Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Ni-catalyzed asymmetric decarboxylative Mannich reaction for the synthesis of β-trifluoromethyl-β-amino ketones

Ping Qian, Yanling Dai, Haibo Mei, Vadim A. Soloshonok, Jianlin Han* and Yi Pan

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1. General information

β-Keto acids were synthesized according to literature.[1] Sulfinylimine **1** was synthesized due to literature.[2] Other reagents were obtained from commercial suppliers and used without further purification. The reactions were conducted in a closed system in an atmosphere of N_2 and were monitored by TLC. Solvents were dried and distilled prior to use. Flash chromatography was performed using silica gel 60 (300–400 mesh). Thin layer chromatography was carried out on silica gel 60 F-254 TLC plates of 20 cm × 20 cm. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker AVANCE400M spectrometer. High pressure liquid chromatography (HPLC) analyses were performed on a Shimadzu SPD-20A Series instrument equipped with an isostatic pump, using a chiral stationary phase column (Daicel Co. CHIRALPAK), and the UV detection was monitored at 254 nm. The chiral HPLC methods were calibrated with the corresponding racemic mixtures. Melting points were uncorrected. Values of optical rotation were measured on a Rudolph Automatic Polarimeter A21101. Infrared spectra were obtained on a Bruker Vector 22 in KBr pellets. HRMS were conducted on an Agilent 6540Q-TOF LC/MS equipped with an electrospray ionization (ESI) probe operating in positive or negative ion mode.

Reference

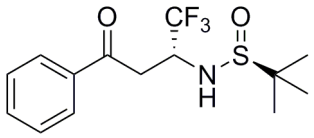
1 Z. Duan, J. L. Han, P. Qian, Y. Wang, Y. Pan, *Org. Biomol. Chem.* **2013**, *11*, 6456-6459.

2 P. Qian, C. Xie, L. M. Wu, H. B. Mei, V. A. Soloshonok, J. L. Han, Y. Pan, *Org. Biomol. Chem.* **2014**, *12*, 7909-7913.

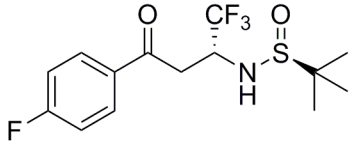
2. Typical procedure for asymmetric addition of sulfinylimine

Into an oven-dried reaction vial flushed with N_2 was taken β-keto acids (0.16 mmol), sulfinylimine (0.1 mmol), $Ni(OTf)_2$ (10 mol %) and anhydrous THF (0.5 mL). Then the reaction was stirred at room temperature for 24 hours. The reaction was quenched with brine (2 mL) and was extracted with DCM (2 × 20 mL). The combined organic layers were washed with water (30 mL) and brine (30 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude mixture was charged onto silica gel and purified by flash chromatography to furnish the corresponding product.

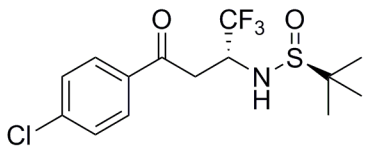
3. Characterization data of compounds 3



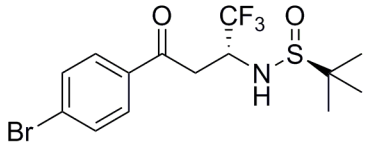
(*S*)-2-methyl-*N*-((*R*)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)propane-2-sulfinamide (3a): Colorless solid (29.5 mg, 92% yield, >99:1 dr), mp 64–68 °C, $[\alpha]_D^{25}$ = +61.2 (*c* = 0.60, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* =7.3 Hz, 2H), 7.60 (t, *J* = 7.4Hz, 1H), 7.48 (t, *J* =7.7 Hz, 2H), 4.54–4.45 (m, 1H), 4.44–4.34 (m, 1H), 3.57 (dd, *J* = 17.6, 6.1 Hz, 1H), 3.43 (dd, *J* = 17.6, 4.8 Hz, 1H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.47. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 136.2, 133.9, 128.8, 128.2, 125.2 (q, J_{FC} = 281.1 Hz), 56.9, 55.2 (q, $^2J_{FC}$ = 31.0 Hz), 38.2, 22.4. IR (cm^{-1}): *v* 3193, 2961, 2926, 2855, 1692, 1598, 1581, 1450, 1416, 1365, 1274, 1220, 1169, 1124, 1067, 1003, 919. HRMS (ESI): calcd for $C_{14}H_{18}F_3NO_2SNa$ $[M+Na]^+$ 344.0908, found 344.0909.



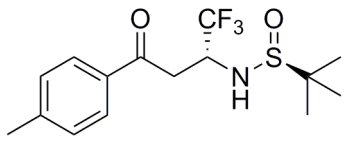
(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-oxobutan-2-yl)propane-2-sulfinamide (3b): Colorless solid (30.5 mg, 90% yield, 98:2 dr), mp 73–76 °C, $[\alpha]_D^{25}$ = +40.6 (*c* = 1.31, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.7, 5.4 Hz, 2H), 7.15 (t, *J* = 8.5 Hz, 2H), 4.56–4.44 (m, 1H), 4.41 (m, 1H), 3.54 (dd, *J* = 17.5, 6.2 Hz, 1H), 3.40 (dd, *J* = 17.5, 4.6 Hz, 1H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.52, -103.65. ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 166.2 (d, *J* = 256.2 Hz, 1H), 132.6 (d, *J* = 2.9 Hz), 131.0 (d, *J* = 9.5 Hz), 125.1 (q, J_{FC} = 281.0 Hz), 116.0 (d, *J* = 22.0 Hz), 56.9, 55.2 (q, $^2J_{FC}$ = 31.0 Hz), 38.2, 22.4. IR (cm^{-1}): *v* 3188, 3075, 2963, 2928, 2873, 1691, 1599, 1509, 1475, 1535, 1509, 1413, 1367, 1326, 1274, 1232, 1162, 1126, 1067, 1027. HRMS (ESI): calcd for $C_{14}H_{17}F_4NO_2SNa$ $[M+Na]^+$ 362.0814, found: 362.0812.



(S)-N-((R)-4-(4-chlorophenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3c): Yellow solid (29.5 mg, 83%, 97:3 dr), mp 114–118 °C, $[\alpha]_D^{25}$ = +53.75 (*c* = 0.32, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.6, 2H), 7.38 (d, *J* = 8.4Hz, 2H), 4.51–4.33 (m, 1H), 4.22 (s, 1H), 3.45 (dd, *J* = 17.6, 6.1 Hz, 1H), 3.32 (dd, *J* = 17.6, 4.9 Hz, 1H), 1.15 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.45. ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.3, 140.5, 134.5, 129.6, 129.2, 125.1 (q, J_{FC} = 281.1 Hz), 56.9, 55.2 (q, $^2J_{FC}$ = 31.0 Hz), 38.3, 22.3. IR (cm^{-1}): *v* 3462, 3224, 3140, 2963, 2922, 2851, 1690, 1590, 1572, 1471, 1403, 1369, 1275, 1268, 1212, 1163, 1129, 1105, 1092, 1054, 1008, 992, 836. HRMS (ESI): calcd for $C_{14}H_{17}ClF_3NO_2SNa$ $[M+Na]^+$ 378.0518, found: 378.0518.

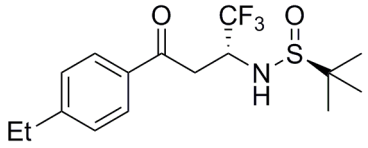


(S)-N-((R)-4-(4-bromophenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3d): White solid (34.0 mg, 85%, 95:5 dr), mp 125–130 °C, $[\alpha]_D^{25}$ = +44.9 (*c* = 1.49, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 4.56–4.44 (m, 1H), 4.33 (d, *J* = 8.8 Hz, 1H), 3.52 (dd, *J* = 17.5, 6.3 Hz, 1H), 3.38 (dd, *J* = 17.6, 4.6 Hz, 1H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.53. ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.4, 134.9, 132.1, 129.7, 129.2, 125.0 (q, J_{FC} = 263.6Hz), 57.0, 55.2 (q, $^2J_{FC}$ = 31.1 Hz), 38.3, 22.4. IR (cm^{-1}): *v* 3504, 3171, 2928, 2871, 1690, 1586, 1570, 1476, 1399, 1366, 1276, 1218, 1165, 1126, 1070, 1052, 1031, 1010, 990, 930, 883. HRMS (ESI): calcd for $C_{14}H_{17}BrF_3NO_2SNa$ $[M+Na]^+$ 422.0013, found: 422.0012.

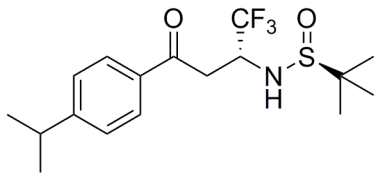


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-oxo-4-(p-tolyl)butan-2-yl)propane-2-sulfinamide (3e):

Colorless solid (32.5 mg, 97%, 98:2 dr), mp 115–120 °C, [α] = +67.9 (*c* = 0.54, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.55–4.39 (m, 1H), 4.46 (s, 1H), 3.53 (dd, *J* = 17.5, 5.6 Hz, 1H), 3.39 (dd, *J* = 17.5, 4.3 Hz, 1H), 2.41 (s, 3H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.47. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 144.9, 133.7, 129.5, 128.4, 125.2 (q, J_{FC} = 281.2 Hz), 56.9, 55.3 (q, $^2J_{FC}$ = 31.0 Hz), 37.9, 22.4, 21.7. IR (cm^{-1}): *v* 3166, 2988, 2959, 2925, 2869, 1682, 1606, 1574, 1466, 1429, 1365, 1282, 1226, 1183, 1153, 1123, 1094, 1052, 939, 883. HRMS (ESI): calcd for $C_{15}H_{20}F_3NO_2SNa$ $[M+Na]^+$ 358.1065, found: 358.1061.

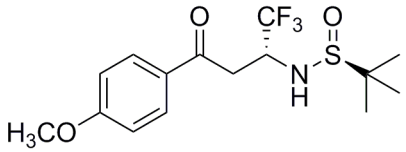


(S)-N-((R)-4-(4-ethylphenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3f): Colorless solid (34.6 mg, 99%, >99:1 dr), mp 90–94 °C, [α] = +65.2 (*c* = 1.41, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.51–4.42 (m, 2H), 3.54 (dd, *J* = 17.4, 5.7 Hz, 1H), 3.40 (dd, *J* = 17.4, 4.6 Hz, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.8 Hz, 3H), 1.25 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.45. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 151.1, 128.5, 125.2 (q, J_{FC} = 281.3 Hz), 56.8, 55.3 (q, $^2J_{FC}$ = 30.9 Hz), 37.9, 29.0, 22.4, 15.1. IR (cm^{-1}): *v* 3218, 2965, 2931, 2875, 1681, 1606, 1571, 1474, 1463, 1434, 1417, 1360, 1281, 1268, 1223, 1154, 1131, 1111, 1056, 1023, 989, 836. HRMS (ESI): calcd for $C_{16}H_{22}F_3NO_2SNa$ $[M+Na]^+$ 372.1221, found: 372.1220.

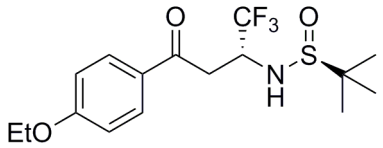


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(4-isopropylphenyl)-4-oxobutan-2-yl)propane-2-sulfinamide (3g): Colorless solid (36.0 mg, 99%, >99:1 dr), mp 58–62 °C, [α] = +54.6 (*c* = 1.58, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 4.48 (m, 2H), 3.54 (dd, *J* = 17.4, 5.5 Hz, 1H), 3.40 (dd, *J* = 17.4, 4.5 Hz, 1H), 3.03–2.90 (m, 1H),

1.26 (d, J = 6.9 Hz, 6H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.45. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 155.6, 134.1, 128.5, 126.9, 125.2 (q, J_{FC} = 281.1 Hz), 56.8, 55.3 (q, $^2J_{FC}$ = 30.9 Hz), 37.9, 34.3, 23.6, 22.4. IR (cm^{-1}): v 3483, 3128, 2966, 2985, 2928, 2874, 1689, 1607, 1473, 1416, 1366, 1278, 1224, 1164, 1130, 1109, 1029, 1016, 993, 837, 677. HRMS (ESI): $[M+Na]^+$ calcd for $C_{17}H_{24}F_3NO_2SNa$: 386.1378, found: 386.1374.

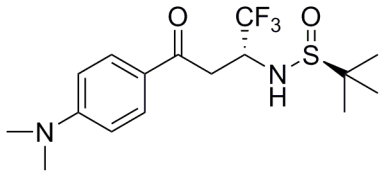


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(4-methoxyphenyl)-4-oxobutan-2-yl)propane-2-sulfinamide (3h): Colorless solid (33.0 mg, 94% yield, 98:2 dr), mp 47–51 °C, $[\alpha]_D^{25}$ = +59.2 (c = 0.36, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 4.46 (m, 2H), 3.88 (s, 3H), 3.50 (dd, J = 17.1, 4.8 Hz, 1H), 3.44–3.30 (m, 1H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.43. ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 164.2, 130.7, 129.3, 125.2 (q, J_{FC} = 281.1 Hz), 114.0, 25.2 (q, J_{FC} = 281.1 Hz), 56.8, 55.3 (q, $^2J_{FC}$ = 30.9 Hz), 37.5, 22.4. IR (cm^{-1}): v 3221, 2960, 2925, 2852, 1680, 1602, 1576, 1513, 1466, 1422, 1365, 1265, 1227, 1172, 1125, 1059, 1032, 888, 680, 590. HRMS (ESI): calcd for $C_{15}H_{20}F_3NO_3SNa$ $[M+Na]^+$ 374.1014, found: 374.1012.

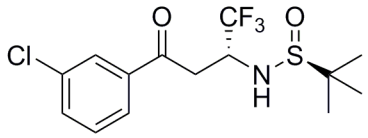


(S)-N-((R)-4-(4-ethoxyphenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3i): Colorless solid (35.4 mg, 97% yield, >99:1 dr), mp 88–91 °C, $[\alpha]_D^{25}$ = +58.6 (c = 1.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.90 (m, 2H), 7.30–6.90 (m, 2H), 4.56–4.42 (m, 2H), 4.09 (q, J = 7.0 Hz, 2H), 3.51 (dd, J = 17.3, 6.1 Hz, 1H), 3.35 (dd, J = 17.3, 4.8 Hz, 1H), 1.43 (t, J = 7.0 Hz, 3H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.43. ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 163.6, 130.7, 129.1, 125.3 (q, J_{FC} = 281.2 Hz), 114.4, 55.8, 55.3 (q, $^2J_{FC}$ = 30.8 Hz), 54.9, 37.5, 22.4, 14.6. IR (cm^{-1}): v 3222, 2977, 2989, 2936, 2901, 2871, 1677, 1603, 1575, 1510, 1479, 1424, 1398, 1367, 1320, 1267, 1222, 1161, 1131, 1112, 1057, 1023, 988, 806.

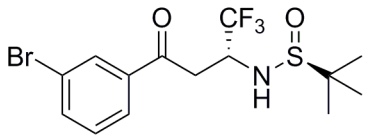
HRMS (ESI): calcd for $C_{16}H_{22}F_3NO_3SNa$ $[M+Na]^+$ 388.1170, found: 388.1169.



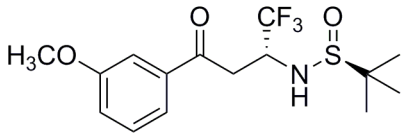
(S)-N-((R)-4-(4-(dimethylamino)phenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3j): Yellow solid (33.2 mg, 91%, 97:3 dr), mp 110–114 °C, $[\alpha]_D^{25}$ = +67.5 (*c* = 0.53, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.1 Hz, 2H), 6.65 (d, *J* = 9.1 Hz, 2H), 4.72 (d, *J* = 7.8 Hz, 1H), 4.53–4.25 (m, 1H), 3.45 (dd, *J* = 16.8, 5.9 Hz, 1H), 3.28 (dd, *J* = 16.8, 5.1Hz, 1H), 3.07 (s, 6H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.34. ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 153.9, 130.6, 125.3 (q, *J* = 281.5 Hz), 110.7, 56.7, 55.5 (q, $^2J_{FC}$ = 30.8 Hz), 36.4, 22.4. IR (cm^{-1}): *v* 3282, 3094, 2985, 2962, 2925, 2871, 2827, 1660, 1610, 1548, 1537, 1474, 1437, 1415, 1379, 1367, 1351, 1289, 1271, 1246, 1225, 1209, 1191, 1165, 1117, 1073, 943, 917, 816. HRMS (ESI): calcd for $C_{16}H_{23}F_3N_2O_2SNa$ $[M+Na]^+$ 387.1330, found: 387.1326.



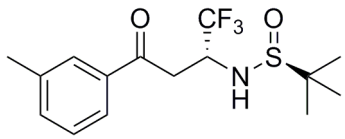
(S)-N-((R)-4-(3-chlorophenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3k): Colorless solid (31.3 mg, 88%, 96:4 dr), mp 52–56 °C, $[\alpha]_D^{25}$ = +64.9 (*c* = 0.94, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (t, *J* = 1.6 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.60–7.53 (m, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 4.58–4.41 (m, 1H), 4.30 (d, *J* = 8.3 Hz, 1H), 3.54 (dd, *J* = 17.7, 6.1 Hz, 1H), 3.42 (dd, *J* = 17.7, 4.9 Hz, 1H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.51. ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.3, 137.7, 135.2, 133.8, 130.2, 128.3, 126.3, 125.1 (q, J_{FC} = 281.1 Hz), 56.9, 55.09 (q, $^2J_{FC}$ = 31.1 Hz), 38.5, 22.4. IR (cm^{-1}): *v* 3225, 2978, 2927, 2871, 1692, 1573, 1474, 1432, 1418, 1366, 1281, 1262, 1217, 1159, 1131, 1115, 1054, 951, 885. HRMS (ESI): calcd for $C_{14}H_{17}ClF_3NO_2SNa$ $[M+Na]^+$ 378.0518, found: 378.0520.



(S)-N-((R)-4-(3-bromophenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3l): Colorless oil (28.0 mg, 70%, 97:3 dr), $[\alpha]_D^{25}$ = +49.9 (*c* = 1.03, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 4.58–4.52 (m, 2H), 3.57 (dd, *J* = 17.8, 6.2 Hz, 1H), 3.38 (dd, *J* = 17.8, 3.7 Hz, 1H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.79. ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 137.8, 136.7, 131.3, 130.4, 129.3, 126.7, 125.1 (q, J_{FC} = 281.0 Hz), 57.2, 55.1 (q, $^2J_{FC}$ = 31.1 Hz), 38.4, 22.4. IR (cm^{-1}): *v* 3205, 3070, 2962, 2928, 2873, 2117, 2052, 1696, 1567, 1475, 1463, 1420, 1365, 1274, 1213, 1172, 1126, 1068, 903, 788. HRMS (ESI): calcd for $C_{14}H_{17}BrF_3NO_2SNa$ $[M+Na]^+$ 422.0013, found: 422.0009.

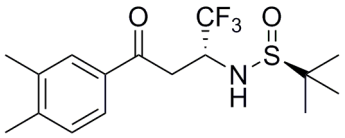


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(3-methoxyphenyl)-4-oxobutan-2-yl)propane-2-sulfinamide (3m): Colorless oil (31.3 mg, 91%, 94:6 dr), $[\alpha]_D^{25}$ = +68.6 (*c* = 0.72, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.12 (dd, *J* = 8.0, 2.3 Hz, 1H), 4.60–4.45 (m, 1H), 4.51 (s, 1H), 3.84 (s, 3H), 3.57 (dd, *J* = 17.5, 5.7 Hz, 1H), 3.41 (dd, *J* = 17.5, 3.9 Hz, 1H), 1.25 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.51. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 159.9, 137.4, 129.7, 125.2 (q, J_{FC} = 281.0 Hz), 120.8, 120.5, 112.3, 57.0, 55.4, 55.23 (q, $^2J_{FC}$ = 30.9 Hz), 38.3, 22.4. IR (cm^{-1}): *v* 3219, 2963, 1691, 1598, 1585, 1487, 1463, 1432, 1364, 1332, 1275, 1171, 1125, 1073, 1014, 948, 876. HRMS (ESI): calcd for $C_{15}H_{20}F_3NO_3SNa$ $[M+Na]^+$ 374.1014, found: 374.1014.

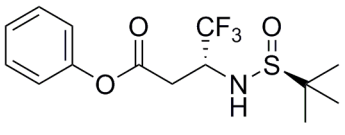


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-oxo-4-(m-tolyl)butan-2-yl)propane-2-sulfinamide (3n):

Colorless solid (30.2 mg, 90%, >99:1 dr), mp 44–47 °C, $[\alpha]_D^{25}$ = +49.4 (*c* = 1.9, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.78–7.70 (m, 2H), 7.37(m, 2H), 4.56–4.40 (m, 2H), 3.55 (dd, *J* = 17.6, 5.6 Hz, 1H), 3.42 (dd, *J* = 17.6, 4.5 Hz, 1H), 2.4 (s, 3H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.46. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 138.7, 134.7, 128.8, 125.5, 125.2 (q, J_{FC} = 281.1 Hz), 56.8, 55.2 (q, $^2J_{FC}$ = 31.0 Hz), 38.2, 22.4, 21.3. IR (cm^{-1}): *v* 3210, 2961, 2927, 2871, 1687, 1587, 1459, 1420, 1366, 1276, 1165, 1124, 1057, 939, 916. HRMS (ESI): calcd for $C_{15}H_{20}F_3NO_2SNa$ $[M+Na]^+$ 358.1065, found: 358.1063.

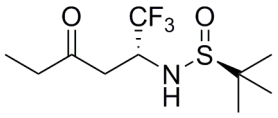


(S)-N-((R)-4-(3,4-dimethylphenyl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3o): Colorless solid (34.2 mg, 98%, >99:1 dr), mp 51–53 °C, $[\alpha]_D^{25}$ = +47.8 (*c* = 0.41, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.65 (s, 1H), 7.59 (m, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 4.41 (m, 1H), 4.32 (m, 1H), 3.45 (dd, *J* = 17.3, 5.9 Hz, 1H), 3.31 (dd, *J* = 17.3, 4.9 Hz, 1H), 2.24 (s, 6H), 1.16 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.44. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 143.7, 137.3, 134.1, 130.0, 129.4, 128.0 (q, J_{FC} = 278.3 Hz), 126, 56.8, 55.3 (q, $^2J_{FC}$ = 30.9 Hz), 37.8, 22.4, 20.1, 19.8. IR (cm^{-1}): *v* 3219, 2959, 2927, 2856, 1687, 1608, 1573, 1456, 1409, 1365, 1274, 1240, 1212, 1167, 1123, 1072, 1020, 988, 930. HRMS (ESI): calcd for $C_{16}H_{22}F_3NO_2SNa$ $[M+Na]^+$ 372.1221, found: 372.1219.

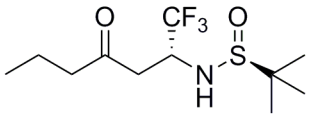


phenyl (R)-3-(((S)-tert-butylsulfinyl)amino)-4,4,4-trifluorobutanoate (3p): Colorless solid (27.0 mg, 80%, 96:4 dr), mp 103–105 °C, $[\alpha]_D^{25}$ = +56.9 (*c* = 1.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.36 (m, 2H), 7.25 (t, *J* = 7.5Hz, 1H), 7.17–7.14 (m, 2H), 4.56 (d, 1H), 4.29 (m, 1H), 3.15 (dd, *J* = 16.2, 5.2 Hz, 1H), 3.02 (dd, *J* = 16.2, 6.3 Hz, 1H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.08. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 150.2, 129.6, 126.4, 124.7 (q, J_{FC} =

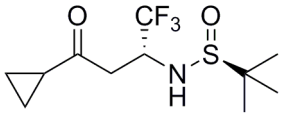
281.3 Hz), 121.5, 57.0, 55.9 (q, $^2J_{FC}$ = 31.3 Hz), 35.0, 22.4. IR (cm^{-1}): *v* 3210, 2989, 2960, 2926, 2867, 1759, 1592, 1489, 1458, 1387, 1366, 1290, 1271, 1236, 1120, 1153, 1129, 1057, 953, 768. HRMS (ESI): calcd for $C_{14}H_{18}F_3NO_3SNa$ $[M+Na]^+$ 360.0857, found: 360.0859.



(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-oxohexan-2-yl)propane-2-sulfinamide (3q): Colorless solid (24.9 mg, 91%, 99:1 dr), mp 57–61 °C, $[\alpha]_D^{25}$ = +70.4 (*c* = 0.09, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 4.39 (d, *J* =8.6 Hz, 1H), 4.28 (m, 1H), 3.00–2.86 (m, 2H), 2.52 (q, *J* =7.2 Hz, 2H), 1.23 (s, 9H), 1.09 (t, *J* =7.2 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.78. ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 125.0 (q, J_{FC} =280.9 Hz), 56.9, 55.2 (q, $^2J_{FC}$ = 31.1Hz), 41.5, 37.2, 22.4, 7.3. IR (cm^{-1}): *v* 3151, 2986, 2963, 2927, 1725, 1460, 1367, 1277, 1167, 1122, 1056, 923, 810. HRMS (ESI): calcd for $C_{10}H_{18}F_3NO_2SNa$ $[M+Na]^+$ 296.0908, found: 296.0907.

