Supporting Information

Palladium-Catalyzed Domino C–S Coupling/Carbonylation Reactions: An Efficient Synthesis of 2-Carbonylbenzo[b]thiophene Derivatives

*Fanlong Zeng, Howard Alper**

Centre for Catalysis Research and Innovation, Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada, K1N 6N5

E-mail: howard.alper@uottawa.ca

Table of Contents

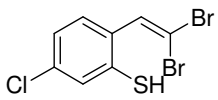
I General Considerations

Unless otherwise noted, all the materials were purchased from commercial suppliers and used as received. Solvents were freshly distilled by standard procedures prior to use. All ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Bruker 400 MHz spectrometer. The NMR chemical shift values refer to $CDCl_3$ (δ (^{1}H), 7.26 ppm; δ (^{13}C), 77.16 ppm). Mass spectra were obtained on a VG7070E mass spectrometer. IR Spectra were recorded on a Shimadzu FTIR−8400S spectrometer. Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

II General Procedures for the Preparation of the Starting Materials

All the 2-*gem*-dihalothiophenols **1a**-**1g** were synthesized according to the literature methods (2-*gem*-thiophenols **1a-1d** and **1g** were prepared using the procedure A, and 2-*gem*-thiophenols **1e** and **1f** were generated by the procedure B).[a]

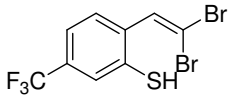
2-*Gem*-dibromovinyl-5-chlorobenzothiol



1b

^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.45-7.37 (m, 2 H), 7.37-7.32 (m, 1 H), 7.14-7.20 (m, 1 H), 3.44 (s, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 134.7, 134.6, 133.4, 132.8, 130.7, 129.8, 126.2, 94.3; MS (EI) *m/z* 326 [M^+]; HRMS (EI) m/z calcd for $C_8H_5Br_2ClS$ [M^+] 325.8167, found 325.8153.

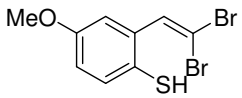
2-*Gem*-dibromovinyl-5-trifluoromethylbenzothiol



1d

^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.55-7.64 (m, 2 H), 7.40-7.52 (m, 2 H), 3.54 (s, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 138.3, 134.6, 132.4, 131.1 (q, J = 33.1 Hz), 130.1, 127.0 (q, J = 2.2 Hz), 123.6 (q, J = 279.8 Hz), 122.7 (q, J = 3.0 Hz), 95.4; MS (EI) *m/z* 360 [M^+]; HRMS (EI) m/z calcd for $C_9H_5Br_2F_3S$ [M^+] 359.8431, found 359.8420.

2-*Gem*-dibromovinyl-4-methoxylbenzothiol



1e

^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.52-7.55 (s, 1 H), 7.26-7.31 (d, J = 8.6 Hz, 1 H), 7.05-7.10 (d, J = 2.8 Hz, 1 H), 6.75-6.87 (dd, J = 8.6 Hz and 2.8 Hz, 1 H), 3.80 (s, 3 H), 3.21 (s, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 158.3, 137.2, 136.0, 133.1, 119.9, 115.2, 114.9, 92.9, 55.5; MS (EI) *m/z* 322 [M^+]; HRMS (EI) m/z calcd for $C_9H_8Br_2OS$ [M^+] 321.8663, found 321.8671.

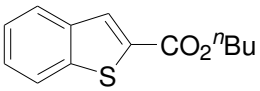
III General Procedure for Synthesis of 2-Carbonylbenzo[b]thiophene Derivatives 3a-3n

Typical procedure for the synthesis of esters: A mixture of **1** (0.50 mmol), base (1.50 mmol), $Pd(OAc)_2$, (0.020 mmol), Ruphos, (0.020 mmol), and 6 mL of MeOH/THF (v/v = 1:1) were sequentially added to a 45 mL glass-lined autoclave. After sealing, the autoclave was purged three times with carbon monoxide, and then pressurized with 150 psi of CO. The resulting mixture was stirred at 110°C for 15 h. The autoclave was cooled to room temperature, and the excess carbon monoxide was released. The reaction mixture was filtered. The filtrate was concentrated in a rotary evaporator. The residue was purified by flash chromatography on silica gel using a mixture of hexanes and ethyl acetate (7:1 to 4:1) as the eluant to afford the products.

Typical procedure for the synthesis of amides: A mixture of **1** (0.50 mmol), the corresponding amine (2.0 mmol), base (1.50 mmol), $Pd(OAc)_2$, (0.020 mmol), Ruphos, (0.020 mmol), and 6 mL of THF were sequentially added to a 45 mL glass-lined autoclave. After sealing, the autoclave was purged three times with carbon monoxide, and then pressurized with 150 psi of CO. The resulting mixture was stirred at 110°C for 15 h. The autoclave was cooled to room temperature and the excess carbon monoxide was released. The reaction mixture was filtered. The filtrate was concentrated in a rotary evaporator. The residue was purified by flash chromatography on silica gel using a mixture of hexanes and ethyl acetate (4:1 to 2:1)

as the eluant to afford the products.

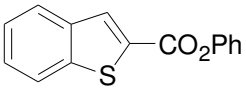
^{n}Butyl benzo[b]thiophene-2-carboxylate



3c

IR (neat) cm^{-1}: 1713, 1526, 1521, 1286, 1245, 1182, 1157, 1078, 1060, 760, 723; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 8.04-8.08 (m, 1 H), 7.82-7.90 (m, 2 H), 7.36-7.49 (m, 2 H), 4.36 (t, J = 6.6 Hz, 2 H), 1.72-1.82 (m, 2 H), 1.43-1.56 (m, 2 H), 1.00 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 163.0, 142.3, 138.9, 134.0, 130.4, 127.0, 125.6, 125.0, 122.9, 65.5, 30.9, 19.4, 13.9; MS (EI) *m/z* 234 [M^+]; HRMS (EI) m/z calcd for $C_{13}H_{14}O_2S$ [M^+] 234.0715, found 234.0697.

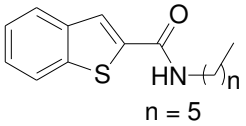
Phenyl benzo[b]thiophene-2-carboxylate



3d

White solid, mp 108-109 ^{o}C; IR (neat) cm^{-1}: 1734, 1722, 1554, 1522, 1494, 1456, 1339, 1275, 1250, 1236, 1180, 1072, 1028, 752, 733, 723, 690; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 8.23-8.26 (d, J = 0.8 Hz, 1 H), 7.86-7.95 (m, 2 H), 7.39-7.51 (m, 4 H), 7.22-7.32 (m, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 161.4, 150.7, 142.8, 138.8, 132.8, 132.0, 129.7, 127.5, 126.3, 125.9, 125.2, 123.0, 121.7; MS (EI) *m/z* 254 [M^+]; HRMS (EI) m/z calcd for $C_{15}H_{10}O_2S$ [M^+] 254.0402, found 254.0385.

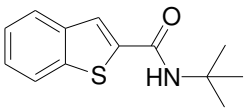
***N*-*n*-hexyl benzo[b]thiophene-2-carboxamide**



3e

Pale yellow solid, mp 49-50 ^{o}C; IR (neat) cm^{-1}: 2927, 2856, 1626, 1564, 1544, 1458, 1431, 1296, 1278, 1204, 758, 743, 723, 710, 669, 636; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.76-7.86 (m, 3 H), 7.33-7.44 (m, 2 H), 6.43 (br, 1 H), 3.40-3.50 (m, 2 H), 1.57-1.68 (m, 2 H), 1.20-1.42 (m, 6 H), 0.81-0.94 (m, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 162.4, 140.8, 139.3, 138.9, 126.3, 125.1, 125.1, 124.9, 122.8, 40.4, 31.6, 29.7, 26.8, 22.7, 14.1; MS (EI) *m/z* 261 [M^+]; HRMS (EI) m/z calcd for $C_{15}H_{19}ONS$ [M^+] 261.1187, found 261.1169.

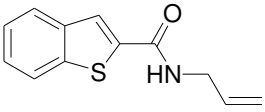
***N-tert*-butyl benzo[b]thiophene-2-carboxamide**



3g

White solid, mp 162-163 ^{o}C; IR (neat) cm^{-1}: 3286, 1632, 1564, 1545, 1456, 1307, 1220, 866, 841, 824, 764, 741, 723; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.79-7.87 (m, 2 H), 7.66-7.69 (d, J = 0.8 Hz, 1 H), 7.36-7.44 (m, 2 H), 5.92 (br. s, 1 H), 1.49 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 161.7, 140.8, 140.2, 139.3, 126.2, 124.9, 124.9, 124.5, 122.7, 52.3, 29.0; MS (EI) *m/z* 233 [M^{+}]; HRMS (EI) m/z calcd for $C_{13}H_{15}ONS$ [M^{+}] 233.0874, found 233.0870.

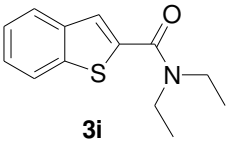
***N*-allyl benzo[b]thiophene-2-carboxamide**



3h

Pale yellow solid, mp 109-111 ^{o}C; IR (neat) cm^{-1}: 3327, 1628, 1595, 1564, 1541, 1508, 1419, 1337, 1300, 1258, 1248, 1213, 989, 916, 758, 739, 717, 629; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.78-7.88 (m, 3 H), 7.36-7.48 (m, 2 H), 6.30 (br. s, 1 H), 5.89-6.02 (m, 1 H), 5.25-5.33 (dq, J = 17 and 1.4 Hz, 1 H), 5.18-5.24 (dq, J = 10 and 1.3 Hz,, 1 H), 4.07-4.14 (tt, J = 5.8 and 1.5 Hz, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 162.4, 140.9, 139.2, 138.5, 133.9, 126.4, 125.4, 125.1, 124.9, 122.8, 117.0, 42.6; MS (EI) *m/z* 217 [M^{+}]; HRMS (EI) m/z calcd for $C_{12}H_{11}ONS$ [M^{+}] 217.0561, found 217.0546.

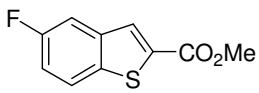
***N*,*N*-diethyl benzo[b]thiophene-2-carboxamide**



3i

IR (neat) cm^{-1}: 2972, 1616, 1522, 1460, 1437, 1421, 1381, 1312, 1281, 1217, 1157, 1074, 822, 754, 727; ^{1}H NMR (400 MHz, $CDCl_3$, 23 ^{o}C): δ 7.76-7.86 (m, 2 H), 7.48 (s, 1 H), 7.32-7.42 (m, 2 H), 3.48-3.62 (q, J = 7.2 Hz, 4 H), 1.26 (t, J = 7.2 Hz, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 ^{o}C): δ 164.3, 140.1, 138.9, 137.9, 125.6, 124.7, 124.5, 124.2, 122.3, 30.4, 12.9; MS (EI) *m/z* 233 [M^{+}]; HRMS (EI) m/z calcd for $C_{13}H_{15}ONS$ [M^{+}] 233.0874, found 233.0862.

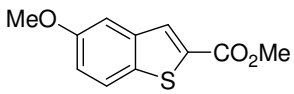
Methyl 5-fluorobenzo[b]thiophene-2-carboxylate



3k

White solid, mp 75-76 °C; IR (neat) cm^{-1}: 1720, 1609, 1526, 1445, 1429, 1327, 1298, 1286, 1254, 1242, 1207, 1186, 1146, 1078, 1063, 922, 881, 804, 752, 714; ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ 7.97-8.01 (d, J = 0.4 Hz, 1 H), 7.75-7.82 (m, 1 H), 7.48-7.55 (dd, J = 9.0 and 2.4 Hz, 1 H), 7.18-7.25 (m, 1 H), 3.95 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 °C): δ 163.0, 161.0 (d, J = 244.3 Hz), 139.7 (d, J = 9.6 Hz), 137.8, 135.8, 130.1 (d, J = 5.2 Hz), 124.2 (d, J = 8.8 Hz), 116.3 (d, J = 25.8 Hz), 110.7 (d, J = 22.8 Hz), 52.7; MS (EI) *m/z* 210 [M^+]; HRMS (EI) m/z calcd for $C_{10}H_7O_2FS$ [M^+] 210.0151, found 210.0133.

Methyl 5-methoxylbenzo[b]thiophene-2-carboxylate



3m

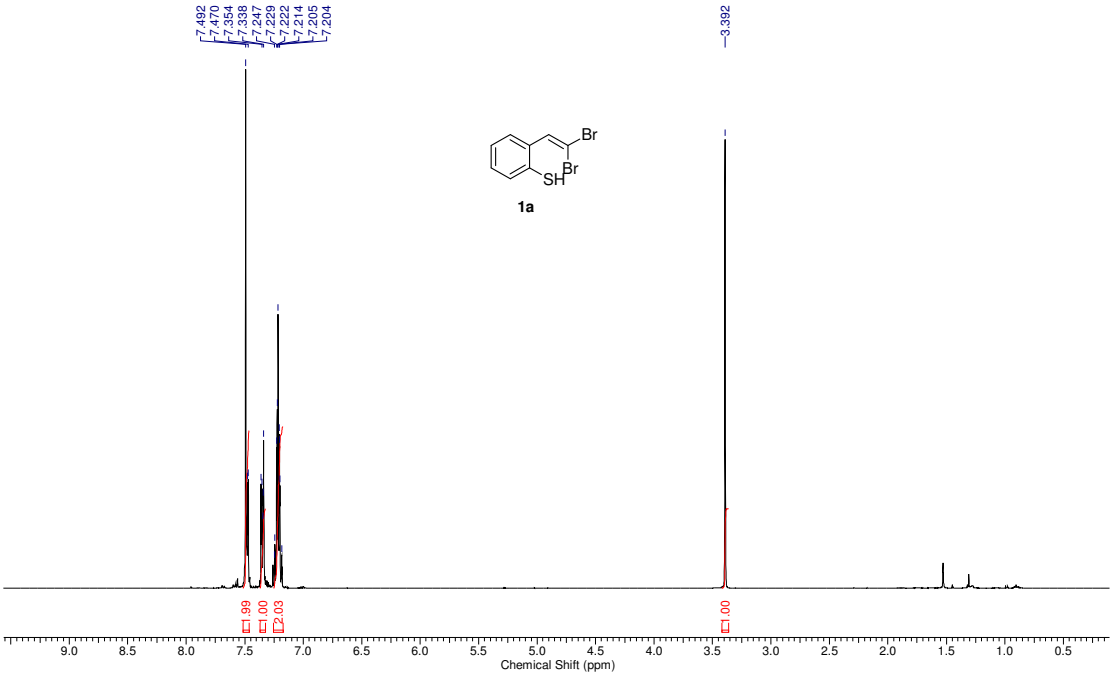
White solid, mp 102-103 °C; IR (neat) cm^{-1}: 1709, 1607, 1526, 1456, 1425, 1342, 1300, 1290, 1229, 1155, 1082, 1020, 926, 872, 833, 798, 754, 714; ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ 7.93-7.97 (d, J = 0.4 Hz, 1 H), 7.66-7.72 (d, J = 8.8 Hz, 1 H), 7.23-7.27 (d, J = 2.4 Hz, 1 H), 7.06-7.12 (dd, J = 8.8 and 2.4 Hz, 1 H), 3.91 (s, 3 H), 3.85 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$, 23 °C): δ 163.4, 157.9, 139.8, 135.0, 134.3, 130.4, 123.6, 118.2, 106.5, 55.6, 52.6; MS (EI) *m/z* 222 [M^+]; HRMS (EI) m/z calcd for $C_{11}H_{10}O_3S$ [M^+] 222.0351, found 222.0332.

