Supporting Information *for*

Synthesis of Polysubstituted 5-Trifluoromethyl Isoxazoles *via* Denitrogenative Cyclization of Vinyl Azides with Trifluoroacetic Anhydride

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General information

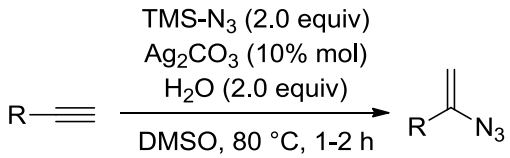
^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded using Bruker AVIII 400 spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. Coupling constants (*J*) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference: ^{1}H NMR ($CDCl_3$ δ 7.26), ^{13}C NMR ($CDCl_3$ δ 77.0), ^{1}H NMR (DMSO-d_6 δ 2.50) and ^{13}C NMR (DMSO-d_6 δ 39.50). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Solvents were freshly dried and degassed according to the published procedures prior to use. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60.

Caution: One should keep in mind the inherent toxicity, instability, shock sensitivity, and explosive nature of azides. All users should exercise appropriate caution. We have never experienced a safety problem with these materials.

General procedure of synthesis of vinyl azide substrates 2

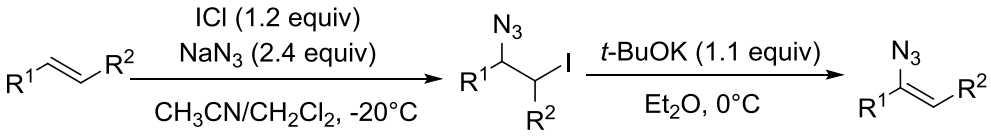
Vinyl azides **2a**–**2i**, **2k**–**2p**, **2-4l**, **2-4q**, **2-4r**, **2-5a**–**2-5e**, **2-6a**, **2-6b** were known compounds and prepared according to the reported procedures.[1]

Typical synthetic procedure A[1a] (with **2a** as an example):



To a solution of Ag_2CO_3 (138 mg, 0.10 equiv), phenylacetylene (0.51g, 5 mmol), TMS-N_3 (1.15g, 10 mmol) and H_2O (1800 μL) in DMSO (6 mL) was stirred for 1-2 h at 80 °C. The resulting mixture was washed with Et_2O and brine (4 × 20 mL), dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with petroleum ether to give (1-azidovinyl)benzene.

Typical synthetic procedure B[1b] (with **2a** as an example):

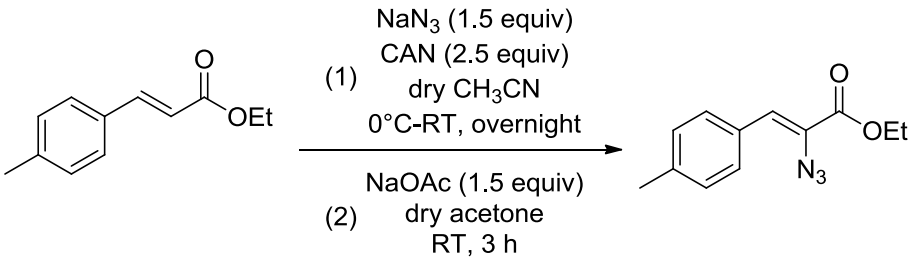


To a suspension of NaN_3 (1.56 g, 24 mmol) in CH_3CN (5 mL) was added dropwise a solution of iodine monochloride (1.95 g, 12 mmol) in CH_3CN (5 mL) at −20 °C, and the mixture was kept stirring at −20 ℃ for 30 min. A solution of styrene (1.04 g, 10 mmol) in CH_2Cl_2 (5 mL) was added slowly dropwise, and the mixture was stirred at -20 ℃–RT for overnight. The reaction was quenched with saturated aqueous $Na_2S_2O_3$, and the resulting mixture were extracted with Et_2O (3 × 15 mL) and the organic layer were washed with brine and dried over $MgSO_4$. The solvent was removed by rotary

evaporation and the resulting crude materials were used immediately for the next step without any further purification.

To a solution of the obtained crude materials above in Et_2O (10 mL) was added *t*-BuOK (1.23 g, 11 mmol) at 0 ℃, and the mixture was stirred for 1.5 h at the same temperature. The reaction was quenched by adding Saturated $NaHCO_3$, and the mixture was extracted with Et_2O, washed with brine, and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with petroleum ether to give (1-azidovinyl)benzene.

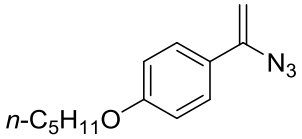
Typical synthetic procedure C[1c]



In a dried 100 mL round bottom flask equipped with a stir bar were added ethyl 4-methylcinnamate (0.95 g, 5.0 mmol) and NaN_3 (0.49 g, 7.5 mmol) in dry CH_3CN (5 mL) under N_2 atmosphere, a solution of CAN (6.85 g, 12.5 mmol) in the same solvent (15 mL) was added dropwise at 0 ℃ and was kept stirring at 0 ℃-RT for overnight. The resulting mixture were extracted with CH_2Cl_2 (3 × 10 mL) and the organic layer were washed with brine and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting crude materials were used immediately for the next step without any further purification.

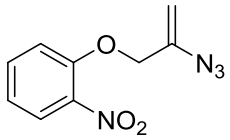
To a solution of the obtained crude materials above in dry acetone (5 mL) was added anhydrous sodium acetate (0.62 g, 7.5 mmol) at RT for 3 h. The mixture was extracted with CH_2Cl_2, washed with brine, and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with PE/EA to give ethyl 2-azido-3-(*p*-tolyl)acrylate.

The following new compounds were synthesized by Procedure A:



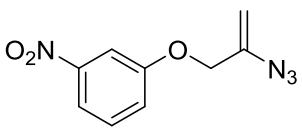
1-(1-Azidovinyl)-4-(pentyloxy)benzene (2j)

Prepared on a 5.0 mmol scale. Obtained as a yellow solid in 58% yield (670 mg). Mp: 38.0-38.5 ℃. R_f (*n*-pentane:dichloromethane 10:1) = 0.78. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 2H), 5.31 (s, 1H), 4.85 (s, 1H), 3.97 (t, *J* = 6.4 Hz, 2H), 1.84 – 1.75 (m, 2H), 1.50 – 1.35 (m, 4H), 0.95 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9 (s), 144.7 (s), 126.8 (s), 126.6 (s), 114.3 (s), 96.0 (s), 68.0 (s), 28.9 (s), 28.1 (s), 22.4 (s), 14.0 (s). IR (ATR): ν 2955, 2932, 2870, 2136, 2101, 1606, 1509, 1469, 1295, 1249, 1175, 1022, 829 cm^{-1}. GC-MS (EI) m/z (%): 203 $[M\text{-}N_2]^+$ (100).



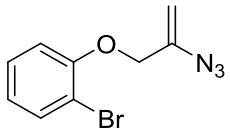
1-((2-Azidoallyl)oxy)-2-nitrobenzene (2-4a)

Prepared on a 7.3 mmol scale. Obtained as a yellow solid in 80% yield (1285 mg). Mp: 36.6-37.9 ℃. R_f (*n*-pentane:ethyl acetate 10:1) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.14 – 7.00 (m, 2H), 5.18 (s, 1H), 4.93 (s, 1H), 4.52 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1 (s), 140.9 (s), 140.1 (s), 134.1 (s), 125.6 (s), 121.2 (s), 115.1 (s), 101.0 (s), 68.5 (s). IR (ATR): ν 2952, 2873, 2110, 1638, 1605, 1521, 1486, 1348, 1272, 1255, 1235, 1165, 1091, 1045, 1002, 858, 772, 694 cm^{-1}. GC-MS (EI) m/z: 192 $[M\text{-}N_2]^+$ (3.93), 139 (100).



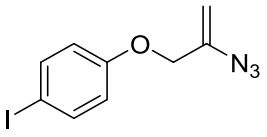
1-((2-Azidoallyl)oxy)-3-nitrobenzene (2-4b)

Prepared on a 7.0 mmol scale. Obtained as a yellow oily liquid in 85% yield (1309 mg). R_f (*n*-pentane:ethyl acetate 10:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.73 (s, 1H), 7.43 (t, *J* = 8.1 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 5.08 (s, 1H), 4.94 (s, 1H), 4.50 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (s), 149.1 (s), 141.2 (s), 130.1 (s), 121.8 (s), 116.5 (s), 109.3 (s), 101.6 (s), 68.1 (s). IR (ATR): ν 3099, 2934, 2872, 2110, 1637, 1524, 1480, 1349, 1281, 1237, 1028, 859, 716, 798, 670 cm^{-1}. GC-MS (EI) m/z (%): 192 $[M-N_2]^+$ (0.57), 139 (100).



1-((2-Azidoallyl)oxy)-2-bromobenzene (2-4c)

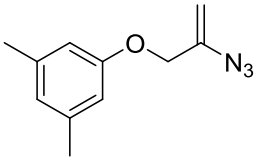
Prepared on a 6.0 mmol scale. Obtained as a yellow oily liquid in 83% yield (1260 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.72. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.84 (m, 2H), 5.17 (s, 1H), 4.94 (s, 1H), 4.49 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3 (s), 141.5 (s), 133.5 (s), 128.4 (s), 122.7 (s), 113.9 (s), 112.5 (s), 100.8 (s), 68.2 (s). IR (ATR): ν 3065, 2931, 2868, 2107, 1637, 1585, 1476, 1442, 1271, 1231, 1052, 1030, 859, 745, 655, 437 cm^{-1}. GC-MS (EI) m/z (%): 225 $[M-N_2]^+$ (10.85), 54 (100).



1-((2-Azidoallyl)oxy)-4-iodobenzene (2-4d)

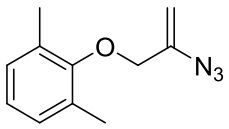
Prepared on a 5.4 mmol scale. Obtained as a yellow oily liquid in 75% yield (1219 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.72. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 5.03 (s, 1H), 4.91 (s, 1H), 4.41 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7 (s), 141.6 (s), 138.3 (s), 117.2 (s), 101.1 (s), 83.8 (s), 67.6 (s). IR (ATR): ν 3065, 2938, 2868, 2108, 1637, 1584, 1483, 1277, 1223,

1173, 1050, 1027, 1000, 859, 817, 684, 503 cm^{-1}. GC-MS (EI) m/z: 259 $[M\text{-}N_3]^+$ (%) (48.74), 219 (100).



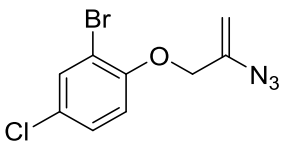
1-((2-Azidoallyl)oxy)-3,5-dimethylbenzene (2-4e)

Prepared on a 4.3 mmol scale. Obtained as a light yellow liquid in 91% yield (794 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.72. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (s, 1H), 6.59 (s, 2H), 5.05 (s, 1H), 4.91 (s, 1H), 4.44 (s, 2H), 2.32 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0 (s), 142.2 (s), 139.2 (s), 123.3 (s), 112.6 (s), 100.8 (s), 67.5 (s), 21.4 (s). IR (ATR): ν 3018, 2920, 2865, 2107, 1637, 1594, 1455, 1320, 1288, 1273, 1151, 1064, 847, 828, 686 cm^{-1}. GC-MS (EI) m/z: 175 $[M\text{-}N_2]^+$ (%) (61.82), 105 (100).



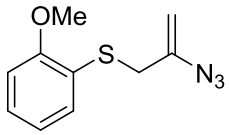
2-((2-Azidoallyl)oxy)-1,3-dimethylbenzene (2-4f)

Prepared on a 5.6 mmol scale. Obtained as a light yellow liquid in 90% yield (1023 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.72. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 – 6.90 (m, 3H), 5.12 (s, 1H), 4.93 (s, 1H), 4.21 (s, 2H), 2.31 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3 (s), 143.0 (s), 130.9 (s), 128.9 (s), 124.2 (s), 100.8 (s), 71.3 (s), 16.3 (s). IR (ATR): ν 3022, 2924, 2862, 2113, 1634, 1475, 1264, 1198, 1013, 997, 860, 769 cm^{-1}. GC-MS (EI) m/z (%): 175 $[M\text{-}N_2]^+$ (21.48), 54 (100).



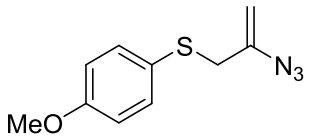
1-((2-Azidoallyl)oxy)-2-bromo-4-chlorobenzene (2-4g)

Prepared on a 5.0 mmol scale. Obtained as a yellow oily liquid in 78% yield (1119 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 1H), 5.14 (s, 1H), 4.93 (s, 1H), 4.45 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2 (s), 141.3 (s), 133.1 (s), 128.2 (s), 127.1 (s), 114.6 (s), 113.1 (s), 101.0 (s), 68.6 (s). IR (ATR): ν 3071, 2928, 2868, 2106, 1638, 1473, 1386, 1278, 1261, 1246, 1047, 1011, 863, 801 cm^{-1}. GC-MS (EI) m/z: 247 $[M\text{-}N_3]^+$ (%) (7.53), 43 (100).



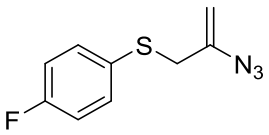
(2-Azidoallyl)(2-methoxyphenyl)sulfane (2-4h)

Prepared on a 4.6 mmol scale. Obtained as a yellow oily liquid in 82% yield (834 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 7.7 Hz, 1H), 6.95 – 6.84 (m, 2H), 4.64 (s, 1H), 4.63 (s, 1H), 3.90 (s, 3H), 3.49 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (s), 142.4 (s), 132.9 (s), 128.9 (s), 121.9 (s), 120.9 (s), 110.6 (s), 100.7 (s), 55.7 (s), 36.0 (s). IR (ATR): ν 3065, 3006, 2938, 2837, 2136, 2098, 1625, 1580, 1476, 1433, 1294, 1273, 1244, 1069, 1023, 852, 727, 647 cm^{-1}. GC-MS (EI) m/z (%): 193 $[M\text{-}N_2]^+$ (18.86), 138 (100).



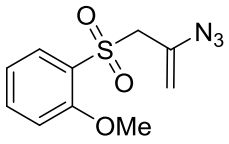
(2-azidoallyl)(4-methoxyphenyl)sulfane (2-4i)

Prepared on a 5.0 mmol scale. Obtained as a yellow oily liquid in 88% yield (972 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 4.62 (s, 1H), 4.52 (s, 1H), 3.80 (s, 3H), 3.36 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (s), 142.4 (s), 135.0 (s), 124.6 (s), 114.5 (s), 101.0 (s), 55.3 (s), 39.9 (s). IR (ATR): ν 3004, 2960, 2939, 2836, 2135, 2097, 1624, 1591, 1493, 1461, 1285, 1244, 1174, 1030, 826, 647, 524 cm^{-1}. GC-MS (EI) m/z (%): 193 $[M\text{-}N_2]^+$ (36.98), 139 (100).



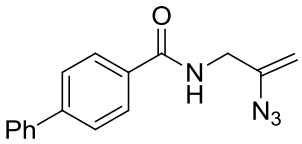
(2-Azidoallyl)(4-fluorophenyl)sulfane (2-4j)

Prepared on a 8.2 mmol scale. Obtained as a colorless liquid in 94% yield (1611 mg). R_f (*n*-pentane) = 0.48. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 2H), 7.17 – 6.92 (m, 2H), 4.63 (s, 1H), 4.56 (s, 1H), 3.39 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.5 – -113.7 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2 (d, *J* = 247.8 Hz), 142.0 (s), 134.3 (d, *J* = 8.2 Hz), 129.3 (d, *J* = 3.3 Hz), 115.8 (d, *J* = 21.9 Hz), 100.8 (s), 39.0 (s). IR (ATR): ν 2134, 2096, 1624, 1589, 1488, 1397, 1290, 1222, 1156, 1090, 852, 824, 629, 513, 450 cm^{-1}. GC-MS (EI) m/z (%): 181 $[M-N_2]^+$ (30.89), 141 (100).



1-((2-Azidoallyl)sulfonyl)-2-methoxybenzene (2-4k)

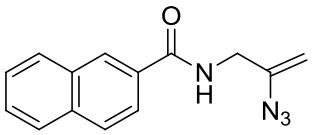
Prepared on a 5.6 mmol scale. Obtained as a yellow oily liquid in 74% yield (1048 mg). R_f (*n*-pentane:ethyl acetate 5:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.15 – 6.97 (m, 2H), 4.90 (s, 2H), 4.01 (s, 2H), 3.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3 (s), 135.9 (s), 135.4 (s), 130.9 (s), 126.0 (s), 120.7 (s), 112.3 (s), 106.2 (s), 58.1 (s), 56.3 (s). IR (ATR): ν 2944, 2844, 2142, 2107, 1724, 1627, 1591, 1479, 1435, 1314, 1279, 1241, 1148, 1064, 1014, 867, 802, 755, 595, 525, 485 cm^{-1}. GC-MS (EI) m/z (%): 253 $[M]^+$ (2.98), 191 (100).



***N*-(2-Azidoallyl)-[1,1'-biphenyl]-4-carboxamide (2-4m)**

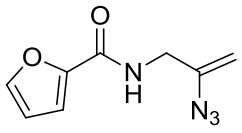
Prepared on a 7.0 mmol scale. Obtained as a white solid in 35% yield (681 mg). Mp: 120.0-120.9 ℃. R_f (*n*-pentane:ethyl acetate 5:2) = 0.77. ^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.88 (d, *J* = 7.6 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.39 (d, *J* = 6.8 Hz, 1H), 6.78 (s, 1H), 5.00 (s, 1H), 4.81 (s, 1H), 4.05 (d, *J* = 5.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (s), 144.5 (s), 143.3 (s), 139.8 (s), 132.6 (s), 128.9 (s), 128.0 (s), 127.5 (s), 127.2 (s), 127.1 (s), 99.3 (s), 42.0 (s). IR (ATR): ν 3317, 3060, 2922, 2852, 2106, 1637, 1609, 1531, 1483, 1290, 1250, 1186, 851, 744, 689, 601, 462 cm^{-1}. GC-MS (EI) m/z (%): 278 $[M]^+$ (1.46), 205 (100).



_N_-(2-Azidoallyl)-2-naphthamide (2-4n)

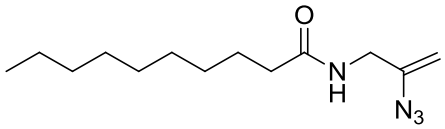
Prepared on a 5.0 mmol scale. Obtained as a white solid in 40% yield (504 mg). Mp: 87.6-88.5 ℃. R_f (*n*-pentane:ethyl acetate 5:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.00 – 7.78 (m, 4H), 7.64 – 7.46 (m, 2H), 7.00 – 6.51 (br m, 1H), 5.02 (d, *J* = 14.2 Hz, 1H), 4.82 (d, *J* = 12.6 Hz, 1H), 4.14 – 4.03 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5 (d, *J* = 19.3 Hz), 143.3 (s), 134.8 (s), 132.6 (s), 131.2 (s), 128.9 (s), 128.5 (d, *J* = 5.8 Hz), 127.8 (d, *J* = 0.9 Hz), 127.6 (d, *J* = 7.2 Hz), 126.8 (d, *J* = 4.0 Hz), 123.5 (d, *J* = 6.5 Hz), 99.5 (d, *J* = 15.4 Hz), 42.2 (d, *J* = 4.1 Hz). IR (ATR): ν 3311, 3060, 2927, 2247, 2108, 1643, 1535, 1505, 1423, 1270, 1203, 863, 777, 648, 477 cm^{-1}. GC-MS (EI) m/z (%): 253 $[M]^+$ (5.39), 155 (100).



_N_-(2-Azidoallyl)furan-2-carboxamide (2-4o)

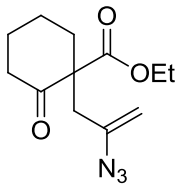
Prepared on a 4.3 mmol scale. Obtained as a colorless oily liquid in 44% yield (363 mg). R_f (*n*-pentane:ethyl acetate 5:2) = 0.53. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.14 (s, 1H), 6.58 (br s, 1H), 6.51 (s, 1H), 4.99 (s, 1H), 4.80 (s, 1H), 3.99 (d, *J* = 5.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1 (s), 147.5 (s), 144.1 (s), 143.2 (s), 114.7 (s), 112.2 (s), 99.4 (s), 41.1 (s). IR (ATR): ν 3438, 3319, 2926, 2855, 2251,

2110, 1658, 1594, 1521, 1475, 1272, 1179, 1015, 859, 725, 649, 594 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_8H_7N_4O_2$ $[M-H]^-$: 191.0564; found: 191.0572.



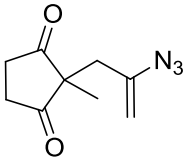
***N*-(2-Azidoallyl)decanamide (2-4p)**

Prepared on a 8.0 mmol scale. Obtained as a yellow oily liquid in 54% yield (1089 mg). R_f (*n*-pentane:ethyl acetate 10:1) = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (s, 1H), 4.89 (s, 1H), 4.74 (s, 1H), 3.82 (d, *J* = 5.4 Hz, 2H), 2.19 (t, *J* = 7.4 Hz, 2H), 1.62 (s, 2H), 1.40 – 1.13 (m, 12H), 0.86 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1 (s), 143.4 (s), 99.1 (s), 41.5 (s), 36.6 (s), 31.8 (s), 29.4 (s), 29.3 (s), 29.2 (s), 29.1 (s), 25.6 (s), 22.6 (s), 14.0 (s). IR (ATR): ν 3287, 3073, 2924, 2104, 1649, 1543, 1463, 1422, 1377, 1265, 846, 466 cm^{-1}. GC-MS (EI) m/z (%): 223 $[M-N_2]^+$ (9.49), 112 (100).



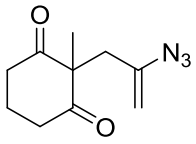
Ethyl 1-(2-azidoallyl)-2-oxocyclohexane-1-carboxylate (2-4s)

Prepared on a 4.0 mmol scale. Obtained as a yellow oily liquid in 64% yield (642 mg). R_f (*n*-pentane:ethyl acetate 10:1) = 0.83. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (d, *J* = 6.6 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.73 (d, *J* = 14.4 Hz, 1H), 2.61 (d, *J* = 13.8 Hz, 1H), 2.49 – 2.32 (m, 2H), 2.26 (d, *J* = 14.4 Hz, 1H), 2.06 – 1.98 (m, 1H), 1.83 – 1.71 (m, 2H), 1.66 – 1.56 (m, 1H), 1.45 – 1.32 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4 (s), 170.3 (s), 142.8 (s), 101.9 (s), 61.4 (s), 60.0 (s), 40.9 (s), 38.7 (s), 35.4 (s), 27.5 (s), 22.3 (s), 14.0 (s). IR (ATR): ν 2941, 2868, 2115, 1713, 1626, 1437, 1297, 1262, 1204, 1181, 1087, 1020, 855, 800 cm^{-1}. GC-MS (EI) m/z (%): 223 $[M-N_2]^+$ (6.79), 150 (100).



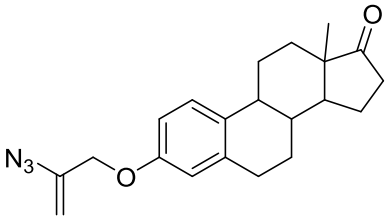
2-(2-Azidoallyl)-2-methylcyclopentane-1,3-dione (2-4t)

Prepared on a 4.1 mmol scale. Obtained as a colorless liquid in 52% yield (411 mg). R_f (*n*-pentane:ethyl acetate 10:2) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (s, 1H), 4.67 (s, 1H), 2.79 (s, 4H), 2.54 (s, 2H), 1.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.4 (s), 141.9 (s), 100.7 (s), 39.1 (s), 35.8 (s), 35.0 (s), 21.1 (s). IR (ATR): ν 3305, 2973, 2255, 2121, 1723, 1629, 1453, 1418, 1288, 1259, 1068, 648 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_9H_{12}N_3O_2$ $[M+H]^+$: 194.0924; found: 194.0932.



2-(2-Azidoallyl)-2-methylcyclohexane-1,3-dione (2-4u)

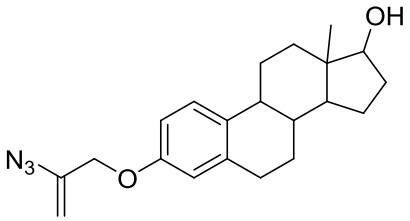
Prepared on a 3.6 mmol scale. Obtained as a yellow oily liquid in 67% yield (500 mg). R_f (*n*-pentane:ethyl acetate 5:1) = 0.83. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.76 (s, 1H), 4.68 (s, 1H), 2.75 – 2.61 (m, 6H), 2.09 – 1.90 (m, 2H), 1.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6 (s), 142.5 (s), 100.6 (s), 62.6 (s), 39.6 (s), 38.1 (s), 22.6 (s), 17.4 (s). IR (ATR): ν 2969, 2254, 2125, 1727, 1697, 1627, 1270, 1093, 1024, 723, 649 cm^{-1}. GC-MS (EI) m/z (%): 207 $[M]^+$ (1.36), 95 (100).



3-((2-Azidoallyl)oxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclope nta[*a*]phenanthren-17-one (2-7a)

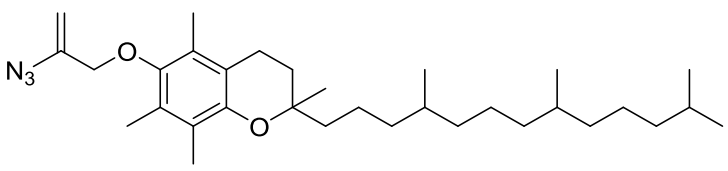
Prepared on a 8.5 mmol scale. Obtained as a white solid in 87% yield (2596 mg). Mp: 113.0-114.5 ℃. R_f (*n*-pentane:ethyl acetate 10:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.5 Hz, 1H), 6.74 (d, *J* = 8.6 Hz, 1H), 6.68 (s, 1H), 5.03 (s, 1H), 4.89 (s,

1H), 4.43 (s, 2H), 2.89 (d, *J* = 5.3 Hz, 2H), 2.52 (dd, *J* = 18.8, 8.6 Hz, 1H), 2.39 (d, *J* = 9.7 Hz, 1H), 2.25 (t, *J* = 9.1 Hz, 1H), 2.20 – 1.92 (m, 4H), 1.68 – 1.37 (m, 6H), 0.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0 (s), 142.1 (s), 137.9 (s), 133.0 (s), 126.4 (s), 115.0 (s), 112.4 (s), 100.9 (s), 67.7 (s), 50.4 (s), 48.0 (s), 44.0 (s), 38.3 (s), 35.8 (s), 31.6 (s), 29.6 (s), 26.5 (s), 25.9 (s), 21.6 (s), 13.8 (s). IR (ATR): ν 2928, 2861, 2107, 1736, 1638, 1608, 1497, 1454, 1277, 1233, 1158, 1056, 1007, 870, 817 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{21}H_{26}N_3O_2$ $[M+H]^+$: 352.2020; found: 352.2032.



3-((2-Azidoallyl)oxy)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclope -nta[*a*]phenanthren-17-ol (2-7b)

Prepared on a 8.2 mmol scale. Obtained as a white solid in 84% yield (1743 mg). Mp: 92.5-93.0 ℃. R_f (*n*-pentane:ethyl acetate 10:1) = 0.25. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 6.67 (s, 1H), 5.03 (s, 1H), 4.89 (s, 1H), 4.43 (s, 2H), 3.73 (t, *J* = 8.3 Hz, 1H), 2.90 – 2.81 (m, 2H), 2.31 (d, *J* = 13.4 Hz, 1H), 2.24 – 2.07 (m, 2H), 2.00 – 1.84 (m, 2H), 1.76 – 1.61 (m, 2H), 1.54 – 1.16 (m, 7H), 0.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8 (s), 142.1 (s), 138.1 (s), 133.5 (s), 126.3 (s), 114.9 (s), 112.2 (s), 100.8 (s), 81.8 (s), 67.6 (s), 50.0 (s), 43.9 (s), 43.2 (s), 38.7 (s), 36.6 (s), 30.5 (s), 29.7 (s), 27.1 (s), 26.2 (s), 23.1 (s), 11.0 (s). IR (ATR): ν 3410, 2924, 2868, 2246, 2108, 1638, 1608, 1497, 1275, 1250, 1232, 1054, 1022, 863, 728, 648, 447 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{21}H_{26}N_3O_2$ $[M-H]^-$: 352.2020; found: 352.2032.

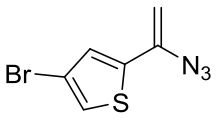


6-((2-Azidoallyl)oxy)-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chromane

(2-7c)

Prepared on a 9.0 mmol scale. Obtained as a yellow oily liquid in 86% yield (3955 mg). R_f (*n*-pentane:dichloromethane 10:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14 (s, 1H), 4.91 (s, 1H), 4.09 (s, 2H), 2.59 (t, *J* = 6.3 Hz, 2H), 2.20 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H), 1.91 – 1.71 (m, 3H), 1.65 – 1.51 (m, 3H), 1.49 – 0.99 (m, 20H), 0.94 – 0.82 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1 (s), 147.7 (s), 143.2 (s), 127.8 (s), 125.8 (s), 123.0 (s), 117.6 (s), 100.5 (s), 74.9 (s), 72.0 (s), 40.0 (d, *J* = 3.9 Hz), 39.4 (s), 37.6 – 37.2 (m), 32.8 (d, *J* = 1.8 Hz), 32.7 (d, *J* = 1.9 Hz), 31.2 (d, *J* = 4.9 Hz), 28.0 (s), 24.8 (s), 24.4 (s), 23.9 (s), 22.7 (d, *J* = 9.3 Hz), 21.0 (s), 20.6 (s), 19.9 – 19.1 (m), 12.7 (s), 11.9 (s), 11.8 (s). IR (ATR): ν 2926, 2867, 2249, 2154, 2109, 1635, 1459, 1414, 1378, 1292, 1274, 1255, 1158, 1089, 1063, 1014, 857, 650 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{32}H_{52}N_3O_2$ $[M-H]^-$: 510.4054; found: 510.4031.

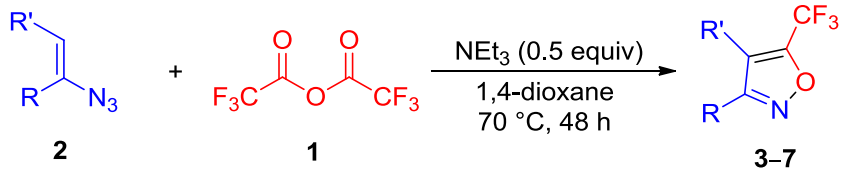
The following new compounds were synthesized by Procedure B:



2-(1-Azidovinyl)-4-bromothiophene (2q)

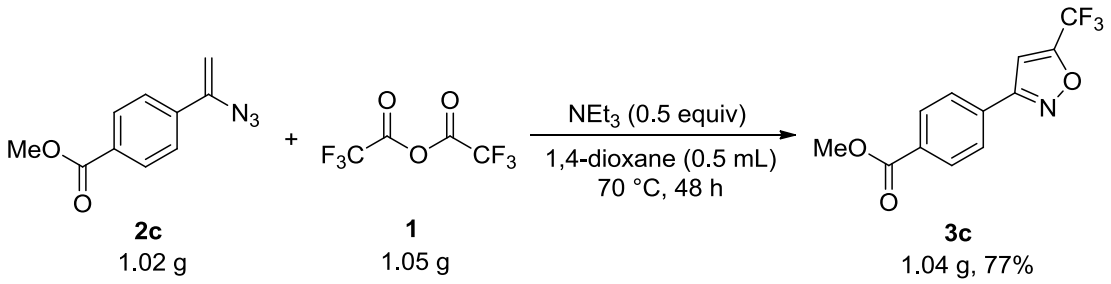
Prepared on a 2.0 mmol scale. Obtained as a yellow oily liquid in 88% yield (403 mg). R_f (*n*-pentane) = 0.96. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (s, 2H), 5.37 (s, 1H), 4.89 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3 (s), 138.9 (s), 127.3 (s), 123.2 (s), 110.3 (s), 97.1 (s). IR (ATR): ν 3110, 2924, 2855, 2140, 2107, 1460, 1175, 1158, 1020 cm^{-1}. GC-MS (EI) m/z (%): 203 $[M]^+$ (81.52), 95 (100).

General procedure of the synthesis of 5-trifluoromethyl isoxazole



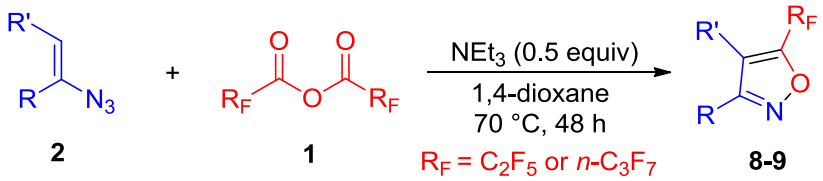
In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added vinyl azides **2** (0.30 mmol, 1.0 equiv), trifluoroacetic anhydride **1** (3.00 mmol, 10.0 equiv or 1.50 mmol, 5.0 equiv), NEt_3 (0.15 mmol, 0.5 equiv) and 1,4-dioxane (0.5 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 70 °C for 48 h. After cool to room temperature, the crude mixture was diluted with water (5 mL × 3) and CH_2Cl_2 (15 mL). The organic phase was extracted and dried over $MgSO_4$, filtered, and the solvent was removed by rotary evaporation. The resulting isoxazole products **3**–**7** was purified by column chromatography on silica gel with *n*-pentane/CH_2Cl_2 or *n*-pentane/ethyl acetate.

Procedure for gram scale reaction for synthesis of methyl 4-(5-(trifluoromethyl)isoxazol-3-yl)benzoate (3c)



In a glove box filled with nitrogen, to an oven-dried 25 mL pressure tube equipped with a stir bar were added vinyl azide **2c** (1.02 g, 5.0 mmol, 1.0 equiv), trifluoroacetic anhydride **1** (10.50 g, 50.0 mmol, 10.0 equiv), NEt_3 (0.25 g, 2.5 mmol, 0.5 equiv) and 1,4-dioxane (2.5 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 70℃ for 48 h. After cool to room temperature, the crude mixture was diluted with water (20 mL × 3) and CH_2Cl_2 (50 mL). The organic phase was extracted and dried over $MgSO_4$, filtered, and the solvent was removed by rotary evaporation. The resulting residue was purified by column chromatography on silica gel with *n*-pentane/ CH_2Cl_2 (4:1) to give 1.04 g of product **3c** (77% yield).

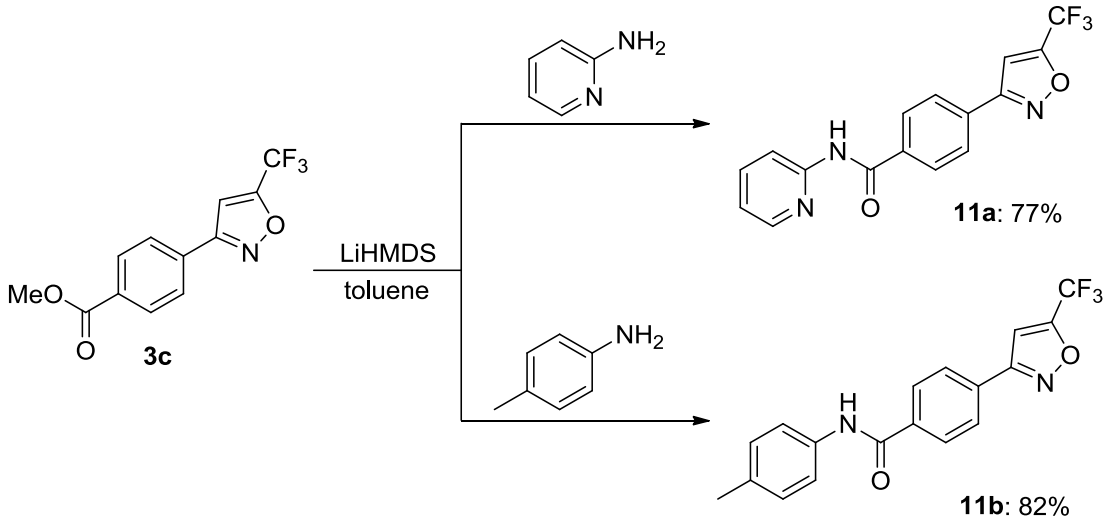
General procedure of the synthesis of 5-perfluoroalkyl isoxazole



In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added vinyl azides **2** (0.30 mmol, 1.0 equiv), perfluorocarboxylic anhydride (3.00 mmol, 10.0 equiv), NEt_3 (0.15 mmol, 0.5 equiv) and 1,4-dioxane (0.5 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 70 °C for 48 h. After cool to room temperature, the crude mixture was diluted with water (5 mL × 3) and CH_2Cl_2 (15 mL). The organic phase was extracted and dried over $MgSO_4$, filtered, and the solvent was removed by rotary evaporation. The resulting 5-perfluoroalkyl isoxazole products **8–9** was purified by column chromatography on silica gel with *n*-pentane/CH_2Cl_2.

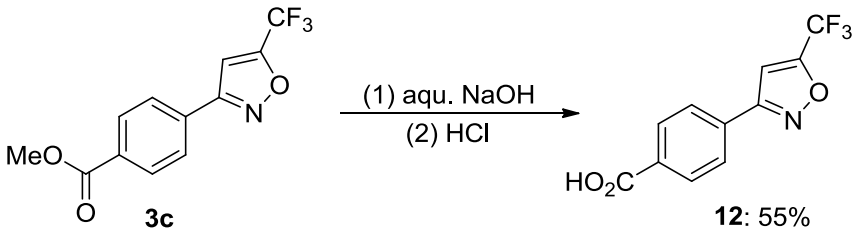
Synthetic utility of trifluoromethylated isoxazoles

General procedure for the transformation of 3 to 11



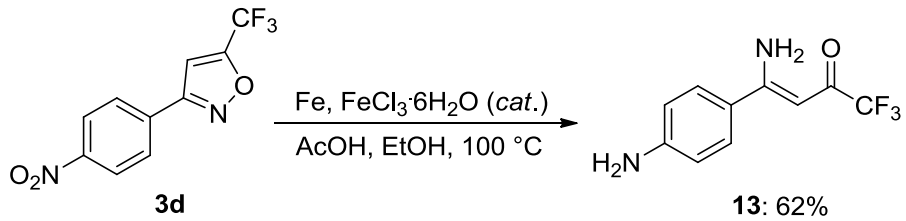
An oven-dried vial equipped with a stir bar was charged with methyl 4-(5-(trifluoromethyl)isoxazol-3-yl)benzoate **3c** (54.2 mg, 0.20 mmol, 1.0 equiv), 2-aminopyridine (37.6 mg, 0.40 mmol, 2.0 equiv) or *p*-toluidine (42.9 mg, 0.40 mmol, 2.0 equiv). The vial was placed under a positive pressure of N_2, and subjected to three evacuation/backfilling cycles. Toluene (1 mL) and LiHMDS (1.0 M in THF, 400 μL, 2.0 equiv) were sequentially added with vigorous stirring at room temperature for 20 h. The reaction mixture was quenched with saturated NH_4Cl, diluted with EtOAc (20 mL). The organic layer was washed with water (10 mL), brine (10 mL) and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting residue was purified by column chromatography on silica gel with petro ether/EtOAc to give **11a** (77%) and **11b** (82%), respectively.

Procedure for the transformation of 3c to 12



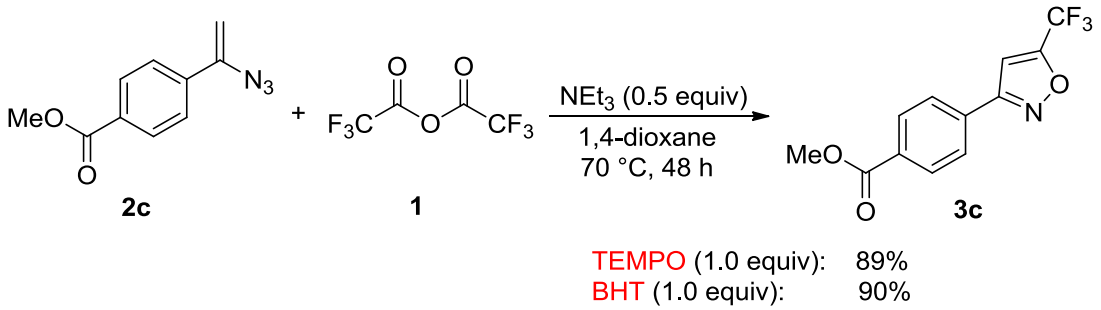
The methyl 4-(5-(trifluoromethyl)isoxazol-3-yl)benzoate **3c** (54.2 mg, 0.20 mmol) was stirred with a 1.2 N aqueous sodium hydroxide (0.5 mL) and dimethylformamide (0.5 mL) at ambient temperature for 1 h. The reaction mixture was acidified with 6 N HCl. The solid carboxylic acid was collected and the aqueous portion was extracted with Et_2O (2 × 10 mL) , brine (2 × 10 mL) and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting product was purified by recrystallization with Et_2O/petro ether to give **12** (55% yield).

Procedure for the transformation of 3d to 13



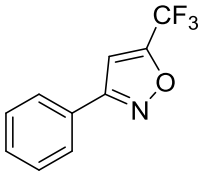
A solution of 3-(4-nitrophenyl)-5-(trifluoromethyl)isoxazole **3d** (129.0 mg, 0.50 mmol) and AcOH (86 μL, 3.0 equiv) in EtOH (2 mL) was heated to reflux with stirring for 10 min before iron powder (19.5 g, 3.5 mmol, 7 equiv) and $FeCl_3$ $6H_2O$ (13.5 mg, 0.48 mmol, 0.1 equiv) were added. The resulting mixture was heated to reflux with stirring for 4 h before it was cooled to room temperature, diluted with EtOAc (30 mL). The organic layer was washed with water (2 × 10 mL), brine (2 × 10 mL) and dried over $MgSO_4$. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with petro ether/EtOAc to give **13** (62% yield).

Radical inhibition experiments



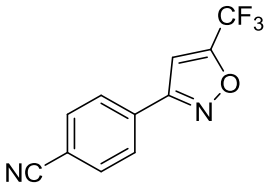
In a dry-box, **2c** (20.3 mg, 0.10 mmol), trifluoroacetic anhydride **1** (140 μL, 1.0 mmol, 10.0 equiv), NEt_3 (7 μL, 0.05 mmol, 0.5 equiv), TEMPO (1.0 equiv) or BHT (1.0 equiv), and 1,4-dioxane (0.5 mL) were added to a oven-dried 5 mL test tube with Teflon screw cap. The tube was sealed and the solution was stirred at 70 °C for 48 h. After cool to room temperature, the 10 μL (trifluoromethoxy)benzene was added as an internal standard. The reaction mixture was then filtered through a layer of celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of **3c** was calculated to be 89% and 90% yield, respectively.

Data for compounds 3–13



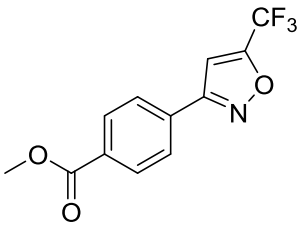
3-Phenyl-5-(trifluoromethyl)isoxazole (3a)

Obtained as a white solid in 57% yield (37 mg). Mp: 62.9–63.8 ℃. R_f (*n*-pentane) = 0.62. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.79 (m, 2H), 7.57 – 7.43 (m, 3H), 7.01 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.4 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (s), 159.1 (q, *J* = 42.4 Hz), 130.8 (s), 129.1 (s), 127.2 (s), 126.8 (s), 117.9 (q, *J* = 270.1 Hz), 103.4 (q, *J* = 2.0 Hz). IR (ATR): ν 3118, 2956, 2923, 1470, 1445, 1244, 1178, 1143, 1119, 968, 950, 909, 849, 770, 692 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_7F_3NO$ $[M+H]^+$: 214.0474; found: 214.0475.



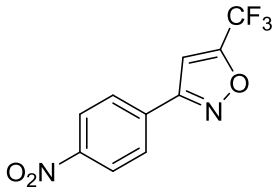
4-(5-(Trifluoromethyl)isoxazol-3-yl)benzonitrile (3b)

Obtained as a white solid in 98% yield (70 mg). Mp: 84.2–85.9 ℃. R_f (*n*-pentane) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.9 Hz, 2H), 7.79 (d, *J* = 7.9 Hz, 2H), 7.09 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (s), 159.9 (q, *J* = 42.9 Hz), 132.9 (s), 131.5 (s), 127.5 (s), 117.9 (s), 117.6 (q, *J* = 270.5 Hz), 114.5 (s), 103.4 (q, *J* = 2.0 Hz). IR (ATR): ν 3135, 2958, 2923, 2232, 1462, 1430, 1316, 1304, 1264, 1239, 1186, 1156, 1114, 968, 824, 735, 704, 554 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_6F_3N_2O$ $[M+H]^+$: 239.0432; found: 239.0437.



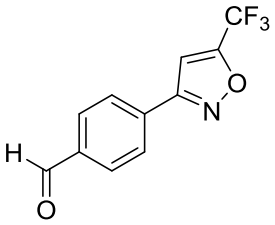
Methyl 4-(5-(trifluoromethyl)isoxazol-3-yl)benzoate (3c)

Obtained as a white solid in 98% yield (80 mg). Mp: 99.2–100.8 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.60. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.06 (s, 1H), 3.94 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1 (s), 161.7 (s), 159.6 (q, *J* = 42.7 Hz), 132.2 (s), 131.3 (s), 130.3 (s), 126.9 (s), 117.7 (q, *J* = 270.4 Hz), 103.5 (q, *J* = 2.0 Hz), 52.3 (s). IR (ATR): ν 3136, 2959, 2923, 2852, 1724, 1432, 1315, 1284, 1240, 1182, 1161, 1107, 1020, 972, 834, 776, 702 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_9F_3NO_3$ $[M+H]^+$: 272.0529; found: 272.0527.



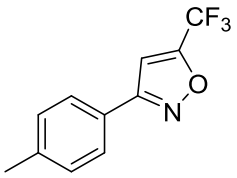
3-(4-Nitrophenyl)-5-(trifluoromethyl)isoxazole (3d)

Obtained as a light yellow crystalline solid in 92% yield (71 mg). Mp: 107.2–108.5 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 8.3 Hz, 2H), 7.14 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (s), 160.1 (q, *J* = 43.0 Hz), 149.2 (s), 133.2 (s), 127.9 (s), 124.4 (s), 117.6 (q, *J* = 270.6 Hz), 103.6 (q, *J* = 1.9 Hz). IR (ATR): ν 3141, 2924, 2854, 1605, 1521, 1345, 1310, 1239, 1188, 1150, 1116, 968, 852, 737, 698 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6F_3N_2O_3$ $[M+H]^+$: 259.0331; found: 259.0325.



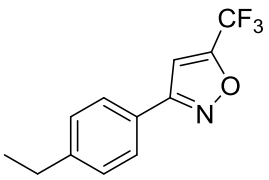
4-(5-(Trifluoromethyl)isoxazol-3-yl)benzaldehyde (3e)

Obtained as a yellow solid in 43% yield (31 mg). Mp: 71.3–72.1 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.05 – 7.96 (m, 4H), 7.09 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3 (s), 161.6 (s), 159.9 (q, *J* = 42.7 Hz), 137.8 (s), 132.7 (s), 130.4 (s), 127.6 (s), 117.7 (q, *J* = 270.5 Hz), 103.6 (q, *J* = 1.9 Hz). IR (ATR): ν 3143, 2957, 2924, 2852, 1692, 1611, 1431, 1316, 1177, 1161, 1114, 969, 923, 827, 748, 693 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_7F_3NO_2$ $[M+H]^+$: 242.0423; found: 242.0427.



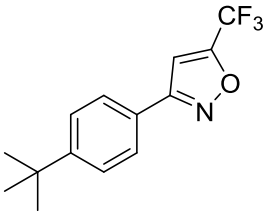
3-(*p*-Tolyl)-5-(trifluoromethyl)isoxazole (3f)

Obtained as a white solid in 55% yield (38 mg). Mp: 80.7–81.5 ℃. R_f (*n*-pentane) = 0.62. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.4 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 2H), 6.97 (s, 1H), 2.42 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (s), 159.0 (q, *J* = 42.7 Hz), 141.2 (s), 129.8 (s), 126.8 (s), 124.5 (s), 117.9 (q, *J* = 270.4 Hz), 103.3 (q, *J* = 2.0 Hz), 21.4 (s). IR (ATR): ν 3120, 2924, 2854, 1619, 1461, 1319, 1242, 1180, 1142, 1117, 968, 908, 850, 820, 749 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_9F_3NO$ $[M+H]^+$: 228.0631; found: 228.0632.



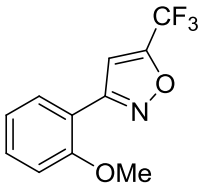
3-(4-Ethylphenyl)-5-(trifluoromethyl)isoxazole (3g)

Obtained as a white solid in 57% yield (41 mg). Mp: 46.3–47.1 ℃. R_f (*n*-pentane) = 0.62. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 2H), 6.98 (s, 1H), 2.72 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 6.8 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (s), 159.0 (q, *J* = 42.3 Hz), 147.5 (s), 128.7 (s), 126.9 (s), 124.7 (s), 117.9 (q, *J* = 270.3 Hz), 103.3 (q, *J* = 1.9 Hz), 28.8 (s), 15.2 (s). IR (ATR): ν 3129, 2962, 2925, 1739, 1614, 1463, 1433, 1318, 1244, 1186, 1165, 1144, 1117, 968, 830 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{11}F_3NO$ $[M+H]^+$: 242.0793; found: 242.0787.



3-(4-(*tert*-Butyl)phenyl)-5-(trifluoromethyl)isoxazole (3h)

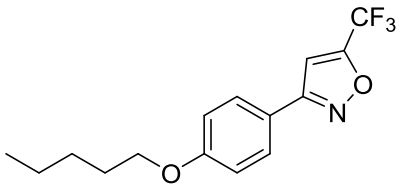
Obtained as a colorless liquid in 57% yield (46 mg). R_f (*n*-pentane) = 0.63. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 2H), 7.52 (d, *J* = 7.9 Hz, 2H), 6.99 (s, 1H), 1.37 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (s), 159.0 (q, *J* = 42.6 Hz), 154.4 (s), 126.7 (s), 126.1 (s), 124.5 (s), 117.9 (q, *J* = 270.3 Hz), 103.4 (q, *J* = 1.9 Hz), 34.9 (s), 31.1 (s). IR (ATR): ν 3141, 2965, 2871, 1616, 1462, 1430, 1319, 1306, 1238, 1184, 1154, 1101, 967, 912, 821, 732, 559 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{14}H_{15}F_3NO$ $[M+H]^+$: 270.1100; found: 270.1103.



3-(2-Methoxyphenyl)-5-(trifluoromethyl)isoxazole (3i)

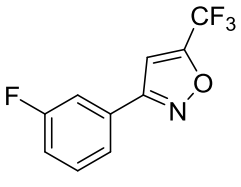
Obtained as a colorless oily liquid in 55% yield (40 mg). R_f

(*n*-pentane:dichloromethane 4:1) = 0.63. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.23 (s, 1H), 7.12 – 6.99 (m, 2H), 3.93 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2 (s), 157.9 (q, *J* = 42.2 Hz), 157.2 (s), 132.1 (s), 129.5 (s), 121.1 (s), 118.1 (q, *J* = 270.4 Hz), 116.2 (s), 111.5 (s), 106.9 (q, *J* = 2.1 Hz), 55.6 (s). IR (ATR): ν 2955, 2923, 2852, 1740, 1463, 1438, 1377, 1317, 1253, 1185, 1159, 1083, 1026 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_9F_3NO_2$ $[M+H]^+$: 244.0580; found: 244.0581.



3-(4-(Pentyloxy)phenyl)-5-(trifluoromethyl)isoxazole (3j)

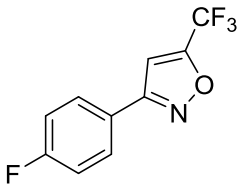
Obtained as a light yellow solid in 25% yield (23 mg). Mp: 54.6–55.6 ℃. R_f (*n*-pentane) = 0.45. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.94 (s, 1H), 4.01 (t, *J* = 6.5 Hz, 2H), 1.87 – 1.77 (m, 2H), 1.51 – 1.33 (m, 4H), 0.94 (t, *J* = 6.9 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2 (s), 161.3 (s), 158.8 (q, *J* = 42.3 Hz), 128.3 (s), 119.4 (s), 117.9 (q, *J* = 270.3 Hz), 115.0 (s), 103.2 (q, *J* = 2.0 Hz), 68.2 (s), 28.8 (s), 28.1 (s), 22.4 (s), 14.0 (s). IR (ATR): ν 3119, 2960, 2935, 2871, 1612, 1461, 1436, 1318, 1258, 1177, 1148, 1116, 1014, 968, 795, 738 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{15}H_{17}F_3NO_2$ $[M+H]^+$: 300.1206; found: 300.1208.



3-(3-Fluorophenyl)-5-(trifluoromethyl)isoxazole (3k)

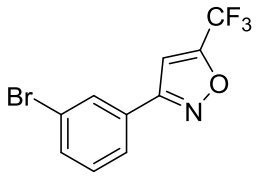
Obtained as a white crystalline solid in 97% yield (67 mg). Mp: 53.6–54.4 ℃. R_f (*n*-pentane) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 9.4 Hz, 1H), 7.49 – 7.41 (m, 1H), 7.19 (t, *J* = 8.3 Hz, 1H), 6.99 (s, 1H). ^{19}F NMR

(376 MHz, $CDCl_3$) δ -64.4 (s, 3F), -111.4 (dd, *J* = 14.9, 7.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0 (d, *J* = 247.6 Hz), 161.6 (d, *J* = 2.6 Hz), 159.5 (q, *J* = 42.7 Hz), 130.9 (d, *J* = 8.3 Hz), 129.3 (d, *J* = 8.3 Hz), 122.7 (d, *J* = 3.1 Hz), 117.9 (d, *J* = 21.2 Hz), 117.8 (q, *J* = 270.3 Hz), 113.9 (d, *J* = 23.5 Hz), 103.4 (q, *J* = 2.0 Hz). IR (ATR): ν 3145, 2956, 2924, 2854, 1591, 1450, 1314, 1255, 1198, 1186, 1159, 1112, 967, 855, 789 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6F_4NO$ $[M+H]^+$: 232.0380; found: 232.0382.



3-(4-Fluorophenyl)-5-(trifluoromethyl)isoxazole (3l)

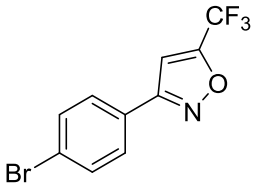
Obtained as a colorless oily liquid in 57% yield (40 mg). R_f (*n*-pentane) = 0.45. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (t, *J* = 5.4 Hz, 2H), 7.19 (t, *J* = 8.1 Hz, 2H), 6.97 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F), -108.8 (dd, *J* = 7.7, 5.5 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3 (d, *J* = 251.6 Hz), 161.6 (s), 159.4 (q, *J* = 42.3 Hz), 129.0 (d, *J* = 8.7 Hz), 123.6 (d, *J* = 3.3 Hz), 117.8 (q, *J* = 270.4 Hz), 116.4 (d, *J* = 22.1 Hz), 103.3 (q, *J* = 1.9 Hz). IR (ATR): ν 3141, 2956, 2924, 2854, 1450, 1316, 1253, 1199, 1188, 1160, 1112, 967, 854 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6F_4NO$ $[M+H]^+$: 232.0380; found: 232.0381.



3-(3-Bromophenyl)-5-(trifluoromethyl)isoxazole (3m)

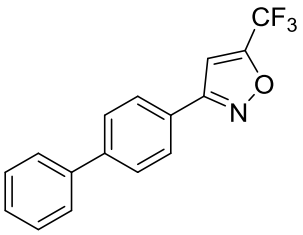
Obtained as a white crystalline solid in 99% yield (86 mg). Mp: 41.2–42.5 ℃. R_f (*n*-pentane) = 0.73. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 6.99 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3 (s), 159.5 (q, *J* =

42.7 Hz), 133.8 (s), 130.7 (s), 129.9 (s), 129.2 (s), 125.4 (s), 123.2 (s), 117.7 (q, *J* = 270.4 Hz), 103.3 (q, *J* = 2.0 Hz). IR (ATR): ν 3140, 2960, 2925, 1568, 1468, 1312, 1236, 1186, 1155, 1121, 1047, 1019, 968, 788, 754, 693 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6BrF_3NO$ $[M+H]^+$: 291.9579; found: 291.9581.



3-(4-Bromophenyl)-5-(trifluoromethyl)isoxazole (3n)

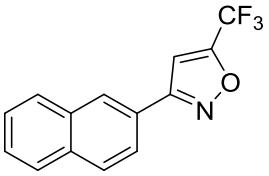
Obtained as a white solid in 99% yield (86 mg). Mp: 70.6–71.3 ℃. R_f (*n*-pentane:dichloromethane 8:1) = 0.70. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 6.98 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6 (s), 159.4 (q, *J* = 42.6 Hz), 132.4 (s), 128.3 (s), 126.2 (s), 125.4 (s), 117.7 (q, *J* = 270.4 Hz), 103.2 (q, *J* = 2.0 Hz). IR (ATR): ν 3127, 1619, 1597, 1321, 1250, 1179, 1162, 1118, 828 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6BrF_3NO$ $[M+H]^+$: 291.9579; found: 291.9580.



3-([1,1'-Biphenyl]-4-yl)-5-(trifluoromethyl)isoxazole (3o)

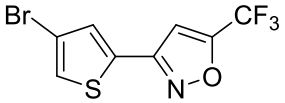
Obtained as a white solid in 51% yield (44 mg). Mp: 160.9–161.8 ℃. R_f (*n*-pentane:dichloromethane 8:1) = 0.88. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 2H), 7.64 (d, *J* = 6.8 Hz, 2H), 7.55 – 7.35 (m, 3H), 7.04 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (s), 159.2 (q, *J* = 42.5 Hz), 143.7 (s), 139.9 (s), 131.0 (s), 129.0 (s), 128.0 (s), 127.8 (s), 127.4 (s), 127.1 (s), 117.9 (q, *J* = 270.4 Hz), 103.4 (q, *J* = 1.5 Hz). IR (ATR): ν 3116, 2955, 2921, 2851, 1462, 1450, 1322, 1247, 1181, 1144, 1120, 968,

838, 766, 726, 689 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{11}F_3NO$ $[M+H]^+$: 290.0787; found: 290.0789.



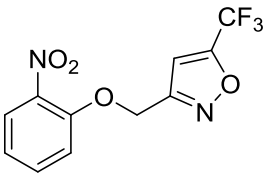
3-(Naphthalen-2-yl)-5-(trifluoromethyl)isoxazole (3p)

Obtained as a yellow solid in 66% yield (52 mg). Mp: 93.6–94.3 ℃. R_f (*n*-pentane) = 0.46. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.93 (s, 2H), 7.89 (t, *J* = 8.5 Hz, 2H), 7.48 – 7.62 (m, 2H), 7.11 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (s), 159.2 (q, *J* = 42.5 Hz), 134.3 (s), 133.0 (s), 129.1 (s), 128.5 (s), 127.9 (s), 127.5 (s), 127.0 (s), 126.9 (s), 124.6 (s), 123.5 (s), 117.9 (q, *J* = 270.3 Hz), 103.5 (q, *J* = 2.0 Hz). IR (ATR): ν 3128, 2956, 2923, 2852, 1490, 1312, 1256, 1224, 1176, 1147, 1107, 968, 903, 828, 752, 487 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{14}H_9F_3NO$ $[M+H]^+$: 264.0631; found: 264.0636.



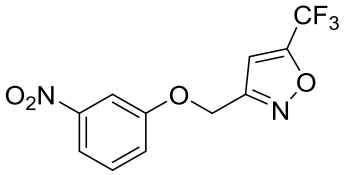
3-(4-Bromothiophen-2-yl)-5-(trifluoromethyl)isoxazole (3q)

Obtained as a colorless oily liquid in 36% yield (32 mg). Mp: 35.0–36.2 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.83. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.38 (s, 1H), 6.91 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6 (q, *J* = 42.9 Hz), 156.8 (s), 130.9 (s), 130.0 (s), 125.9 (s), 117.6 (q, *J* = 270.6 Hz), 110.9 (s), 103.2 (q, *J* = 2.0 Hz). IR (ATR): ν 3114, 2921, 2851, 1554, 1461, 1310, 1229, 1188, 1159, 1098, 967, 929, 817, 747, 583 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_8H_4BrF_3NOS$ $[M+H]^+$: 297.9149; found: 297.9151.



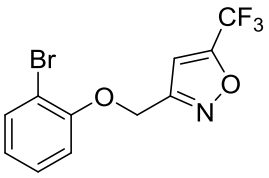
3-((2-Nitrophenoxy)methyl)-5-(trifluoromethyl)isoxazole (4a)

Obtained as a white solid in 49% yield (42 mg). Mp: 56.0–57.1 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.22 – 7.09 (m, 2H), 6.98 (s, 1H), 5.34 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3 (s), 159.5 (q, *J* = 42.8 Hz), 150.7 (s), 140.2 (s), 134.4 (s), 125.9 (s), 122.0 (s), 117.6 (q, *J* = 270.3 Hz), 115.1 (s), 105.0 (q, *J* = 1.9 Hz), 62.6 (s). IR (ATR): ν 3146, 2955, 2922, 1607, 1526, 1488, 1351, 1314, 1280, 1210, 1183, 1151, 966, 743 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8F_3N_2O_4$ $[M+H]^+$: 289.0436; found: 289.0431.



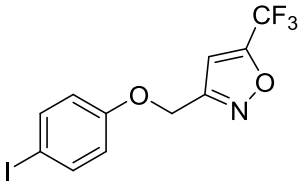
3-((3-Nitrophenoxy)methyl)-5-(trifluoromethyl)isoxazole (4b)

Obtained as a white solid in 65% yield (56 mg). Mp: 68.5–69.1 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 1.3 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 6.88 (s, 1H), 5.29 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1 (s), 159.7 (q, *J* = 42.9 Hz), 158.0 (s), 149.3 (s), 130.4 (s), 121.3 (s), 117.6 (q, *J* = 270.5 Hz), 117.0 (s), 109.4 (s), 104.7 (q, *J* = 2.0 Hz), 61.6 (s). IR (ATR): ν 3145, 2955, 2921, 2852, 1619, 1530, 1352, 1315, 1211, 1183, 1153, 966, 823, 736 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8F_3N_2O_4$ $[M+H]^+$: 289.0436; found: 289.0430.



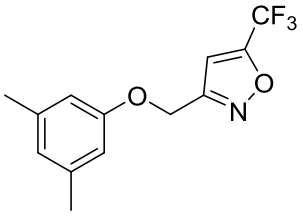
3-((2-Bromophenoxy)methyl)-5-(trifluoromethyl)isoxazole (4c)

Obtained as a white solid in 53% yield (51 mg). Mp: 52.6–53.4 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.02 – 6.88 (m, 3H), 5.26 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0 (s), 159.3 (q, *J* = 42.8 Hz), 154.0 (s), 133.8 (s), 128.7 (s), 123.4 (s), 117.7 (q, *J* = 270.4 Hz), 113.9 (s), 112.5 (s), 105.0 (q, *J* = 2.0 Hz), 62.3 (s). IR (ATR): ν 3146, 2956, 2925, 1586, 1478, 1445, 1317, 1278, 1210, 1182, 1154, 1058, 1031, 966, 827, 747 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8BrF_3NO_2$ $[M+H]^+$: 321.9685; found: 321.9688.



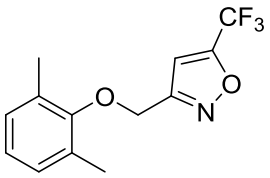
3-((4-Iodophenoxy)methyl)-5-(trifluoromethyl)isoxazole (4d)

Obtained as a white solid in 75% yield (83 mg). Mp: 52.5–53.3 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.63. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.6 Hz, 2H), 6.84 (s, 1H), 6.75 (d, *J* = 7.7 Hz, 2H), 5.16 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7 (s), 159.3 (q, *J* = 42.9 Hz), 157.4 (s), 138.5 (s), 117.7 (q, *J* = 270.3 Hz), 117.0 (s), 104.8 (q, *J* = 1.8 Hz), 84.4 (s), 61.1 (s). IR (ATR): ν 3141, 2957, 2924, 2854, 1584, 1485, 1460, 1317, 1240, 1212, 1179, 1158, 1078, 1046, 1020, 966, 818, 802 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8F_3INO_2$ $[M+H]^+$: 369.9546; found: 369.9547.