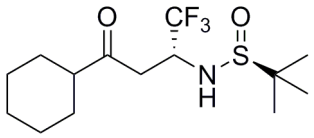


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-oxoheptan-2-yl)propane-2-sulfinamide (3r): Colorless solid (25.9 mg, 90%, 96:4 dr), mp 59–63 °C, $[\alpha]_D^{25}$ = +46.1 (*c* = 0.81, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 4.43 (d, *J* = 9.0Hz, 1H), 4.42–4.19 (m, 1H), 2.99–2.86 (m, 2H), 2.47 (t, *J* = 7.3Hz, 2H), 1.69–1.56 (m, 2H), 1.23 (s, 9H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.76. ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6, 125.1 (q, J_{FC} = 281.0Hz), 56.8, 55.1 (q, $^2J_{FC}$ = 31.1 Hz), 42.3, 22.4, 21.6, 11.8 (d, *J* = 9.*0*Hz, 2C). IR (cm^{-1}): *v* 3189, 3161, 2967, 2937, 2879, 1723, 1460, 1415, 1368, 1275, 1199, 1172, 1128, 1092, 1058, 931, 843. HRMS (ESI): calcd for $C_{11}H_{20}F_3NO_2SNa$ $[M+Na]^+$ 310.0165, found: 310.0164.

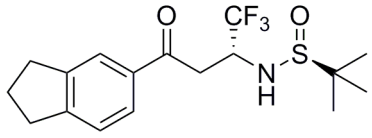


(S)-N-((R)-4-cyclopropyl-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3s): Colorless solid (23.1 mg, 81%, 96:4 dr), mp 81–83 °C, $[\alpha]_D^{25}$ = +67.2 (*c* = 0.98, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (d, J = 8.8 Hz, 1H), 4.34–4.17 (m, 1H), 3.09 (d, J = 5.4 Hz, 2H), 4.60–4.45 (m, 1H), 2.00–1.89 (m, 1H), 1.23 (s, 9H), 1.17–1.09 (m, 1H), 1.02–0.94 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.68. ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6, 125.1 (q, J_{FC} = 281.0 Hz), 56.8, 55.1 (q, $^{2}J_{FC}$ = 31.1 Hz), 42.3, 22.4, 11.8, 11.7. IR (cm^{-1}): v 3139, 2995, 2973, 2929, 2876, 1706, 1480, 1416, 1389, 1365, 1278, 1264, 1216, 1165, 1129, 1093, 1052, 1018, 950, 818, 698. HRMS (ESI): calcd for $C_{11}H_{18}F_3NO_2SNa$ $[M+Na]^+$ 308.0908, found: 308.0909.

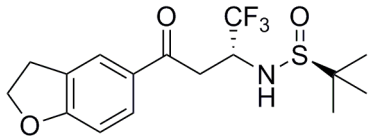


(S)-N-((R)-4-cyclohexyl-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3t): White solid (31.4 mg, 96%, 97:3 dr), mp 103–107 °C, $[\alpha]_D^{25}$ = +63.0 (c = 0.62, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (d, J = 9.1 Hz, 1H), 4.33–4.20 (m, 1H), 2.95 (qd, J = 17.5, 5.3 Hz, 2H), 2.38–2.32 (m, 1H), 1.91–1.83 (m, 2H), 1.83–1.74 (m, 2H), 1.71–1.63 (m, 1H), 1.41–1.26 (m, 5H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.68. ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.8, 125.1 (q, J_{FC} = 281.0 Hz), 56.8, 55.21 (q, $^{2}J_{FC}$ = 31.0 Hz), 51.5, 39.8, 28.0, 25.7, 25.5, 25.4, 22.4. IR (cm^{-1}): v 3196, 2926, 2853, 1714, 1469, 1449, 1379, 1364, 1284, 1266, 1220, 1187, 1159, 1126, 1076, 1055, 1003, 945, 920, 867. HRMS (ESI): calcd for $C_{14}H_{24}F_3NO_2SNa$ $[M+Na]^+$ 350.1378, found: 350.1375.

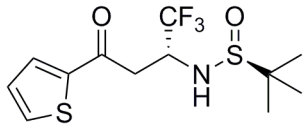


(S)-N-((R)-4-(2,3-dihydro-1H-inden-5-yl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3u): White solid (35.4 mg, 98%, 99:1 dr), mp 88–91 °C, $[\alpha]_D^{25}$ = +58.7 (c = 1.46, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.69–7.63 (m, 1H), 7.22 (d, J = 7.9 Hz, 1H), 4.49–4.24 (m, 2H), 3.46 (dd, J = 17.4, 5.5 Hz, 1H), 3.31 (dd, J = 17.4, 4.3 Hz, 1H), 2.86 (t, J = 7.5 Hz, 4H), 2.03 (p, J = 7.5 Hz, 2H), 1.15 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.68. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 151.3, 145.1, 134.7, 126.8, 125.2 (q, J_{FC} = 281.0 Hz), 124.6, 124.2, 77.4, 77.1, 76.8, 56.8, 55.3 (q, $^{2}J_{FC}$ = 30.8 Hz), 38.0, 33.1, 32.5, 25.3, 22.4. IR (cm^{-1}): v 3221,

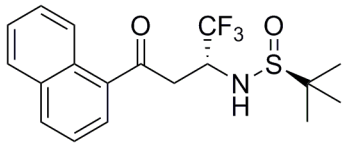
2962, 2930, 2869, 1681, 1606, 1574, 1473, 1462, 1402, 1361, 1268, 1215, 1149, 1130, 1113, 1054, 868, 839. HRMS (ESI): calcd for $C_{17}H_{22}F_3NO_2SNa$ $[M+Na]^+$ 384.1221, found: 384.1218.



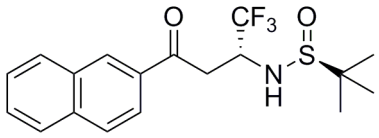
(S)-N-((R)-4-(2,3-dihydrobenzofuran-5-yl)-1,1,1-trifluoro-4-oxobutan-2-yl)-2-methylpropane-2-sulfinamide (3v): Colorless solid (36.0 mg, 99%, >99:1 dr), mp 124–128 °C, $[\alpha]_D^{25}$ = +64.5 (*c* = 1.46, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.85 (s, 1H), 7.77 (d, *J* = 8.5, 1H), 6.80 (d, *J* = 8.4, 1H), 4.66 (t, *J* = 8.8, 2H), 4.47 (s, 2H), 3.48 (dd, *J* = 17.0, 5.1, 1H), 3.34 (dd, *J* = 16.7, 3.1, 1H), 3.24 (t, *J* = 8.7, 2H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.44. ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 165.1, 130.4, 129.6, 128.1, 125.7, 125.2 (q, J_{FC} = 281.1 Hz), 109.2, 72.4, 56.8, 55.35 (q, $^2J_{FC}$ = 30.9 Hz), 37.5, 28.9, 22.4. IR (cm^{-1}): *v* 3226, 2991, 2981, 2961, 2930, 2868, 1669 , 1604, 1496, 1476, 1444, 1423, 1367, 1277, 1269, 1251, 1222,1179, 1120, 1107, 1056, 977,911, 806. HRMS (ESI): calcd for $C_{16}H_{20}F_3NO_3SNa$ $[M+Na]^+$ 386.1014, found: 386.1010.



(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-oxo-4-(thiophen-2-yl)butan-2-yl)propane-2-sulfinamide (3w): Colorless solid (32.4 mg, 99%, >99:1 dr), mp 59–63 °C, $[\alpha]_D^{25}$ = +65.8 (*c* = 1.40, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 3.7Hz, 1H), 7.72 (d, *J* = 4.9 Hz, 1H), 7.16 (t, *J* = 4.3Hz, 1H), 4.62 (d, *J* = 7.2 Hz, 1H), 4.48–4.34 (m, 1H), 3.50 (dd, *J* = 16.9, 5.6 Hz, 1H), 3.37 (dd, *J* = 16.9, 5.1Hz, 1H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.44. ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 141.3, 135.2, 132.9, 128.4, 125.0 (q, J_{FC} = 281.2 Hz), 56.8, 55.4 (q, $^2J_{FC}$ = 31.1 Hz), 38.3, 22.4. IR (cm^{-1}): *v* 3486, 3396, 3118, 2989, 2927, 2873, 1672, 1523, 1473, 1417, 1366, 1275, 1224, 1159, 1131, 1115, 1012, 942, 854. HRMS (ESI): calcd for $C_{12}H_{16}F_3NO_2S_2Na$ $[M+Na]^+$ 350.0472, found: 350.0470.



(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(naphthalen-1-yl)-4-oxobutan-2-yl)propane-2-sulfinamide (3x): Yellow solid (30.8 mg, 96%, 97:3 dr), mp 83–86 °C, $[\alpha]_D^{25}$ = +60.6 (*c* = 1.46, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.5, 1H), 8.01 (d, *J* = 8.2, 1H), 7.87 (t, *J* = 8.0, 2H), 7.64-7.61 (m, 1H), 7.55-7.47 (m, 2H), 4.57-4.50 (m, 2H), 3.65-3.53 (m, 2H), 1.25 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.32. ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 134.7, 134.0, 133.7, 130.1, 128.4, 128.2, 126.7, 125.8, 125.3 (q, J_{FC} = 281.1 Hz), 124.3, 57.0, 55.6 (q, $^2J_{FC}$ = 30.9 Hz), 41.3, 22.4. IR (cm^{-1}): *v* 3220, 2985, 2971, 2930, 2869, 2853, 1671, 1593, 1574, 1509, 1473, 1436, 1366, 1356, 1279, 1253, 1216, 1157, 1130, 1057, 942, 879. HRMS (ESI): calcd for $C_{18}H_{21}F_3NO_2SNa$ $[M+Na]^+$ 394.1065, found: 394.1060.

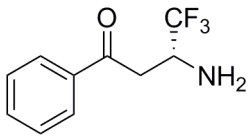


(S)-2-methyl-N-((R)-1,1,1-trifluoro-4-(naphthalen-2-yl)-4-oxobutan-2-yl)propane-2-sulfinamide (3y): Colorless solid (36.4 mg, 98%, >99:1 dr), mp 81–83 °C, $[\alpha]_D^{25}$ = +48.2 (*c* = 1.59, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.93–7.70 (m, 4H), 7.45 (m, *2*H), 4.49 (s, 2H), 3.66–3.60 (m, 1H), 3.55–3.36 (m, 1H), 1.14 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.38. ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 135.8, 133.5, 132.3, 130.2, 129.6, 128.9, 128.7, 127.8, 127.0, 125.3 (q, J_{FC} = 281.1Hz), 123.6, 56.9, 55.3 (q, $^2J_{FC}$ = 31.0Hz), 38.2, 22.4. IR (cm^{-1}): *v* 3494, 3219, 3063, 2983, 2960, 2926, 2870, 1682, 1628, 1597, 1575, 1471, 1437, 1366, 1279, 1217, 1170, 1120, 1057, 938, 816, 747. HRMS (ESI): calcd for $C_{18}H_{21}F_3NO_2SNa$ $[M+Na]^+$ 394.1064, found: 394.1061.

4. Determination of absolute configuration of compound 4

Conversion of 3a affording free β-amino ketone 4

3a (0.5 mmol) and MeOH (5 mL) were placed in a 25 mL round bottom flask and aq HCl (36%, 1 mL) was added. The reaction was stirred at rt for 8 h, during which the cleavage was monitored by TLC. Volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and Et_3N (15 mmol) was added. The mixture was stirred at rt for 1 h, then H_2O (10 mL) was added. The organic layer was taken, washed with H_2O (2×10 mL), dried with anhydrous Na_2SO_4, filtered and the solvent was removed to give the crude product. The residue was purified by silica gel column chromatography, eluting with petroleum ether/ethyl acetate (5:1), to give compound **4a**.



(*R*)-3-amino-4,4,4-trifluoro-1-phenylbutan-1-one

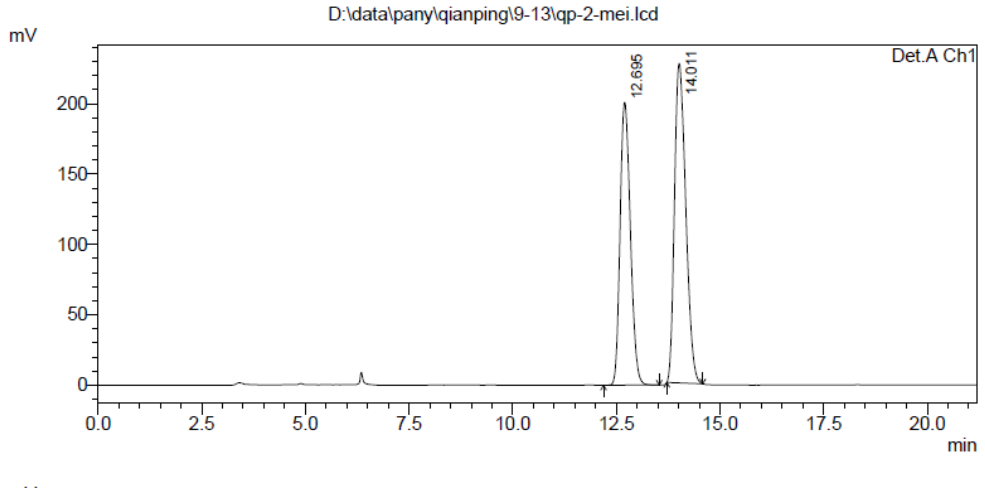
Compound **4**, 98:2 er, colorless solid (97.7 mg, 90%), mp 27-31 °C, $[\alpha]_D^{25}$ = +23.9 (*c* = 1.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 3.95 (m, 1H), 3.32-3.19 (m, 1H), 3.11 (m, 1H), 1.60 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -78.24. ^{13}C NMR (101MHz, $CDCl_3$): δ 196.3, 136.3, 133.8, 128.8, 128.1, 124.6 (q, *J* = 278.9 Hz), 50.2 (q, *J* = 29.7 Hz), 39.3. IR (cm^{-1}): *v* 3389, 3310, 3219, 2958, 2923, 2853, 1689, 1596, 1581,1452, 1416, 1395, 1364, 1335, 1306, 1258, 1188, 1165, 1122, 1098, 1034, 1026, 1001, 930, 896, 876, 826, 763. HRMS (ESI): $[M+H^+]$ calcd for $C_{10}H_{11}F_3NO$ 218.0793, found: 218.0788.

Determination of absolute configuration by the means of HPLC

Conditions: 254 nm, 1 mL/min, 10% *i*-PrOH, Daicel OD chiral column.

(1) The HPLC of racemic compound ((*S*)-**4** and (*R*)-**4**)

<Chromatogram>



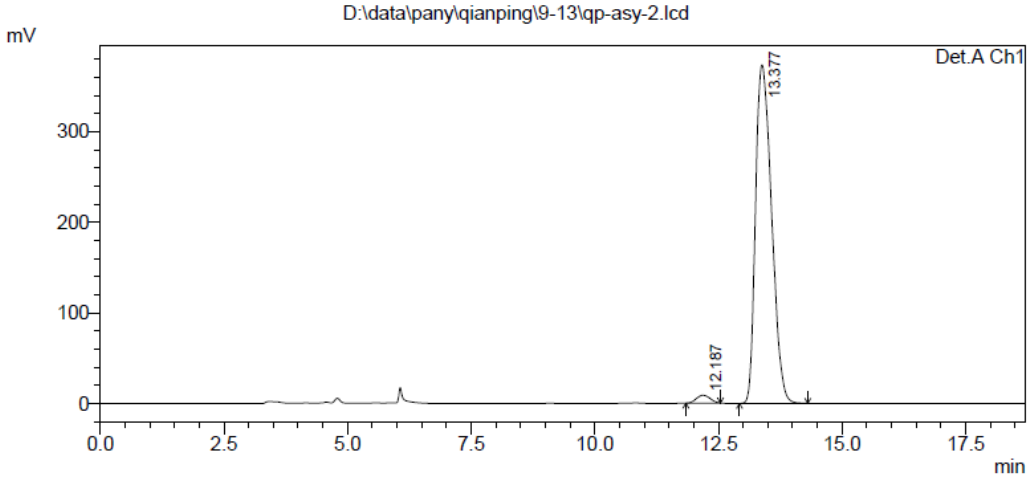
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.695	3475259	200939	44.721	46.949
2	14.011	4295677	227055	55.279	53.051
Total		7770936	427994	100.000	100.000

(2) The HPLC of compound (*R*)-**4**

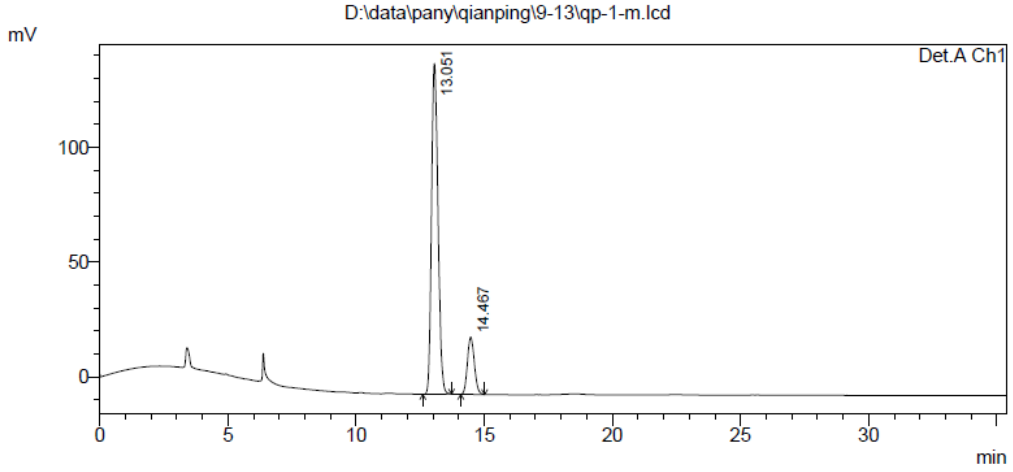
<Chromatogram>



Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.187	165876	8655	1.924	2.265
2	13.377	8457008	373375	98.076	97.735
Total		8622884	382029	100.000	100.000

(3)The HPLC of compound (*S*)-**4**

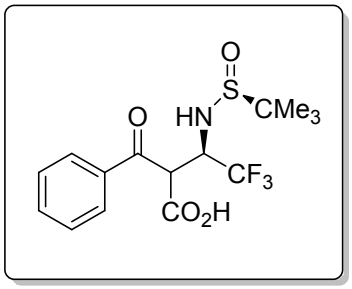
<Chromatogram>



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.051	2538387	144032	84.407	85.239
2	14.467	468925	24941	15.593	14.761
Total		3007311	168974	100.000	100.000

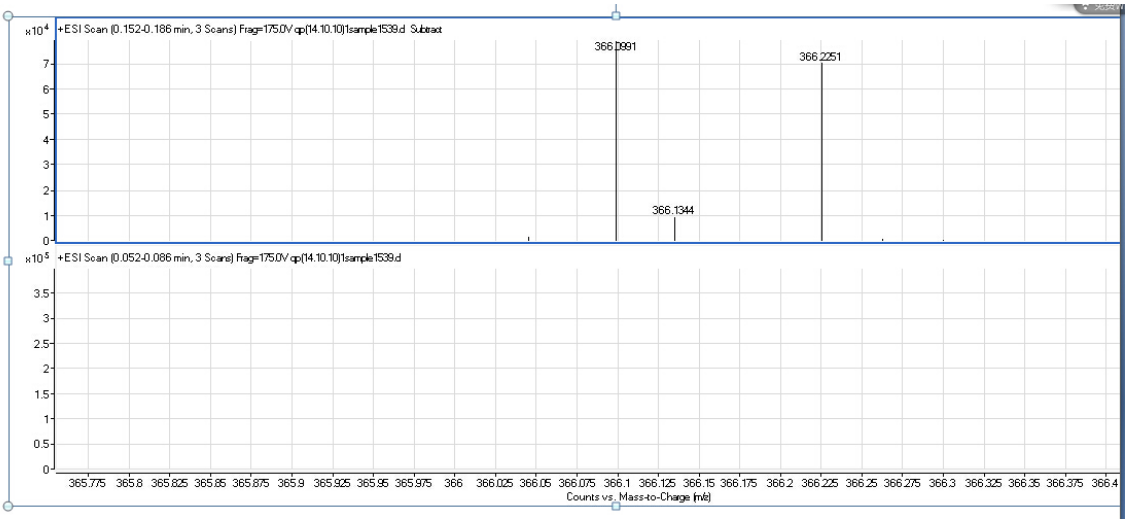
5. ESI-Mass analysis of the mixture of β-ketoacid 2a and imine 1 for the intermediate detection

A mixture of β-keto acid **2a** (26.2 mg, 0.16 mmol) and imine **1** (20.1 mg, 0.10 mmol) in tetrahydrofuran (1.0 mL) was stirred at 25 °C for 5 h and subjected to ESI-mass (positive mode) spectroscopic analysis. Copied below is the ESI-mass spectrum. HRMS (ESI) for intermediate **D**: calcd for $C_{15}H_{19}F_3NO_4S$ $[M+H]^+$ 366.0987, found 366.0991. In addition, calcd for $C_{15}H_{18}F_3NNaO_4S$ $[M+Na]^+$ 388.0806, found 388.0805.

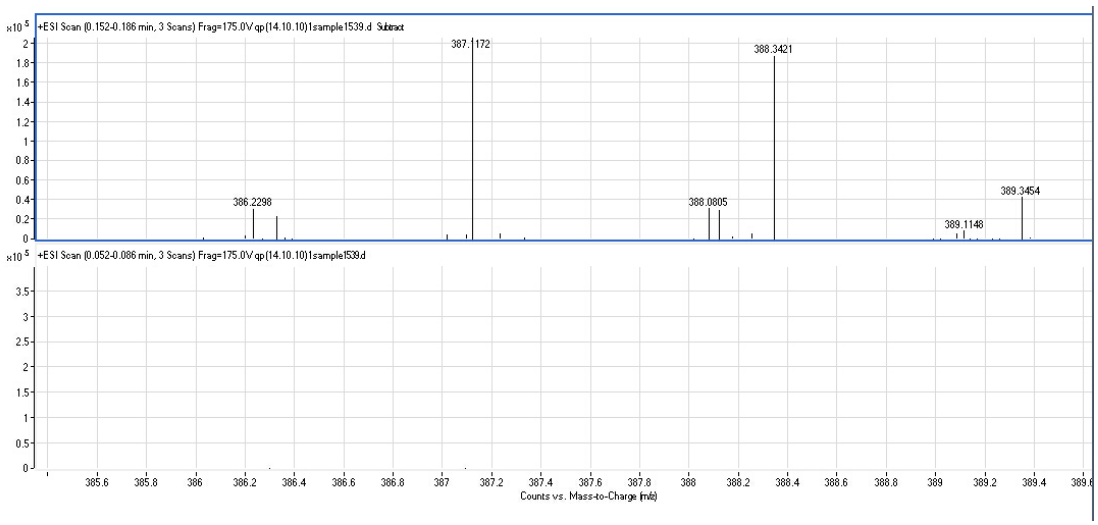


Structure of intermediate **D**.

HRMS (ESI) for $[M+H]^+$



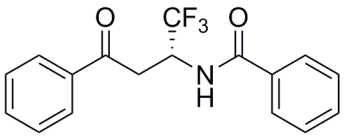
HRMS (ESI) for $[M+Na]^+$


+ESI Scan (0.152-0.186 min, 3 Scans) Frag=175.0V qp(14.10.10)1sample1539.d Subtract
387.1172
388.3421
386.2298
388.0805
389.3454
389.1148
+ESI Scan (0.052-0.086 min, 3 Scans) Frag=175.0V qp(14.10.10)1sample1539.d
Counts vs. Mass-to-Charge (m/z)

6. Cyclization derivatization of β-trifluoromethyl-β-amino ketone 3a

Conversion of 4 affording (*R*)-*N*-(1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)benzamide 5

To a solution of (*R*)-3-amino-4,4,4-trifluoro-1-phenylbutan-1-one (46.2 mg, 0.21 mmol) in dry toluene (10 mL), benzoyl chloride (53.82 mg, 0.38 mmol) was added. The reaction mixture was heated for 6 h at 120 °C in sealing tube, followed by evaporation of the solvent. The residue was purified by silica gel column chromatography, eluting with petroleum ether/ethyl acetate (6:1), to give compound **5**.

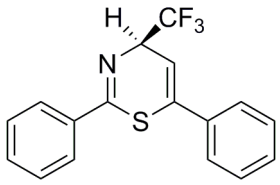


(*R*)-*N*-(1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)benzamide

Compound **5**, 98:2 er, White solid (67.0 mg, 98%), mp 148-153°C, $[\alpha]_D^{25}$ = -29.7 (*c* = 0.15, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 7.0 Hz, 1H), 7.55-7.41 (m, 5H), 5.43 (m, 1H), 3.65 (dd, *J* = 17.4, 5.7 Hz, 1H), 3.34 (dd, *J* = 17.3, 4.6 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.39. ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 167.0, 136.1, 134.1, 133.2, 128.9, 128.7, 128.2, 125.1 (q, J_{FC} = 282.0 Hz), 48.0 (q, $^2J_{FC}$ = 31.8Hz), 35.6. IR (cm^{-1}): *v* 3284, 3189, 3058, 2926, 2854, 1688, 1650, 1598, 1532, 1452, 1352, 1322, 1267, 1228, 1157, 1118, 1101, 1062, 1003, 908, 761, 693, 676,638, 595. HRMS (ESI): $[M+Na]^+$ calcd for $C_{17}H_{14}F_3NO_2Na$: 344.0874, found: 344.0873.

