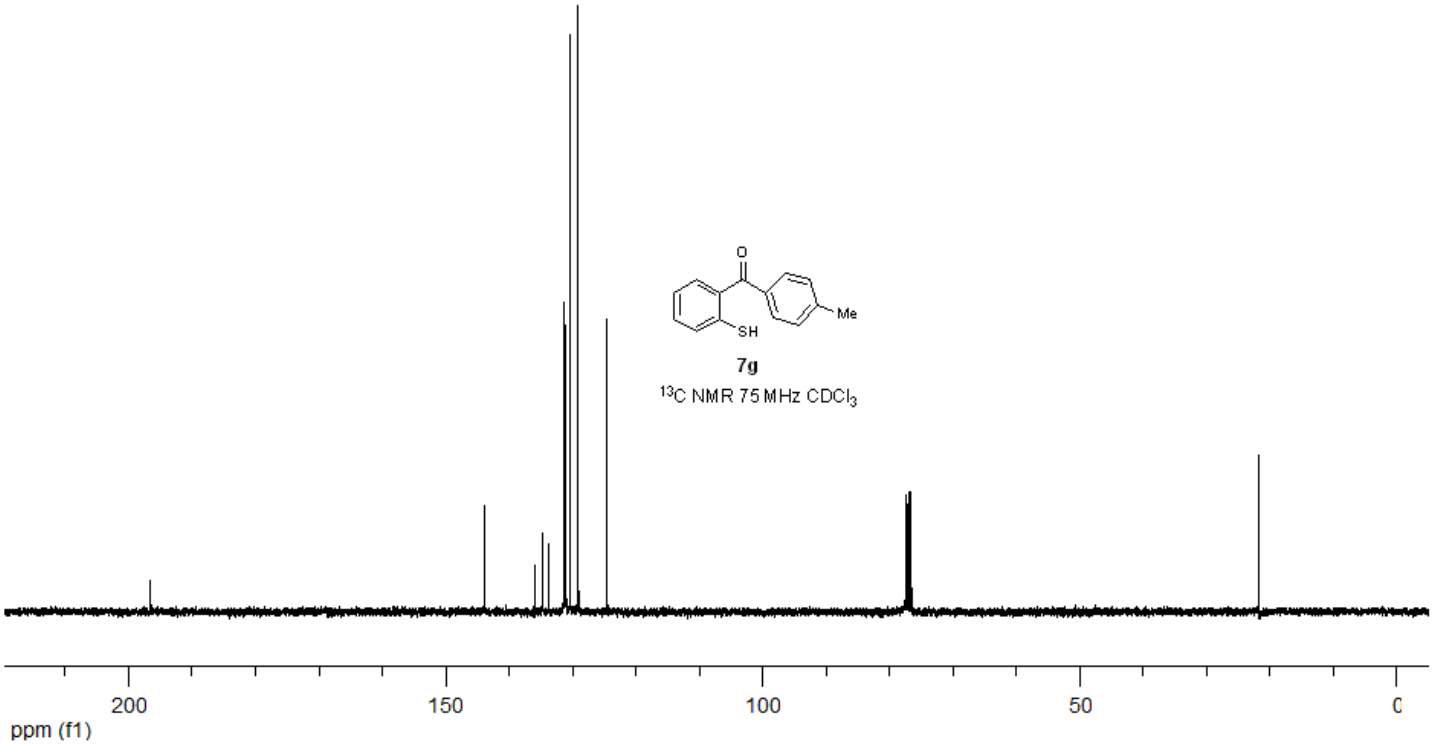
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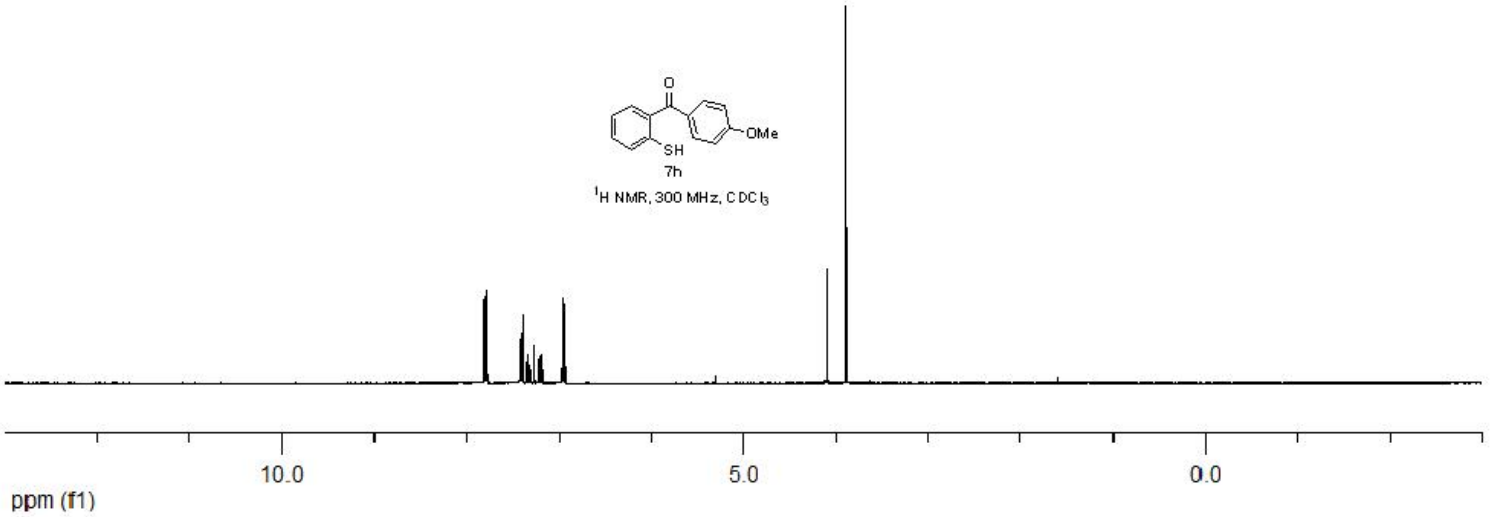
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SH
7h
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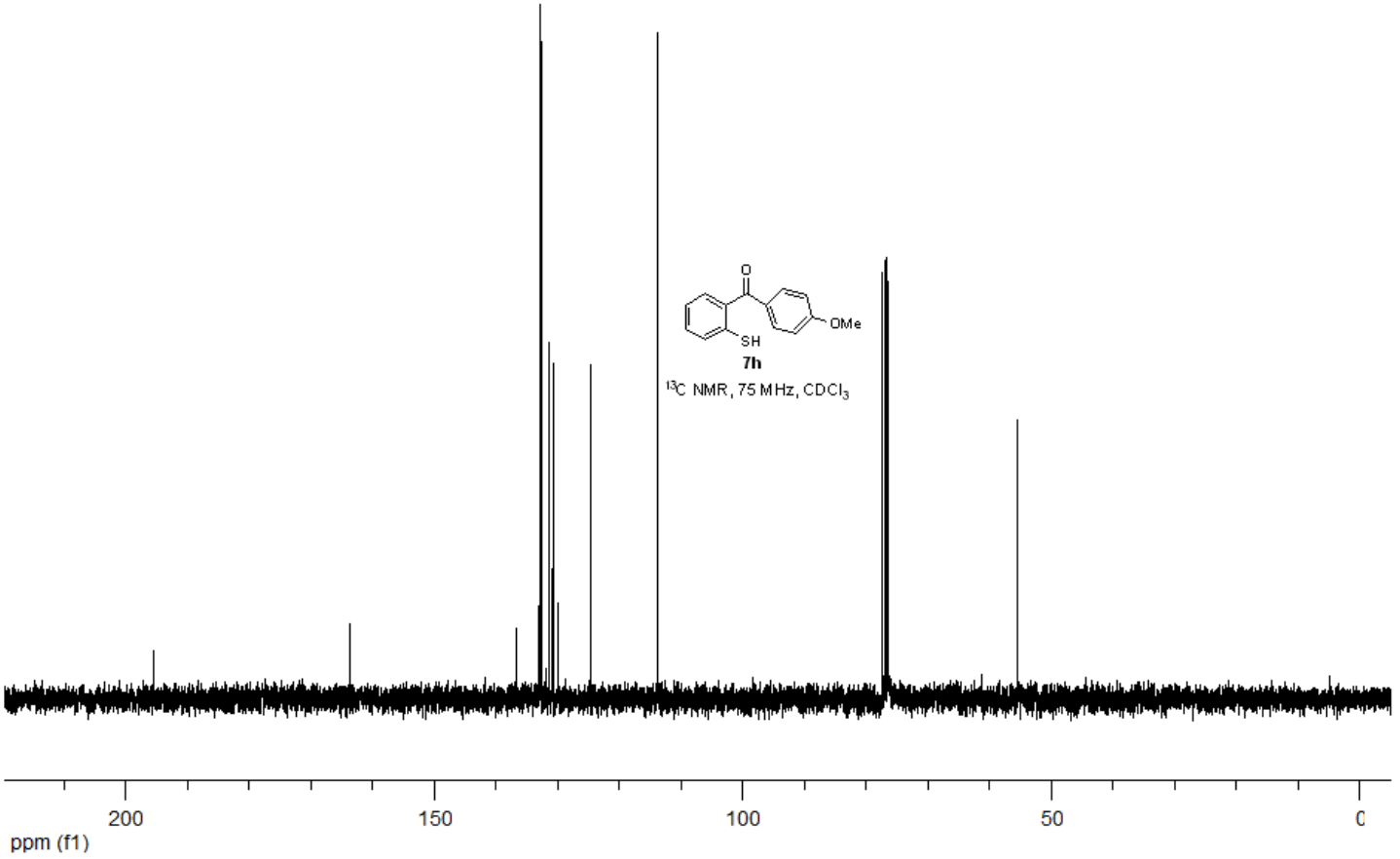