Reference:

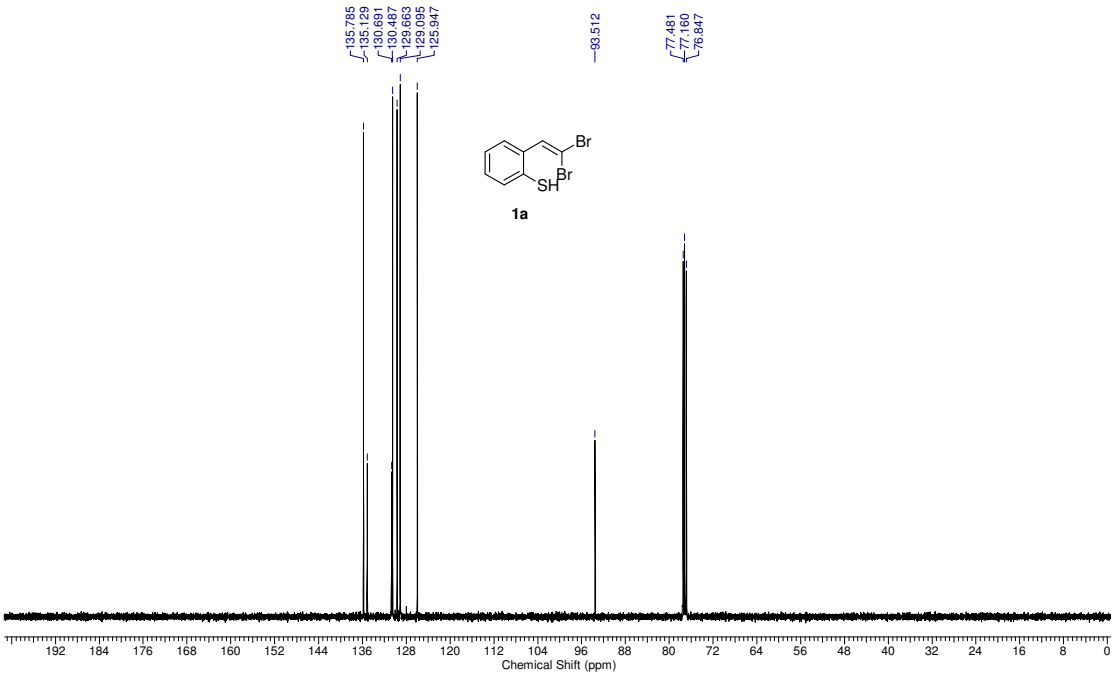
(a) Bryan, C.; Braunger, J. A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 7064.

IV NMR spectra for the starting materials and Products

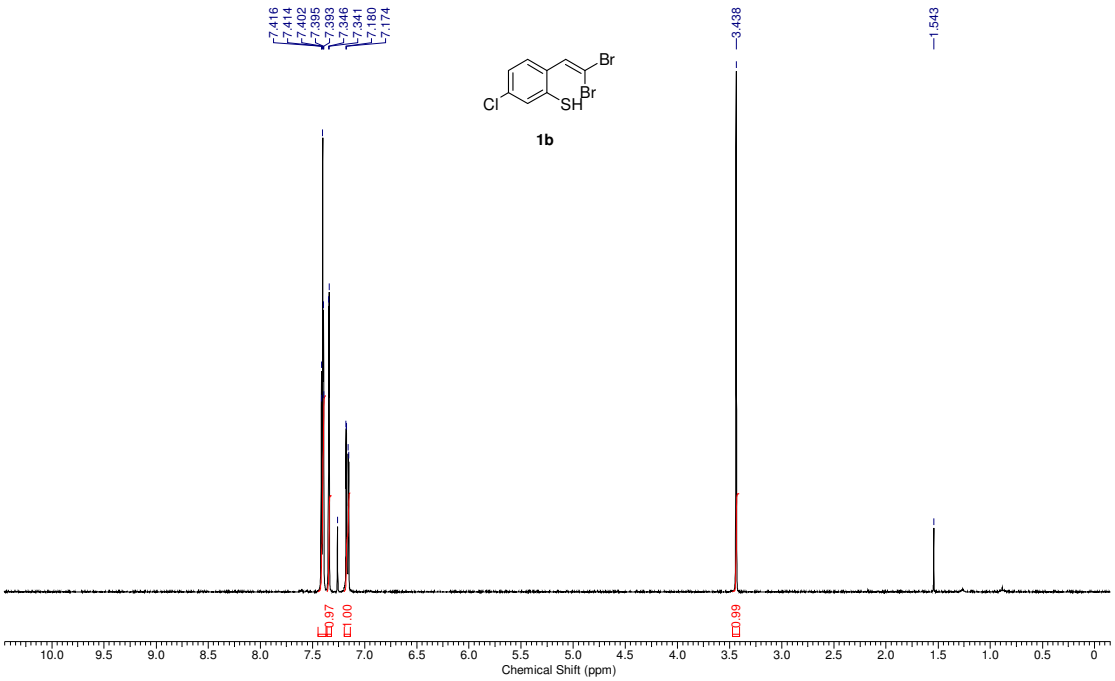
^{1}H NMR of **1a** in $CDCl_3$ (400 MHz)



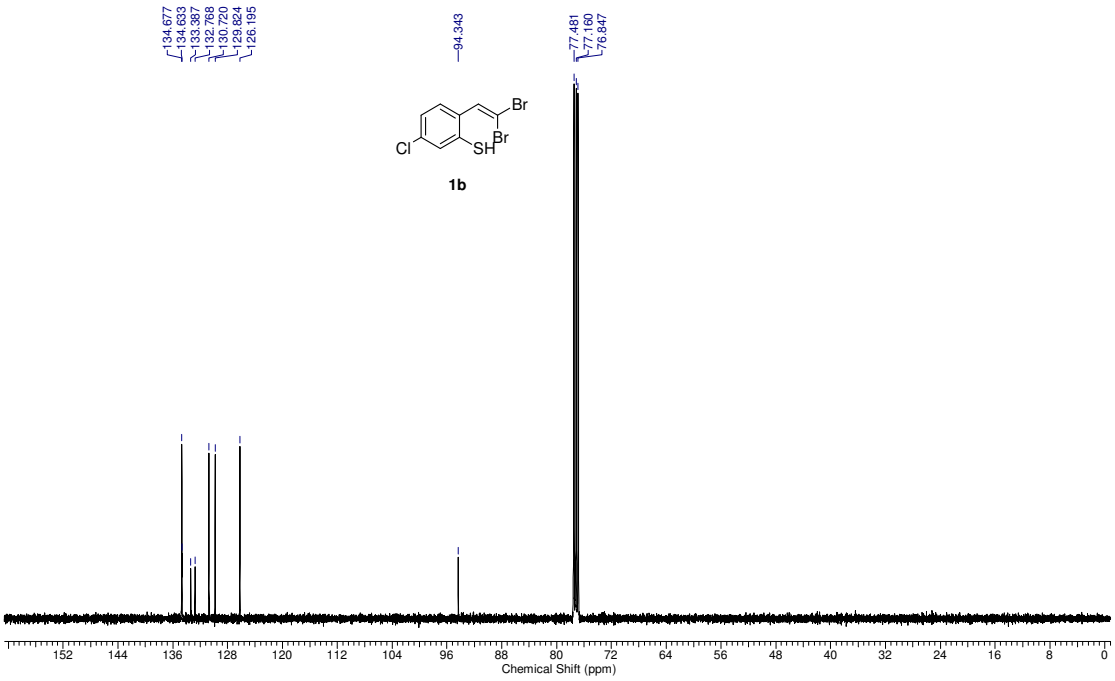
^{13}C NMR of **1a** in $CDCl_3$ (101 MHz)



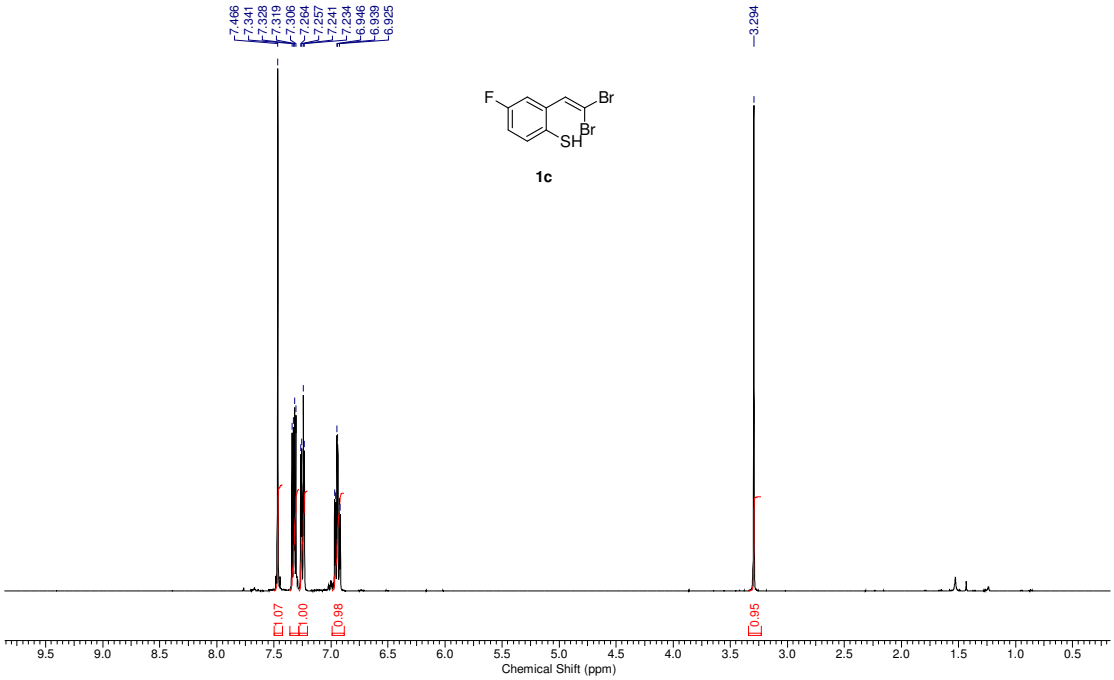
^{1}H NMR of **1b** in $CDCl_3$ (400 MHz)



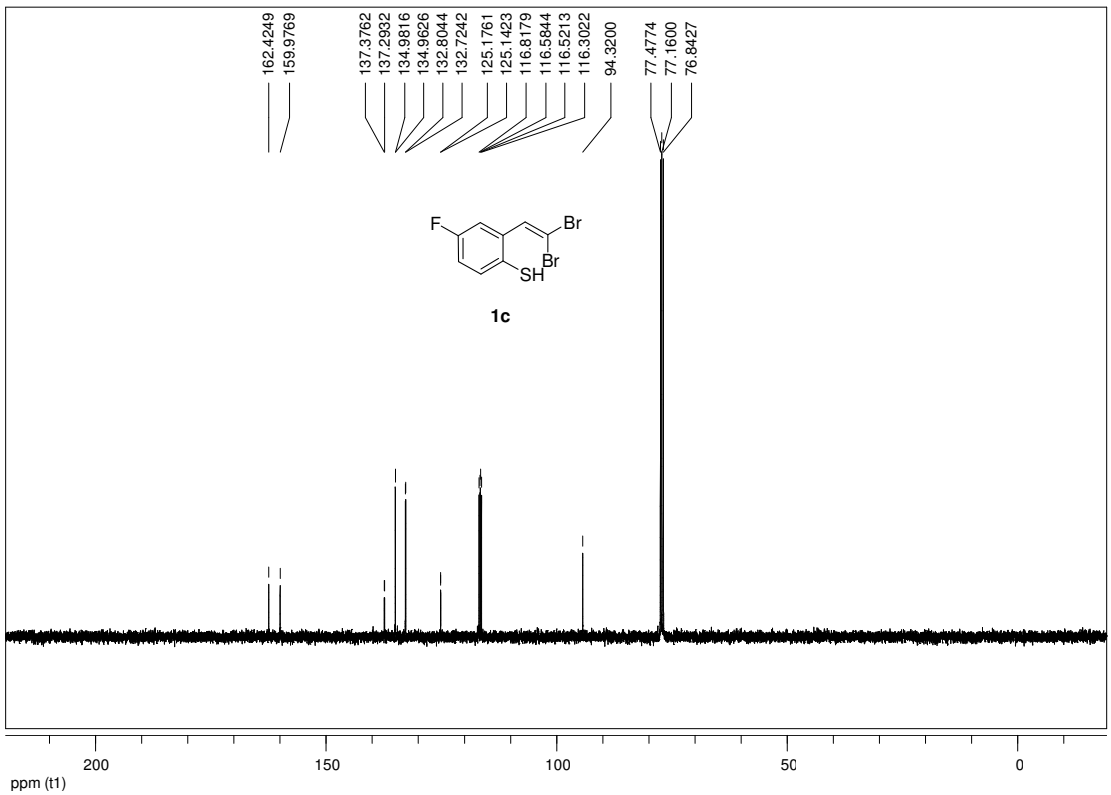
^{13}C NMR of **1b** in $CDCl_3$ (101 MHz)