Conversion of 5 affording (*R*)-2,6-diphenyl-4-(trifluoromethyl)-4*H*-1,3-thiazine 6

To a solution of amide **5** (47.7 mg, 0.15 mmol) in dry toluene (15 mL), phosphorus pentasulfide (66 g, 0.296 mmol) was added and the reaction mixture was boiled with vigorous stirring for 8 h at 120 °C in sealing tube. After cooling, the organic layer was decanted and the solvent was evaporated to give crude oily products. The residue was purified by silica gel column chromatography, eluting with petroleum ether/ethyl acetate (10:1), to give compound **6**.

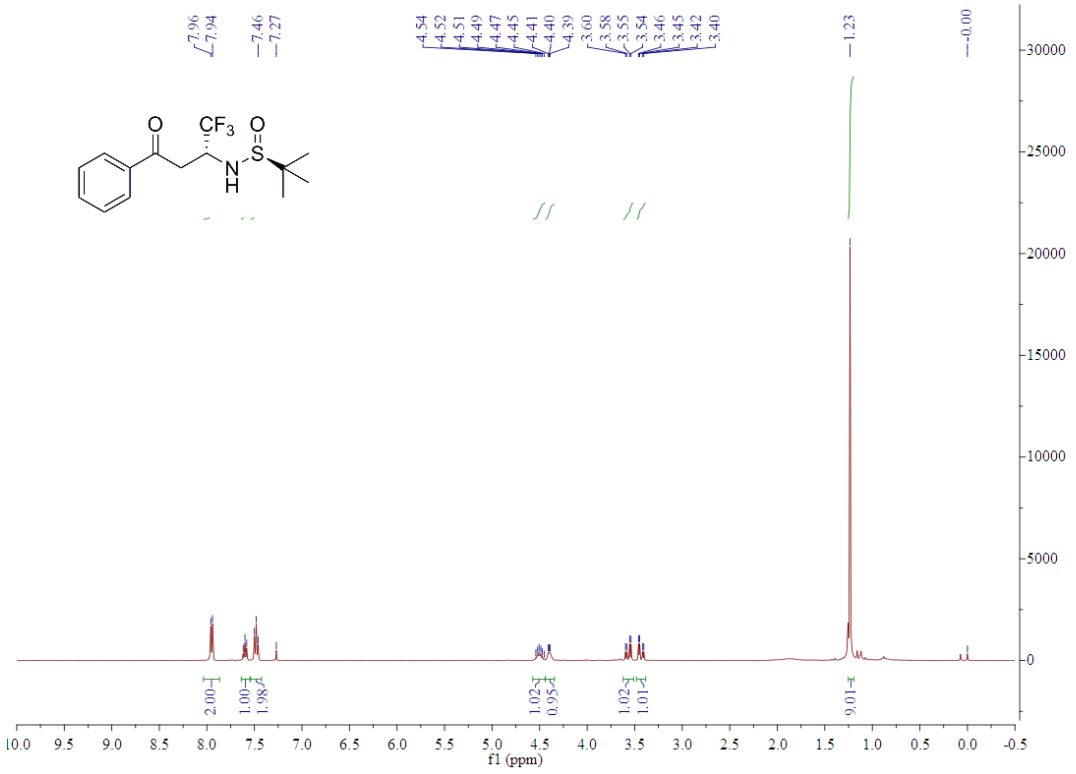


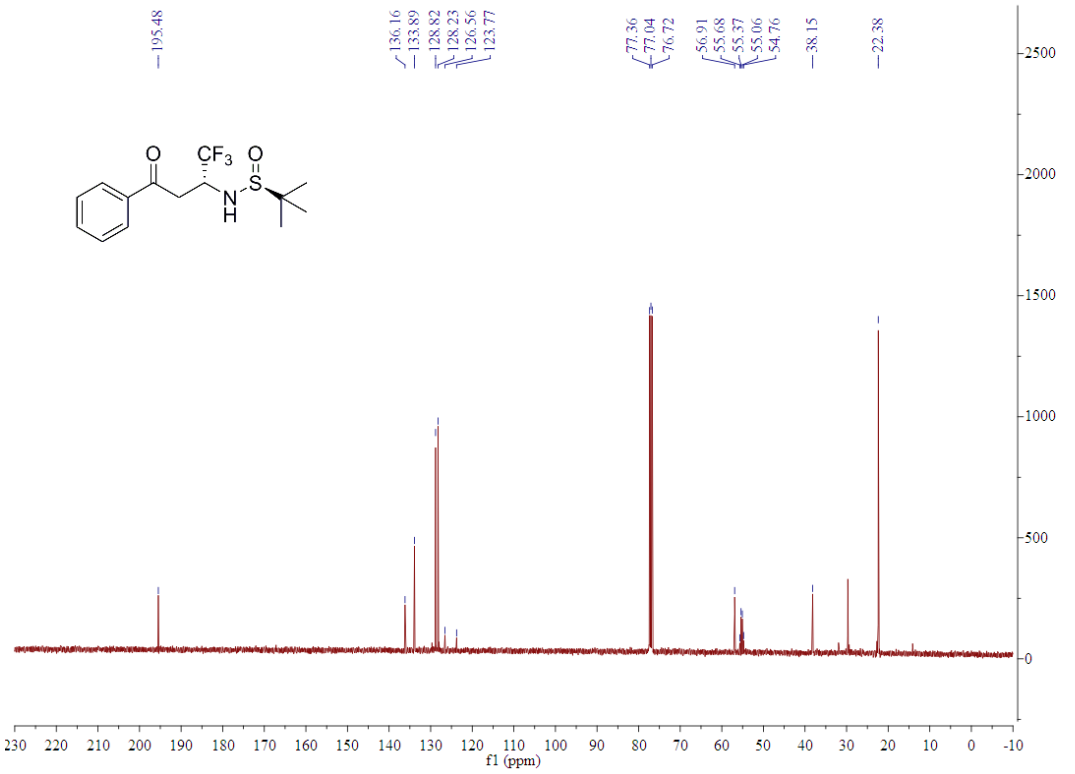
(*R*)-2,6-diphenyl-4-(trifluoromethyl)-4*H*-1,3-thiazine

Compound **6**, 97:3 er, Colorless solid (41.0 mg, 86%), mp 47-52 °C, [α] = -23.7 (*c* = 0.06, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.12-8.08 (m, *2*H), 7.65-7.62 (m, 2H), 7.51-7.42 (m, 6H), 6.17 (d, *J* = 3.1 Hz, 1H), 4.30 (qd, *J* = 8.0, 3.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.56. ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 139.1, 135.9 (d, *J* = 3.3 Hz), 131.9, 129.6, 128.9, 128.7, 128.2, 126.9, 125.3 (q, J_{FC} = 278.4 Hz), 111.0, 64.8 (q, $^2J_{FC}$ = 30.3 Hz). IR (cm^{-1}): *ν* 3067, 2923, 2850, 1625, 1443, 1379, 1257, 1242, 1174, 1124, 1109, 954, 897, 760, 700, 684, 540. HRMS (ESI): $[M+H]^+$ calcd for $C_{17}H_{13}F_3NS$: 320.0721, found: 320.0712.

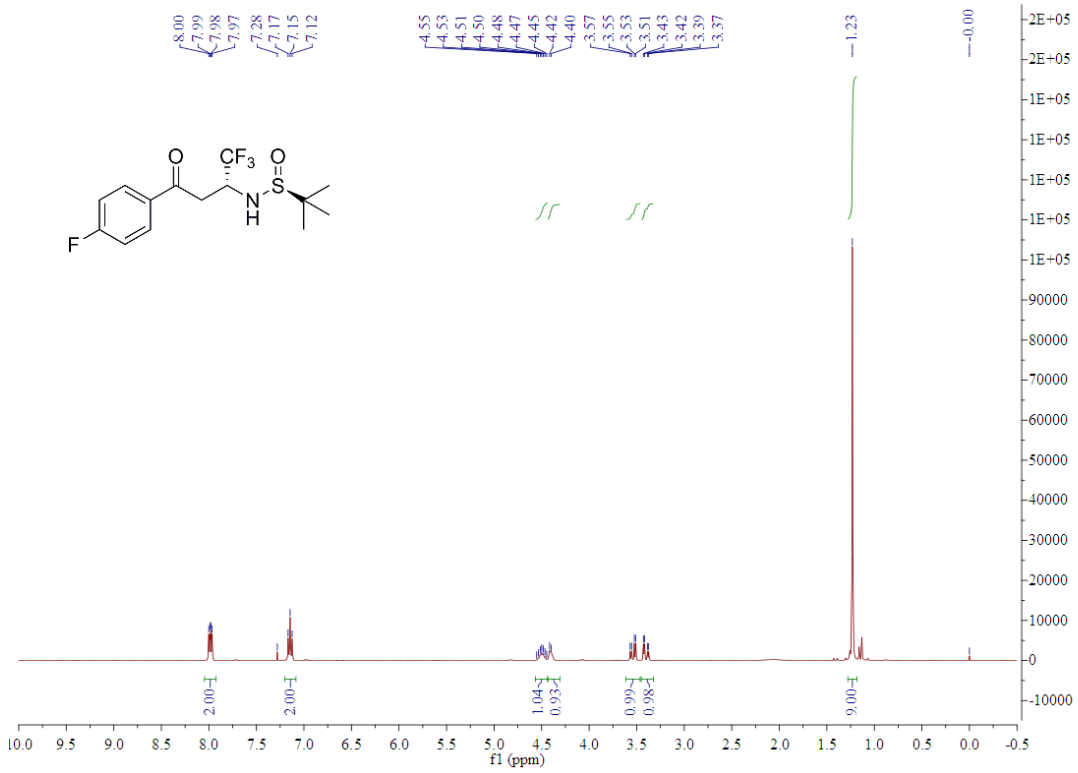
7. ^{1}H and ^{13}C NMR spectra for compounds 3, 4, 5 and 6

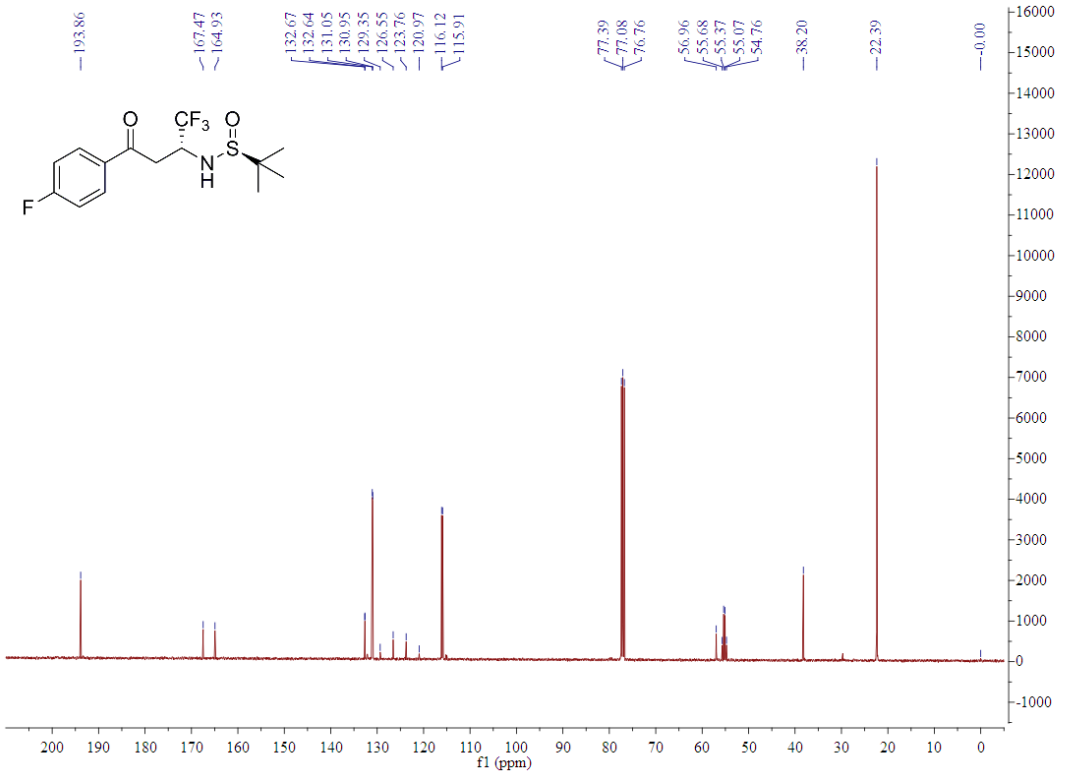
^{1}H NMR and ^{13}C NMR spectrum of **3a**



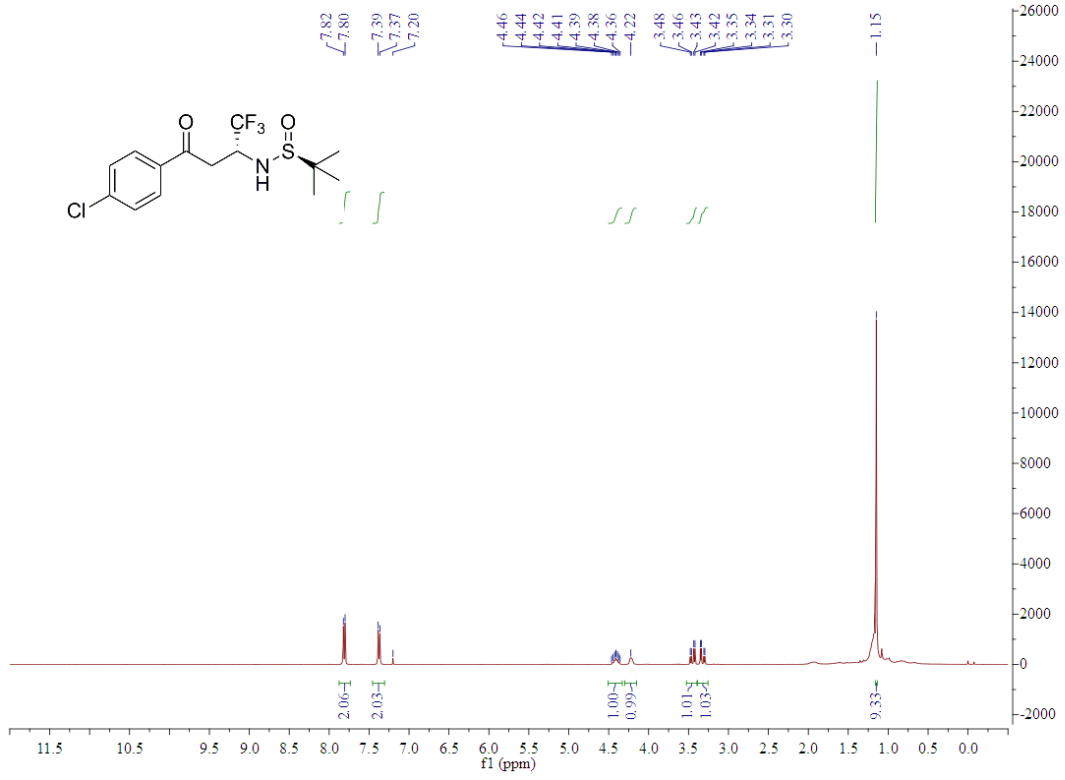


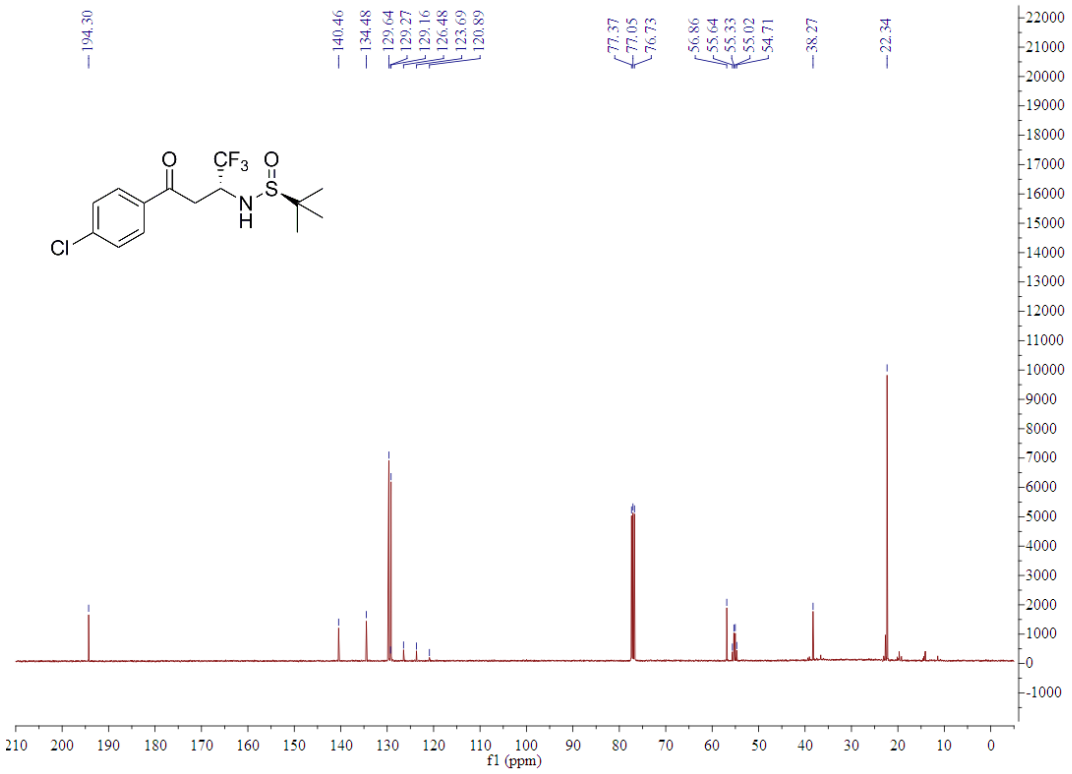
^{1}H NMR and ^{13}C NMR spectrum of **3b**



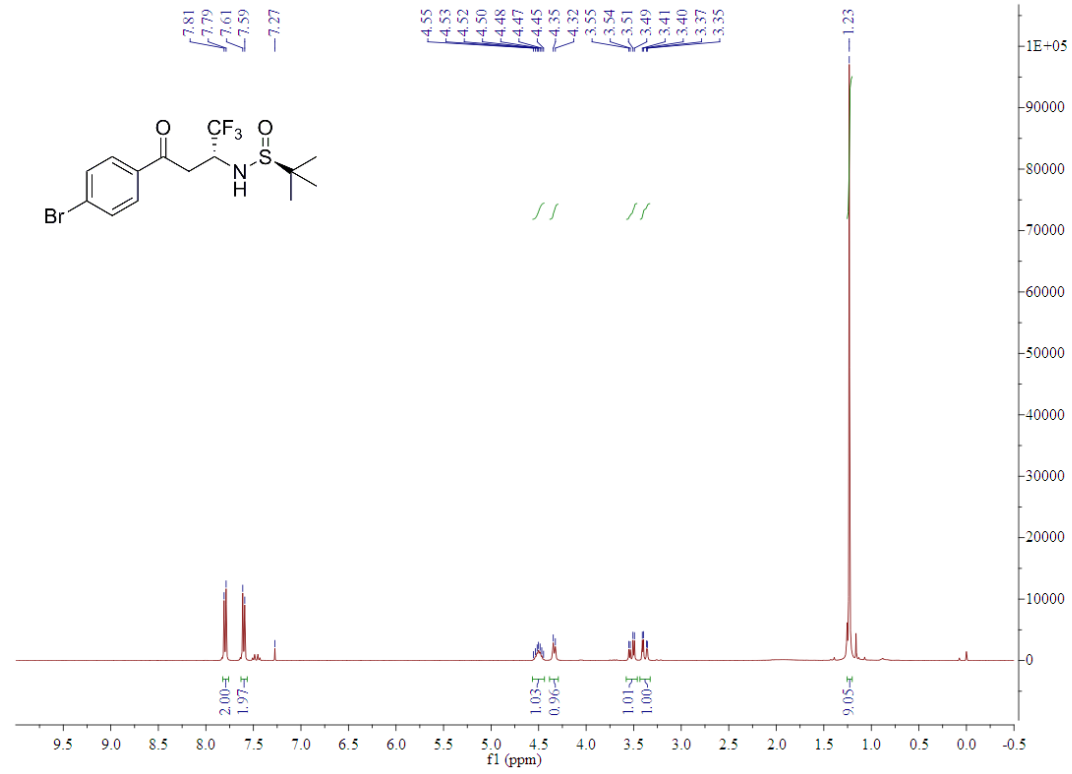


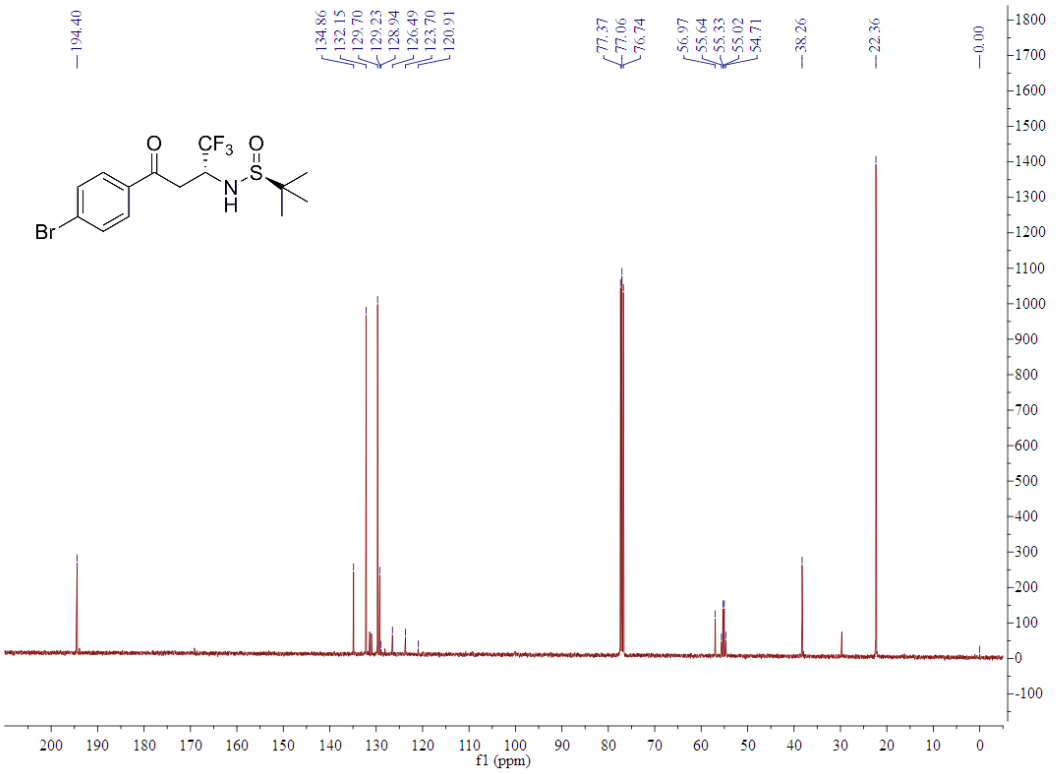
^{1}H NMR and ^{13}C NMR spectrum of **3c**