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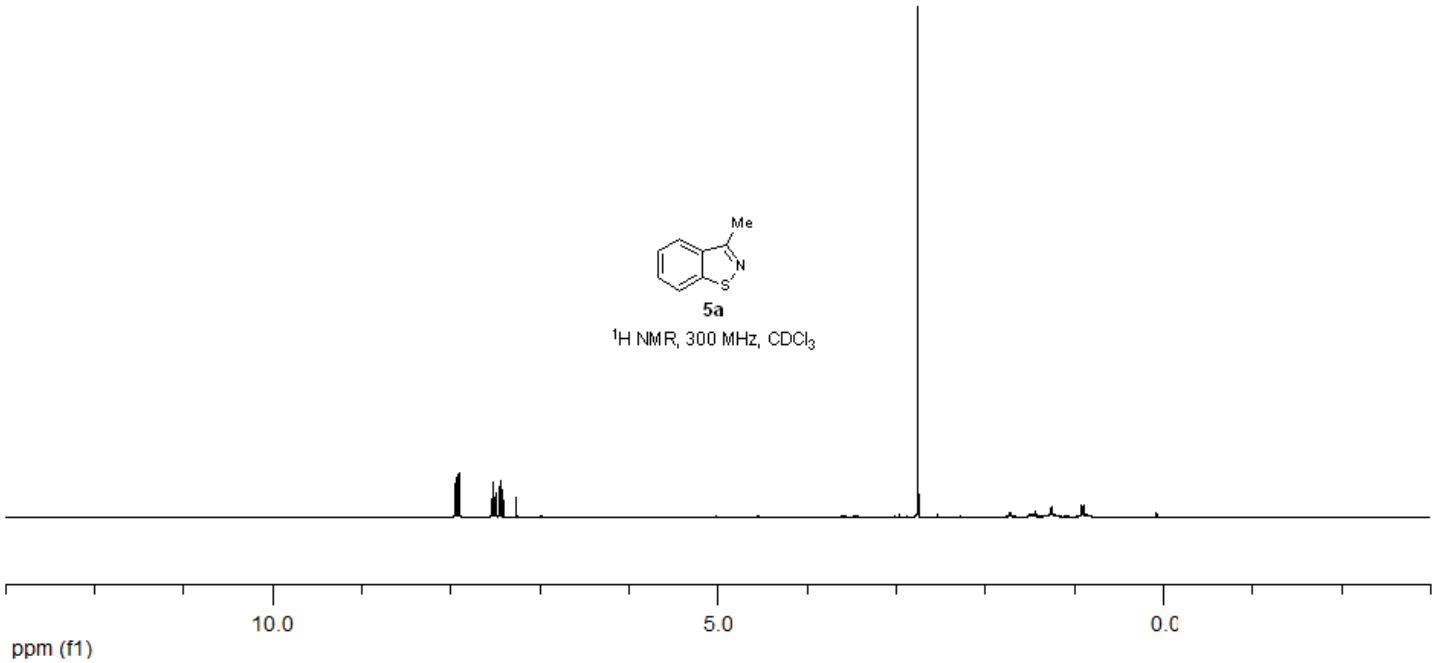
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S
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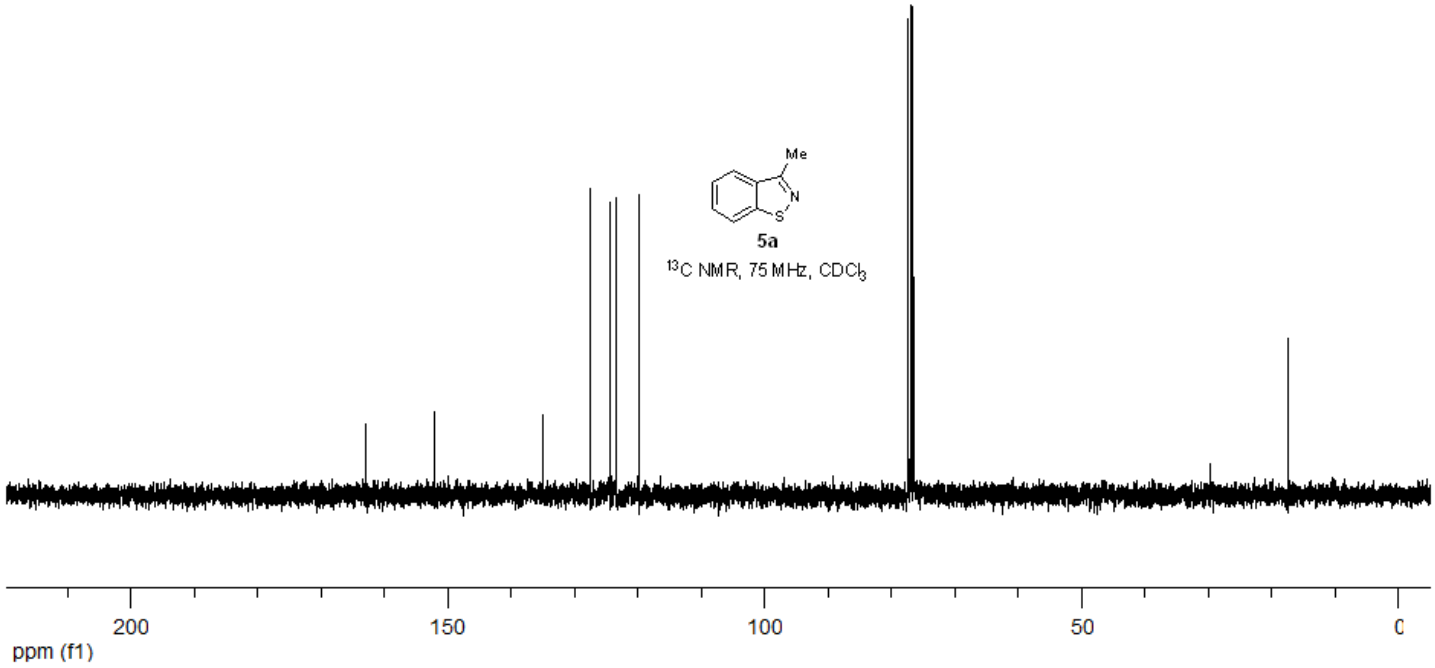
ppm (f1)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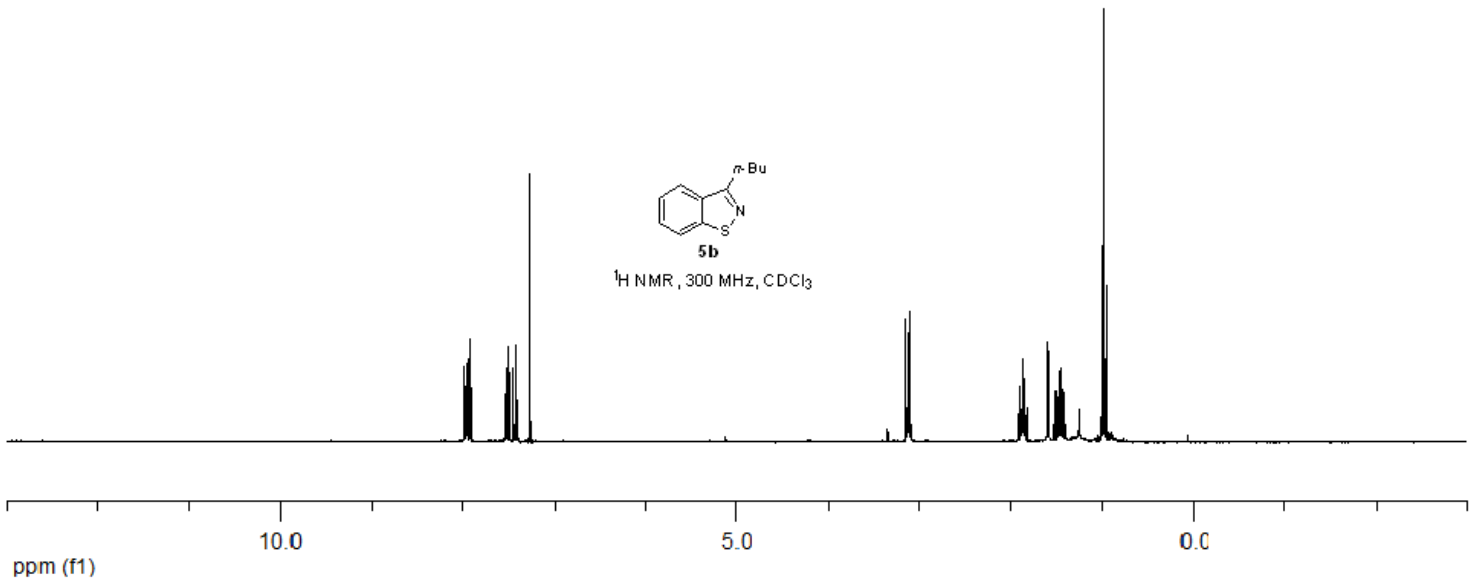