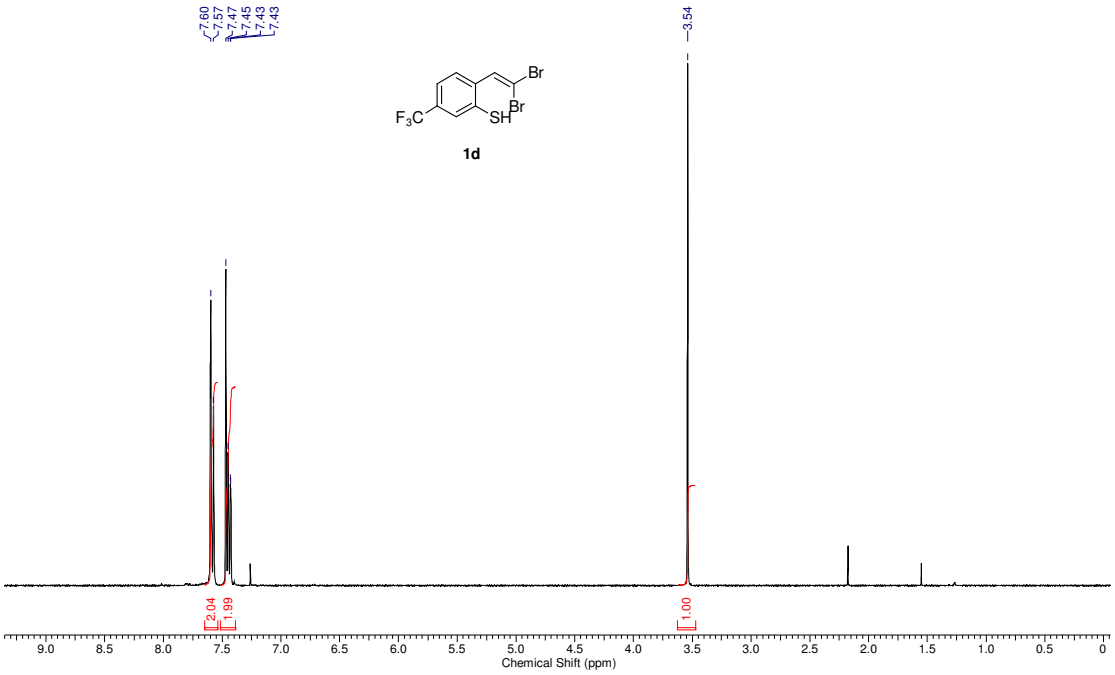
^{1}H NMR of **1c** in $CDCl_3$ (400 MHz)



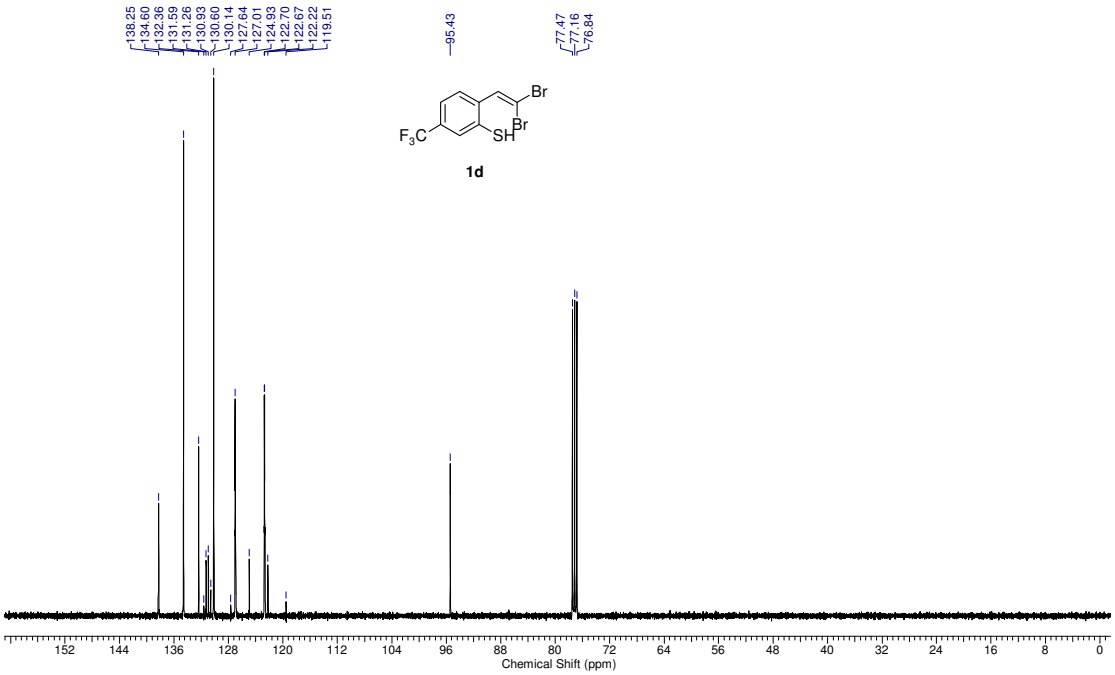
^{13}C NMR of **1c** in $CDCl_3$ (101 MHz)



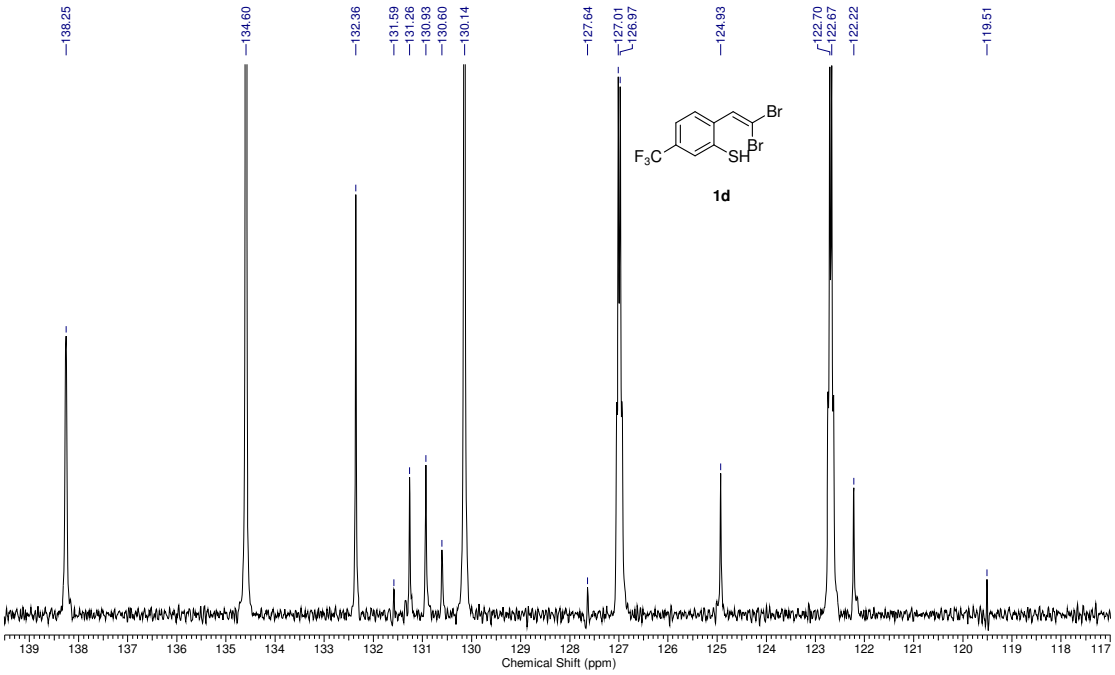
^{1}H NMR of **1d** in $CDCl_3$ (400 MHz)



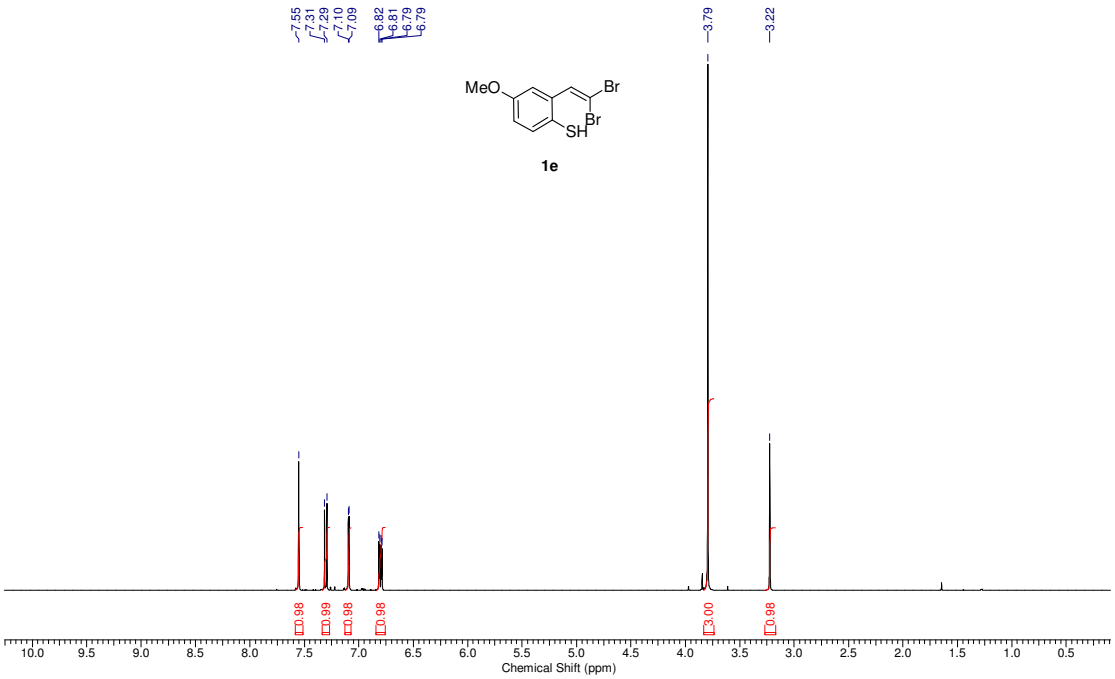
^{13}C NMR of **1d** in $CDCl_3$ (101 MHz)



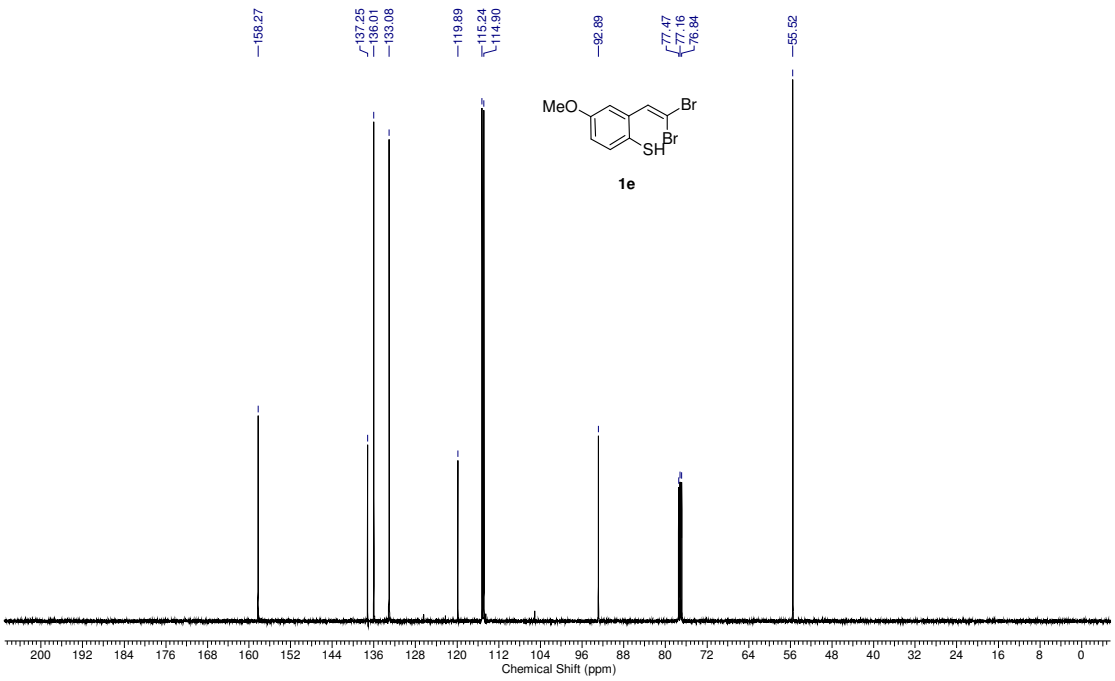
^{13}C NMR of **1d** in $CDCl_3$ (101 MHz)



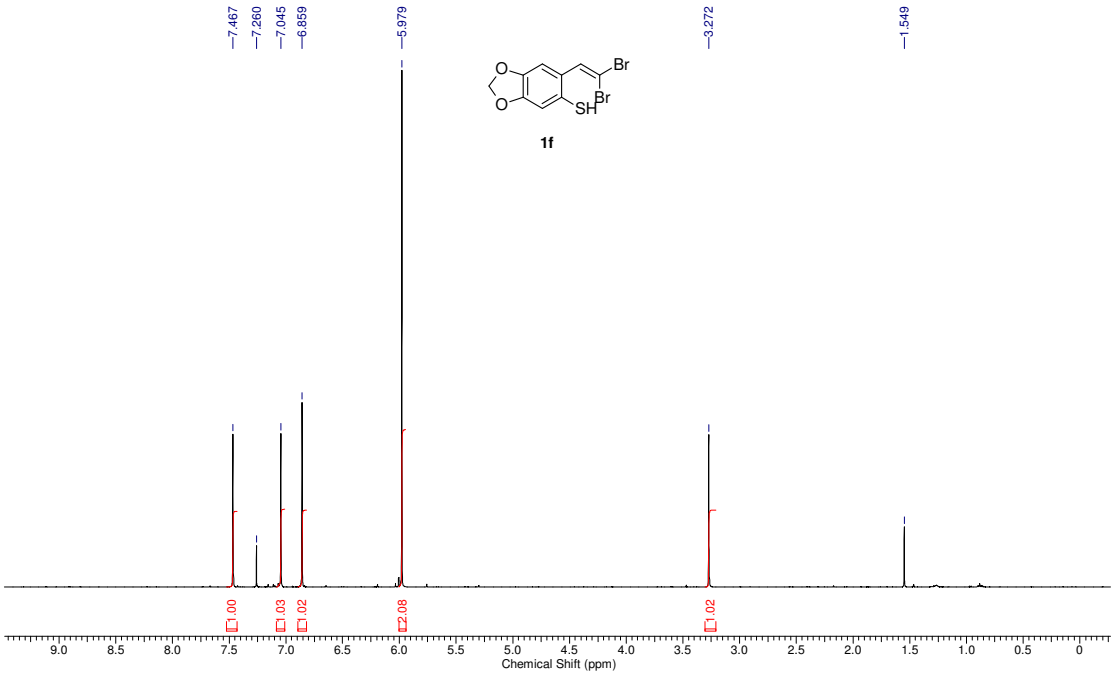
^{1}H NMR of **1e** in $CDCl_3$ (400 MHz)