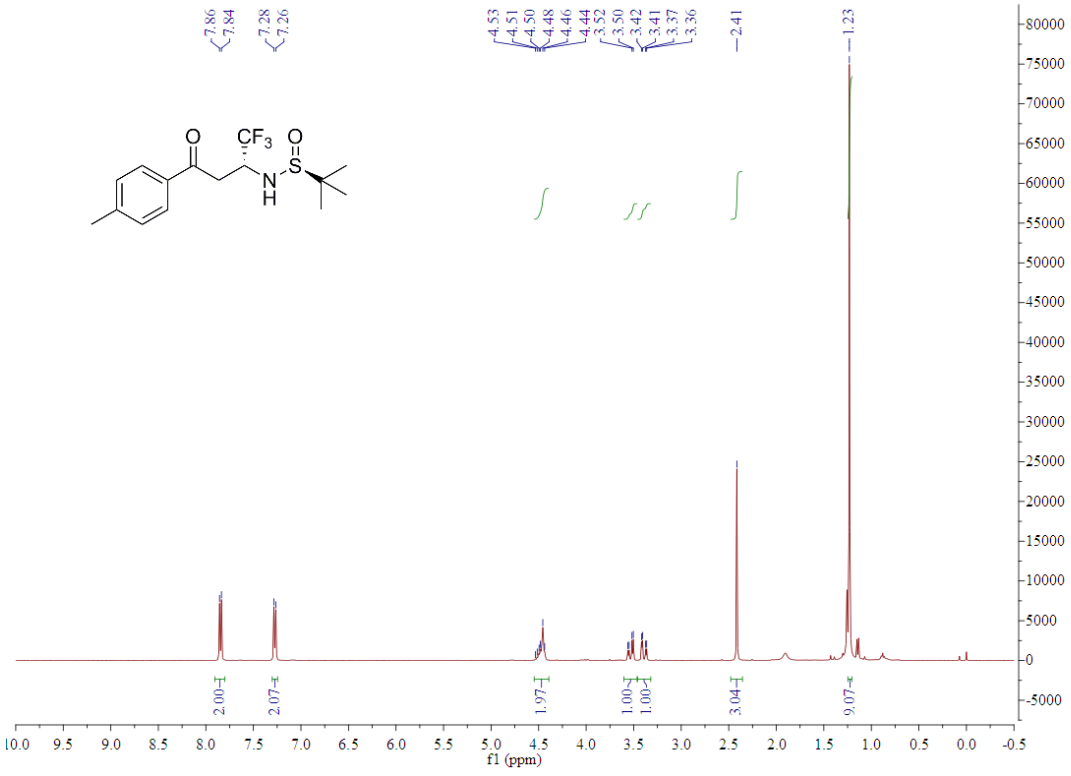


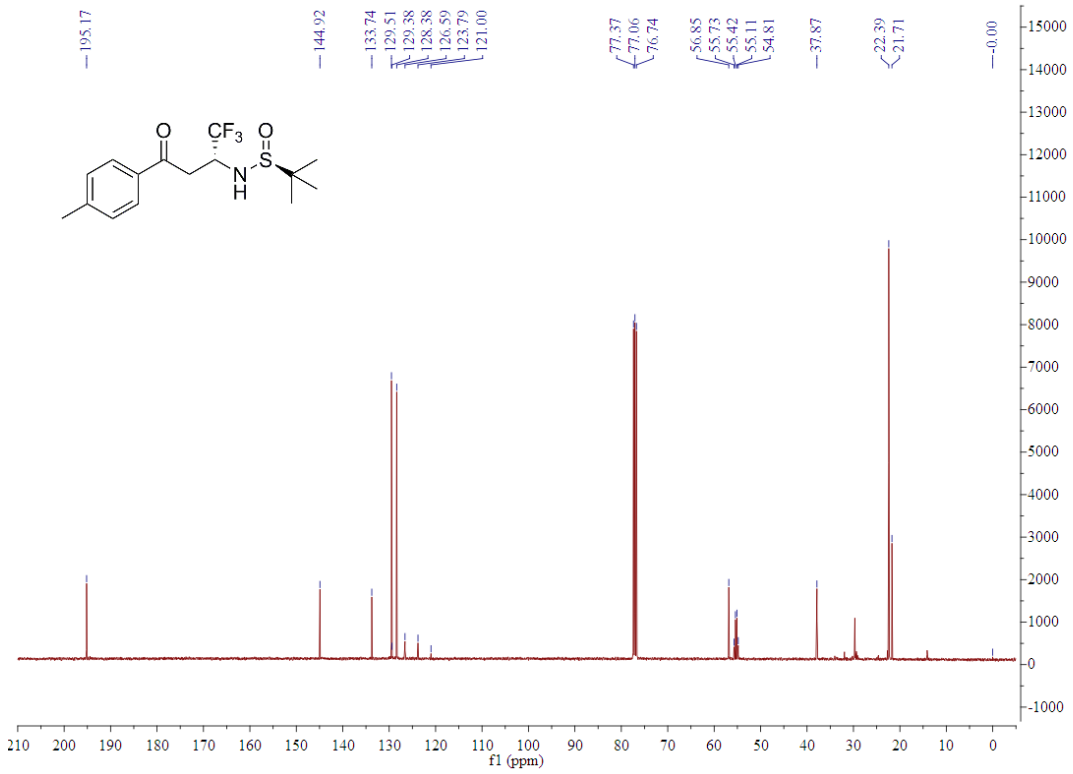
^{1}H NMR and ^{13}C NMR spectrum of **3d**



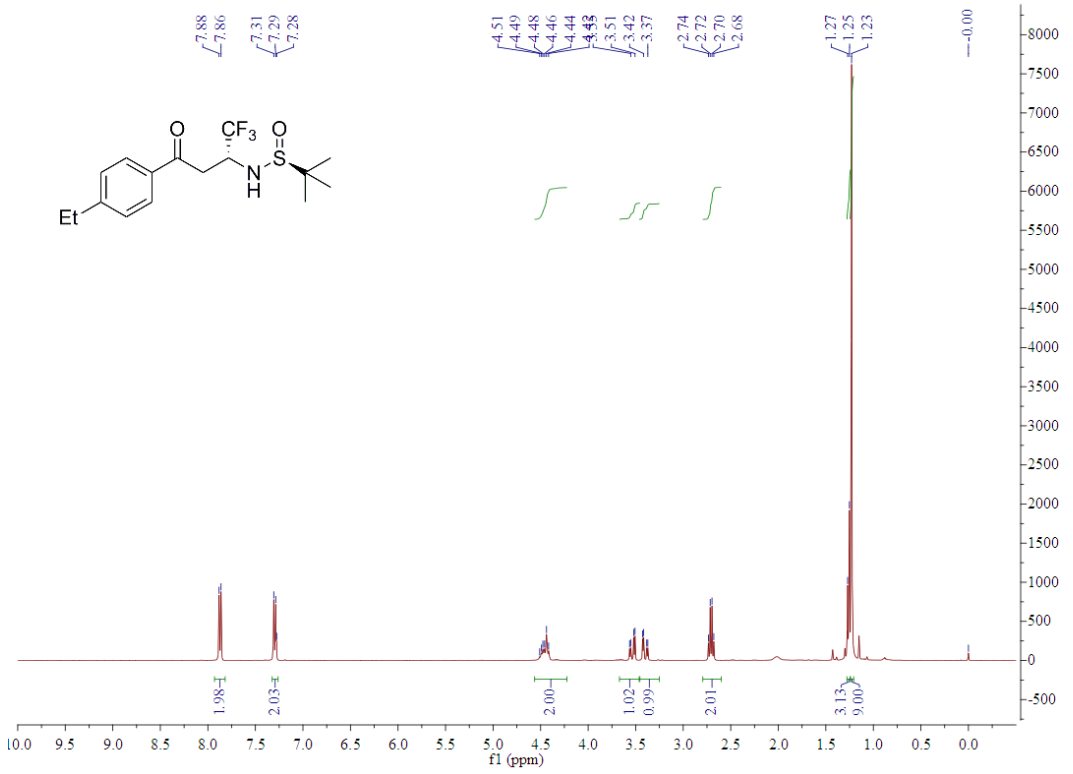


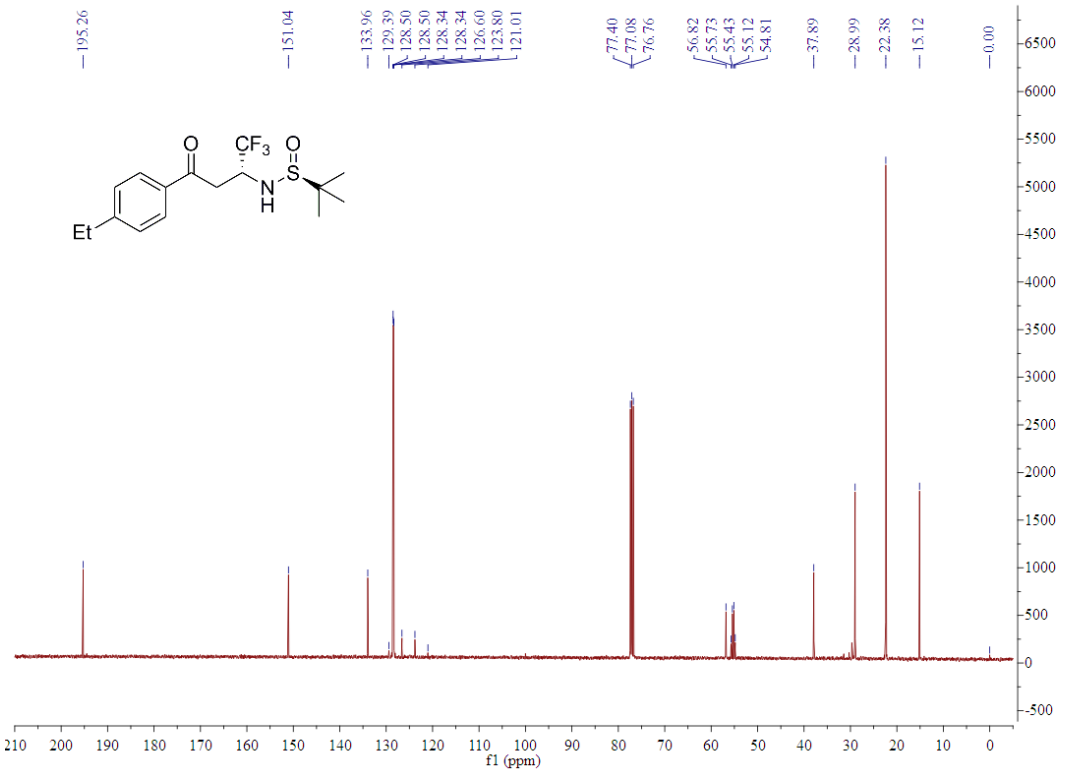
^{1}H NMR and ^{13}C NMR spectrum of **3e**



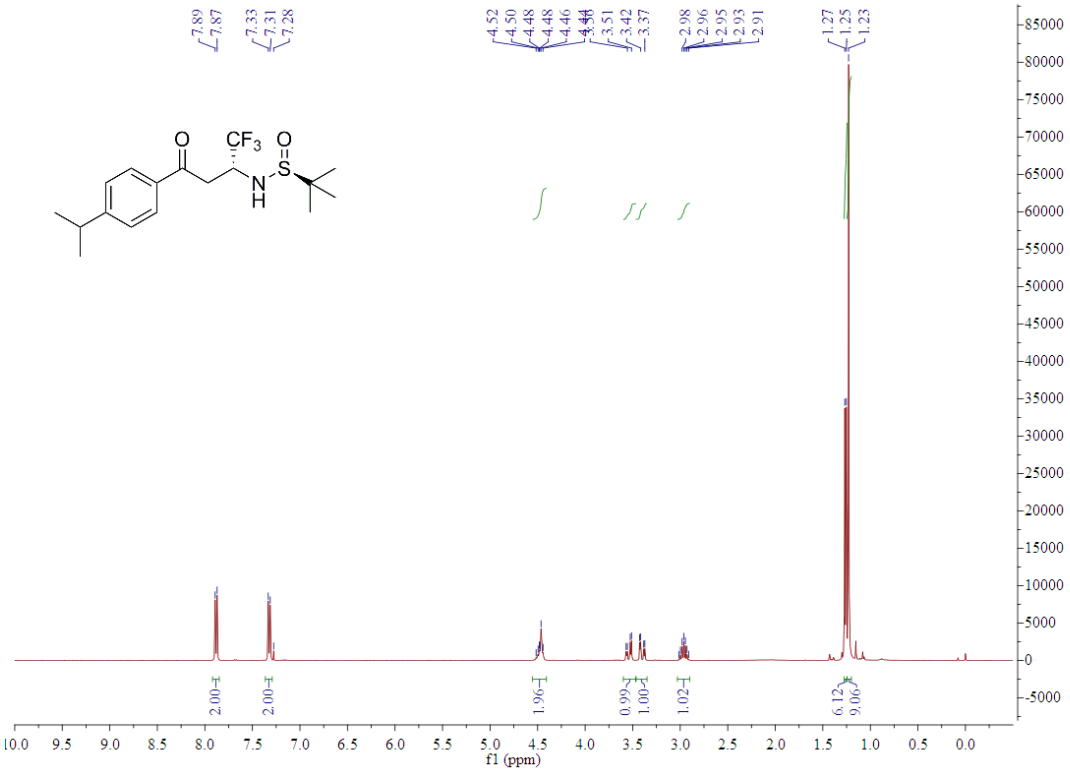


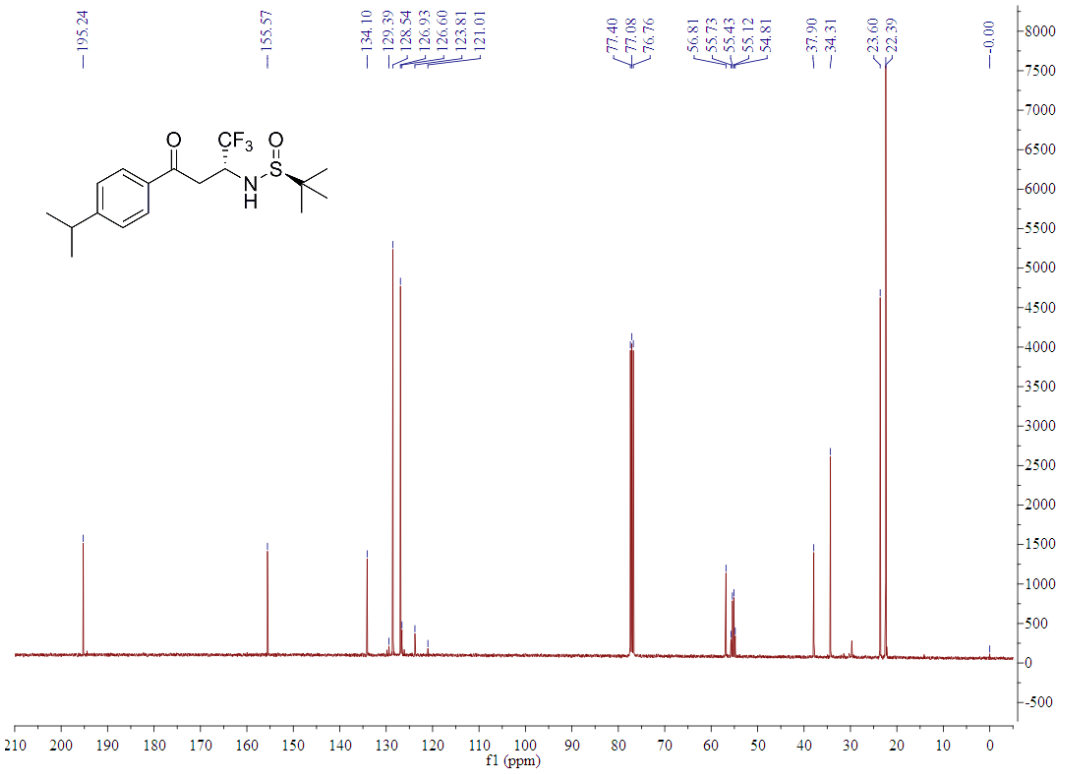
^{1}H NMR and ^{13}C NMR spectrum of **3f**



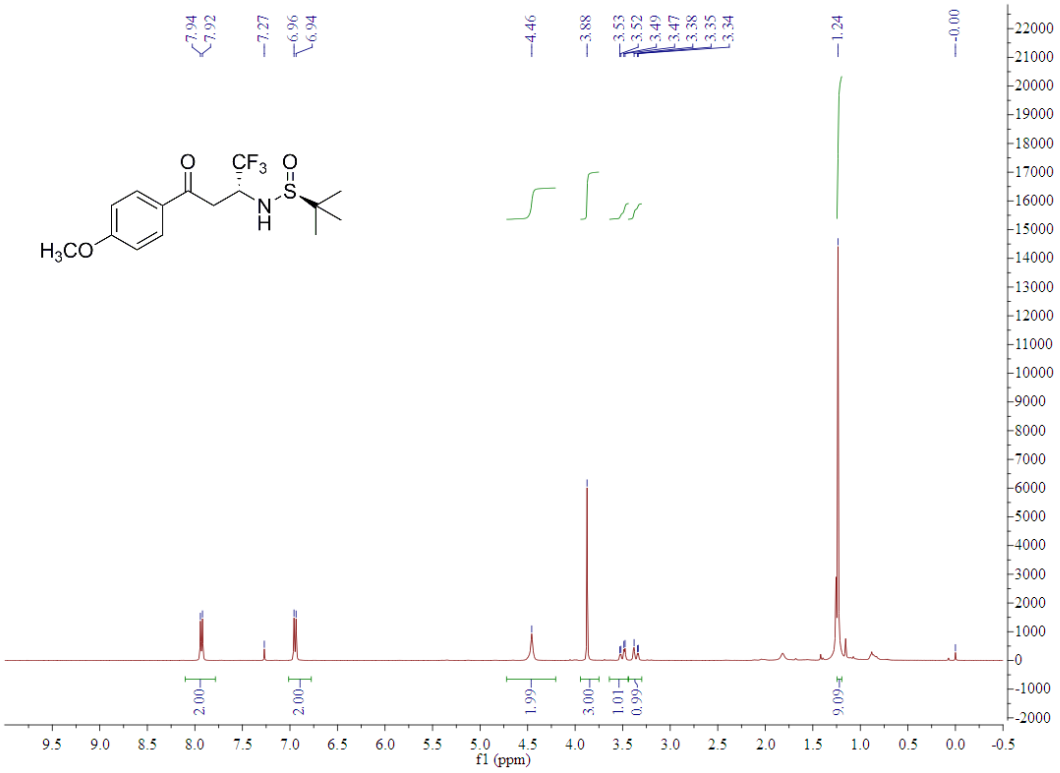


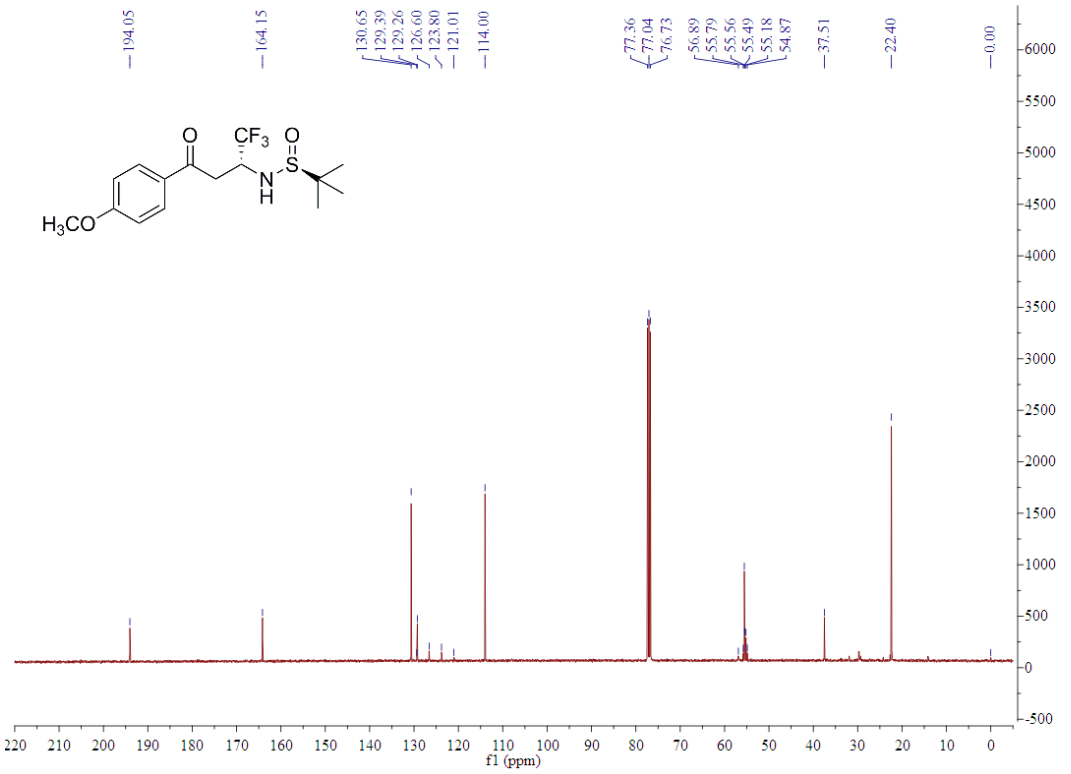
^{1}H NMR and ^{13}C NMR spectrum of **3g**



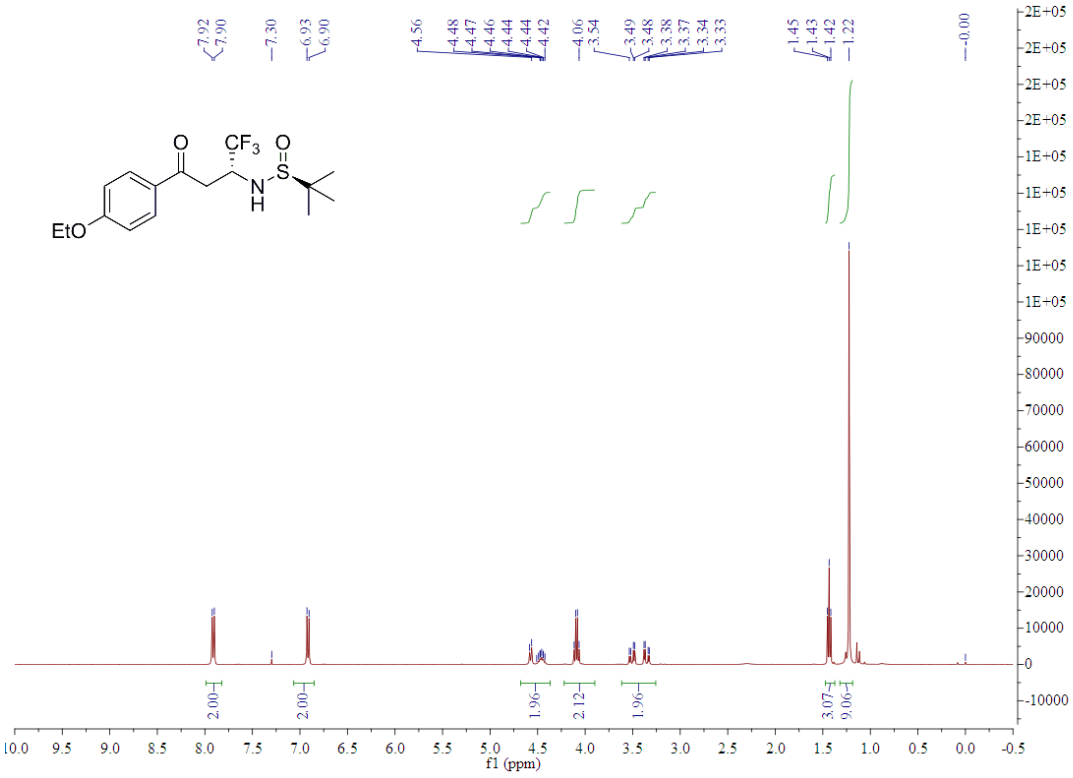


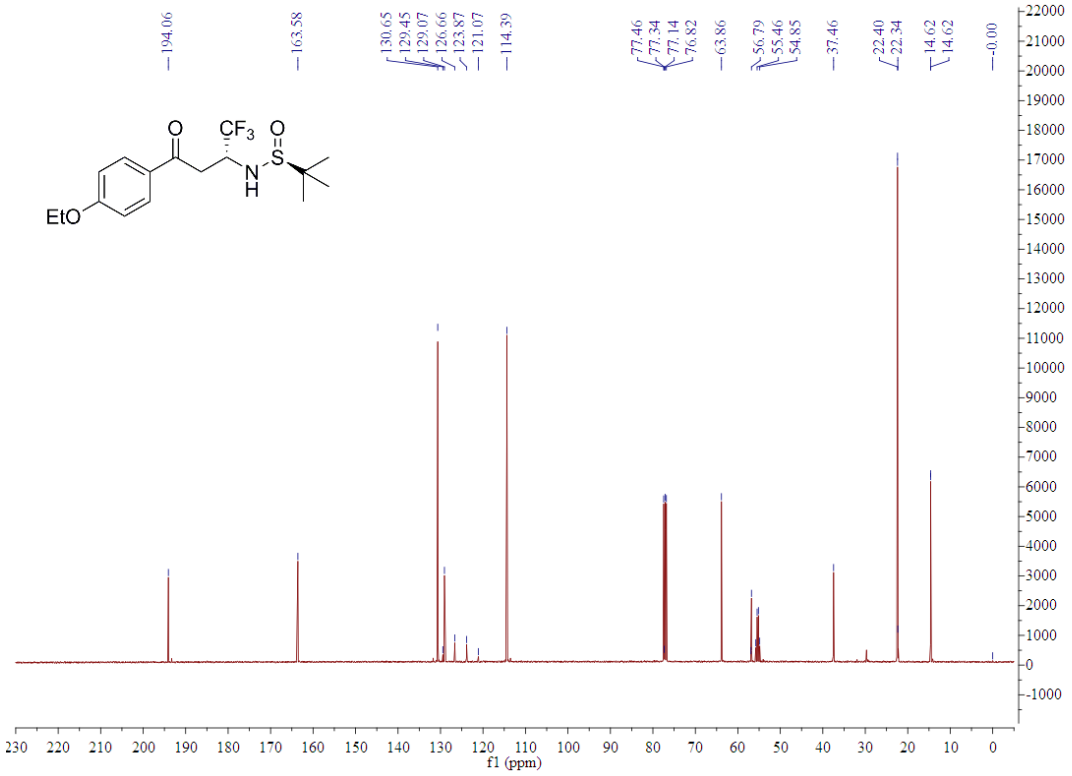
^{1}H NMR and ^{13}C NMR spectrum of **3h**