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S
5b
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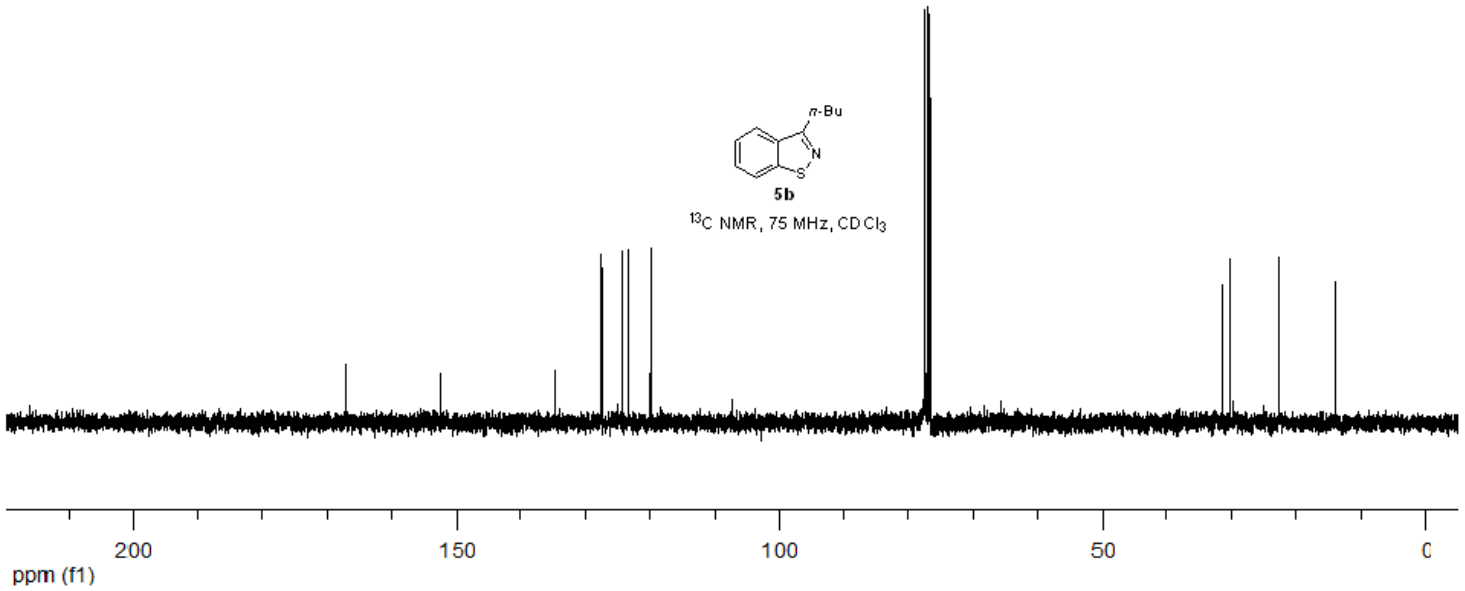
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S
5b
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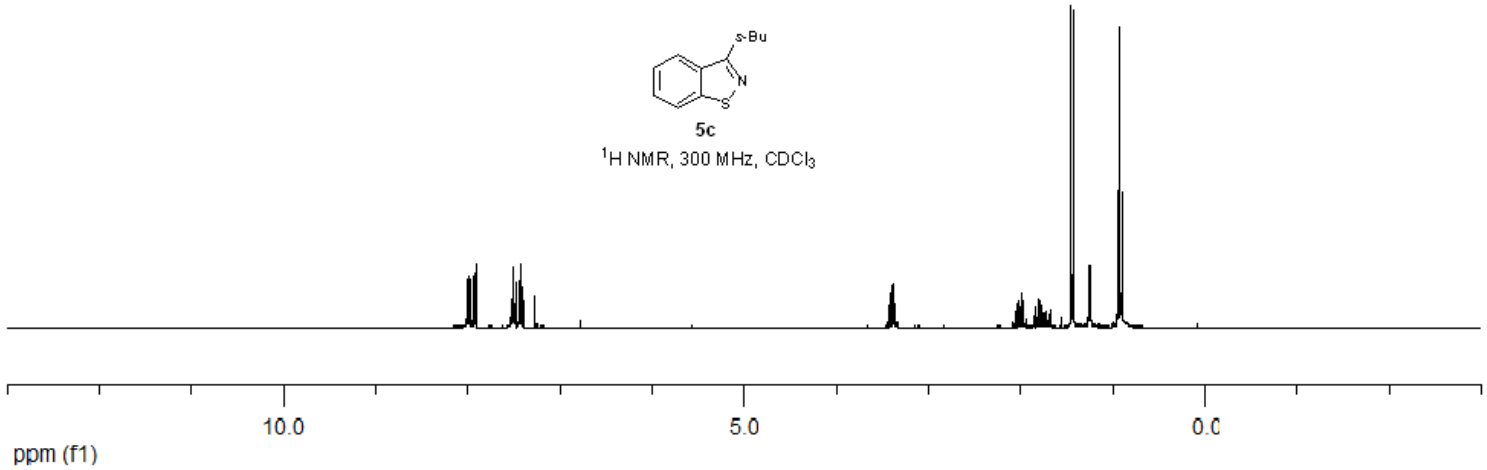