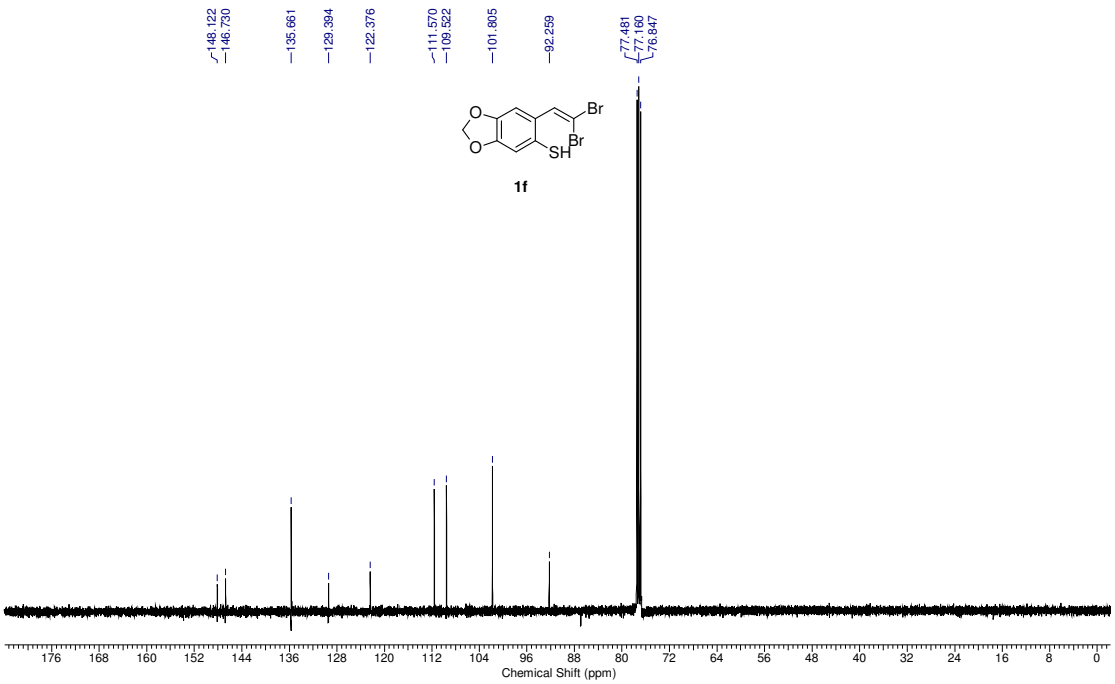
^{13}C NMR of **1e** in $CDCl_3$ (101 MHz)



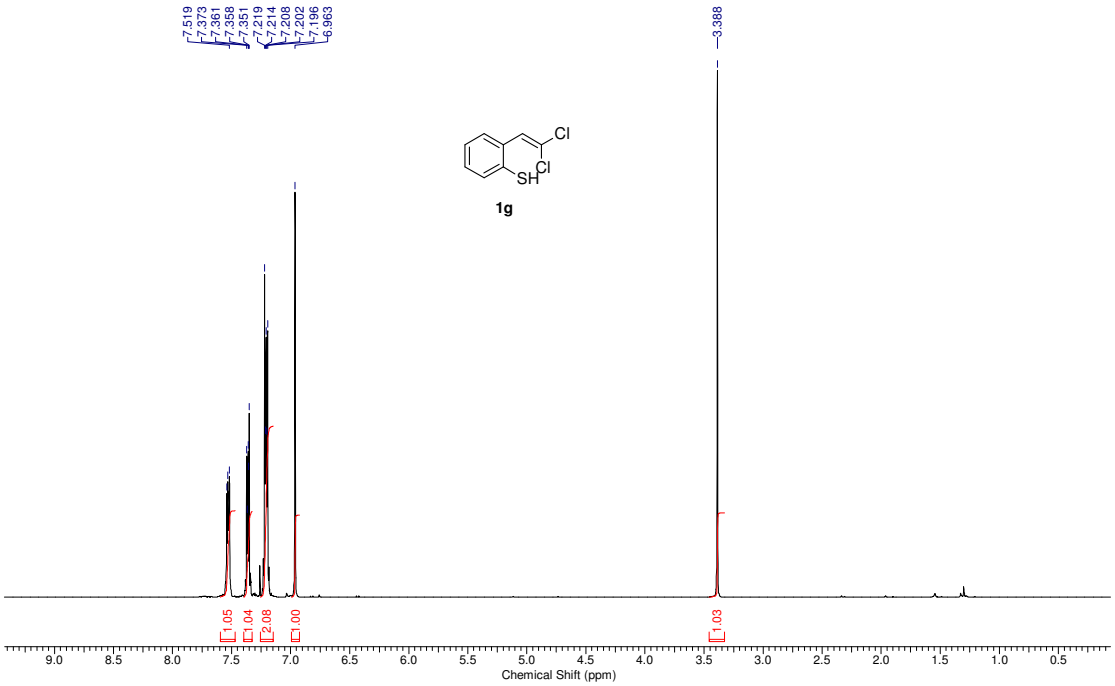
^{1}H NMR of **1f** in $CDCl_3$ (400 MHz)



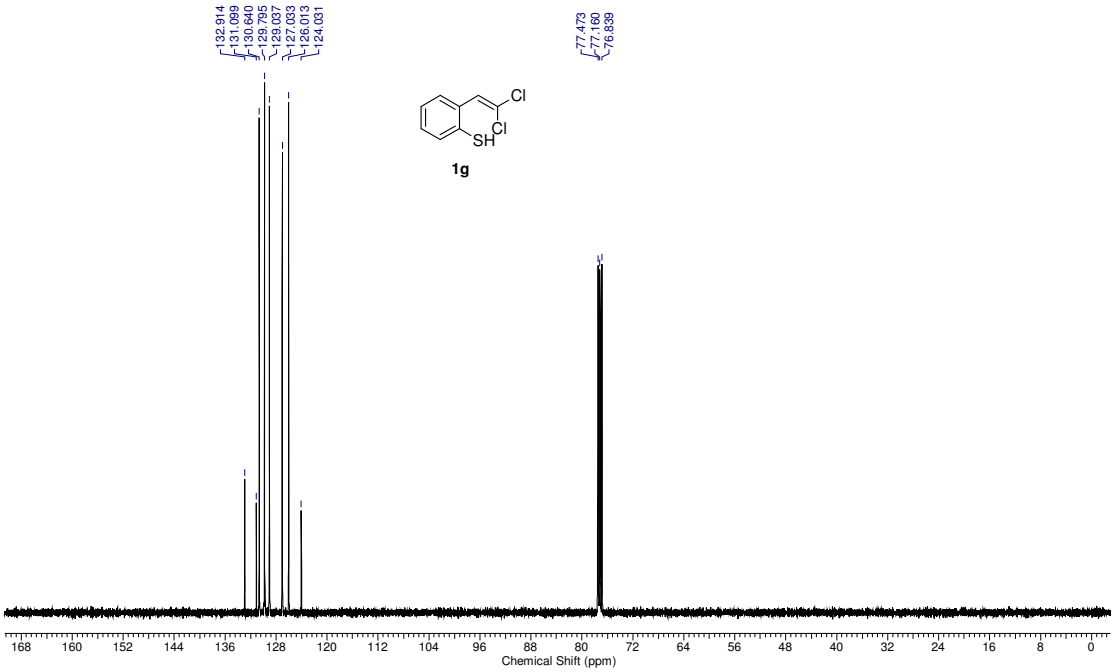
^{13}C NMR of **1f** in $CDCl_3$ (101 MHz)



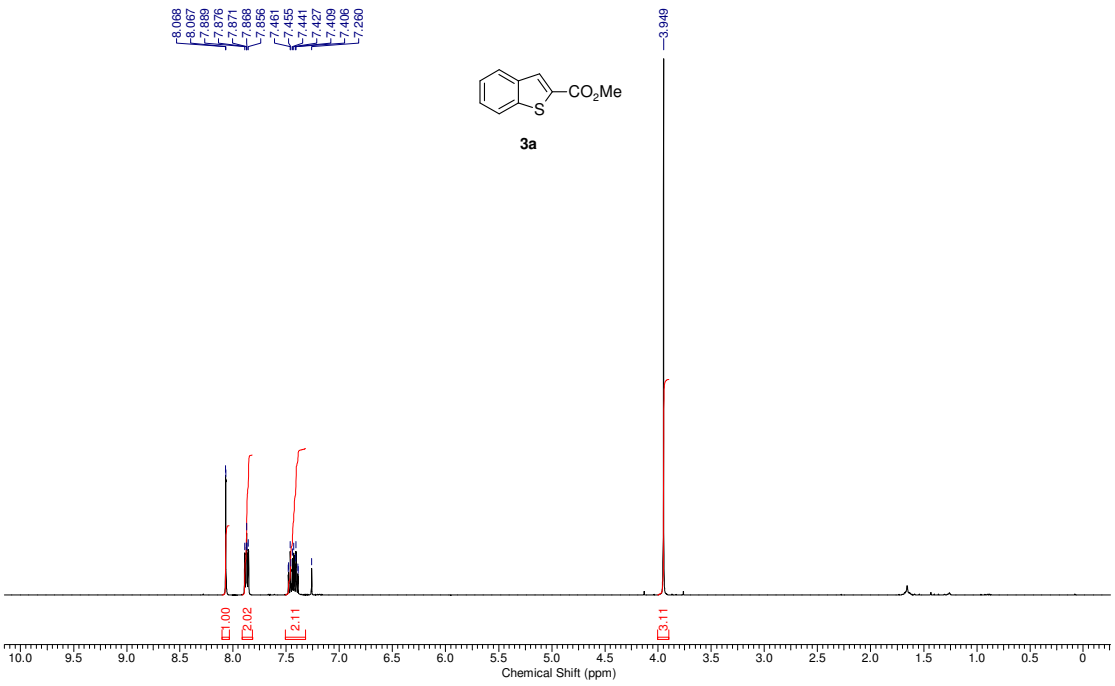
^{1}H NMR of **1g** in $CDCl_3$ (400 MHz)



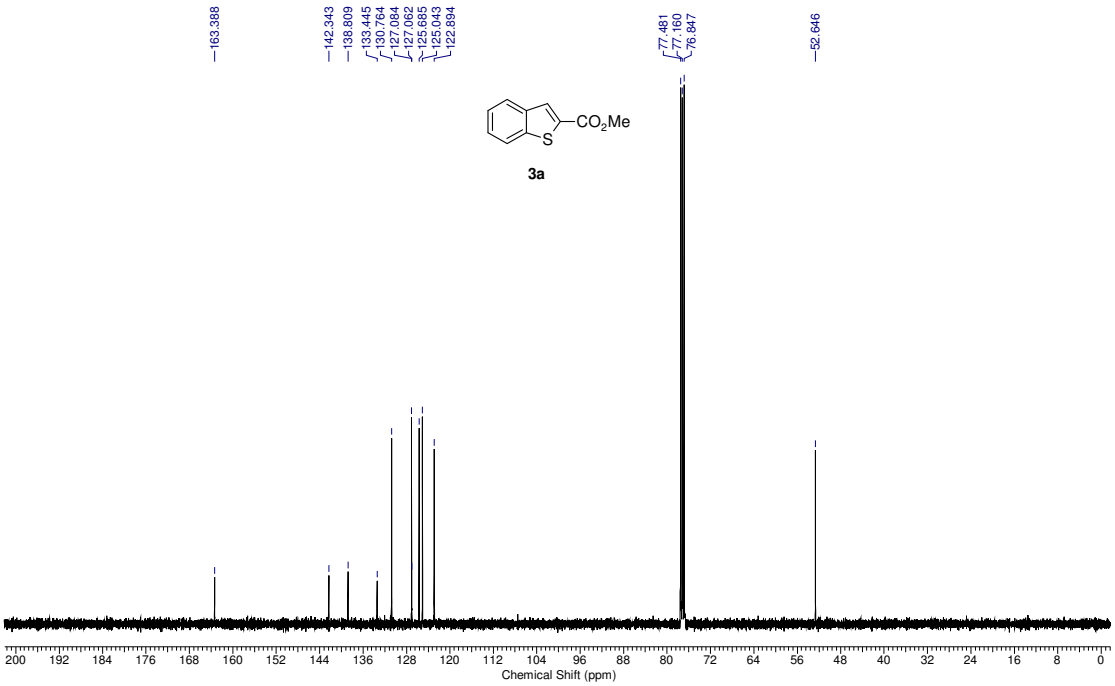
^{13}C NMR of **1g** in $CDCl_3$ (101 MHz)



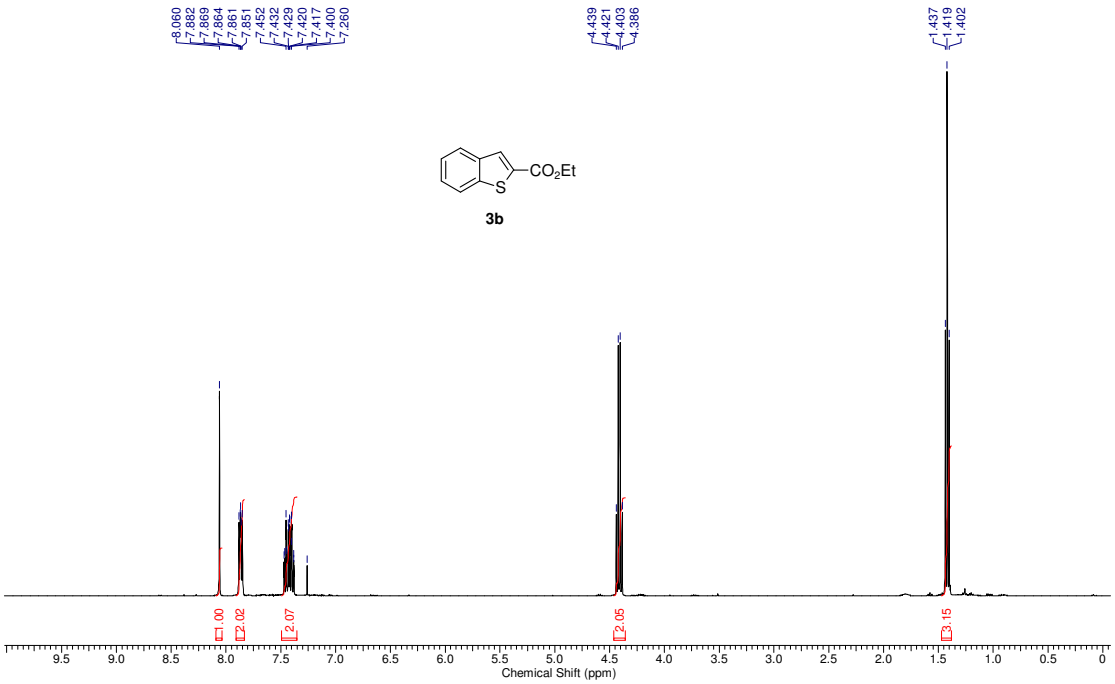
^{1}H NMR of **3a** in $CDCl_3$ (400 MHz)