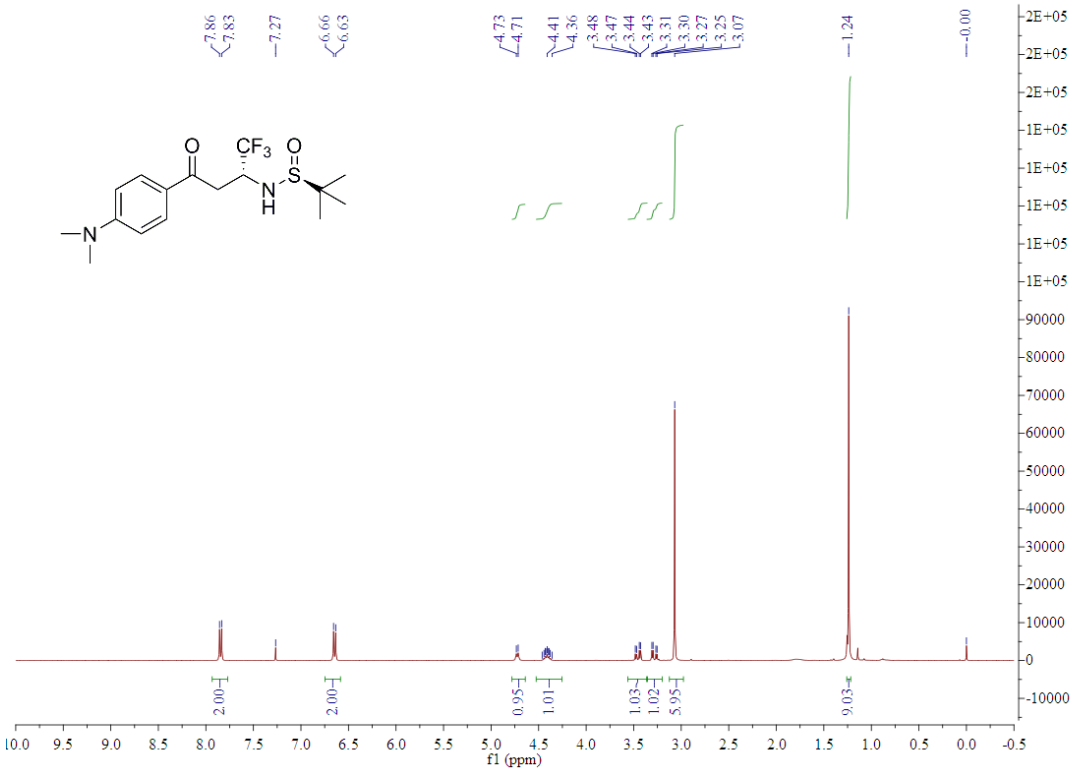


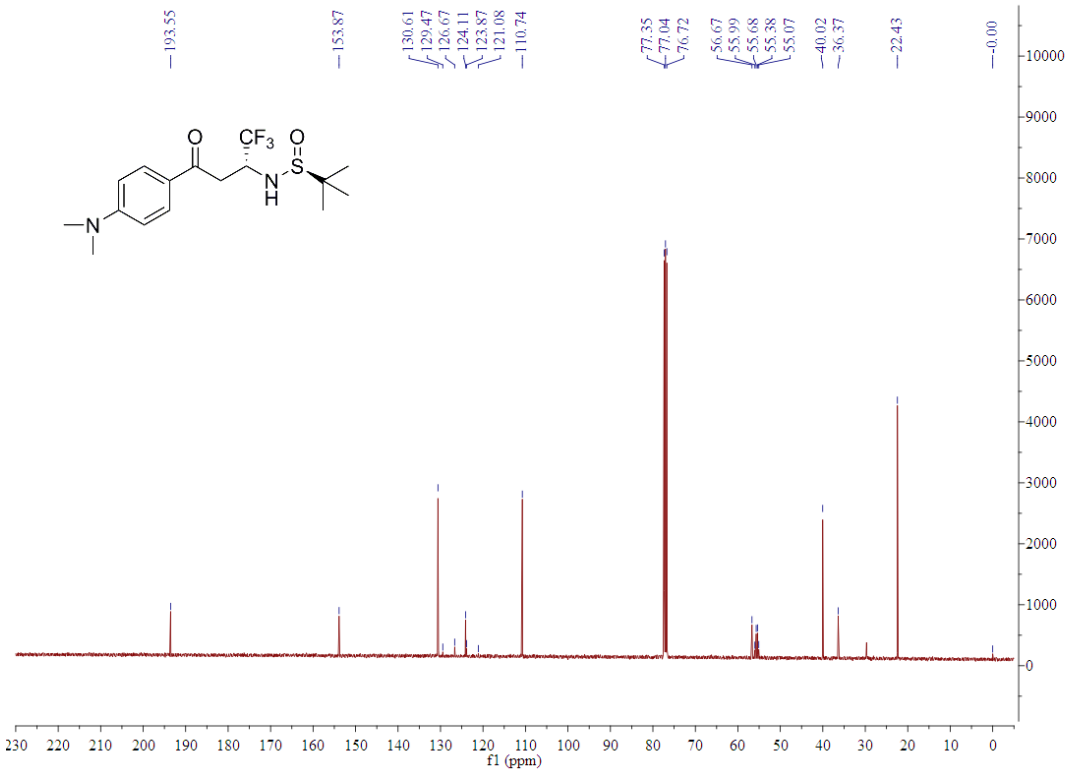
^{1}H NMR and ^{13}C NMR spectrum of **3i**



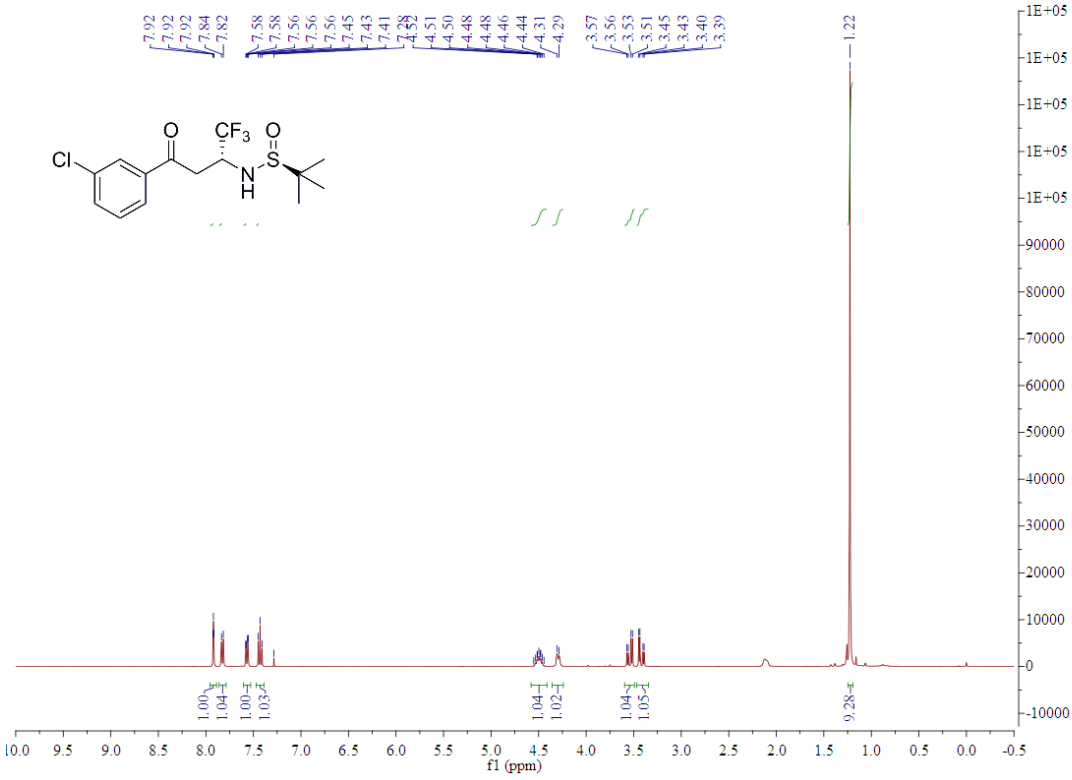


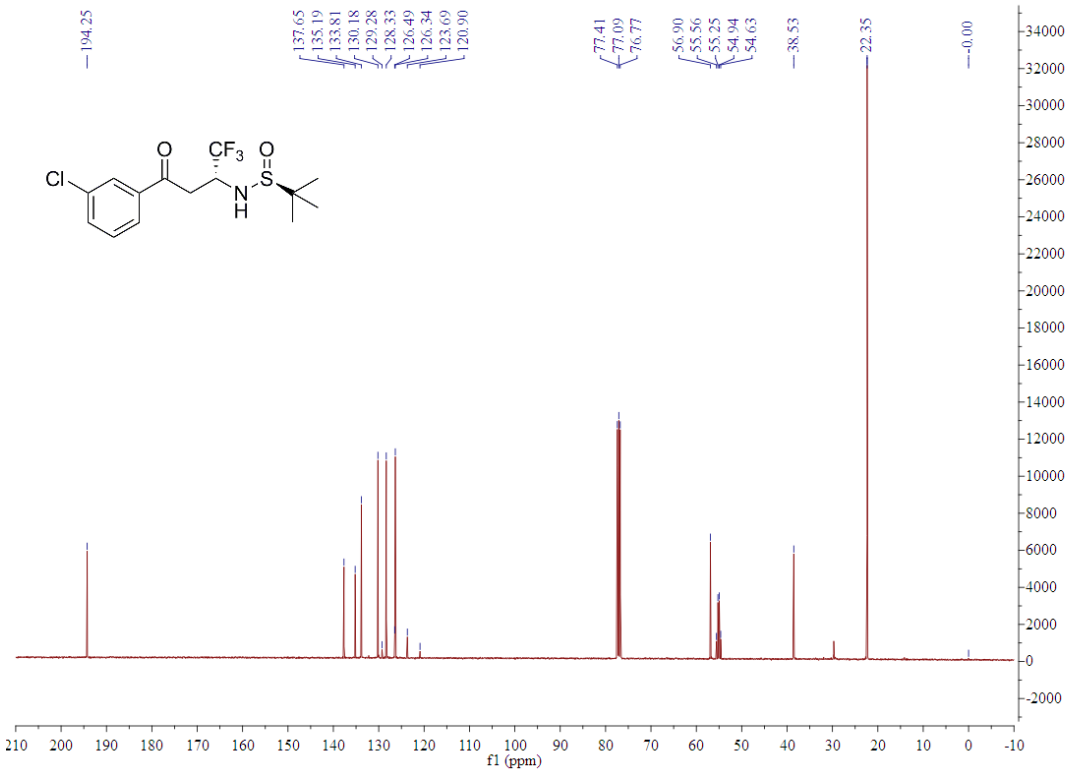
^{1}H NMR and ^{13}C NMR spectrum of **3j**



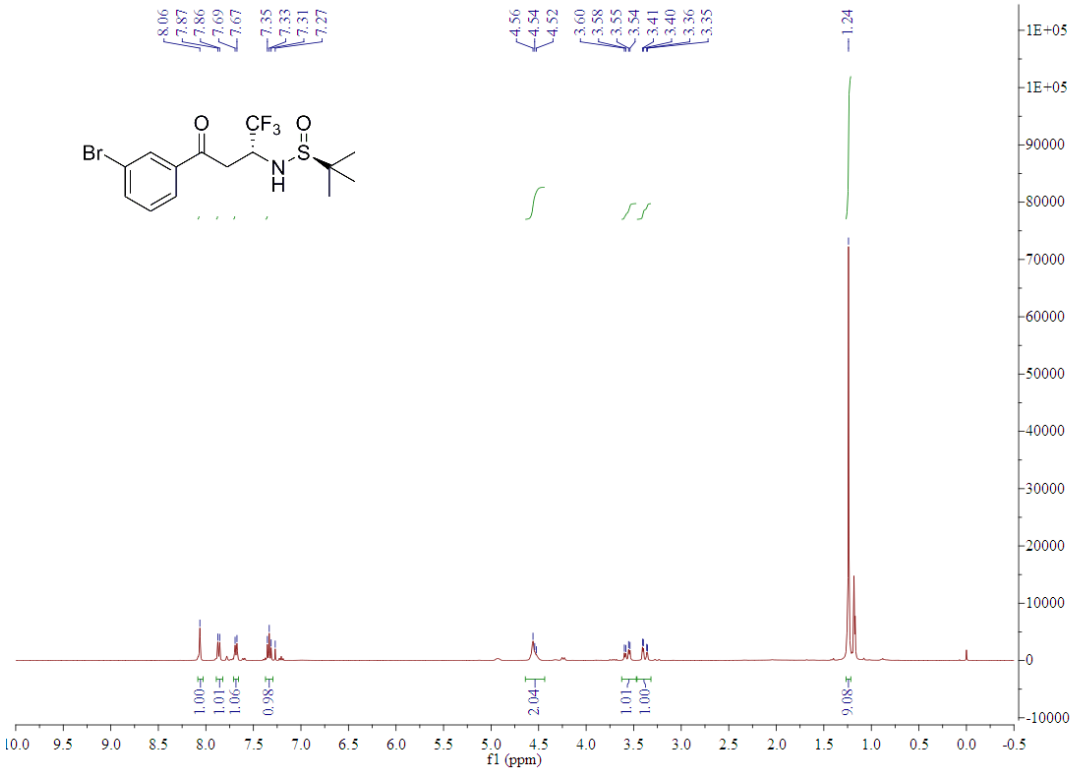


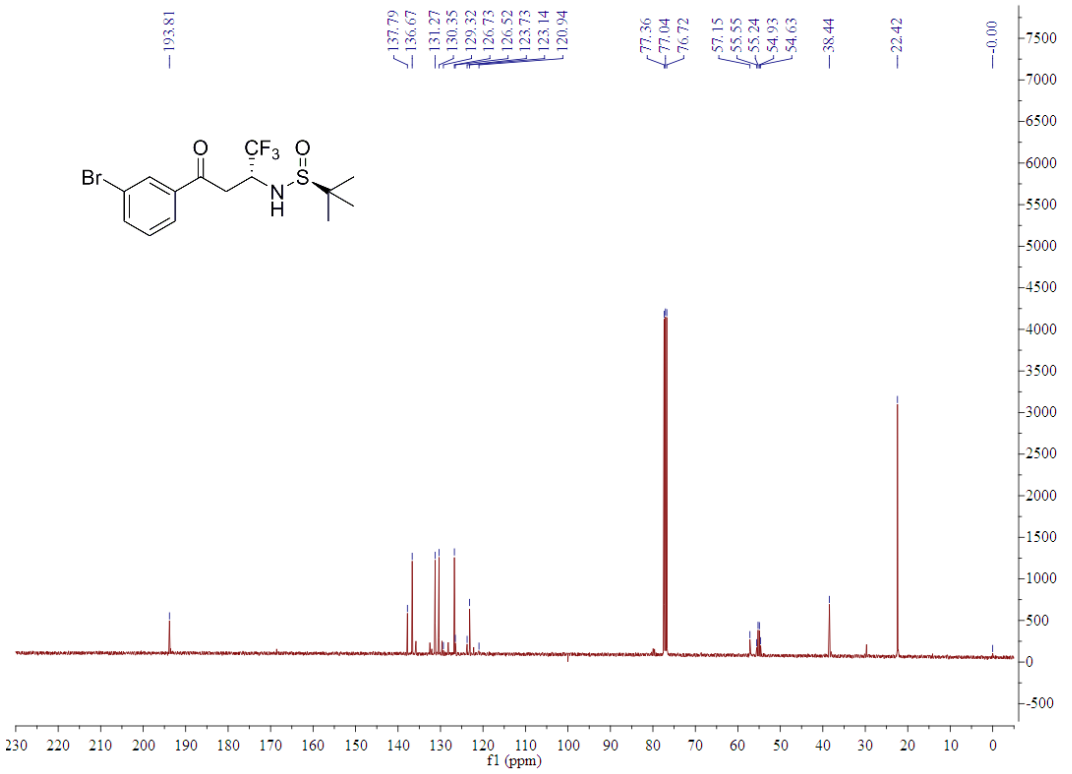
^{1}H NMR and ^{13}C NMR spectrum of **3k**



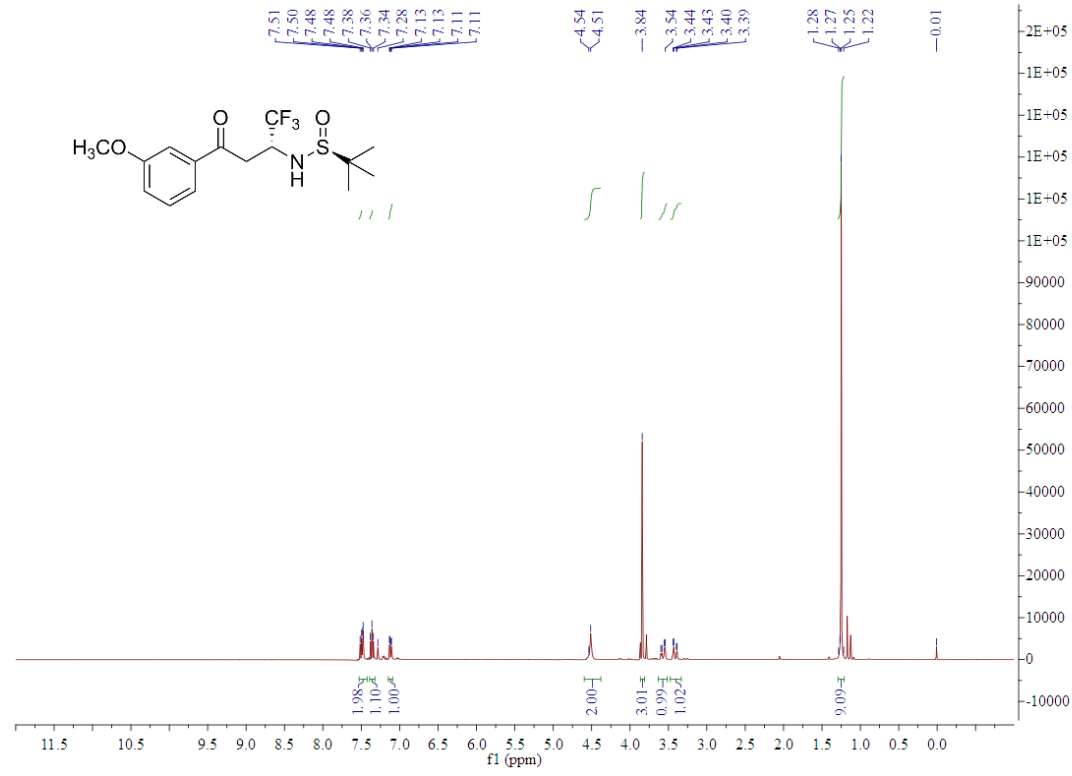


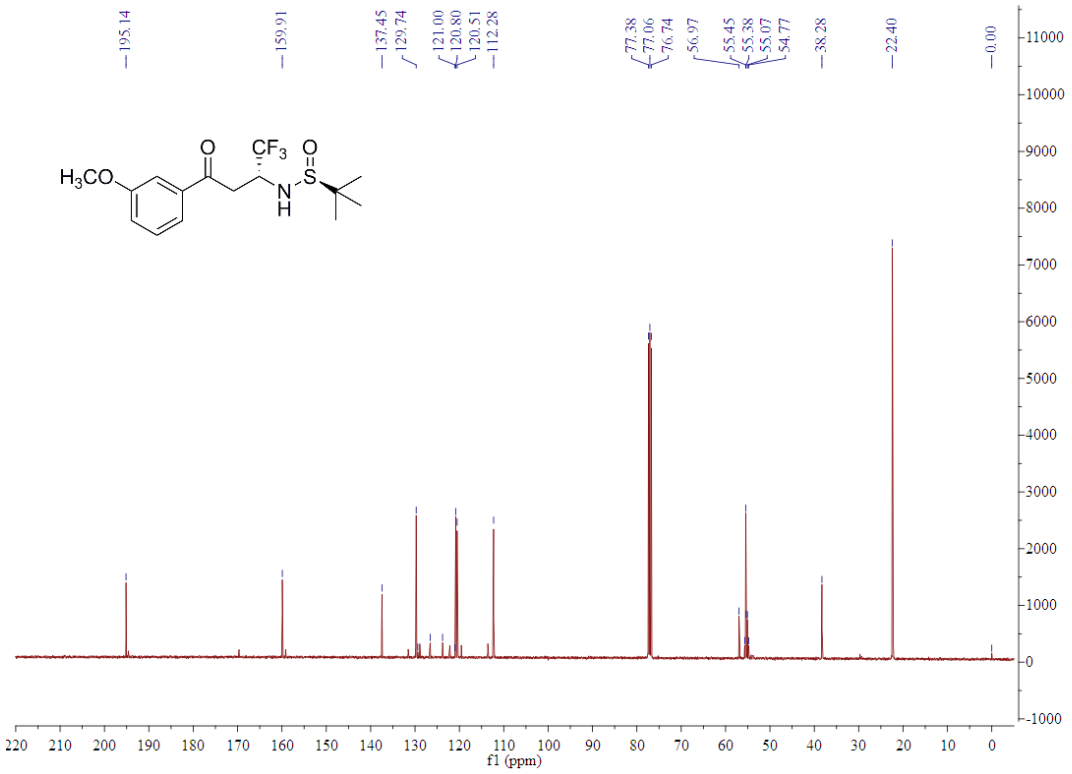
^{1}H NMR and ^{13}C NMR spectrum of **3l**



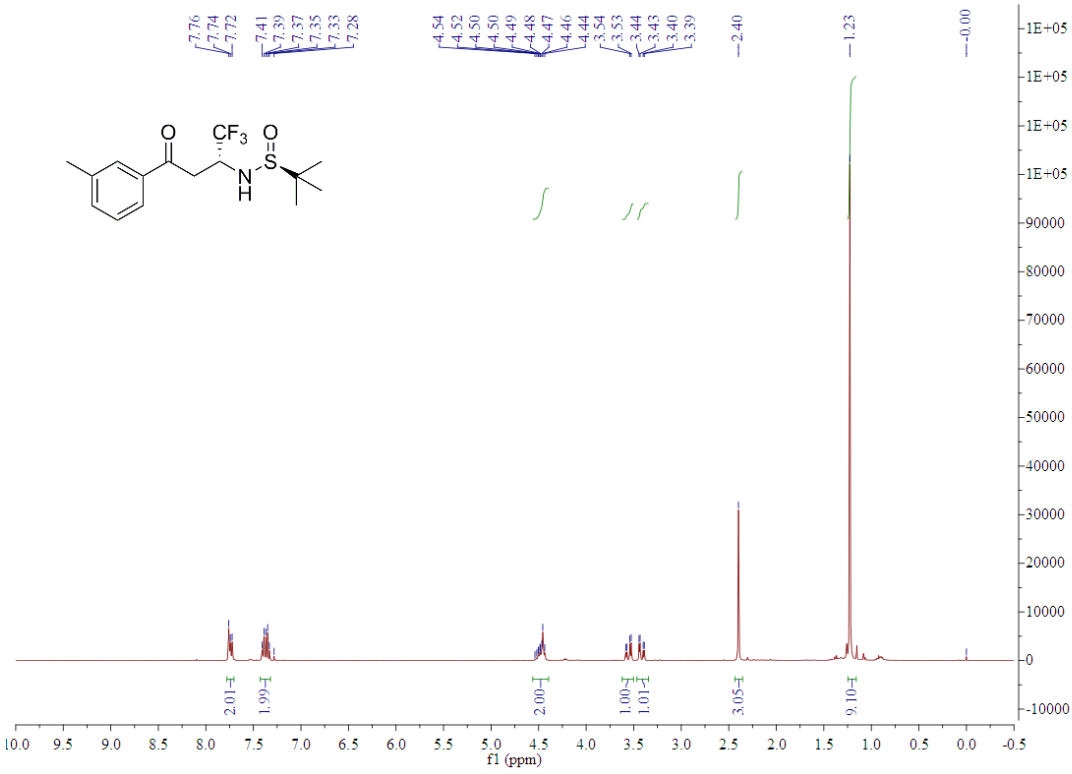


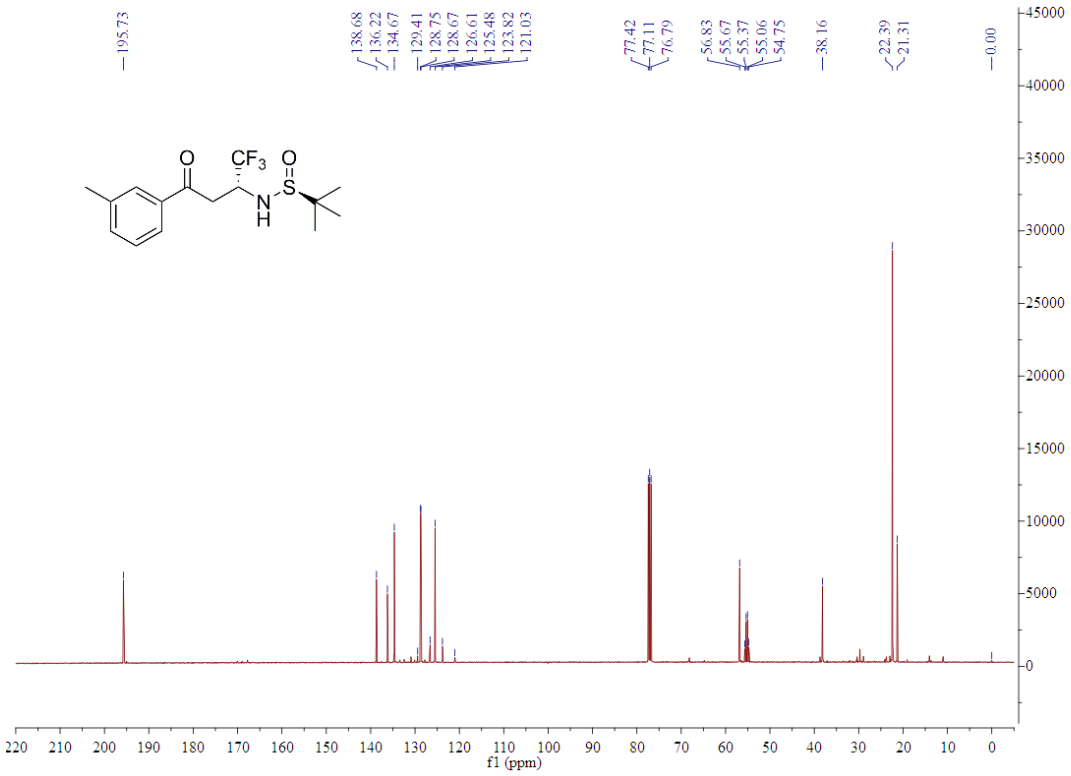
^{1}H NMR and ^{13}C NMR spectrum of **3m**