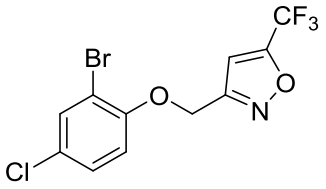
3-((3,5-Dimethylphenoxy)methyl)-5-(trifluoromethyl)isoxazole (4e)

Obtained as a white solid in 78% yield (63 mg). Mp: 51.0–52.0 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.88. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.68 (s, 1H), 6.61 (s, 2H), 5.17 (s, 2H), 2.31 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5 (s), 159.1 (q, *J* = 42.8 Hz), 157.7 (s), 139.6 (s), 123.8 (s), 117.8 (q, *J* = 270.3 Hz), 112.4 (s), 104.9 (q, *J* = 1.8 Hz), 61.0 (s), 21.4 (s). IR (ATR): ν 2955, 2922, 2853, 1740, 1596, 1460, 1315, 1294, 1211, 1156, 1073, 966, 829, 732, 704 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{13}H_{13}F_3NO_2$ $[M+H]^+$: 272.0898; found: 272.0893.



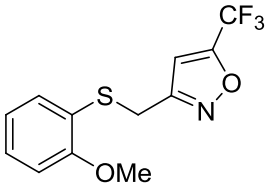
3-((2,6-Dimethylphenoxy)methyl)-5-(trifluoromethyl)isoxazole (4f)

Obtained as a yellow oily liquid in 68% yield (55 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.80. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.3 Hz, 2H), 7.03 – 6.95 (m, 2H), 4.96 (s, 2H), 2.31 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4 (s), 159.1 (q, *J* = 42.8 Hz), 155.0 (s), 130.6 (s), 129.1 (s), 124.8 (s), 117.8 (q, *J* = 270.4 Hz), 104.9 (q, *J* = 2.0 Hz), 64.5 (s), 16.2 (s). IR (ATR): ν 3143, 2955, 2925, 1475, 1317, 1264, 1210, 1185, 1156, 1092, 1077, 1033, 966, 909, 825, 770, 736 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{13}H_{13}F_3NO_2$ $[M+H]^+$: 272.0898; found: 272.0893.



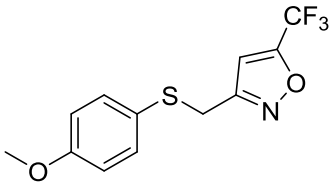
3-((2-Bromo-4-chlorophenoxy)methyl)-5-(trifluoromethyl)isoxazole (4g)

Obtained as a light red solid in 83% yield (88 mg). Mp: 63.8–65.2 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.63. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.00 – 6.83 (m, 2H), 5.23 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5 (s), 159.4 (q, *J* = 42.9 Hz), 152.9 (s), 133.3 (s), 128.5 (s), 127.8 (s), 117.7 (q, *J* = 270.5 Hz), 114.5 (s), 113.0 (s), 104.9 (q, *J* = 2.0 Hz), 62.6 (s). IR (ATR): ν 3163, 3093, 2955, 2923, 1585, 1477, 1316, 1283, 1210, 1151, 1075, 1060, 966, 920, 777, 693 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_7BrClF_3NO_2$ $[M+H]^+$: 357.9275; found: 357.9275.



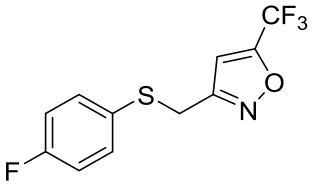
3-(((2-Methoxyphenyl)thio)methyl)-5-(trifluoromethyl)isoxazole (4h)

Obtained as a yellow oily liquid in 98% yield (86 mg). R_f (*n*-pentane:dichloromethane 1:1) = 0.75. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.3 Hz, 1H), 7.26 (d, *J* = 7.3 Hz, 1H), 6.89 (t, *J* = 7.7 Hz, 2H), 6.65 (s, 1H), 4.11 (s, 2H), 3.87 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0 (s), 158.5 (q, *J* = 42.4 Hz), 158.4 (s), 132.5 (s), 129.5 (s), 121.1 (s), 120.9 (s), 117.7 (q, *J* = 270.1 Hz), 110.9 (s), 105.3 (q, *J* = 2.0 Hz), 55.7 (s), 27.4 (s). IR (ATR): ν 2925, 2841, 1581, 1478, 1433, 1315, 1274, 1246, 1211, 1182, 1152, 1072, 1024, 964, 753 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{11}F_3NO_2S$ $[M+H]^+$: 290.0463; found: 290.0457.



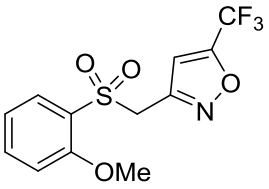
3-(((4-Methoxyphenyl)thio)methyl)-5-(trifluoromethyl)isoxazole (4i)

Obtained as a yellow oily liquid in 98% yield (85 mg). R_f (*n*-pentane:dichloromethane 1:1) = 0.83. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.2 Hz, 2H), 6.83 (d, *J* = 7.2 Hz, 2H), 6.61 (s, 1H), 4.00 (s, 2H), 3.78 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (s), 159.9 (s), 158.7 (q, *J* = 42.4 Hz), 134.5 (s), 123.4 (s), 117.7 (q, *J* = 270.2 Hz), 114.8 (s), 105.1 (q, *J* = 2.0 Hz), 55.2 (s), 30.8 (s). IR (ATR): ν 3136, 2925, 2841, 1744, 1592, 1493, 1463, 1314, 1287, 1246, 1211, 1174, 1149, 1074, 1030, 964, 825 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{11}F_3NO_2S$ $[M+H]^+$: 290.0463; found: 290.0457.



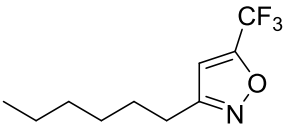
3-(((4-Fluorophenyl)thio)methyl)-5-(trifluoromethyl)isoxazole (4j)

Obtained as a yellow oily liquid in 64% yield (53 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, *J* = 5.8 Hz, 2H), 7.00 (t, *J* = 7.9 Hz, 2H), 6.65 (s, 1H), 4.06 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F), -112.91 – -113.01 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 248.7 Hz), 161.6 (s), 159.0 (q, *J* = 42.8 Hz), 133.9 (d, *J* = 8.3 Hz), 128.3 (d, *J* = 3.4 Hz), 117.7 (q, *J* = 270.4 Hz), 116.5 (d, *J* = 22.1 Hz), 105.0 (q, *J* = 2.0 Hz), 30.1 (s). IR (ATR): ν 3143, 2957, 2926, 2855, 1591, 1492, 1316, 1213, 1185, 1158, 1075, 965, 828 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8F_4NOS$ $[M+H]^+$: 278.0257; found: 278.0259.



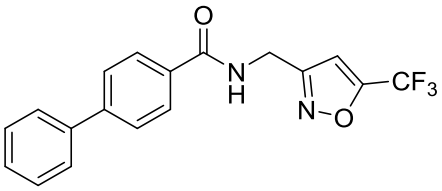
3-(((2-Methoxyphenyl)sulfonyl)methyl)-5-(trifluoromethyl)isoxazole (4k)

Obtained as a light yellow solid in 60% yield (58 mg). Mp: 104.4–104.6 ℃. R_f (dichloromethane) = 0.85. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.12 – 6.99 (m, 2H), 6.91 (s, 1H), 4.77 (s, 2H), 4.01 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3 (q, *J* = 42.9 Hz), 157.4 (s), 154.4 (s), 136.6 (s), 130.6 (s), 125.0 (s), 120.9 (s), 117.5 (q, *J* = 270.6 Hz), 112.5 (s), 106.3 (q, *J* = 2.0 Hz), 56.4 (s), 51.1 (s). IR (ATR): ν 3139, 2952, 2923, 2850, 1593, 1481, 1436, 1314, 1281, 1211, 1185, 1153, 1066, 1016, 966, 760, 520 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{11}F_3NO_4S$ $[M+H]^+$: 322.0361; found: 322.0355.



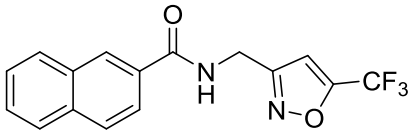
3-Hexyl-5-(trifluoromethyl)isoxazole (4l)

Obtained as a colorless oily liquid in 79% yield (52 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.89. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (s, 1H), 2.71 (t, *J* = 7.3 Hz, 2H), 1.66 (dt, *J* = 14.4, 7.1 Hz, 2H), 1.45 – 1.20 (m, 6H), 0.87 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.4 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2 (s), 158.4 (q, *J* = 42.3 Hz), 118.0 (q, *J* = 270.0 Hz), 104.9 (q, *J* = 1.9 Hz), 31.3 (s), 28.7 (s), 28.0 (s), 25.8 (s), 22.4 (s), 13.9 (s). IR (ATR): ν 2955, 2922, 2853, 1740, 1461, 1377, 1317, 1264, 1183, 1160, 1081, 965, 820, 732, 704 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_{15}F_3NO$ $[M+H]^+$: 222.1100; found: 222.1102.



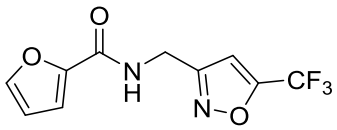
***N*-((5-(Trifluoromethyl)isoxazol-3-yl)methyl)-[1,1'-biphenyl]-4-carboxamide (4m)**

Obtained as a white solid in 34% yield (35 mg). Mp: 202.6–203.2 ℃. R_f (dichloromethane) = 0.75. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.20 (t, J = 5.1 Hz, 1H), 7.96 (d, J = 7.8 Hz, 2H), 7.76 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 7.6 Hz, 2H), 7.46 (t, J = 7.4 Hz, 2H), 7.42 – 7.32 (m, 2H), 4.61 (d, J = 5.4 Hz, 2H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -63.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.3 (s), 163.4 (s), 156.7 (q, J = 41.6 Hz), 143.1 (s), 139.1 (s), 132.4 (s), 129.0 (s), 128.1 (s), 128.0 (s), 126.9 (s), 126.6 (s), 117.9 (q, J = 270.0 Hz), 106.7 (q, J = 2.1 Hz), 34.9 (s). IR (ATR): ν 3380, 2954, 2925, 2855, 1640, 1537, 1310, 1208, 1152, 1046, 1024, 992, 825, 763, 628 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{18}H_{14}F_3N_2O_2$ $[M+H]^+$: 347.1002; found: 347.1005.



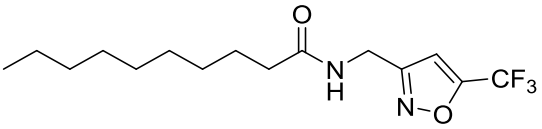
***N*-((5-(Trifluoromethyl)isoxazol-3-yl)methyl)-2-naphthamide (4n)**

Obtained as a white solid in 57% yield (55 mg). Mp: 136.6–137.8 ℃. R_f (dichloromethane) = 0.60. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (t, J = 5.1 Hz, 1H), 8.51 (s, 1H), 8.07 – 7.93 (m, 4H), 7.67 – 7.57 (m, 2H), 7.41 (s, 1H), 4.68 (d, J = 5.4 Hz, 2H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -63.0 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.7 (s), 163.3 (s), 156.7 (q, J = 41.7 Hz), 134.3 (s), 132.1 (s), 131.0 (s), 128.9 (s), 128.0 (s), 127.8 (s), 127.7 (s), 127.6 (s), 126.8 (s), 124.1 (s), 117.9 (q, J = 269.9 Hz), 106.8 (q, J = 2.0 Hz), 34.9 (s). IR (ATR): ν 3388, 3062, 2925, 1651, 1538, 1302, 1207, 1183, 1153, 1049, 1025, 1003, 965, 825, 762, 478 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{12}F_3N_2O_2$ $[M+H]^+$: 321.0851; found: 321.0855.



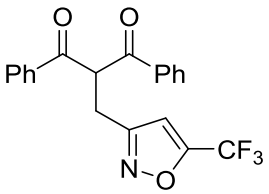
_N_-((5-(Trifluoromethyl)isoxazol-3-yl)methyl)furan-2-carboxamide (4o)

Obtained as a light brown solid in 35% yield (27 mg). Mp: 103.1–103.9 ℃. R_f (dichloromethane) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.17 (s, 1H), 6.99 (br, 1H), 6.80 (s, 1H), 6.52 (d, *J* = 1.6 Hz, 1H), 4.73 (d, *J* = 6.0 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5 (s), 159.2 (q, *J* = 42.7 Hz), 158.6 (s), 147.0 (s), 144.5 (s), 117.7 (q, *J* = 270.3 Hz), 115.3 (s), 112.3 (s), 105.3 (q, *J* = 2.0 Hz), 34.5 (s). IR (ATR): ν 3307, 3119, 2955, 2923, 1649, 1597, 1573, 1538, 1477, 1320, 1309, 1244, 1213, 1178, 1140, 1084, 966, 753 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_8F_3N_2O_3$ $[M+H]^+$: 261.0482; found: 261.0485.



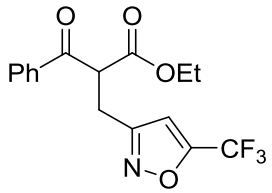
_N_-((5-(Trifluoromethyl)isoxazol-3-yl)methyl)nonanamide (4p)

Obtained as a white solid in 32% yield (31 mg). Mp: 72.3–73.6 ℃. R_f (dichloromethane) = 0.45. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (s, 1H), 6.09 (br, 1H), 4.55 (d, *J* = 5.7 Hz, 2H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.67 – 1.59 (m, 2H), 1.38 – 1.13 (m, 12H), 0.87 (t, *J* = 6.2 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (s), 161.7 (s), 159.1 (q, *J* = 42.8 Hz), 117.7 (q, *J* = 270.4 Hz), 105.2 (q, *J* = 2.0 Hz), 36.4 (s), 35.0 (s), 31.8 (s), 29.4 (s), 29.3 (s), 29.2 (s), 25.5 (s), 22.6 (s), 14.1 (s). IR (ATR): ν 3312, 3131, 2956, 2921, 2851, 1717, 1648, 1542, 1468, 1322, 1220, 1179, 1159, 968 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{15}H_{24}F_3N_2O_2$ $[M+H]^+$: 321.1784; found: 321.1790.



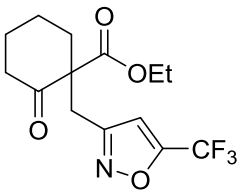
1,3-Diphenyl-2-((5-(trifluoromethyl)isoxazol-3-yl)methyl)propane-1,3-dione (4q)

Obtained as a white solid in 45% yield (50 mg). Mp: 112.3–113.3 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.6 Hz, 4H), 7.59 (t, *J* = 7.3 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 4H), 6.68 (s, 1H), 5.84 (t, *J* = 6.2 Hz, 1H), 3.51 (d, *J* = 6.1 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6 (s), 161.8 (s), 158.6 (q, *J* = 42.5 Hz), 135.2 (s), 134.0 (s), 129.0 (s), 128.6 (s), 117.7 (q, *J* = 270.3 Hz), 106.3 (q, *J* = 1.9 Hz), 54.8 (s), 25.4 (s). IR (ATR): ν 3063, 2955, 2925, 1696, 1674, 1597, 1449, 1314, 1298, 1266, 1184, 1154, 966, 728, 692 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{20}H_{15}F_3NO_3$ $[M+H]^+$: 374.0999; found: 374.0998.



Ethyl 3-oxo-3-phenyl-2-((5-(trifluoromethyl)isoxazol-3-yl)methyl)propanoate (4r)

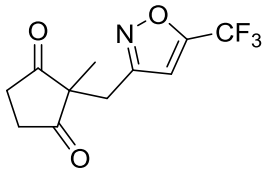
Obtained as a yellow oily liquid in 40% yield (41 mg). R_f (*n*-pentane:dichloromethane 1:1) = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 2H), 6.64 (s, 1H), 4.91 (t, *J* = 7.0 Hz, 1H), 4.14 (q, *J* = 6.8 Hz, 2H), 3.43 (d, *J* = 7.0 Hz, 2H), 1.14 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5 (s), 168.3 (s), 161.4 (s), 158.7 (q, *J* = 42.8 Hz), 135.6 (s), 134.0 (s), 128.9 (s), 128.8 (s), 117.8 (q, *J* = 270.3 Hz), 105.9 (q, *J* = 2.0 Hz), 62.0 (s), 52.1 (s), 25.1 (s), 13.8 (s). IR (ATR): ν 3138, 3065, 2927, 1738, 1688, 1449, 1313, 1235, 1186, 1155, 1081, 966, 689 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{15}F_3NO_4$ $[M+H]^+$: 342.0953; found: 342.0948.



Ethyl

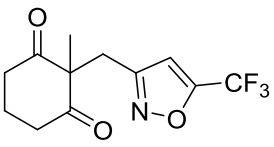
2-oxo-1-((5-(trifluoromethyl)isoxazol-3-yl)methyl)cyclohexane-1-carboxylate (4s)

Obtained as a yellow oily liquid in 54% yield (52 mg). R_f (dichloromethane) = 0.90. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 4.21 – 4.10 (m, 2H), 3.14 (dd, *J* = 54.2, 14.3 Hz, 2H), 2.63 – 2.42 (m, 2H), 2.05 (dd, *J* = 10.9, 3.7 Hz, 1H), 1.85 – 1.46 (m, 5H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.9 (s), 170.6 (s), 160.5 (s), 158.2 (q, *J* = 42.4 Hz), 117.9 (q, *J* = 270.0 Hz), 107.2 (q, *J* = 2.0 Hz), 61.9 (s), 60.9 (s), 40.9 (s), 36.5 (s), 30.8 (s), 27.3 (s), 22.4 (s), 13.8 (s). IR (ATR): ν 2929, 2869, 2109, 1714, 1451, 1314, 1189, 1150, 1091, 1021, 965, 908, 841, 733 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{14}H_{17}F_3NO_4$ $[M+H]^+$: 320.1104; found: 320.1105.



2-Methyl-2-((5-(trifluoromethyl)isoxazol-3-yl)methyl)cyclopentane-1,3-dione (4t)

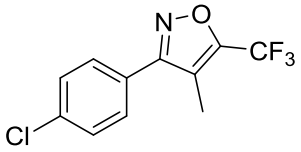
Obtained as a yellow solid in 32% yield (25 mg). Mp: 89.2–90.4 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (s, 1H), 3.13 (s, 2H), 2.92 (s, 4H), 1.25 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.2 (s), 207.0 (s), 160.0 (s), 159.1 (q, *J* = 41.4 Hz), 117.6 (q, *J* = 272.7 Hz), 105.1 (q, *J* = 2.0 Hz), 54.3 (s), 34.7 (s), 30.9 (s), 30.0 (s), 22.0 (s). IR (ATR): ν 2924, 1726, 1493, 1454, 1332, 1297, 1276, 1182, 1154, 1073, 967, 828 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_{11}F_3NO_3$ $[M+H]^+$: 262.0686; found: 262.0693.



2-Methyl-2-((5-(trifluoromethyl)isoxazol-3-yl)methyl)cyclohexane-1,3-dione (4u)

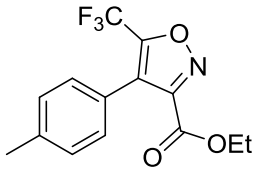
Obtained as a white solid in 70% yield (58 mg). Mp: 72.9–74.3 ℃. R_f (*n*-pentane:dichloromethane 2:1) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (s, 1H),

3.26 (s, 2H), 2.76 – 2.68 (m, 4H), 2.16 – 2.04 (m, 2H), 1.40 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.5 (s), 160.8 (s), 158.3 (q, *J* = 42.4 Hz), 117.8 (q, *J* = 270.2 Hz), 105.6 (q, *J* = 2.0 Hz), 62.3 (s), 37.6 (s), 30.3 (s), 25.3 (s), 17.1 (s). IR (ATR): ν 3135, 2960, 2924, 1729, 1699, 1459, 1331, 1288, 1200, 1181, 1151, 1076, 1023, 966 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{13}F_3NO_3$ $[M+H]^+$: 276.0848; found: 276.0842.



3-(4-Chlorophenyl)-4-methyl-5-(trifluoromethyl)isoxazole (5a)

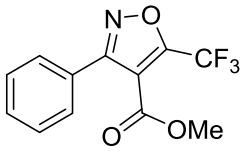
Obtained as a white solid in 56% yield (44 mg). Mp: 47.2–48.3 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.8 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4 (q, *J* = 43.8 Hz), 147.2 (s), 135.1 (s), 133.0 (s), 129.3 (s), 127.1 (s), 125.9 (s), 116.5 (q, *J* = 270.4 Hz), 13.2 (s). IR (ATR): ν 3054, 2927, 2853, 1581, 1492, 1409, 1376, 1264, 1203, 1153, 1095, 1011, 973, 831, 736, 704 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_8ClF_3NO$ $[M+H]^+$: 262.0247; found: 262.0249.



Ethyl 3-(*p*-tolyl)-5-(trifluoromethyl)isoxazole-4-carboxylate (5b)

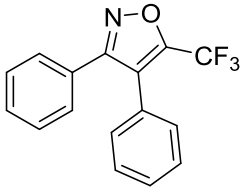
Obtained as a colorless oily liquid in 99% yield (89 mg). Mp: 53.2–54.4 ℃. R_f (*n*-pentane:dichloromethane 4:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 2H), 4.43 (q, *J* = 6.5 Hz, 2H), 2.40 (s, 3H), 1.39 (t, *J* = 6.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.8 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (s), 157.6 (s), 148.1 (q, *J* = 45.0 Hz), 142.0 (s), 129.2 (s), 128.7 (s), 126.9 (s), 122.5 (s), 116.1 (q, *J* = 271.3 Hz), 61.8 (s), 21.4 (s), 14.1 (s). IR (ATR): ν

2984, 2926, 1726, 1601, 1507, 1376, 1344, 1216, 1190, 1157, 1141, 1081, 1030, 823, 788 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{14}H_{13}F_3NO_3$ $[M+H]^+$: 300.0848; found: 300.0849.



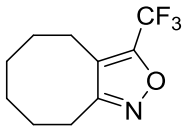
Methyl 3-phenyl-5-(trifluoromethyl)isoxazole-4-carboxylate (5c)

Obtained as a white solid in 60% yield (49 mg). Mp: 68.3–69.4 ℃. R_f (*n*-pentane:dichloromethane 2:1) = 0.48. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 7.95 (m, 2H), 7.63 – 7.41 (m, 3H), 3.97 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.8 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3 (s), 157.5 (q, *J* = 0.7 Hz), 148.5 (q, *J* = 45.1 Hz), 131.6 (s), 128.7 (s), 128.6 (s), 127.1 (s), 125.2 (s), 116.1 (q, *J* = 271.4 Hz), 52.7 (s). IR (ATR): ν 3063, 2956, 2926, 2853, 1731, 1603, 1567, 1494, 1376, 1355, 1223, 1139, 1087, 1037, 1012, 767, 735, 690 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_9F_3NO_3$ $[M+H]^+$: 272.0529; found: 272.0528.



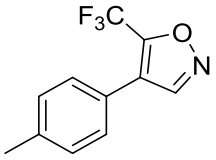
3,4-Diphenyl-5-(trifluoromethyl)isoxazole (5d)

Obtained as a white solid in 44% yield (38 mg). Mp: 70.7–71.9 ℃. R_f (*n*-pentane:dichloromethane 8:1) = 0.73. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.64 (m, 4H), 7.45 – 7.39 (m, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.7 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.1 (q, *J* = 44.0 Hz), 148.0 (s), 136.0 (s), 130.7 (s), 129.8 (s), 128.9 (s), 128.8 (s), 128.7 (s), 128.0 (s), 127.3 (s), 127.1 (s), 116.7 (q, *J* = 270.7 Hz). IR (ATR): ν 2984, 2941, 2909, 1737, 1447, 1372, 1234, 1098, 1044, 938, 847, 634, 608, 461 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{11}F_3NO$ $[M+H]^+$: 290.0787; found: 290.0788.



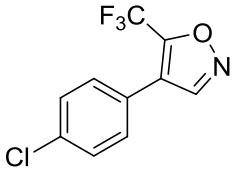
3-(Trifluoromethyl)-4,5,6,7,8,9-hexahydrocycloocta[*c*]isoxazole (5e)

Obtained as a colorless oily liquid in 38% yield (25 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (t, *J* = 6.3 Hz, 2H), 2.65 (t, *J* = 6.1 Hz, 2H), 1.83 – 1.63 (m, 4H), 1.56 – 1.37 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.9 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2 (s), 152.5 (q, *J* = 40.4 Hz), 119.7 (q, *J* = 1.8 Hz), 118.9 (q, *J* = 270.4 Hz), 29.4 (s), 29.0 (s), 25.2 (s), 25.1 (s), 23.7 (s), 19.5 (s). IR (ATR): ν 2927, 2855, 1695, 1414, 1329, 1310, 1202, 1152, 1108, 1080, 1024 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_{13}F_3NO$ $[M+H]^+$: 220.0949; found: 220.0951.



4-(*p*-Tolyl)-5-(trifluoromethyl)isoxazole (6a)

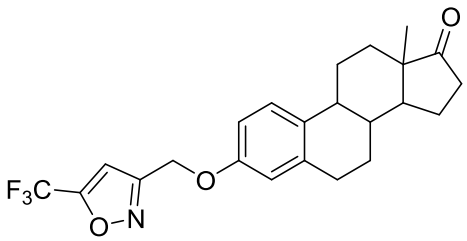
Obtained as a brown oily liquid in 85% yield (58 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.38 (s, 1H), 7.26 (d, *J* = 7.6 Hz, 2H), 2.40 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.7 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2 (s), 149.4 (q, *J* = 43.9 Hz), 140.2 (s), 129.8 (s), 124.8 (s), 123.5 (s), 121.7 (s), 116.6 (q, *J* = 270.2 Hz), 21.3 (s). IR (ATR): ν 2959, 2927, 2165, 2148, 1501, 1376, 1205, 1148, 1103, 964, 815 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_9F_3NO$ $[M+H]^+$: 228.0636; found: 228.0637.



4-(4-Chlorophenyl)-5-(trifluoromethyl)isoxazole (6b)

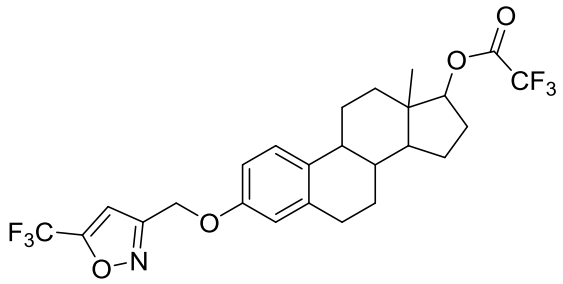
Obtained as a white solid in 90% yield (67 mg). Mp: 53.5–54.4 ℃. R_f

(*n*-pentane:dichloromethane 4:1) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.43 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.7 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9 (s), 149.9 (q, *J* = 44.2 Hz), 135.9 (s), 129.4 (s), 126.1 (s), 124.7 (s), 122.7 (s), 116.4 (q, *J* = 270.4 Hz). IR (ATR): ν 2924, 2853, 1590, 1482, 1410, 1374, 1282, 1208, 1139, 1092, 963, 937, 822, 734, 504 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_6ClF_3NO$ $[M+H]^+$: 248.0090; found: 248.0091.



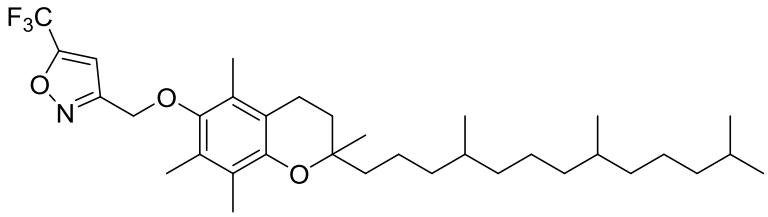
13-Methyl-3-((5-(trifluoromethyl)isoxazol-3-yl)methoxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (7a)

Obtained as a light yellow solid in 79% yield (99 mg). Mp: 123.1–123.7 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 1H), 6.85 (s, 1H), 6.77 (d, *J* = 8.6 Hz, 1H), 6.71 (s, 1H), 5.17 (s, 2H), 2.90 (d, *J* = 5.3 Hz, 2H), 2.51 (dd, *J* = 18.8, 8.6 Hz, 1H), 2.39 (d, *J* = 9.7 Hz, 1H), 2.27 (d, *J* = 9.2 Hz, 1H), 2.20 – 1.92 (m, 4H), 1.63 – 1.37 (m, 6H), 0.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4 (s), 159.1 (q, *J* = 42.7 Hz), 155.6 (s), 138.2 (s), 133.5 (s), 126.6 (s), 117.7 (q, *J* = 270.5 Hz), 114.7 (s), 112.2 (s), 104.9 (q, *J* = 2.0 Hz), 61.1 (s), 50.4 (s), 48.0 (s), 44.0 (s), 38.2 (s), 35.8 (s), 31.5 (s), 29.6 (s), 26.4 (s), 25.9 (s), 21.6 (s), 13.8 (s). IR (ATR): ν 3129, 2925, 2859, 1737, 1609, 1450, 1457, 1315, 1211, 1183, 1154, 1080, 1058, 965, 914, 821 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{23}H_{25}F_3NO_3$ $[M+H]^+$: 420.1781; found: 420.1787.



13-Methyl-3-((5-(trifluoromethyl)isoxazol-3-yl)methoxy)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl 2,2,2-trifluoroacetate (7b)

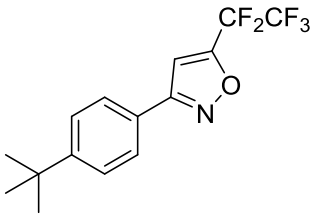
Obtained as a yellow solid in 68% yield (105 mg). Mp: 105.0–106.5 ℃. R_f (*n*-pentane:dichloromethane 1:1) = 0.88. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 1H), 6.86 (s, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.72 (s, 1H), 5.18 (s, 2H), 4.91 (t, *J* = 8.3 Hz, 1H), 2.88 (d, *J* = 6.8 Hz, 2H), 2.38 – 2.18 (m, 3H), 1.99 – 1.64 (m, 4H), 1.57 – 1.26 (m, 6H), 0.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F), -75.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4 (s), 159.1 (q, *J* = 42.7 Hz), 157.5 (q, *J* = 41.8 Hz), 155.6 (s), 138.2 (s), 133.5 (s), 126.6 (s), 117.8 (q, *J* = 270.4 Hz), 114.7 (s), 114.6 (q, *J* = 285.9 Hz), 112.1 (s), 104.9 (q, *J* = 2.0 Hz), 86.7 (s), 61.1 (s), 49.6 (s), 43.6 (s), 43.4 (s), 38.4 (s), 36.6 (s), 29.6 (s), 27.1 (s), 27.0 (s), 26.0 (s), 23.1 (s), 11.8 (s). IR (ATR): ν 2925, 2870, 1781, 1610, 1500, 1460, 1382, 1352, 1316, 1215, 1159, 1078, 966 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{25}H_{26}F_6NO_4$ $[M+H]^+$: 518.1766; found: 518.1771.



3-(((2,5,7,8-Tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl)oxy)methyl)-5-(trifluoromethyl)isoxazole (7c)

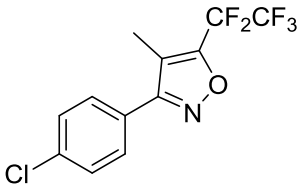
Obtained as a light oily liquid in 95% yield (165 mg). R_f (*n*-pentane:dichloromethane 4:1) = 0.75. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (s, 1H), 4.86 (s, 2H), 2.63 (t, *J* = 6.2 Hz, 2H), 2.23 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 1.92 – 1.76 (m, 2H), 1.71 – 1.05 (m, 24H), 1.00 – 0.76 (m, 12H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.1 (s, 3F). ^{13}C NMR

(101 MHz, $CDCl_3$) δ 161.5 (s), 159.0 (q, *J* = 42.6 Hz), 148.5 (s), 147.5 (s), 127.5 (s), 125.6 (s), 123.3 (s), 117.9 (q, *J* = 270.3 Hz), 117.8 (s), 105.0 (q, *J* = 1.9 Hz), 75.0 (s), 65.2 (s), 40.1 (s), 40.0 (s), 39.4 (s), 37.8 (s), 37.7 (s), 37.6 (s), 37.5 (s), 37.47 (s), 37.41 (s), 37.4 (s), 37.34 (s), 37.3 (s), 32.8 (s), 32.78 (s), 32.7 (s), 32.67 (s), 31.2 (s), 31.17 (s), 28.0 (s), 24.8 (s), 24.4 (s), 23.8 (s), 22.7 (s), 22.6 (s), 21.0 (s), 20.6 (s), 19.7 (s), 19.66 (s), 19.64 (s), 19.60 (s), 19.58 (s), 12.8 (s), 11.9 (s), 11.8 (s). IR (ATR): ν 2925, 2868, 1459, 1413, 1378, 1361, 1315, 1255, 1210, 1182, 1158, 1090, 1010, 966, 909, 827 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{34}H_{53}F_3NO_3$ $[M+H]^+$: 580.3978; found: 580.3990.



3-(4-(*tert*-Butyl)phenyl)-5-(perfluoroethyl)isoxazole (8a)

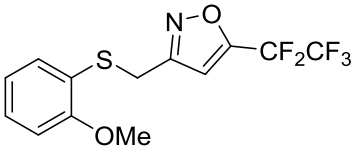
Obtained as a white solid in 55% yield (53 mg). Mp: 41.5-42.1 ℃. R_f (*n*-pentane) = 0.58. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.07 (s, 1H), 1.38 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.1 (s, 3F), -115.1 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7 (s), 158.4 (t, *J* = 31.5 Hz), 154.5 (s), 126.7 (s), 126.2 (s), 124.4 (s), 118.1 (qt, *J* = 286.2, 36.1 Hz), 108.3 (tq, *J* = 254.7, 41.0 Hz), 105.2 (s), 34.9 (s), 31.1 (s). IR (ATR): ν 2964, 2219, 2032, 1985, 1972, 1460, 1212, 1184, 1101, 922, 823, 735 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{15}H_{15}F_5NO$ $[M+H]^+$: 320.1068; found: 320.1066.



3-(4-Chlorophenyl)-4-methyl-5-(perfluoroethyl)isoxazole (8b)

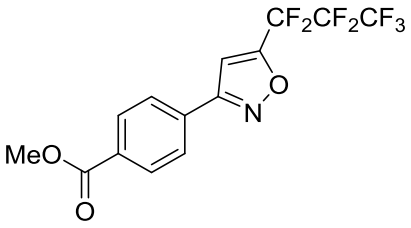
Obtained as a yellow oily liquid in 42% yield (39 mg). R_f (*n*-pentane:dichloromethane 5:1) = 0.73. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 8.3

Hz, 2H), 2.48 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.4 (s, 3F), -115.3 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0 (s), 147.9 (t, *J* = 30.9 Hz), 135.2 (s), 133.6 (s), 129.3 (s), 127.2 (s), 125.8 (s), 118.0 (qt, *J* = 286.4, 35.8 Hz), 107.1 (tq, *J* = 255.2, 40.8 Hz), 13.2 (s). IR (ATR): ν 2960, 2928, 2858, 2106, 1492, 1332, 1220, 1148, 1096, 1038 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_8ClF_5NO$ $[M+H]^+$: 312.0209; found: 312.0212.



3-(((2-Methoxyphenyl)thio)methyl)-5-(perfluoroethyl)isoxazole (8c)

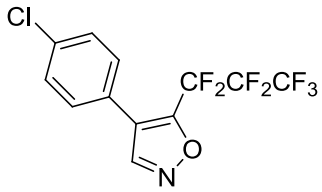
Obtained as a yellow oily liquid in 83% yield (84 mg). R_f (*n*-pentane:dichloromethane 5:1) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 2H), 6.92 – 6.85 (m, 2H), 6.69 (s, 1H), 4.12 (s, 2H), 3.88 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.2 (s, 3F), -115.1 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (s), 158.6 (s), 157.8 (t, *J* = 31.5 Hz), 133.0 (s), 129.6 (s), 121.0 (s), 120.7 (s), 117.9 (qt, *J* = 286.3, 36.1 Hz), 110.9 (s), 108.1 (d, *J* = 254.7, 41.0 Hz), 107.1 (s), 55.6 (s), 27.5 (s). IR (ATR): ν 2927, 2841, 1581, 1477, 1337, 1217, 1189, 1159, 1026, 923, 752 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{13}H_{11}F_5NO_2S$ $[M+H]^+$: 340.0425; found: 340.0423.



Methyl 4-(5-(perfluoropropyl)isoxazol-3-yl)benzoate (9a)

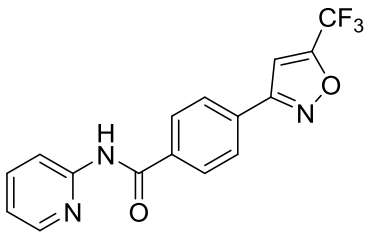
Obtained as a white solid in 96% yield (107 mg). Mp: 93.3-94.5 ℃. R_f (*n*-pentane:dichloromethane 5:1) = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.1 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.12 (s, 1H), 3.92 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.6 (t, *J* = 9.1 Hz, 3F), -112.9 (q, *J* = 9.1 Hz, 2F), -127.0 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1 (s), 161.9 (s), 159.0 (t, *J* = 32.1 Hz), 132.3 (s), 131.2 (s),

130.3 (s), 126.9 (s), 117.5 (qt, J = 287.3, 33.3 Hz), 110.2 (tt, J = 256.7, 32.6 Hz), 108.1 (tq, J = 266.7, 38.6 Hz), 105.5 (s), 52.2 (s). IR (ATR): ν 2957, 2924, 2853, 2111, 1718, 1351, 1279, 1227, 1188, 1153, 1120, 991, 873, 776 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{14}H_9F_7NO_3$ $[M+H]^+$: 372.0465; found: 372.0464.



4-(4-Chlorophenyl)-5-(perfluoropropyl)isoxazole (9b)

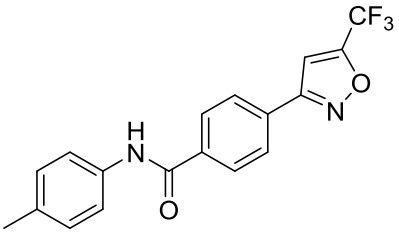
Obtained as a yellow oily liquid in 69% yield (68 mg). R_f (*n*-pentane:dichloromethane 5:1) = 0.80. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 2H), 7.50 (s, 1H), 7.45 (d, J = 7.9 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.5 (t, J = 8.8 Hz, 3F), -113.5 (q, J = 8.4 Hz, 2F), -126.7 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8 (s), 149.5 (t, J = 31.5 Hz), 136.1 (s), 129.5 (s), 126.2 (s), 124.7 (s), 123.3 (s), 117.5 (qt, J = 287.5, 33.4 Hz), 108.9 (tt, J = 258.0, 32.1 Hz), 108.3 (tq, J = 267.4, 38.6 Hz). IR (ATR): ν 2927, 2113, 1613, 1484, 1410, 1368, 1216, 1192, 1124, 873, 826 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_6ClF_7NO$ $[M+H]^+$: 348.0021; found: 348.0024.



***N*-(Pyridin-2-yl)-4-(5-(trifluoromethyl)isoxazol-3-yl)benzamide (11a)**

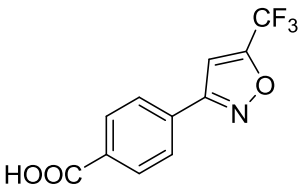
Obtained as a white solid in 77% yield (51 mg). Mp: 207.0–208.5 ℃. R_f (*n*-pentane: ethyl acetate 1:1) = 0.55. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 1H), 8.40 (d, J = 4.0 Hz, 1H), 8.27 – 8.15 (m, 4H), 8.10 (d, J = 8.1 Hz, 2H), 7.86 (t, J = 7.8 Hz, 1H), 7.19 (t, J = 5.7 Hz, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -63.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.2 (s), 162.2 (s), 157.6 (q, J = 41.8 Hz), 152.0 (s), 147.9 (s), 138.1 (s), 136.3 (s), 129.6 (s), 128.9 (s), 126.9 (s), 120.0 (s), 117.8 (q, J = 270.0

Hz), 114.8 (s), 105.8 (q, J = 1.8 Hz). IR (ATR): ν 3365, 3151, 2954, 2923, 2853, 1656, 1537, 1518, 1438, 1322, 1241, 1174, 1140, 969, 778, 737 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{11}F_3N_3O_2$ $[M+H]^+$: 334.0798; found: 334.0799.



N-(p-Tolyl)-4-(5-(trifluoromethyl)isoxazol-3-yl)benzamide (11b)

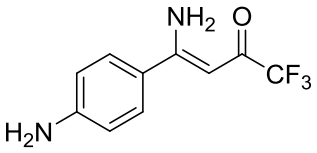
Obtained as a white solid in 82% yield (57 mg). Mp: 239.3–241.0 ℃. R_f (n-pentane: ethyl acetate 1:1) = 0.73. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.19 (s, 1H), 8.12 (s, 4H), 7.67 (d, J = 7.5 Hz, 2H), 7.17 (d, J = 7.7 Hz, 2H), 2.29 (s, 3H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -63.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.4 (s), 162.2 (s), 157.6 (q, J = 41.7 Hz), 137.2 (s), 136.4 (s), 132.9 (s), 129.3 (s), 129.0 (s), 128.5 (s), 127.0 (s), 120.4 (s), 117.8 (q, J = 269.9 Hz), 105.9 (q, J = 1.9 Hz), 20.5 (s). IR (ATR): ν 3054, 2931, 2860, 1668, 1503, 1437, 1407, 1386, 1266, 1091, 730, 701, 659 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{18}H_{14}F_3N_2O_2$ $[M+H]^+$: 347.1002; found: 347.1005.



4-(5-(Trifluoromethyl)isoxazol-3-yl)benzoic acid (12)

Obtained as a white solid in 55% yield (28 mg). Mp: 189.1–190.1 ℃. R_f (n-pentane: ethyl acetate 1:2) = 0.29. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.26 (br, 1H), 8.16 (s, 1H), 8.09 (s, 4H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -63.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.6 (s), 162.2 (s), 157.7 (q, J = 41.8 Hz), 133.0 (s), 130.5 (s), 130.1 (s), 127.2 (s), 117.8 (q, J = 270.0 Hz), 105.9 (q, J = 2.0 Hz). IR (ATR): ν 3485, 3054, 2930, 2860, 1660, 1501, 1438, 1407, 1386, 1256, 1091, 1063, 731, 658 cm^{-1}.

HRMS (ESI) m/z: calcd. for $C_{11}H_7F_3NO_3$ $[M-H]^-$: 256.0216; found: 256.0226.



4-Amino-4-(4-aminophenyl)-1,1,1-trifluorobut-3-en-2-one (13)

Obtained as a yellow solid in 62% yield (71 mg). Mp: 109.8-110.5 ℃. R_f (*n*-pentane: ethyl acetate 4:3) = 0.50. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.83 (s, 1H), 7.55 (d, J = 7.9 Hz, 2H), 6.62 (d, J = 7.9 Hz, 2H), 6.03 (s, 2H), 5.68 (s, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -75.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.1 (q, J = 30.9 Hz), 167.5 (s), 153.2 (s), 128.7 (s), 118.9 (s), 117.9 (q, J = 290.0 Hz), 113.2 (s), 83.5 (q, J = 1.0 Hz). IR (ATR): ν 3353, 3229, 2954, 2924, 2854, 1665, 1597, 1549, 1508, 1445, 1374, 1260, 1188, 1130, 903, 837, 783, 702, 544 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_{10}F_3N_2O$ $[M+H]^+$: 231.0745; found: 231.0740.

Crystal structure analyses

The crystal samples of **3k** were prepared by slow volatilization in a $CH_2Cl_2/CDCl_3$ (3:1) solvent mixture. The suitable crystals of **3k** (CCDC 1972523) were mounted on quartz fibers and X-ray data collected on a Bruker AXS APEX diffractometer, equipped with a CCD detector at -50 ºC, using MoKα radiation (λ 0.71073 Å). The data was corrected for Lorentz and polarisation effect with the **SMART** suite of programs and for absorption effects with SADABS.[2] Structure solution and refinement were carried out with the SHELXTL suite of programs.[2] The structure was solved by direct methods to locate the heavy atoms, followed by difference maps for the light non-hydrogen atoms.

Table S1. Crystal data and structure refinement for compounds

Compound	**3k** (CCDC 1972523)
Empirical formula	C_{10} H_5 F_4 N O
Formula weight	231.15
Temperature/K	273(2)
Wavelength/Å	0.71073
Crystal system	Triclinic
a/Å	5.337(10)
b/Å	7.907(15)
c/Å	11.41(2)
α/°	90.42(3)
β/°	99.00(3)
γ/°	95.19(2)
Volume/$Å^3$	473.6(15)
Z	2
Density (calc.)/cm^3	1.621
Absorption coefficient /mm^{-1}	0.159
F(000)	232
Crystal size/mm	0.50 × 0.40 × 0.20
Theta range for data collection / °	1.81~24.99
Reflections collected	2443
Independent reflections	1582 [R(int) = 0.0179]
Data/restraints/parameters	1582 / 0 / 165
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	0.0680
Final R indexes [all data]	0.1763
Largest diff. peak and hole / e $Å^{-3}$	0.292/-0.361

ORTEP diagrams

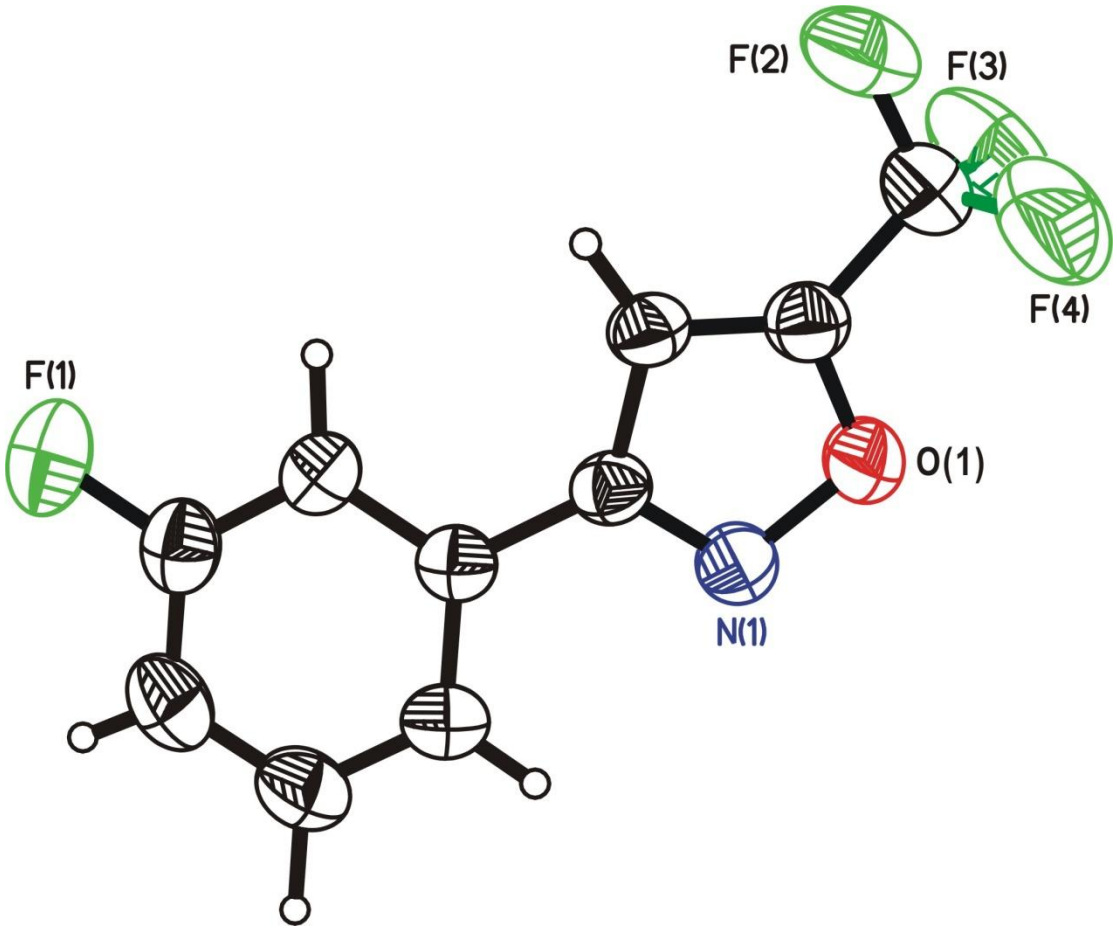


Figure S1. ORTEP diagram of compound 3k. Thermal ellipsoids are drawn at 40% probability

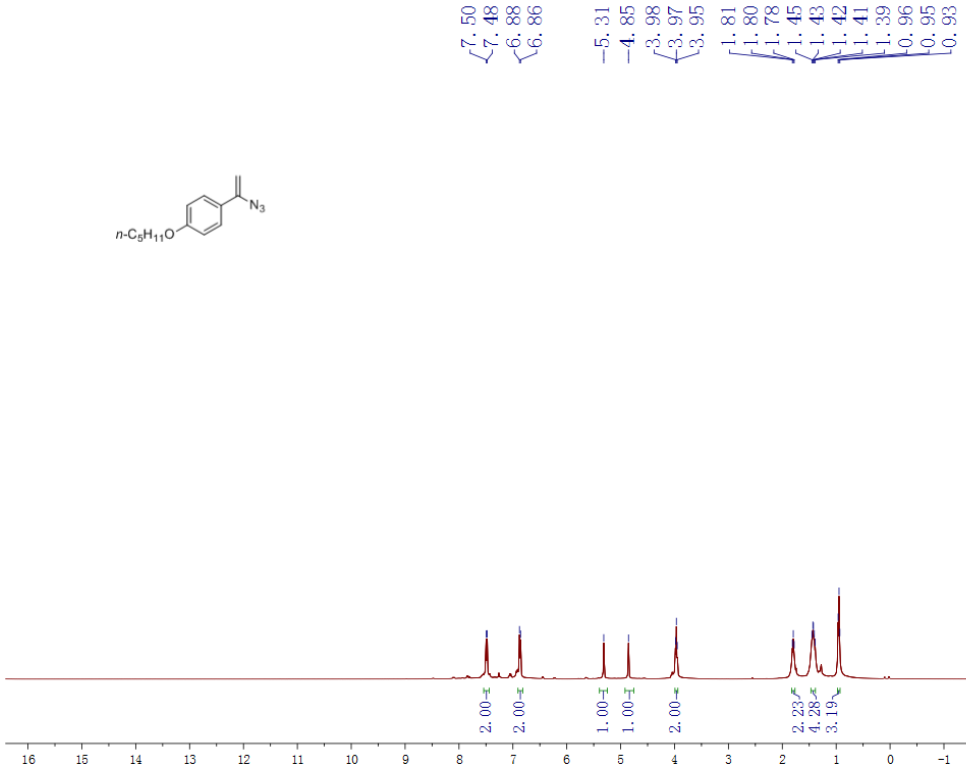
References:

(1) (a) Z. Liu, P. Liao, X. Bi, General silver-catalyzed hydroazidation of terminal alkynes by combining TMS-N_3 and H_2O: synthesis of vinyl azides, *Org. Lett.* 2014, **16**, 3668; (b) Y.-F. Wang, G. H. Lonca, S. Chiba, $PhI(OAc)_2$-mediated radical trifluoromethylation of vinyl azides with Me_3SiCF_3, *Angew. Chem. Int. Ed.* 2014, **53**, 1067; (c) V. Nair, T. G. George, A novel synthesis of α-azidocinnamates, α-azido-α,β-unsaturated ketones and β-azidostyrenes mediated by cerium(IV) ammonium nitrate, *Tetrahedron Lett.* 2000, **41**, 3199.

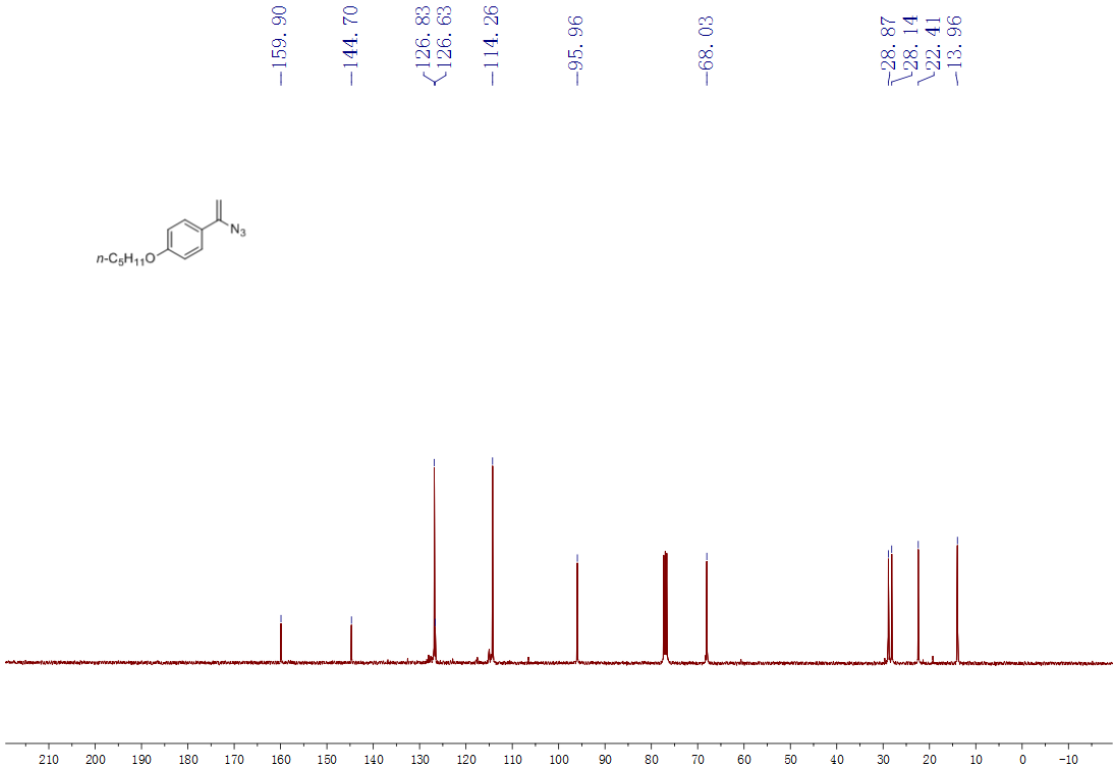
(2) SHELXTL version 5.03; Bruker Analytical X-ray Systems, Madison, WI, 1997.

Copies of ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra

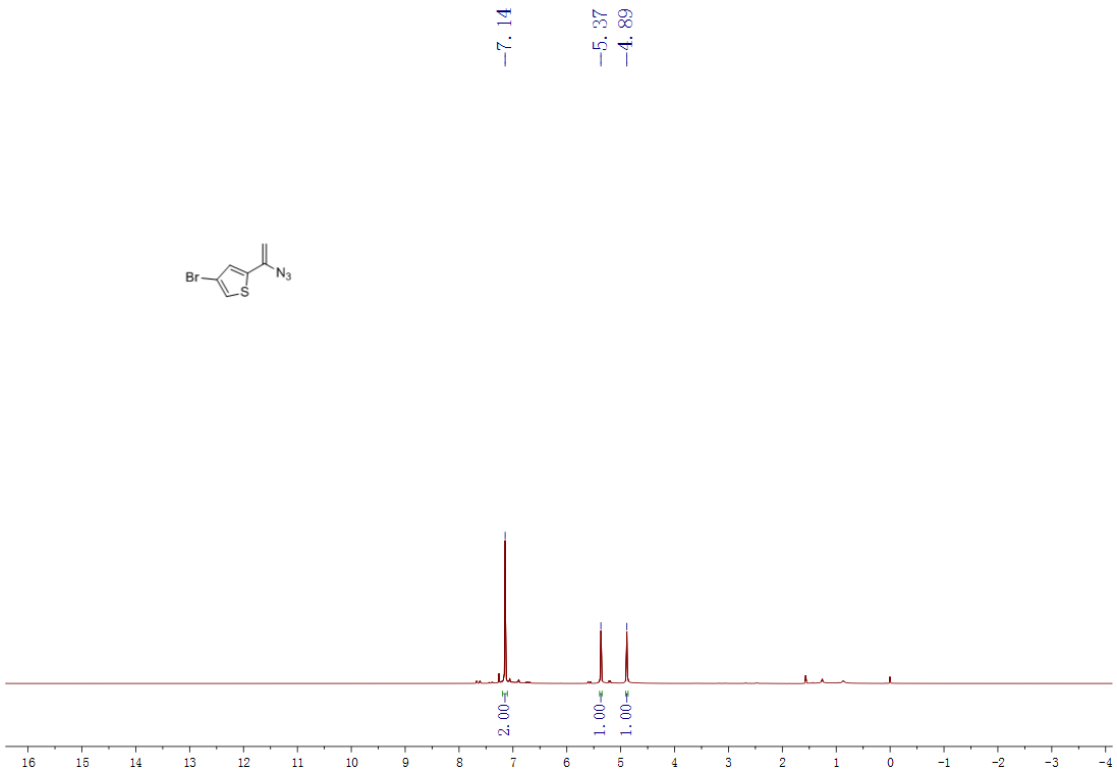
^{1}H NMR spectra of **2j** in $CDCl_3$



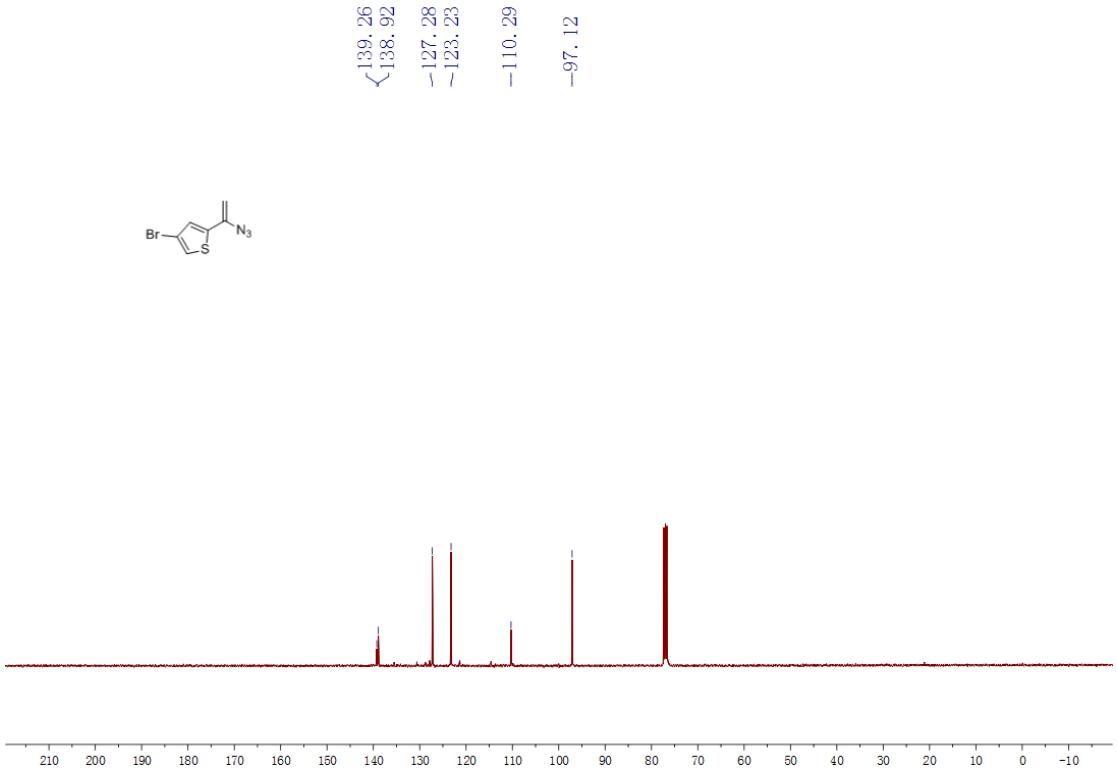
^{13}C NMR spectra of **2j** in $CDCl_3$



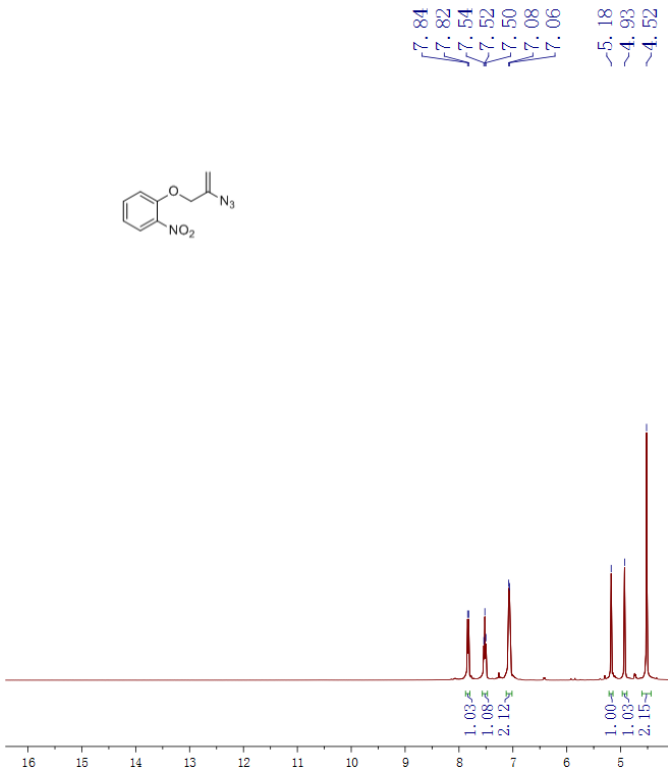
^{1}H NMR spectra of **2q** in $CDCl_3$



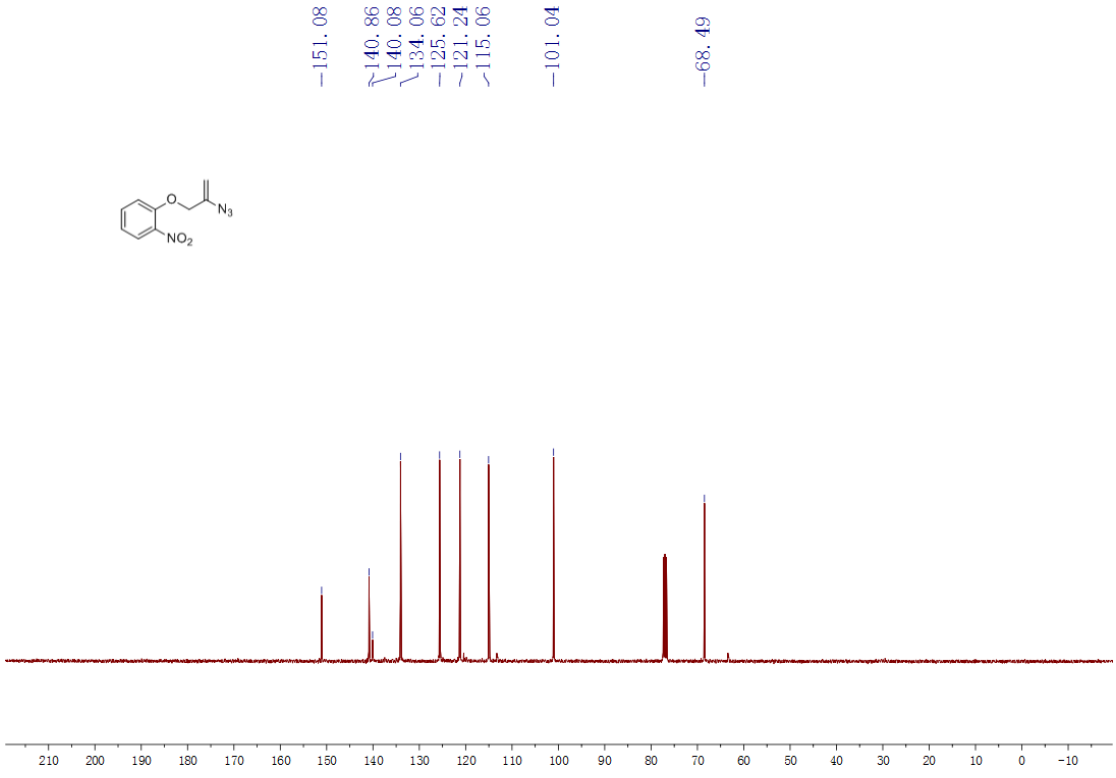
^{13}C NMR spectra of **2q** in $CDCl_3$