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S
5c
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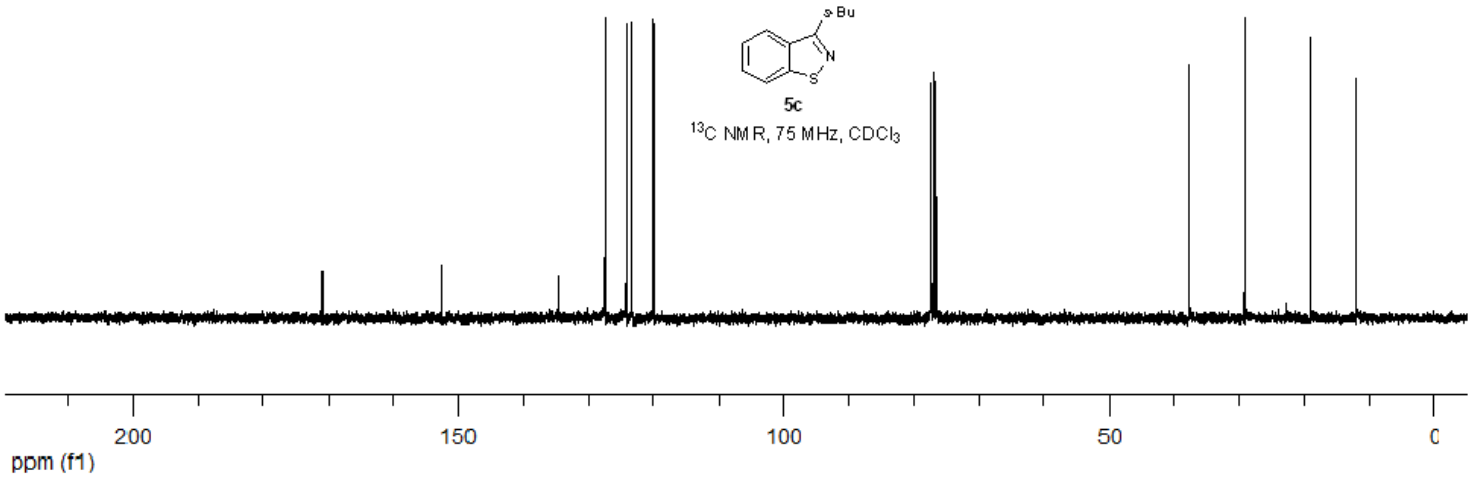
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S
5c
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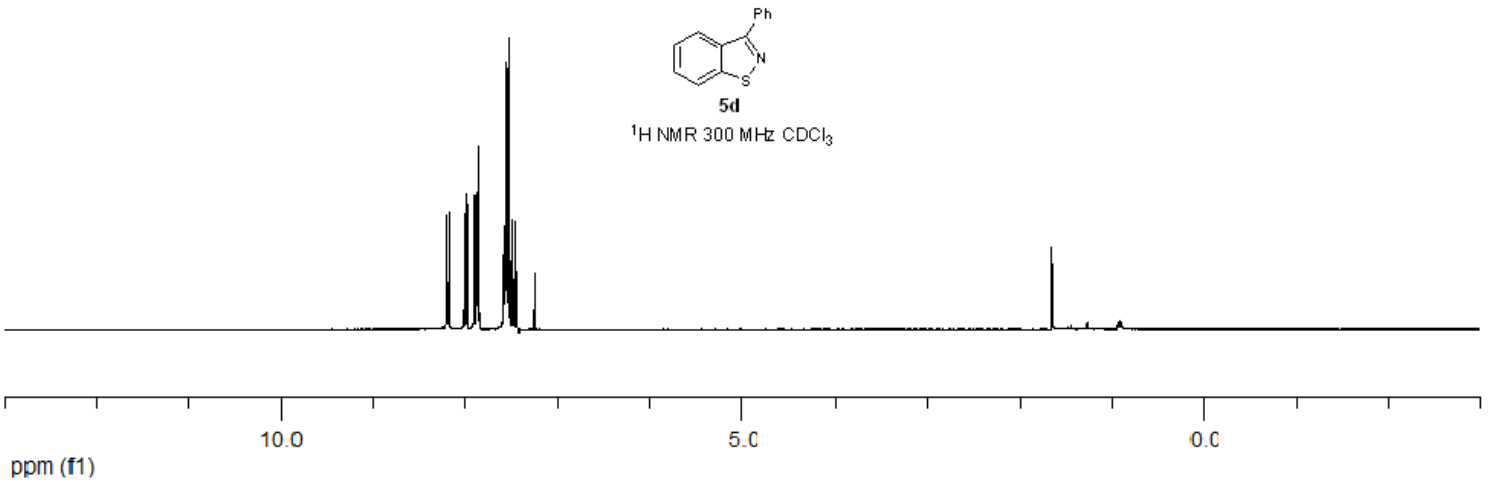
ppm (f1)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S