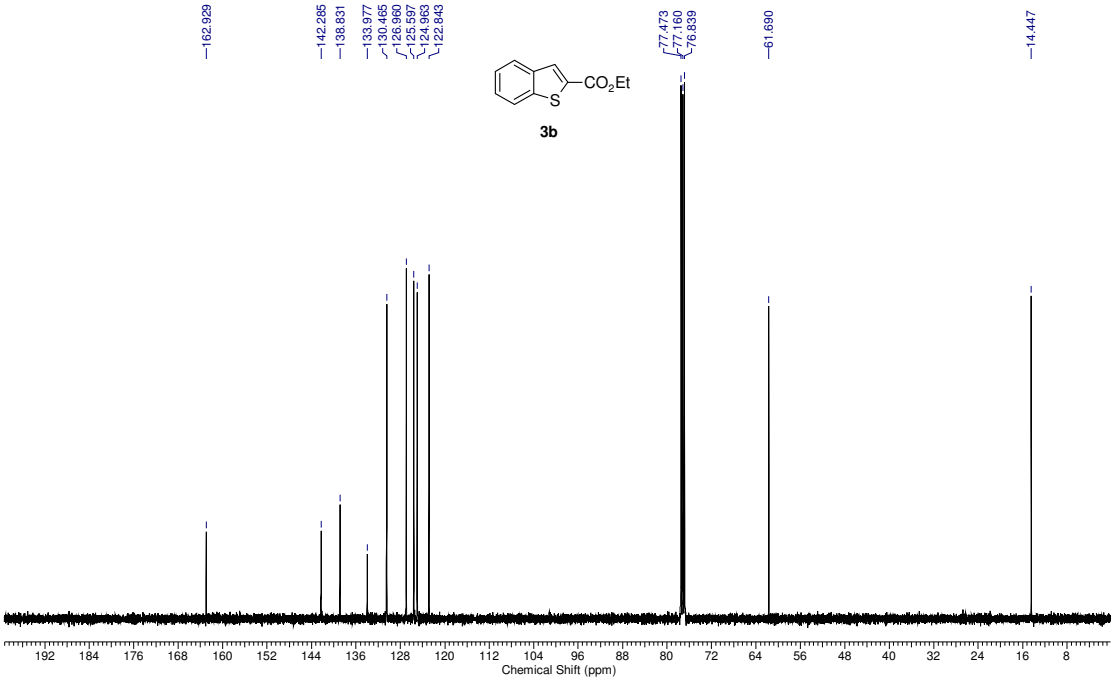
^{13}C NMR of **3a** in $CDCl_3$ (101 MHz)



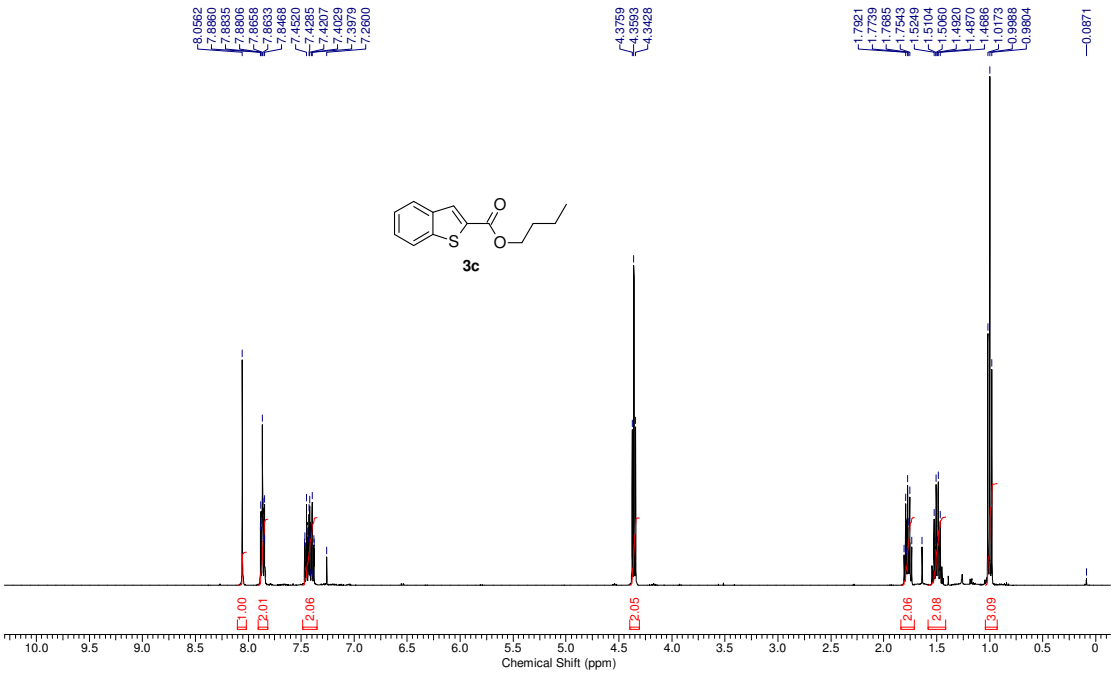
^{1}H NMR of **3b** in $CDCl_3$ (400 MHz)



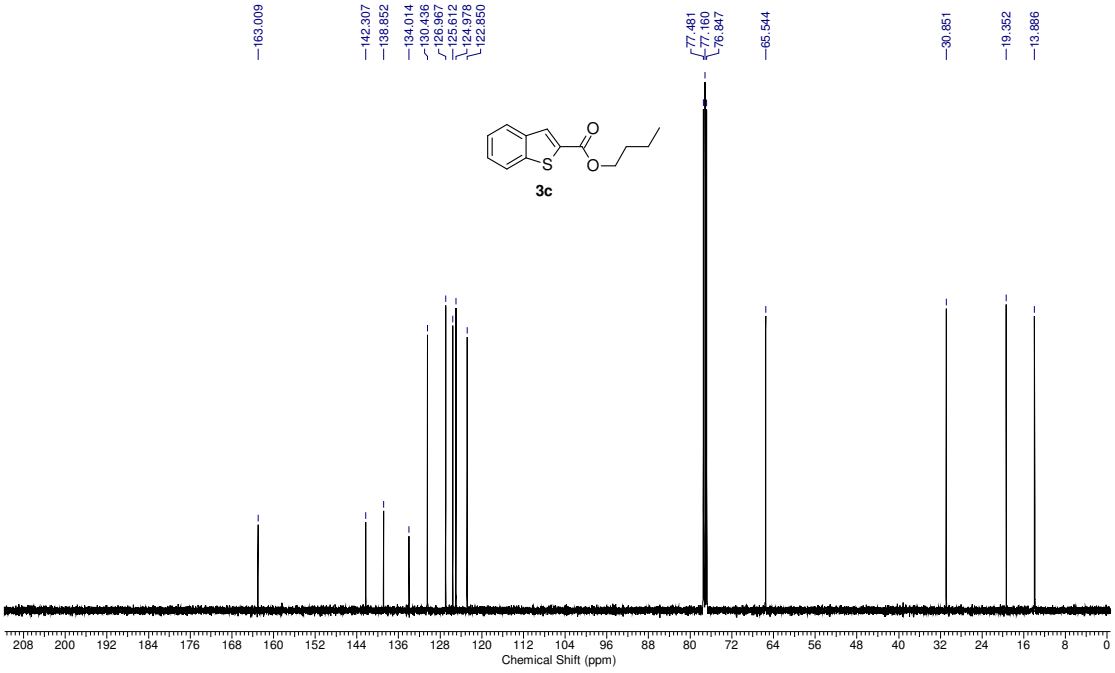
^{13}C NMR of **3b** in $CDCl_3$ (101 MHz)



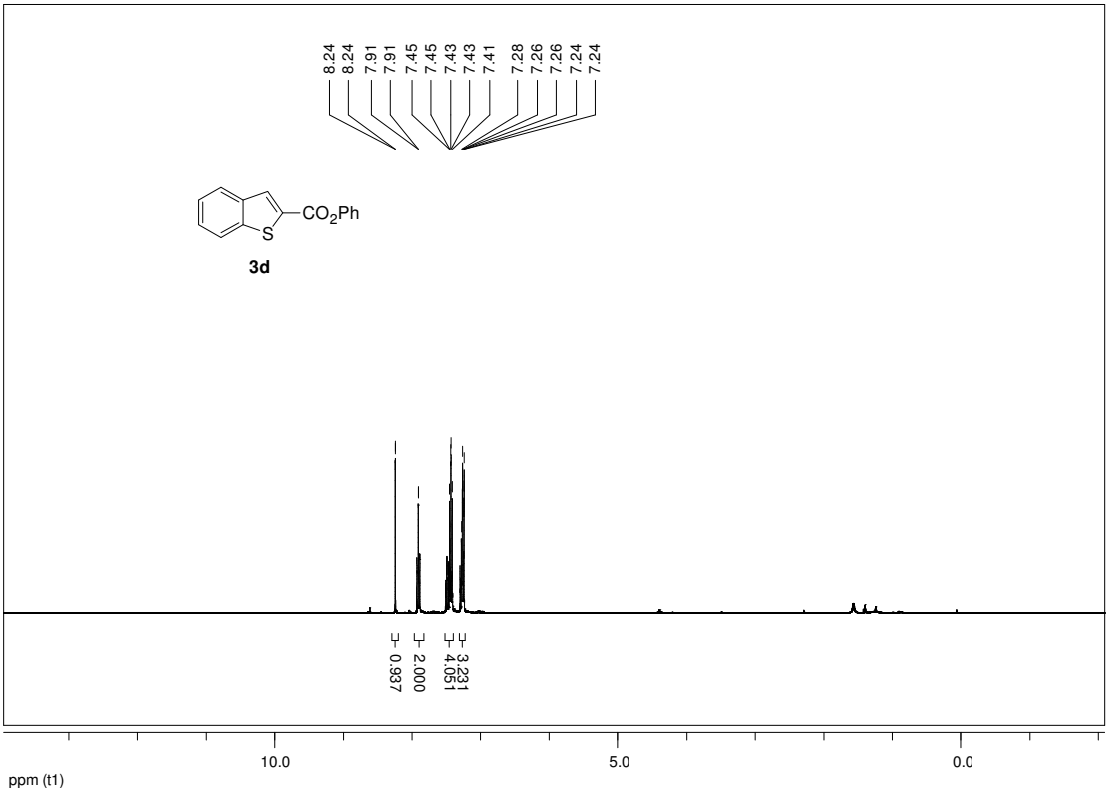
^{1}H NMR of **3c** in $CDCl_3$ (400 MHz)



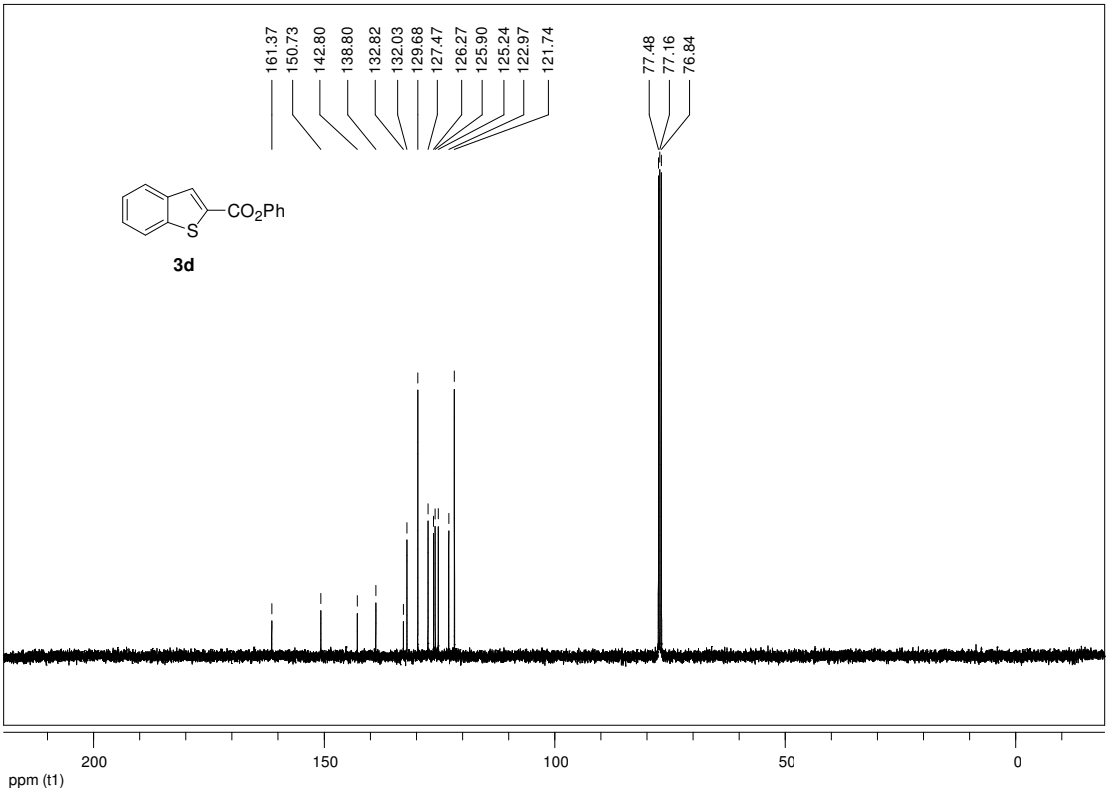
^{13}C NMR of **3c** in $CDCl_3$ (101 MHz)



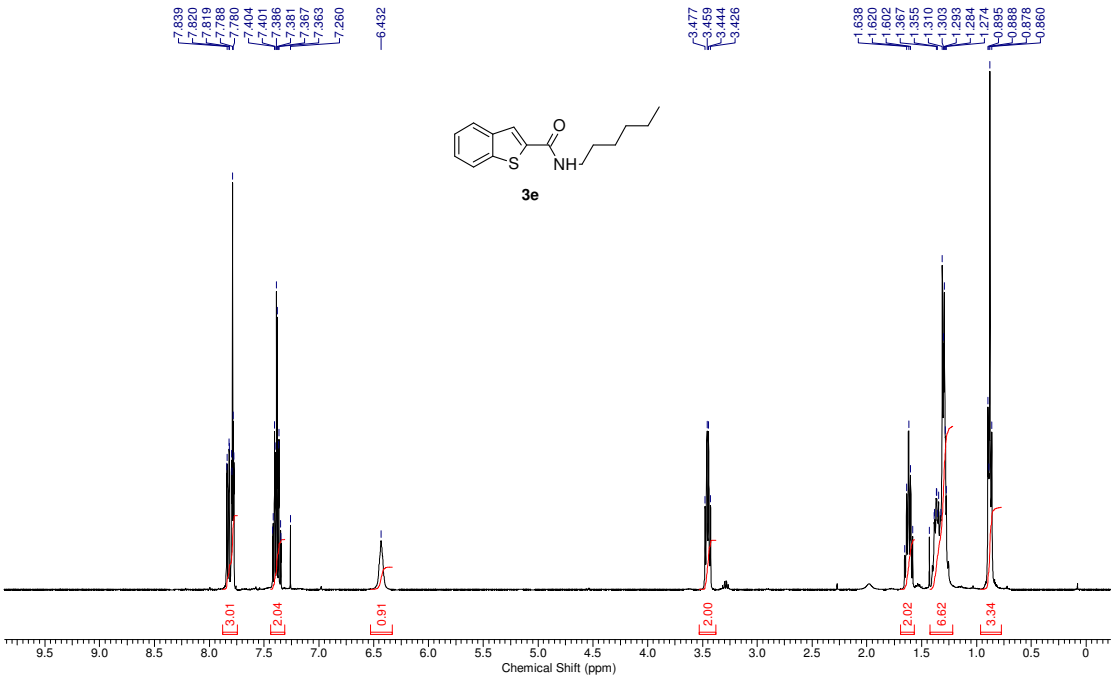
^{1}H NMR of **3d** in $CDCl_3$ (400 MHz)