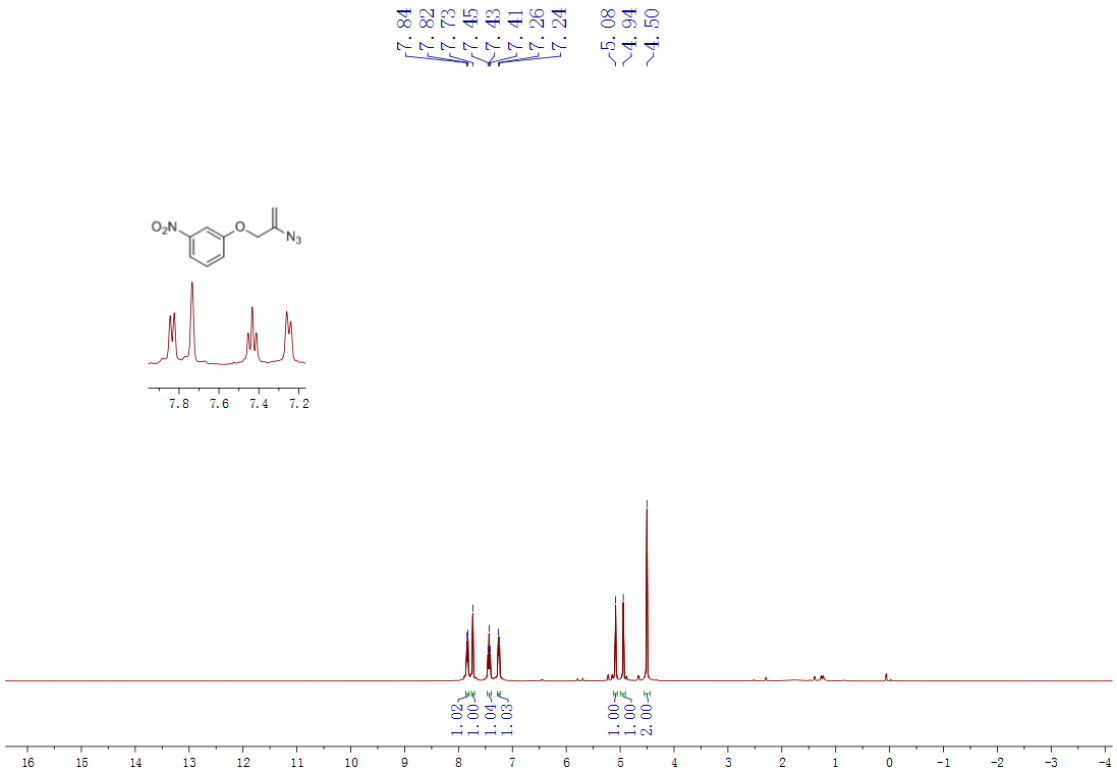
^{1}H NMR spectra of **2-4a** in $CDCl_3$



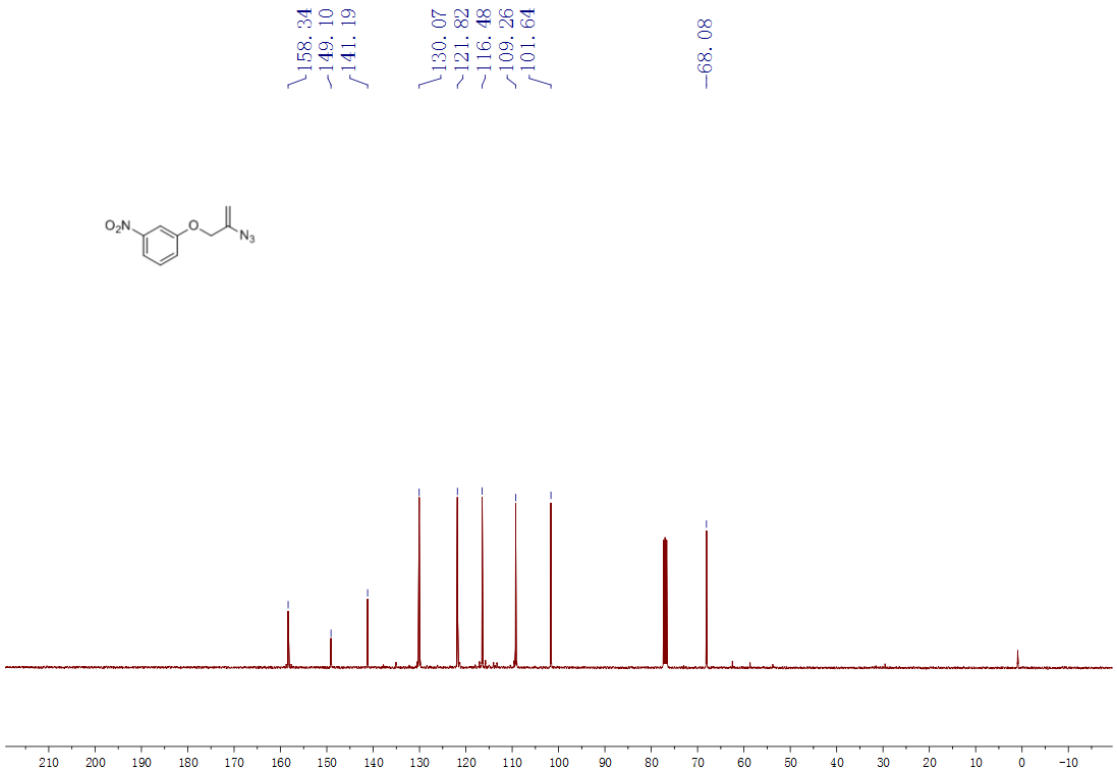
^{13}C NMR spectra of **2-4a** in $CDCl_3$



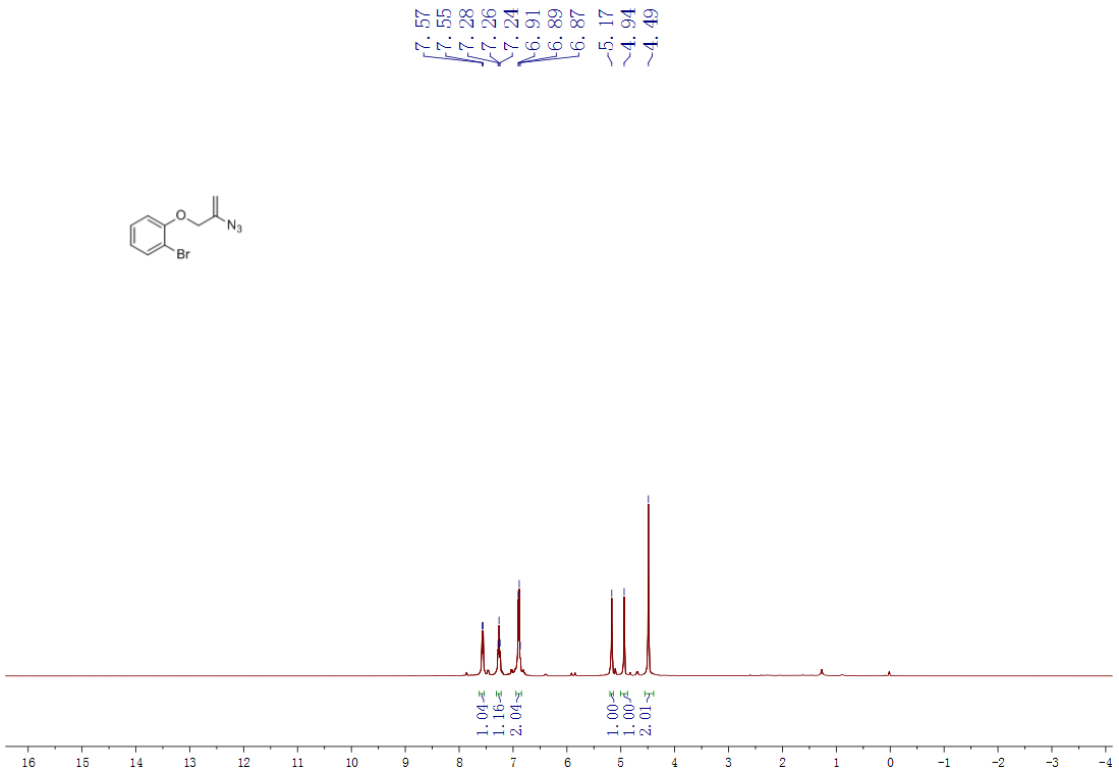
^{1}H NMR spectra of **2-4b** in $CDCl_3$



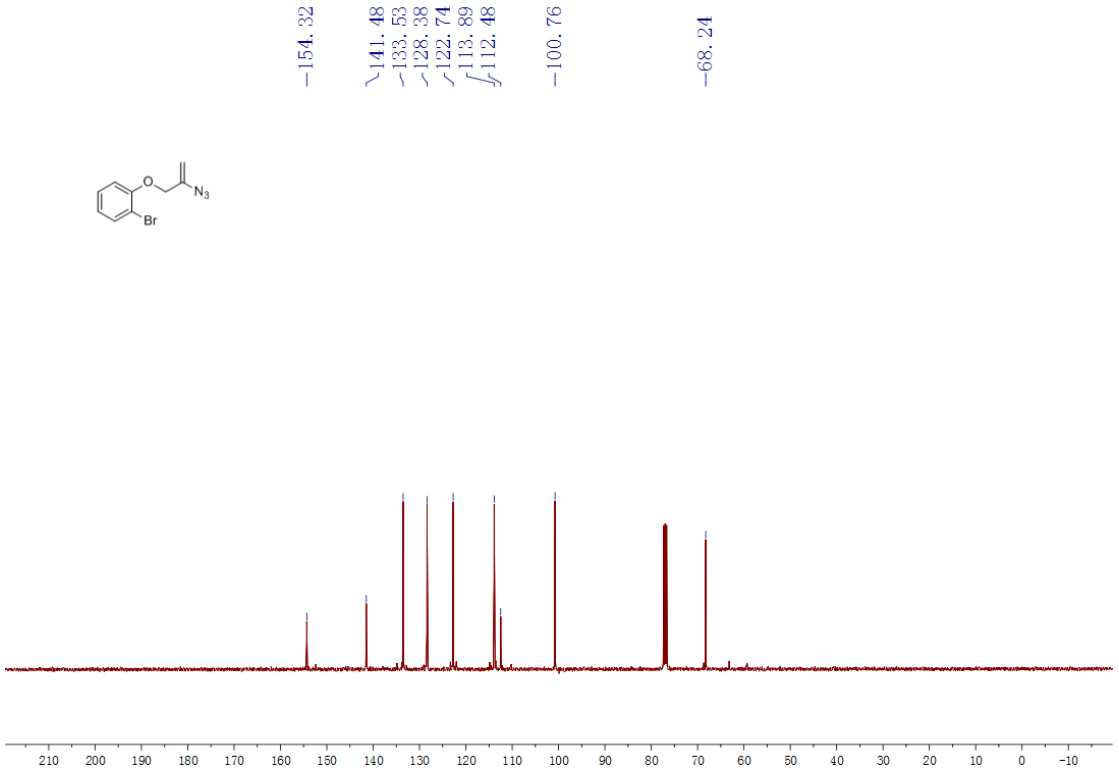
^{13}C NMR spectra of **2-4b** in $CDCl_3$



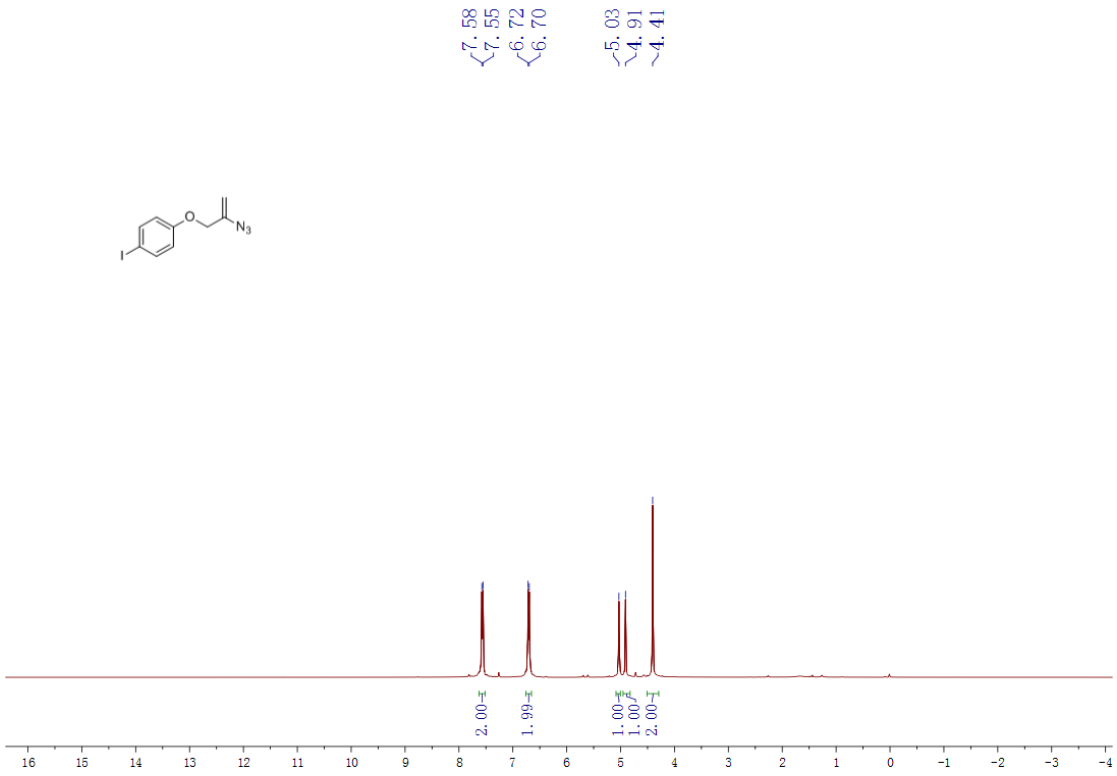
^{1}H NMR spectra of **2-4c** in $CDCl_3$



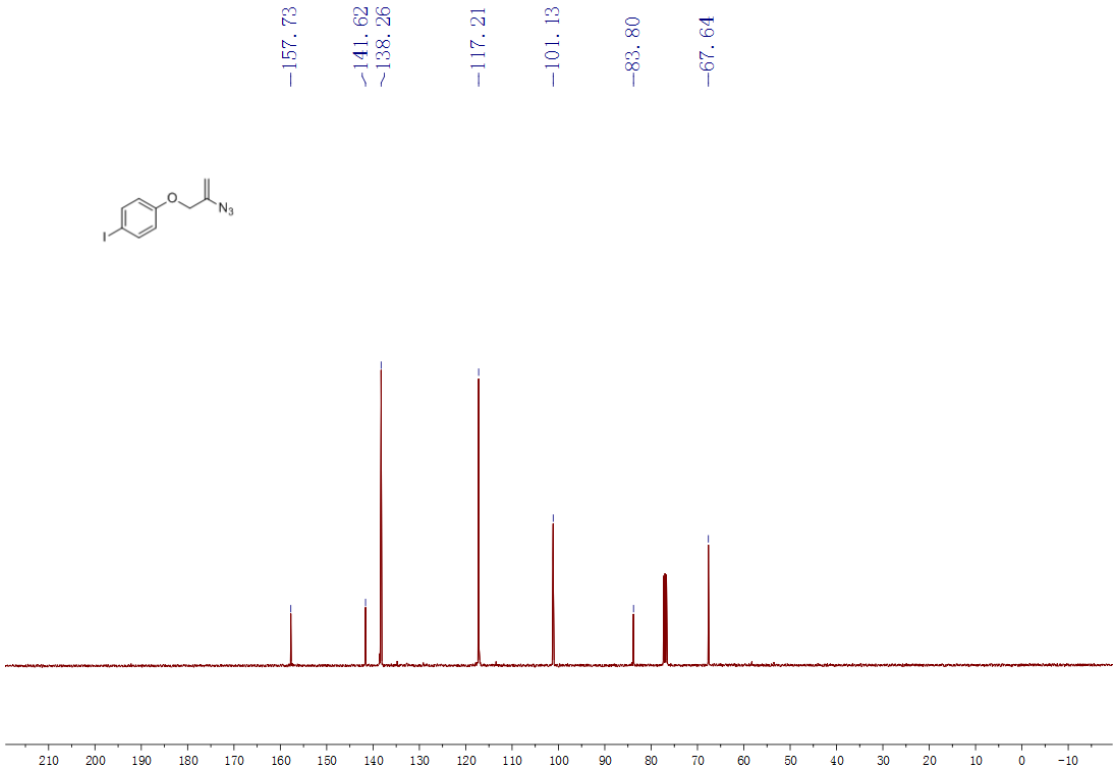
^{13}C NMR spectra of **2-4c** in $CDCl_3$



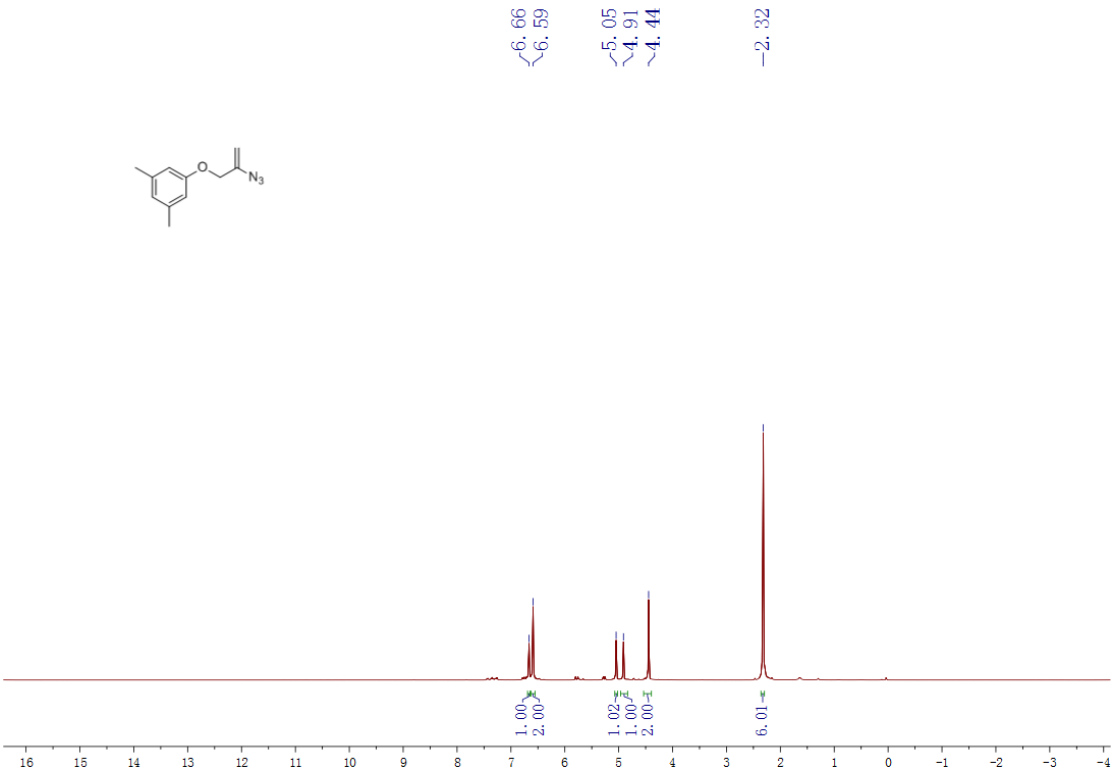
^{1}H NMR spectra of **2-4d** in $CDCl_3$



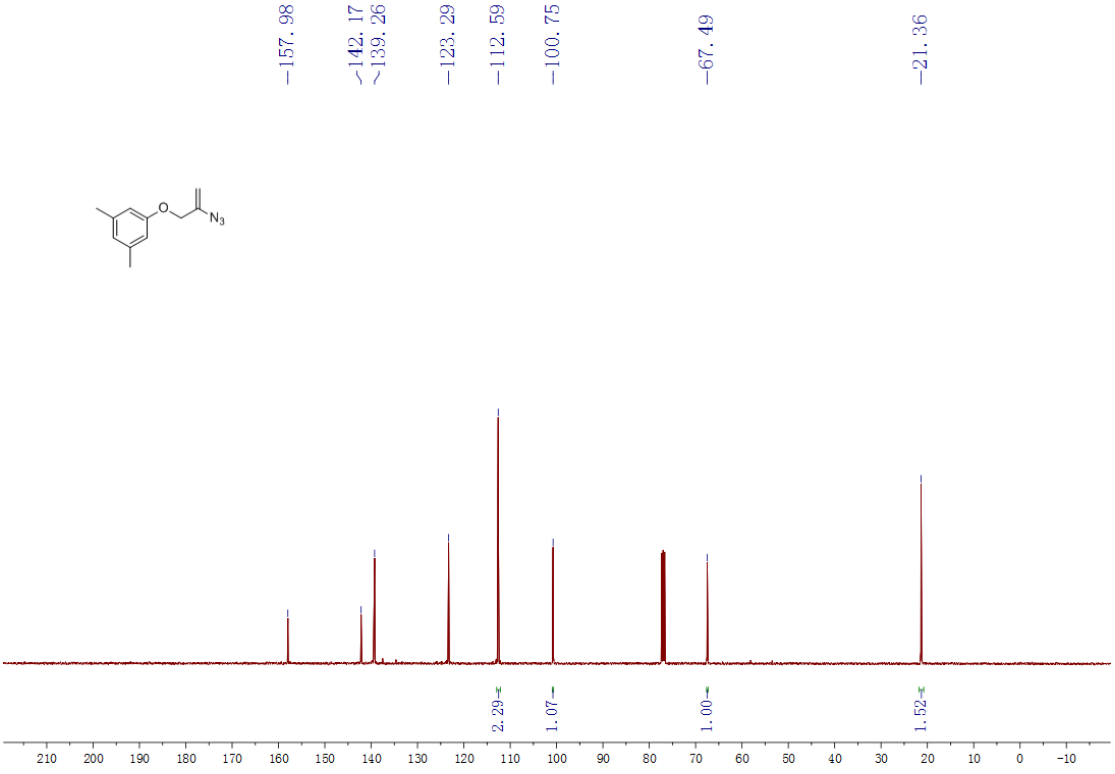
^{13}C NMR spectra of **2-4d** in $CDCl_3$



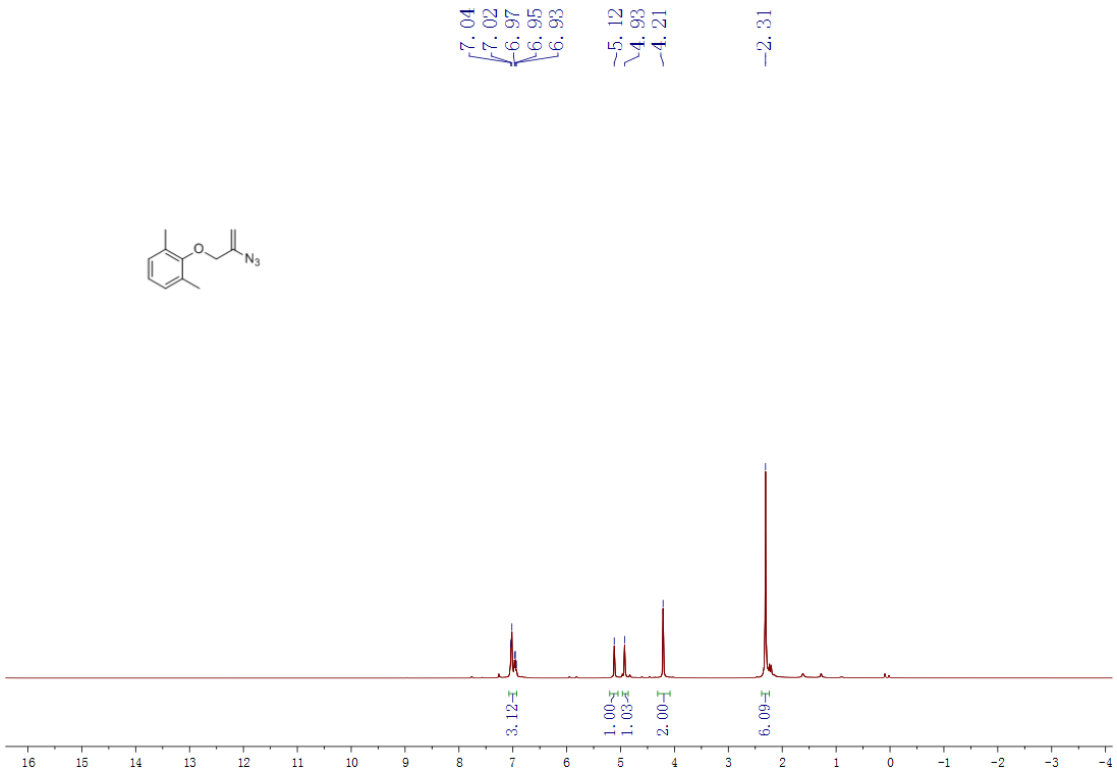
^{1}H NMR spectra of **2-4e** in $CDCl_3$



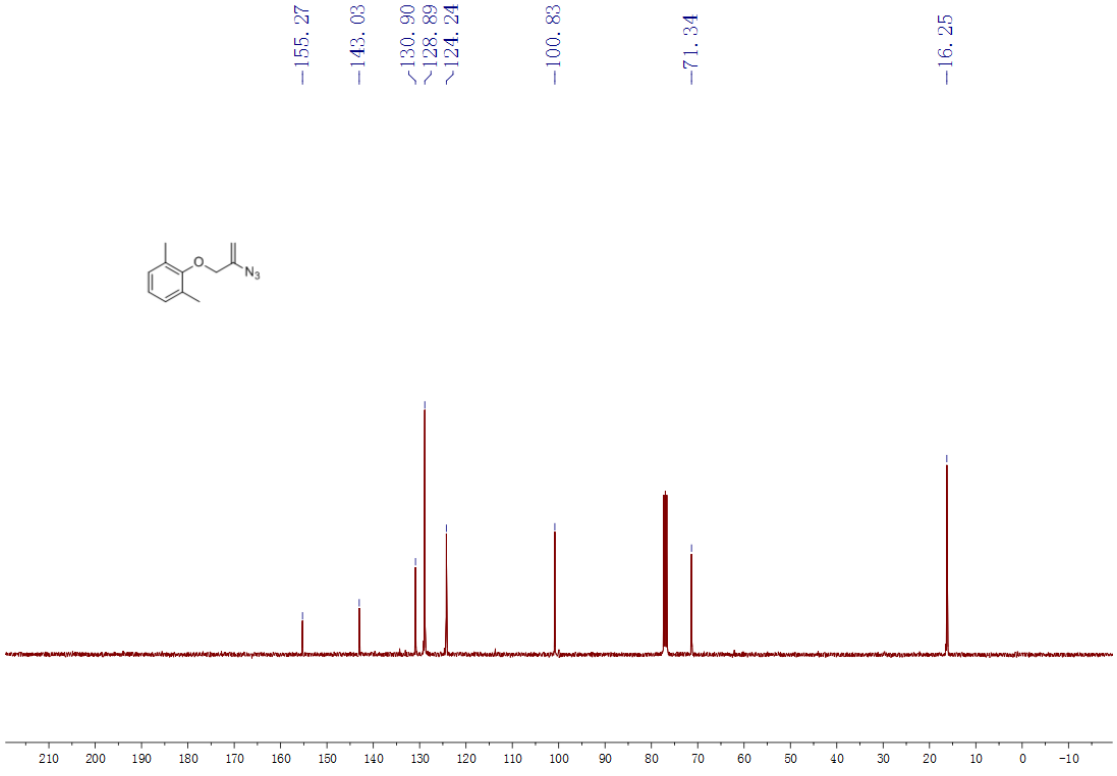
^{13}C NMR spectra of **2-4e** in $CDCl_3$



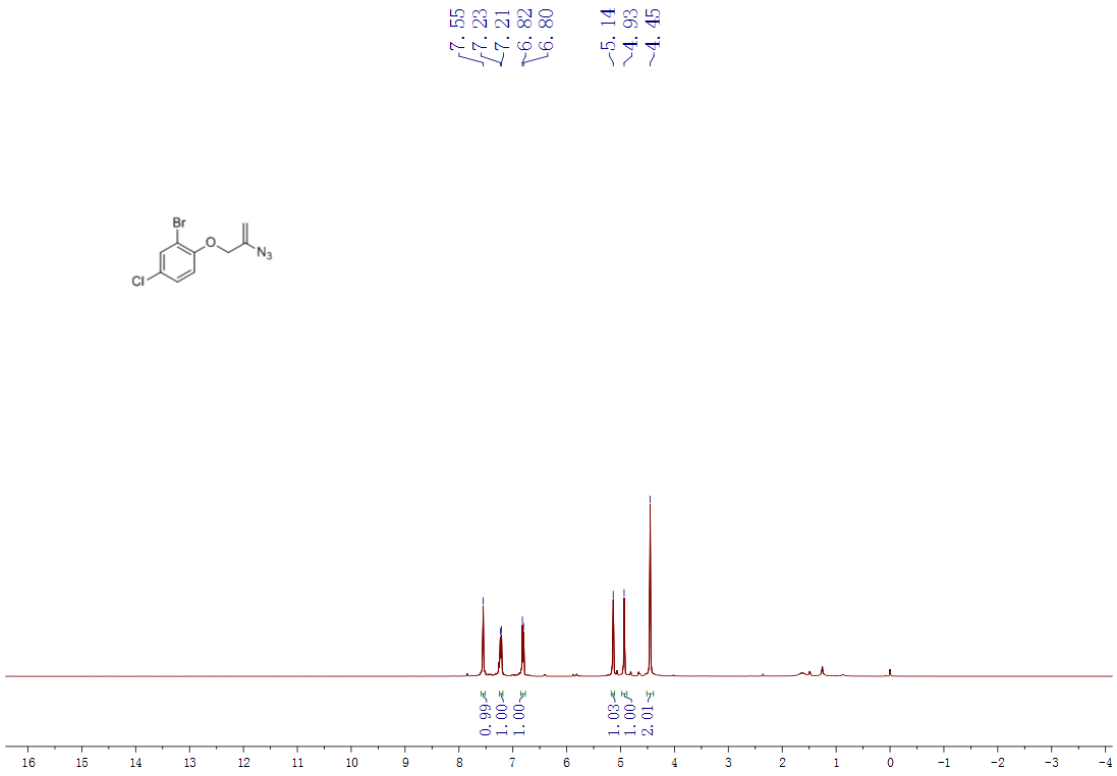
^{1}H NMR spectra of **2-4f** in $CDCl_3$



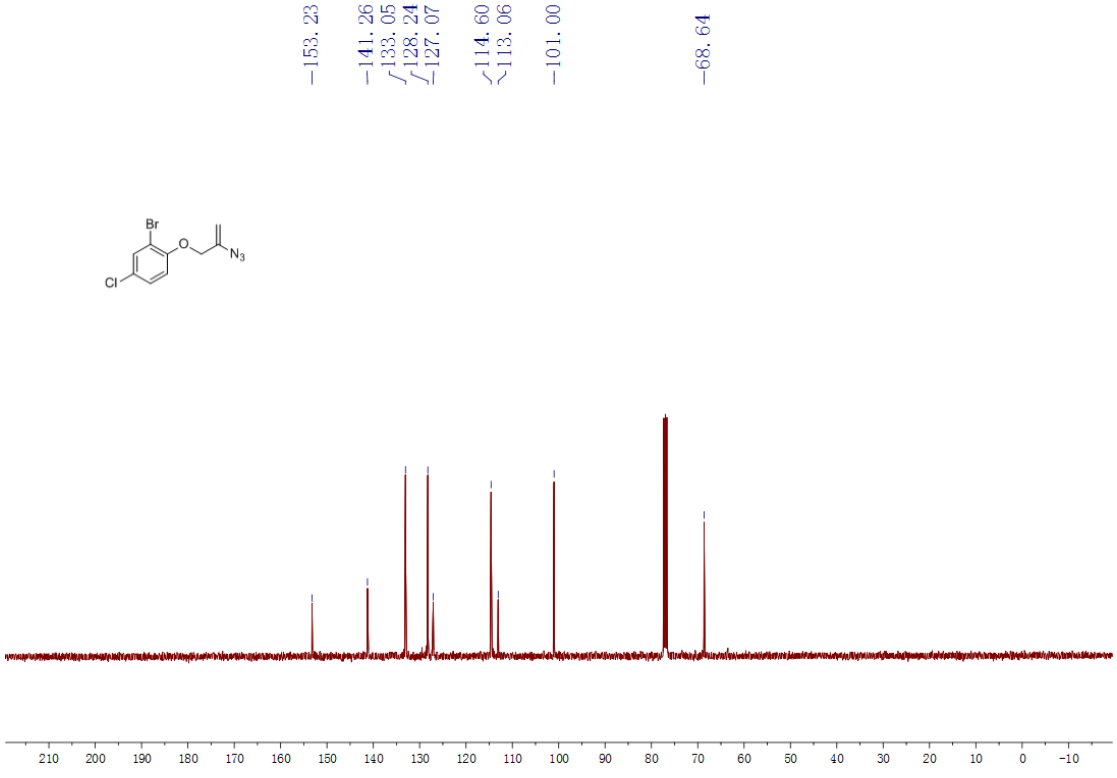
^{13}C NMR spectra of **2-4f** in $CDCl_3$



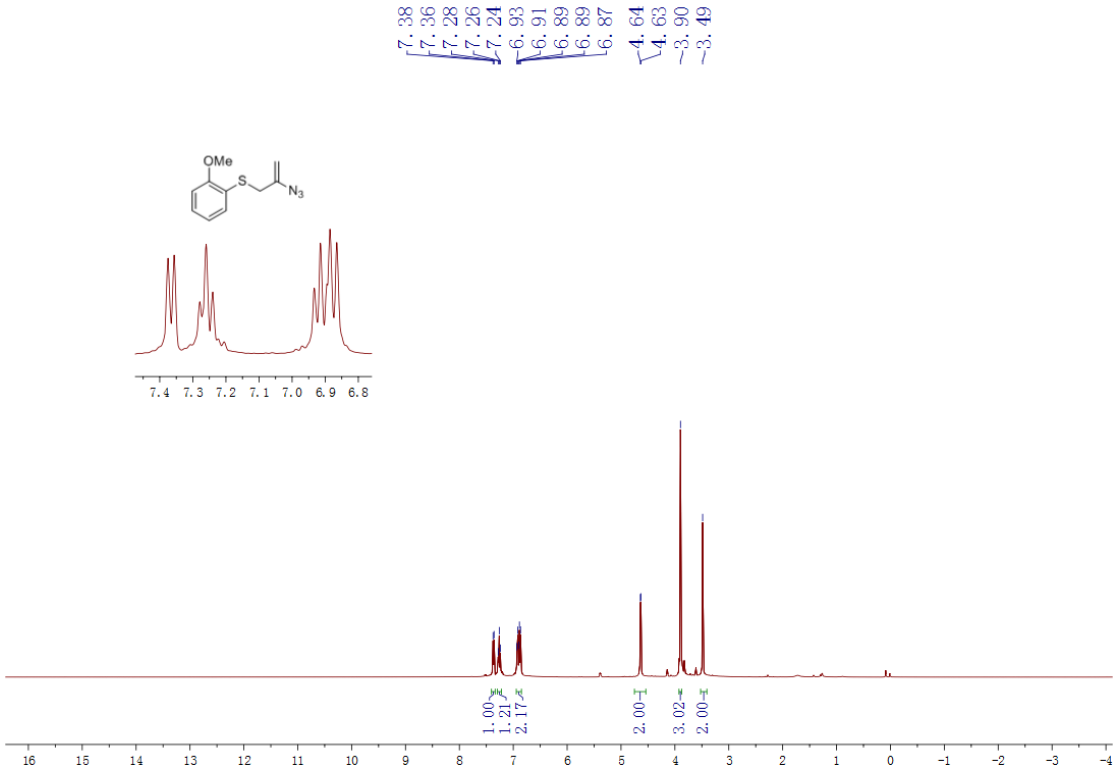
^{1}H NMR spectra of **2-4g** in $CDCl_3$



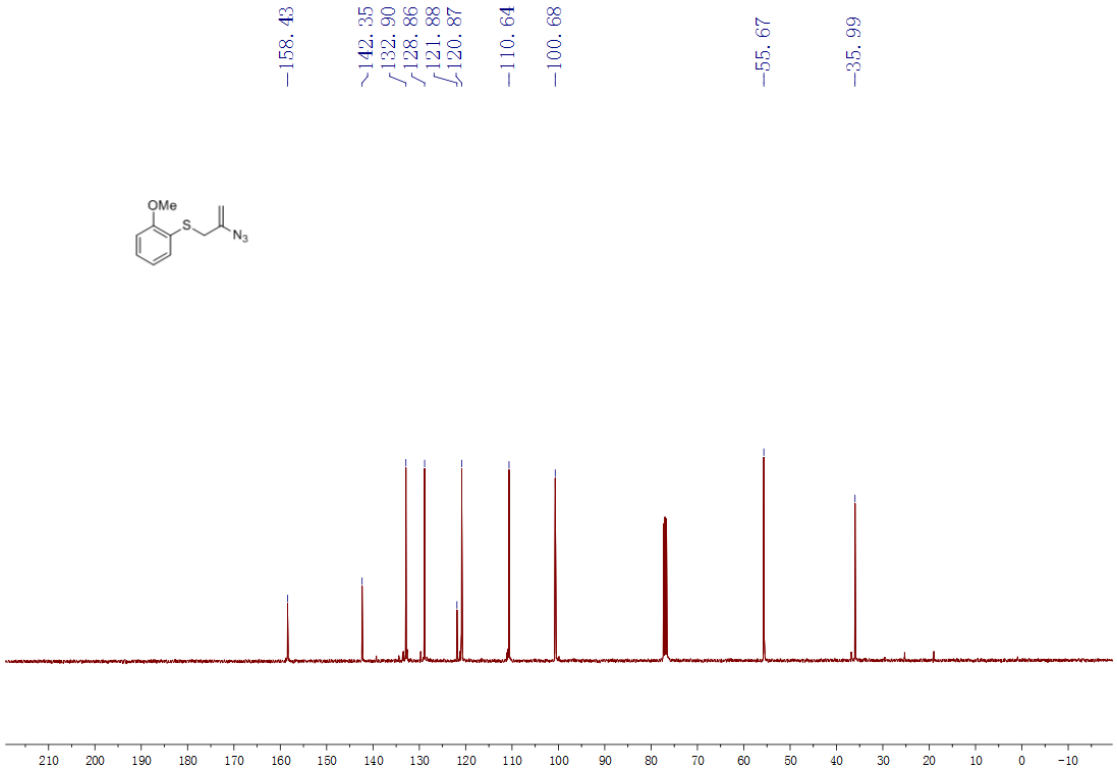
^{13}C NMR spectra of **2-4g** in $CDCl_3$



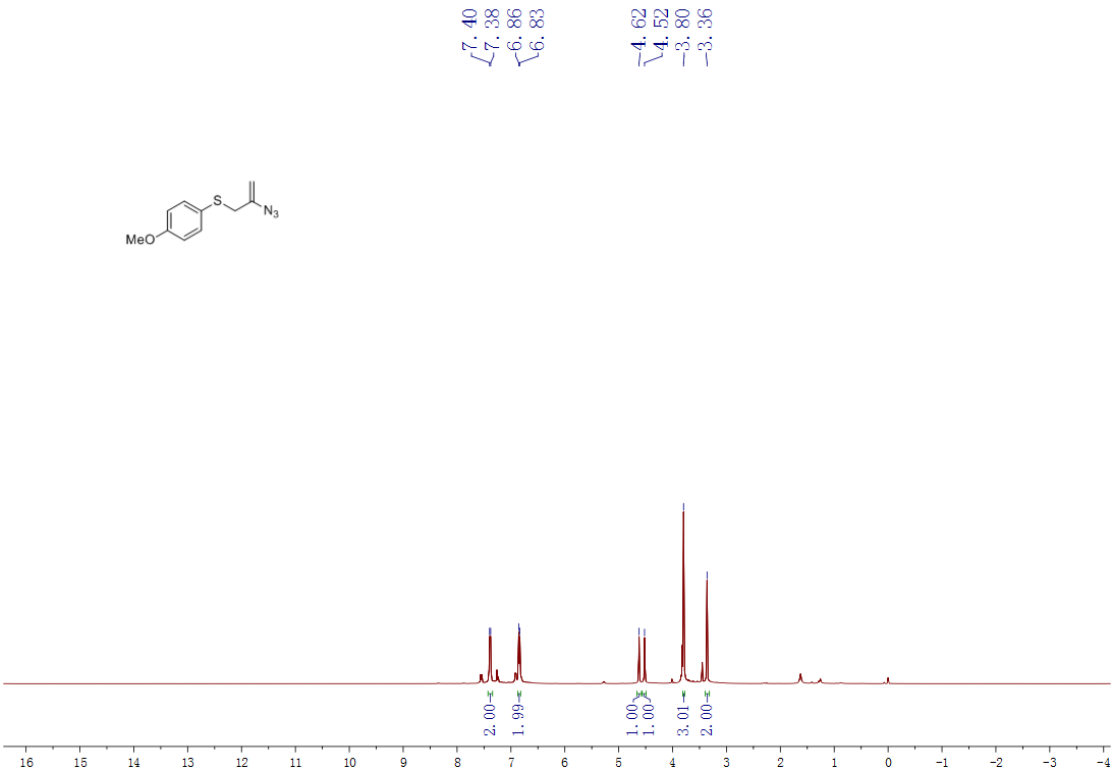
^{1}H NMR spectra of **2-4h** in $CDCl_3$



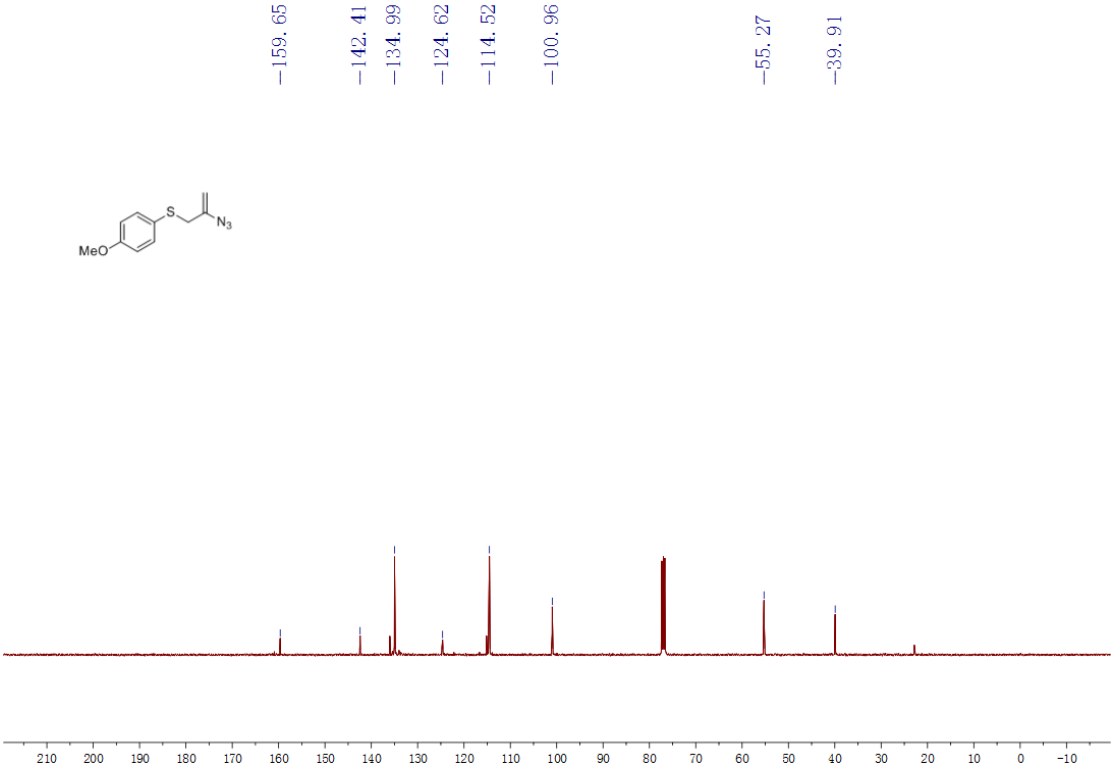
^{13}C NMR spectra of **2-4h** in $CDCl_3$



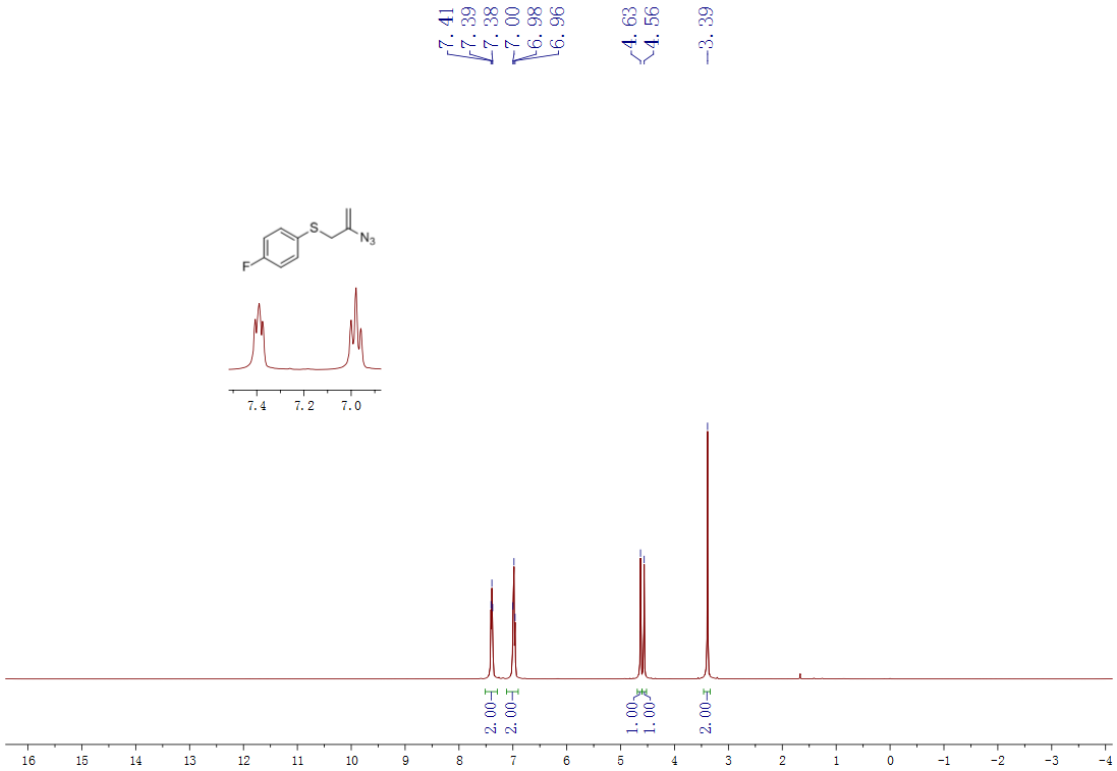
^{1}H NMR spectra of **2-4i** in $CDCl_3$



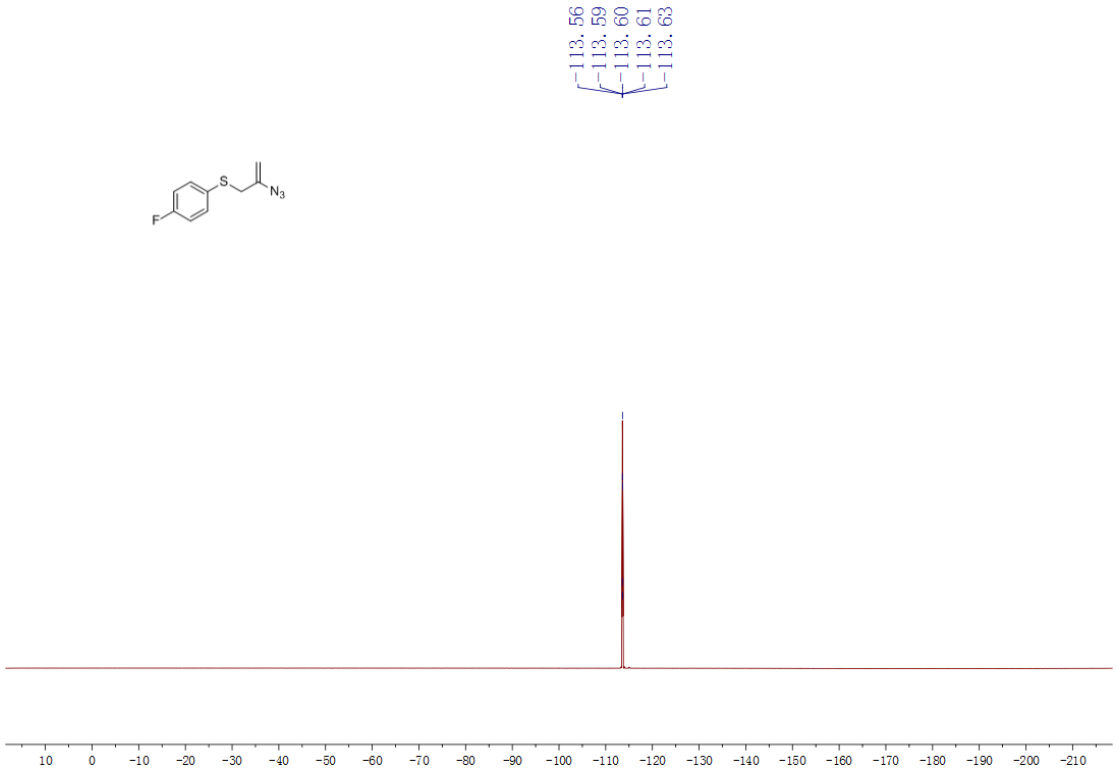
^{13}C NMR spectra of **2-4i** in $CDCl_3$



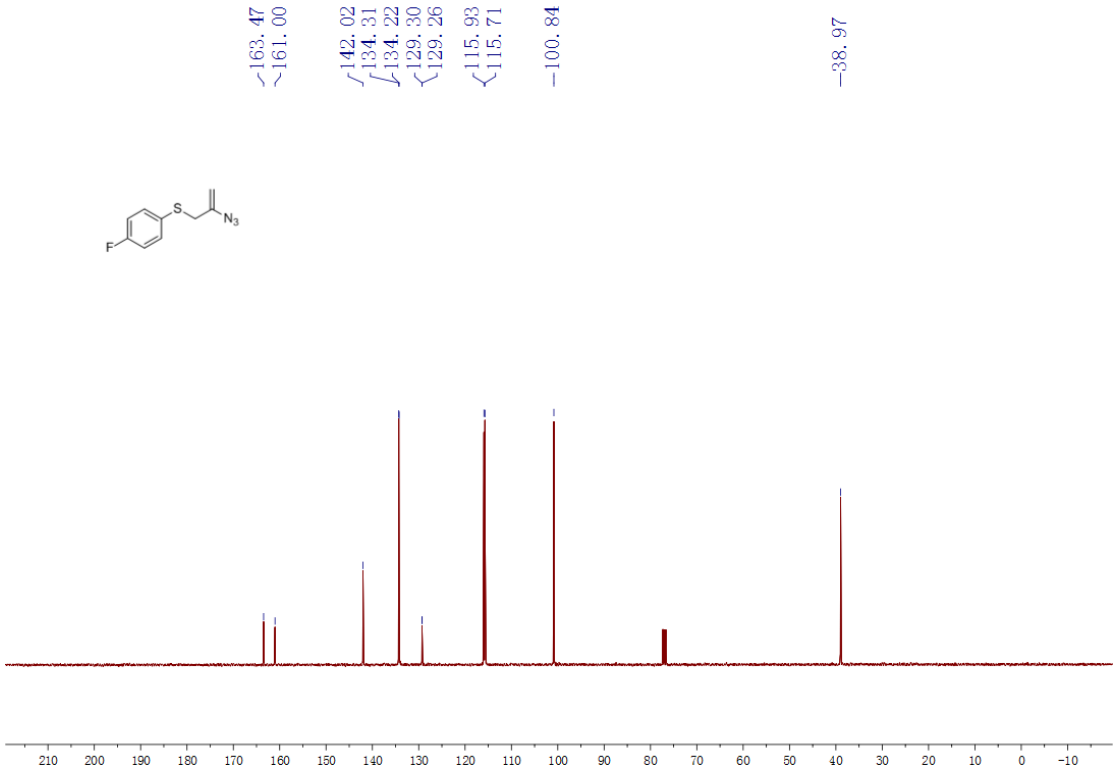
^{1}H NMR spectra of **2-4j** in $CDCl_3$



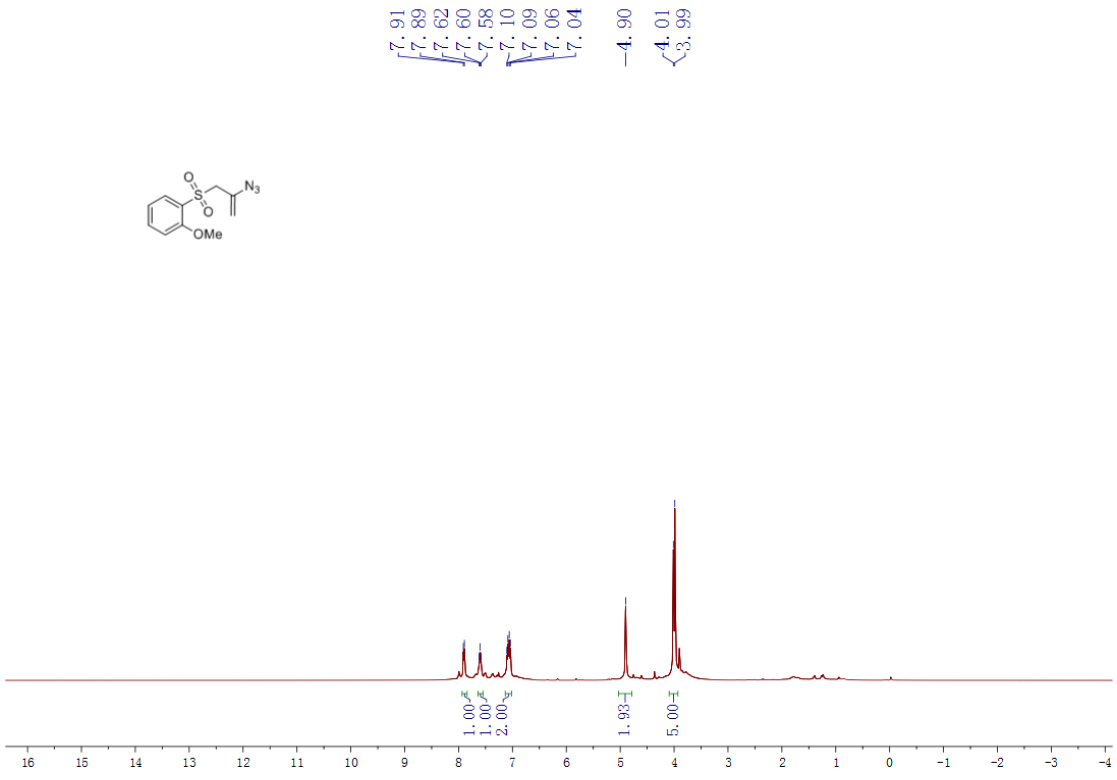
^{19}F NMR spectra of **2-4j** in $CDCl_3$



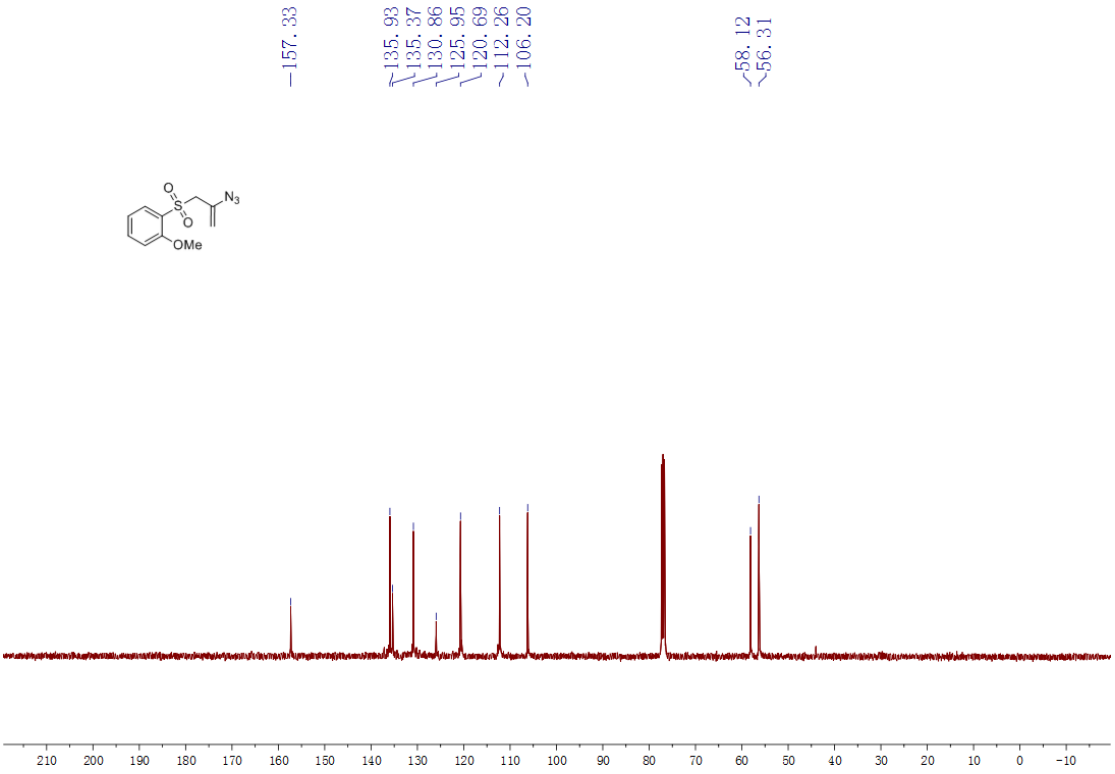
^{13}C NMR spectra of **2-4j** in $CDCl_3$



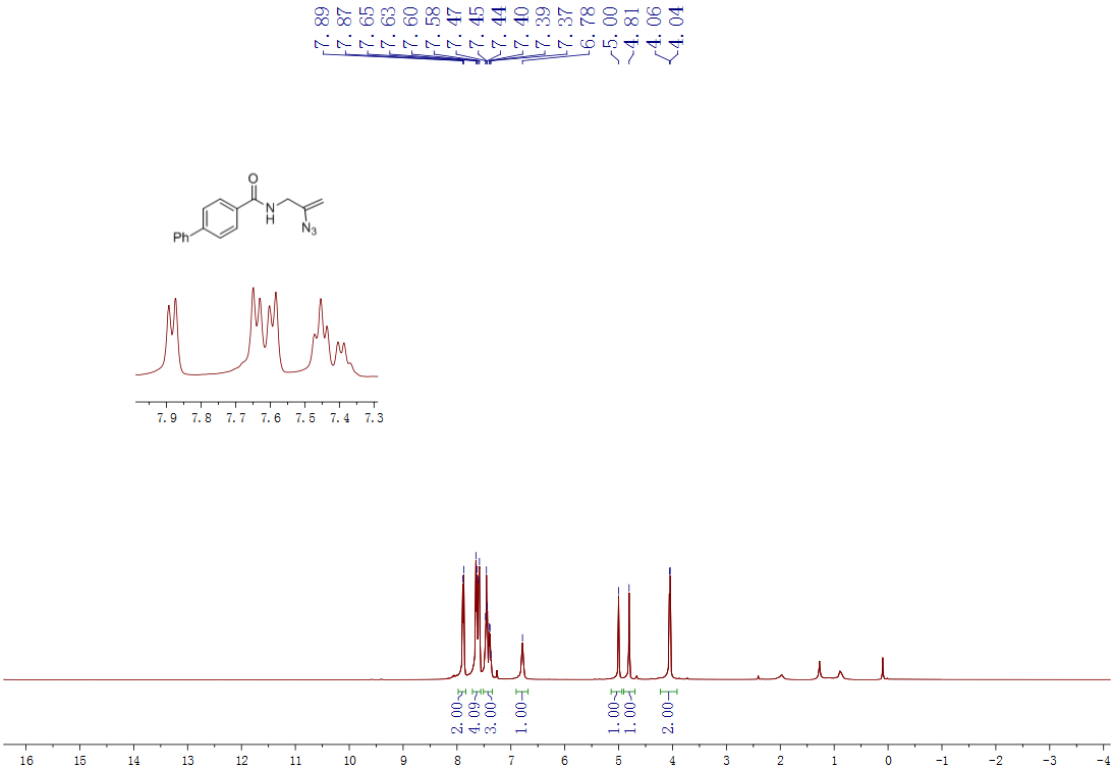
^{1}H NMR spectra of **2-4k** in $CDCl_3$



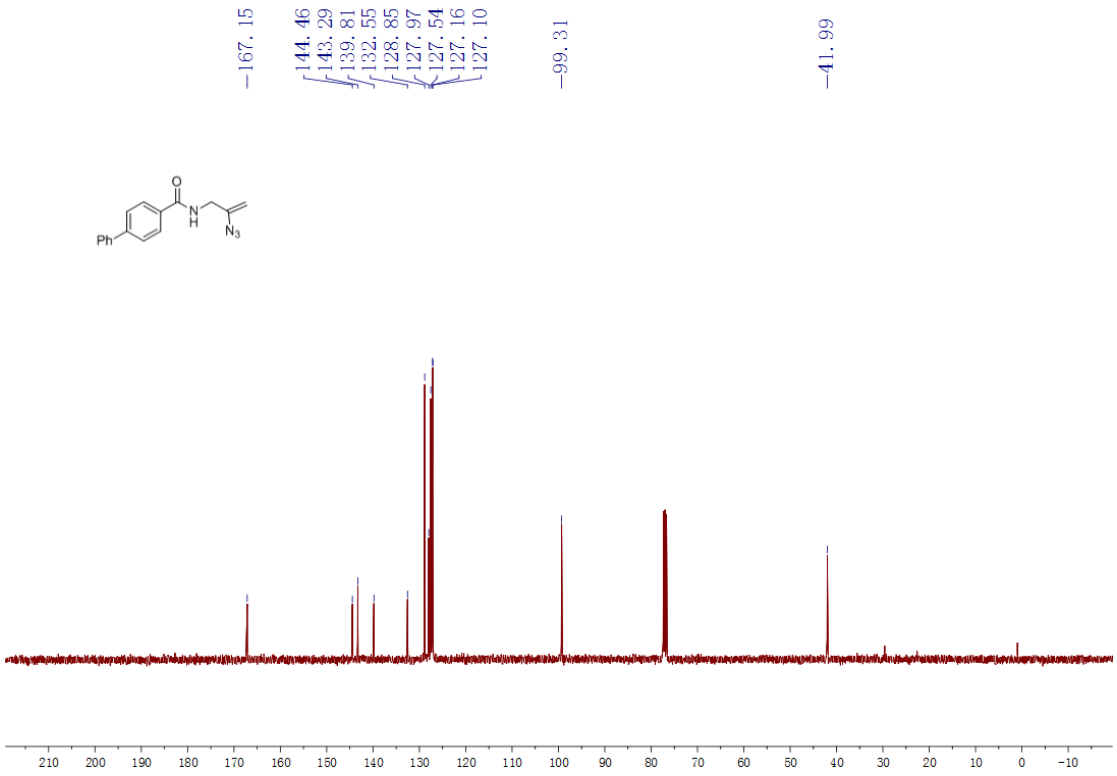
^{13}C NMR spectra of **2-4k** in $CDCl_3$



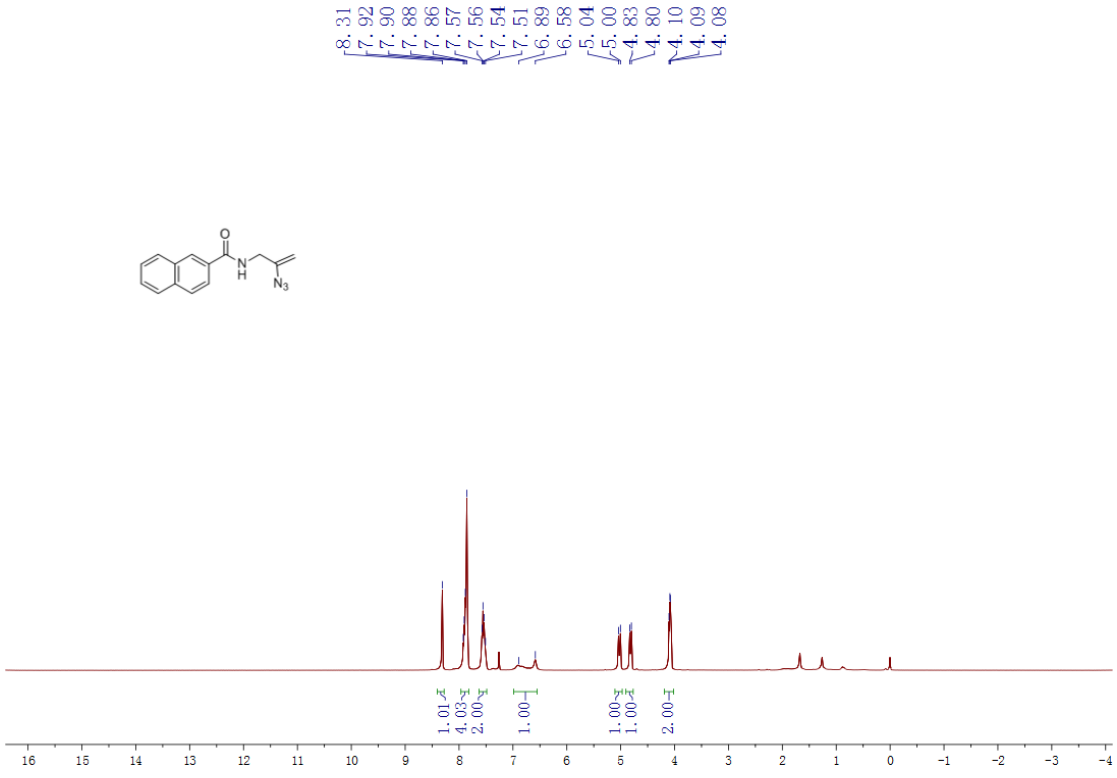
^{1}H NMR spectra of **2-4m** in $CDCl_3$