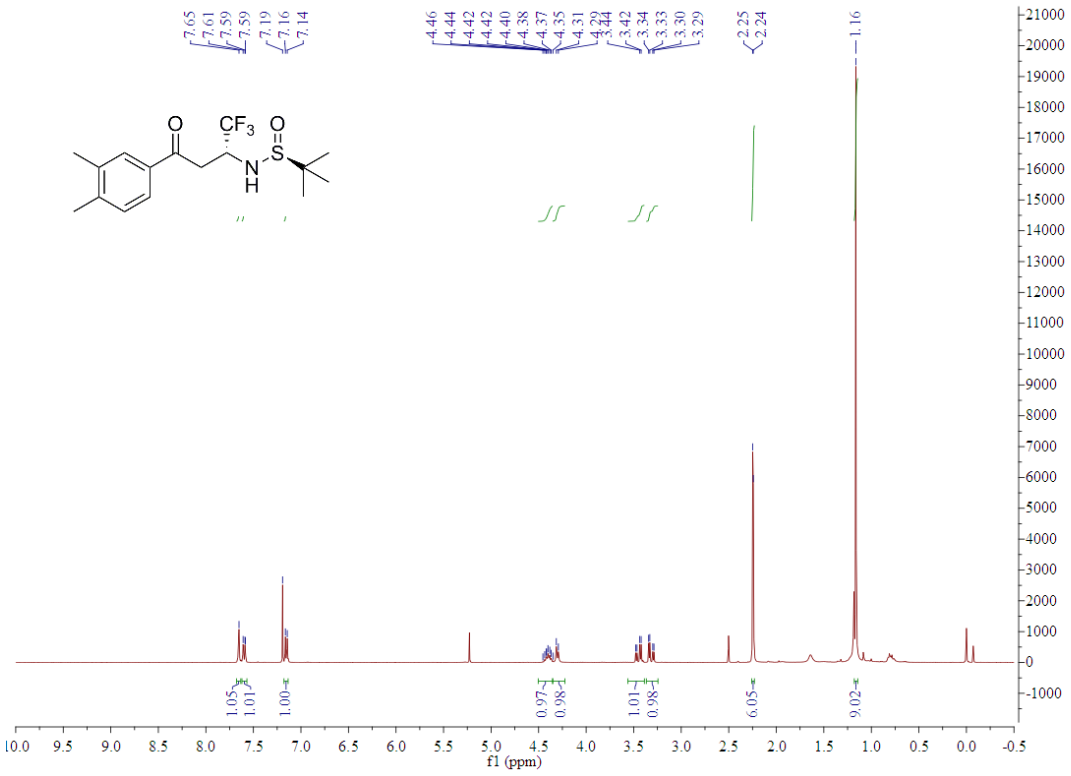


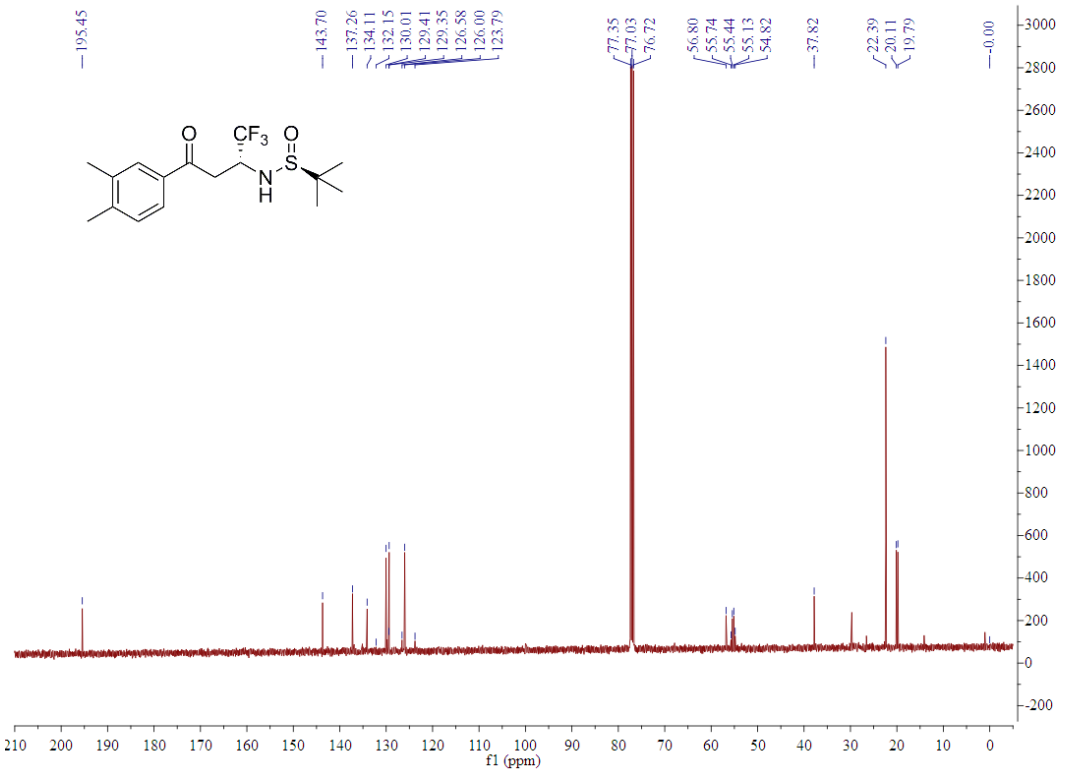
^{1}H NMR and ^{13}C NMR spectrum of **3n**



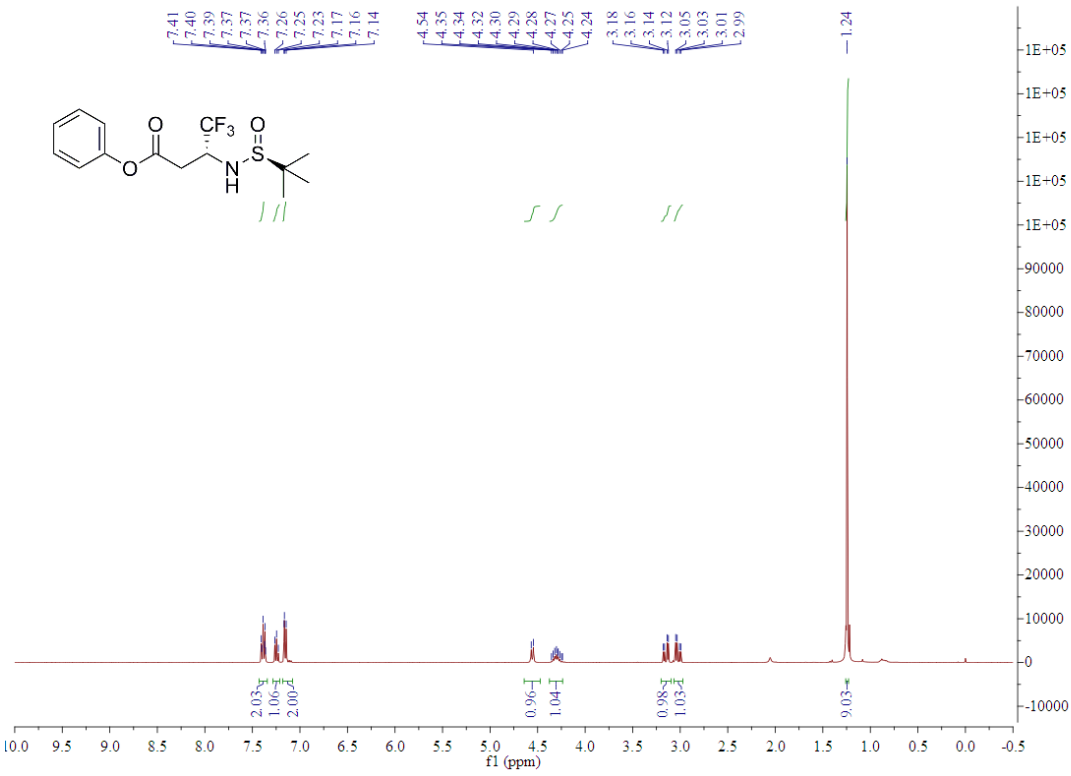


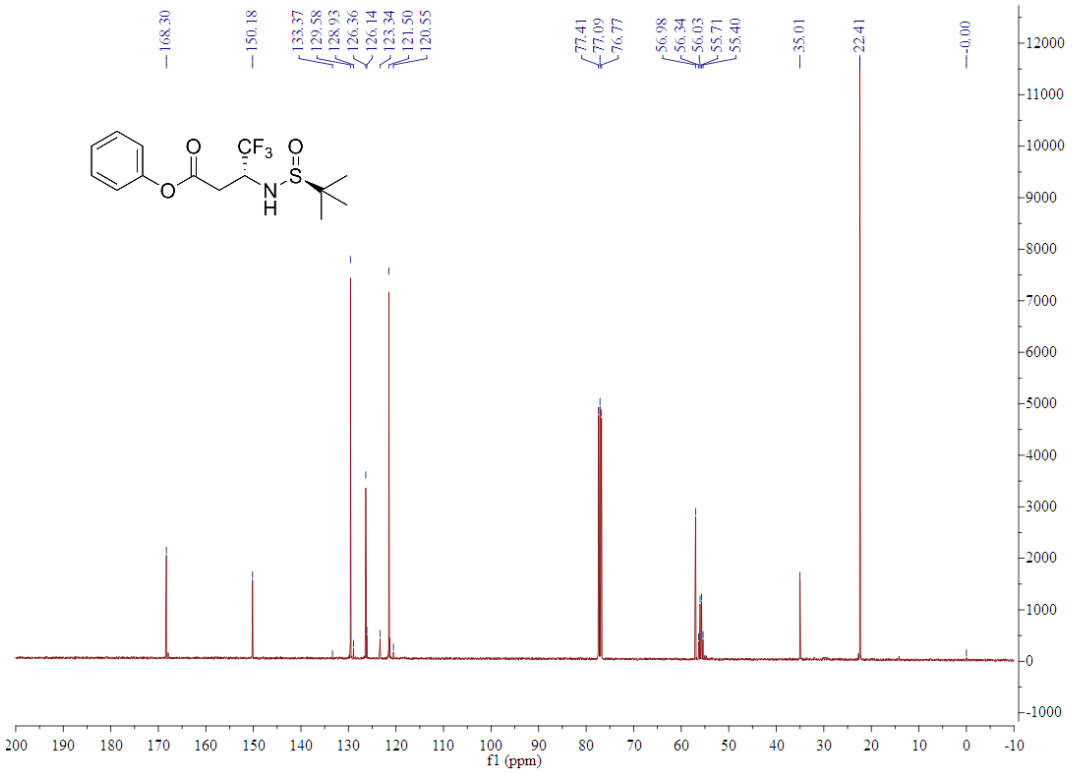
^{1}H NMR and ^{13}C NMR spectrum of **3o**



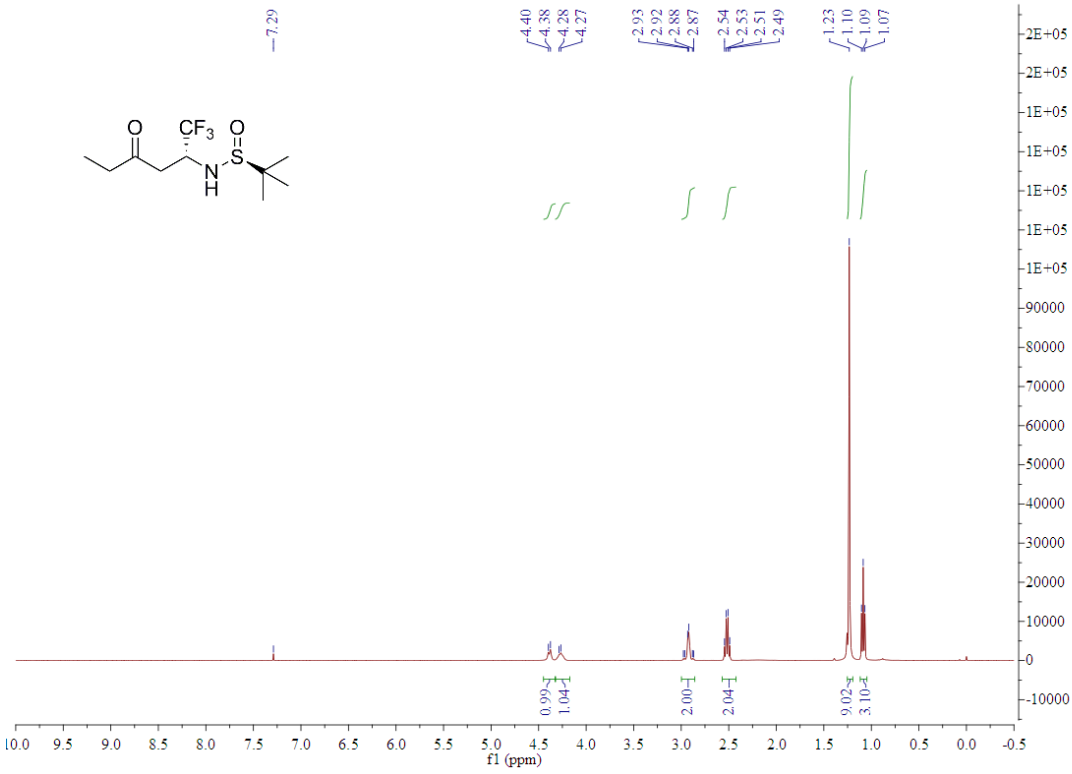


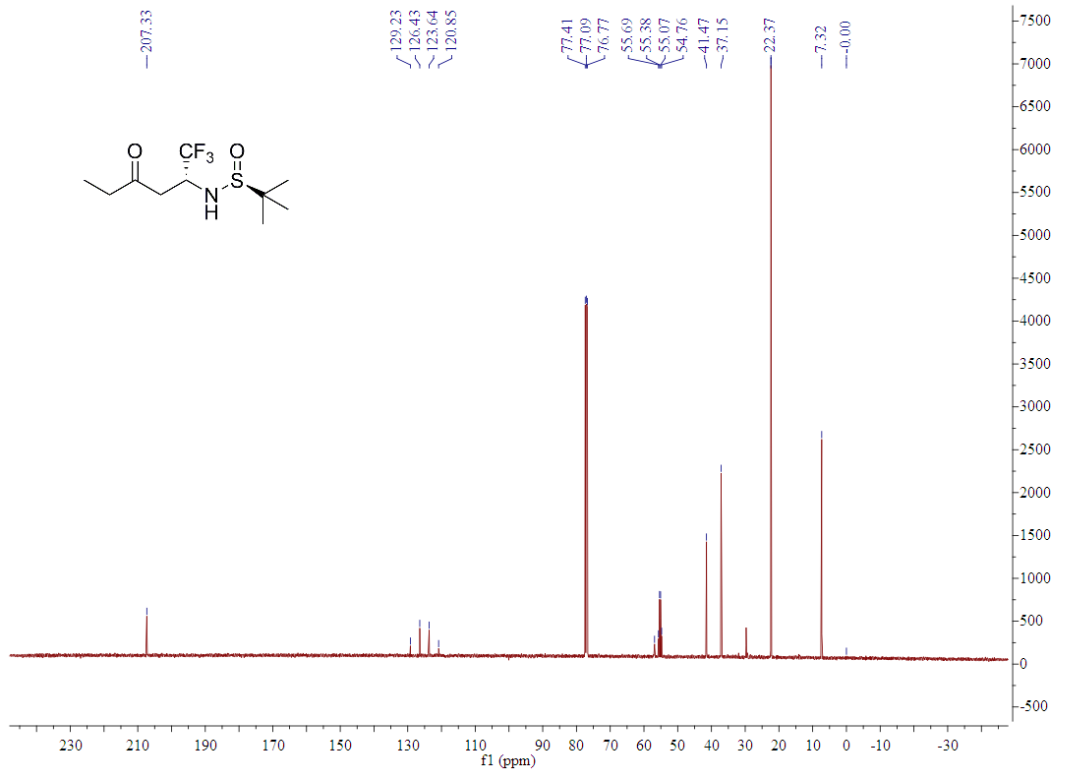
^{1}H NMR and ^{13}C NMR spectrum of **3p**



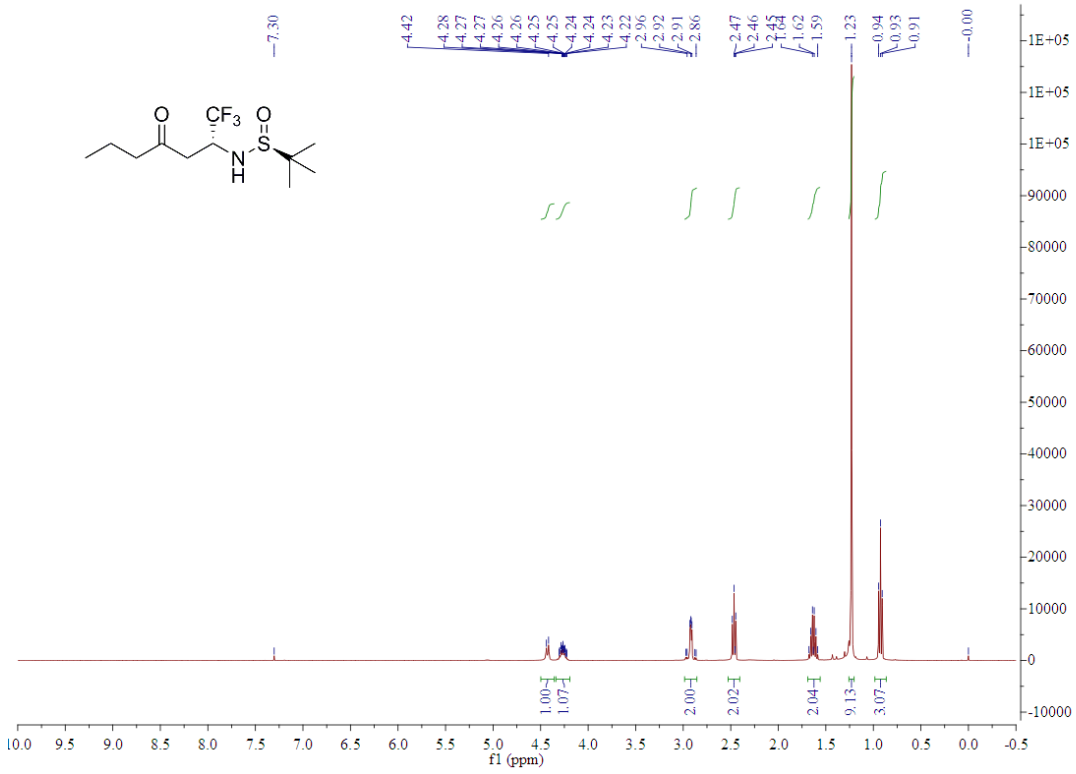


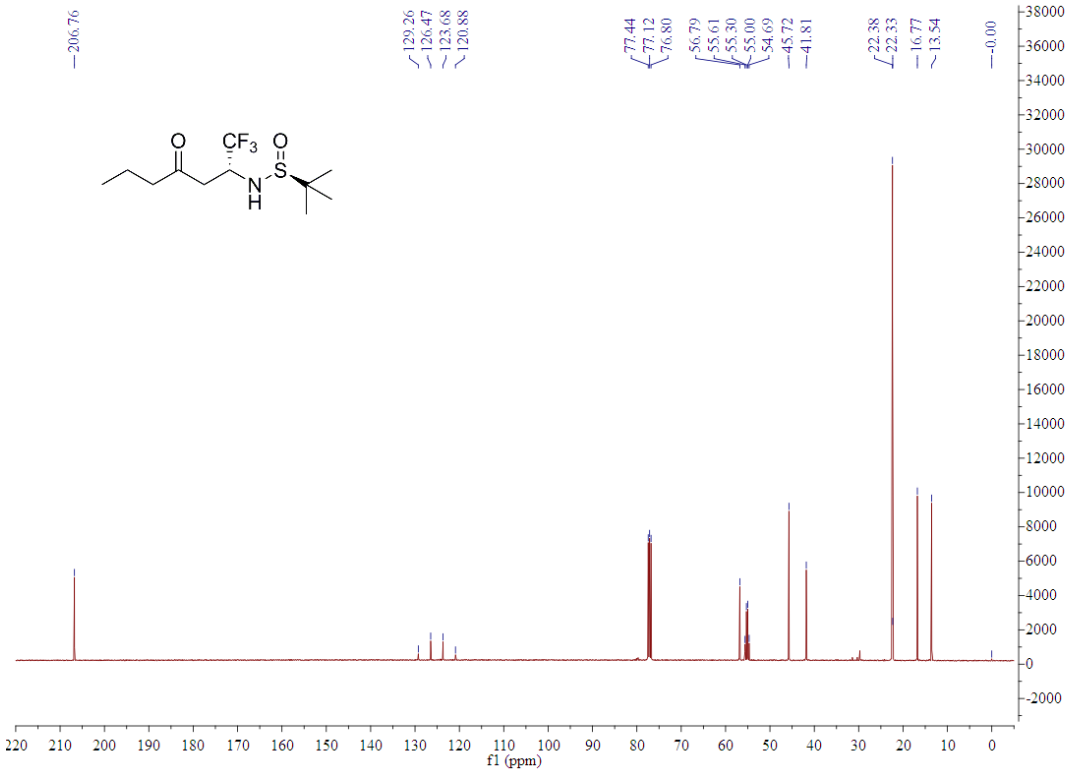
^{1}H NMR and ^{13}C NMR spectrum of **3q**



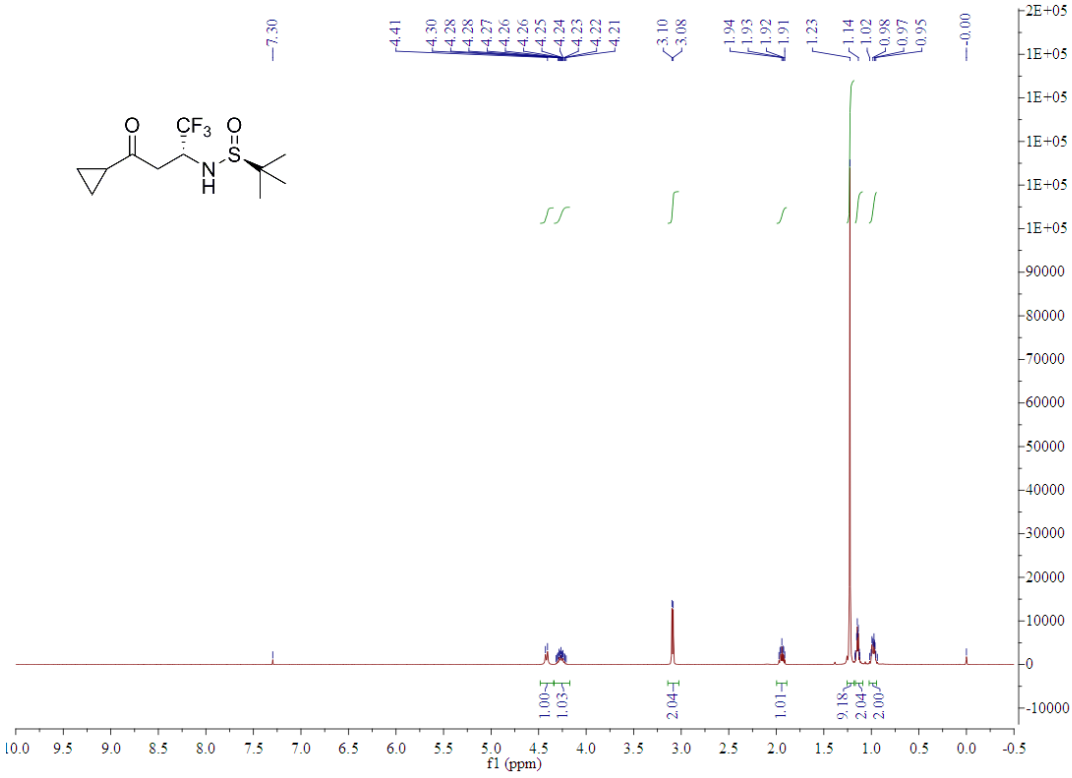


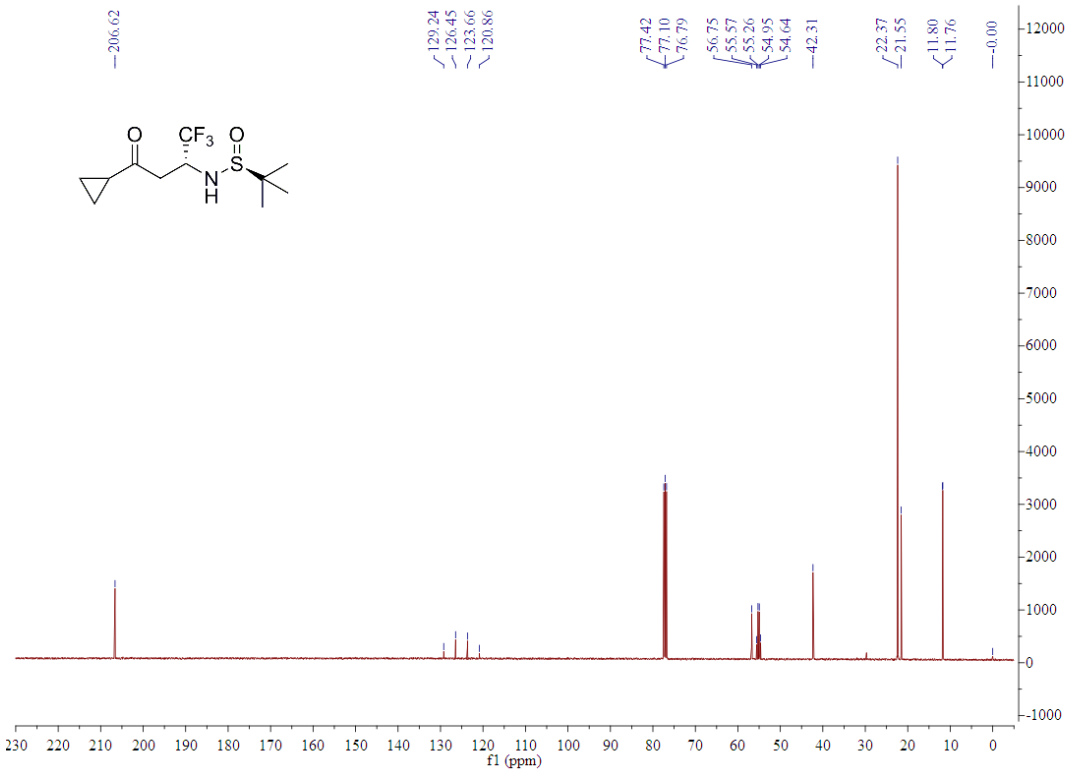
^{1}H NMR and ^{13}C NMR spectrum of **3r**