5d
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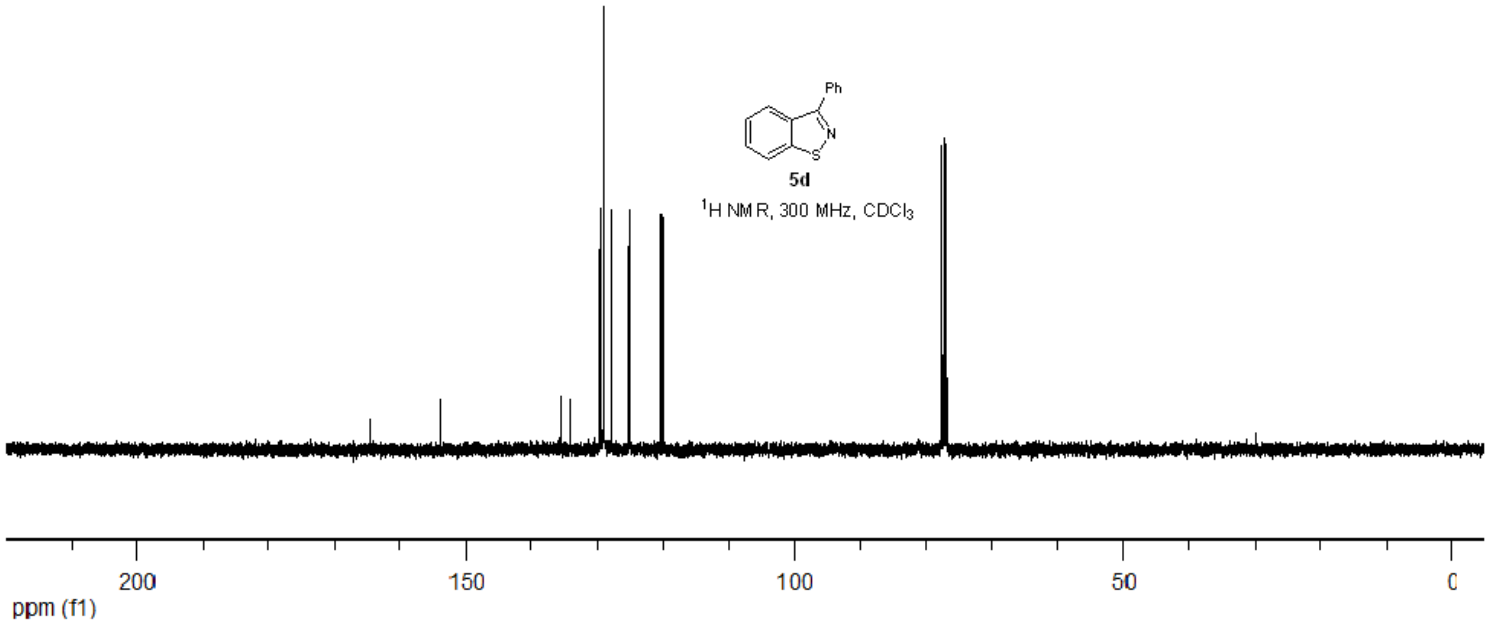
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5d
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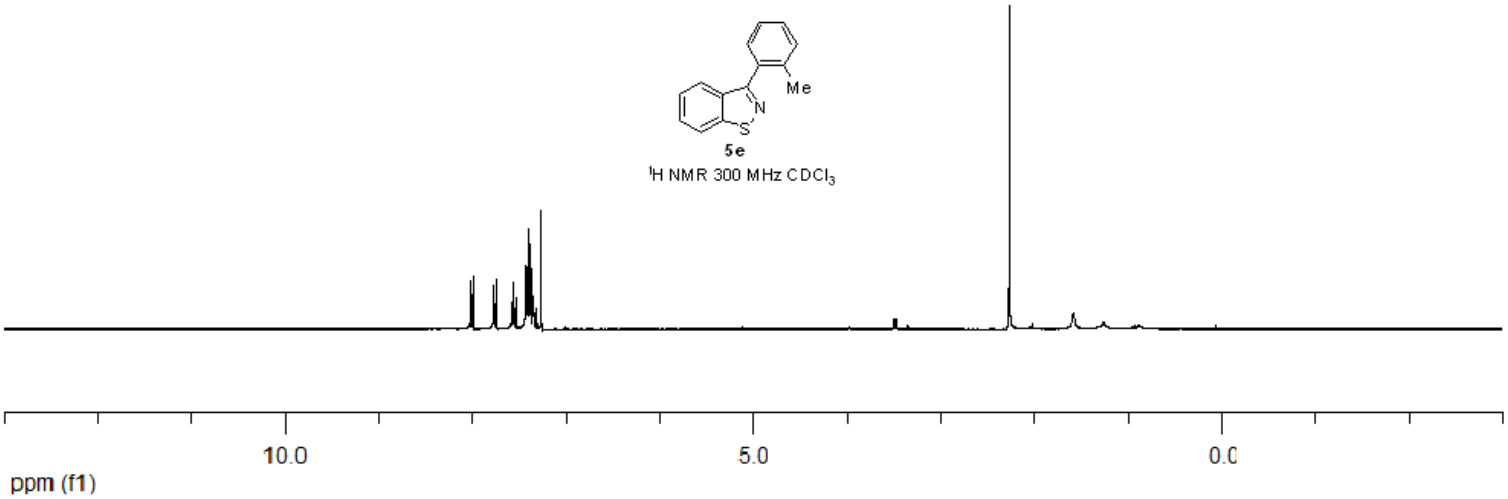
ppm (f1)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S