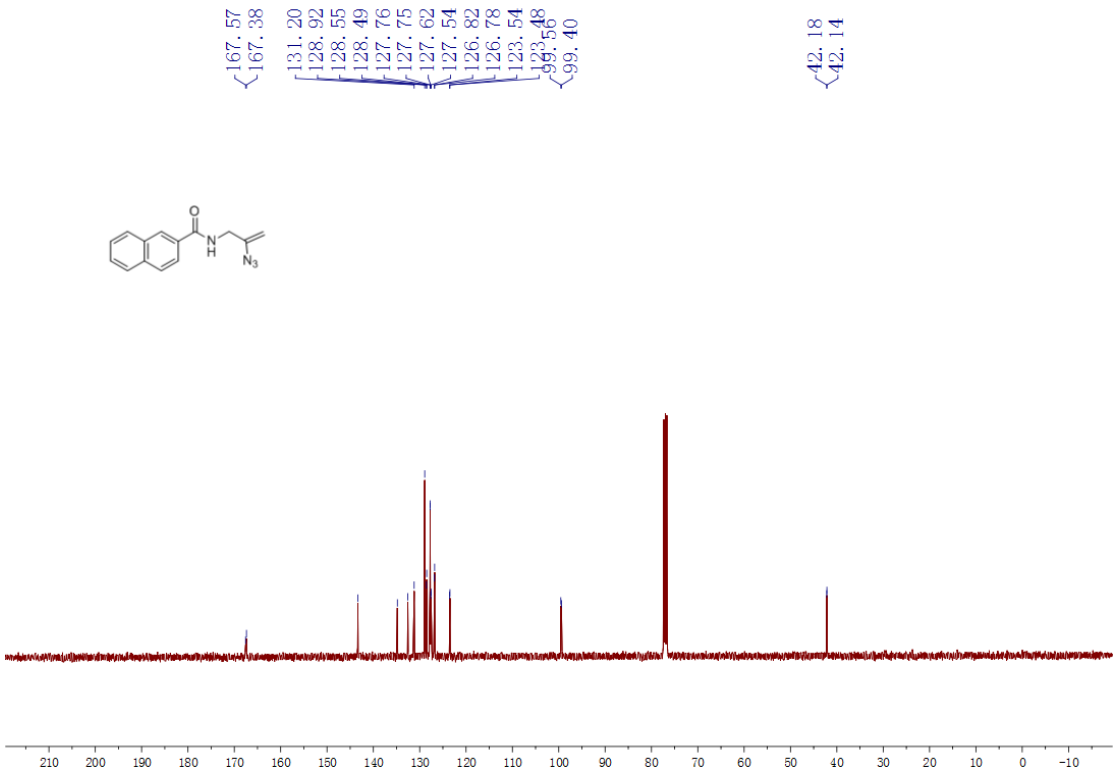
^{13}C NMR spectra of **2-4m** in $CDCl_3$



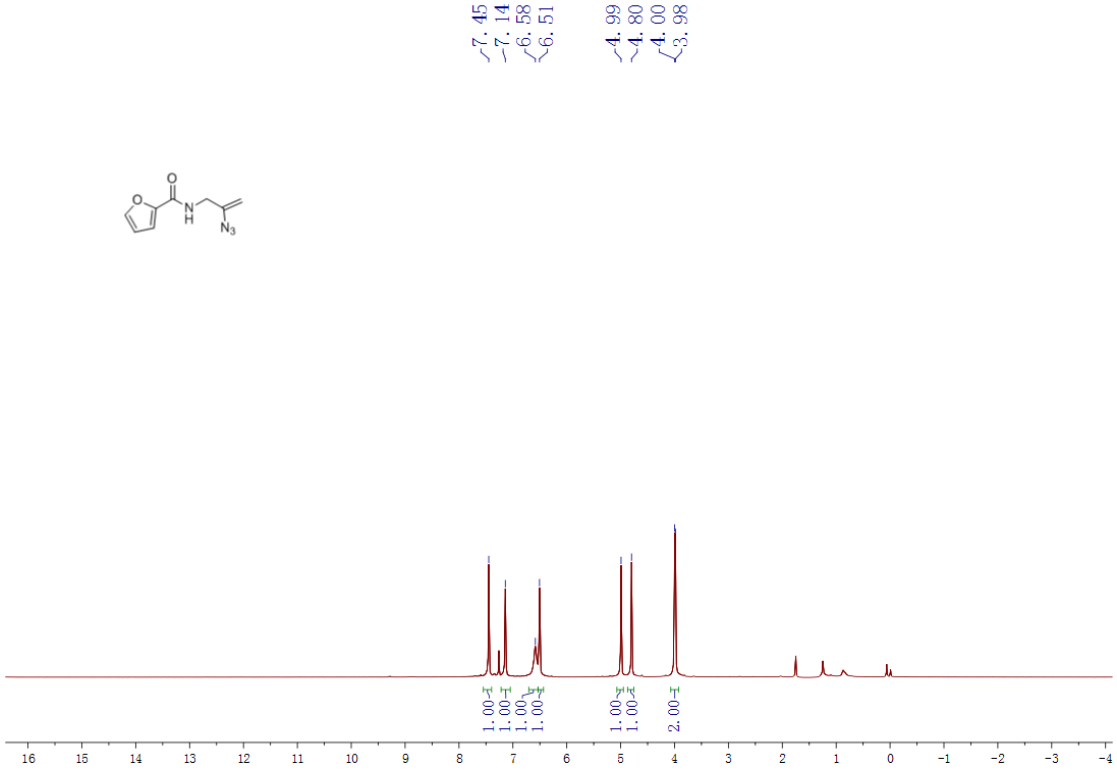
^{1}H NMR spectra of **2-4n** in $CDCl_3$



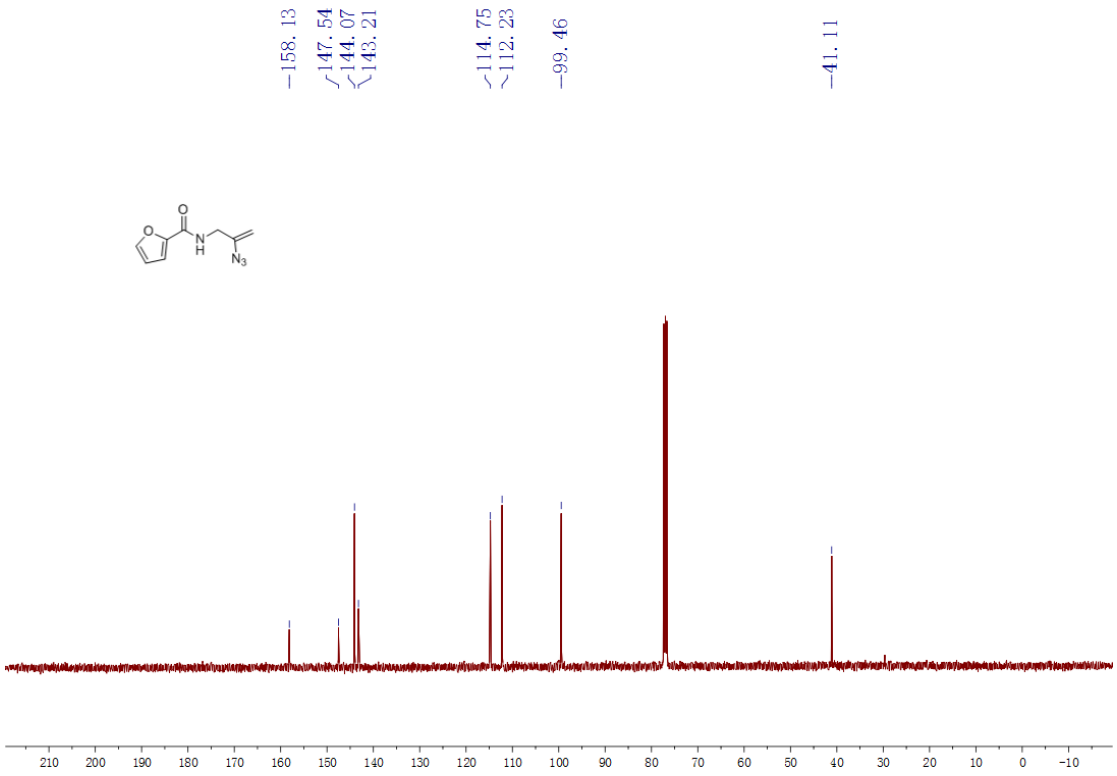
^{13}C NMR spectra of **2-4n** in $CDCl_3$



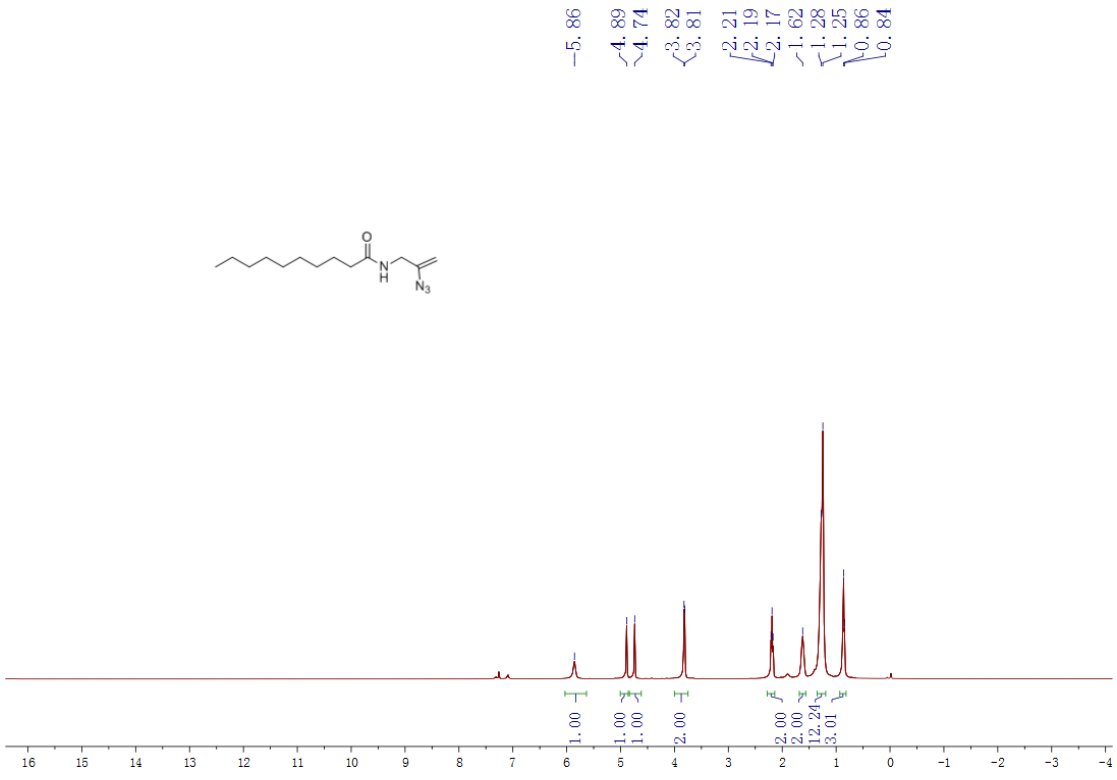
^{1}H NMR spectra of **2-4o** in $CDCl_3$



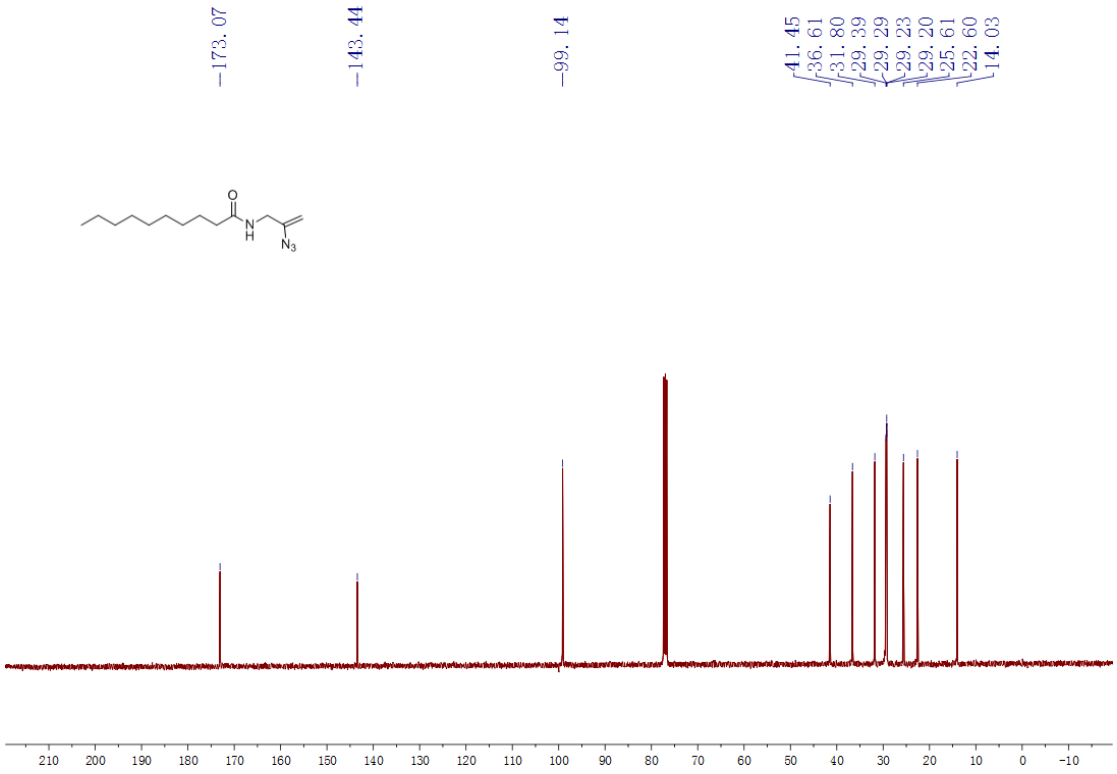
^{13}C NMR spectra of **2-4o** in $CDCl_3$



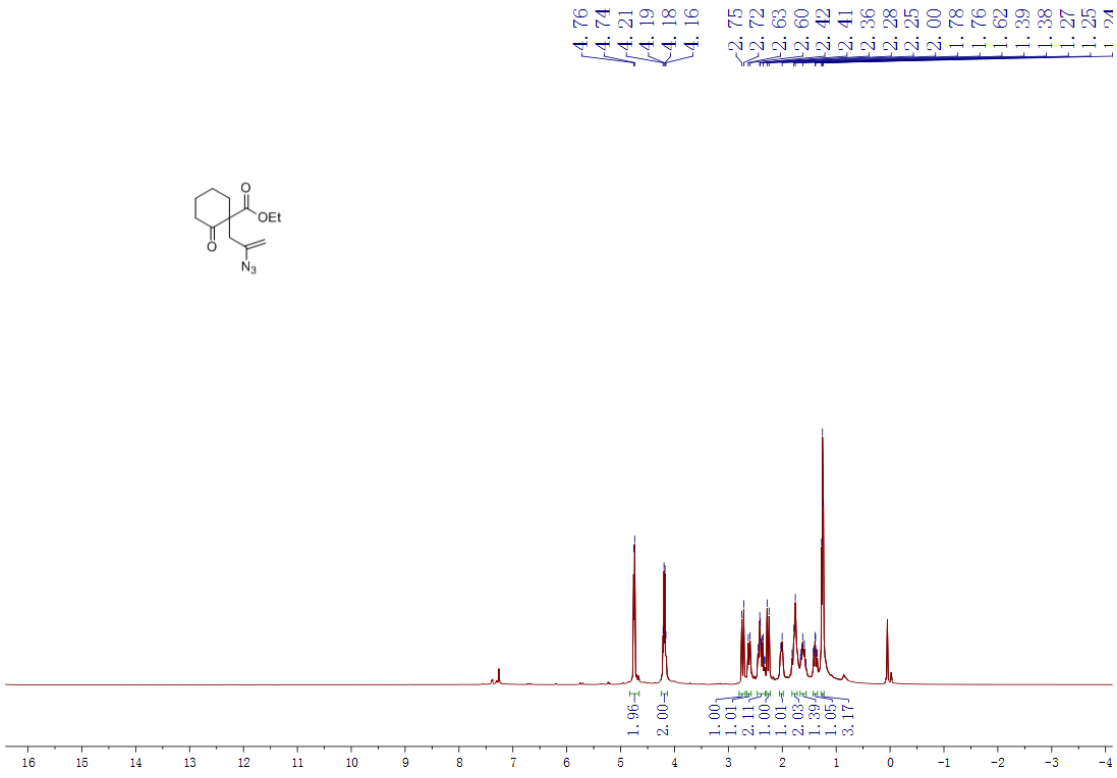
^{1}H NMR spectra of **2-4p** in $CDCl_3$



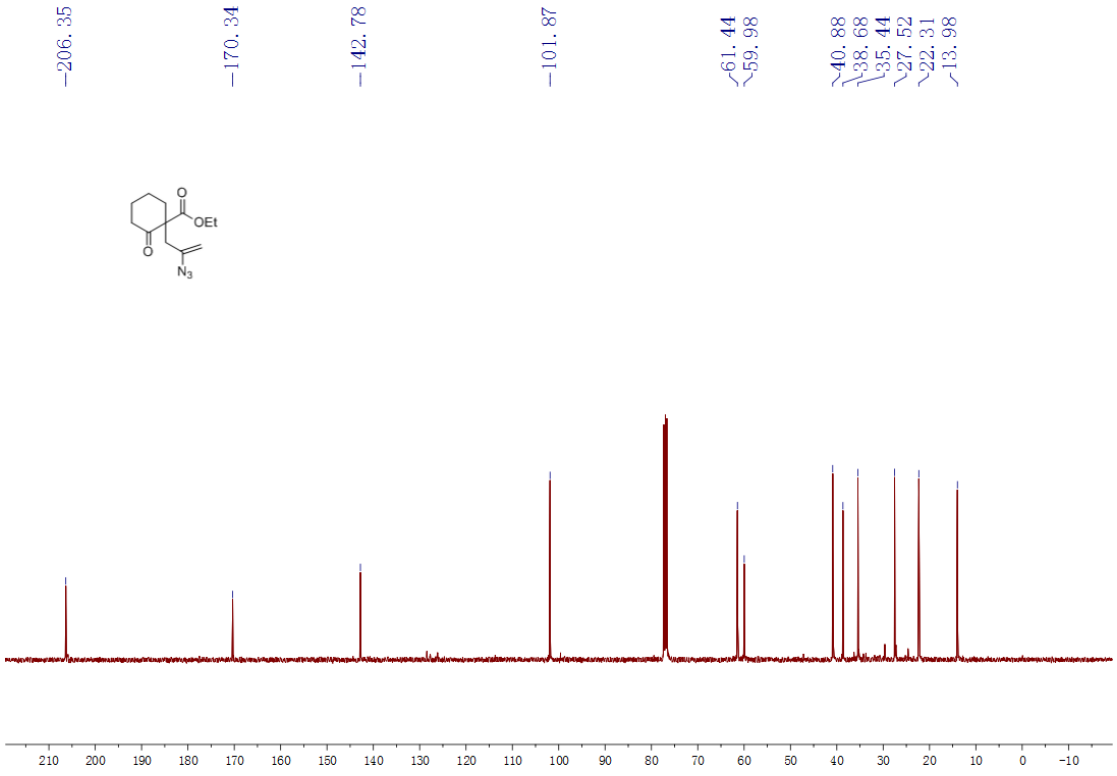
^{13}C NMR spectra of **2-4p** in $CDCl_3$



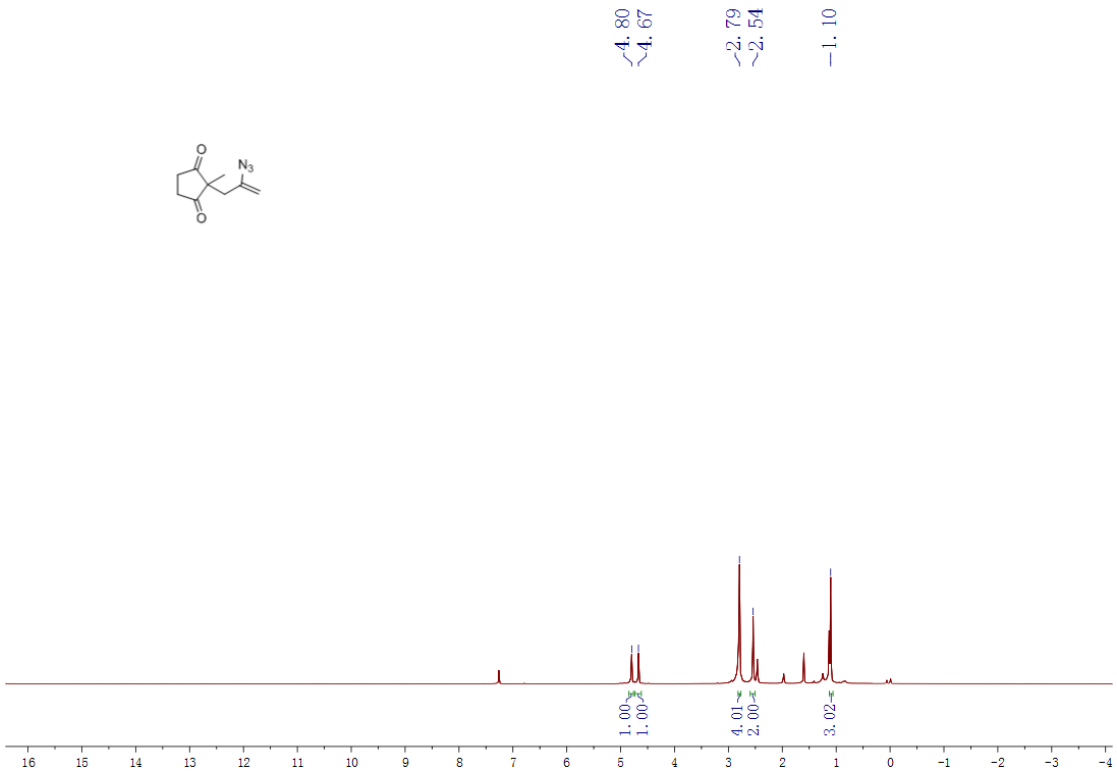
^{1}H NMR spectra of **2-4s** in $CDCl_3$



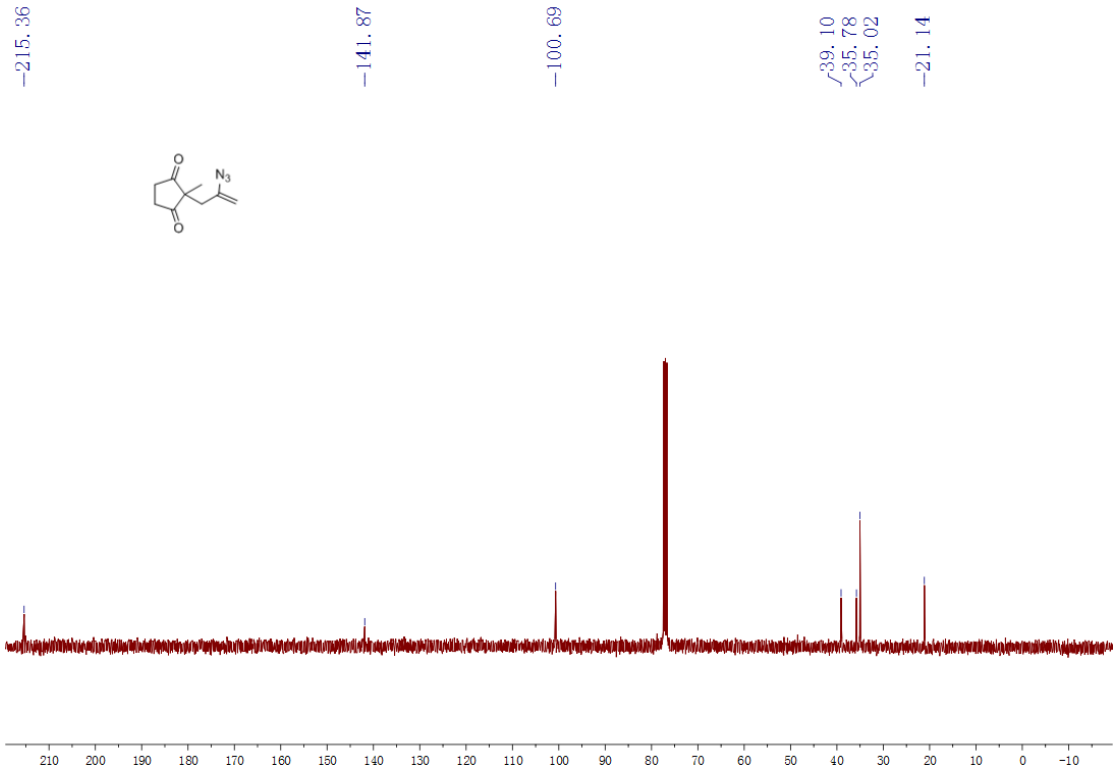
^{13}C NMR spectra of **2-4s** in $CDCl_3$



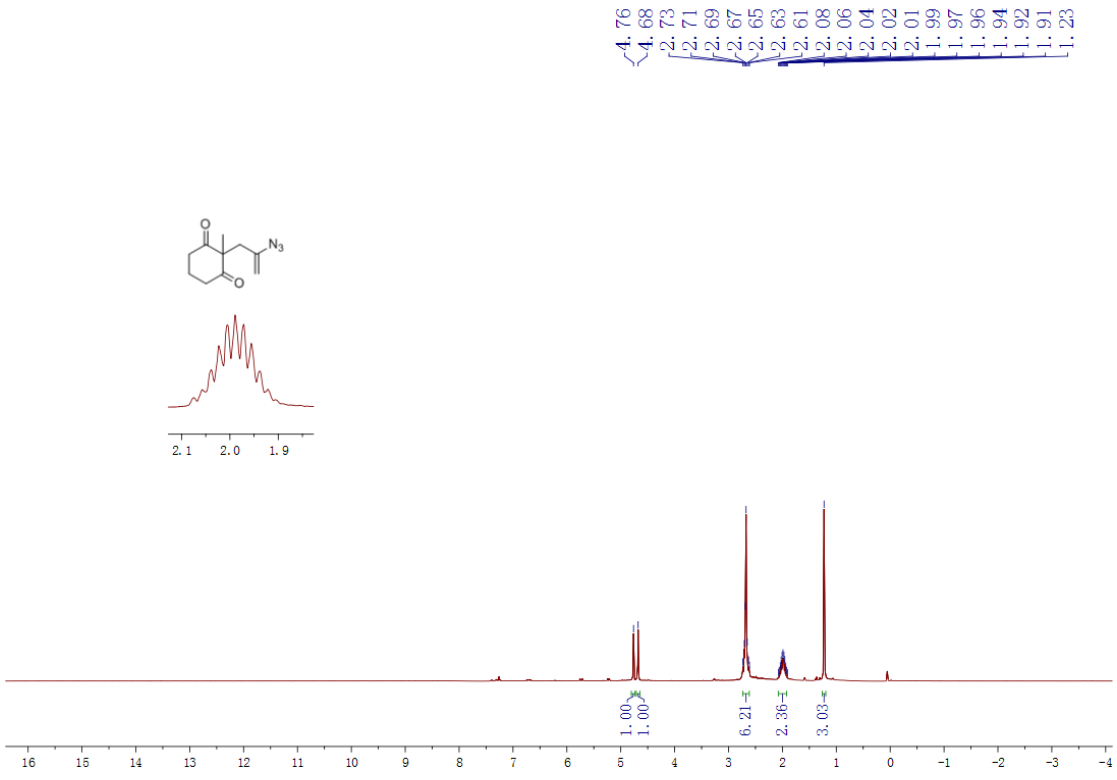
^{1}H NMR spectra of **2-4t** in $CDCl_3$



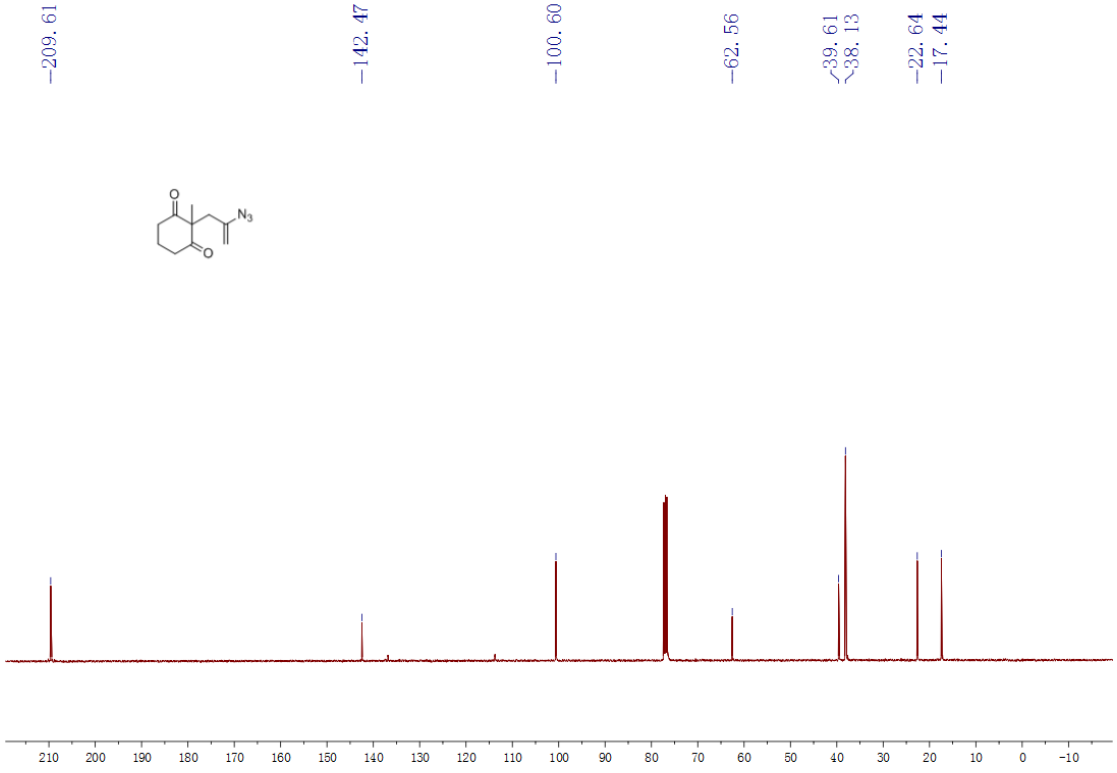
^{13}C NMR spectra of **2-4t** in $CDCl_3$



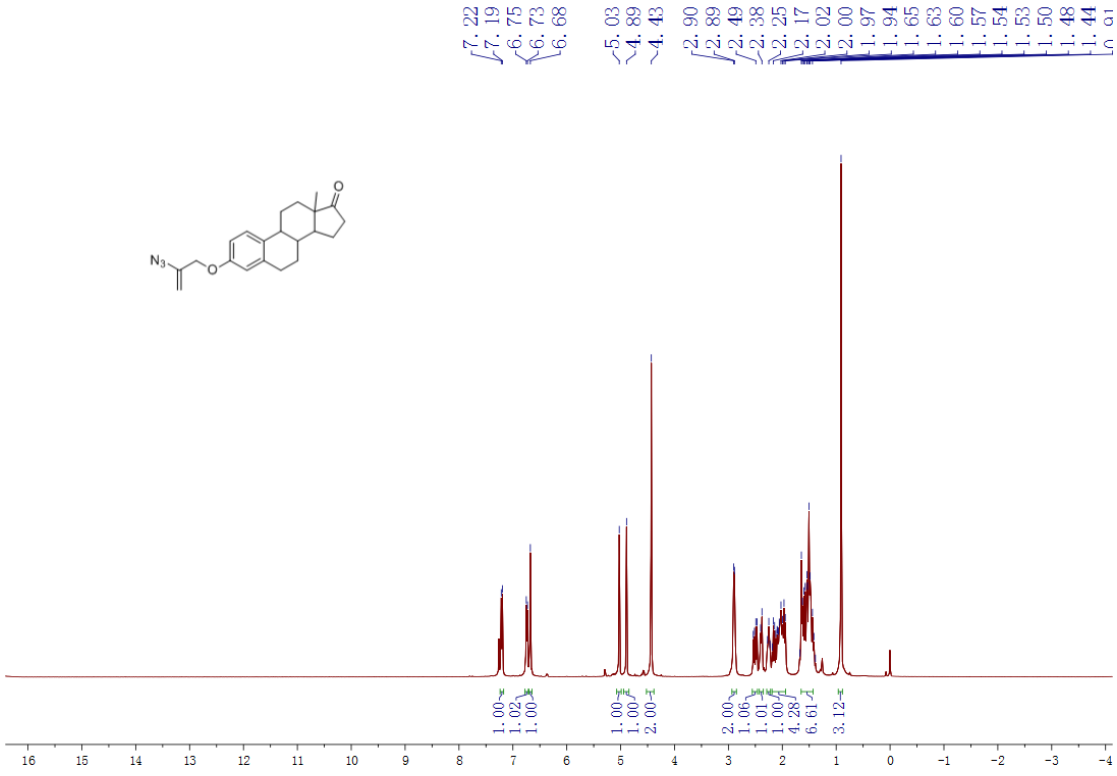
^{1}H NMR spectra of **2-4u** in $CDCl_3$



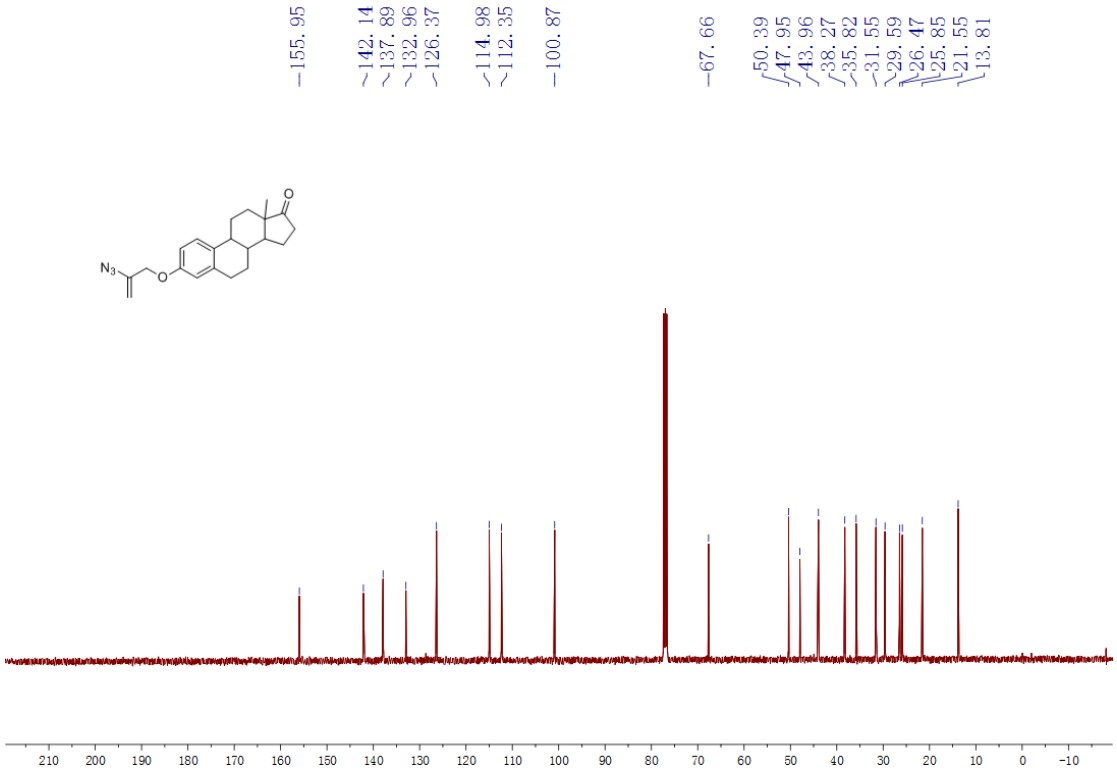
^{13}C NMR spectra of **2-4u** in $CDCl_3$



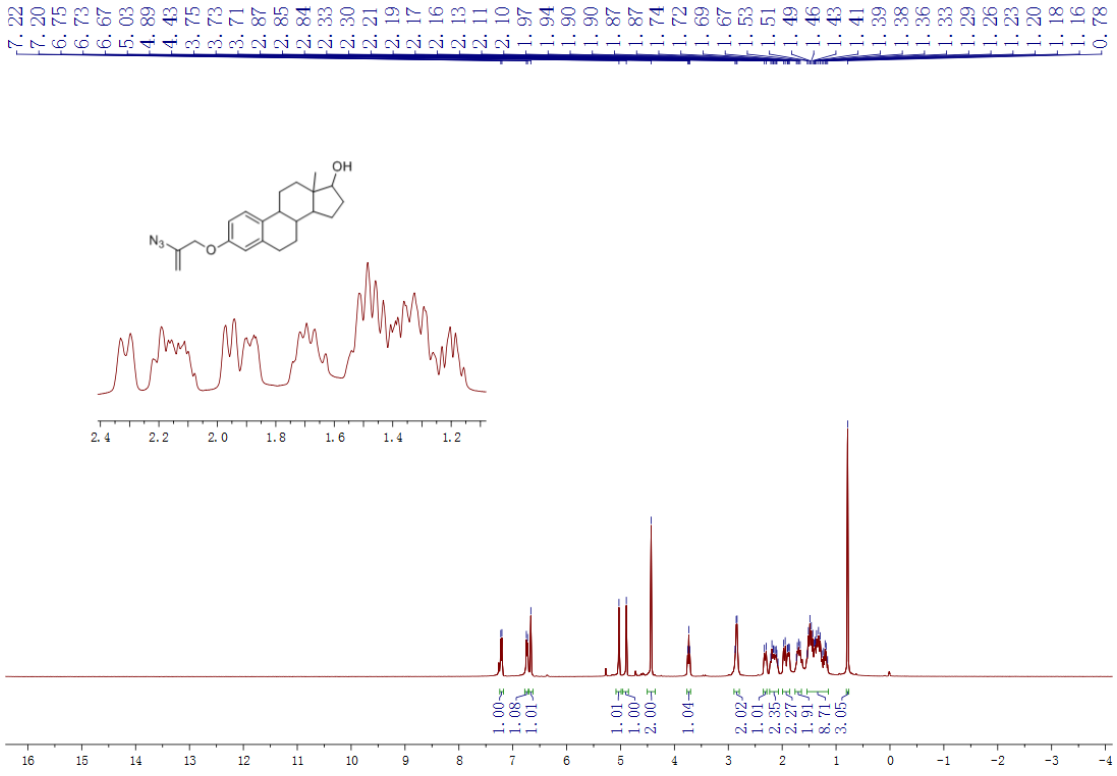
^{1}H NMR spectra of **2-7a** in $CDCl_3$



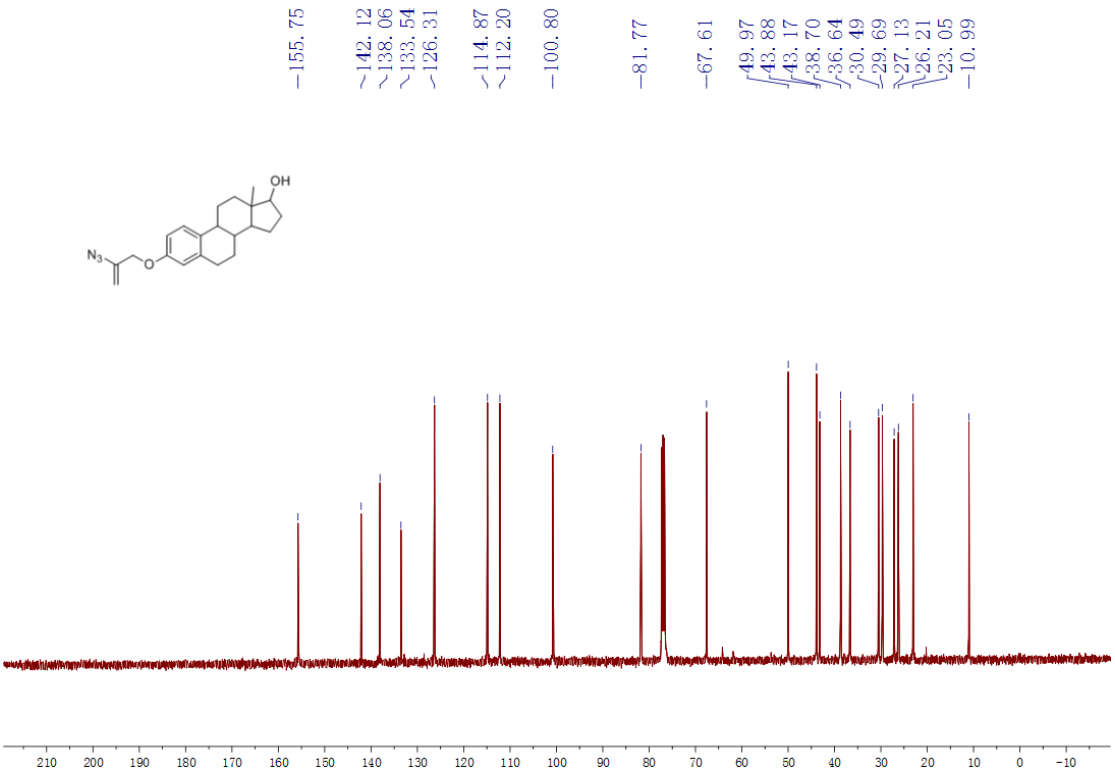
^{13}C NMR spectra of **2-7a** in $CDCl_3$



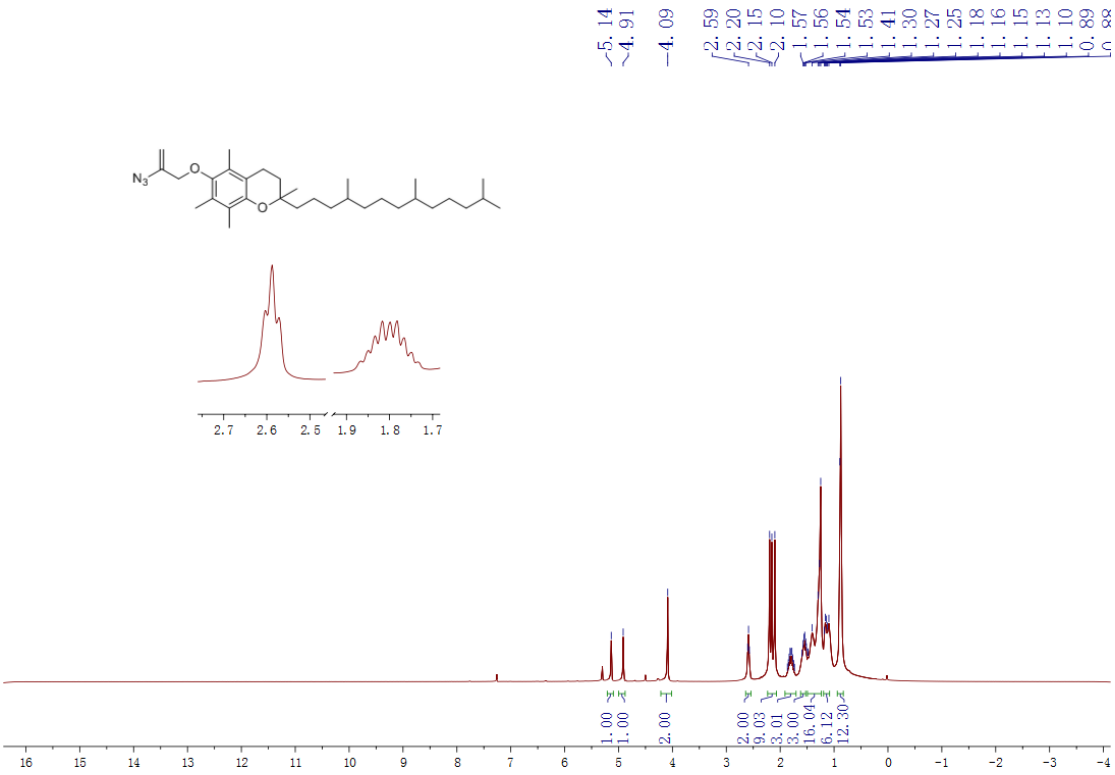
^{1}H NMR spectra of **2-7b** in $CDCl_3$



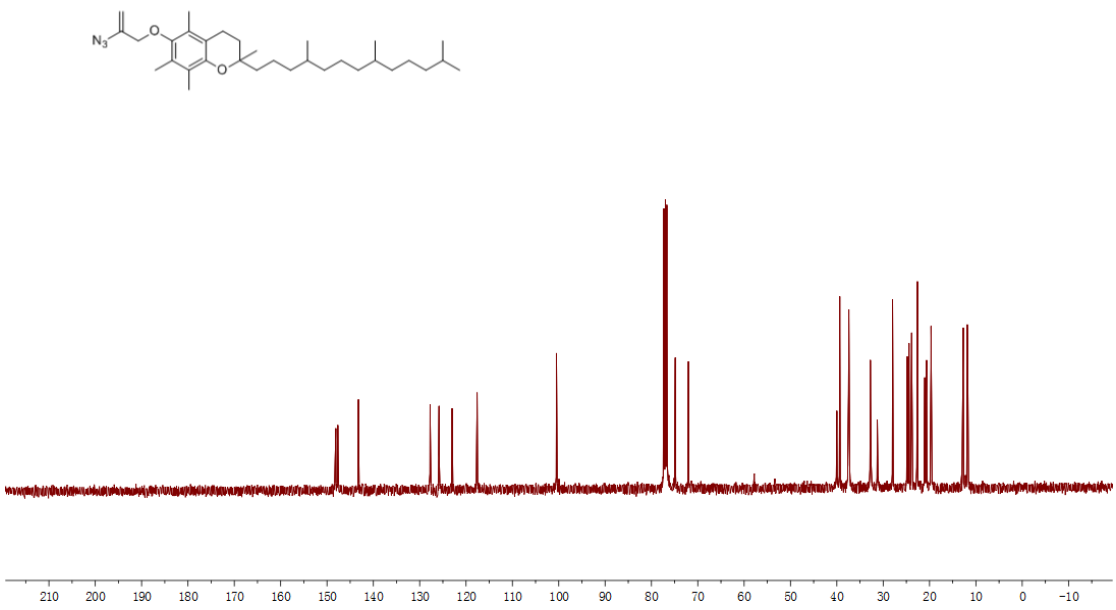
^{13}C NMR spectra of **2-7b** in $CDCl_3$



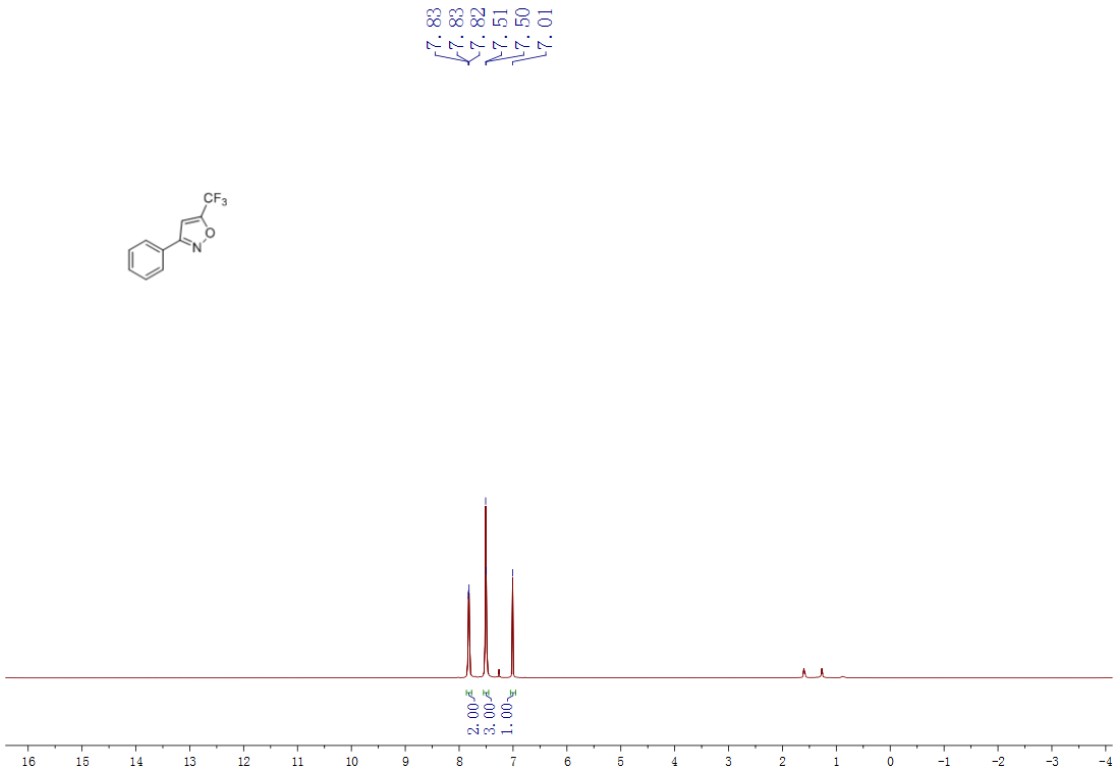
^{1}H NMR spectra of **2-7c** in $CDCl_3$



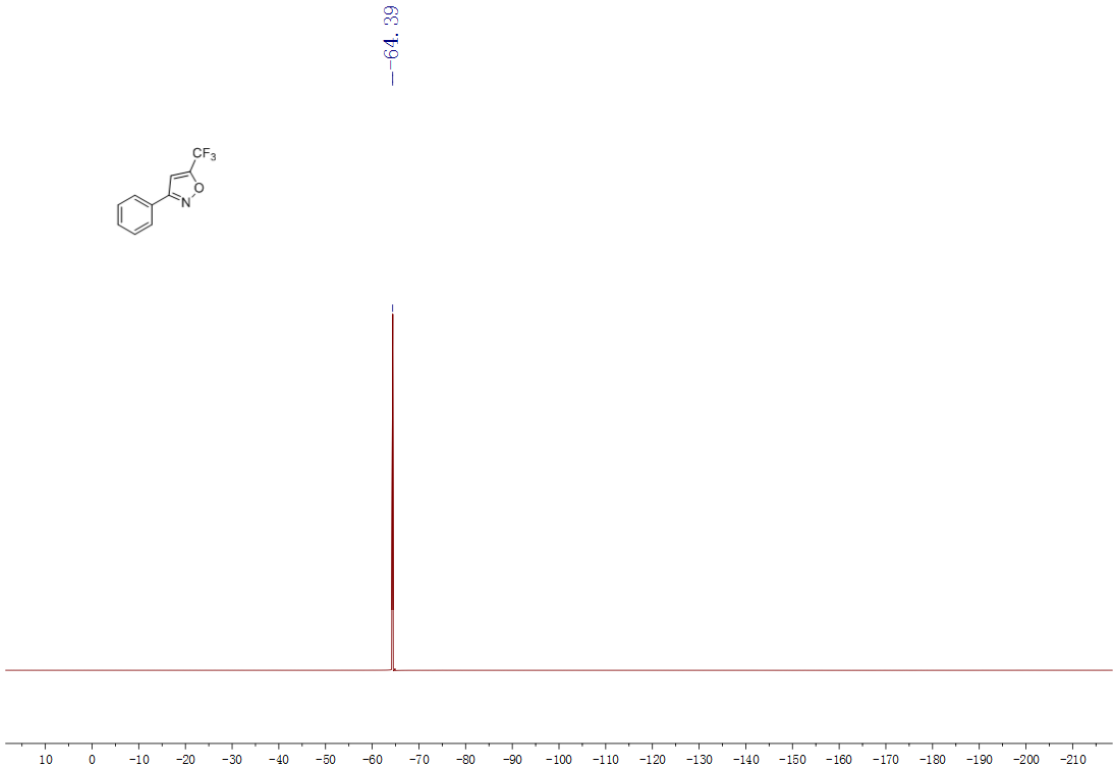
^{13}C NMR spectra of **2-7c** in $CDCl_3$



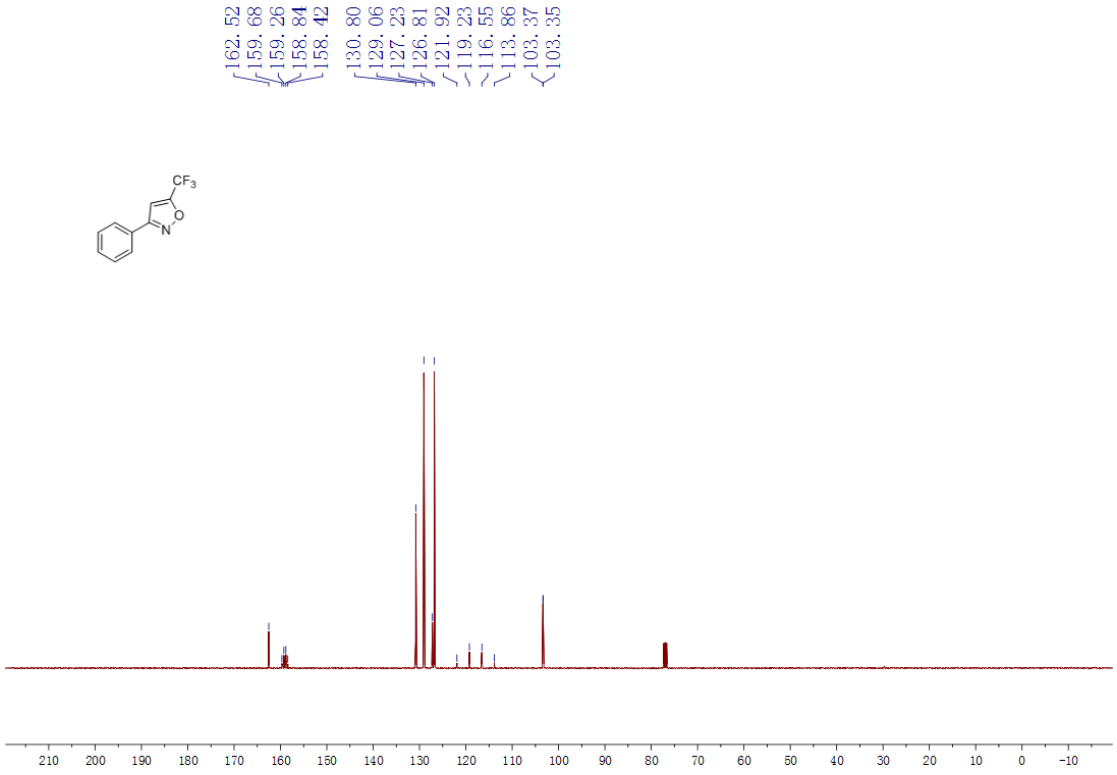
^{1}H NMR spectra of **3a** in $CDCl_3$



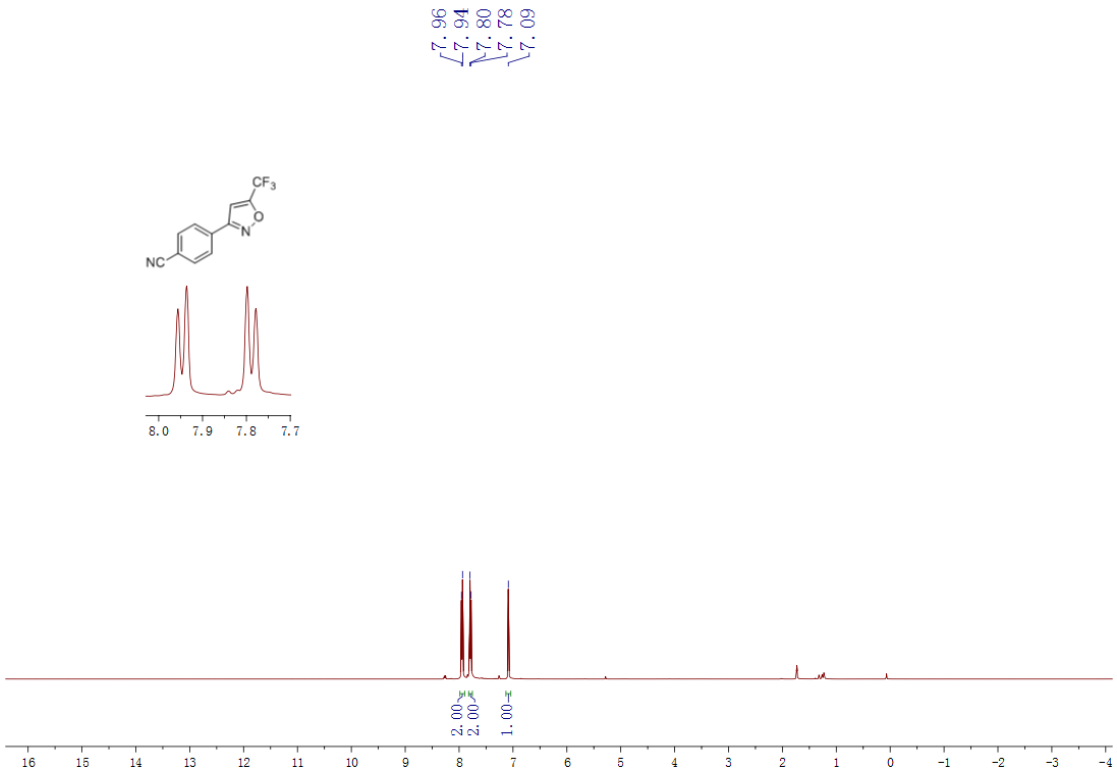
^{19}F NMR spectra of **3a** in $CDCl_3$



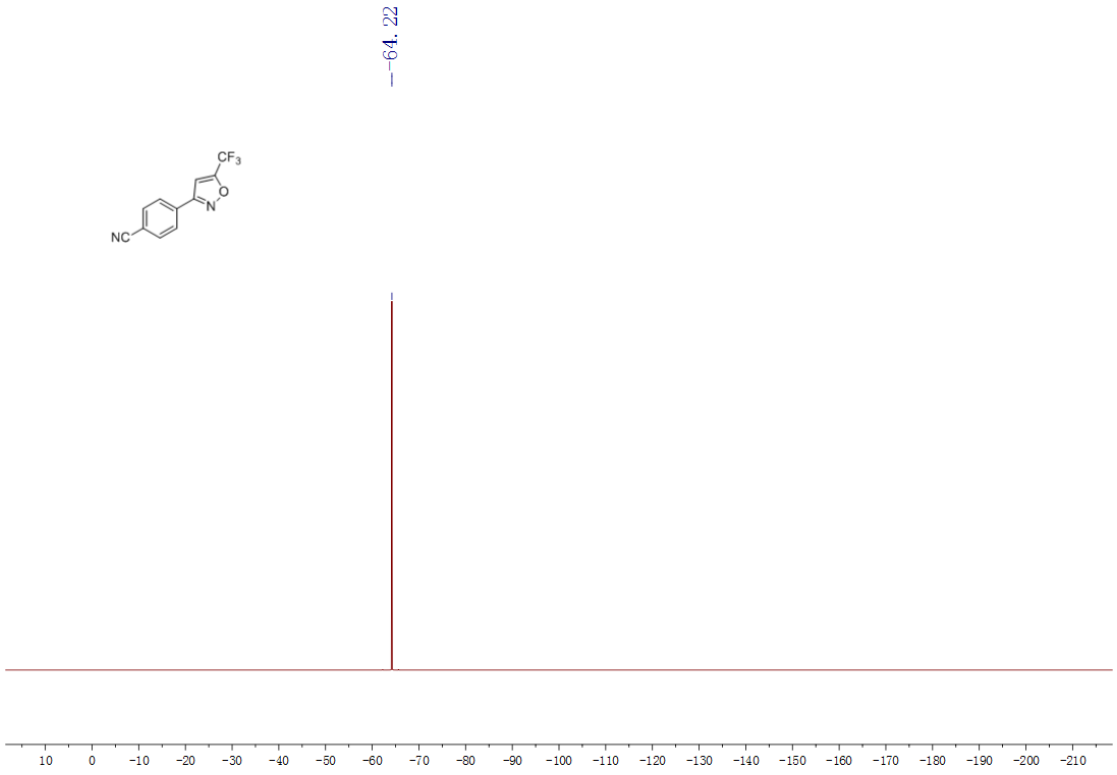
^{13}C NMR spectra of **3a** in $CDCl_3$



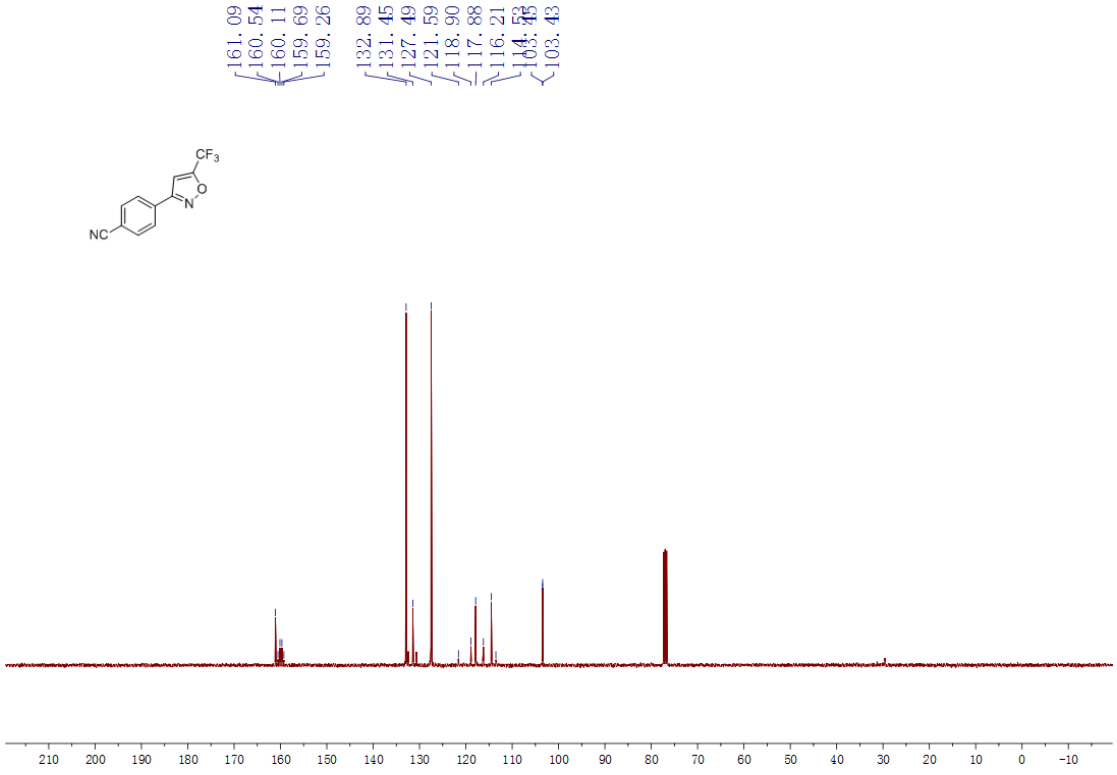
^{1}H NMR spectra of **3b** in $CDCl_3$



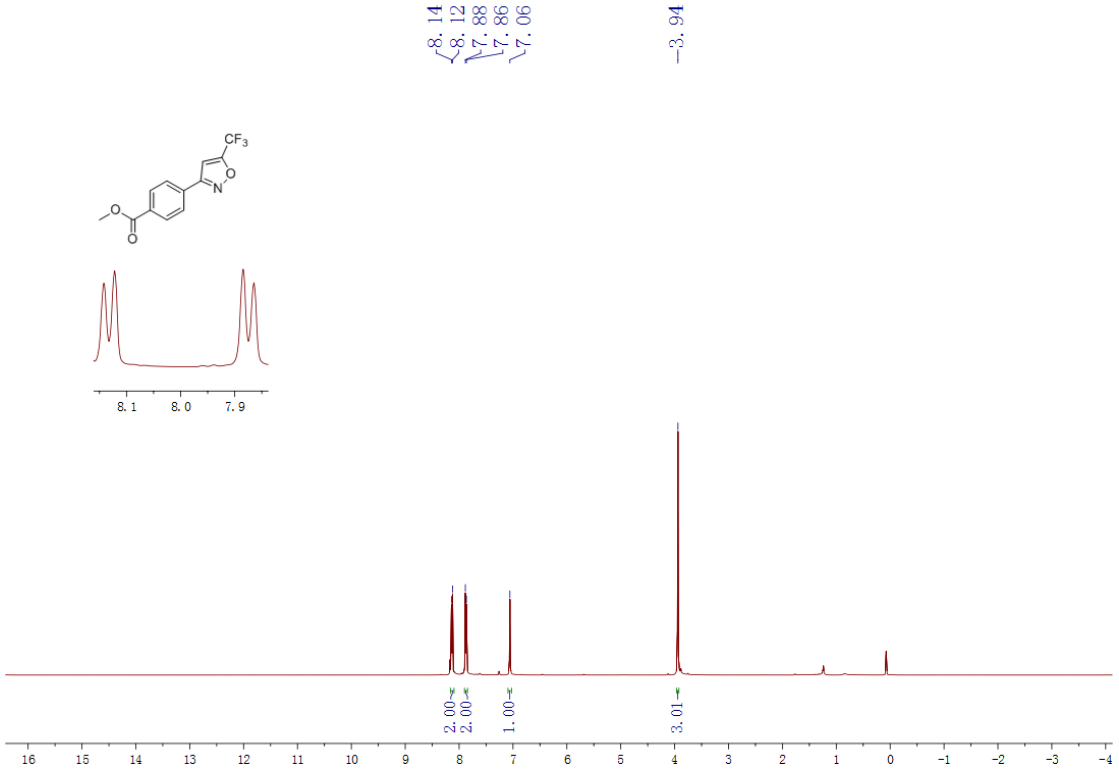
^{19}F NMR spectra of **3b** in $CDCl_3$