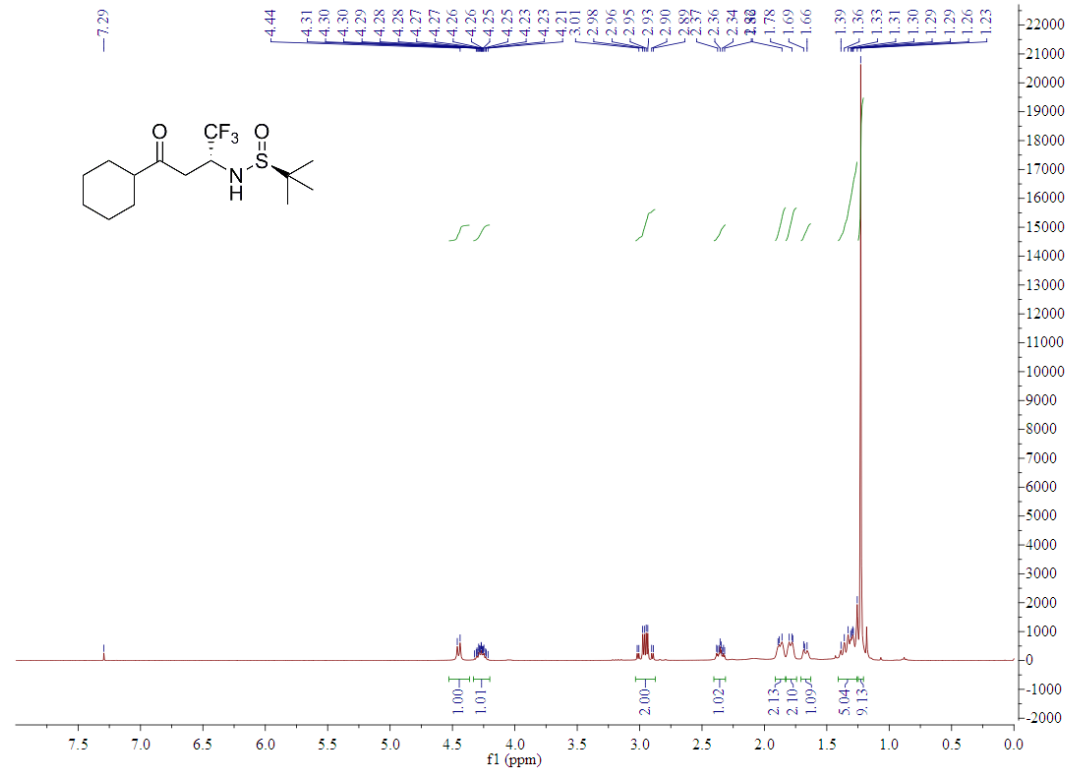


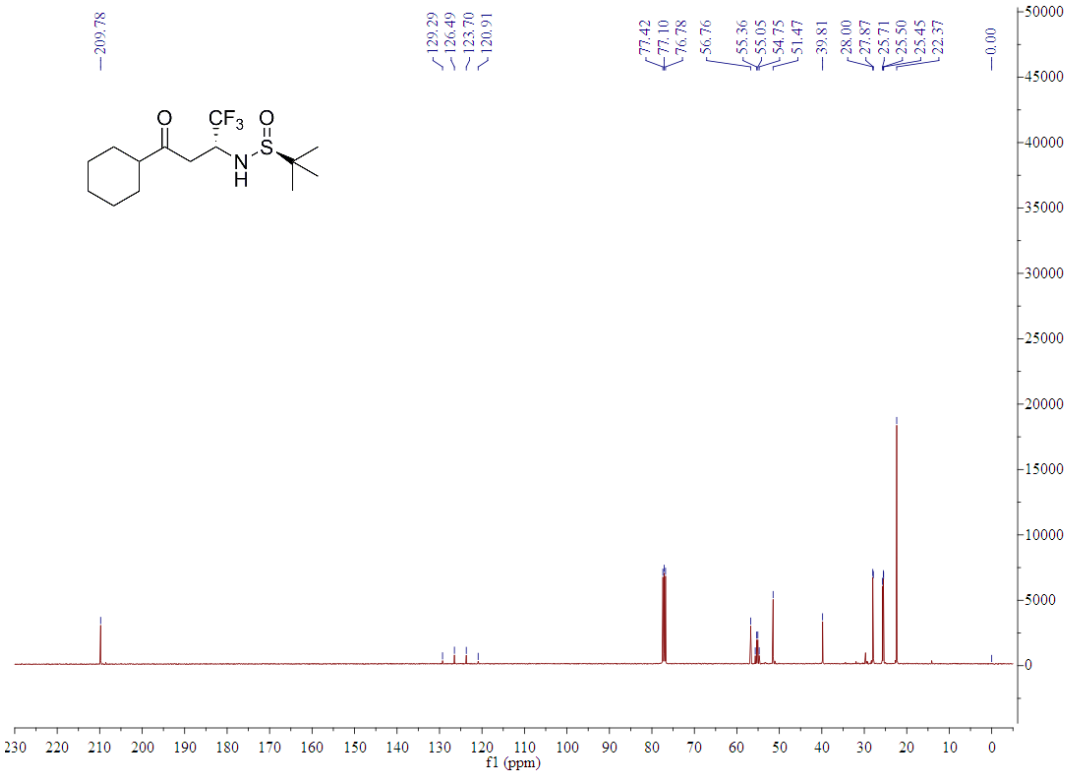
^{1}H NMR and ^{13}C NMR spectrum of **3s**



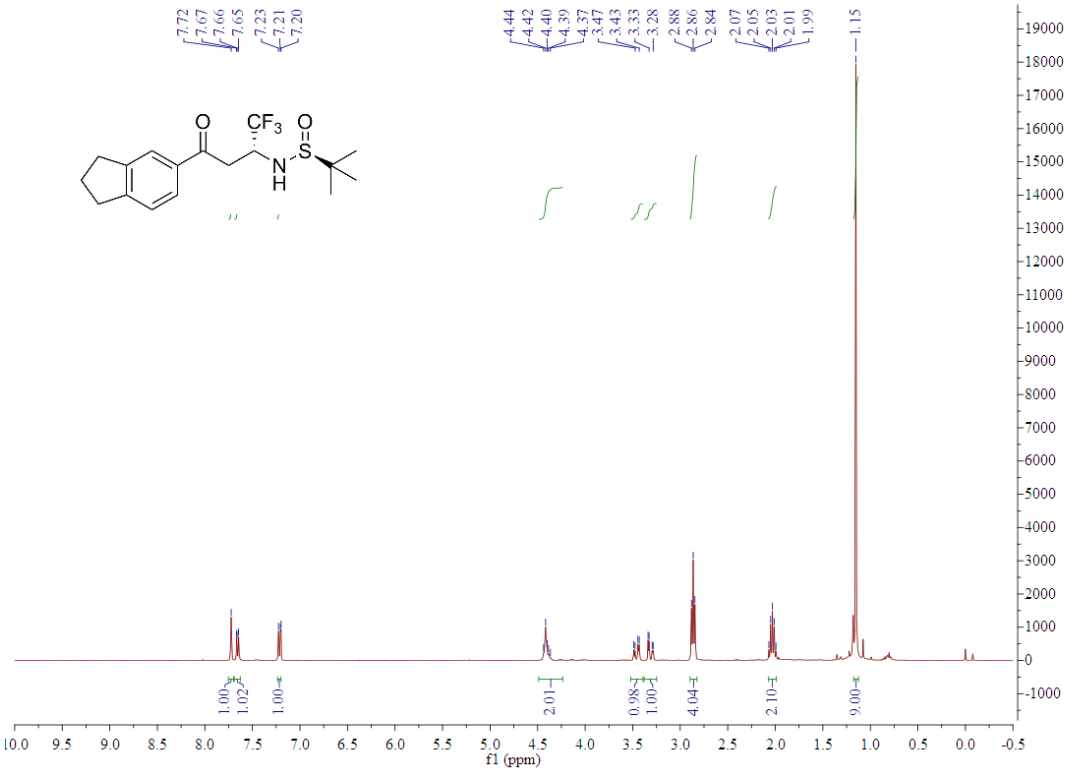


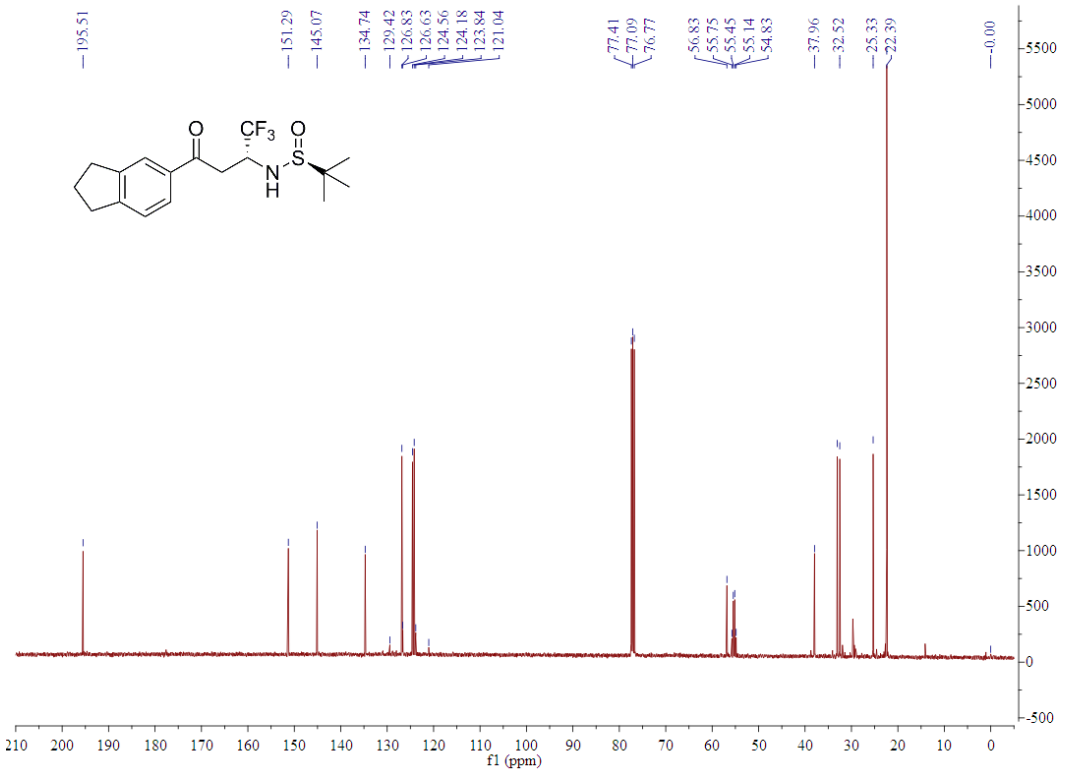
^{1}H NMR and ^{13}C NMR spectrum of **3t**



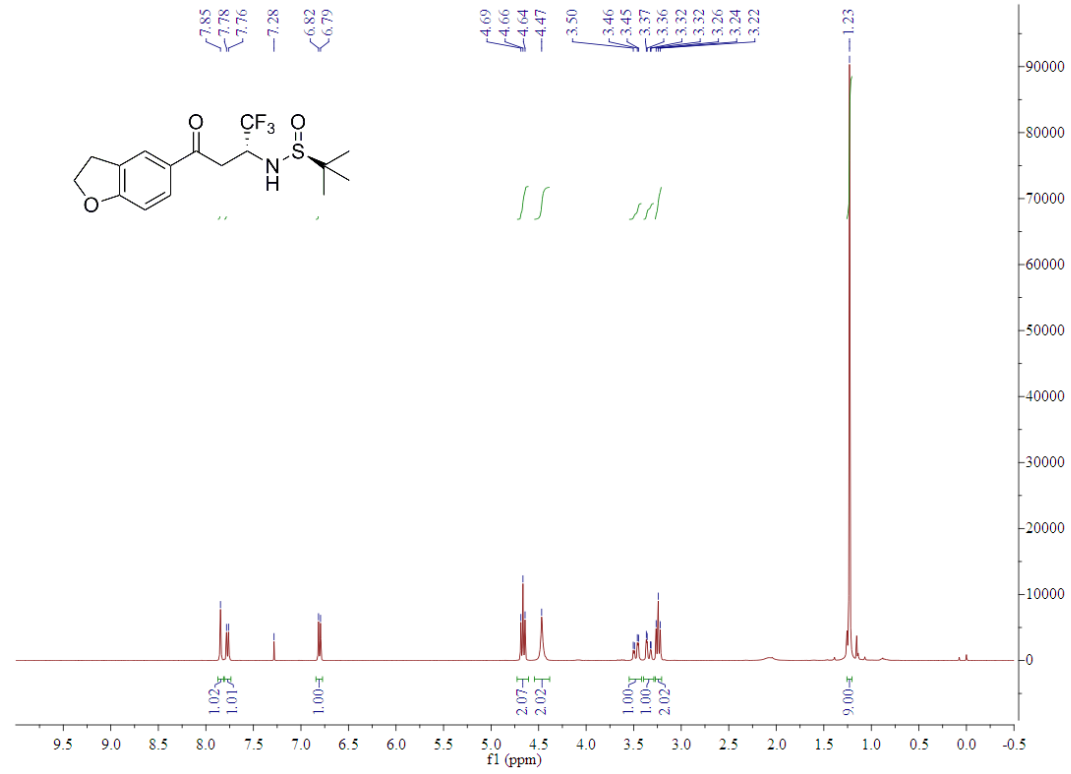


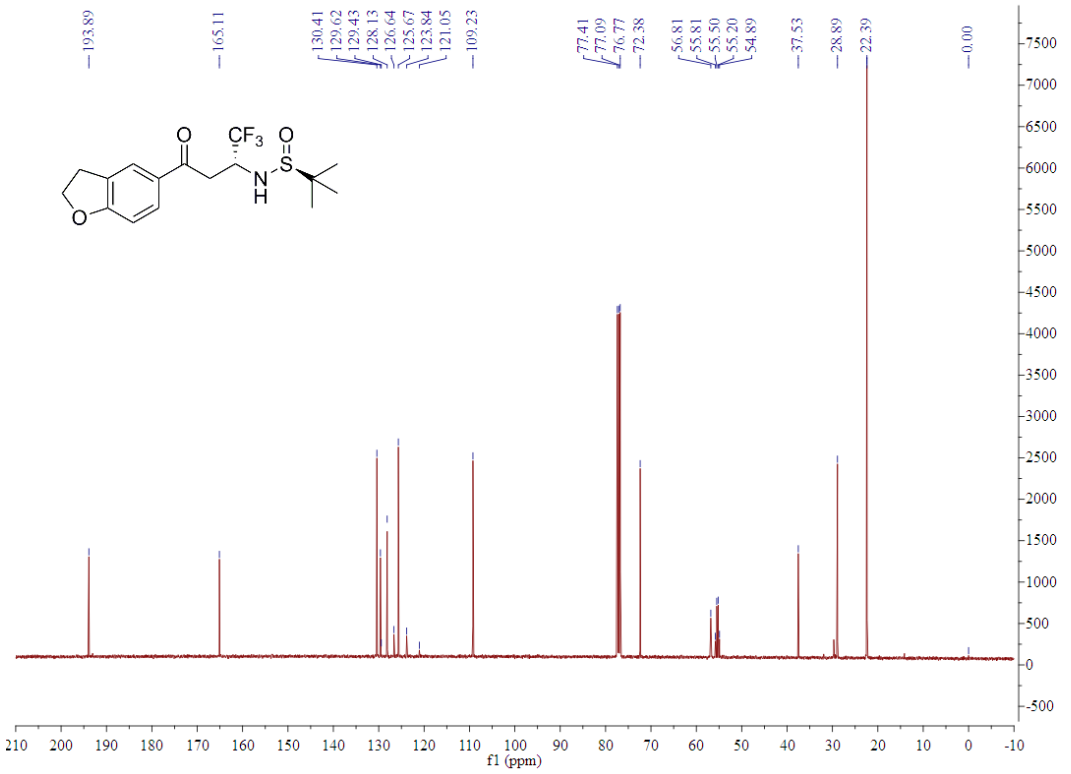
^{1}H NMR and ^{13}C NMR spectrum of **3u**



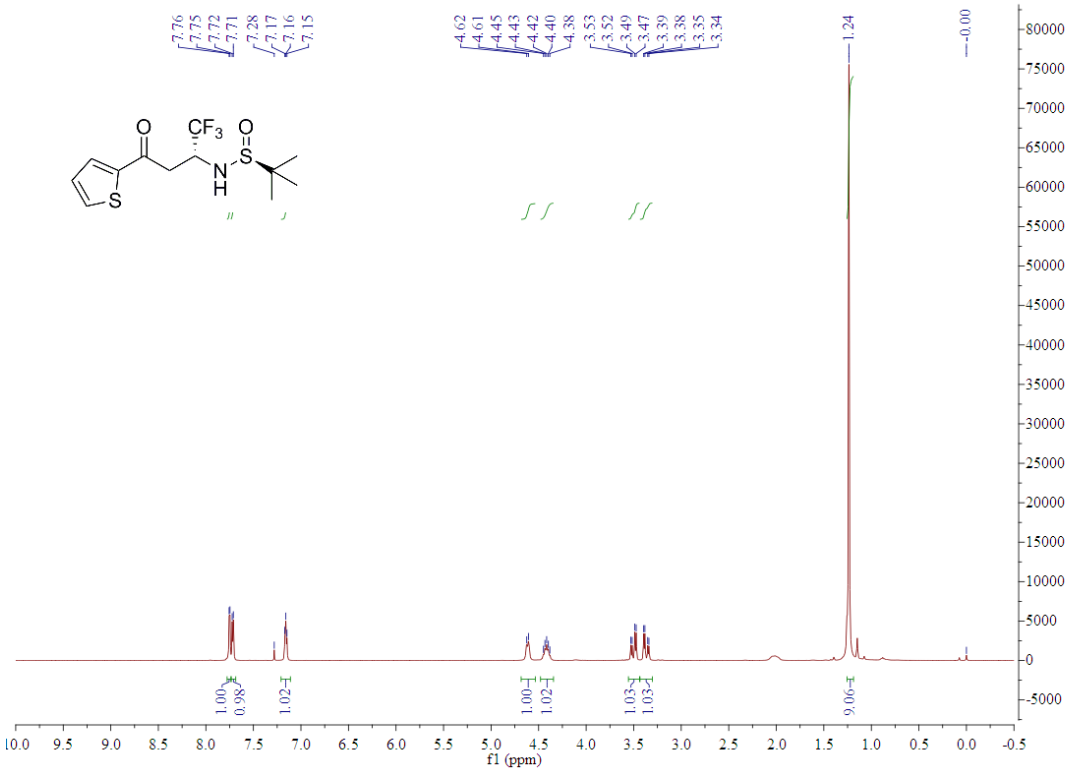


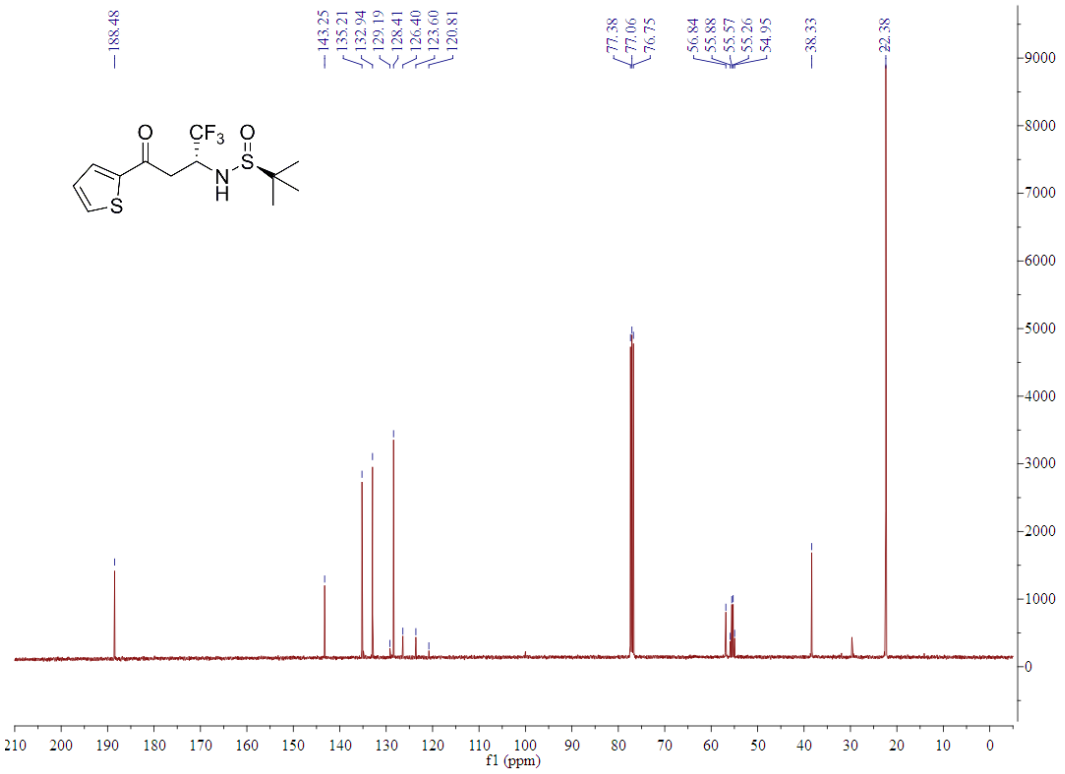
^{1}H NMR and ^{13}C NMR spectrum of **3v**