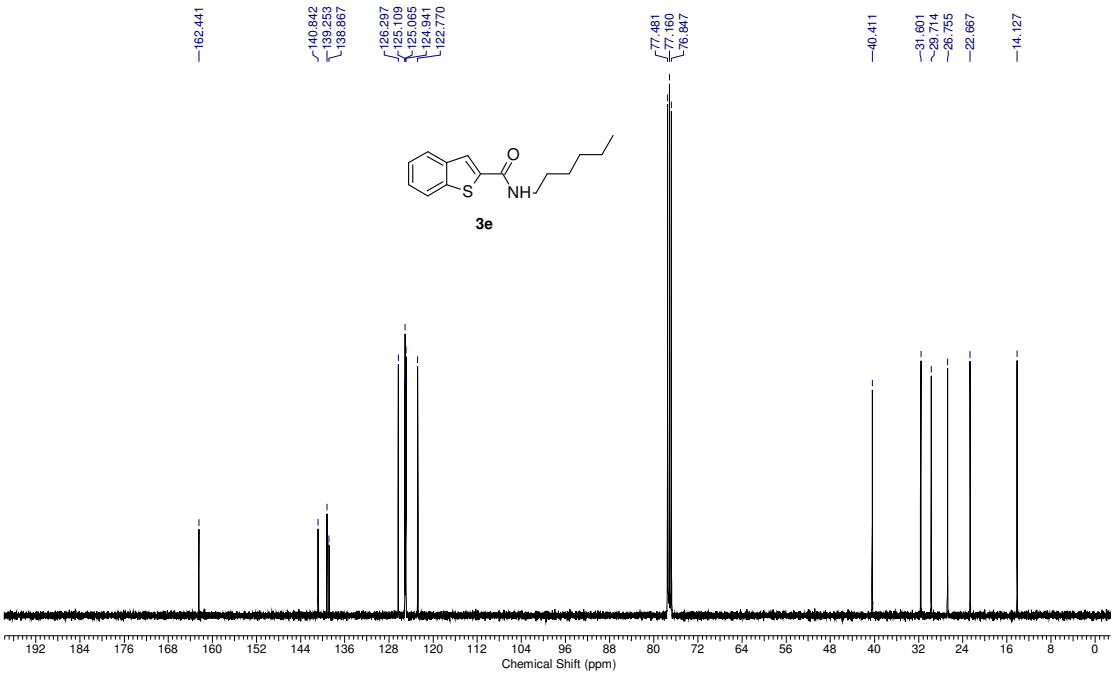
^{13}C NMR of **3d** in $CDCl_3$ (101 MHz)



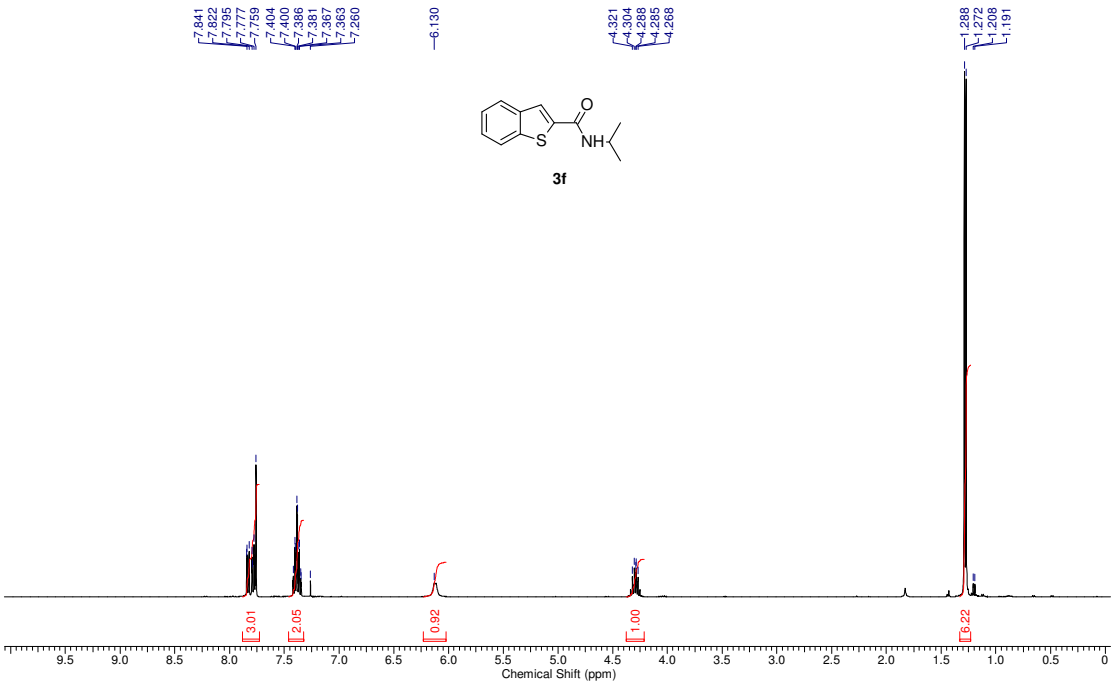
^{1}H NMR of **3e** in $CDCl_3$ (400 MHz)



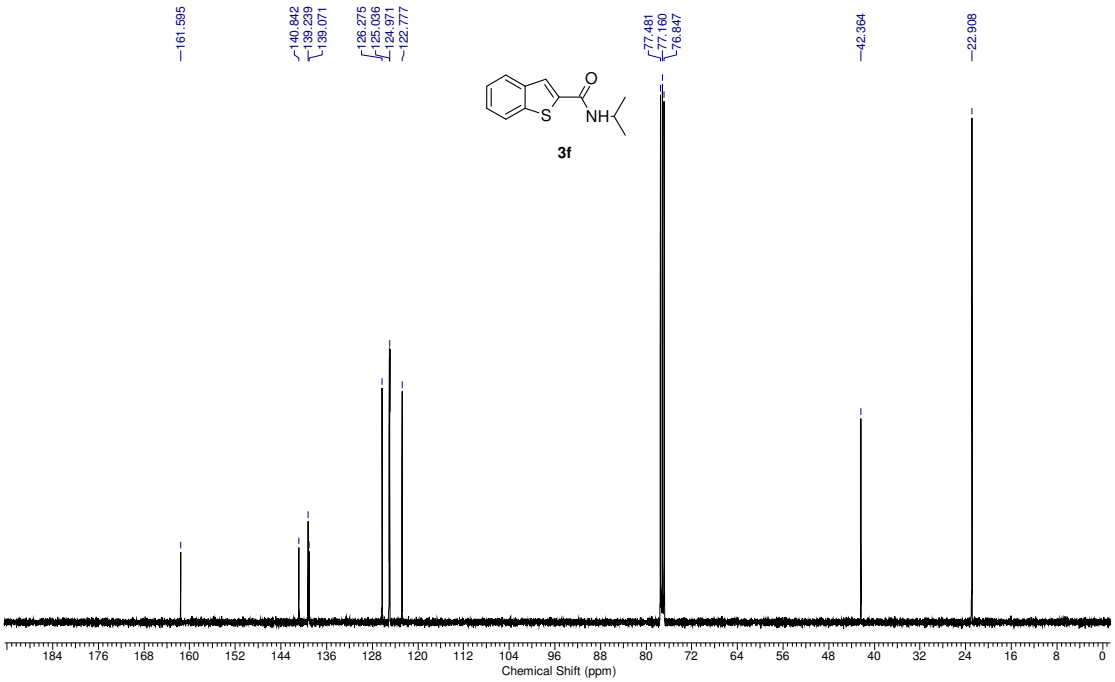
^{13}C NMR of **3e** in $CDCl_3$ (101 MHz)



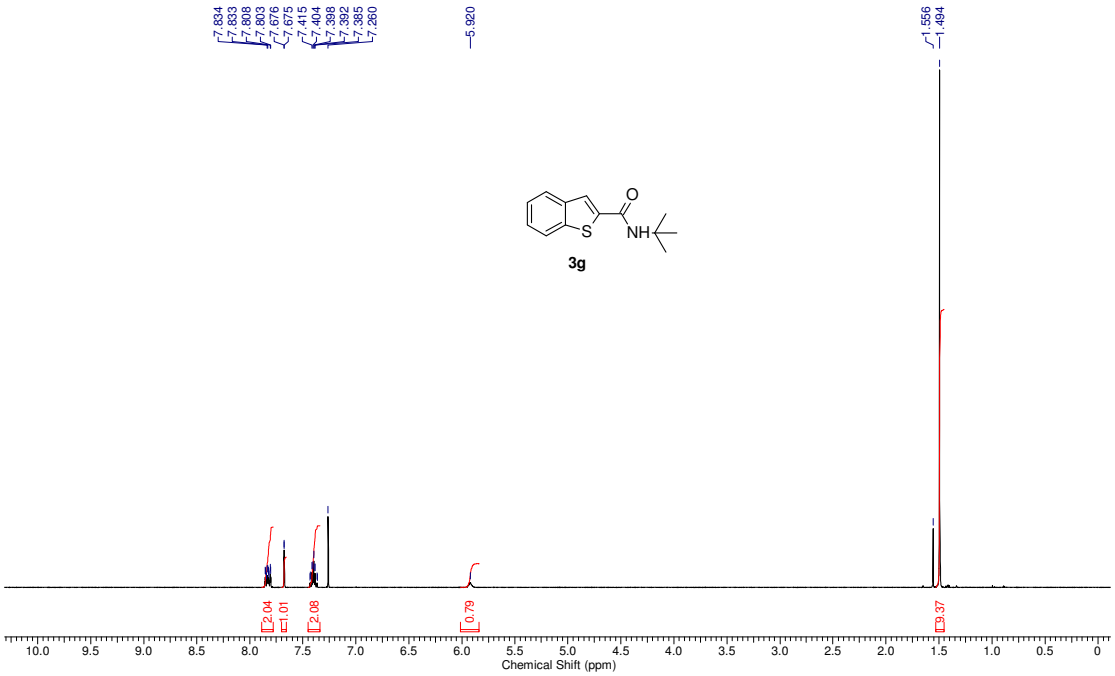
^{1}H NMR of **3f** in $CDCl_3$ (400 MHz)



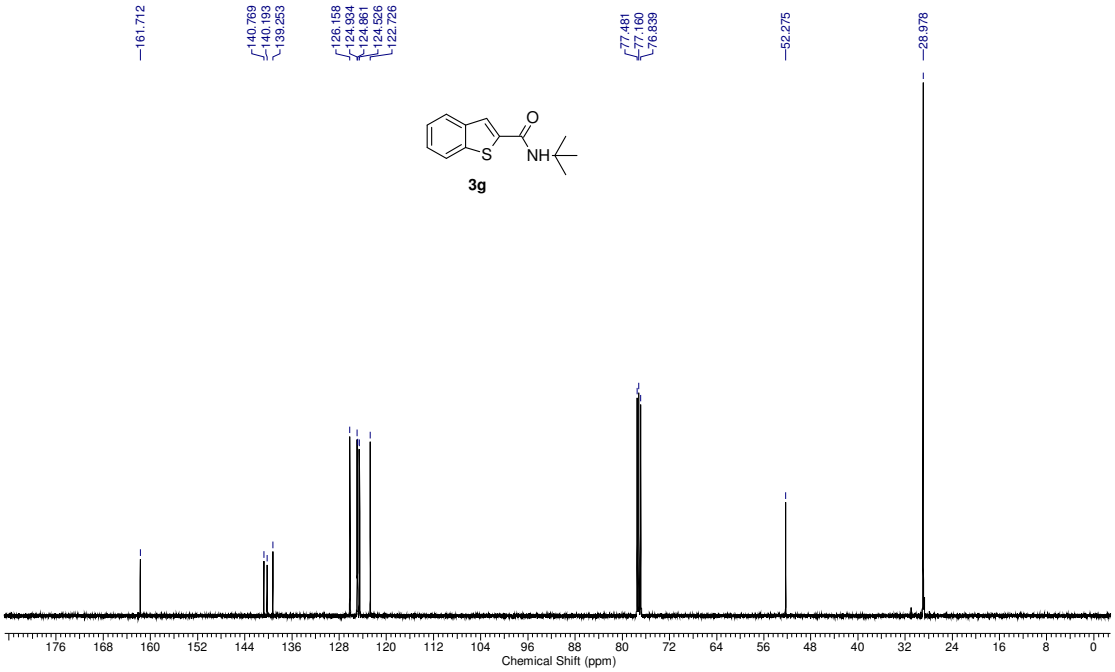
^{13}C NMR of **3f** in $CDCl_3$ (101 MHz)