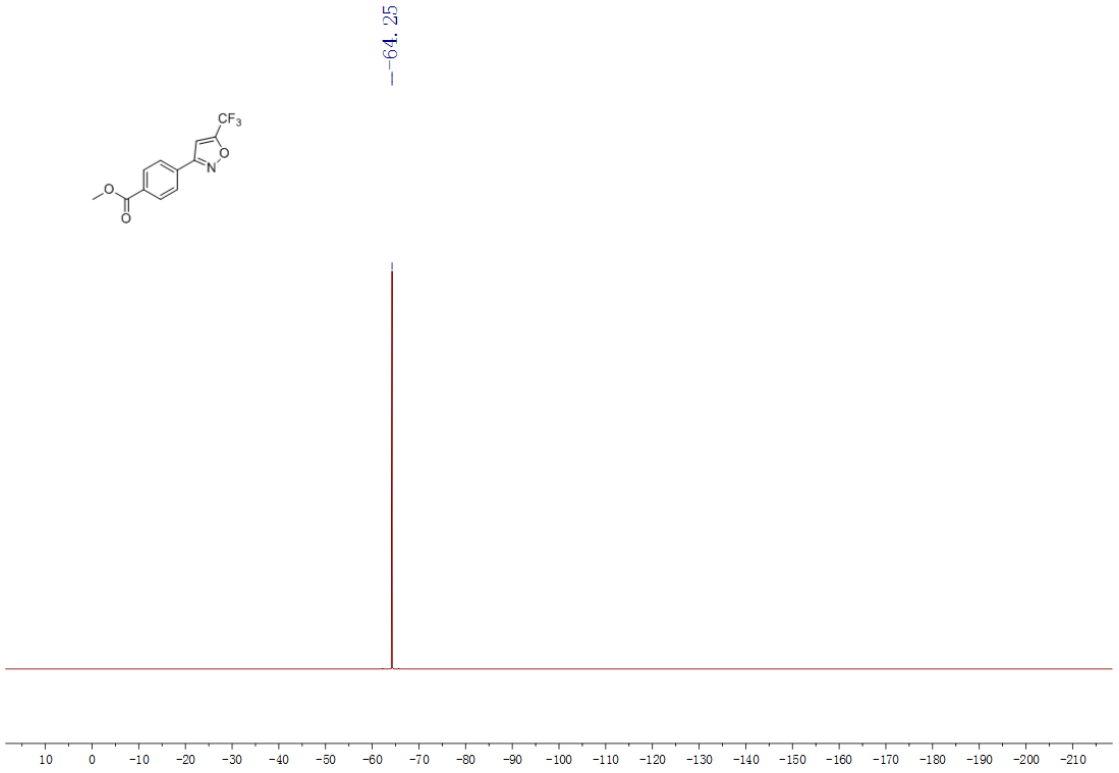
^{13}C NMR spectra of **3b** in $CDCl_3$



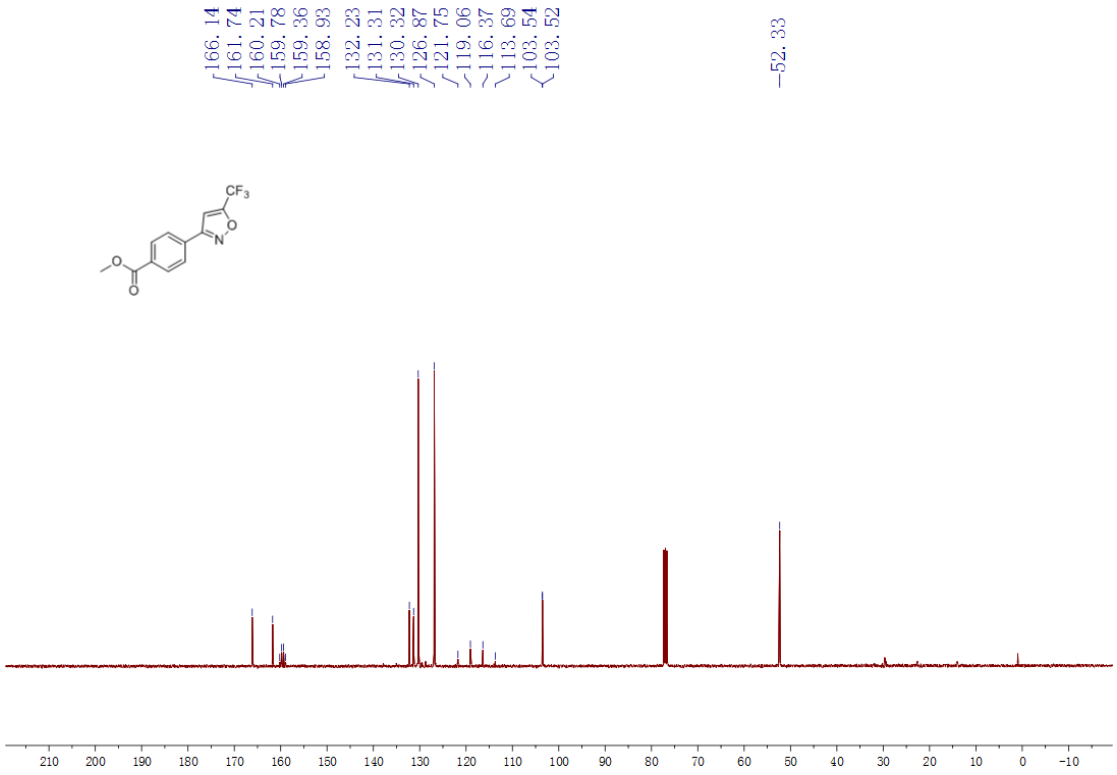
^{1}H NMR spectra of **3c** in $CDCl_3$



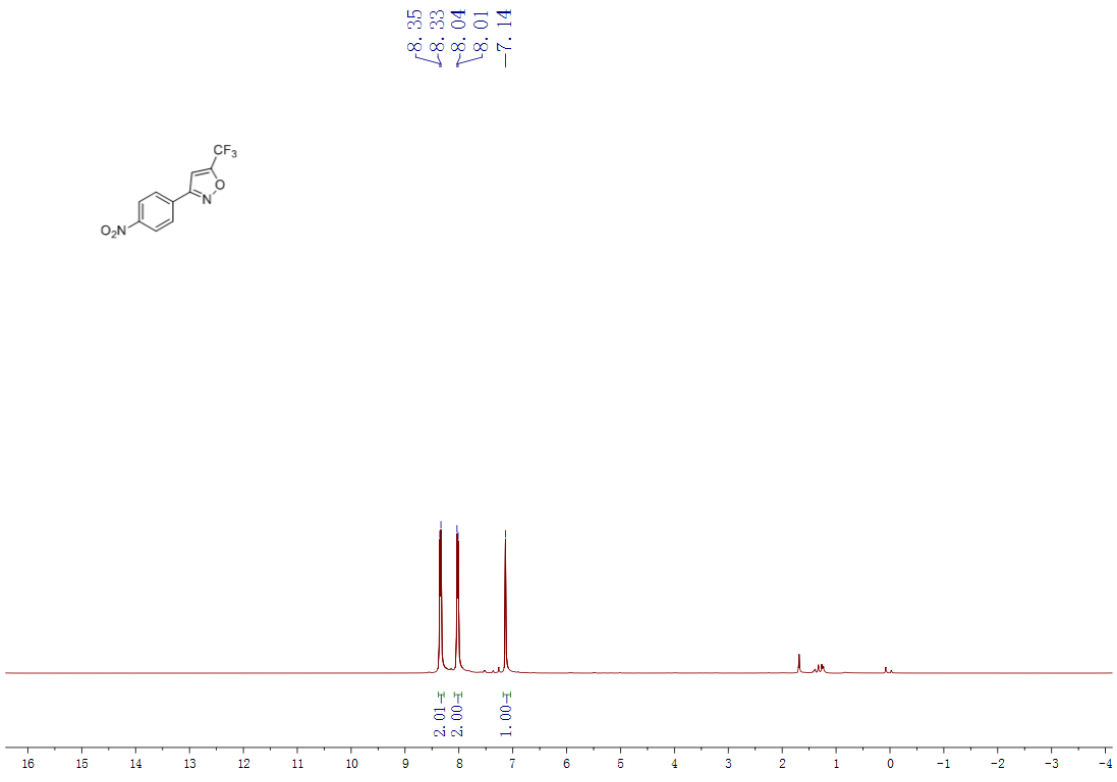
^{19}F NMR spectra of **3c** in $CDCl_3$



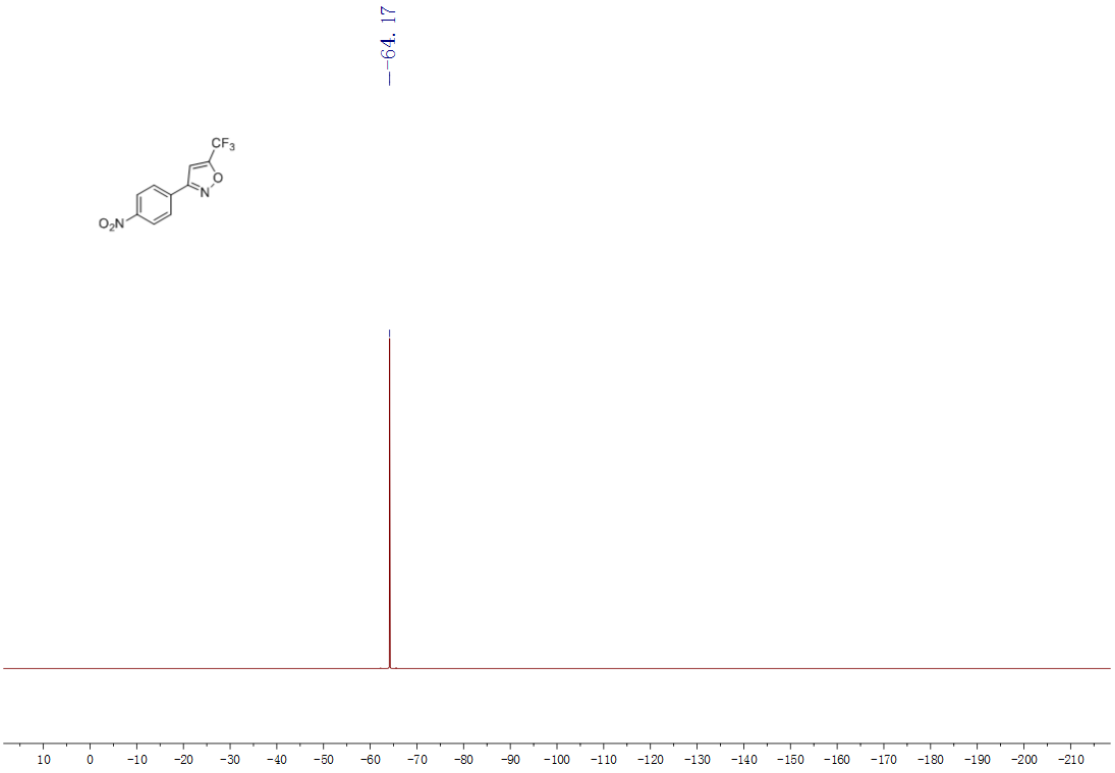
^{13}C NMR spectra of **3c** in $CDCl_3$



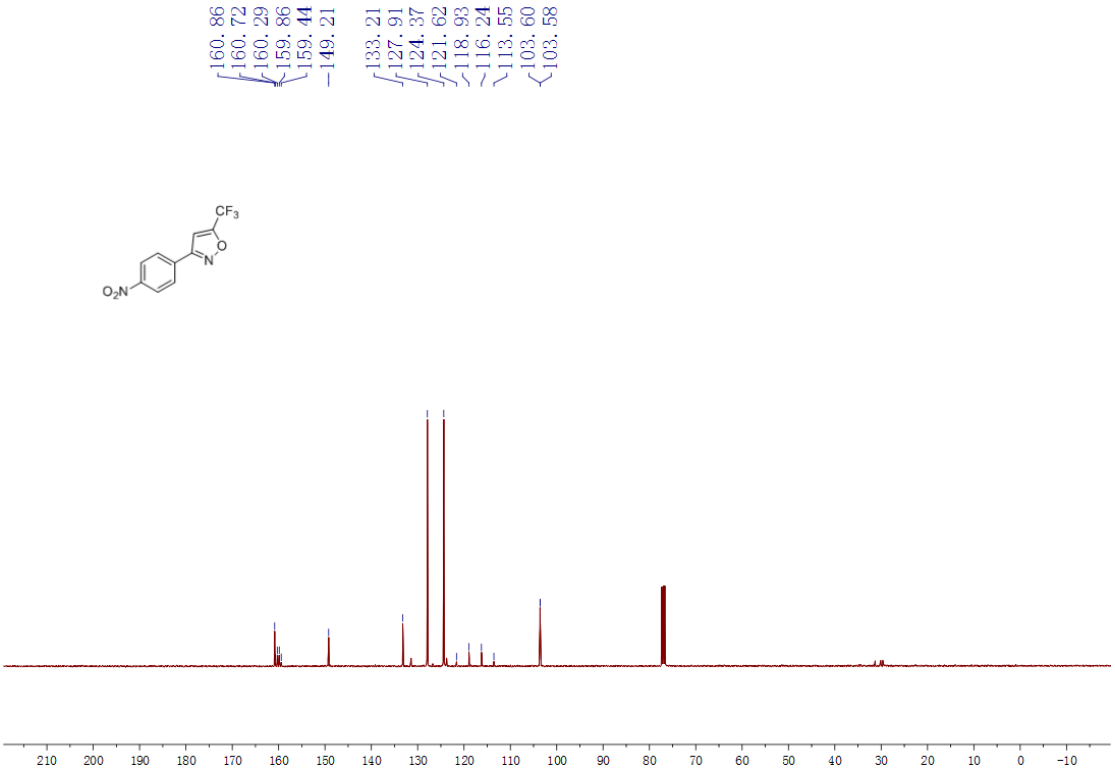
^{1}H NMR spectra of **3d** in $CDCl_3$



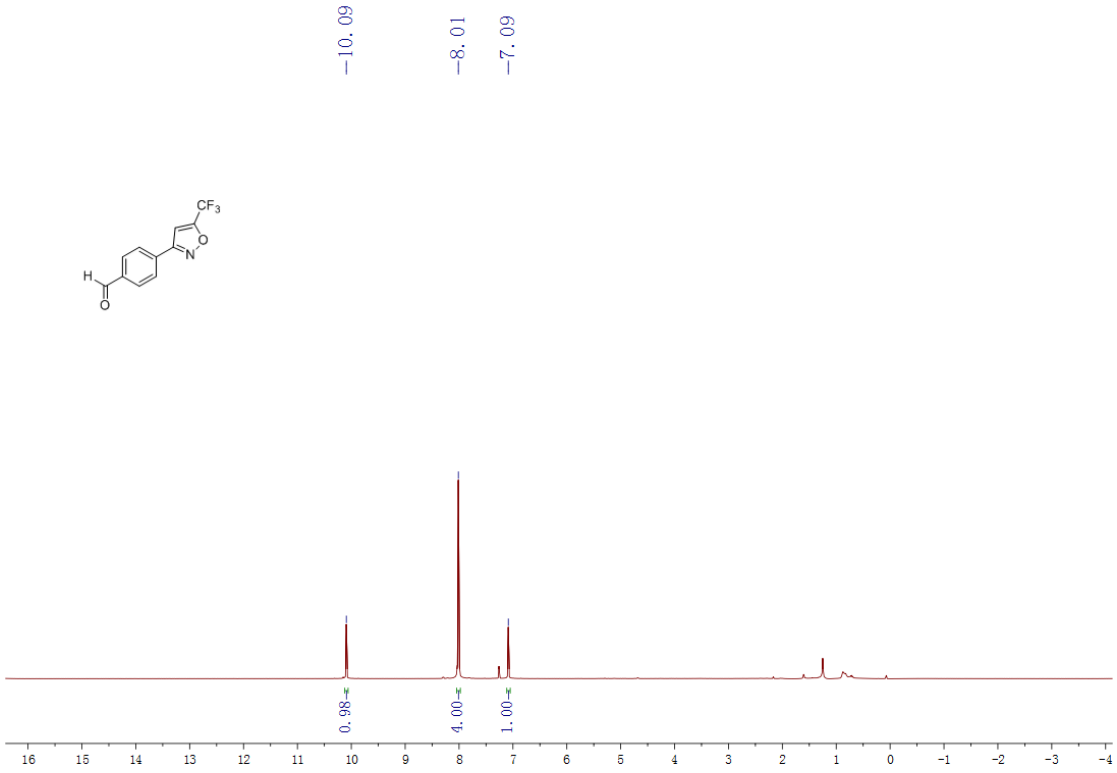
^{19}F NMR spectra of **3d** in $CDCl_3$



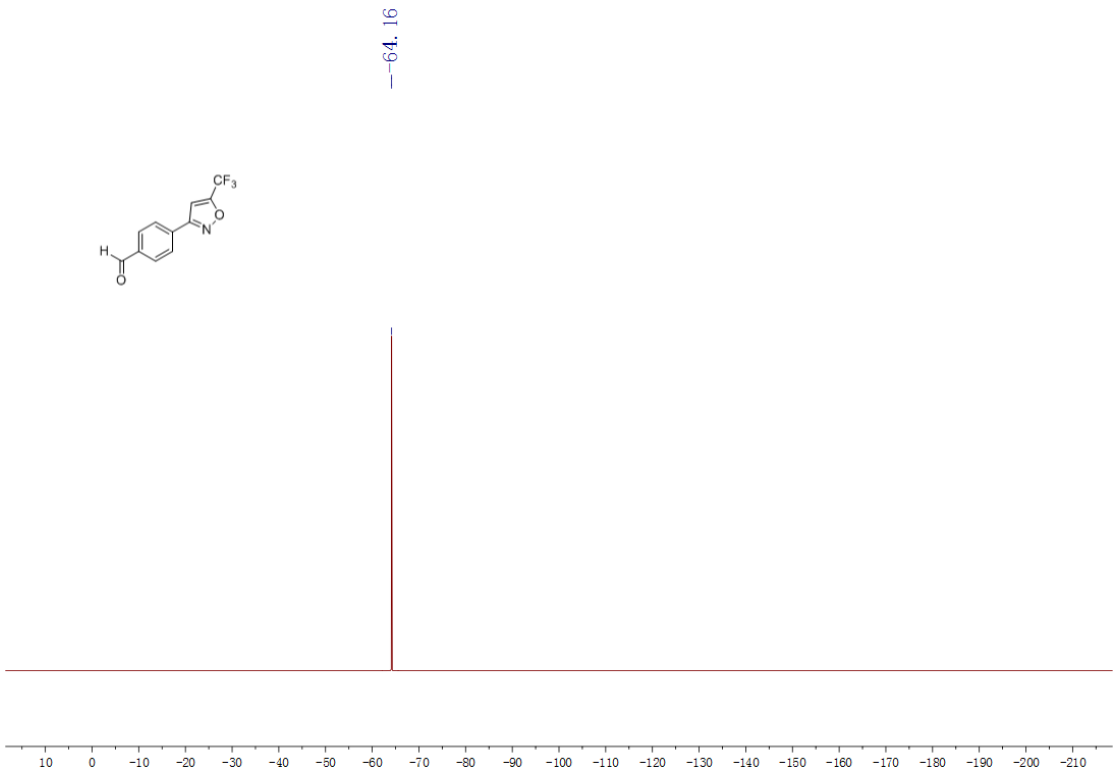
^{13}C NMR spectra of **3d** in $CDCl_3$



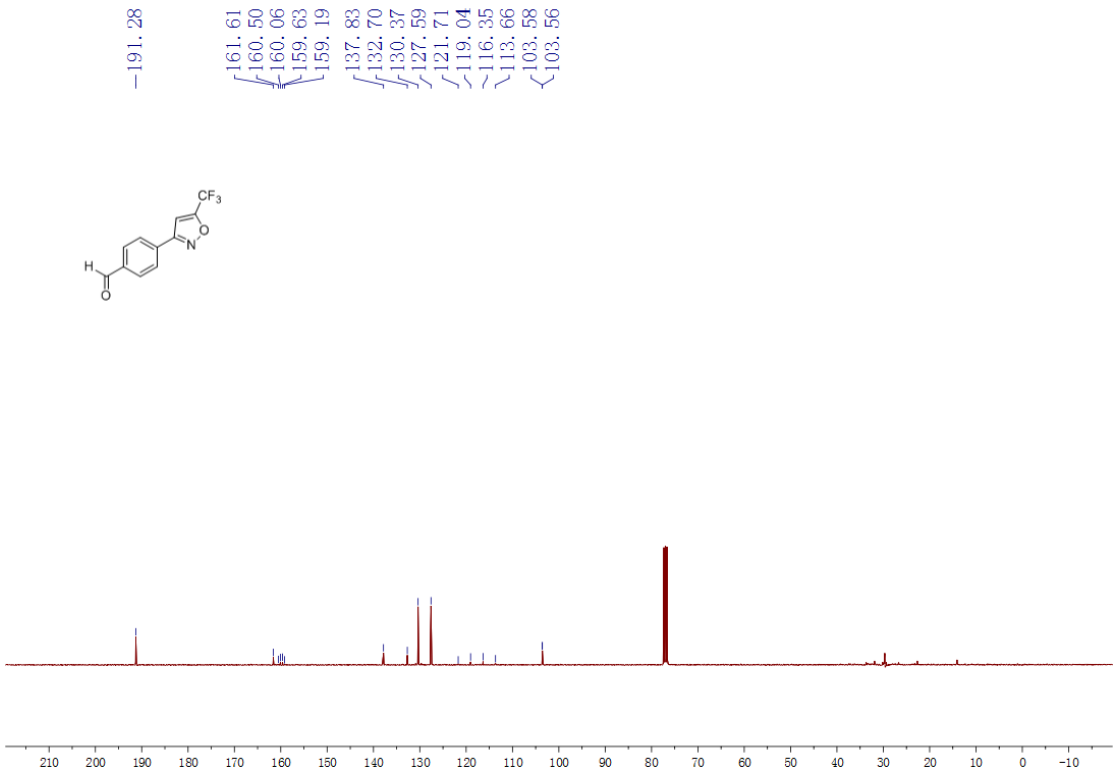
^{1}H NMR spectra of **3e** in $CDCl_3$



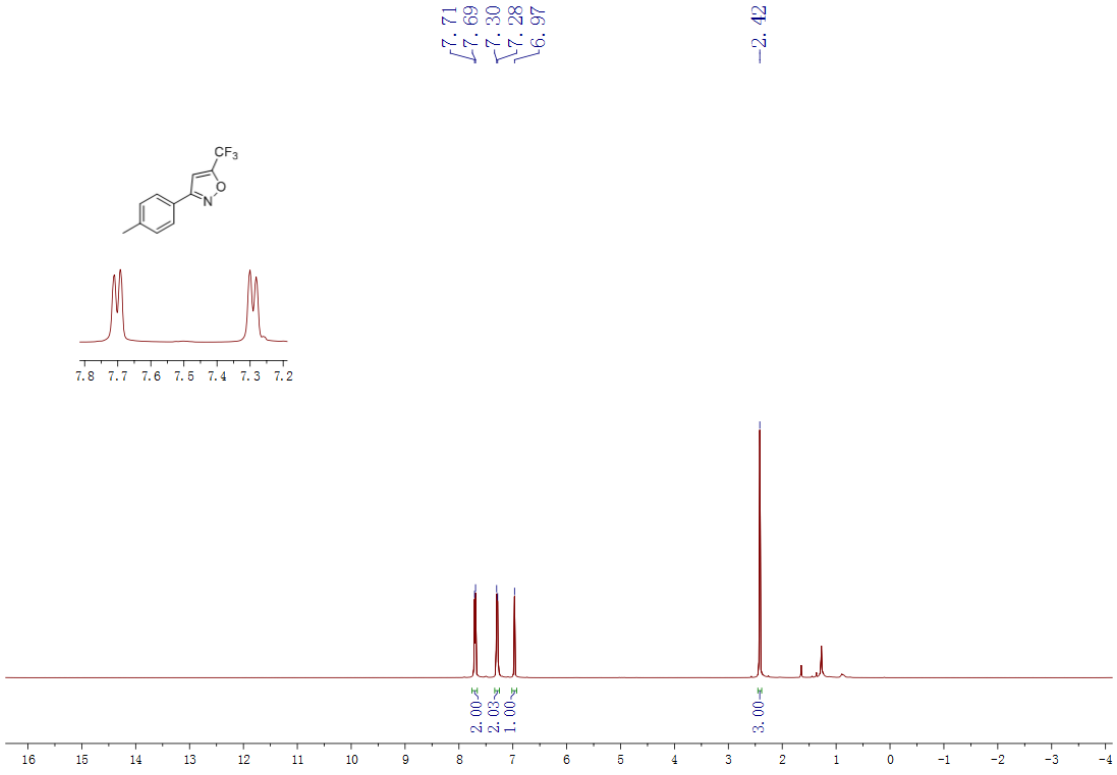
^{19}F NMR spectra of **3e** in $CDCl_3$



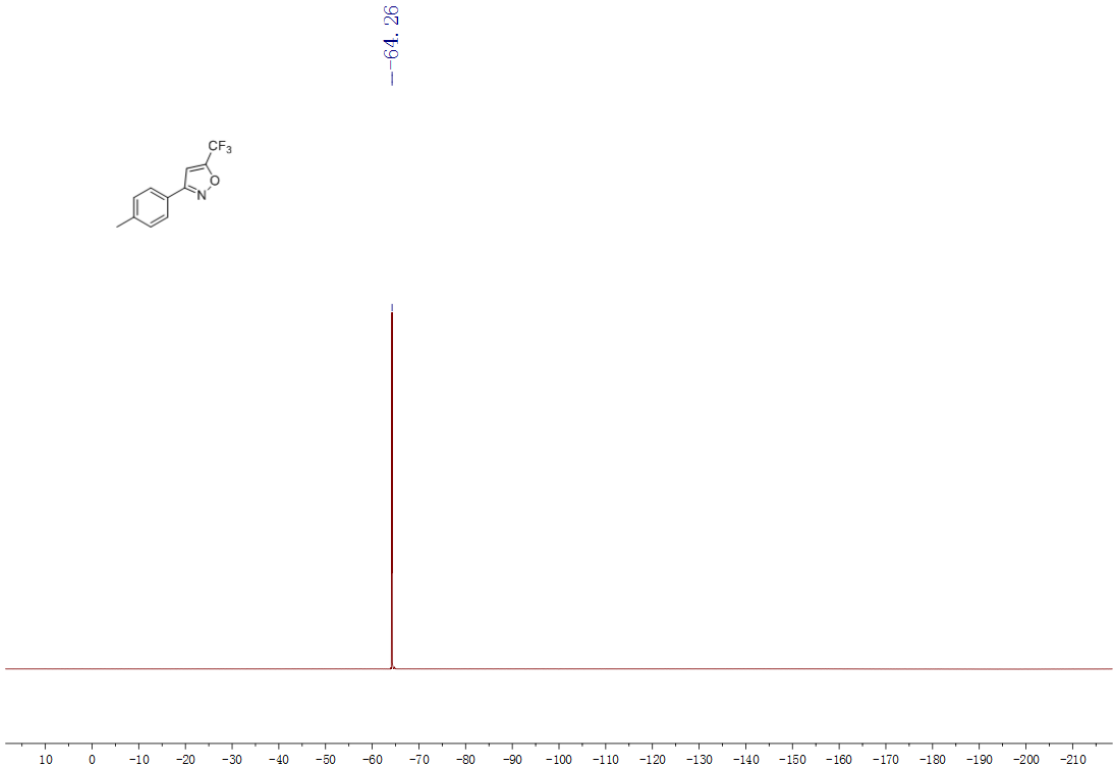
^{13}C NMR spectra of **3e** in $CDCl_3$



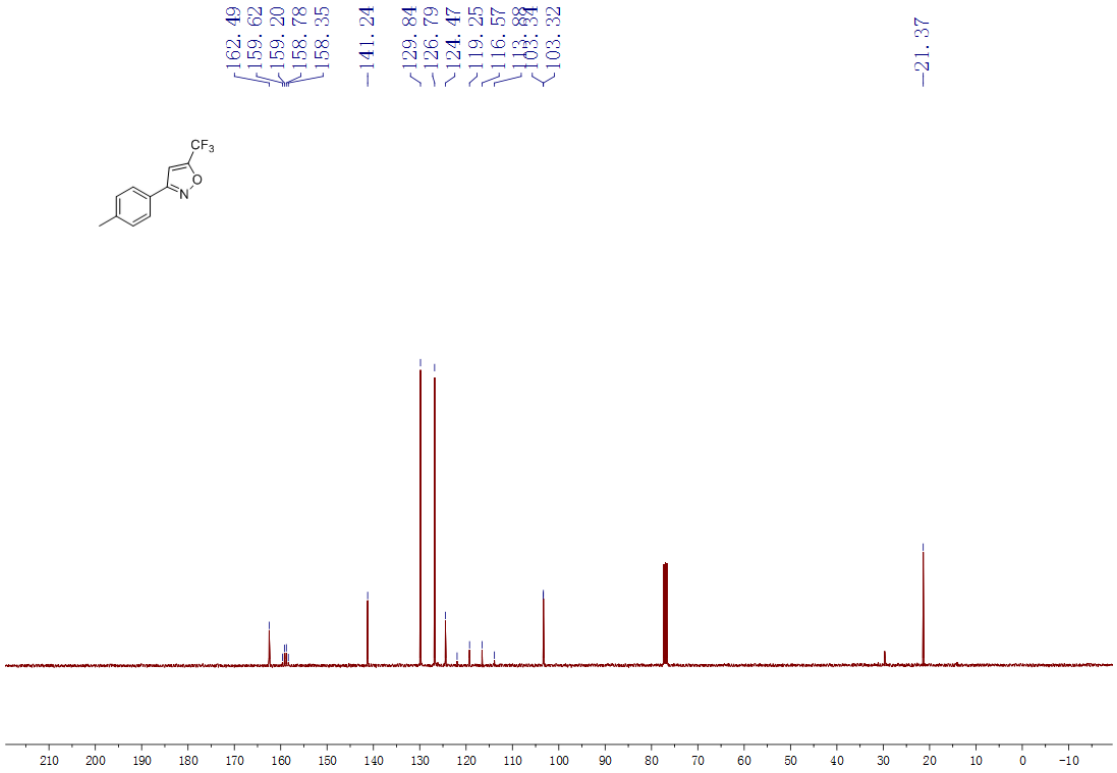
^{1}H NMR spectra of **3f** in $CDCl_3$



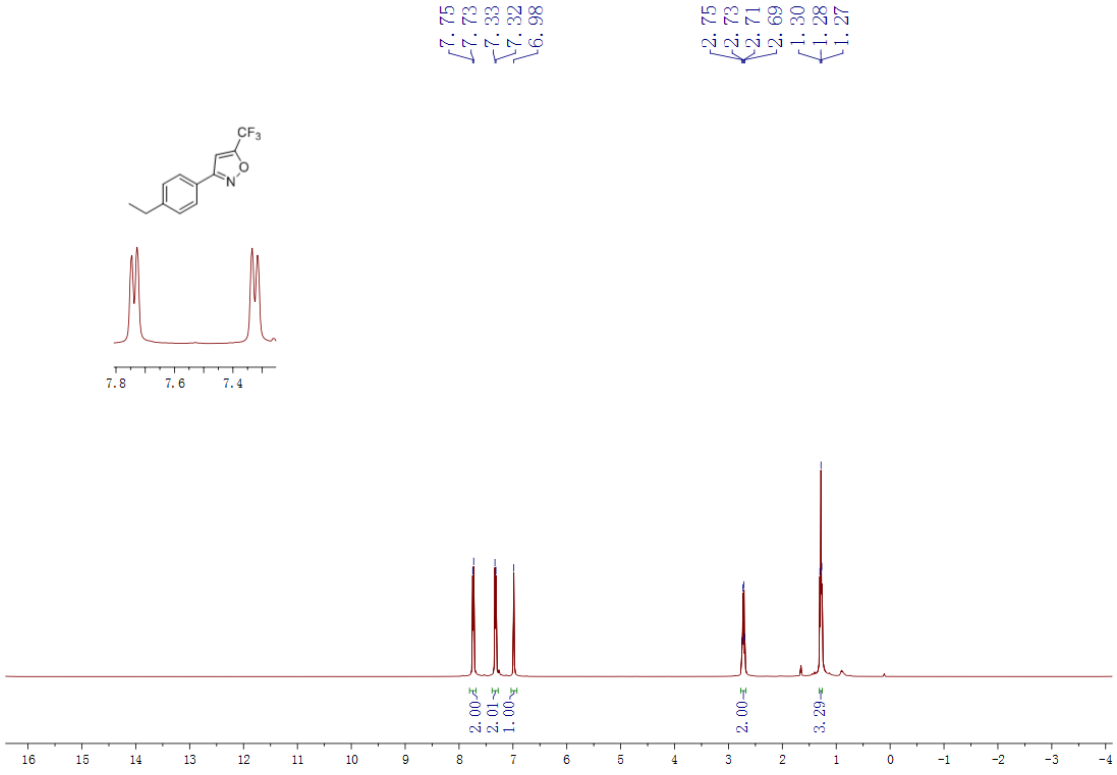
^{19}F NMR spectra of **3f** in $CDCl_3$



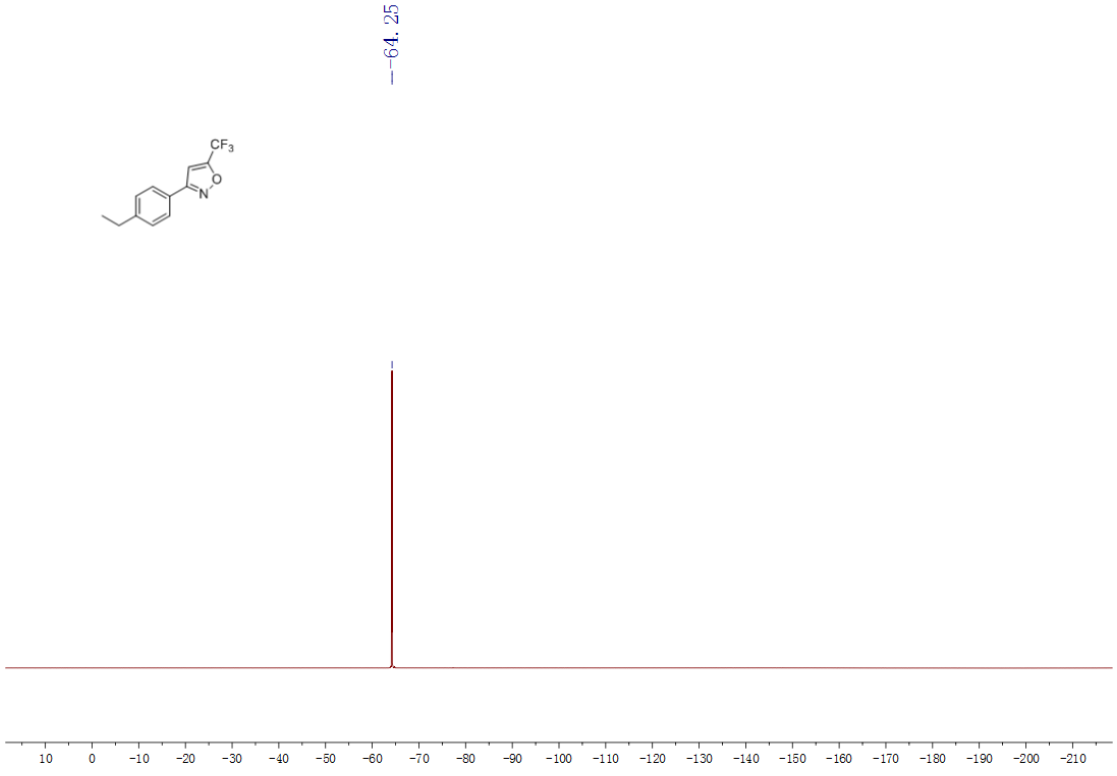
^{13}C NMR spectra of **3f** in $CDCl_3$



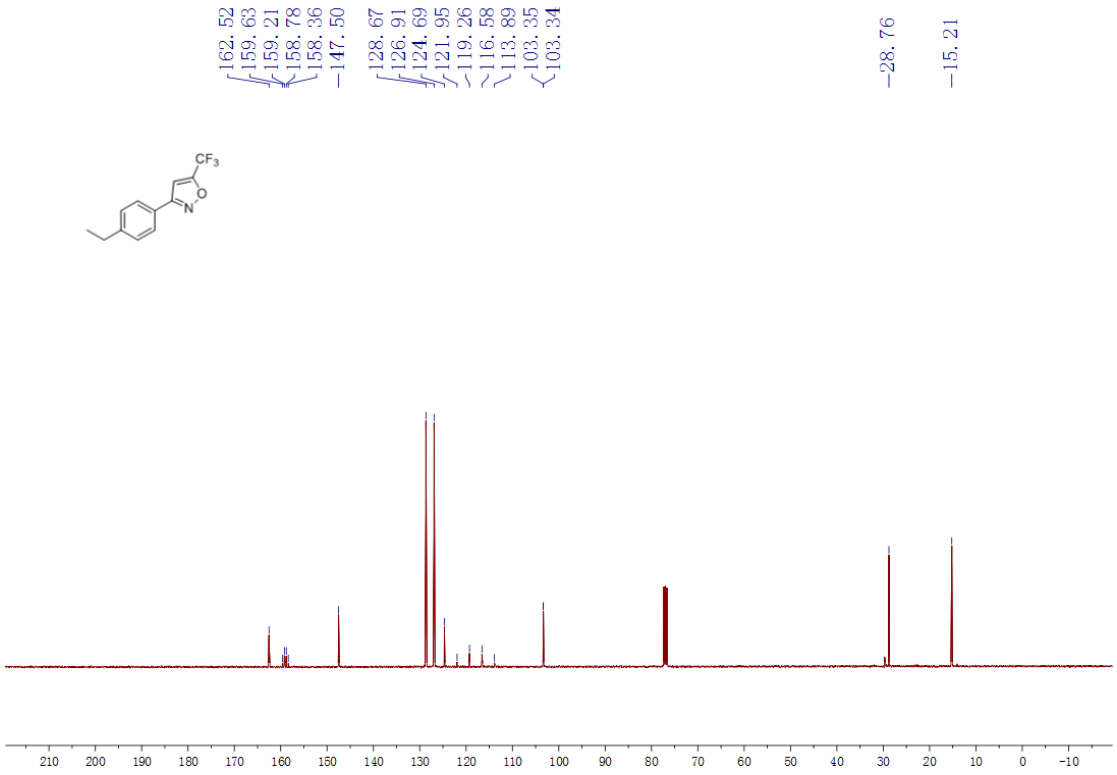
^{1}H NMR spectra of **3g** in $CDCl_3$



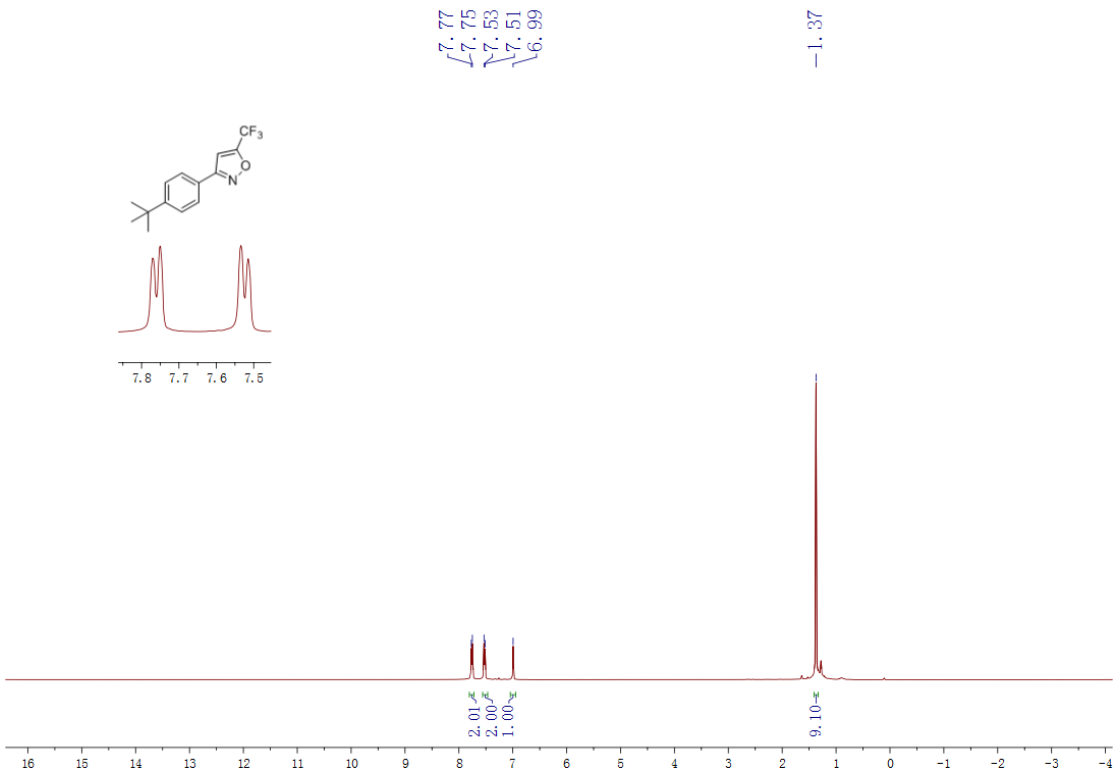
^{19}F NMR spectra of **3g** in $CDCl_3$



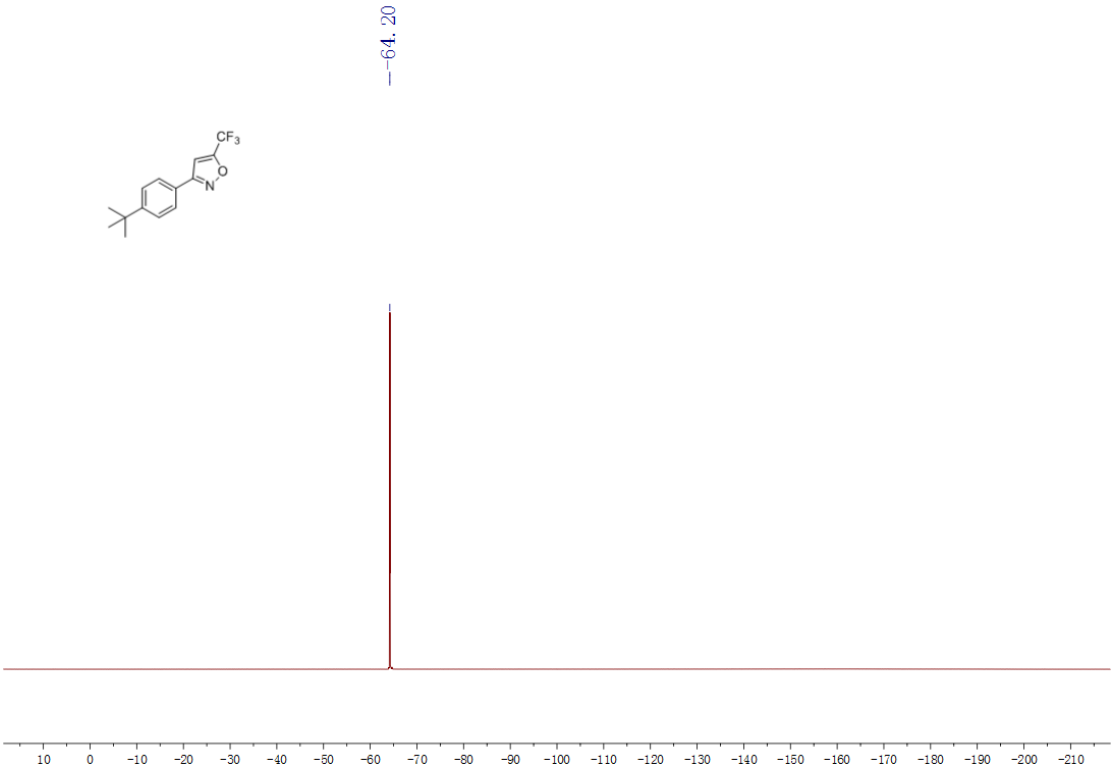
^{13}C NMR spectra of **3g** in $CDCl_3$



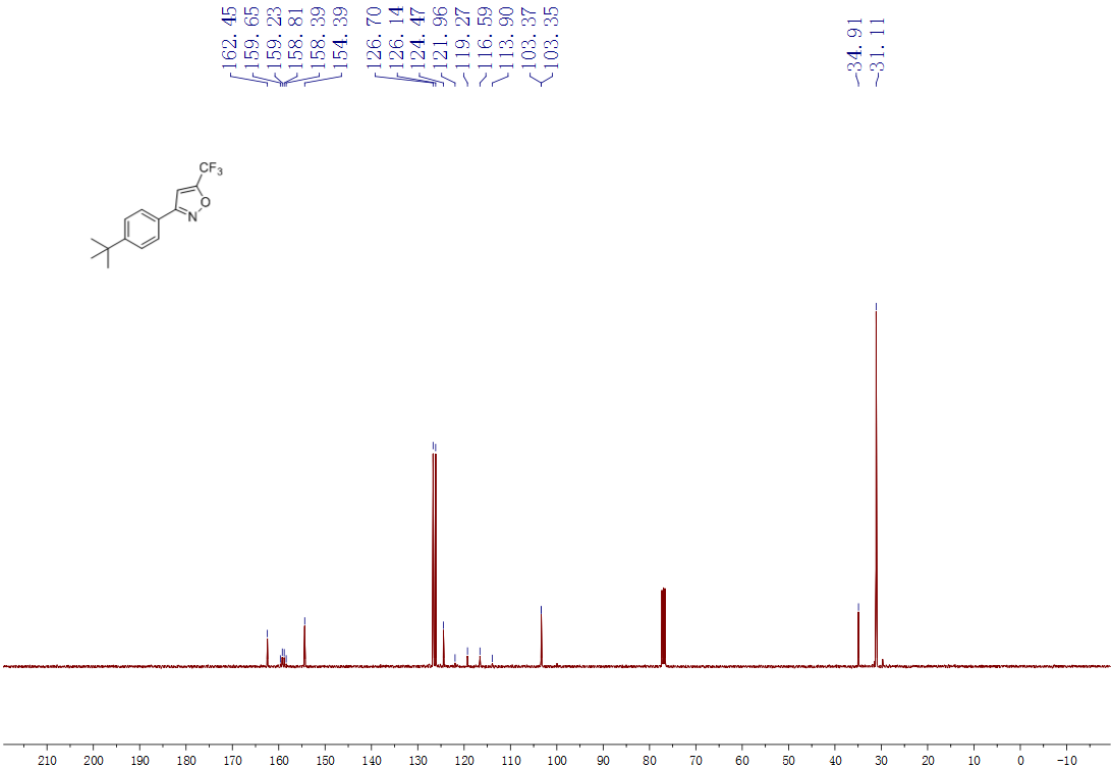
^{1}H NMR spectra of **3h** in $CDCl_3$



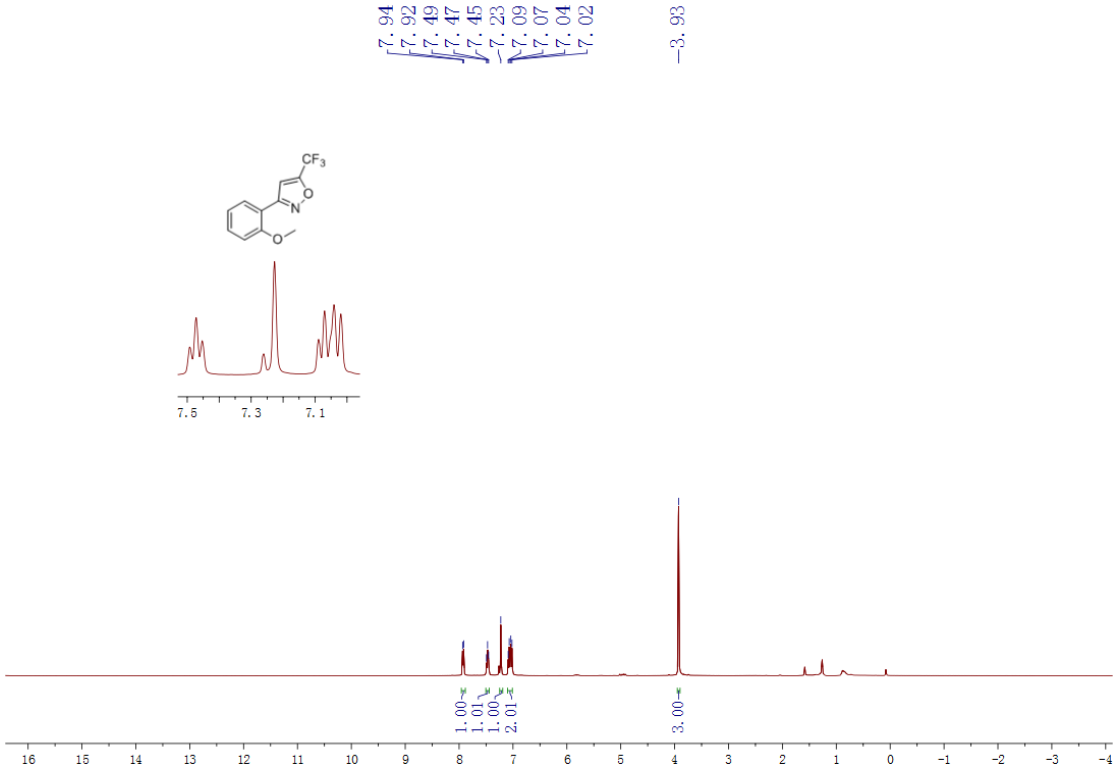
^{19}F NMR spectra of **3h** in $CDCl_3$



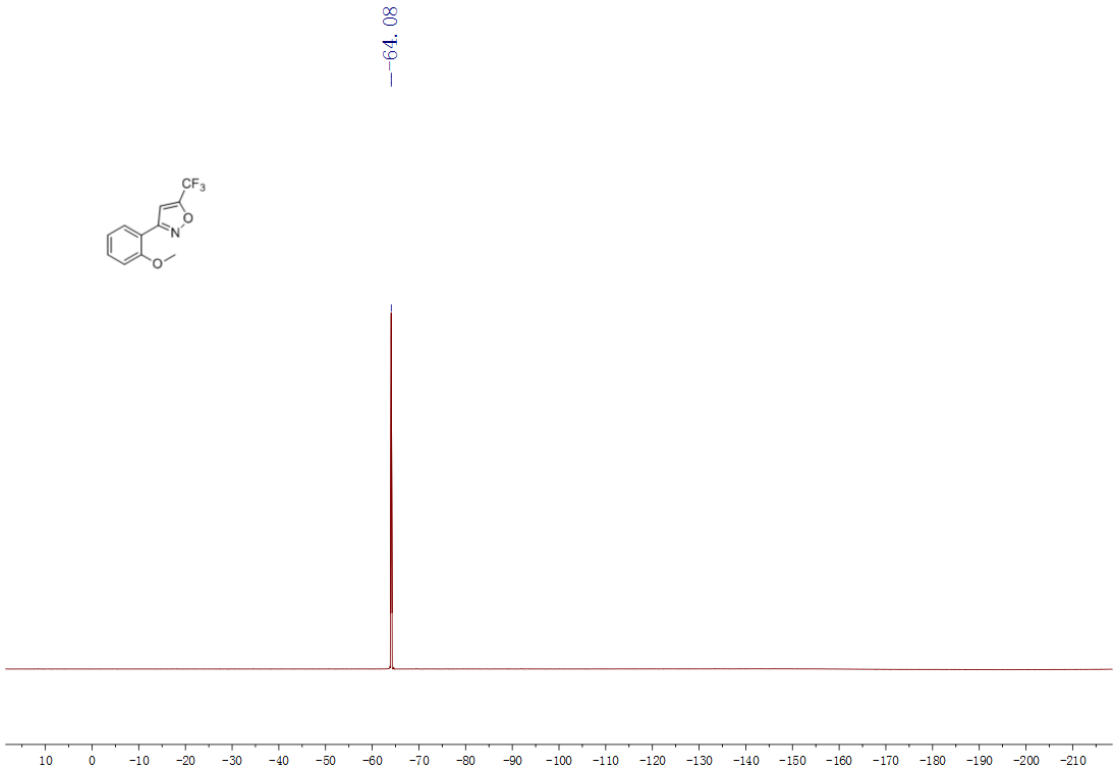
^{13}C NMR spectra of **3h** in $CDCl_3$



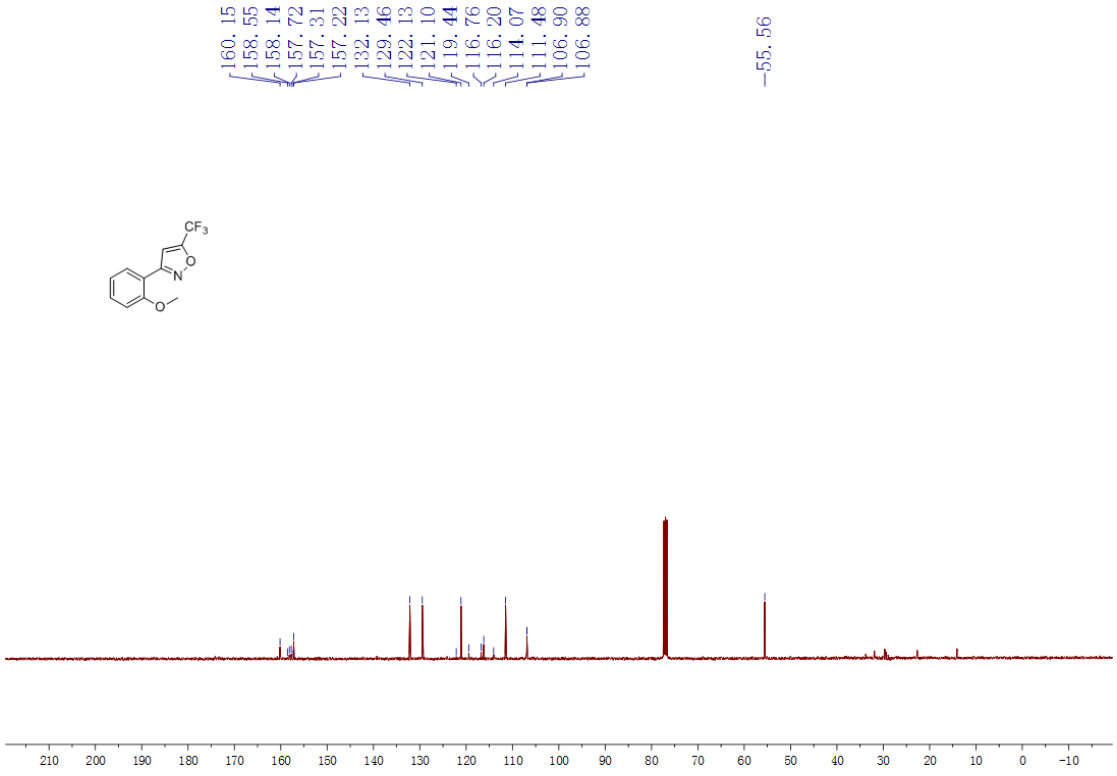
^{1}H NMR spectra of **3i** in $CDCl_3$



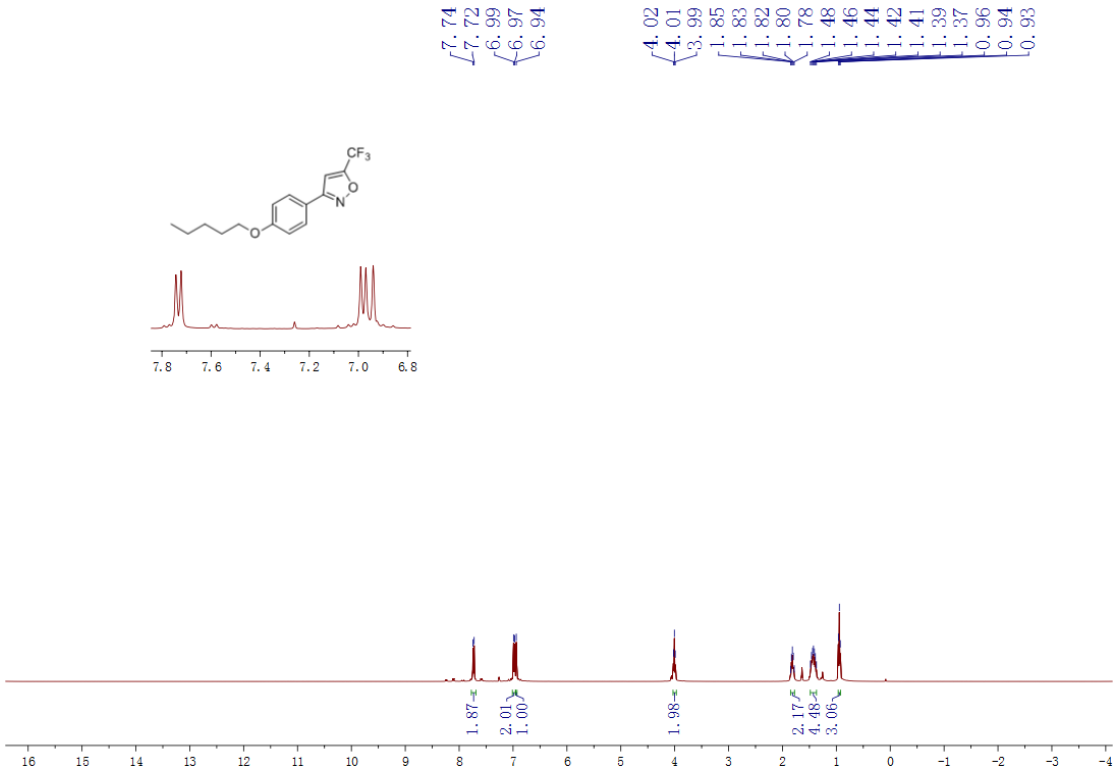
^{19}F NMR spectra of **3i** in $CDCl_3$



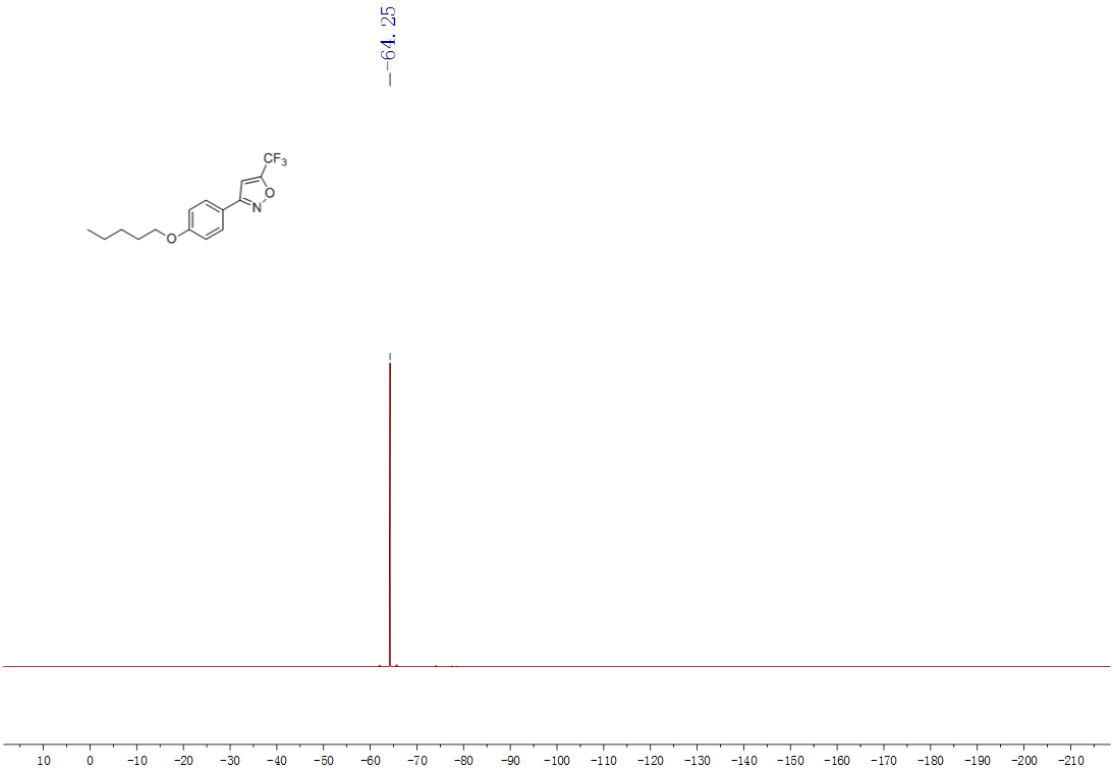
^{13}C NMR spectra of **3i** in $CDCl_3$



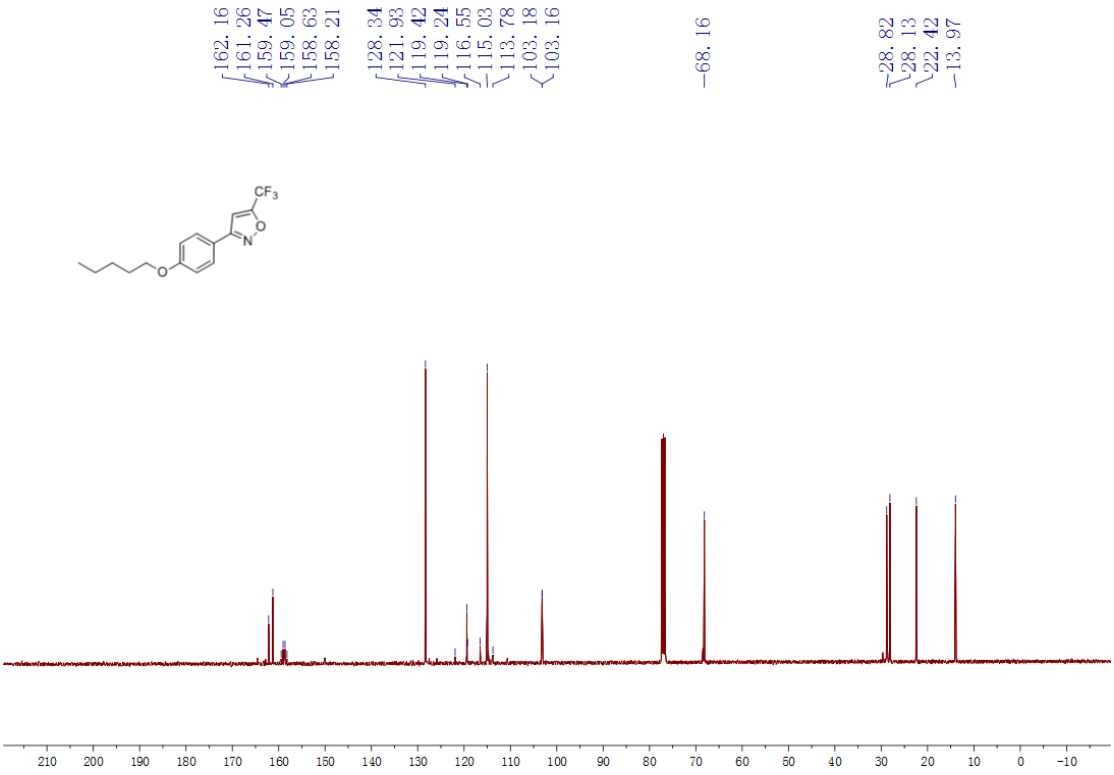
^{1}H NMR spectra of **3j** in $CDCl_3$



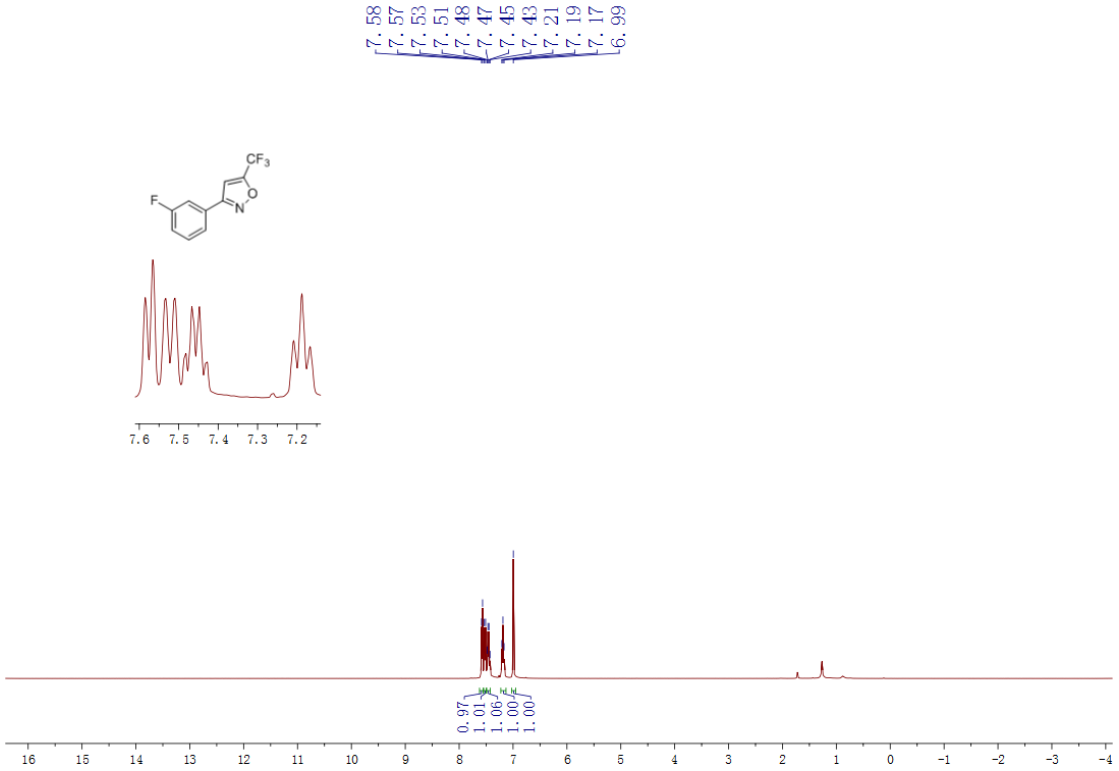
^{19}F NMR spectra of **3j** in $CDCl_3$