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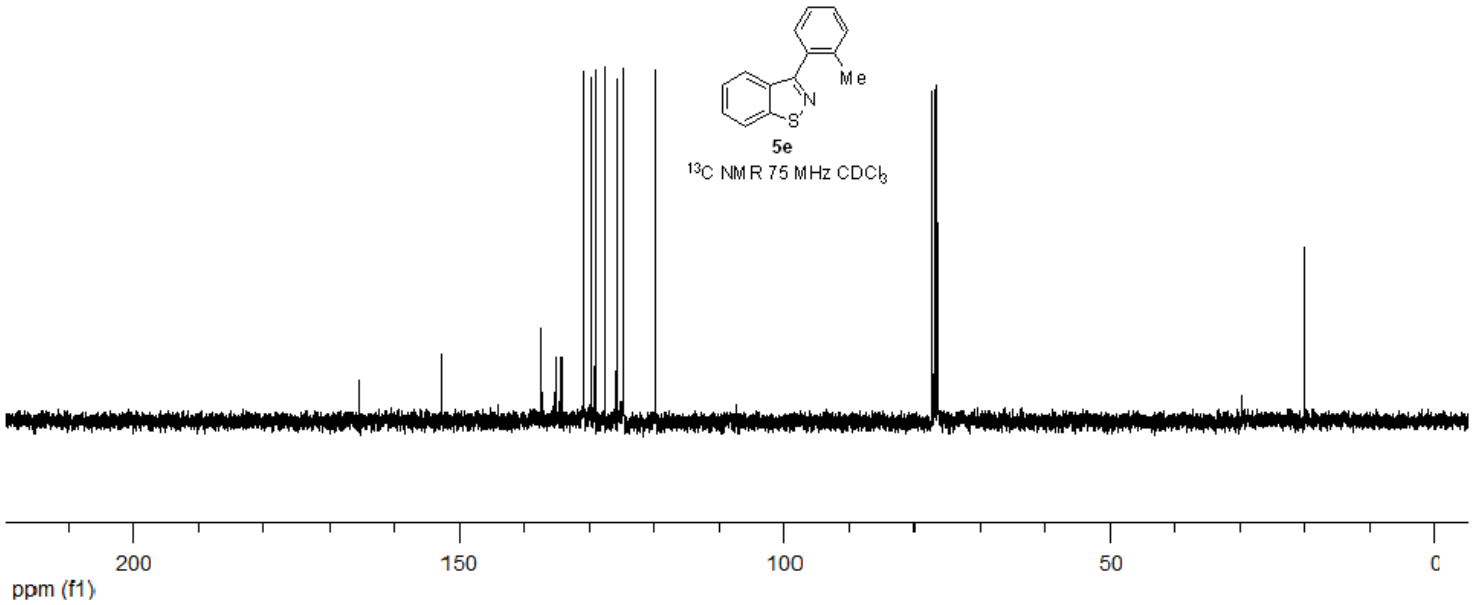
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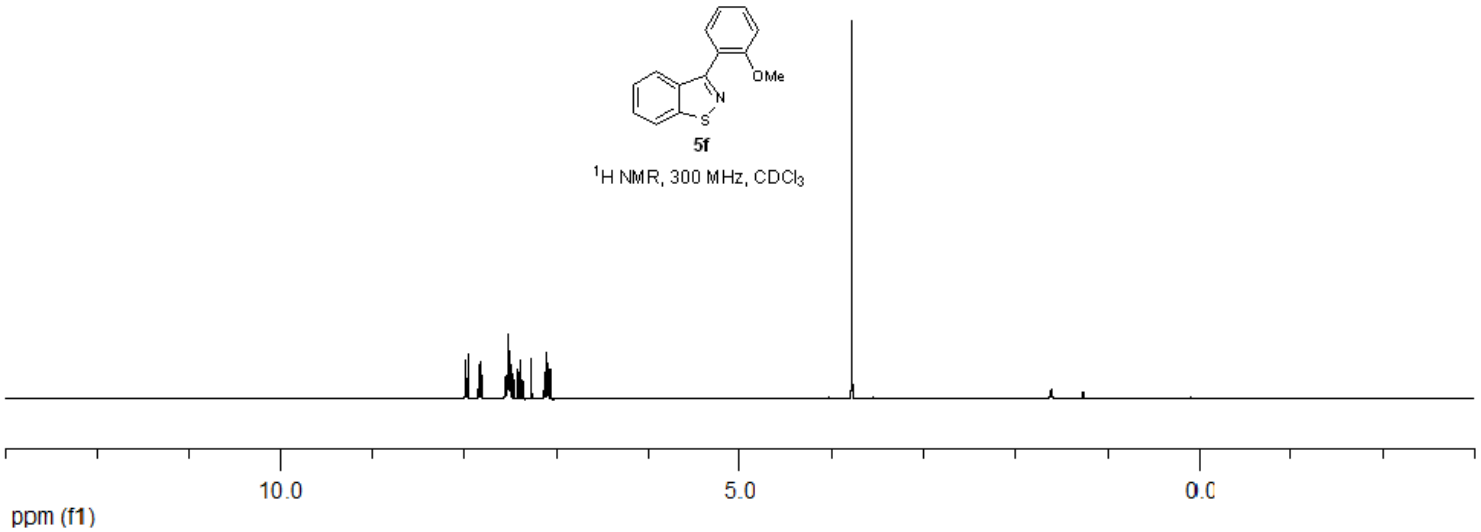
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5f
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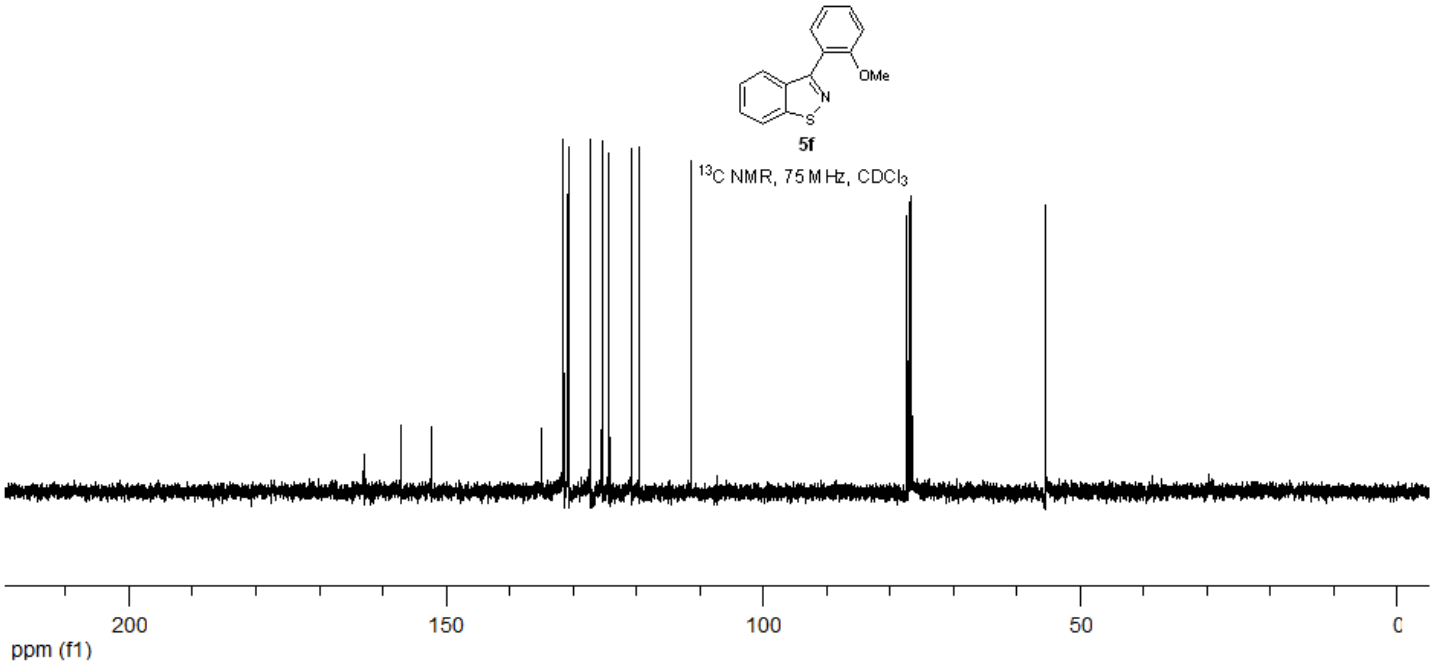