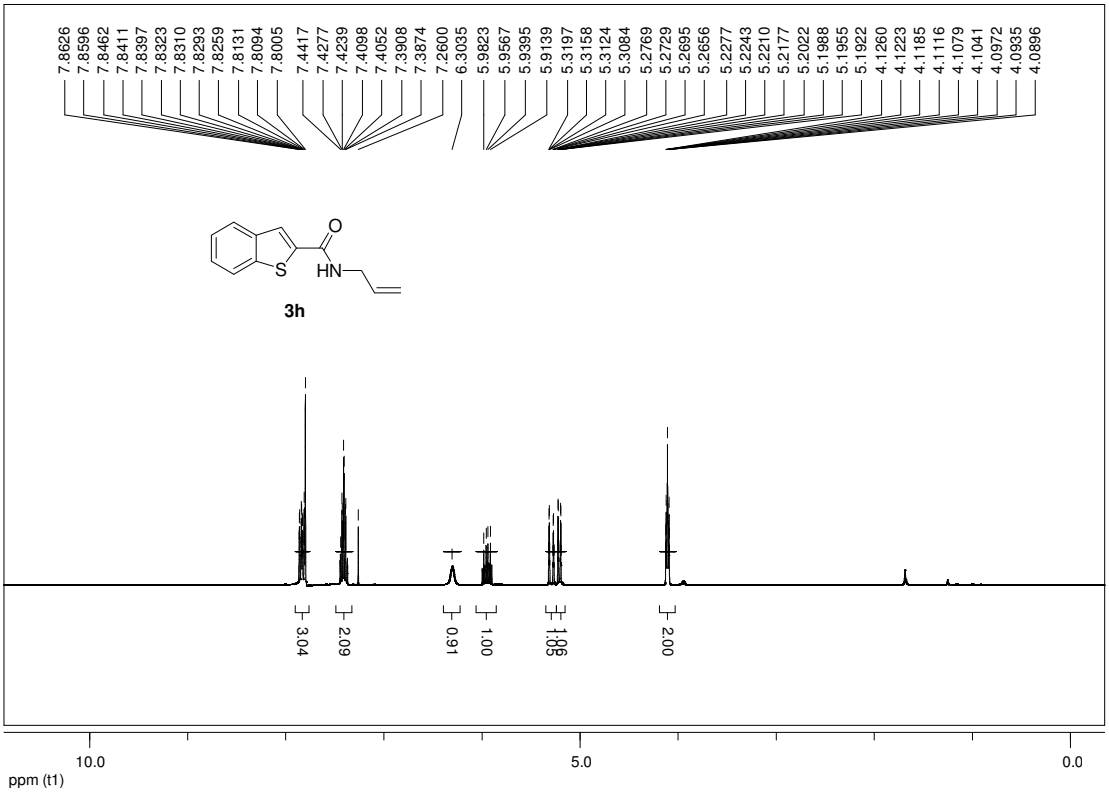
^{1}H NMR of **3g** in $CDCl_3$ (400 MHz)



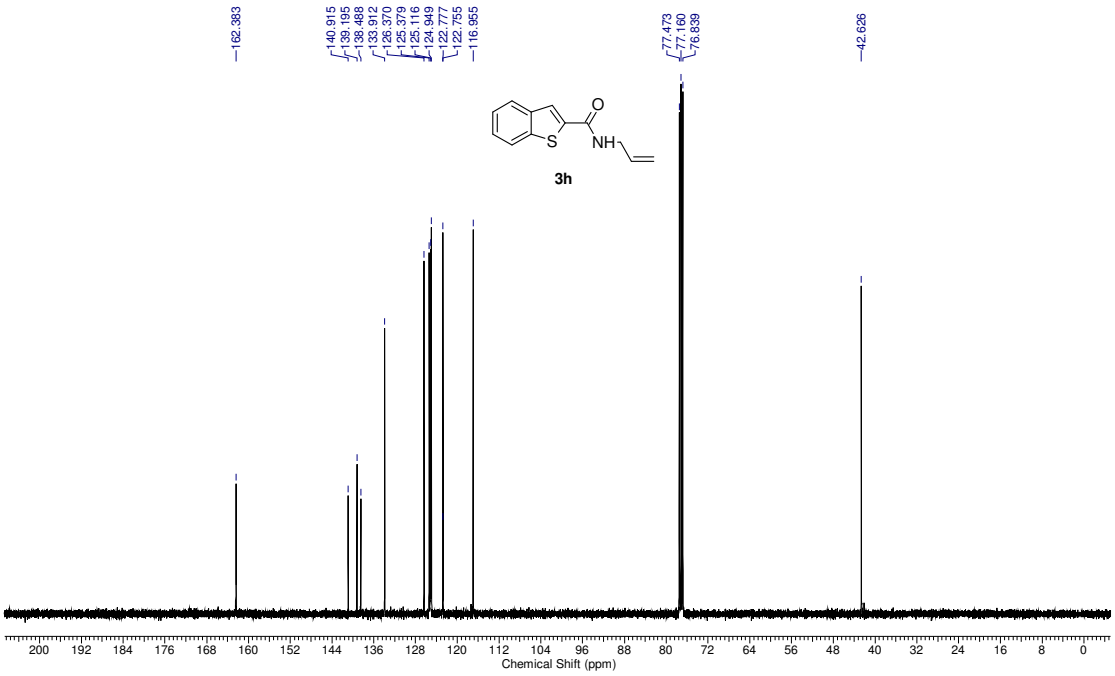
^{13}C NMR of **3g** in $CDCl_3$ (101 MHz)



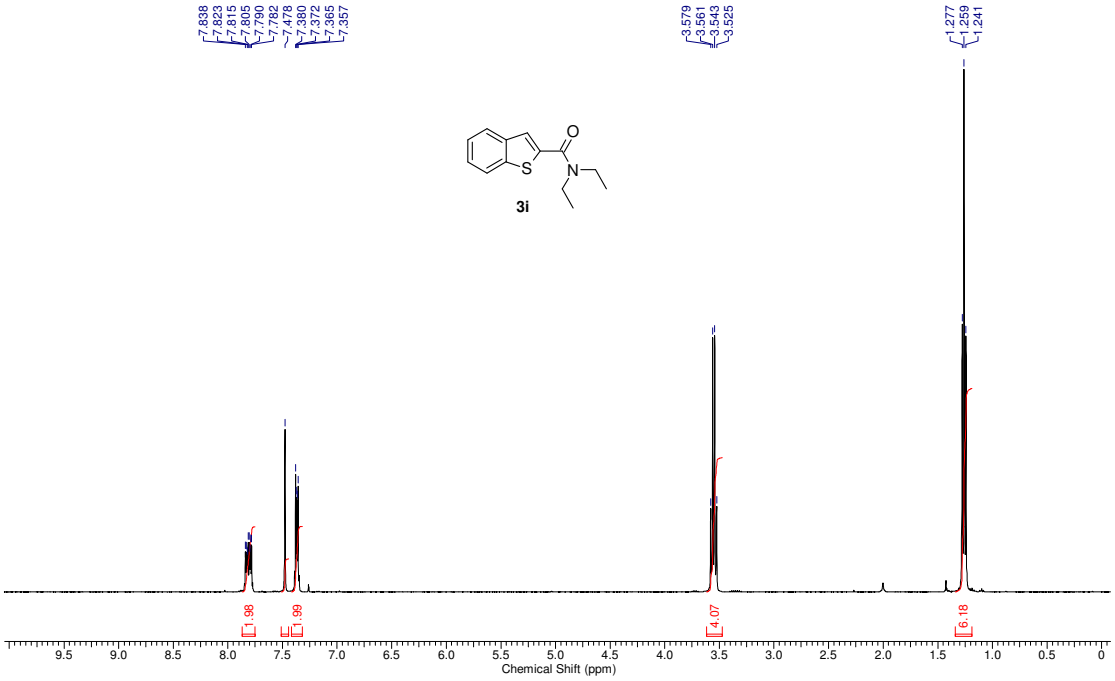
^{1}H NMR of **3h** in $CDCl_3$ (400 MHz)



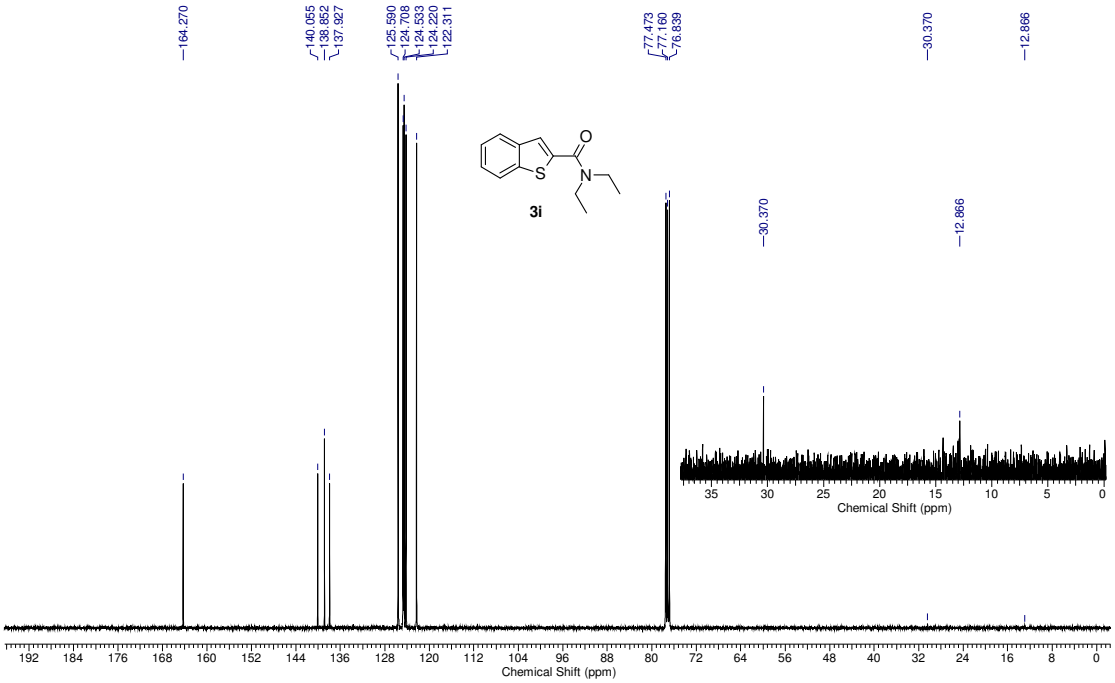
^{13}C NMR of **3h** in $CDCl_3$ (101 MHz)



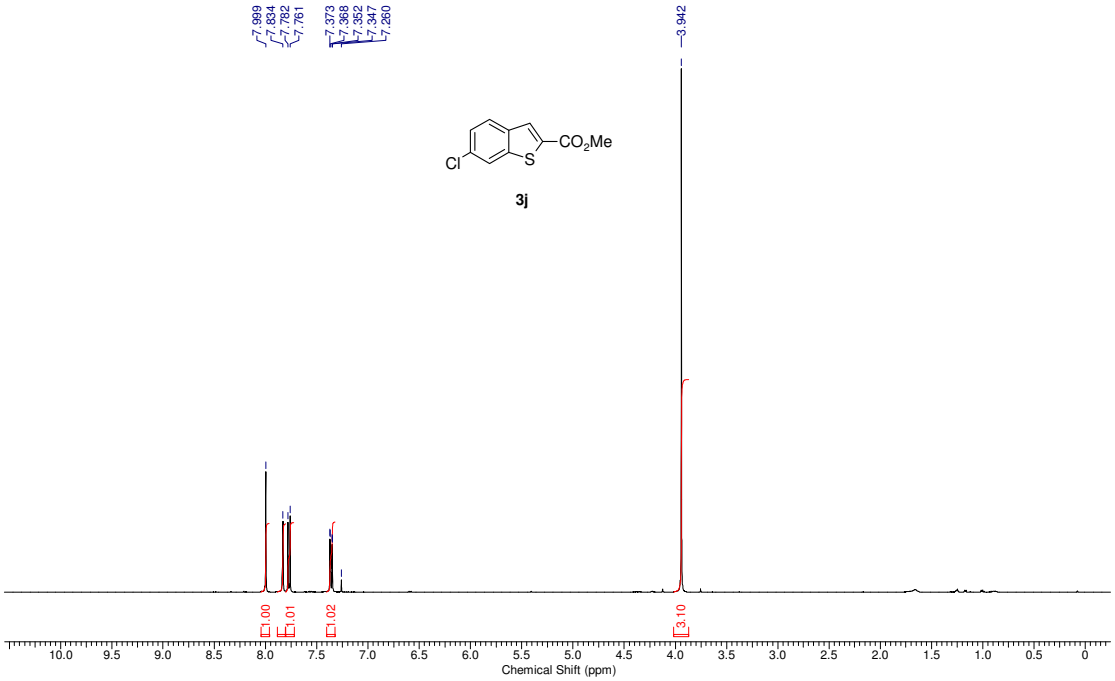
^{1}H NMR of **3i** in $CDCl_3$ (400 MHz)



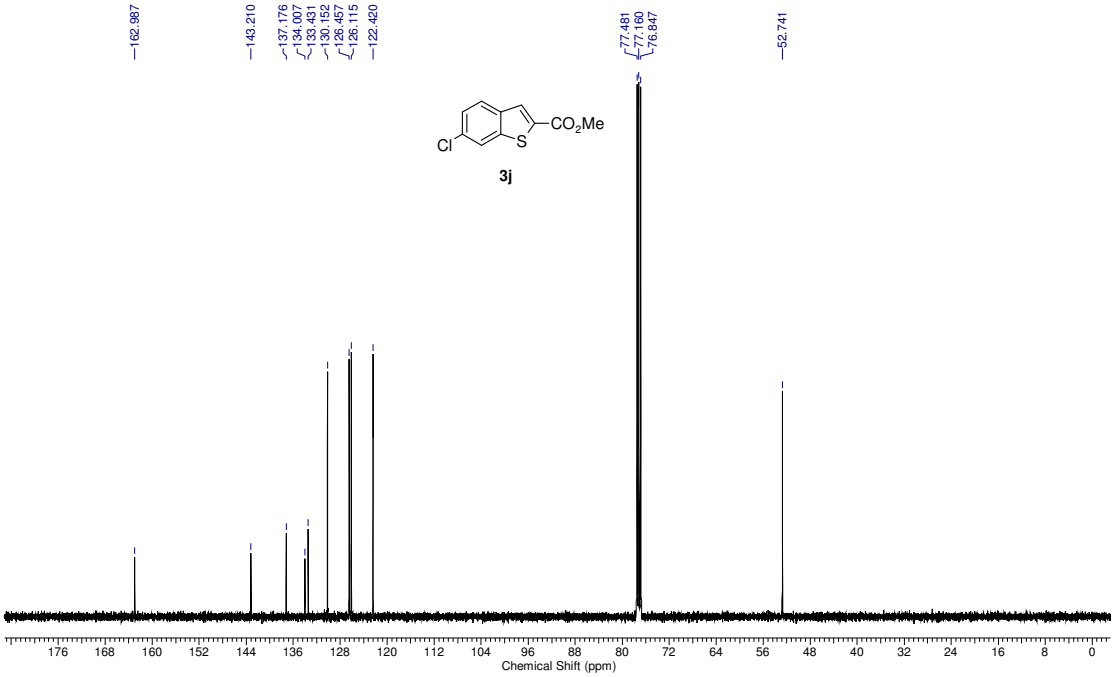
^{13}C NMR of **3i** in $CDCl_3$ (101 MHz)