^{13}C NMR spectra of **3j** in $CDCl_3$

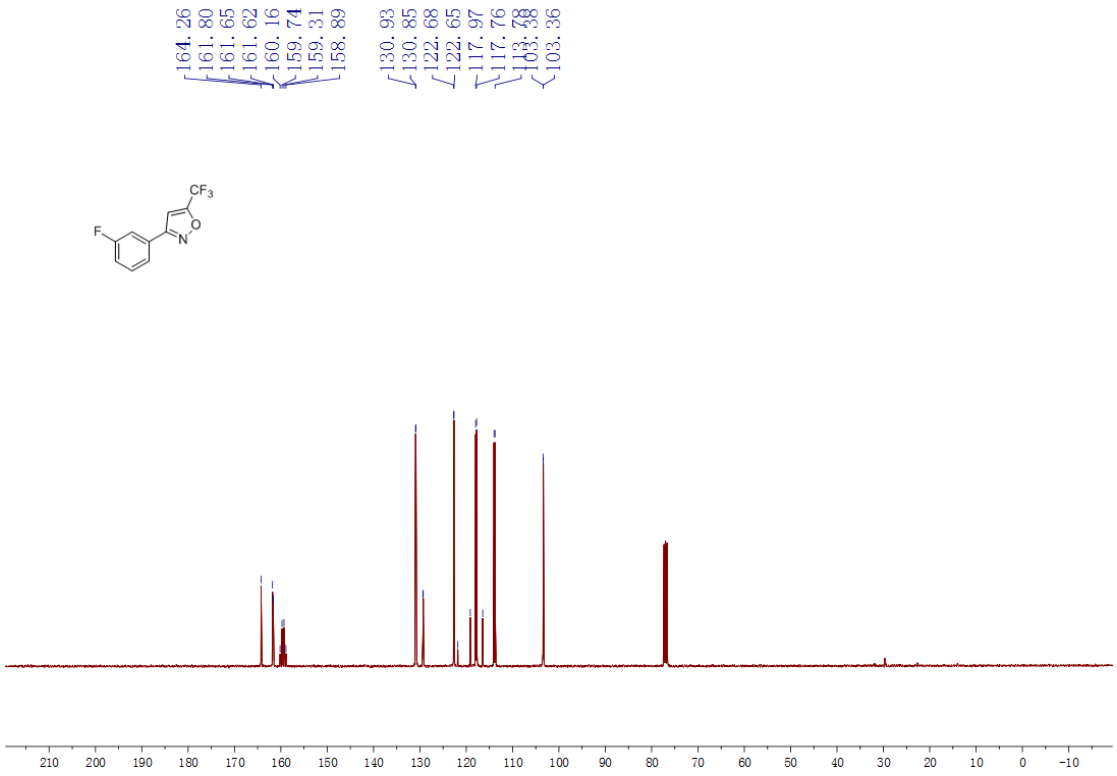


^{1}H NMR spectra of **3k** in $CDCl_3$

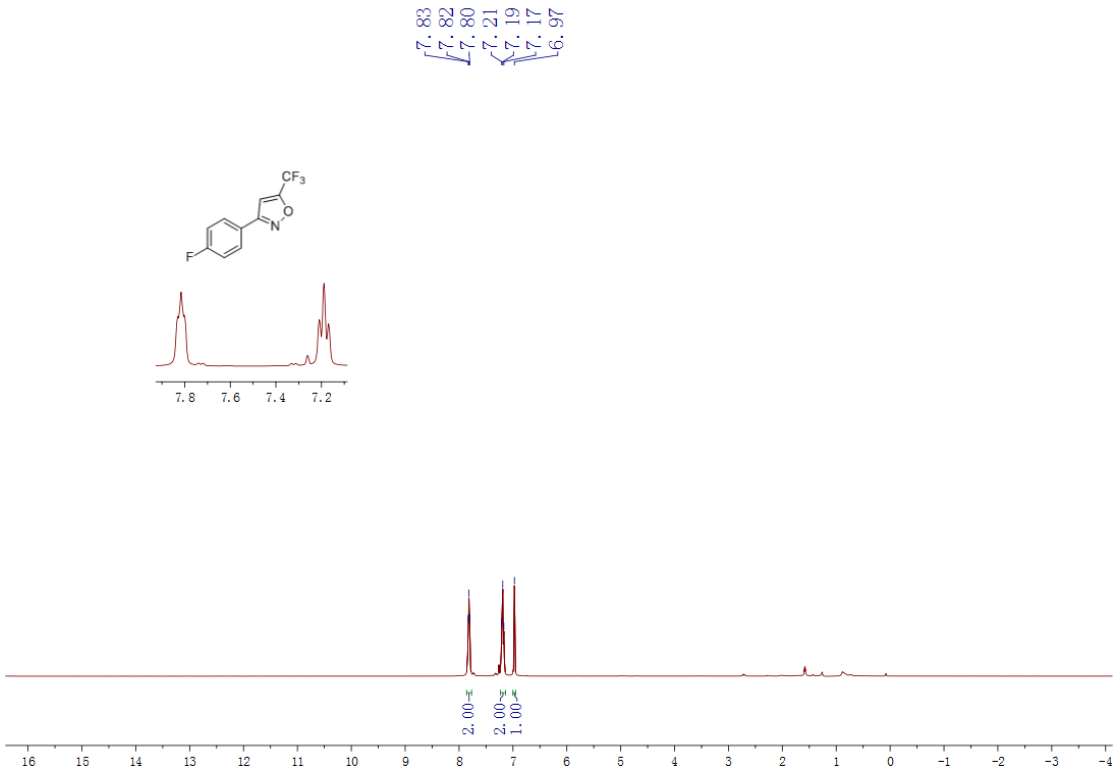


^{19}F NMR spectra of **3k** in $CDCl_3$

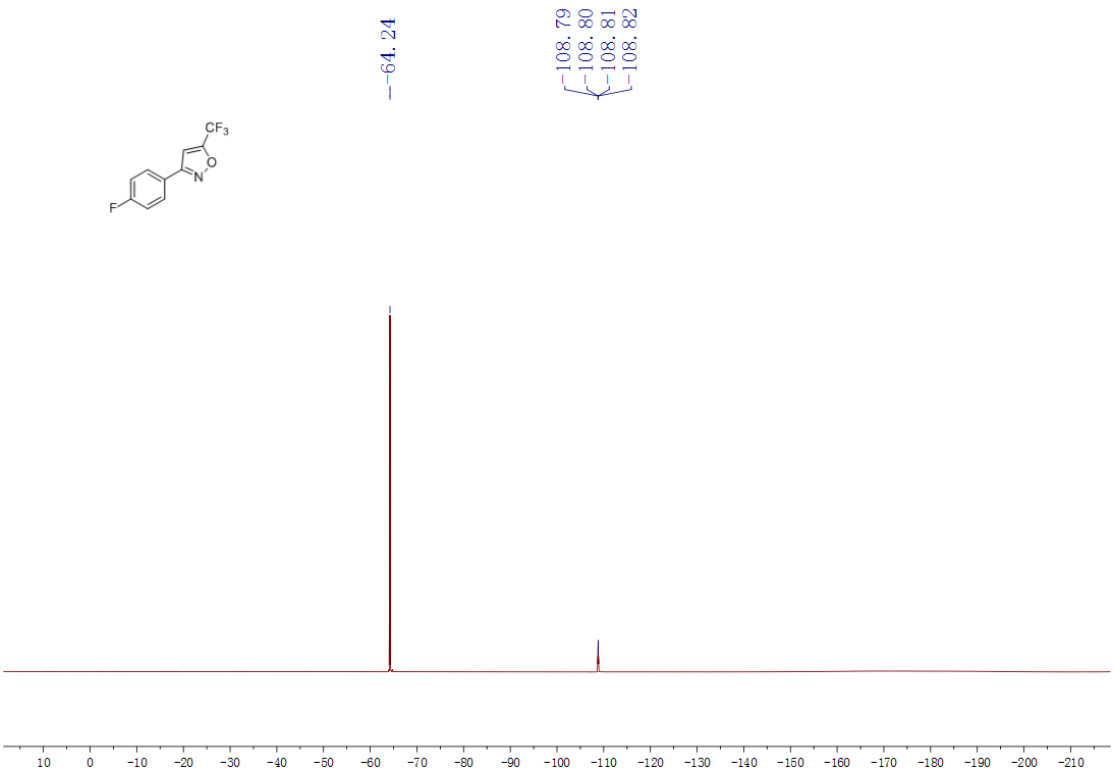
^{13}C NMR spectra of **3k** in $CDCl_3$



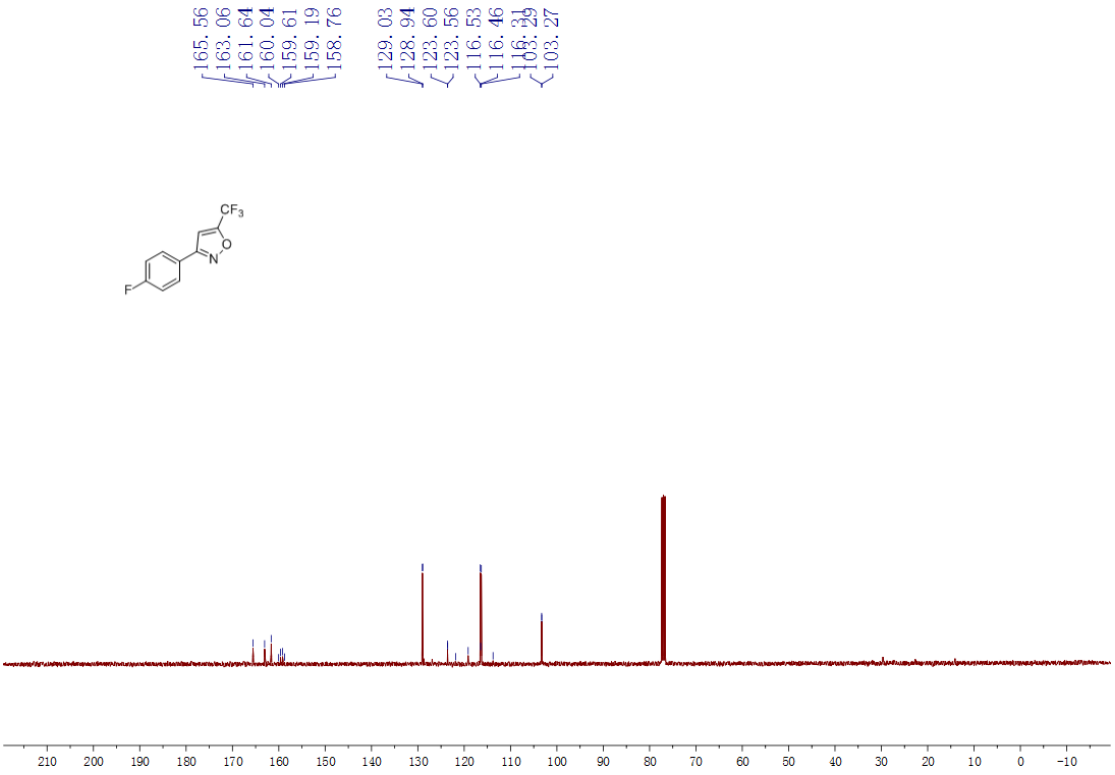
^{1}H NMR spectra of **3l** in $CDCl_3$



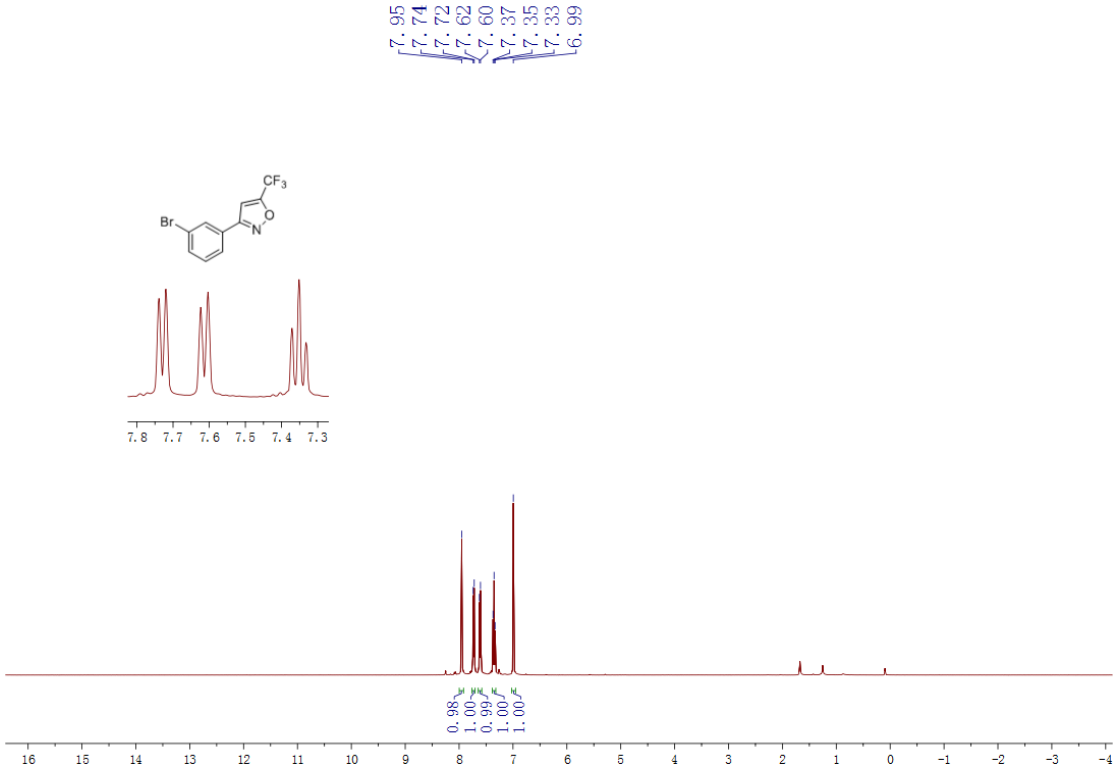
^{19}F NMR spectra of **3l** in $CDCl_3$



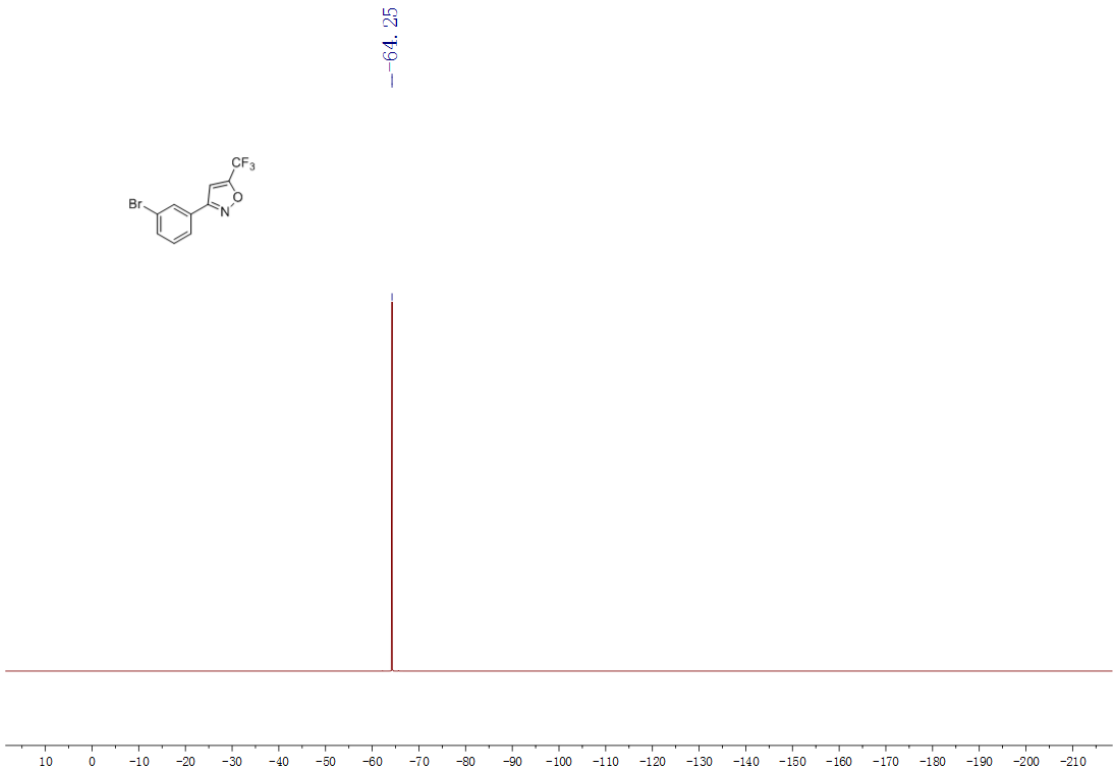
^{13}C NMR spectra of **3l** in $CDCl_3$



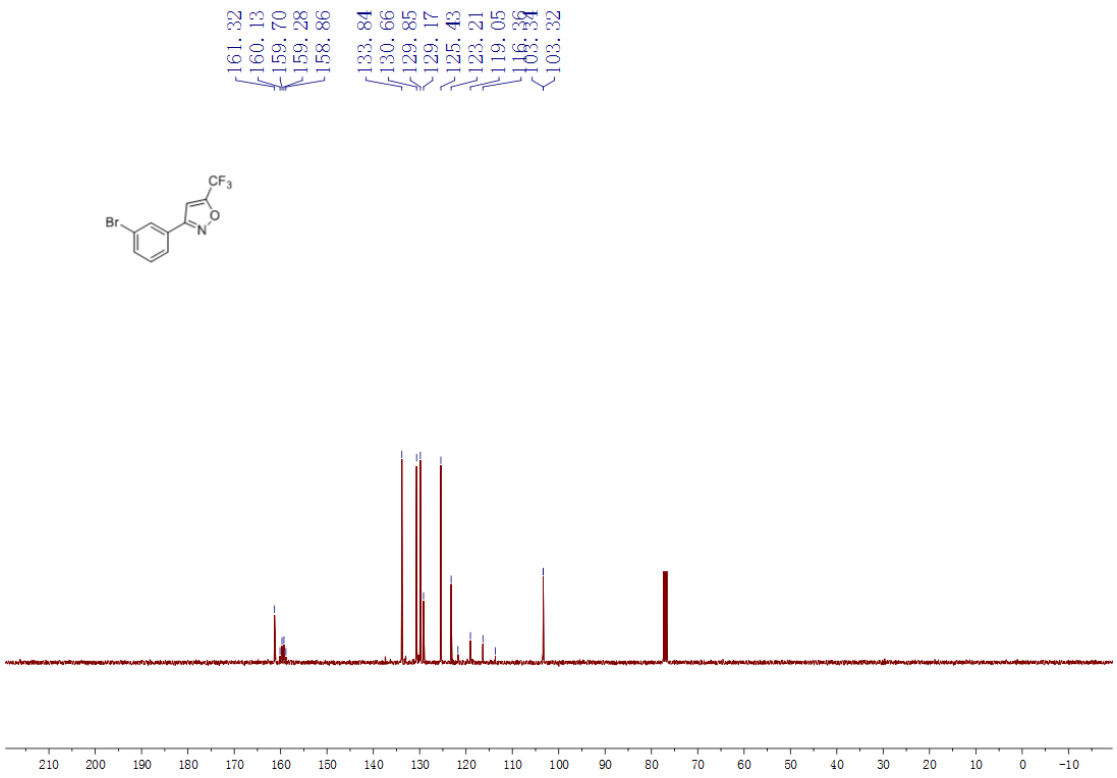
^{1}H NMR spectra of **3m** in $CDCl_3$



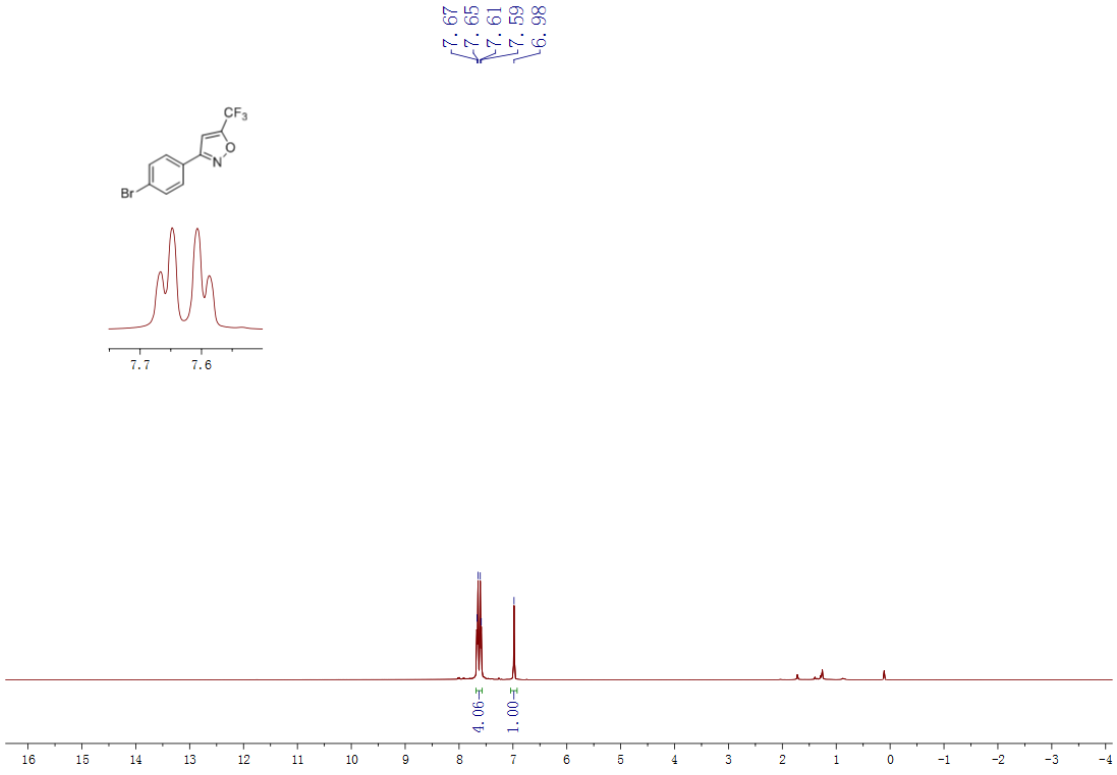
^{19}F NMR spectra of **3m** in $CDCl_3$



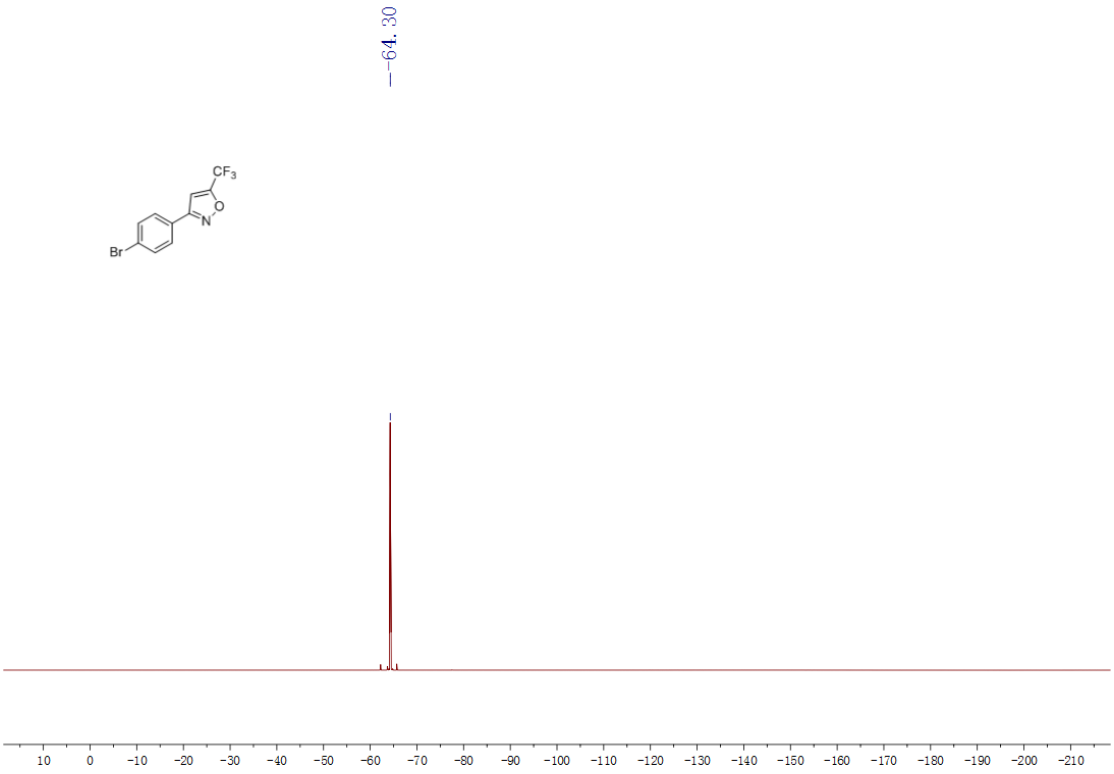
^{13}C NMR spectra of **3m** in $CDCl_3$



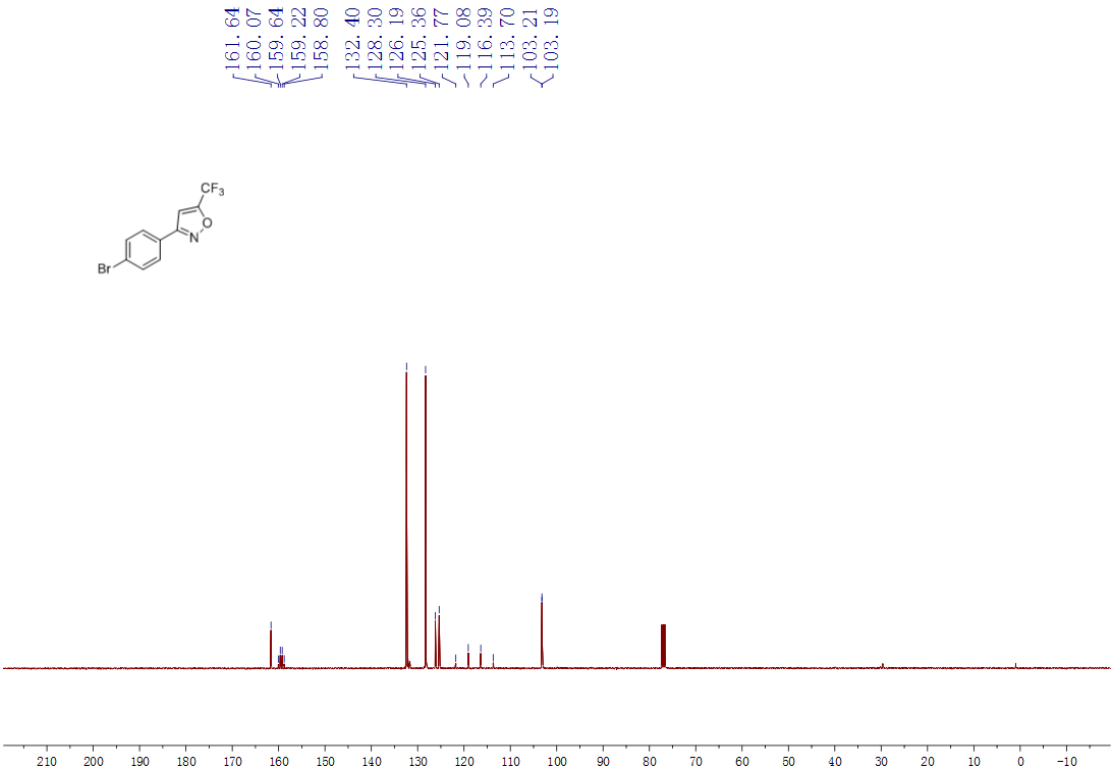
^{1}H NMR spectra of **3n** in $CDCl_3$



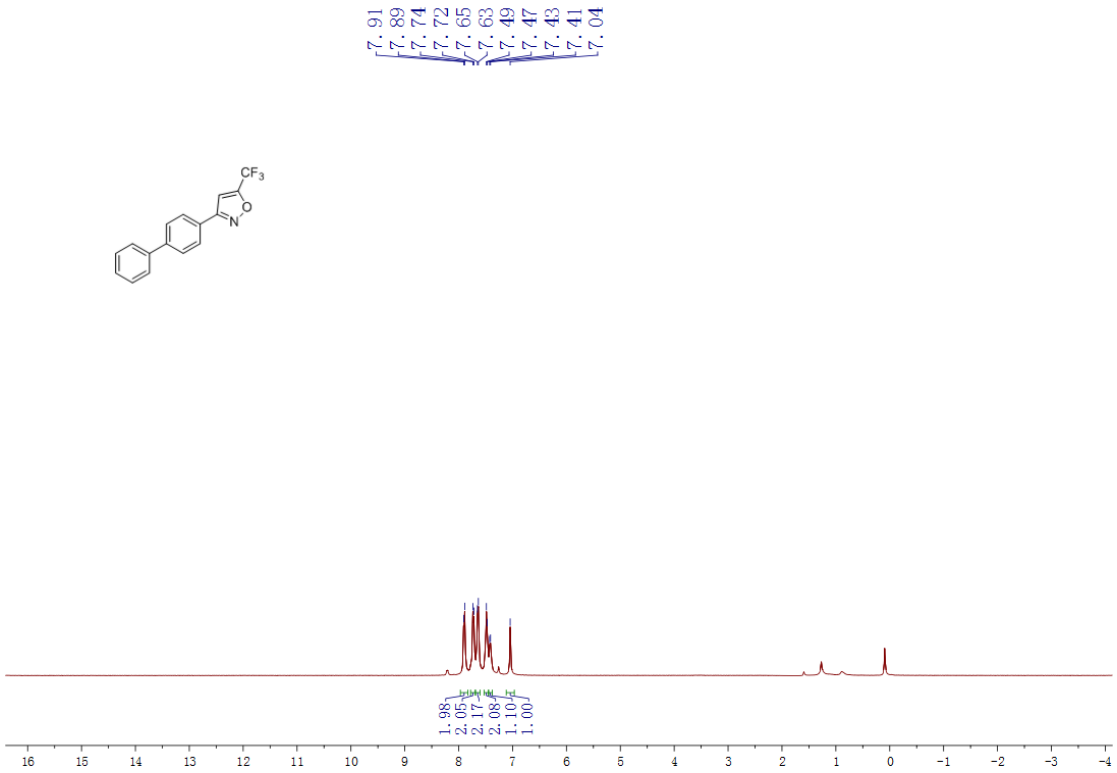
^{19}F NMR spectra of **3n** in $CDCl_3$



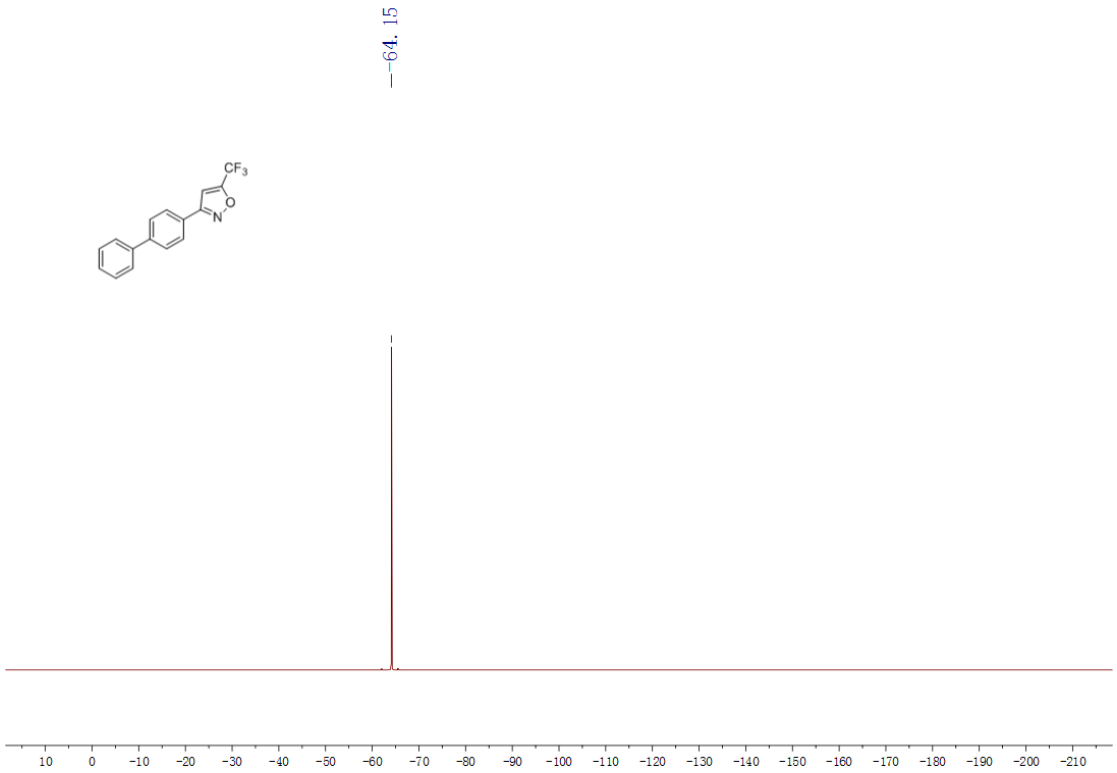
^{13}C NMR spectra of **3n** in $CDCl_3$



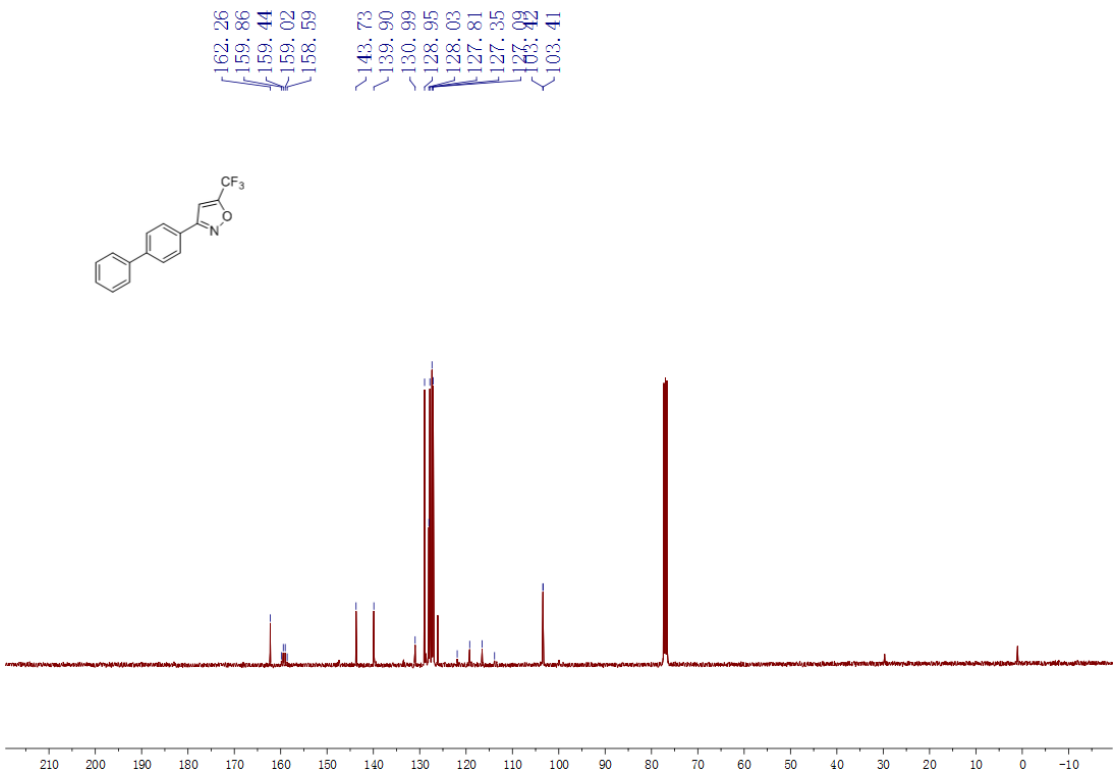
^{1}H NMR spectra of **3o** in $CDCl_3$



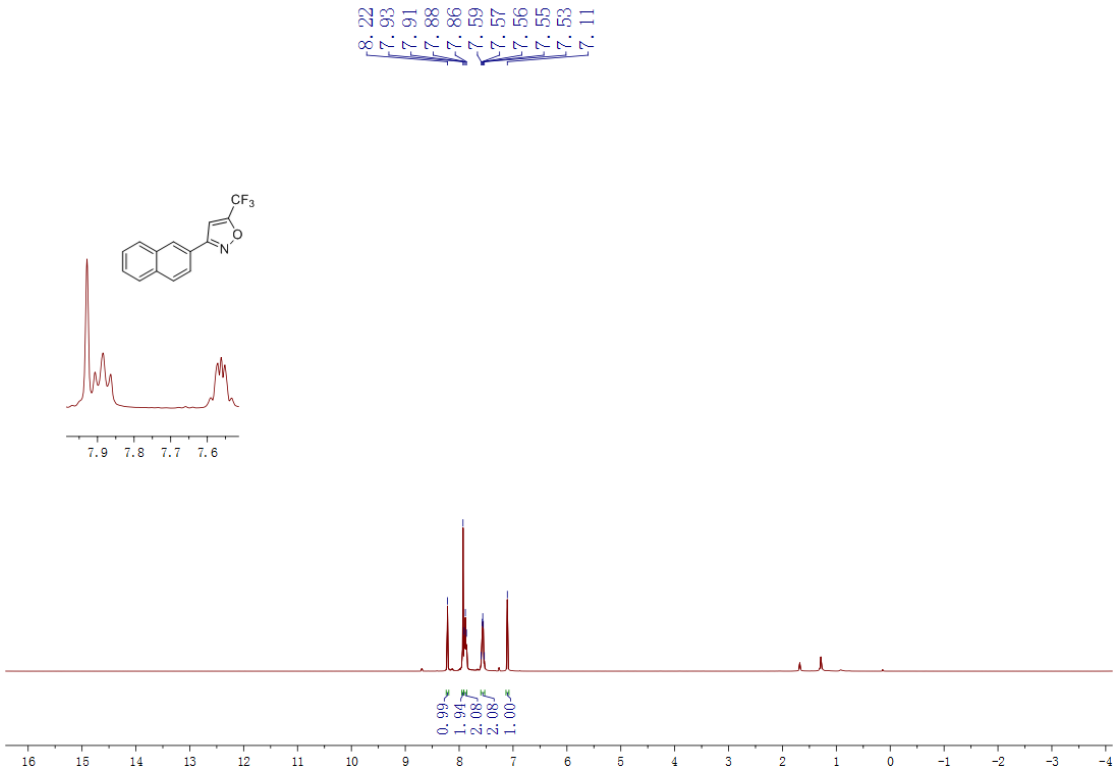
^{19}F NMR spectra of **3o** in $CDCl_3$



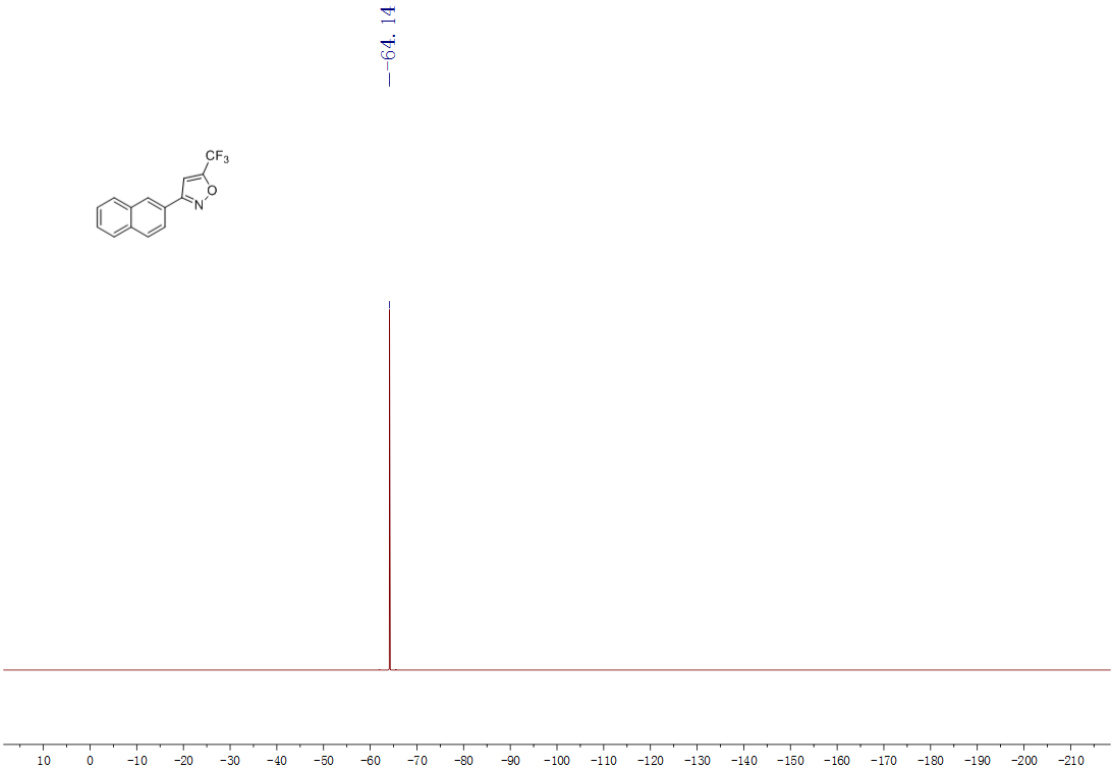
^{13}C NMR spectra of **3o** in $CDCl_3$



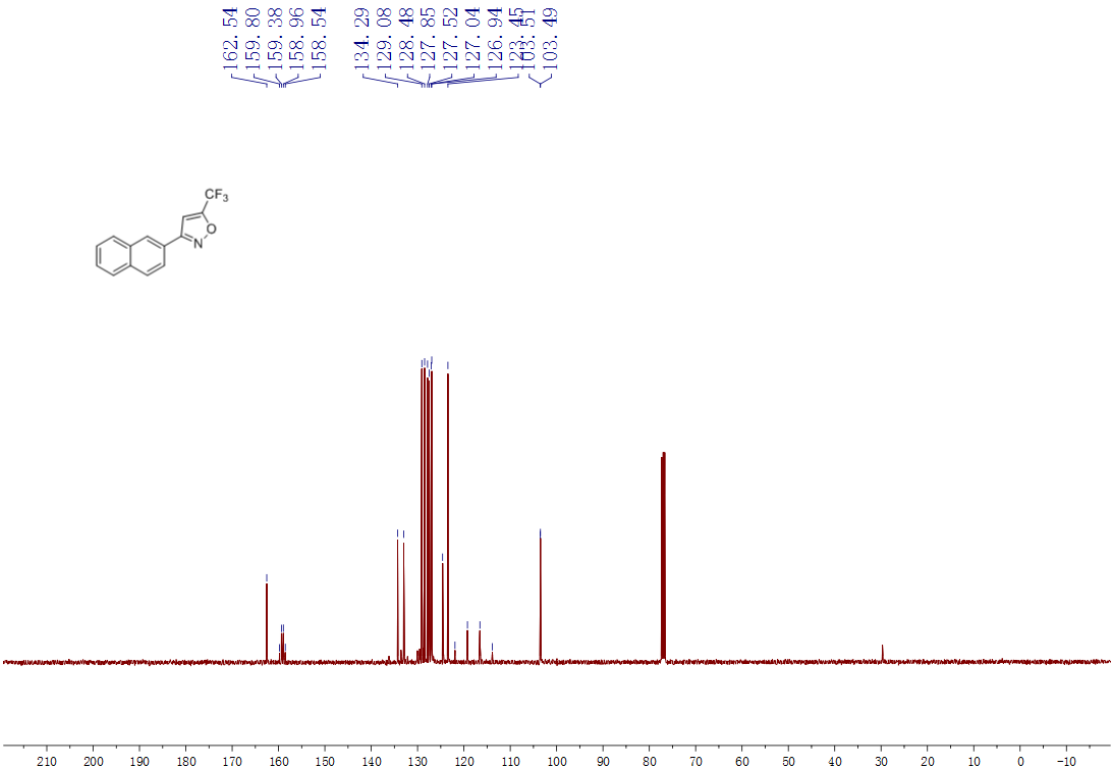
^{1}H NMR spectra of **3p** in $CDCl_3$



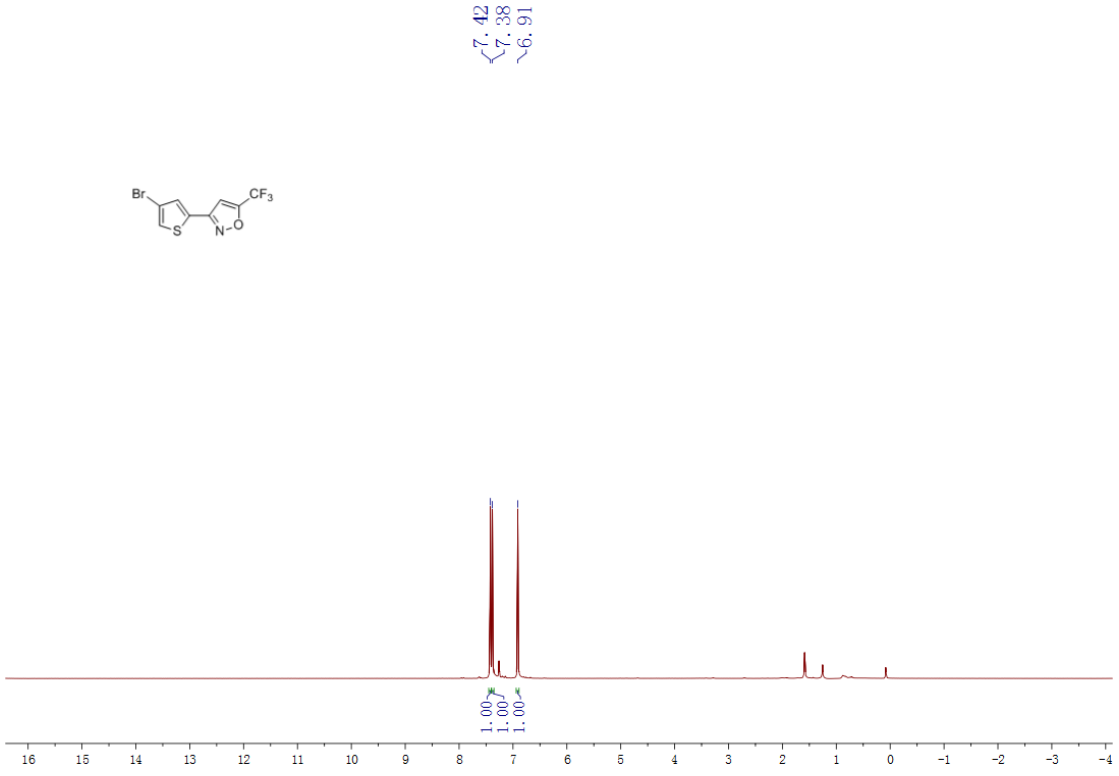
^{19}F NMR spectra of **3p** in $CDCl_3$



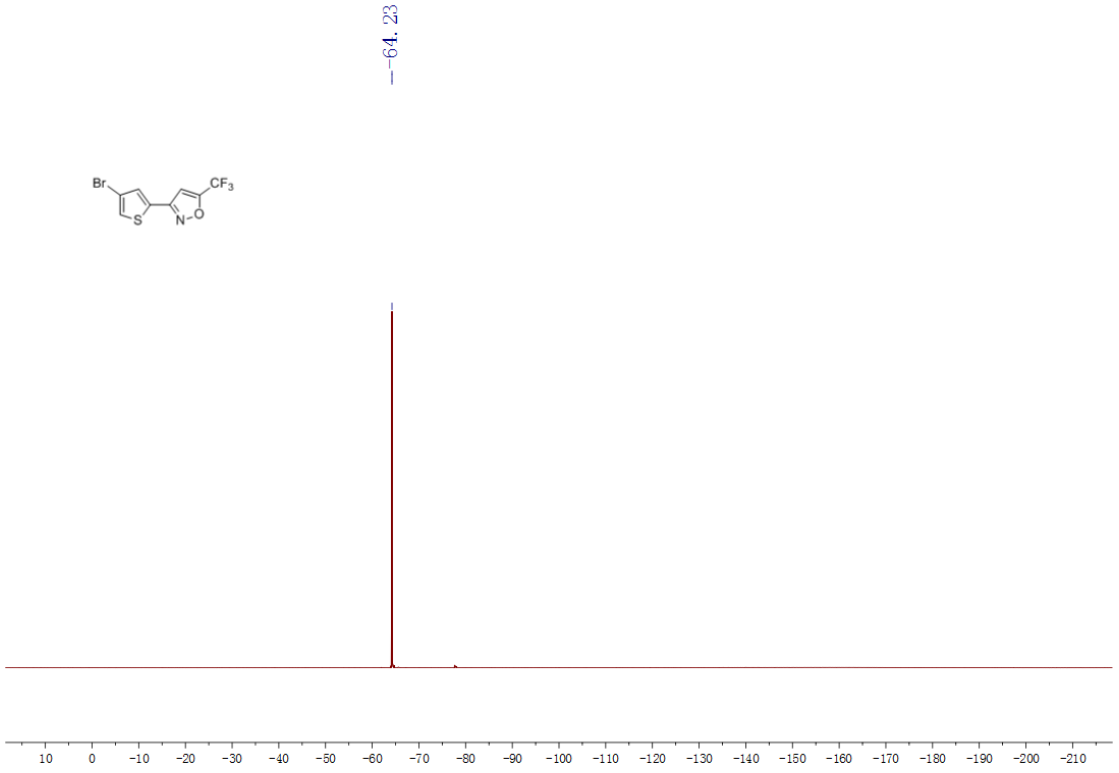
^{13}C NMR spectra of **3p** in $CDCl_3$



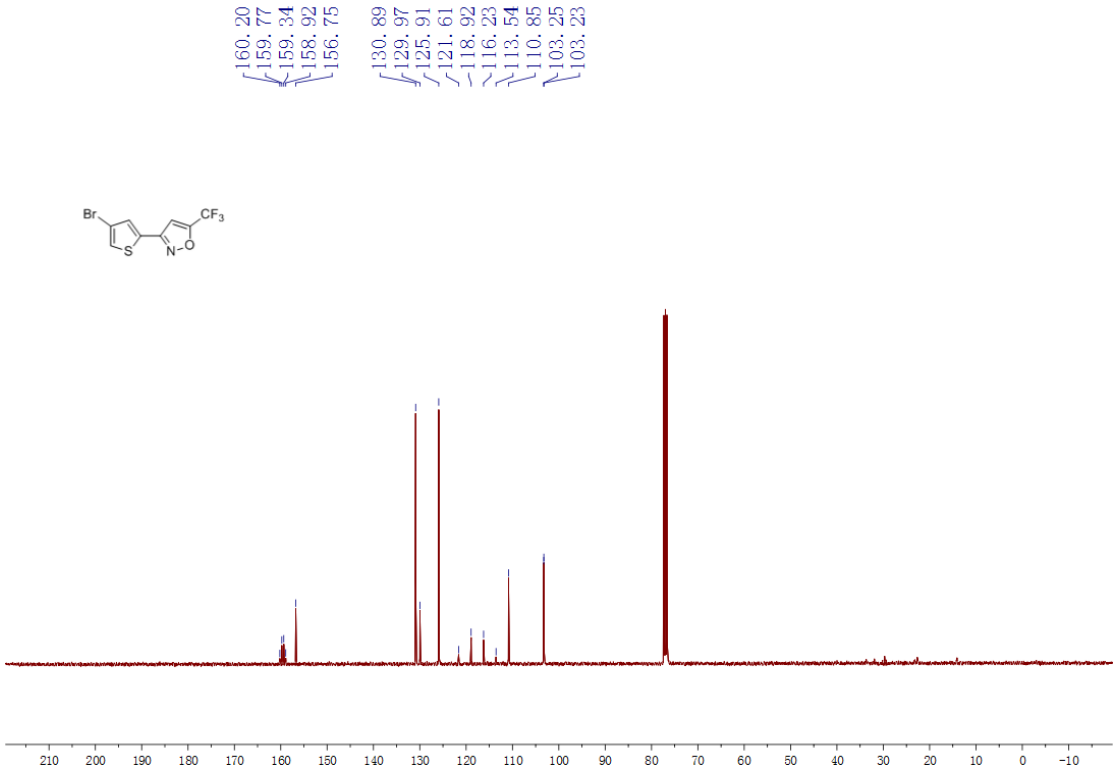
^{1}H NMR spectra of **3q** in $CDCl_3$



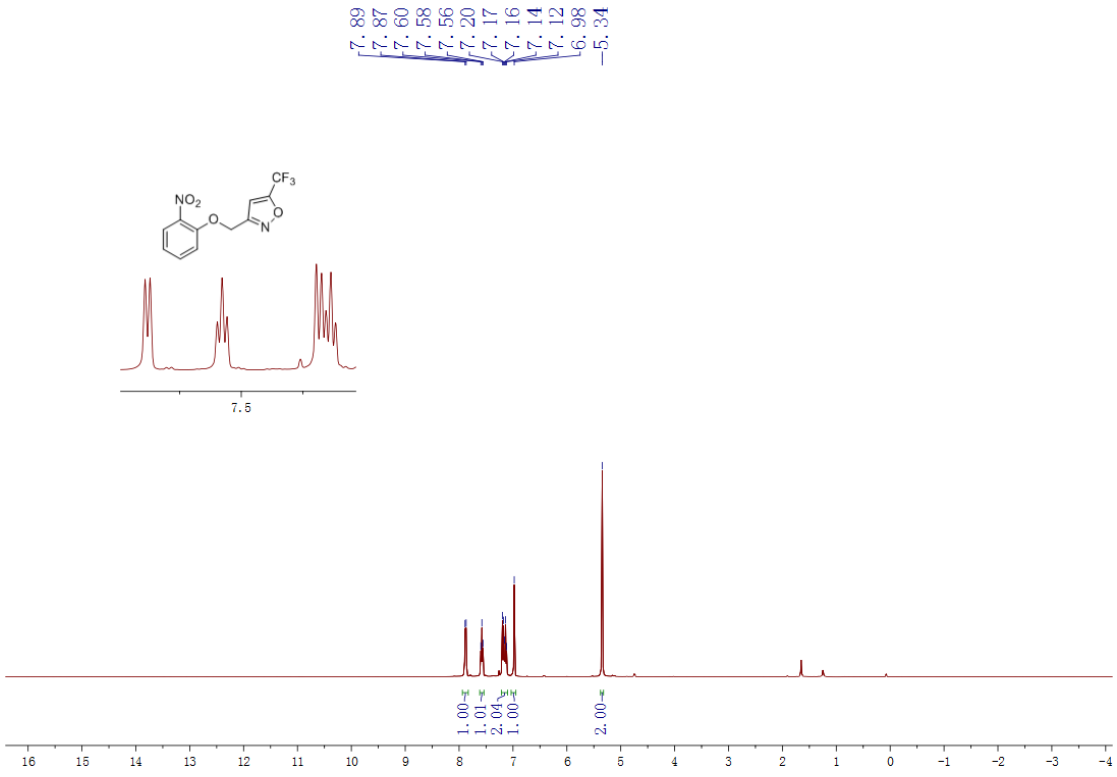
^{19}F NMR spectra of **3q** in $CDCl_3$



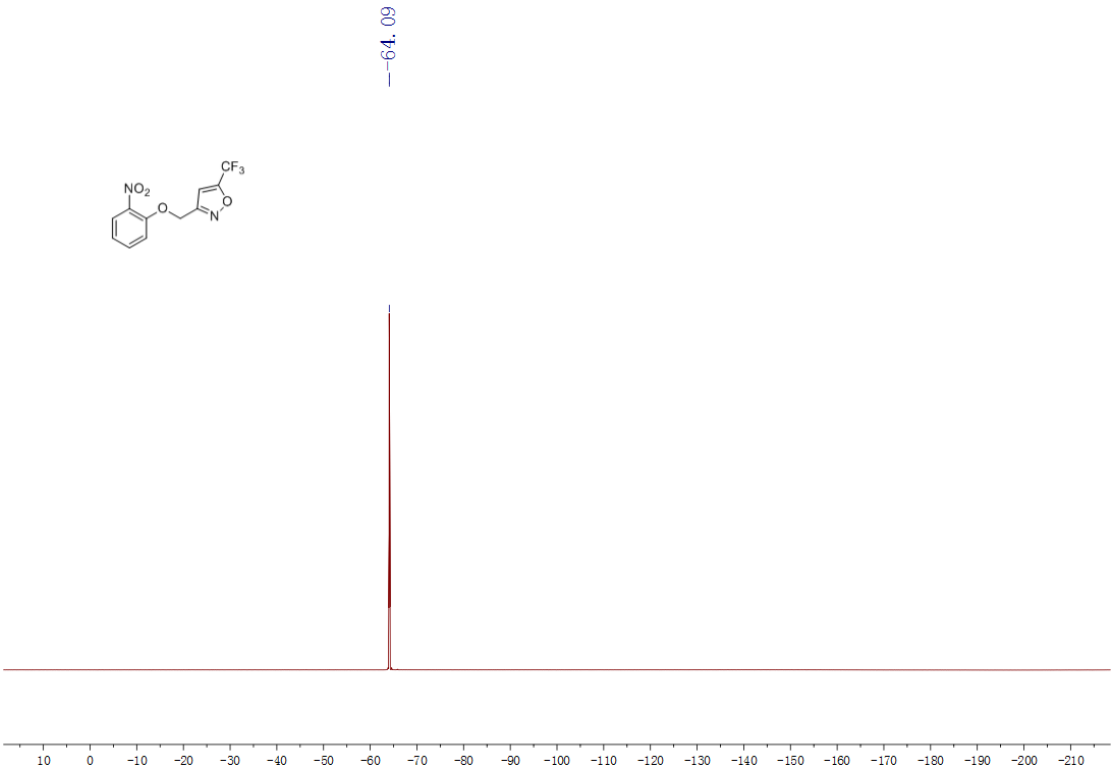
^{13}C NMR spectra of **3q** in $CDCl_3$



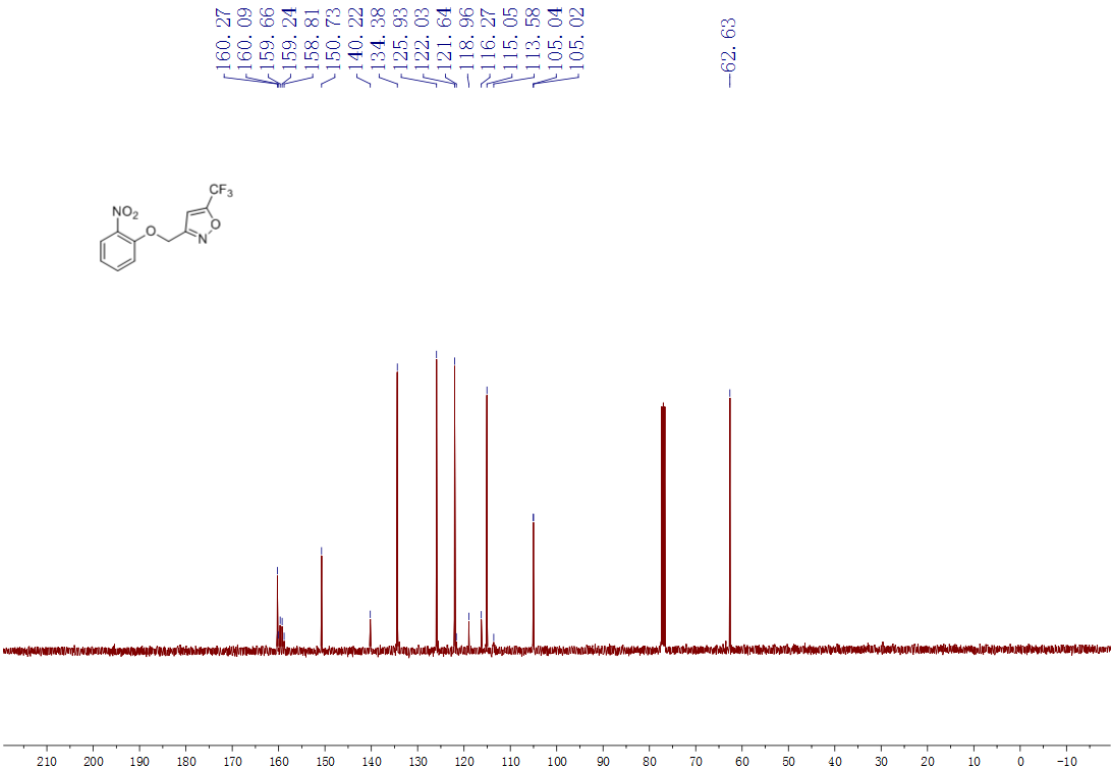
^{1}H NMR spectra of **4a** in $CDCl_3$



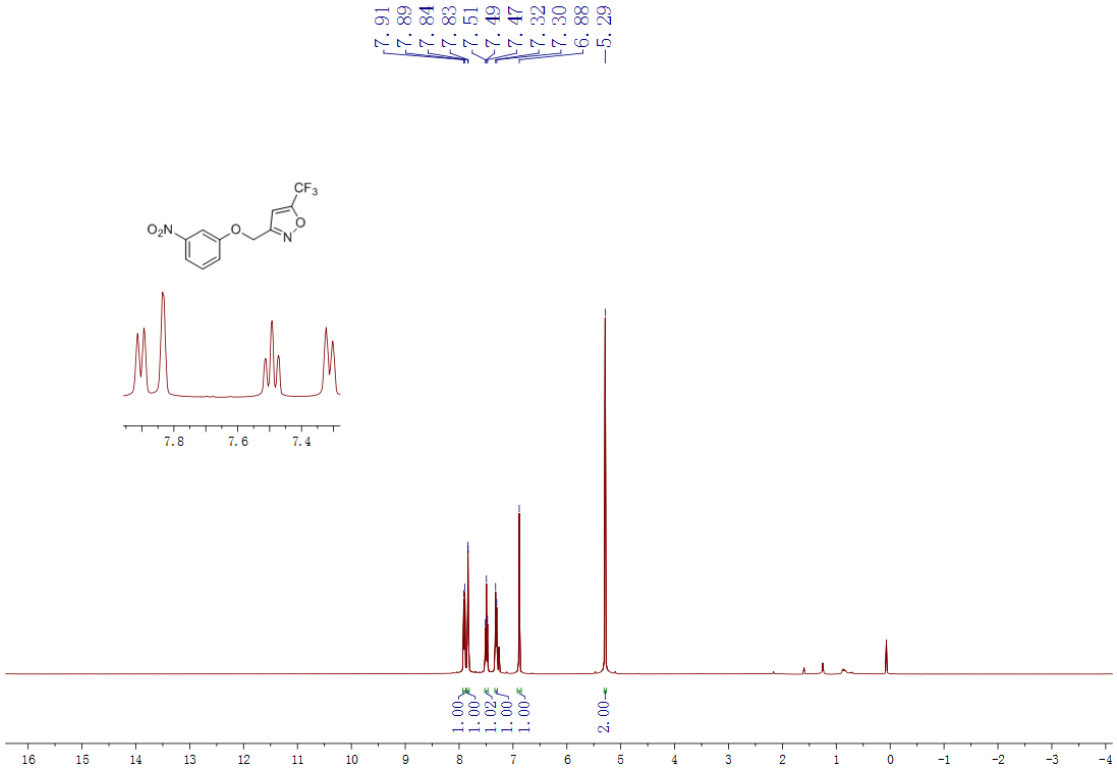
^{19}F NMR spectra of **4a** in $CDCl_3$