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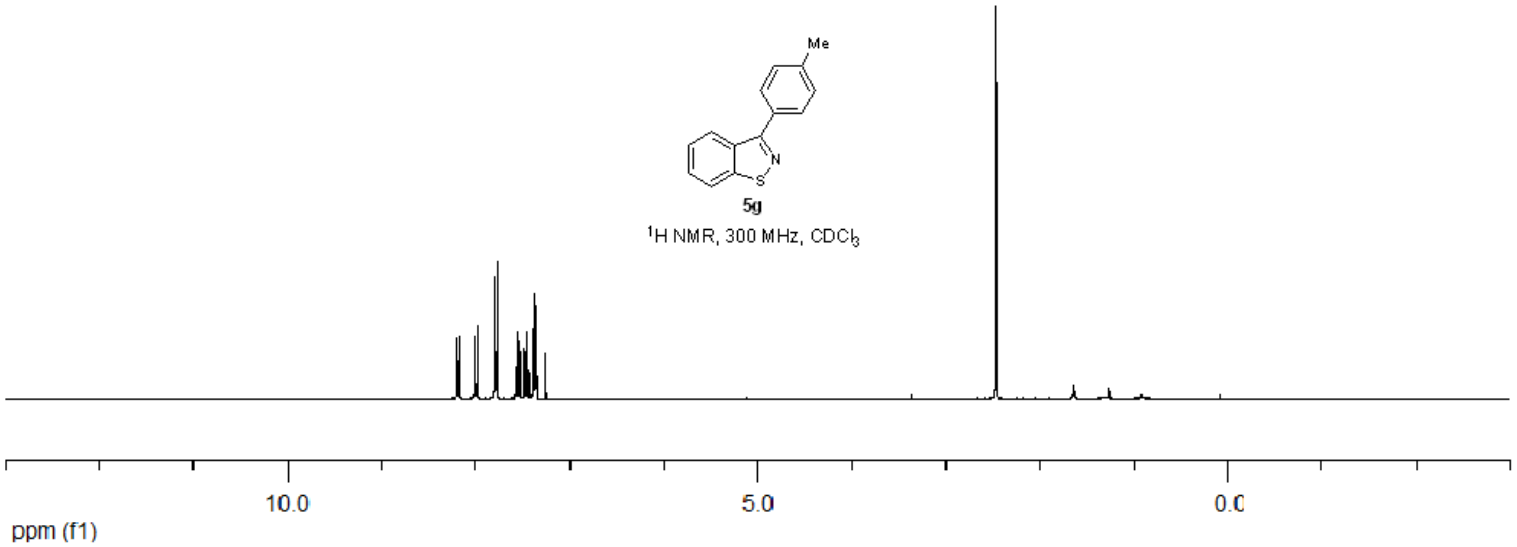
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5g
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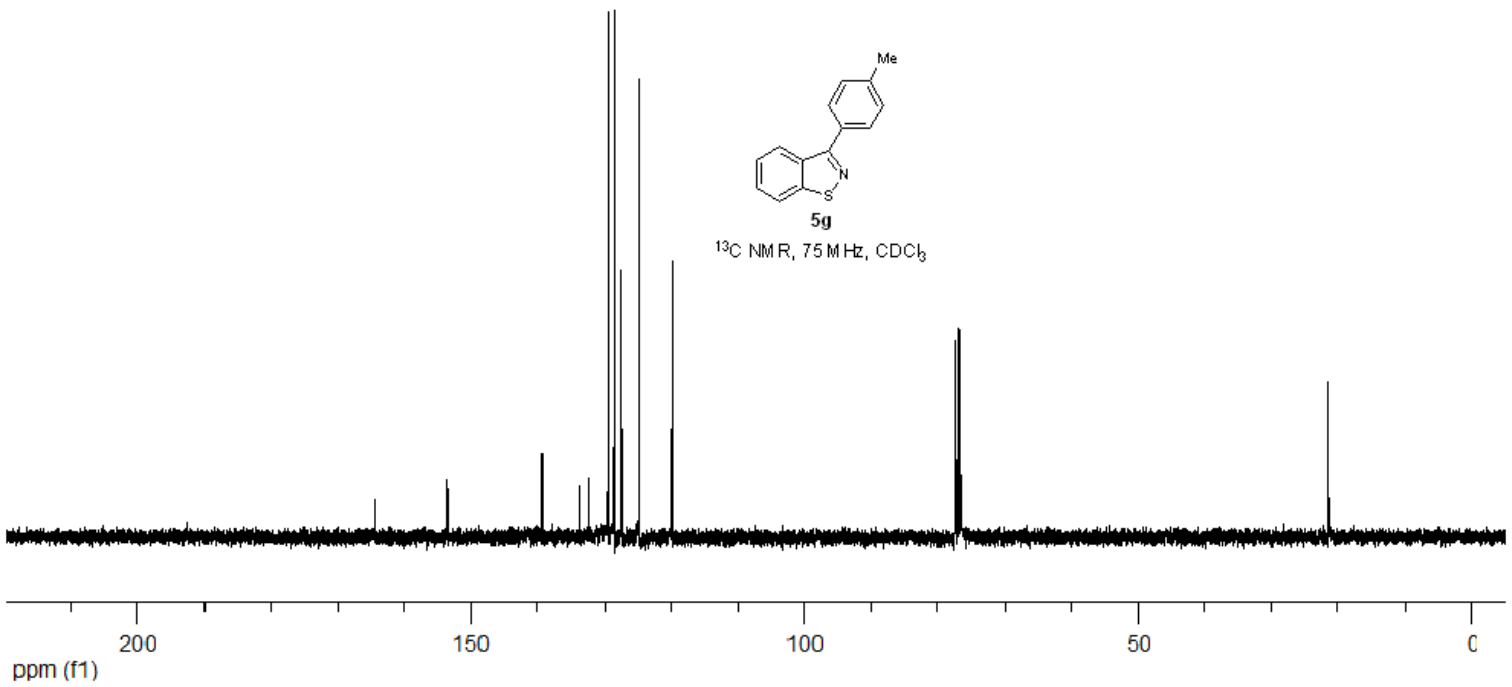