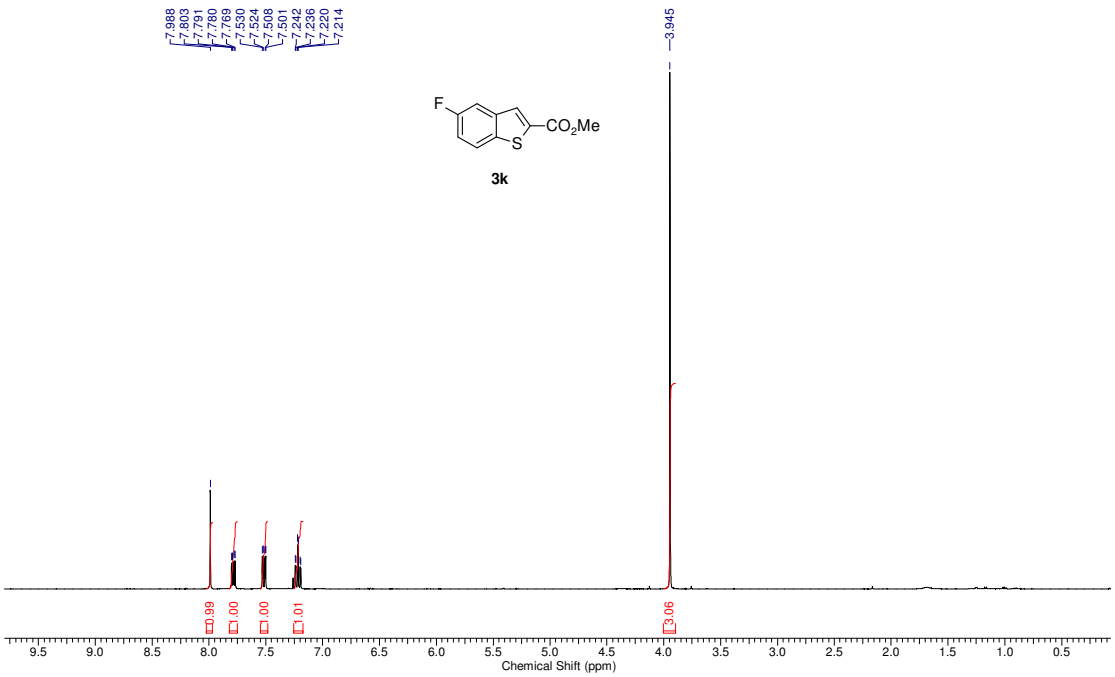
^{1}H NMR of **3j** in $CDCl_3$ (400 MHz)



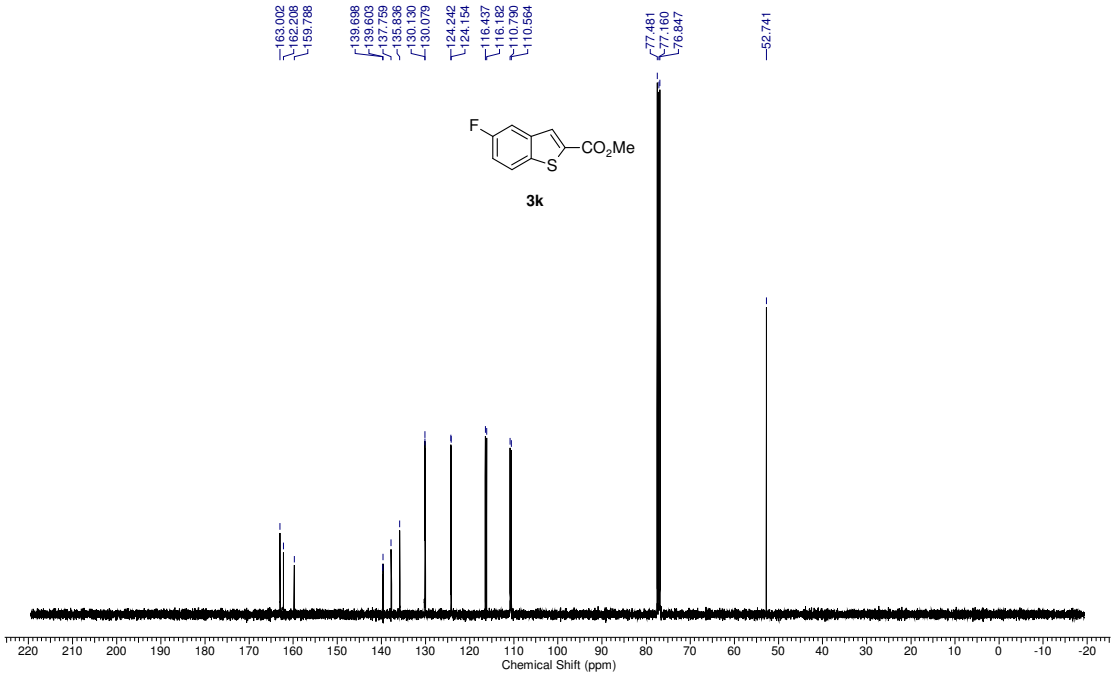
^{13}C NMR of **3j** in $CDCl_3$ (101 MHz)



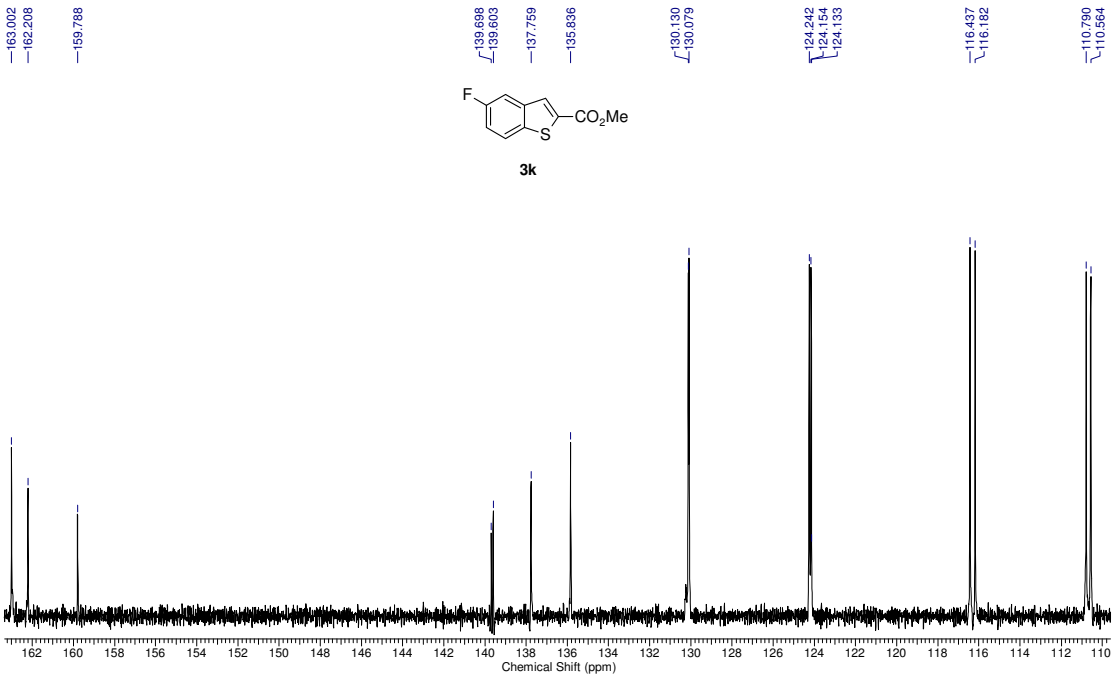
^{1}H NMR of **3k** in $CDCl_3$ (400 MHz)



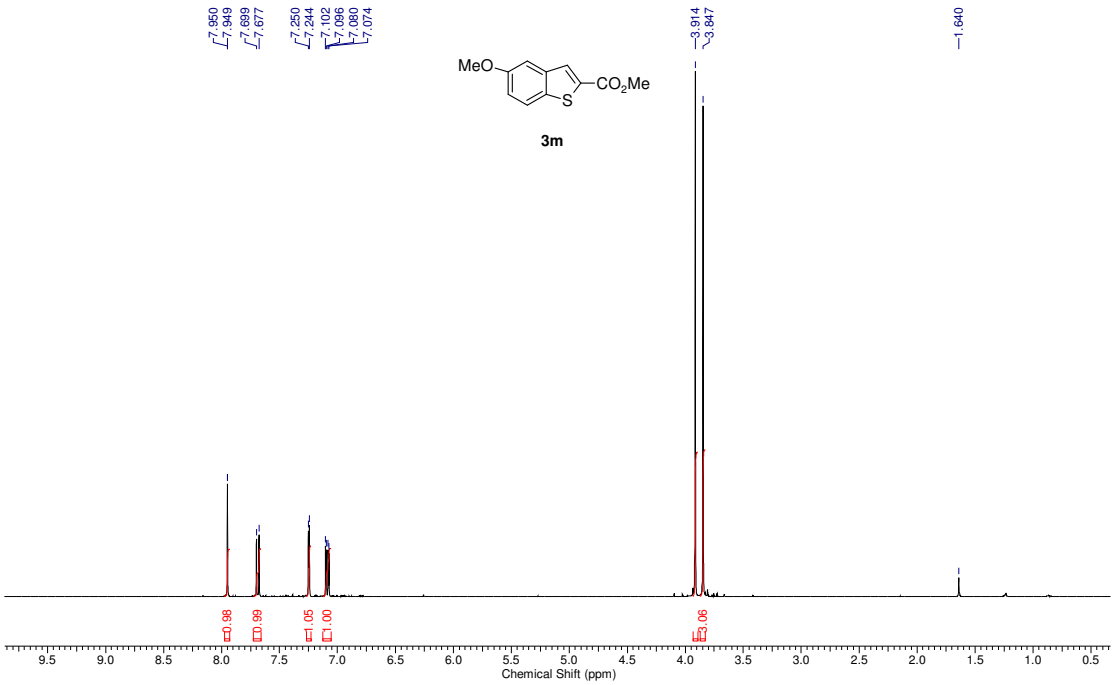
^{13}C NMR of **3k** in $CDCl_3$ (101 MHz)



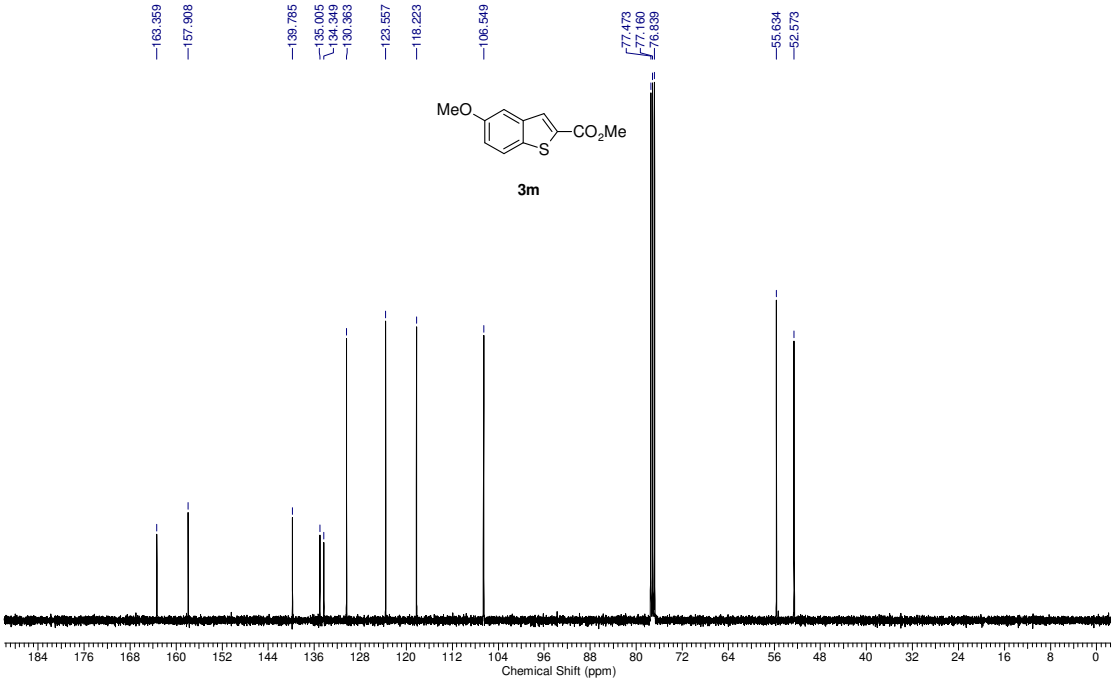
^{13}C NMR of **3k** in $CDCl_3$ (101 MHz)



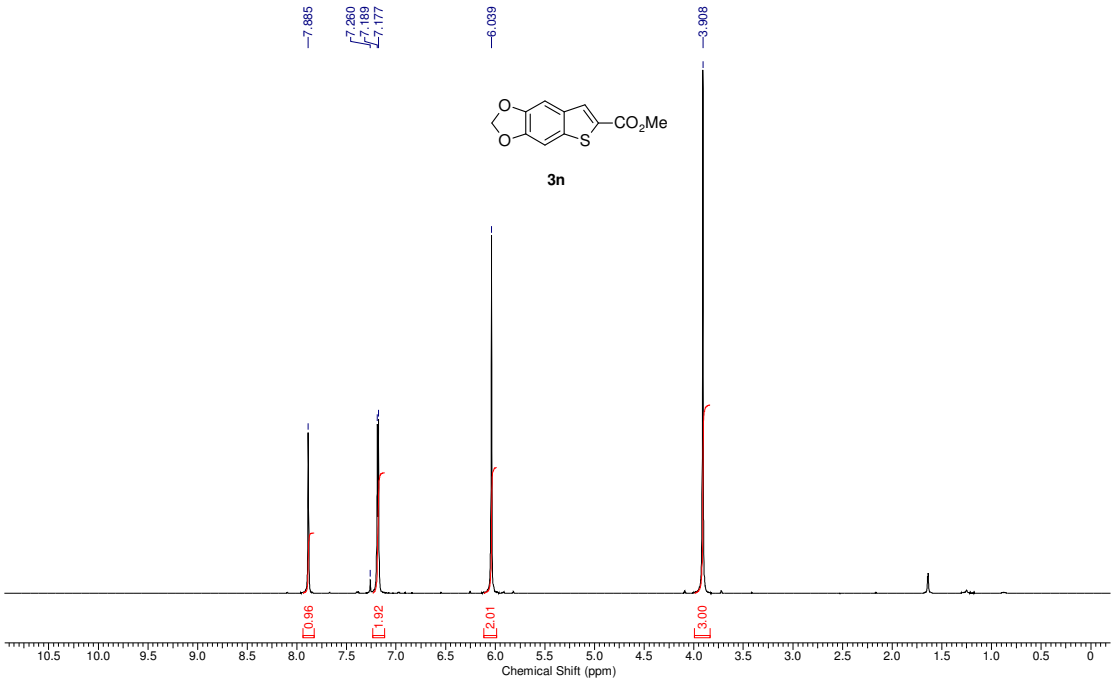
^{1}H NMR of **3m** in $CDCl_3$ (400 MHz)



^{13}C NMR of **3m** in $CDCl_3$ (101 MHz)



^{1}H NMR of **3n** in $CDCl_3$ (400 MHz)



^{13}C NMR of **3n** in $CDCl_3$ (101 MHz)