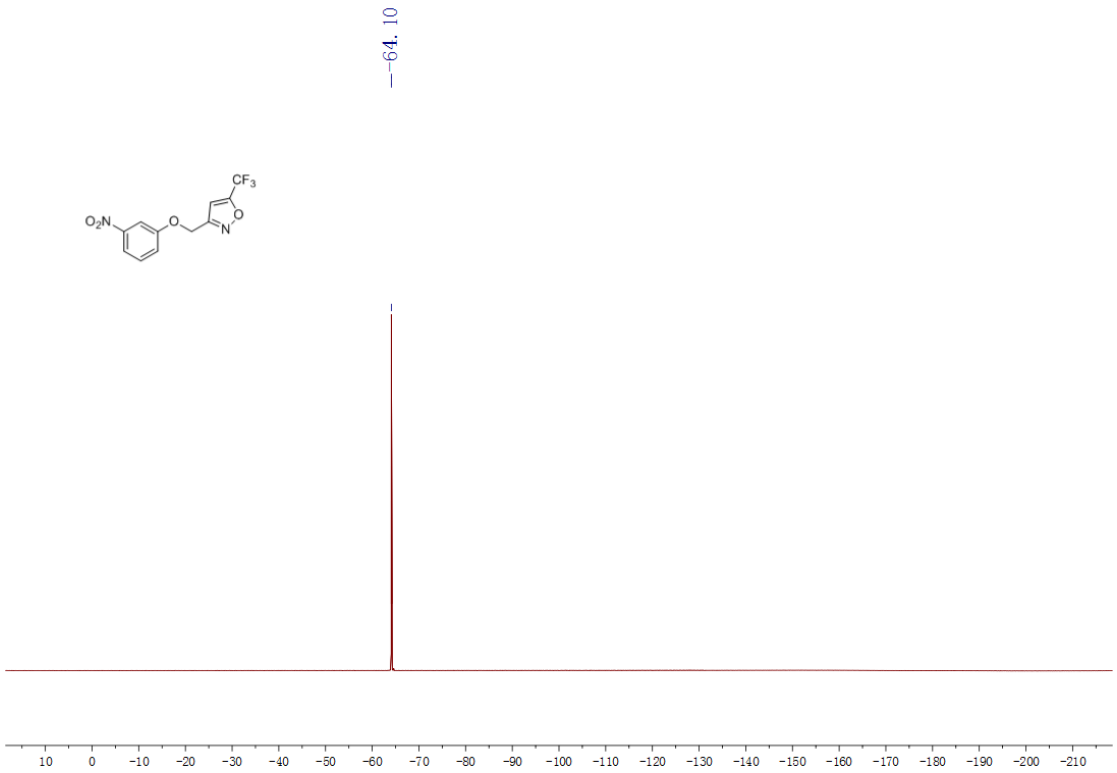
^{13}C NMR spectra of **4a** in $CDCl_3$



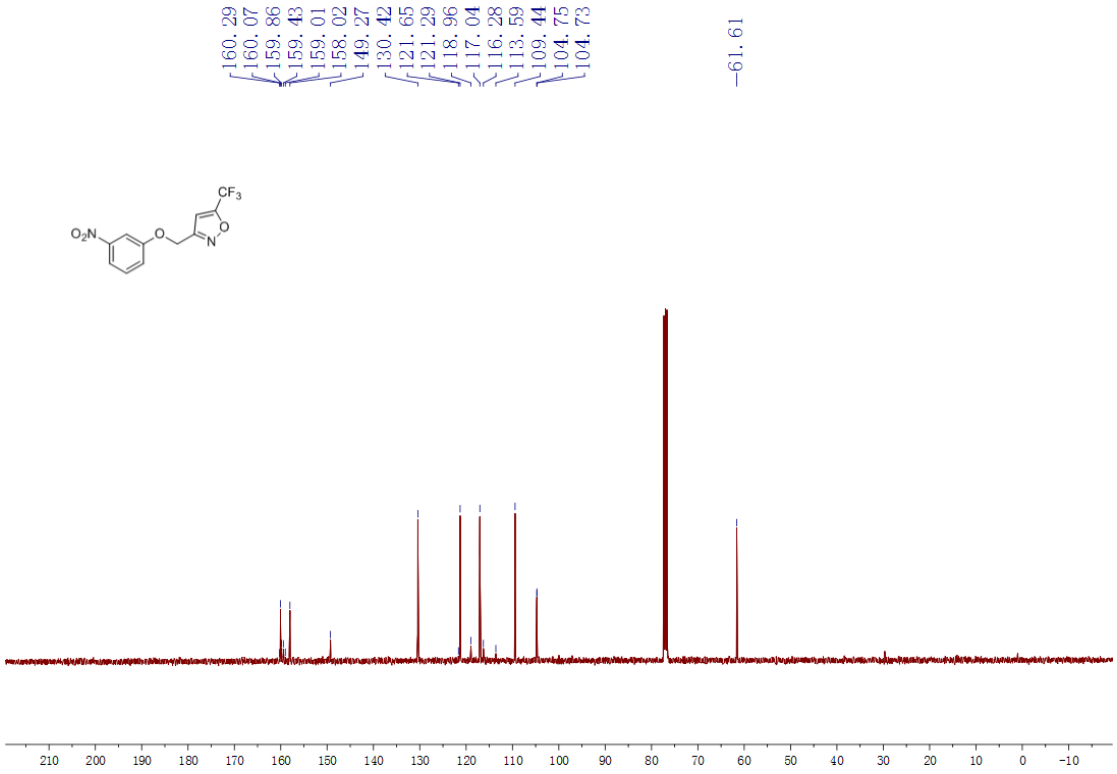
^{1}H NMR spectra of **4b** in $CDCl_3$



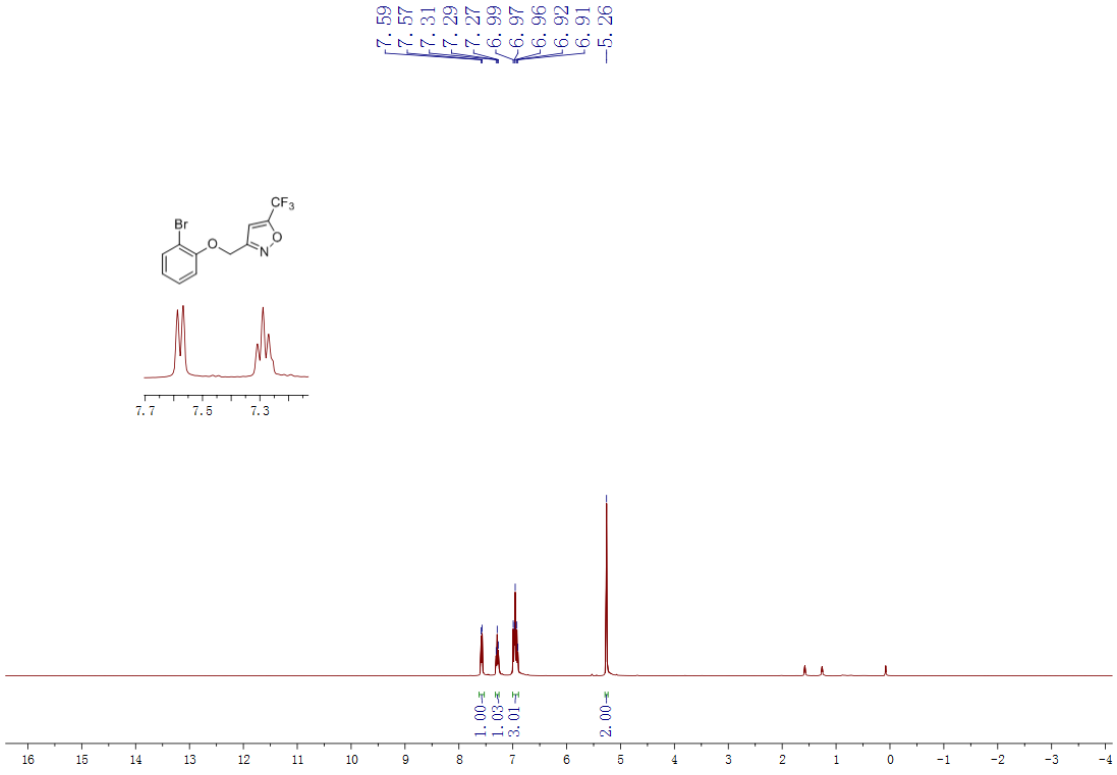
^{19}F NMR spectra of **4b** in $CDCl_3$



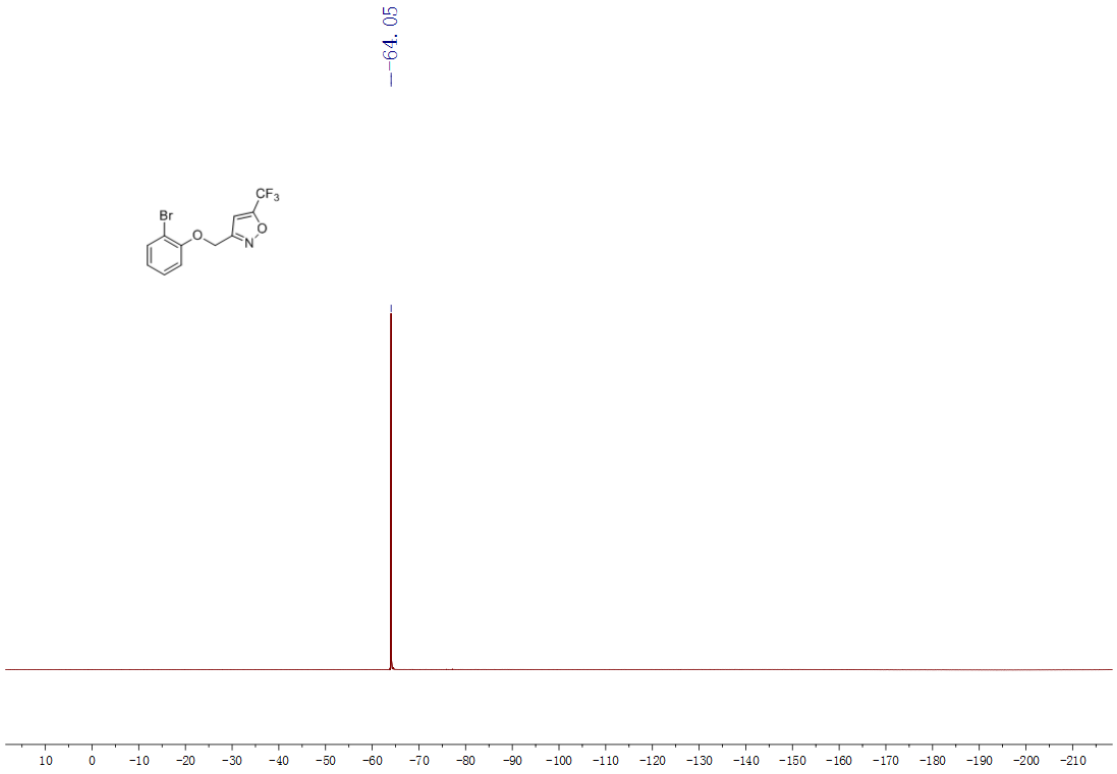
^{13}C NMR spectra of **4b** in $CDCl_3$



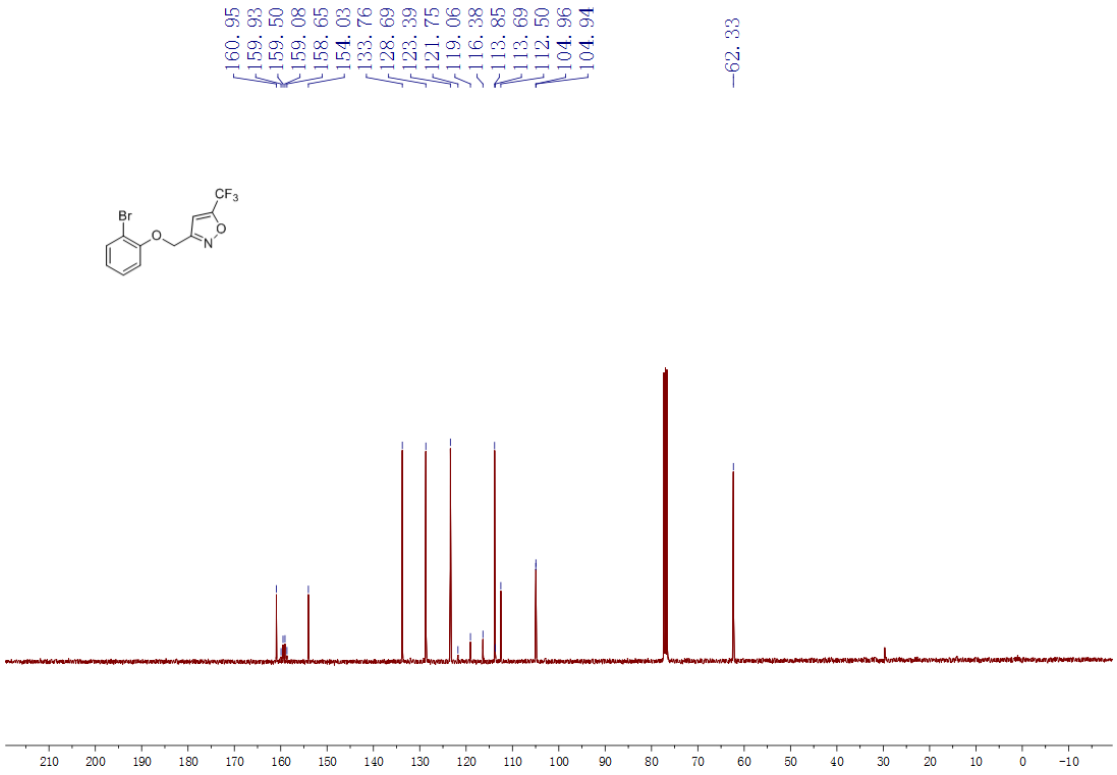
^{1}H NMR spectra of **4c** in $CDCl_3$



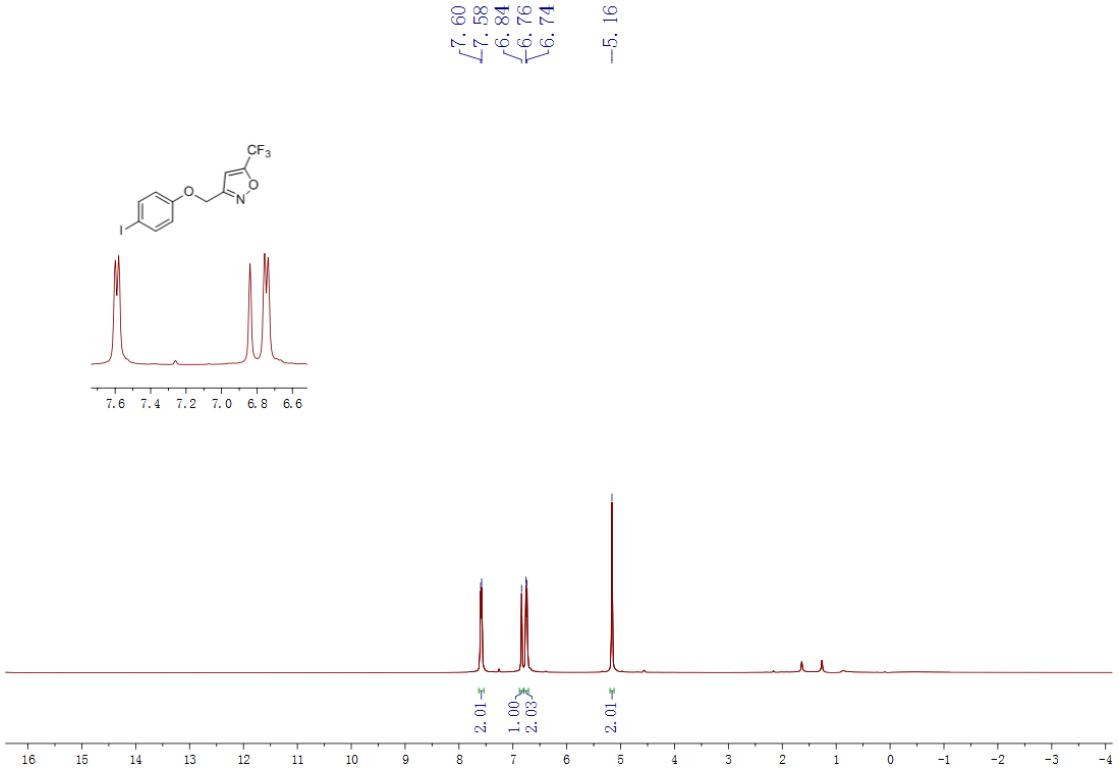
^{19}F NMR spectra of **4c** in $CDCl_3$



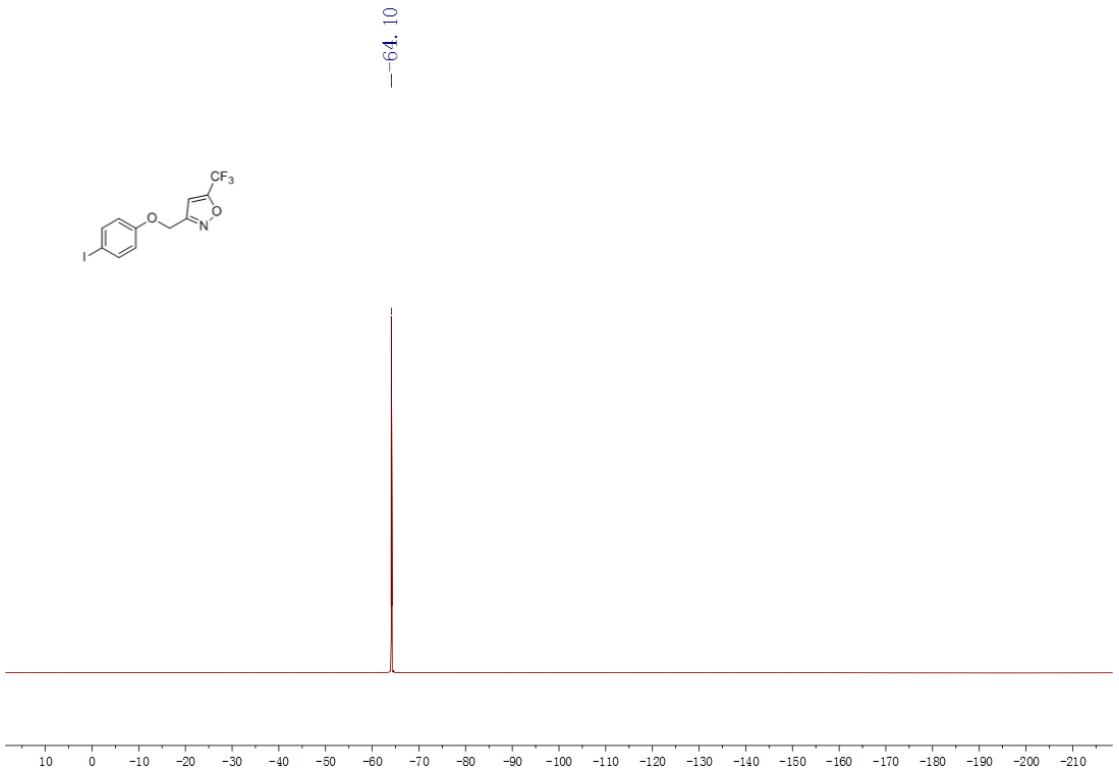
^{13}C NMR spectra of **4c** in $CDCl_3$



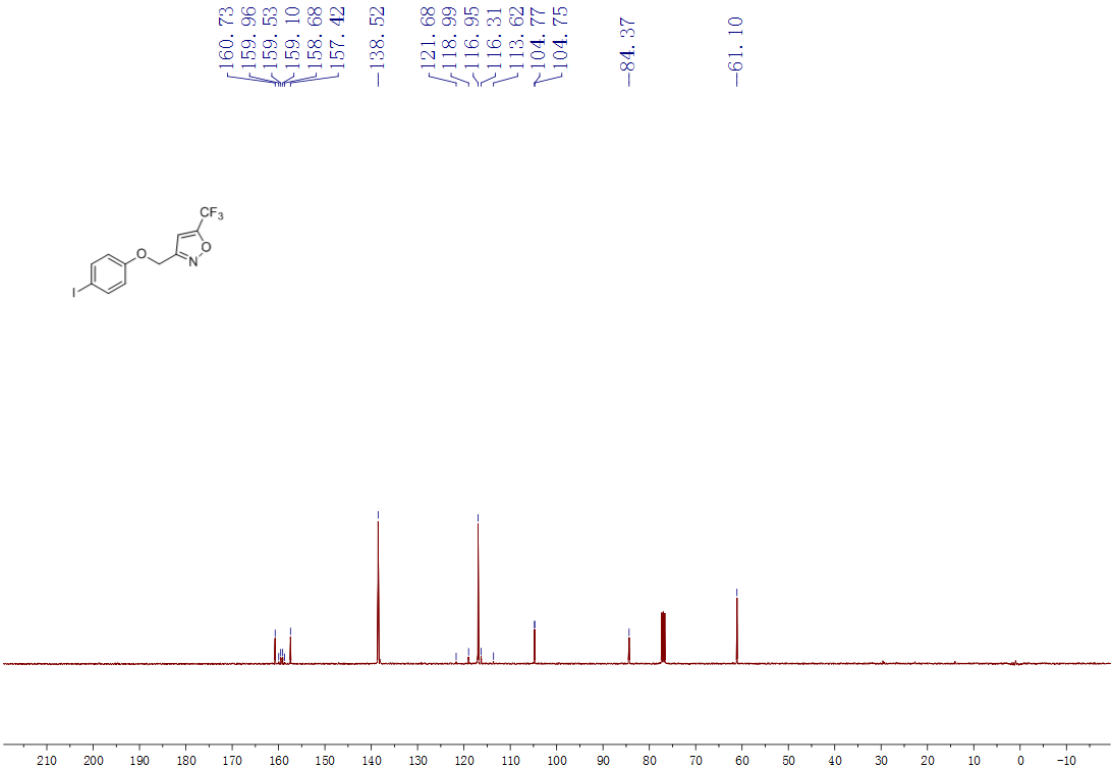
^{1}H NMR spectra of **4d** in $CDCl_3$



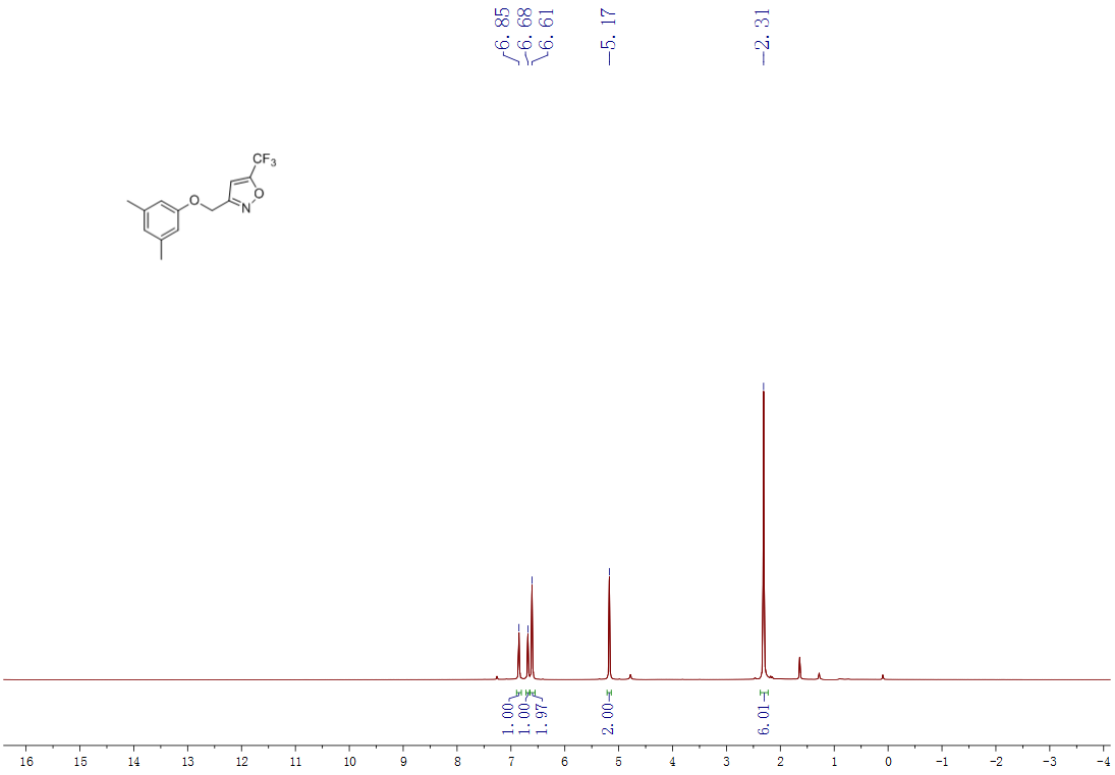
^{19}F NMR spectra of **4d** in $CDCl_3$



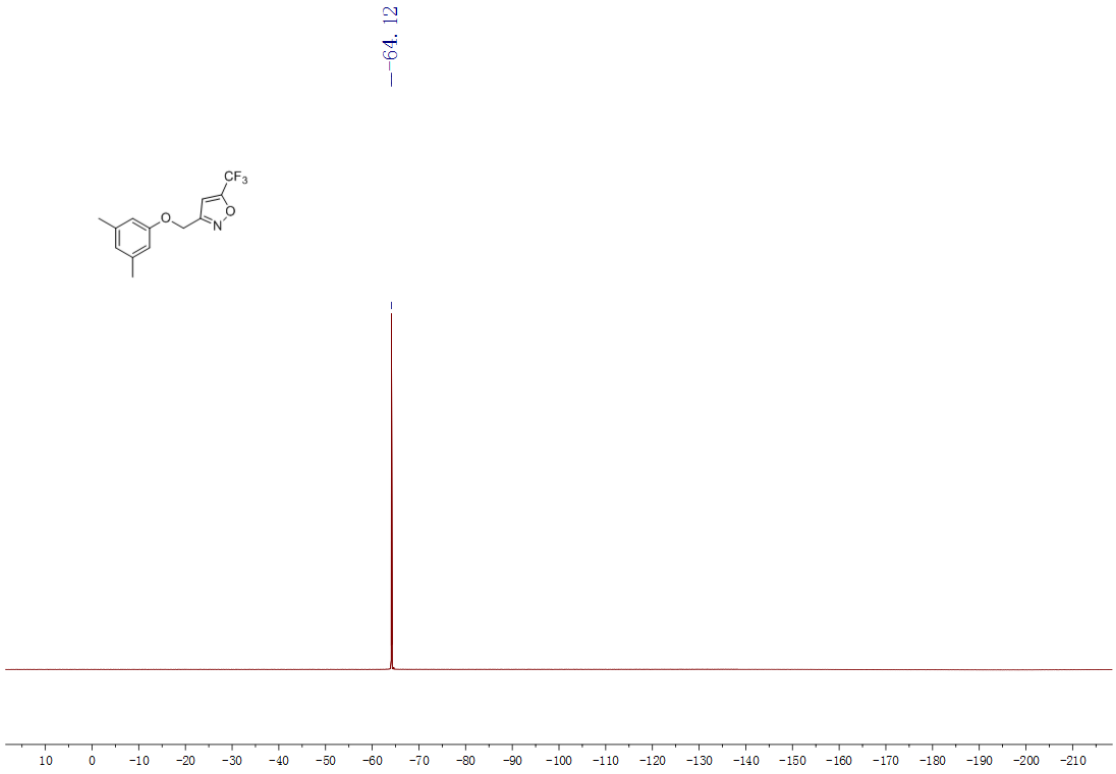
^{13}C NMR spectra of **4d** in $CDCl_3$



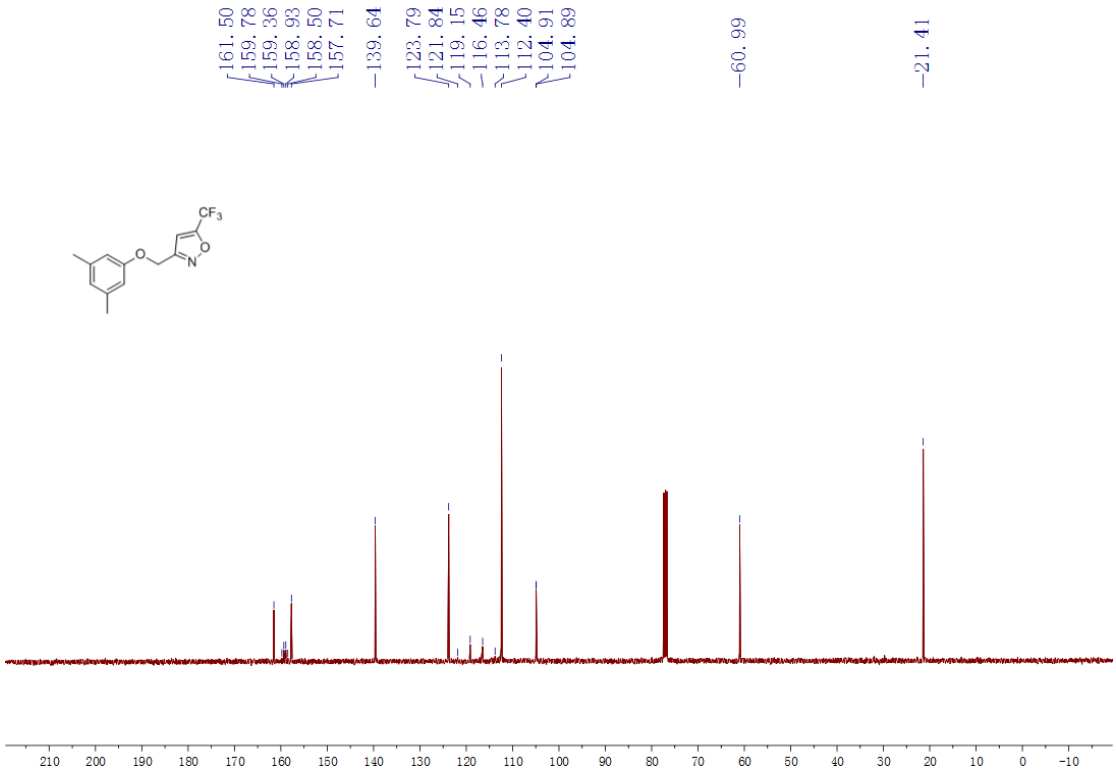
^{1}H NMR spectra of **4e** in $CDCl_3$



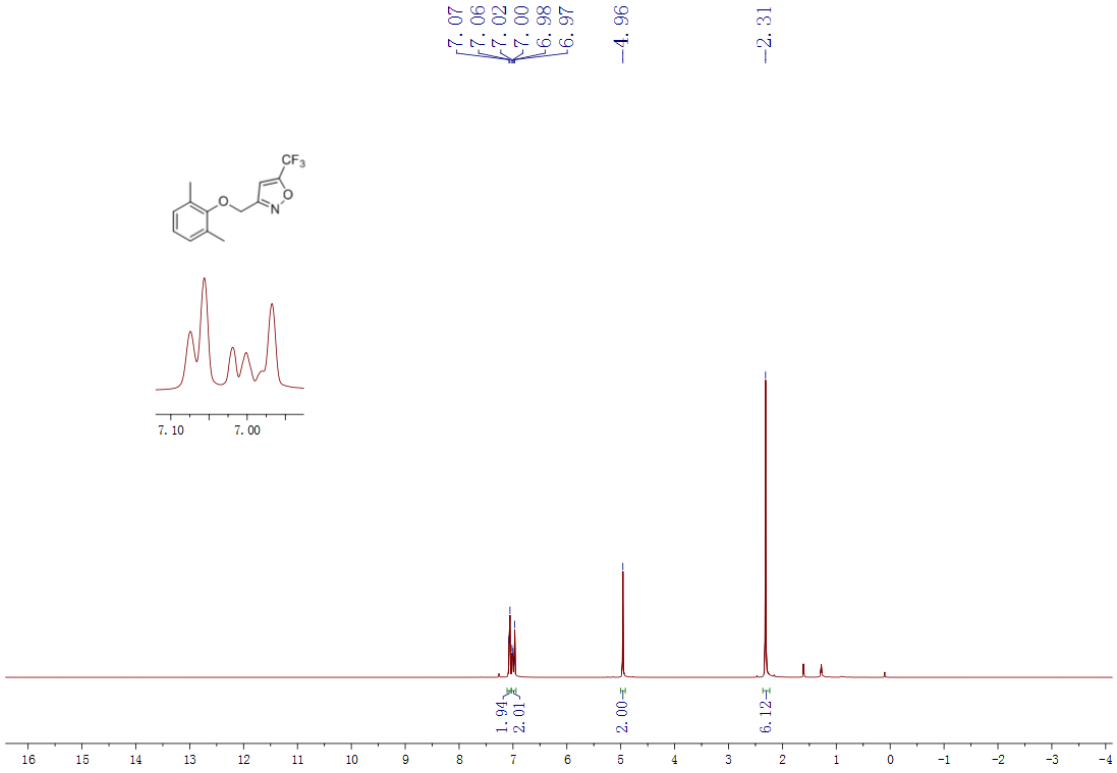
^{19}F NMR spectra of **4e** in $CDCl_3$



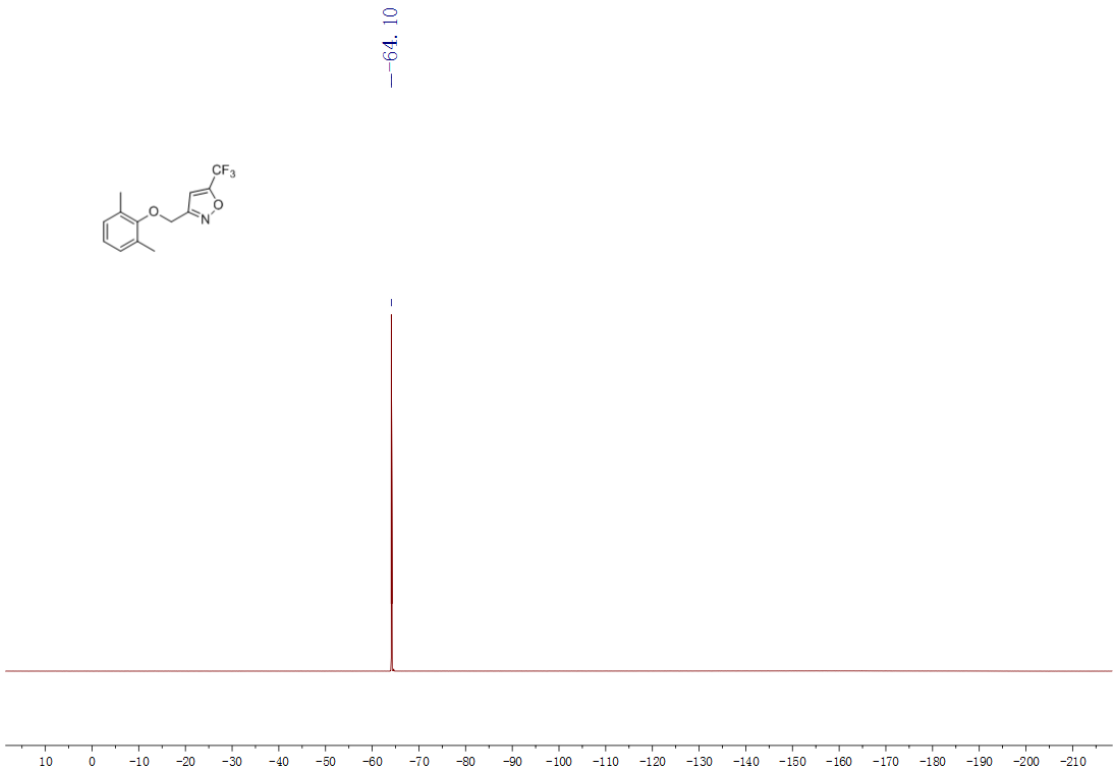
^{13}C NMR spectra of **4e** in $CDCl_3$



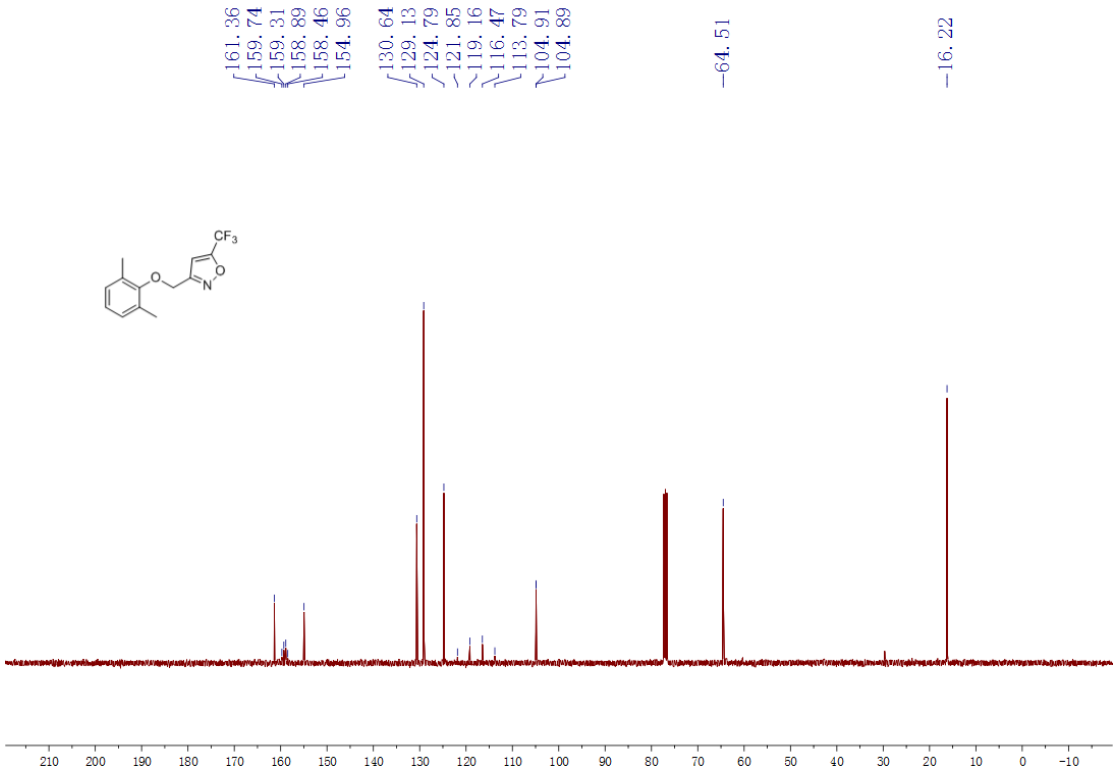
^{1}H NMR spectra of **4f** in $CDCl_3$



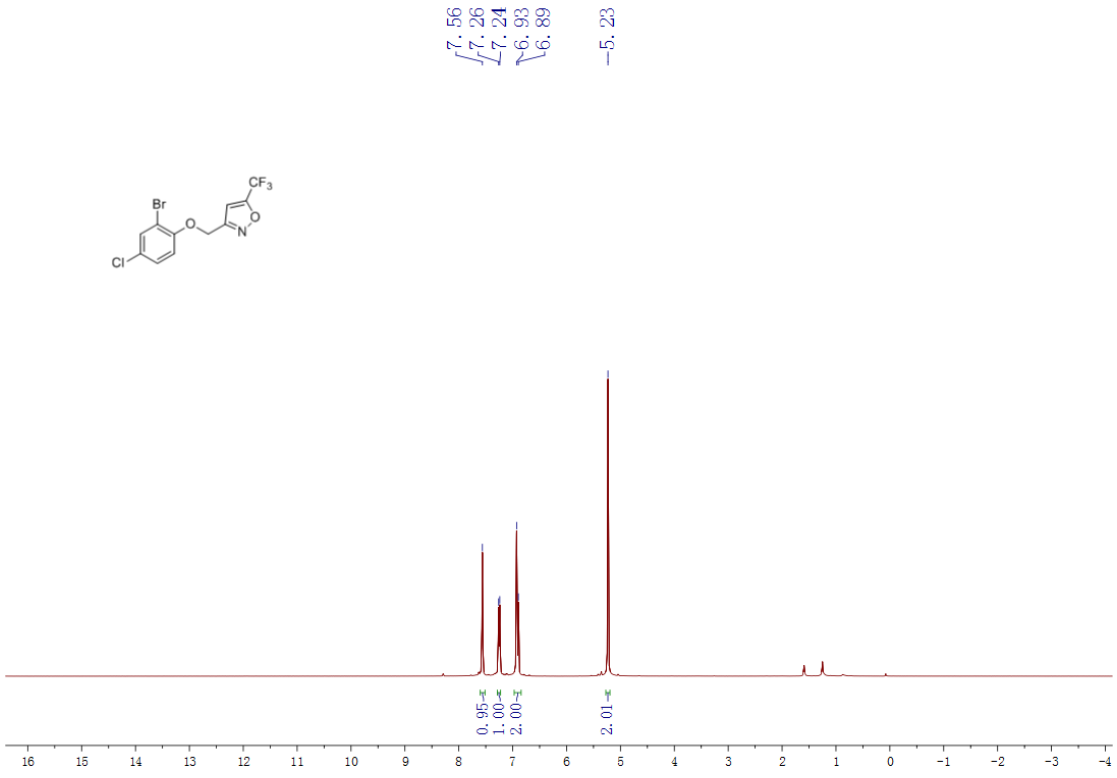
^{19}F NMR spectra of **4f** in $CDCl_3$



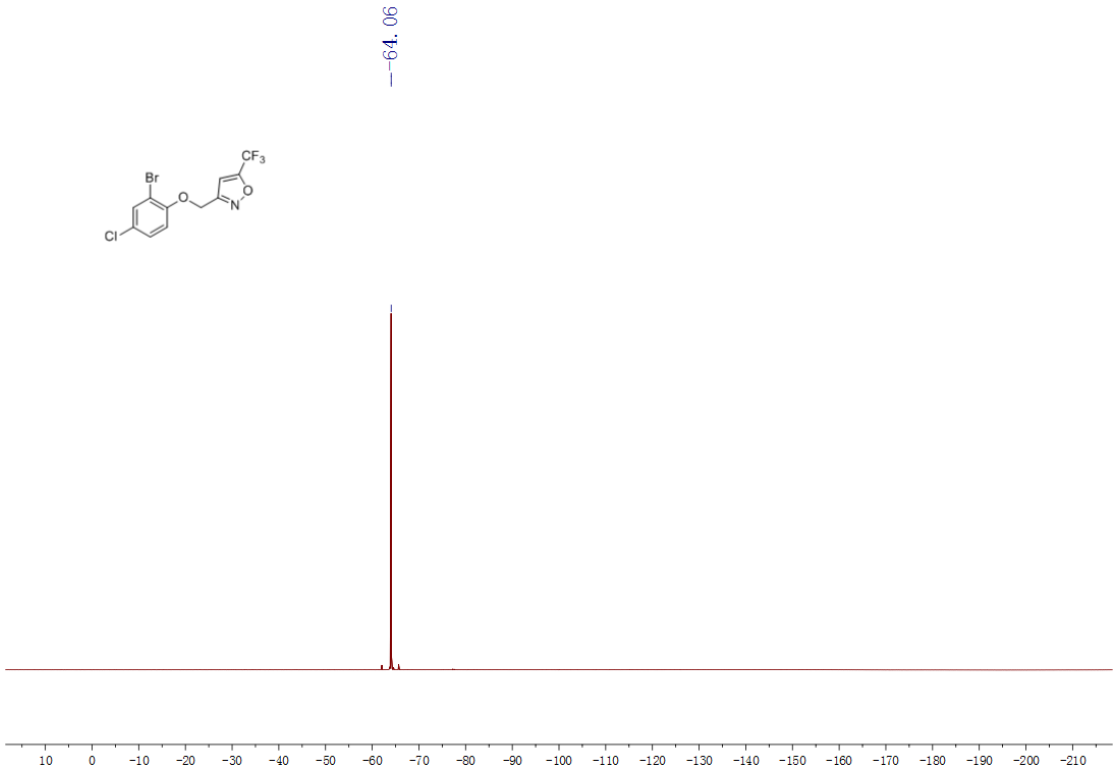
^{13}C NMR spectra of **4f** in $CDCl_3$



^{1}H NMR spectra of **4g** in $CDCl_3$



^{19}F NMR spectra of **4g** in $CDCl_3$



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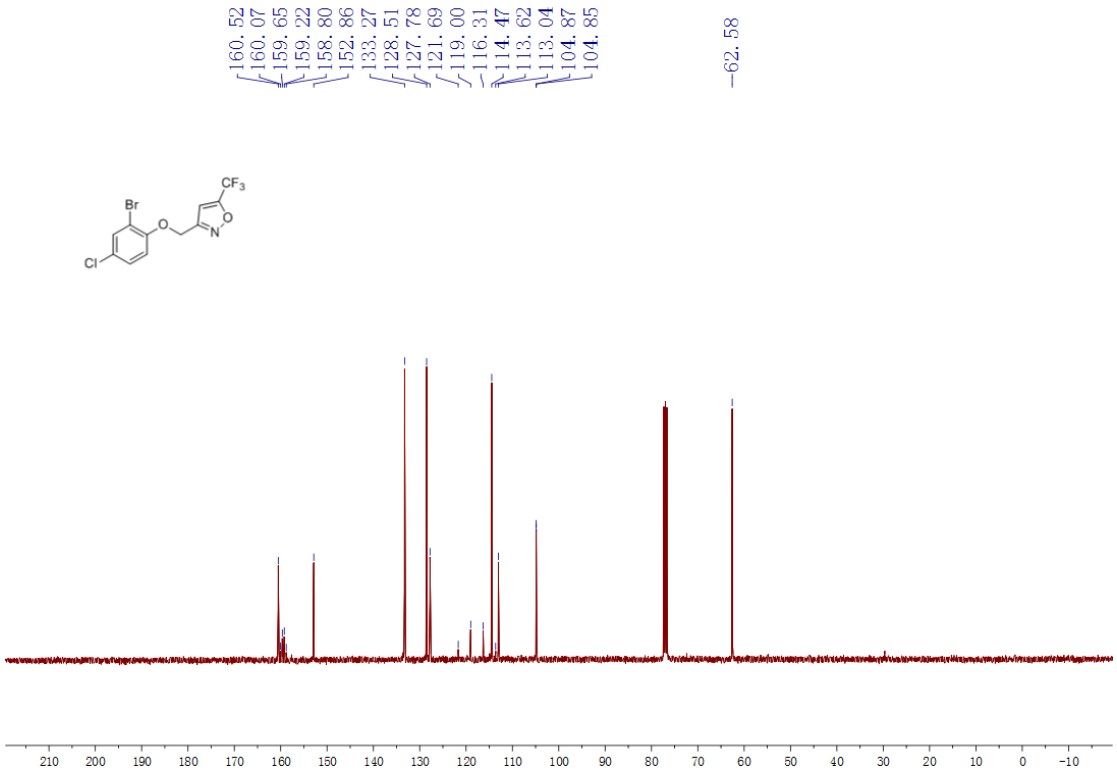
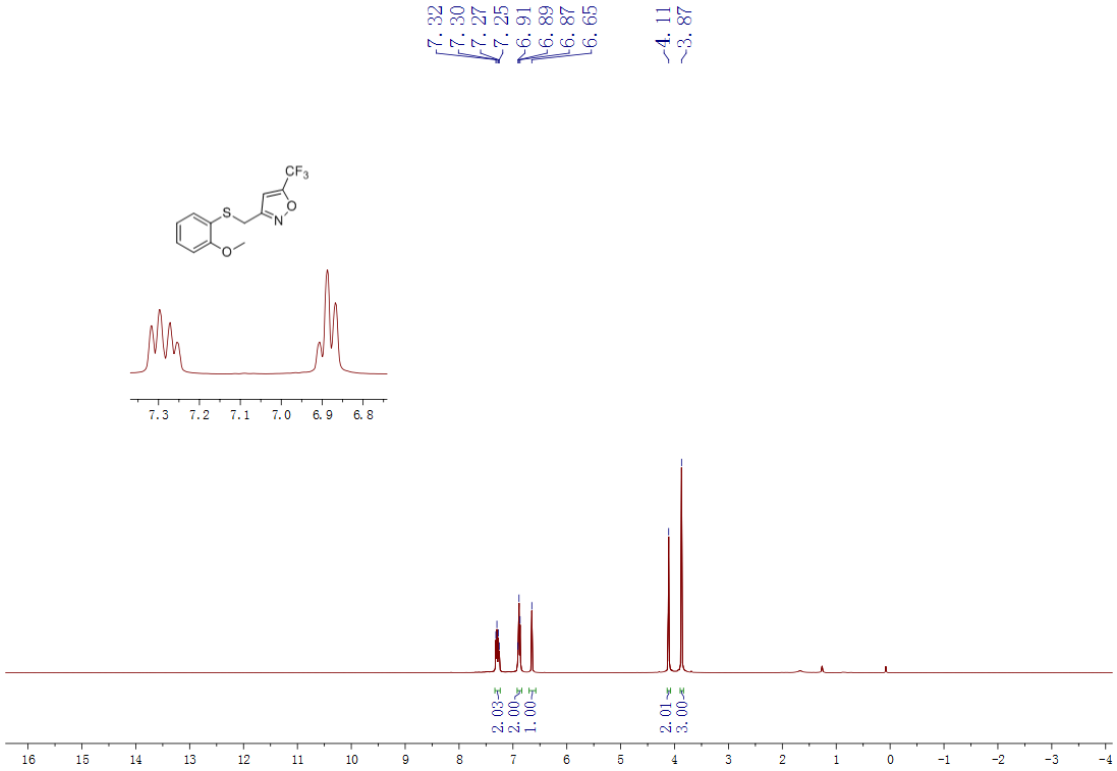
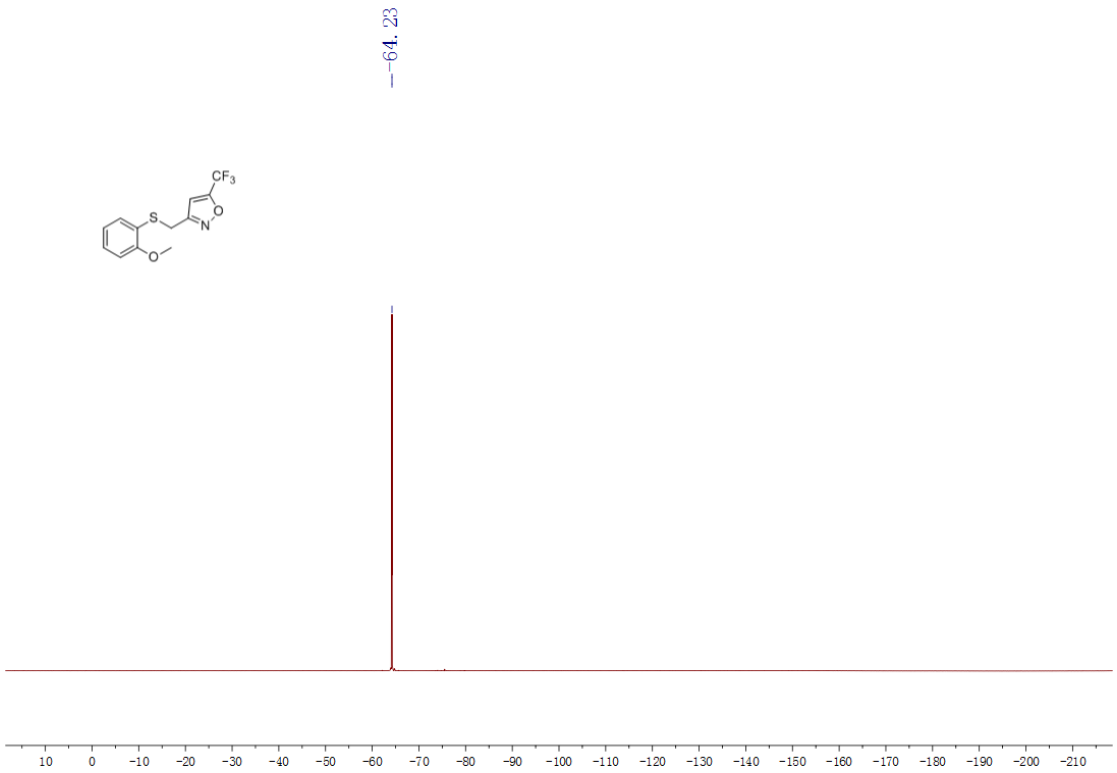


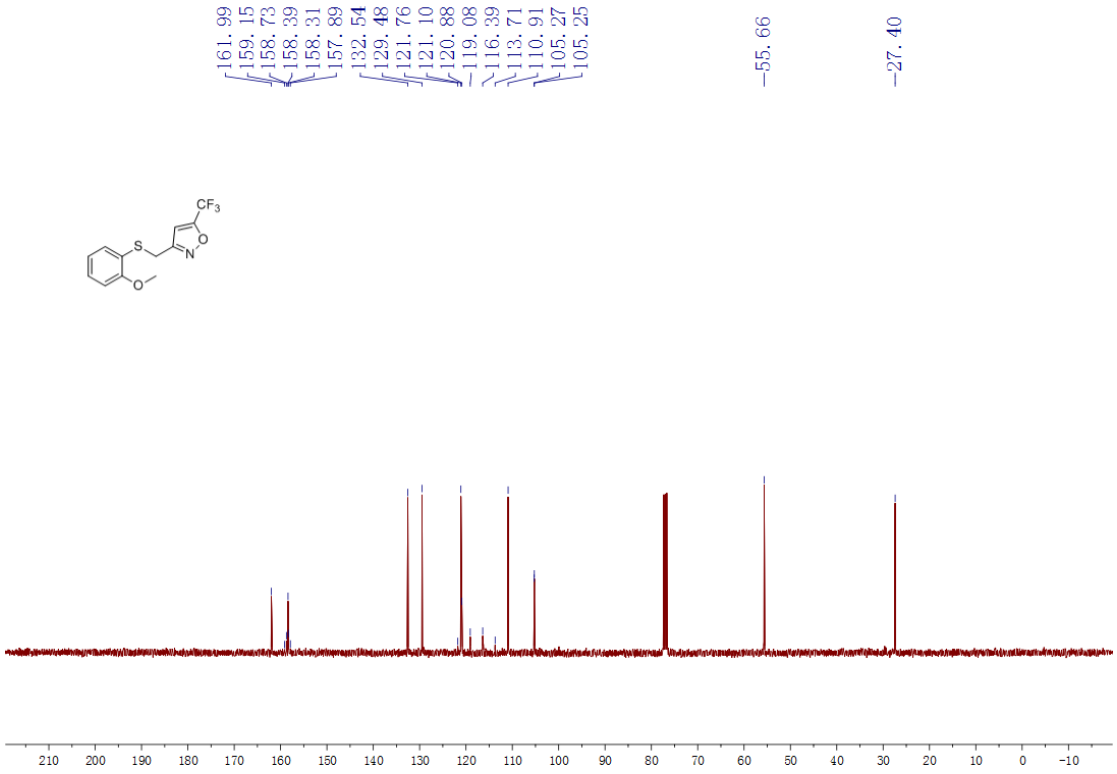
^{1}H NMR spectra of **4h** in $CDCl_3$



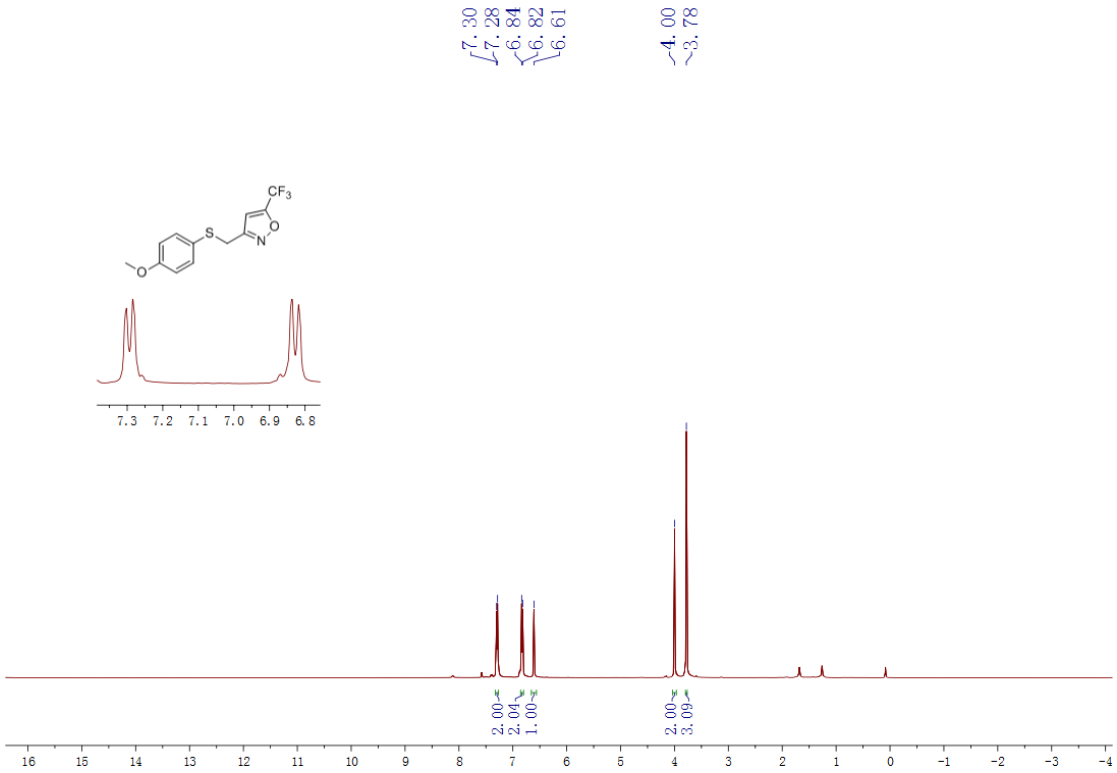
^{19}F NMR spectra of **4h** in $CDCl_3$



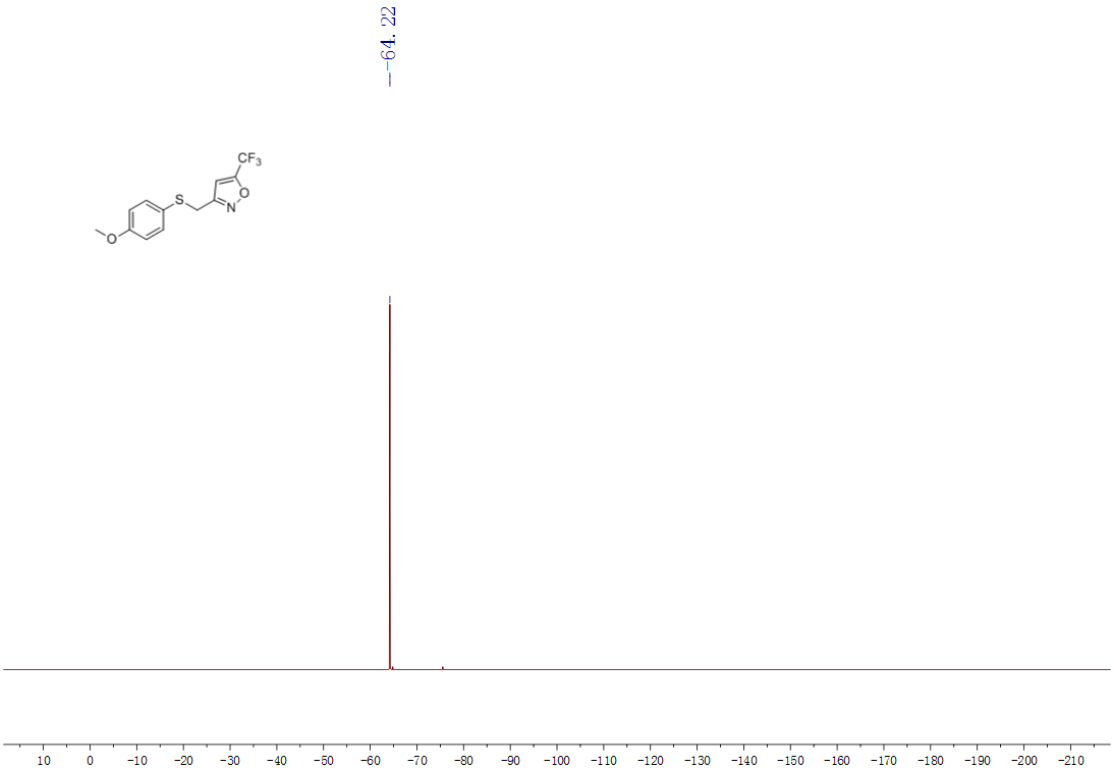
^{13}C NMR spectra of **4h** in $CDCl_3$



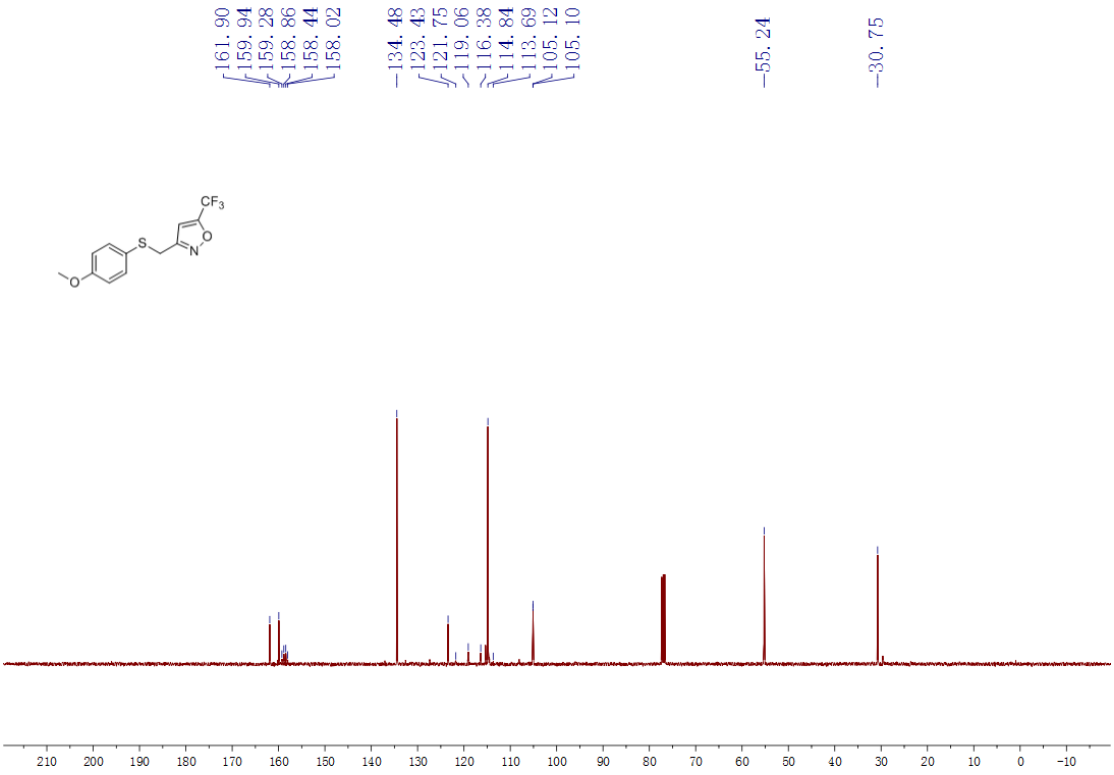
^{1}H NMR spectra of **4i** in $CDCl_3$



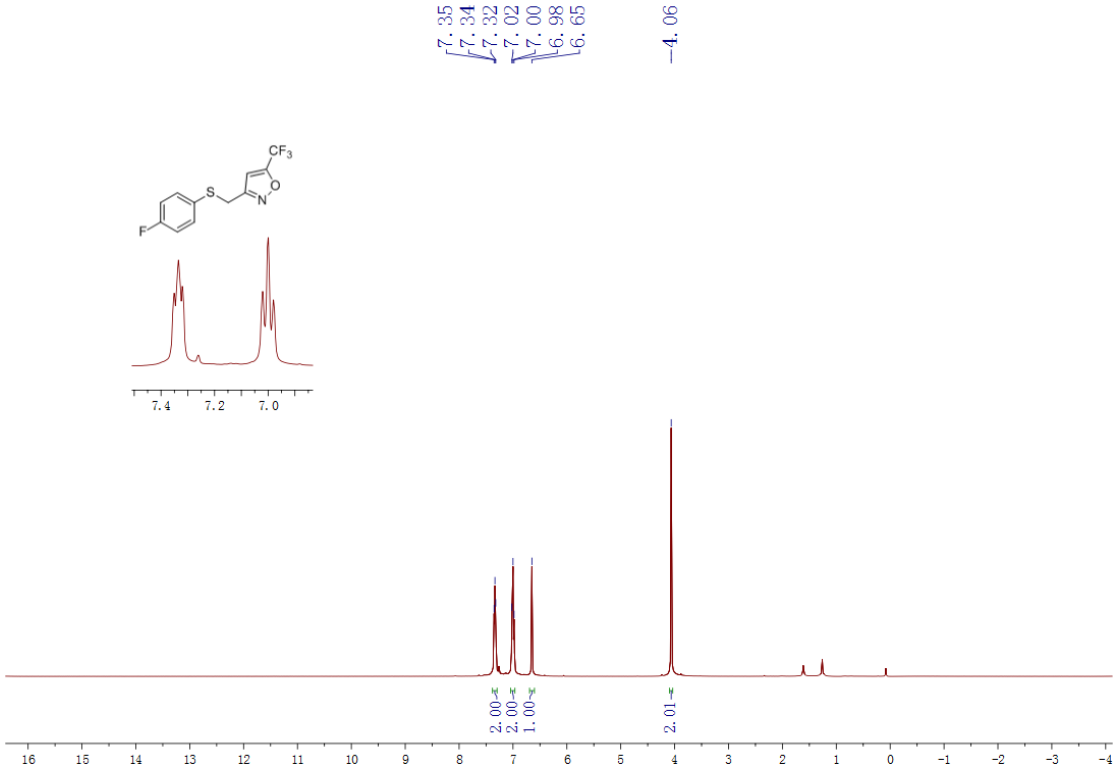
^{19}F NMR spectra of **4i** in $CDCl_3$