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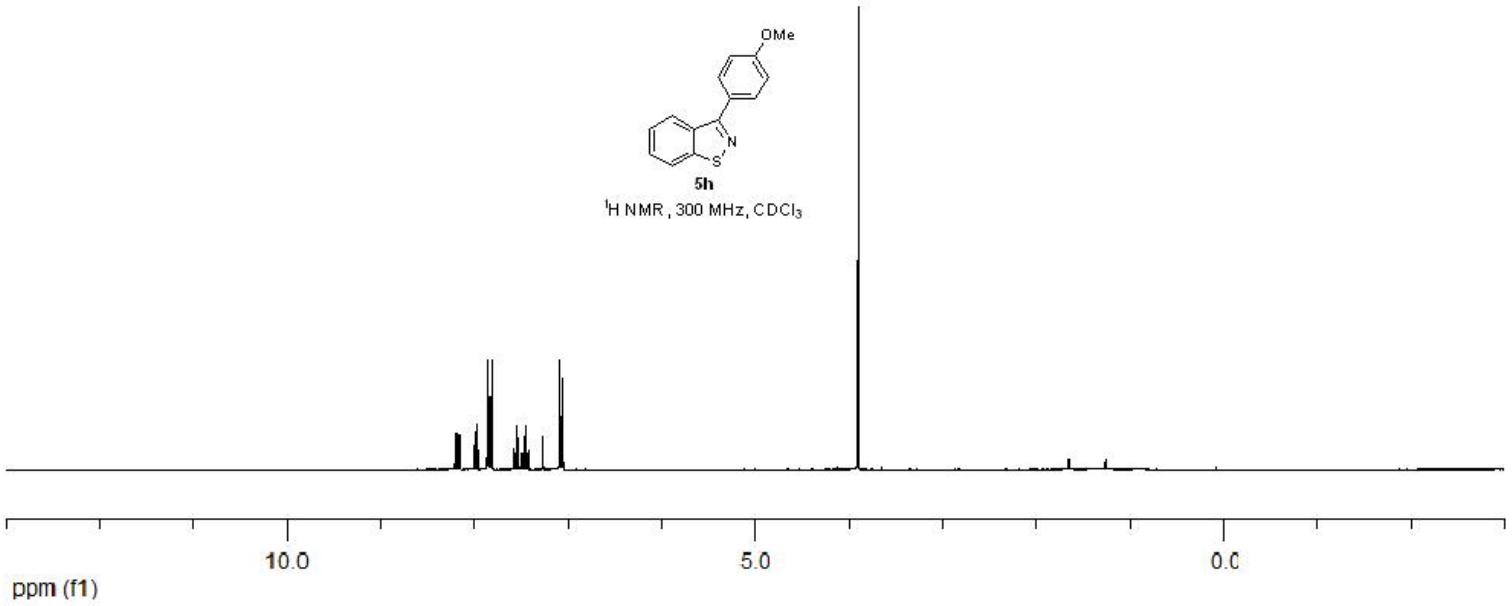
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S
5h
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10.0
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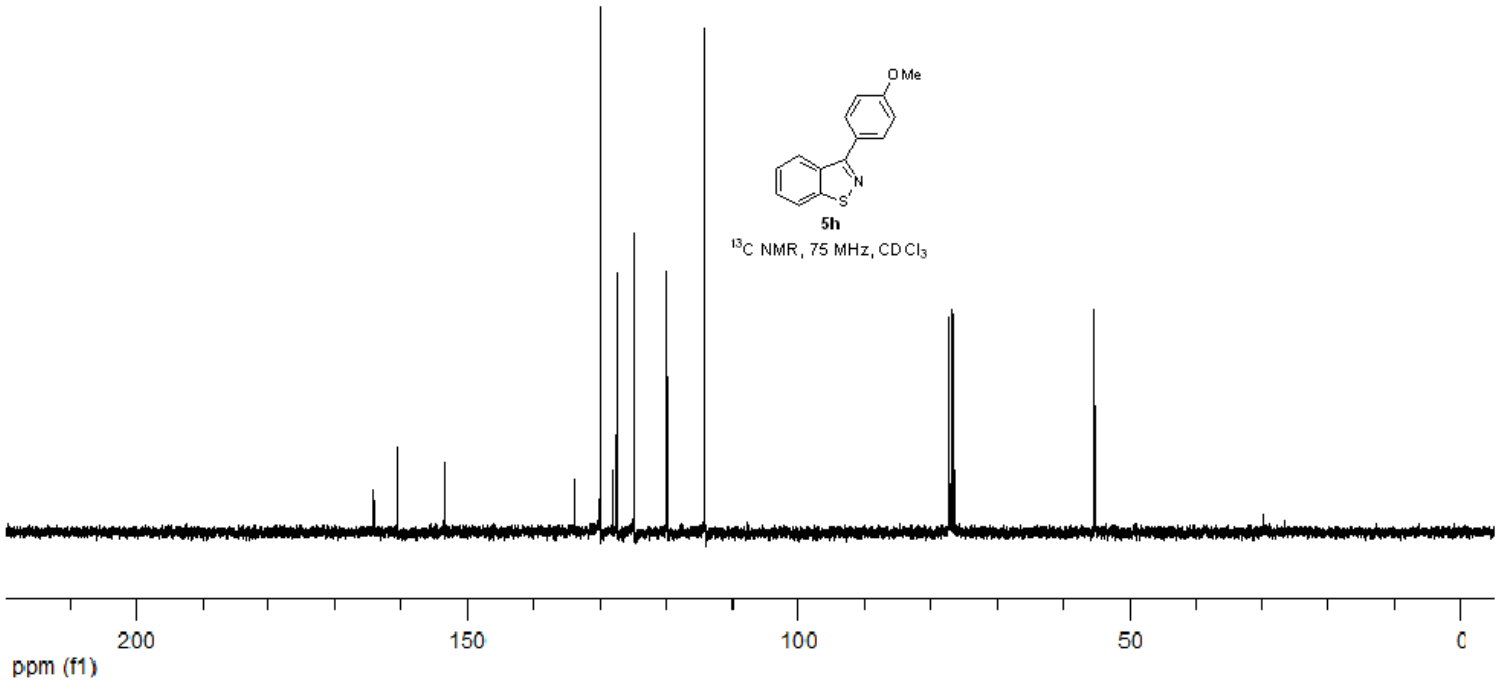
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ppm (f1)