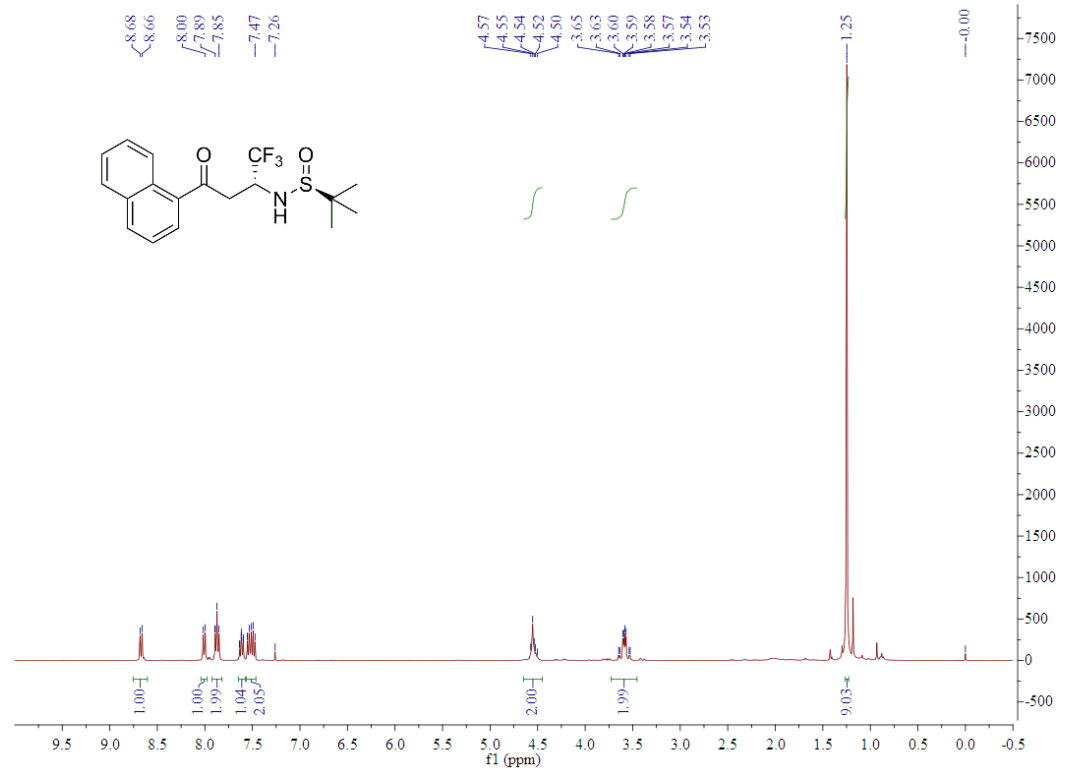


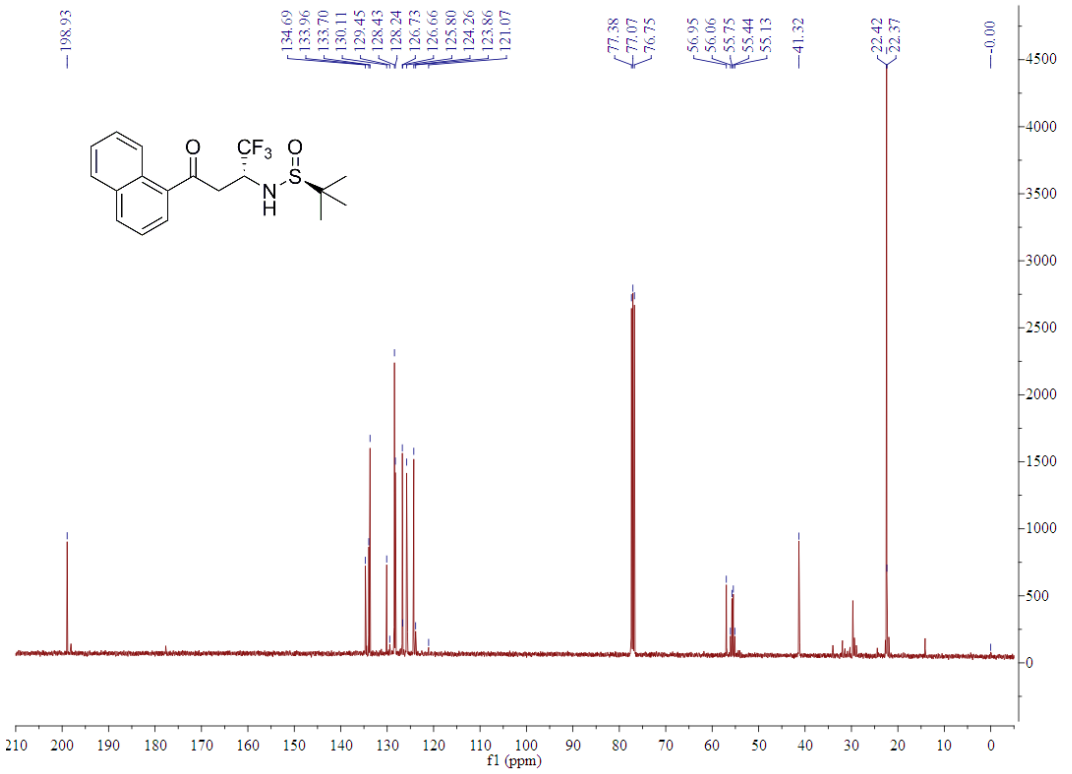
^{1}H NMR and ^{13}C NMR spectrum of **3w**



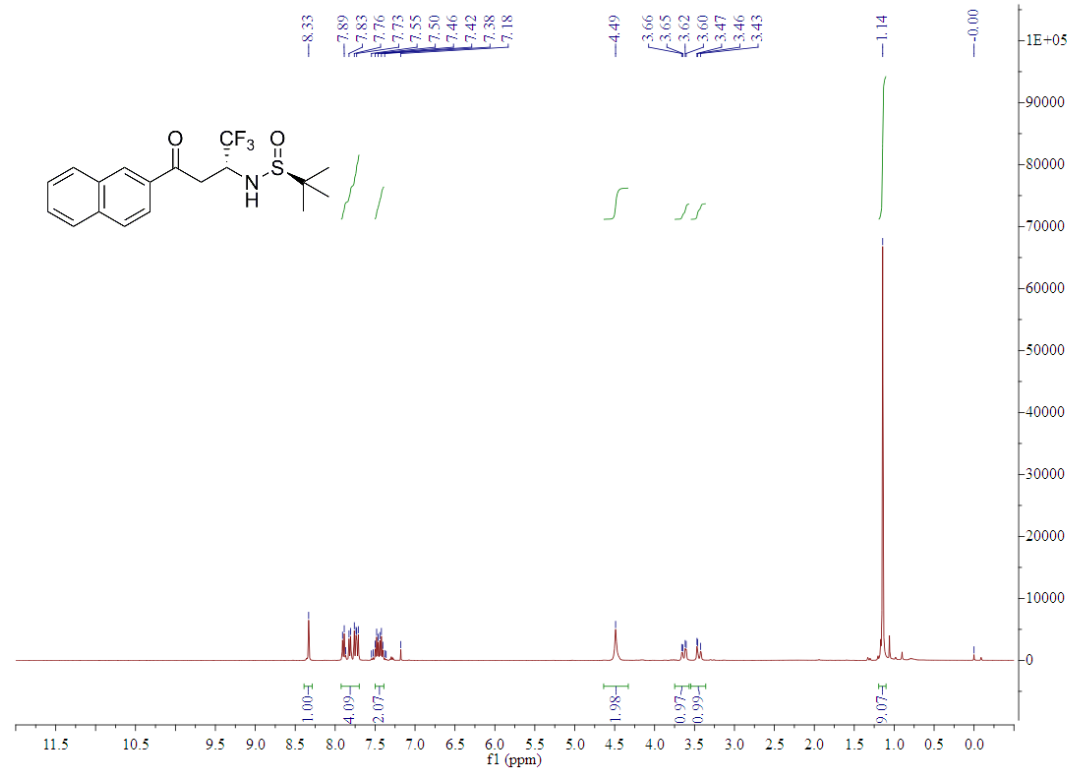


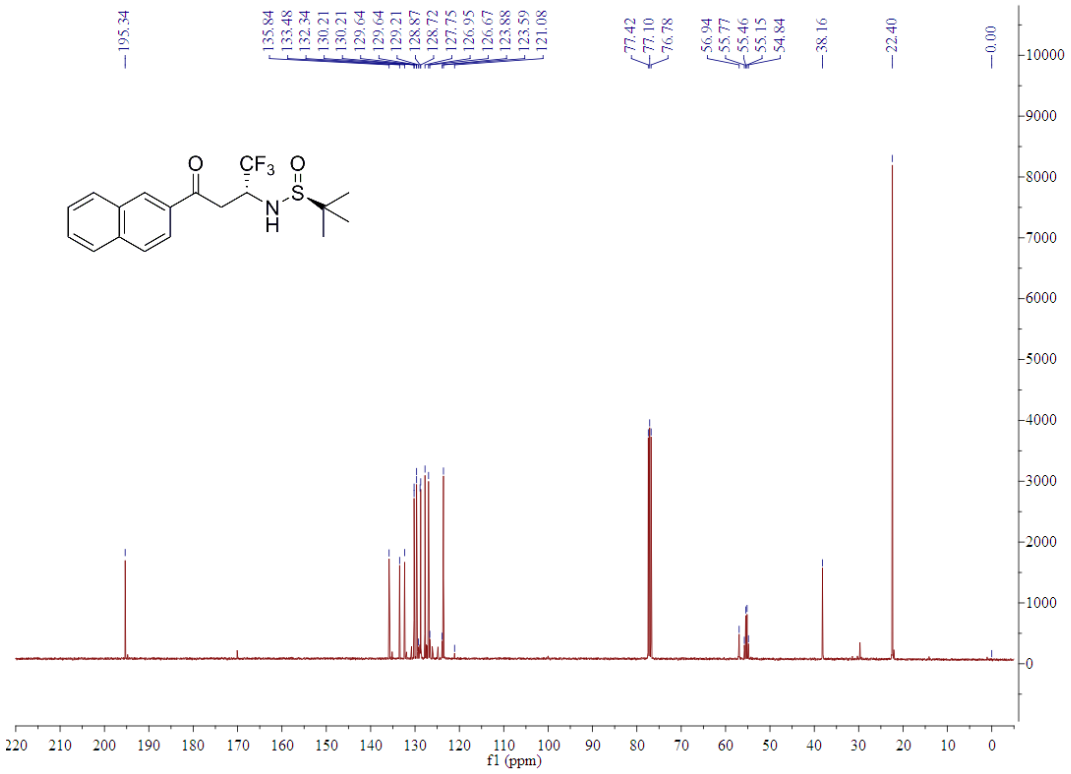
^{1}H NMR and ^{13}C NMR spectrum of **3x**



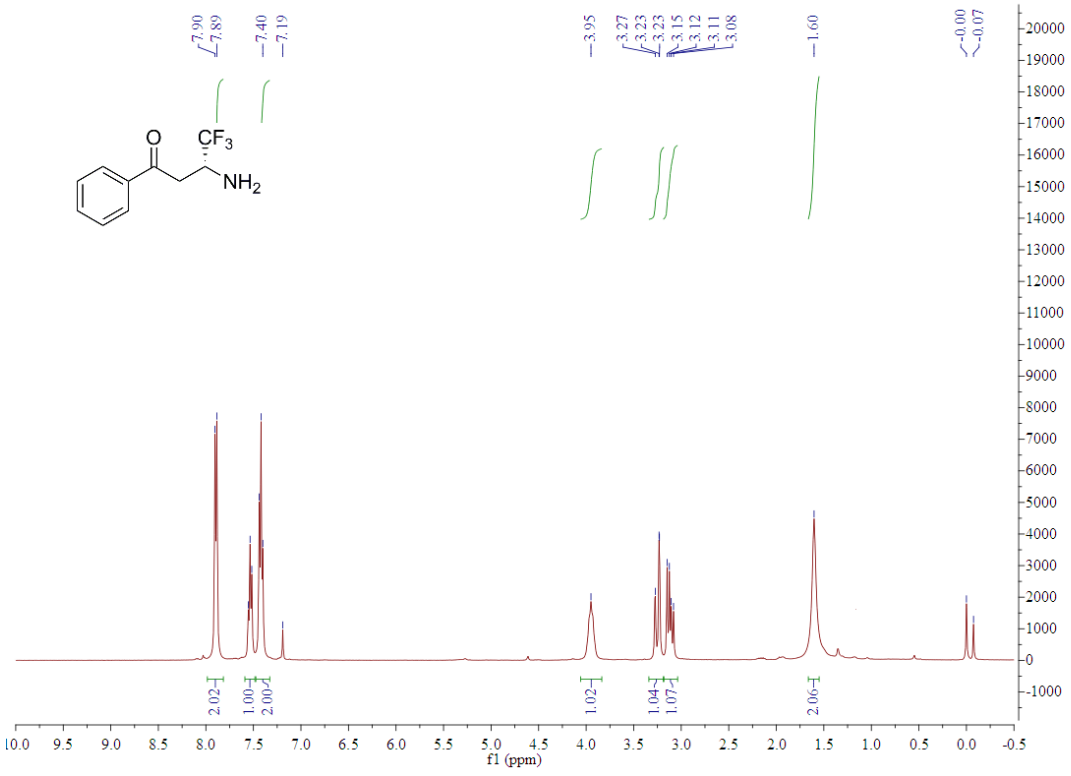


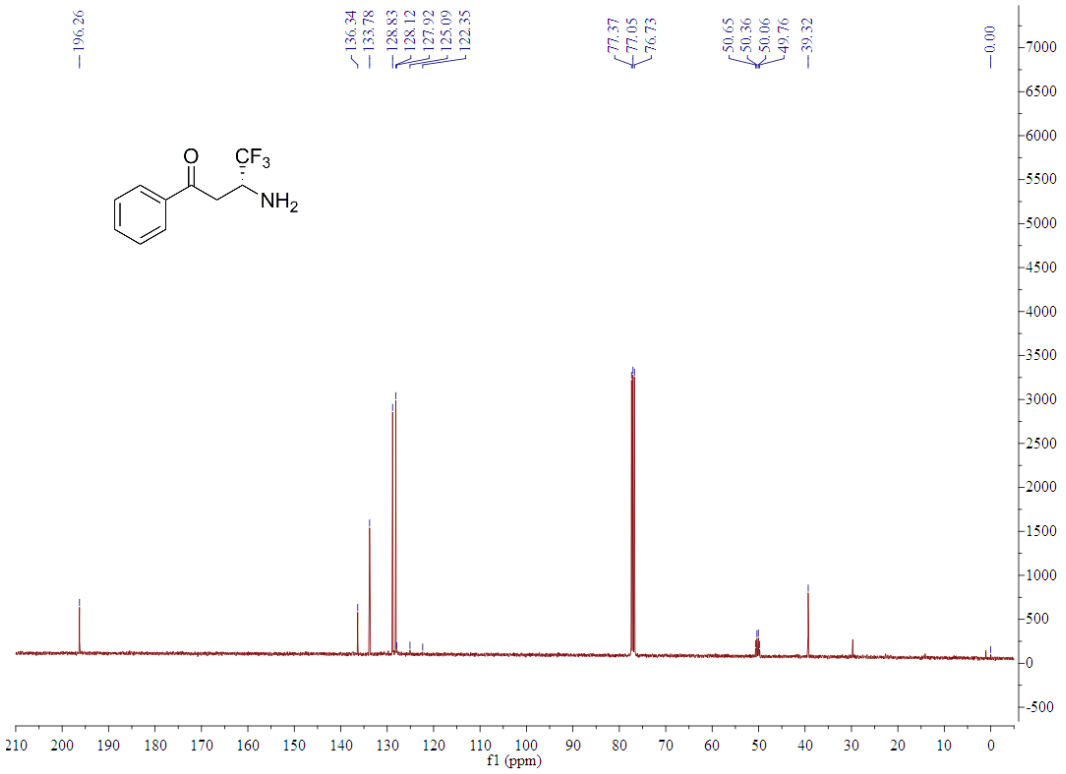
^{1}H NMR and ^{13}C NMR spectrum of **3y**



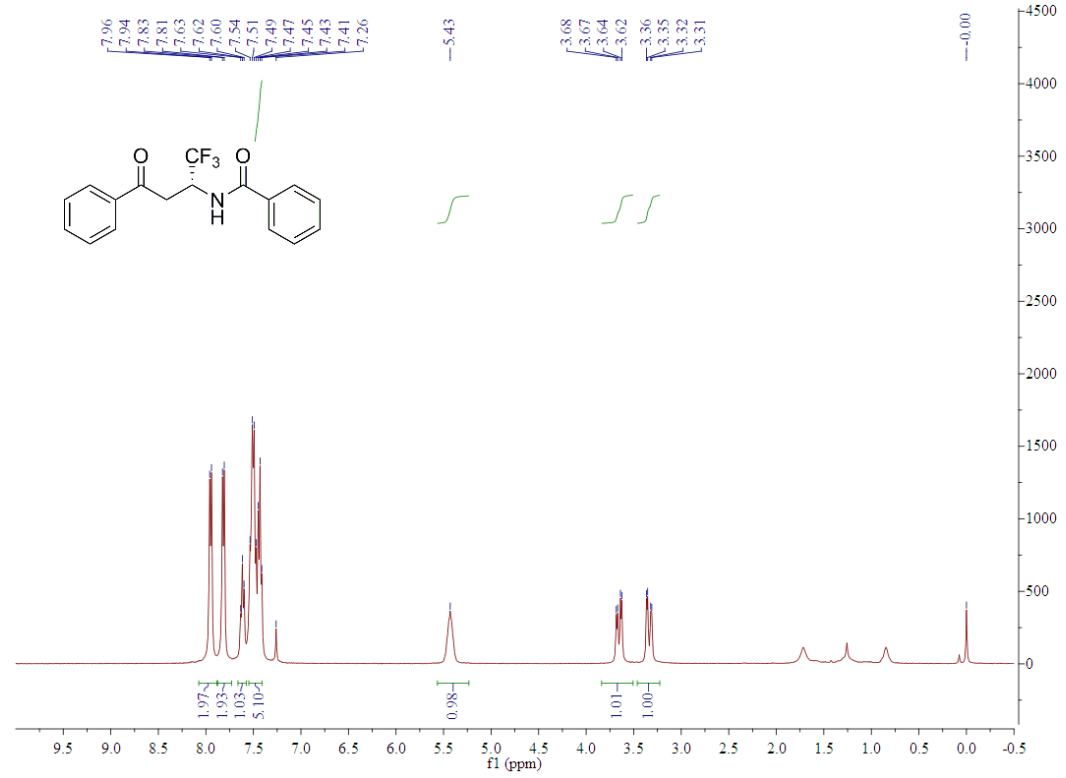


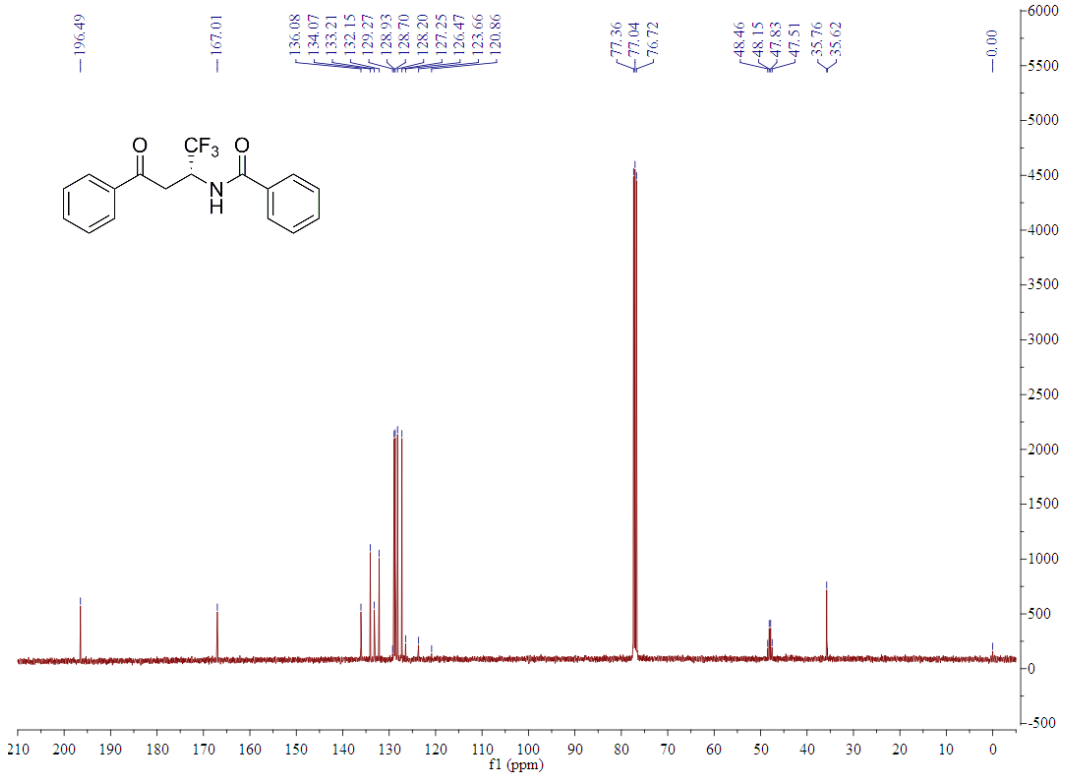
^{1}H NMR and ^{13}C NMR spectrum of (*R*)-**4**



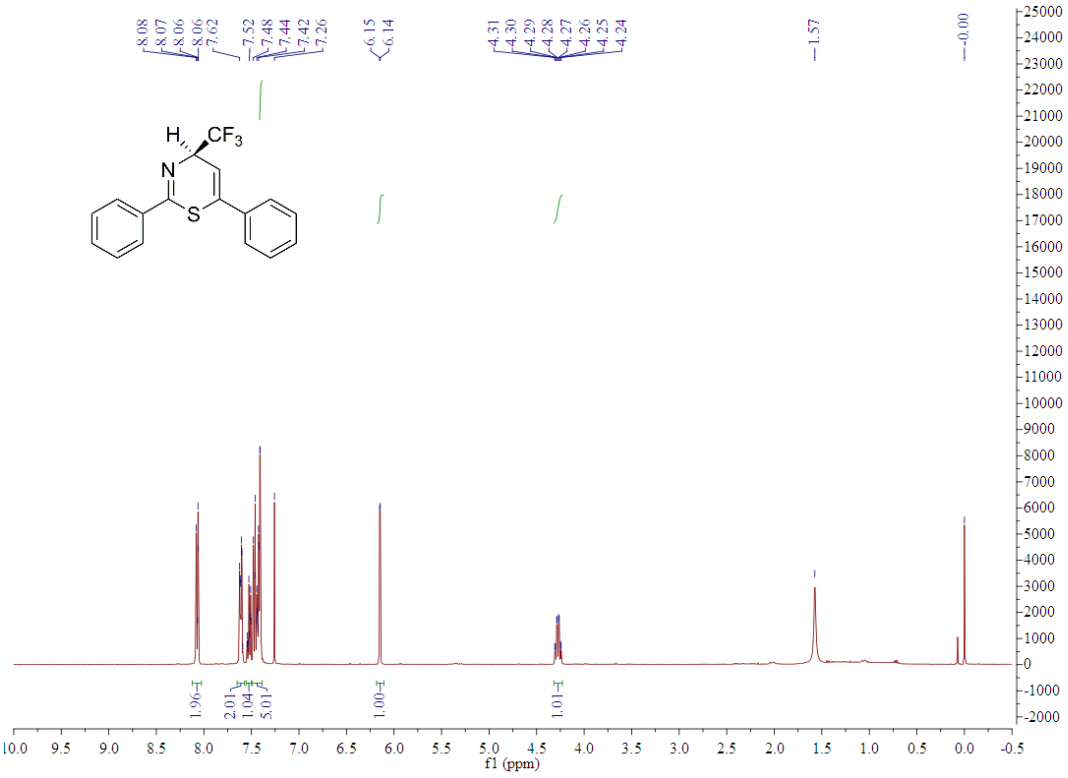


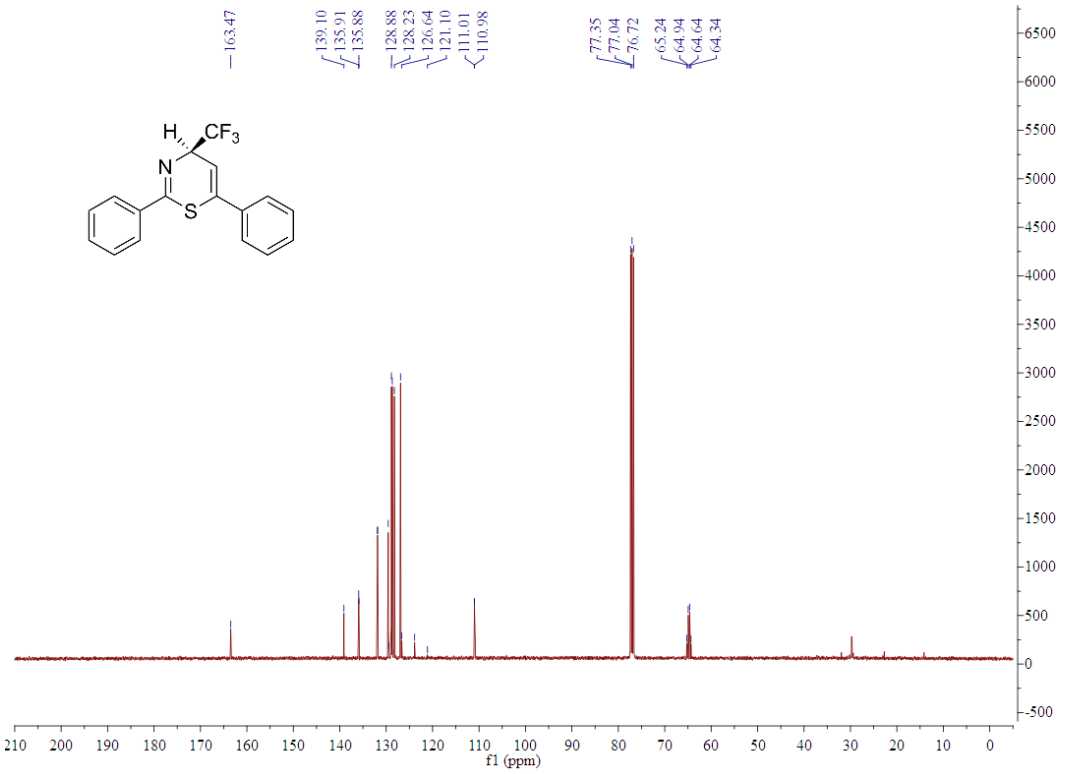
^{1}H NMR and ^{13}C NMR spectrum of **5**





^{1}H NMR and ^{13}C NMR spectrum of **6**

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64.34
H
CF3
N
S
f1 (ppm)