^{13}C NMR spectra of **4i** in $CDCl_3$



^{1}H NMR spectra of **4j** in $CDCl_3$



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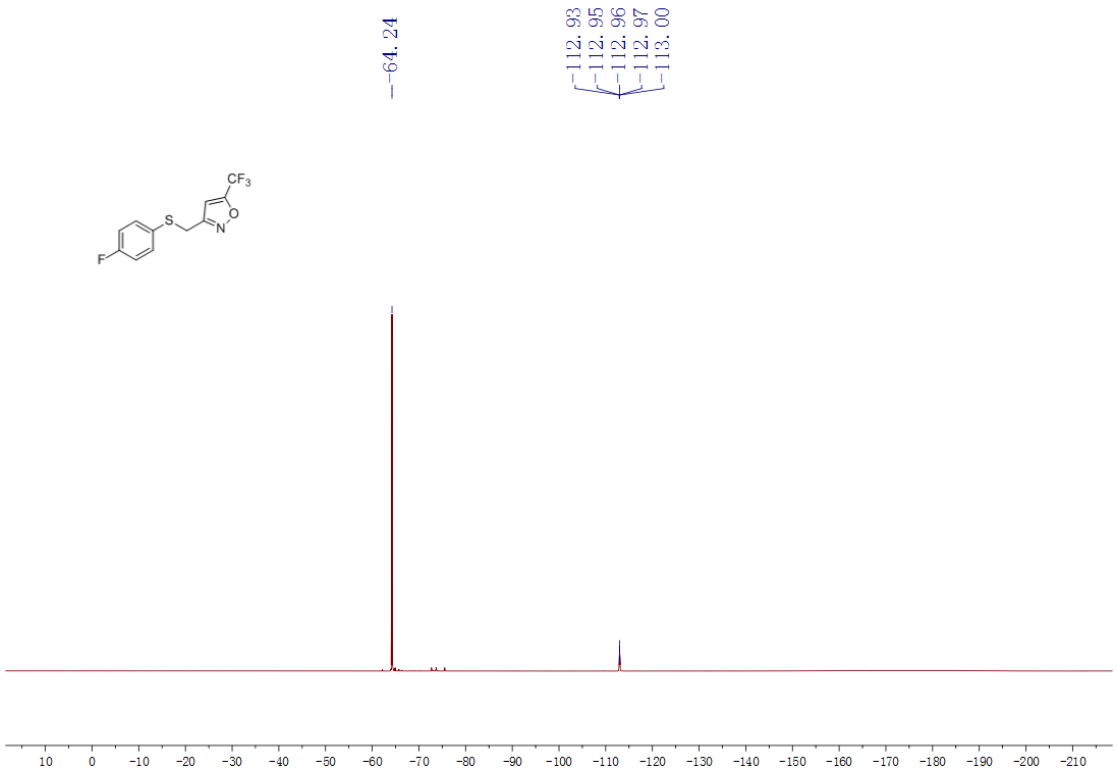
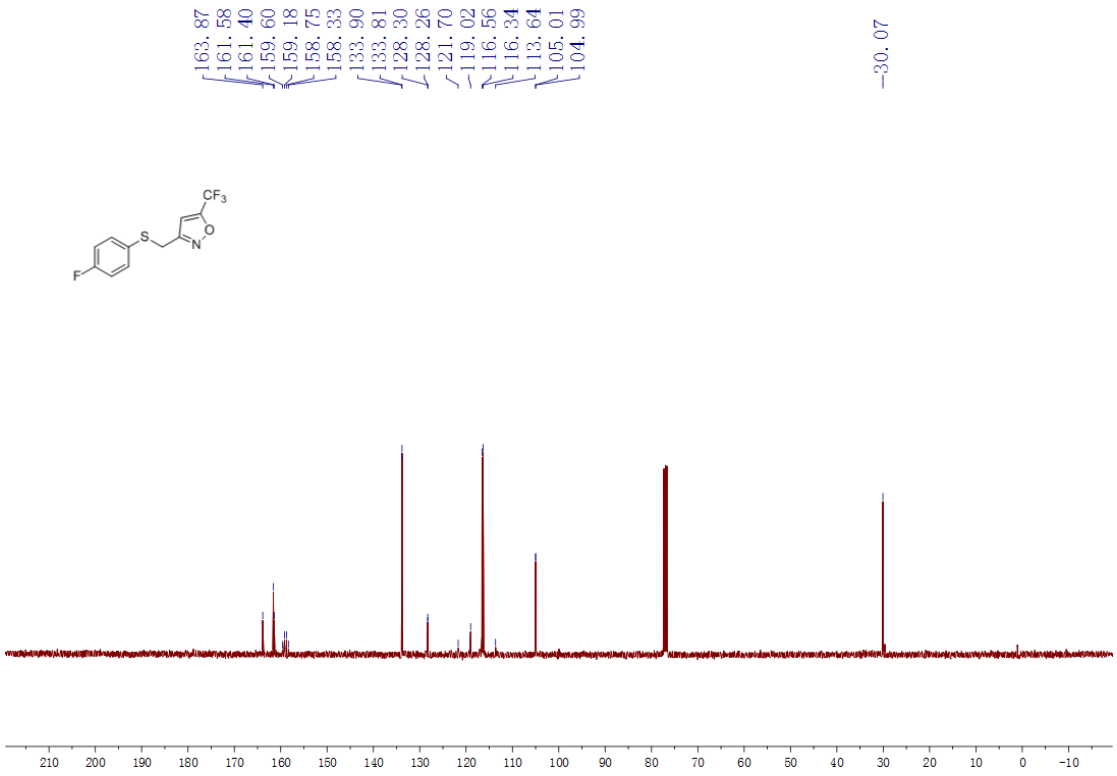
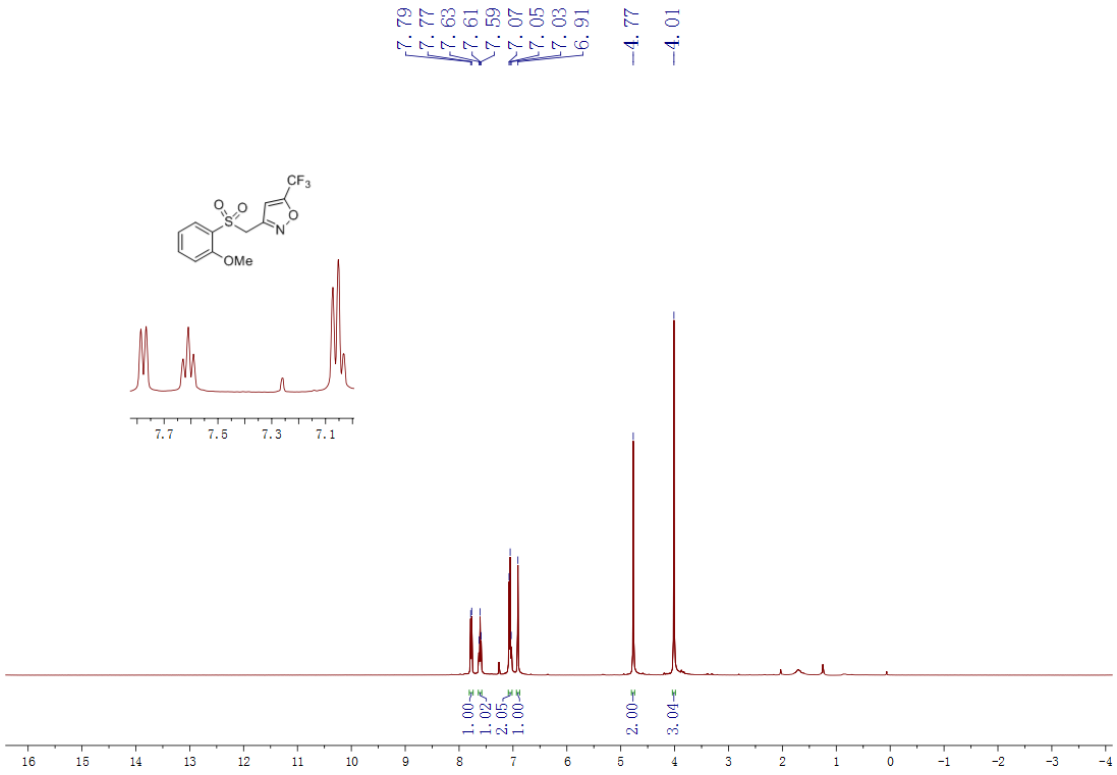


^{13}C NMR spectra of **4j** in $CDCl_3$



^{1}H NMR spectra of **4k** in $CDCl_3$



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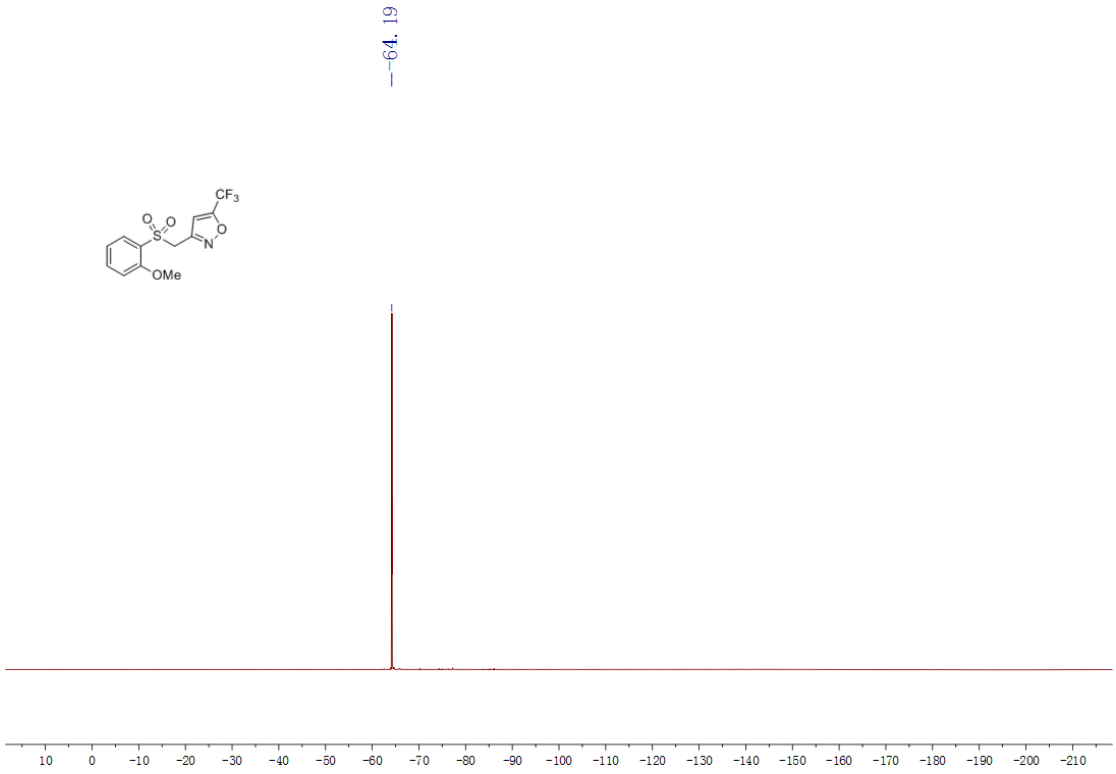
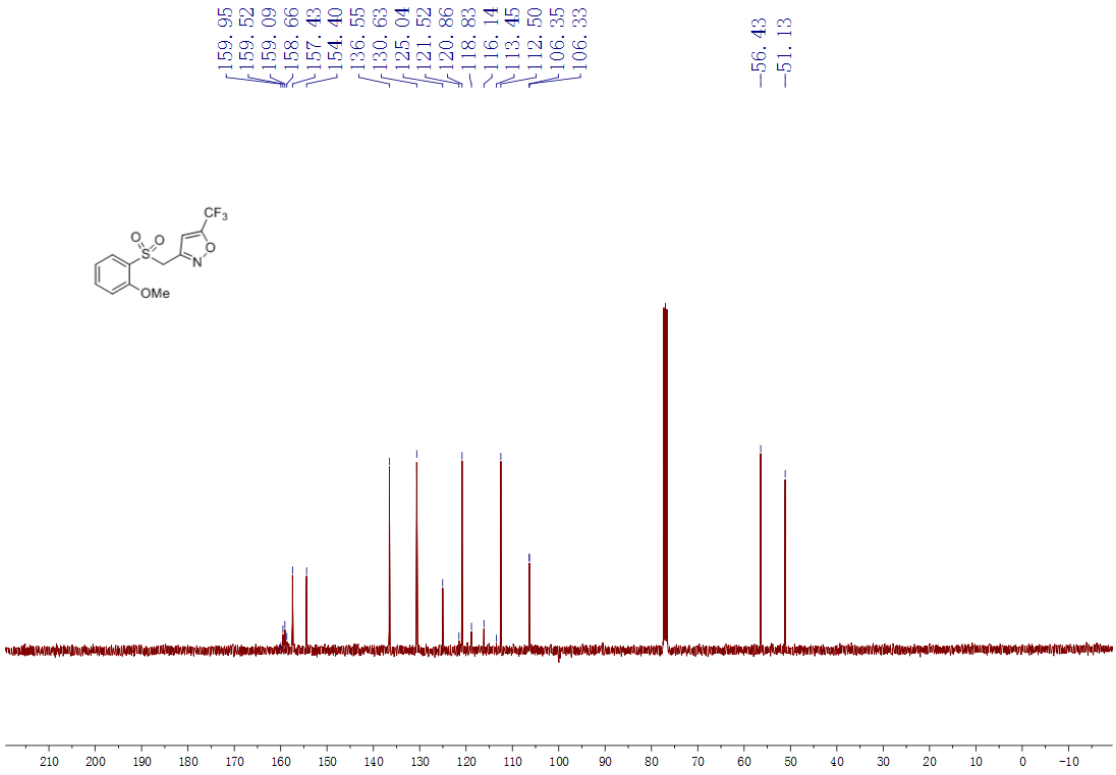
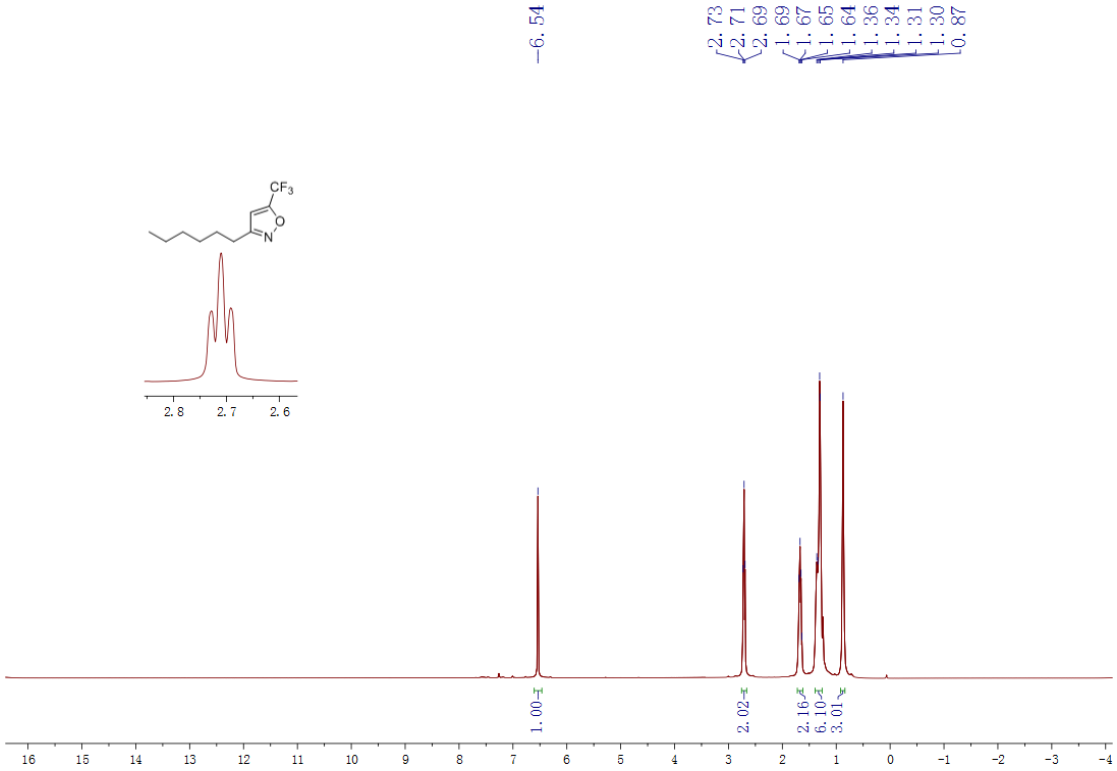


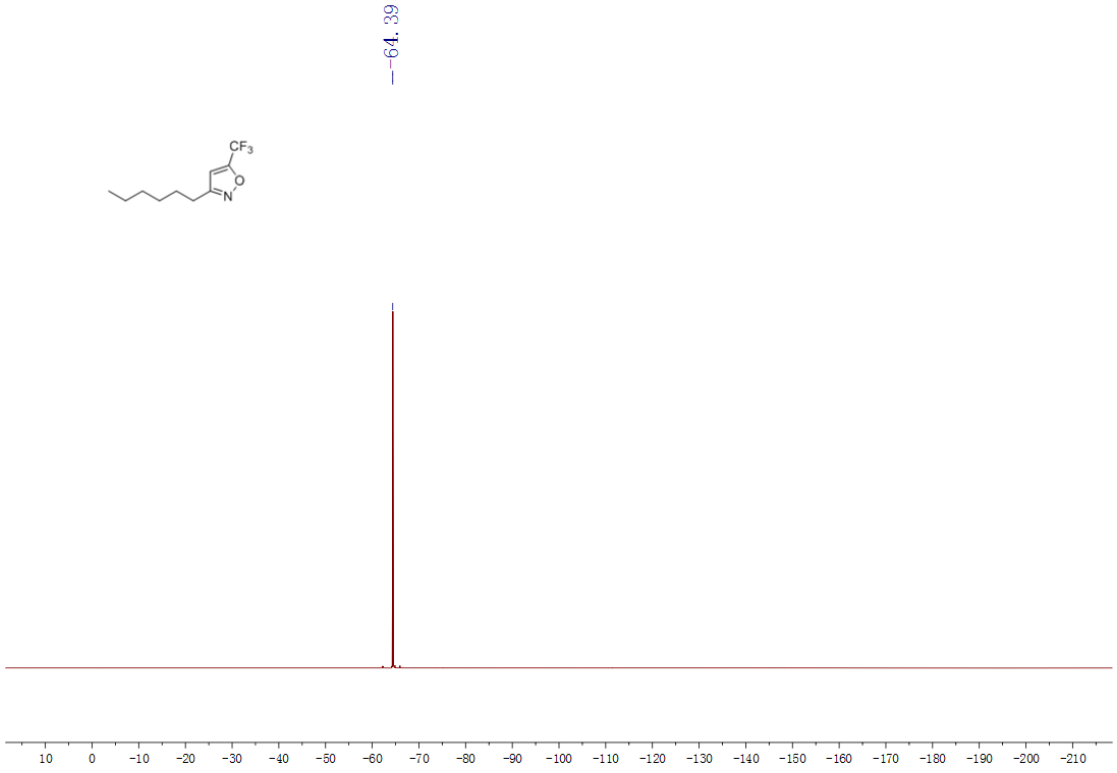
^{13}C NMR spectra of **4k** in $CDCl_3$



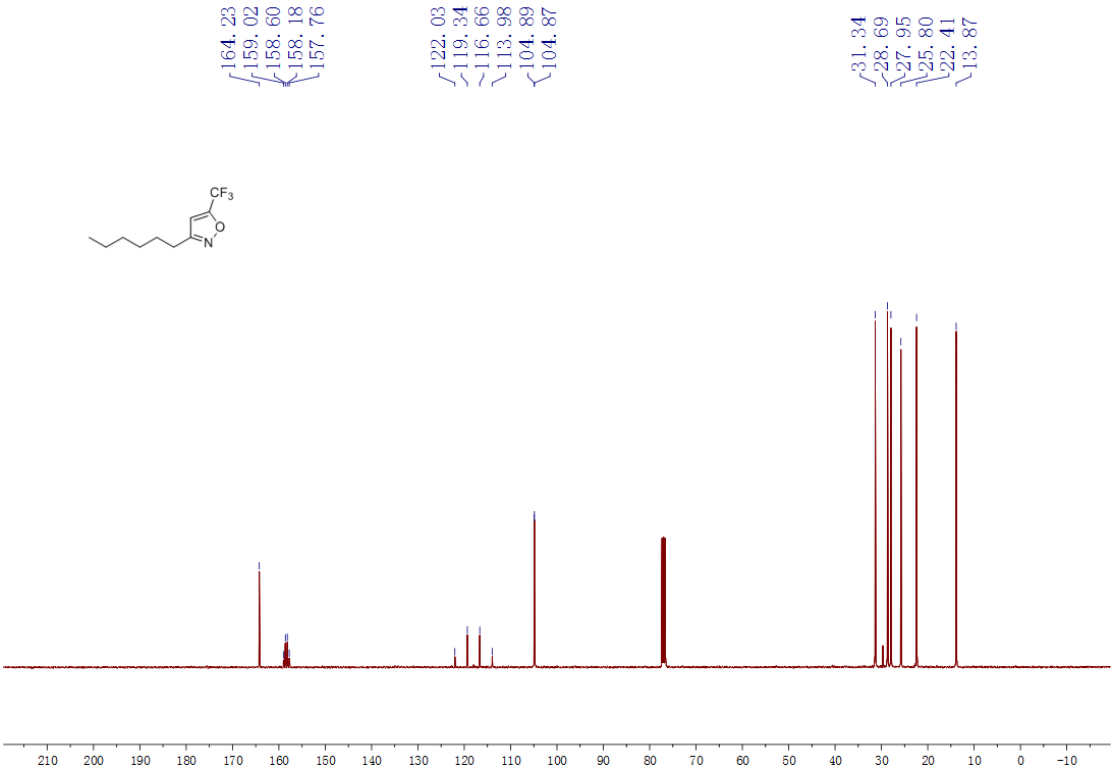
^{1}H NMR spectra of **4l** in $CDCl_3$



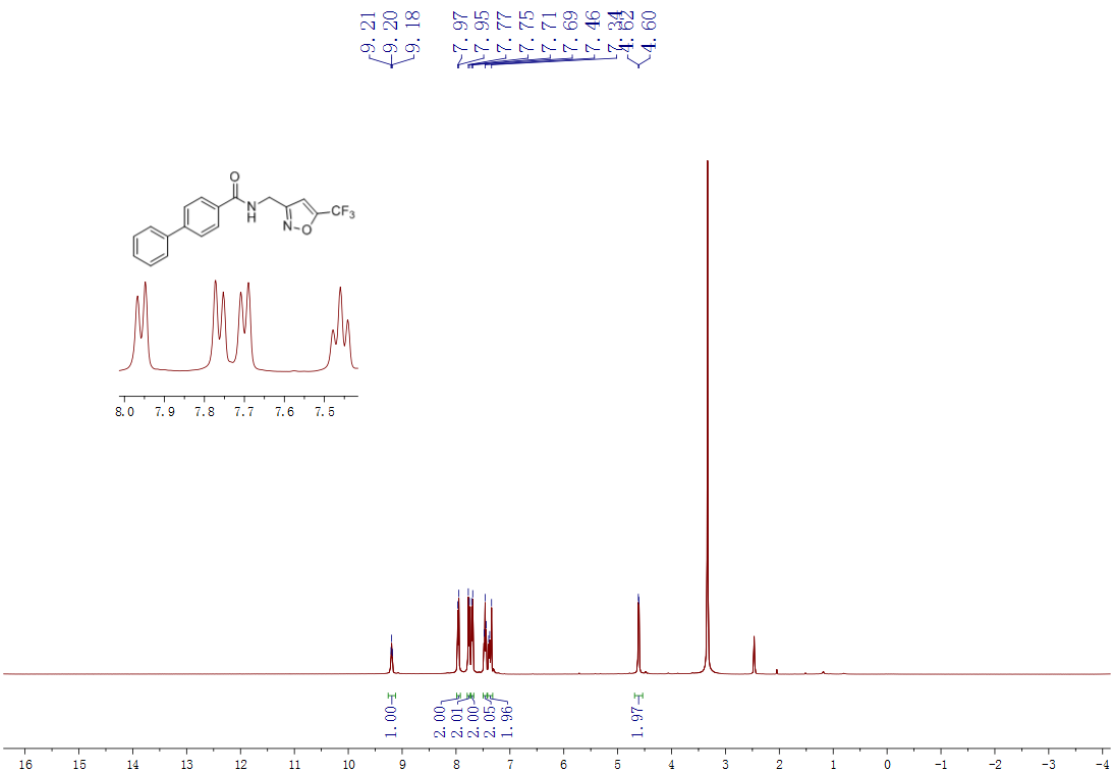
^{19}F NMR spectra of **4l** in $CDCl_3$



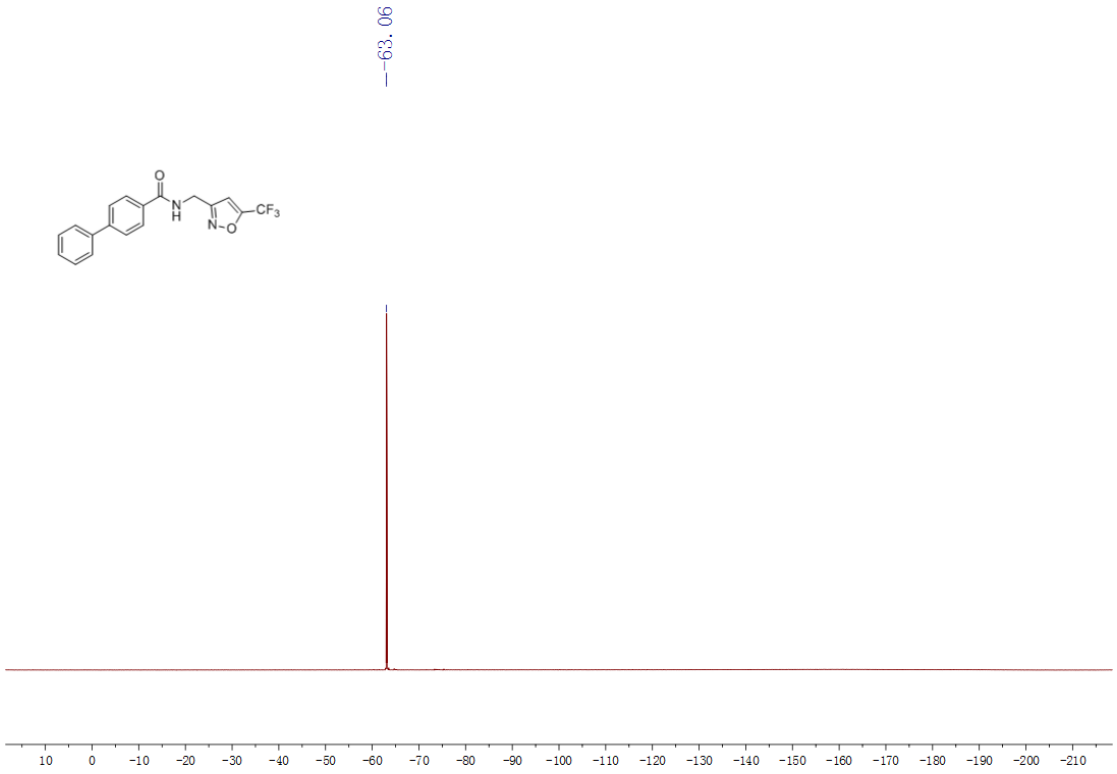
^{13}C NMR spectra of **4l** in $CDCl_3$



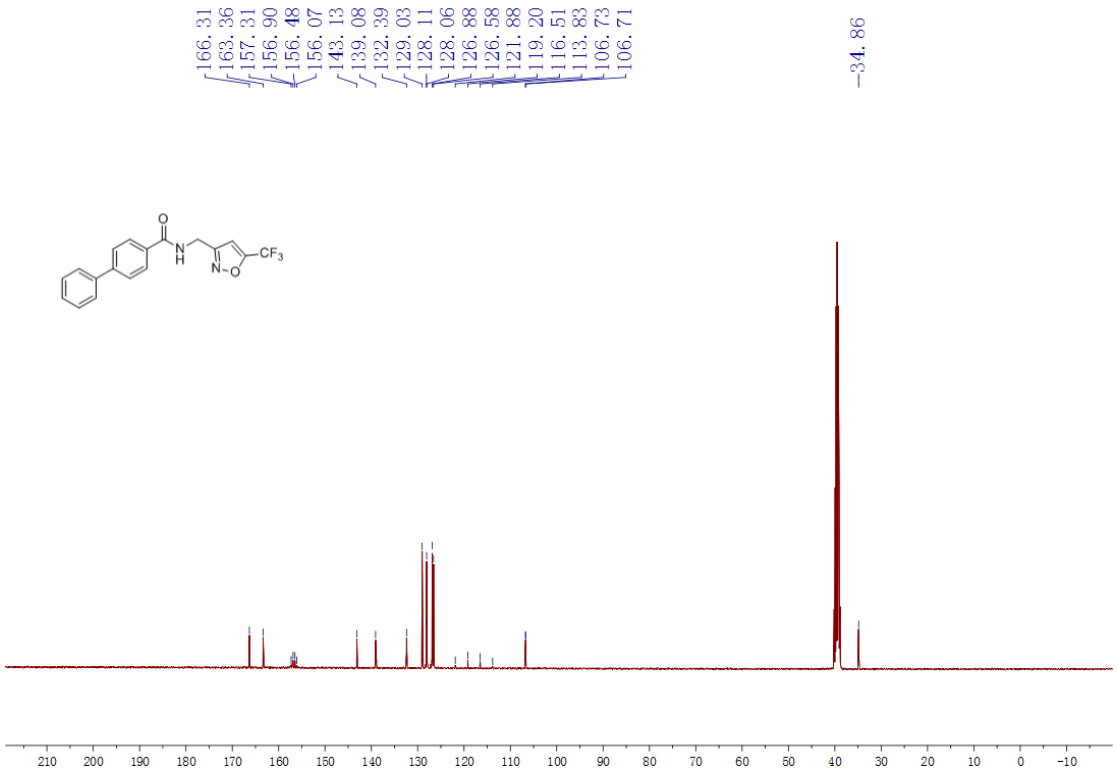
^{1}H NMR spectra of **4m** in DMSO-d_6



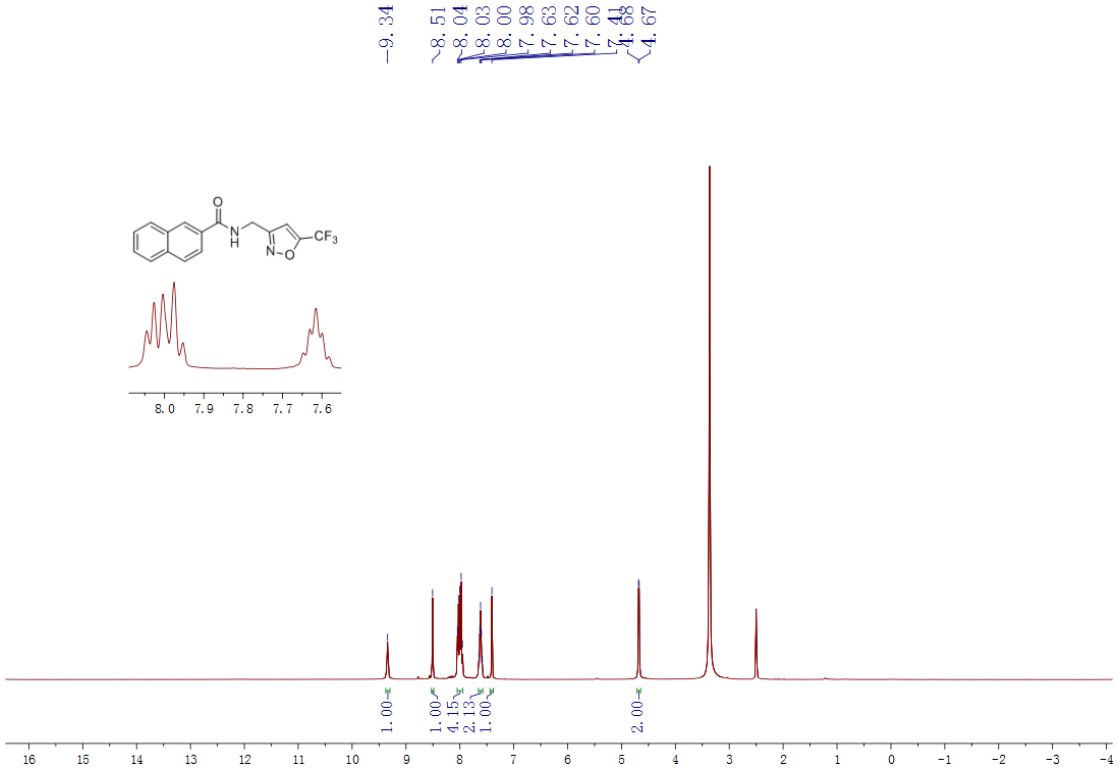
^{19}F NMR spectra of **4m** in DMSO-d_6



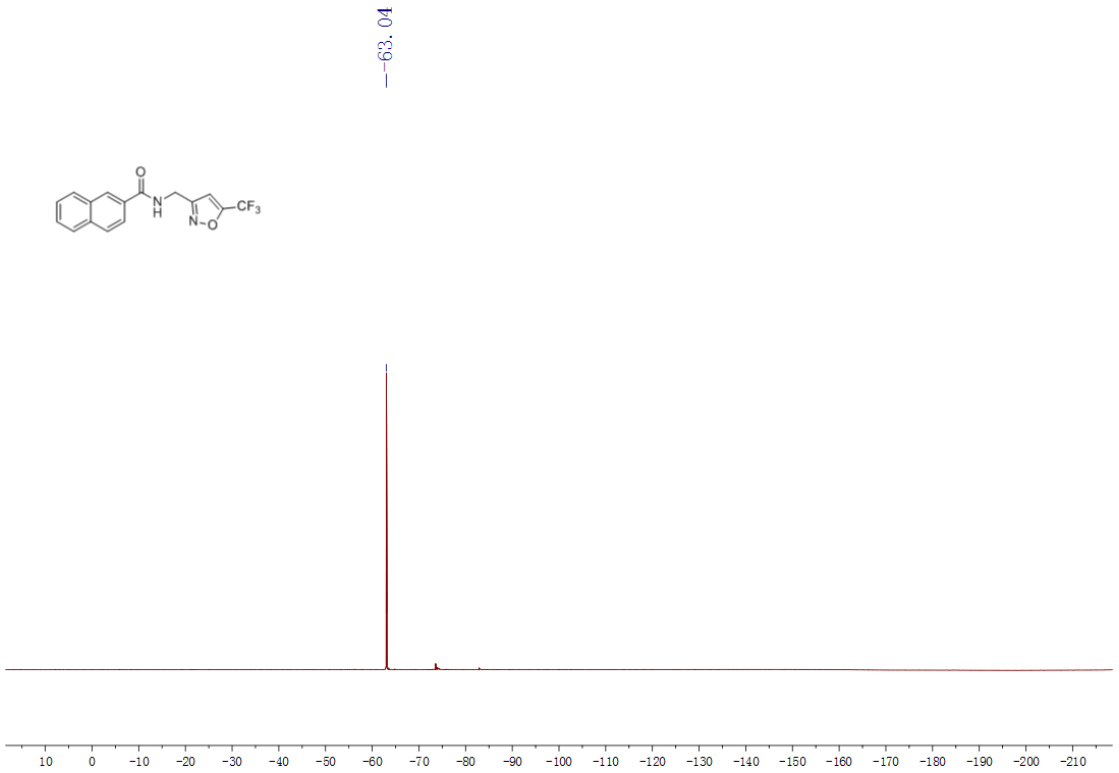
^{13}C NMR spectra of **4m** in DMSO-d_6



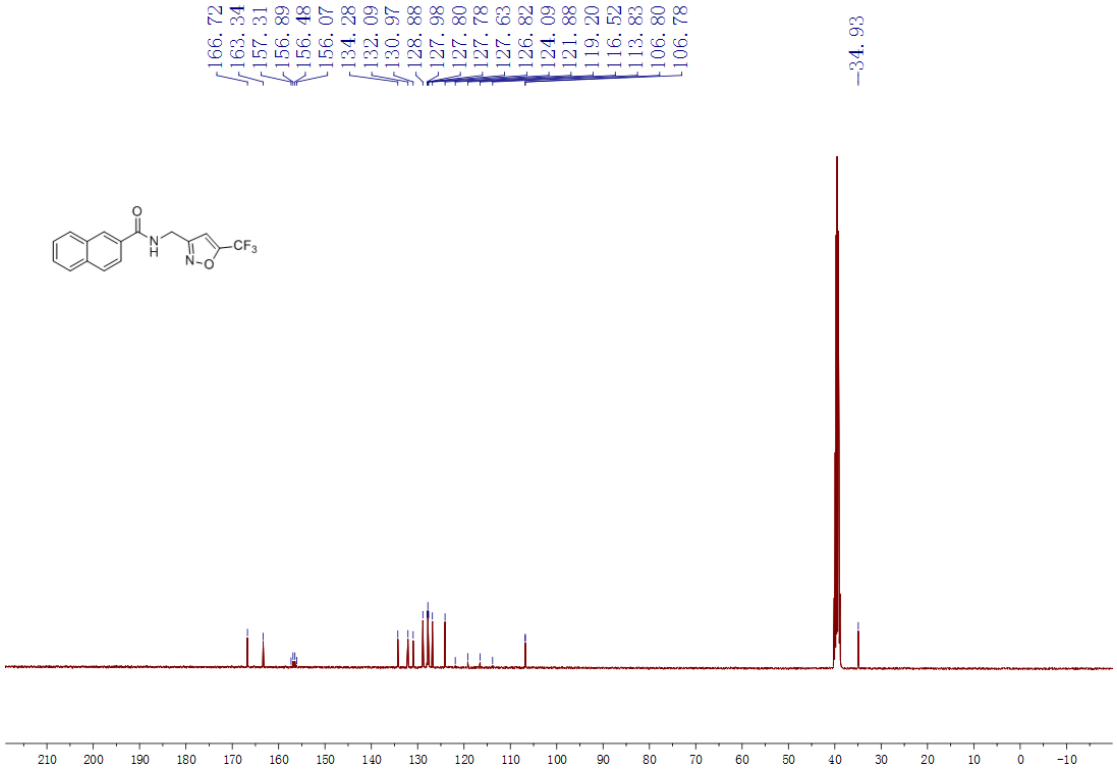
^{1}H NMR spectra of **4n** in DMSO-d_6



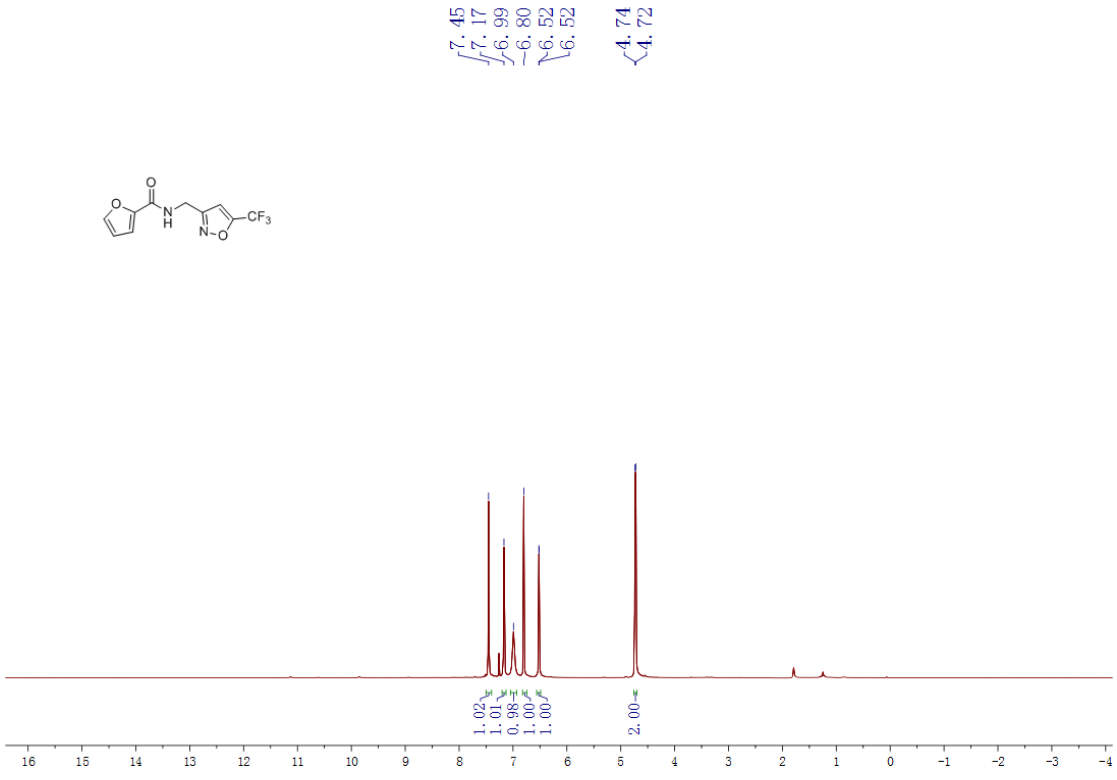
^{19}F NMR spectra of **4n** in DMSO-d_6



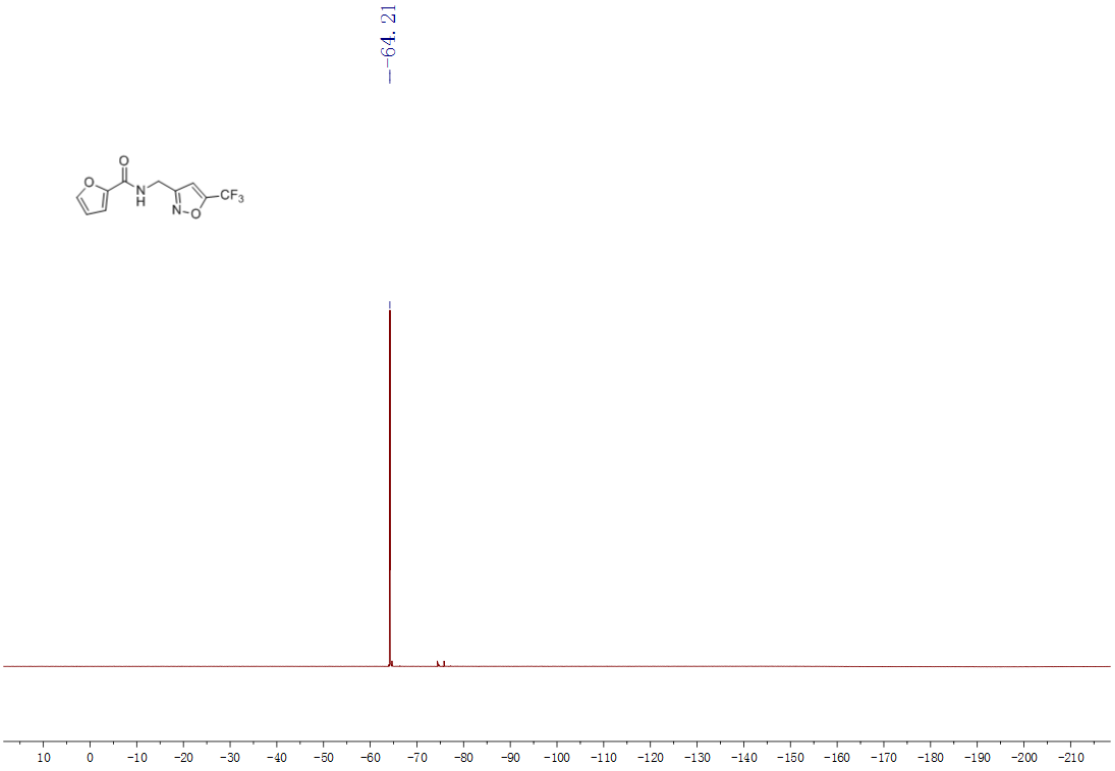
^{13}C NMR spectra of **4n** in DMSO-d_6



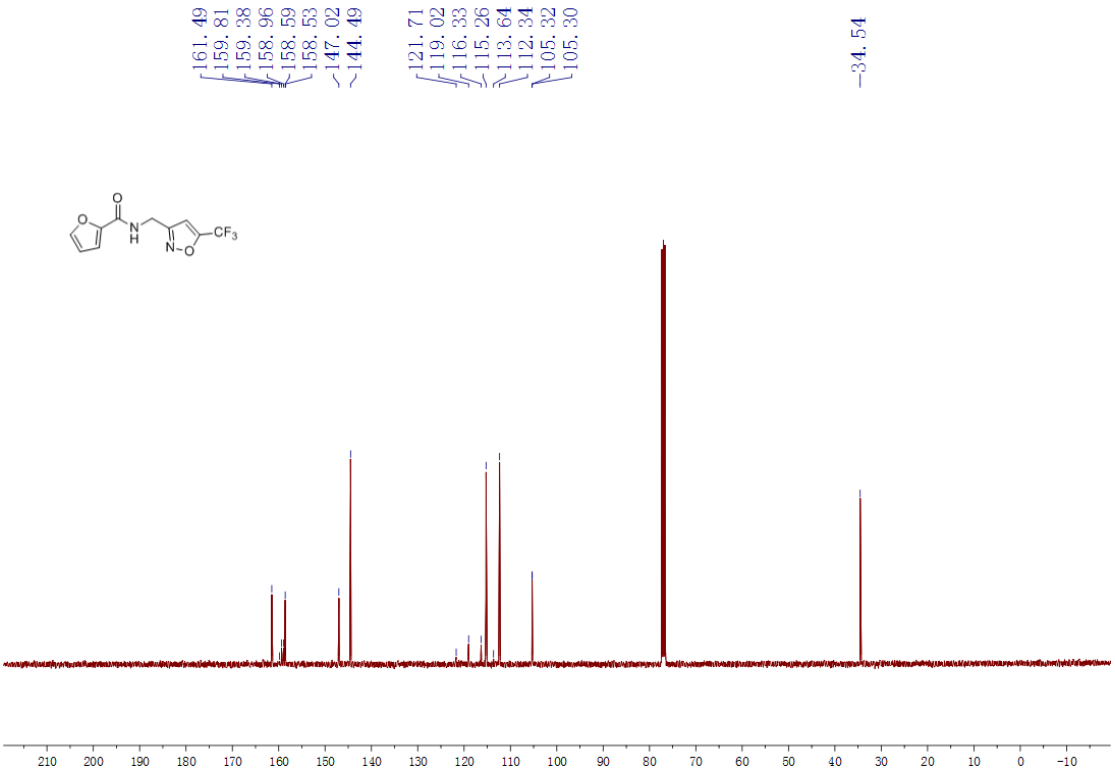
^{1}H NMR spectra of **4o** in $CDCl_3$



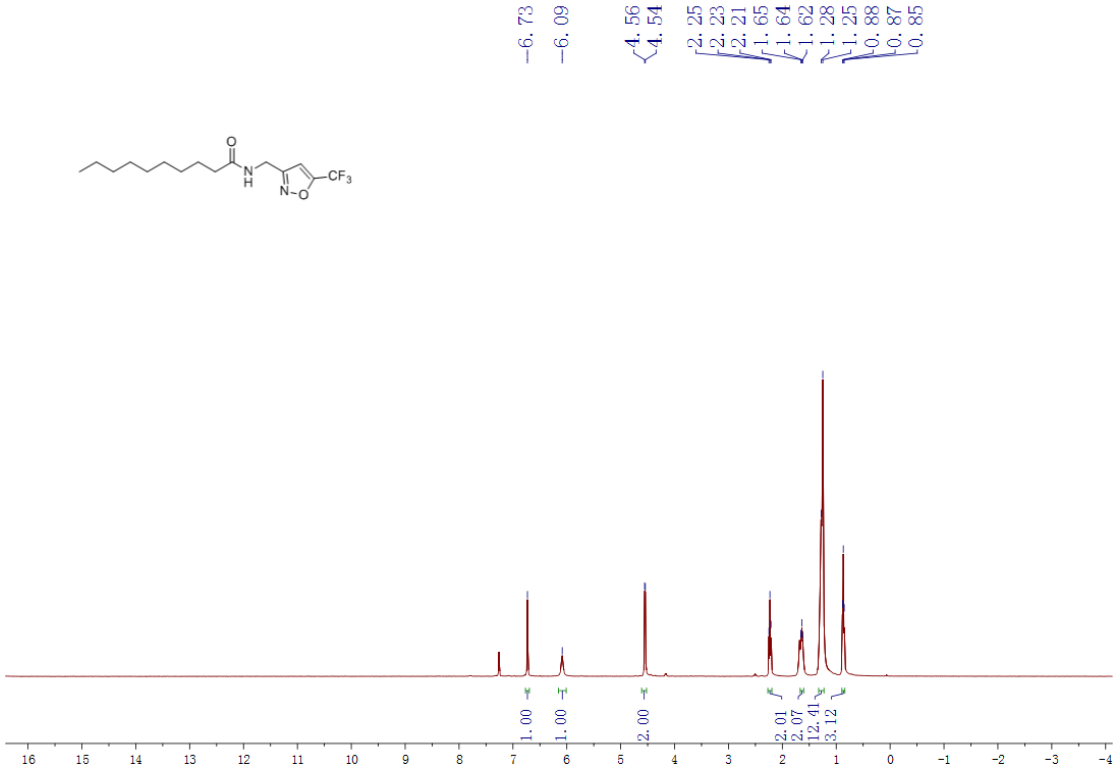
^{19}F NMR spectra of **4o** in $CDCl_3$



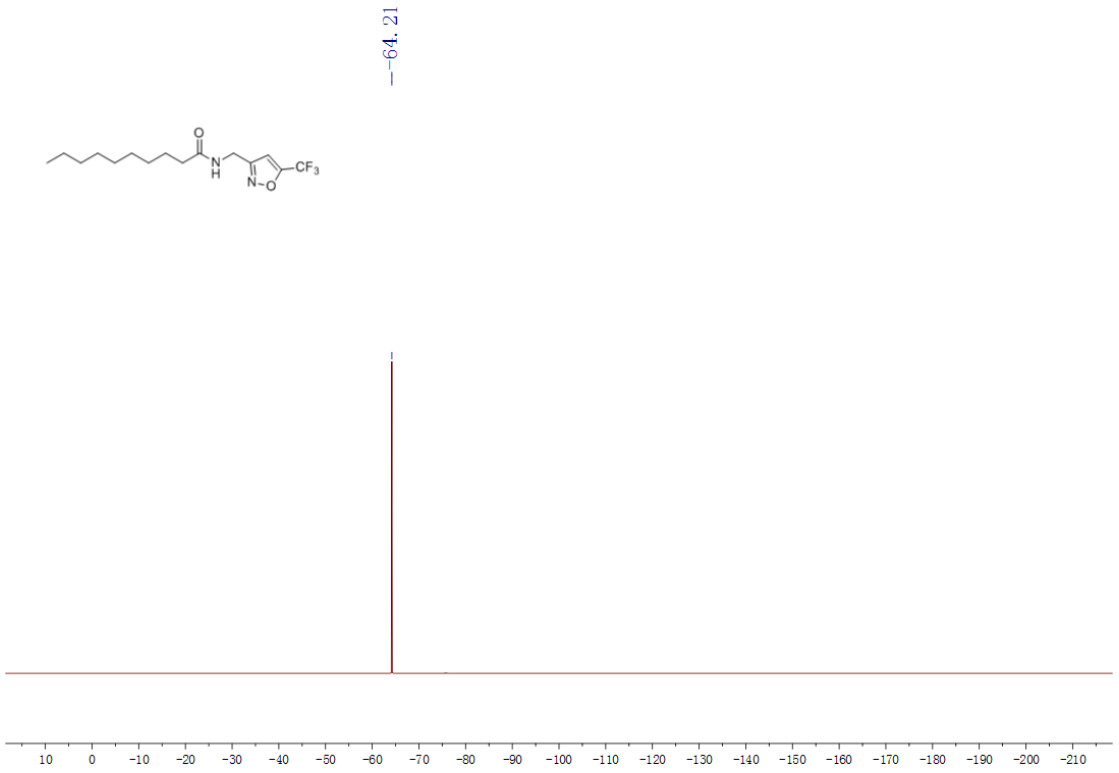
^{13}C NMR spectra of **4o** in $CDCl_3$



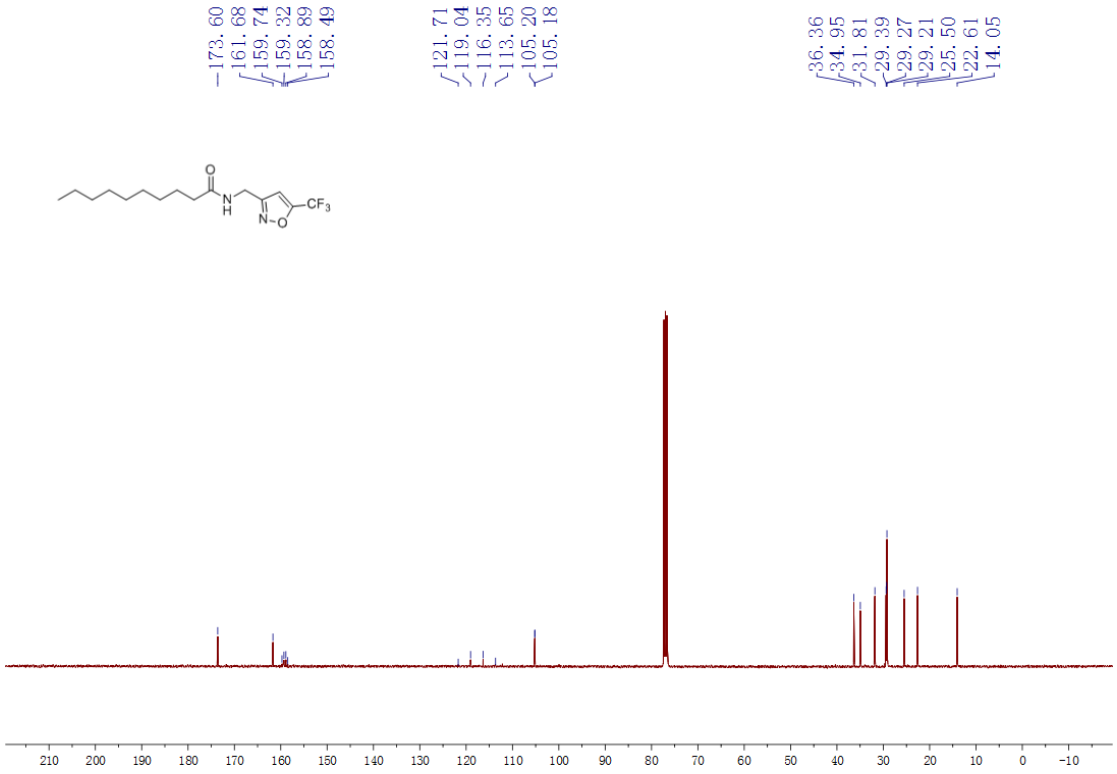
^{1}H NMR spectra of **4p** in $CDCl_3$



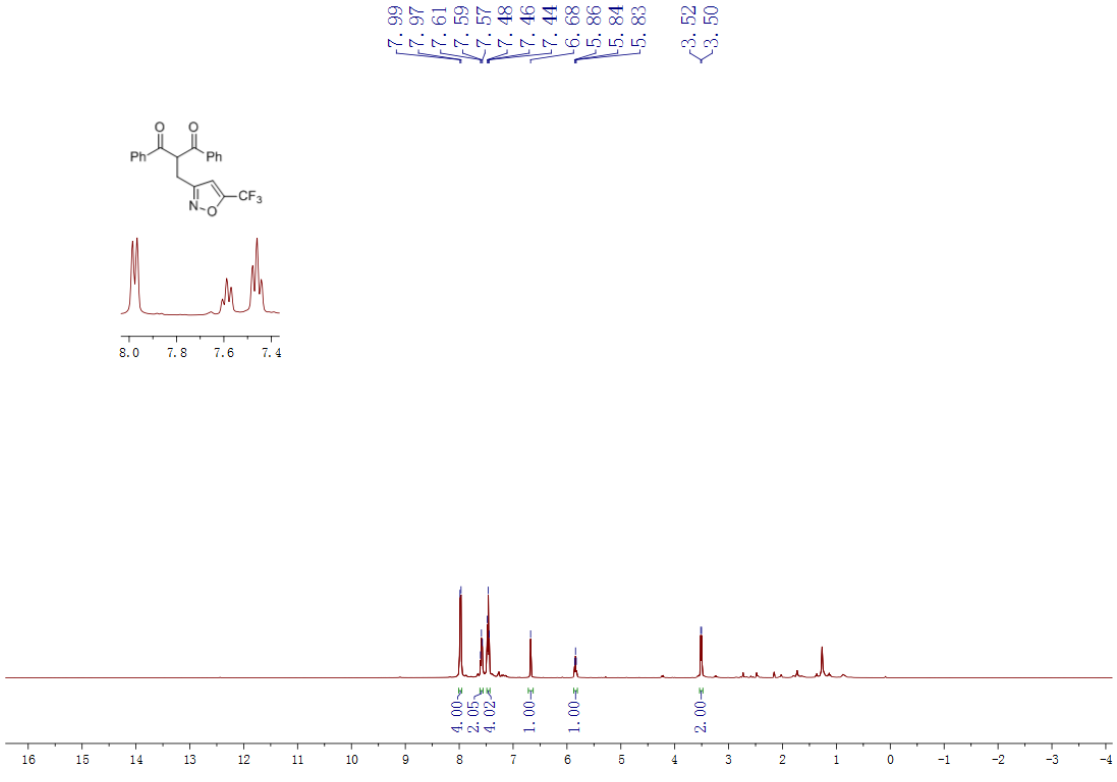
^{19}F NMR spectra of **4p** in $CDCl_3$



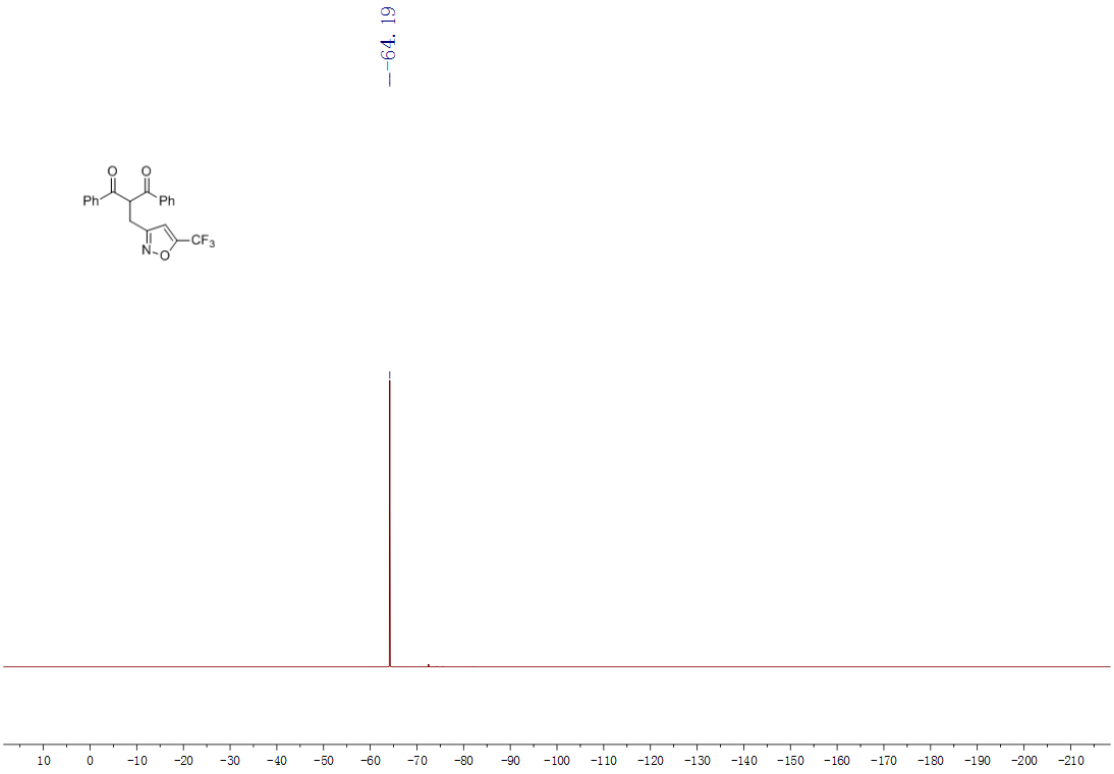
^{13}C NMR spectra of **4p** in $CDCl_3$



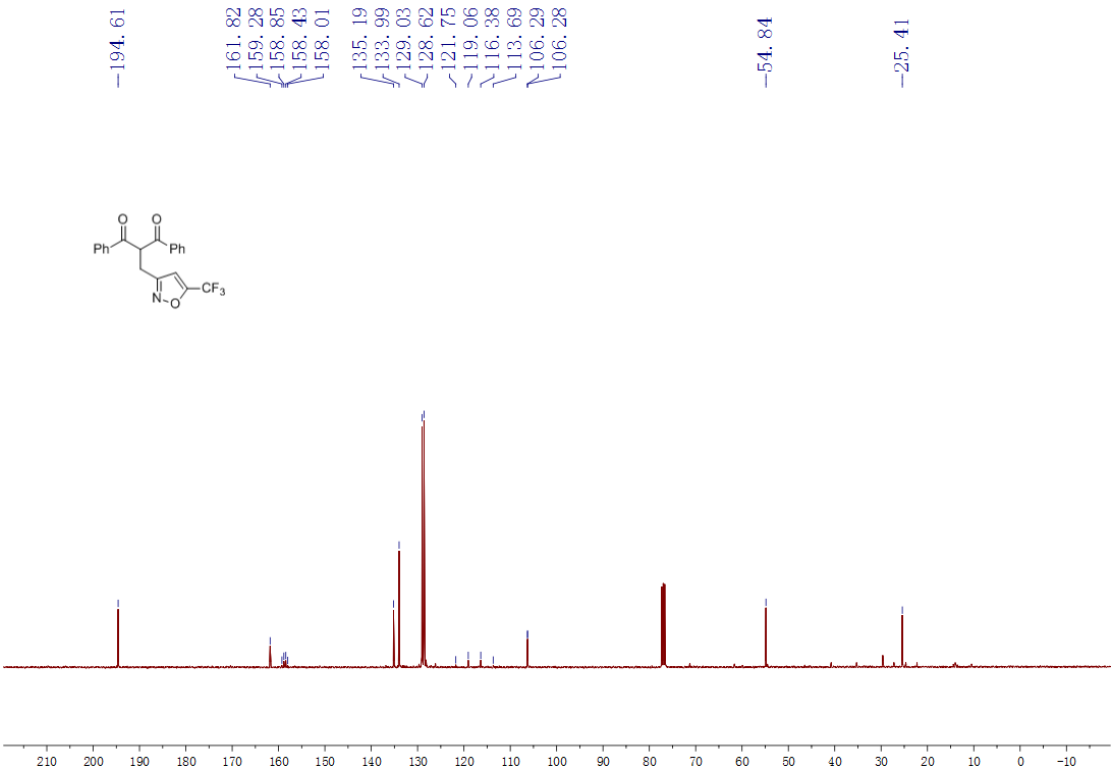
^{1}H NMR spectra of **4q** in $CDCl_3$



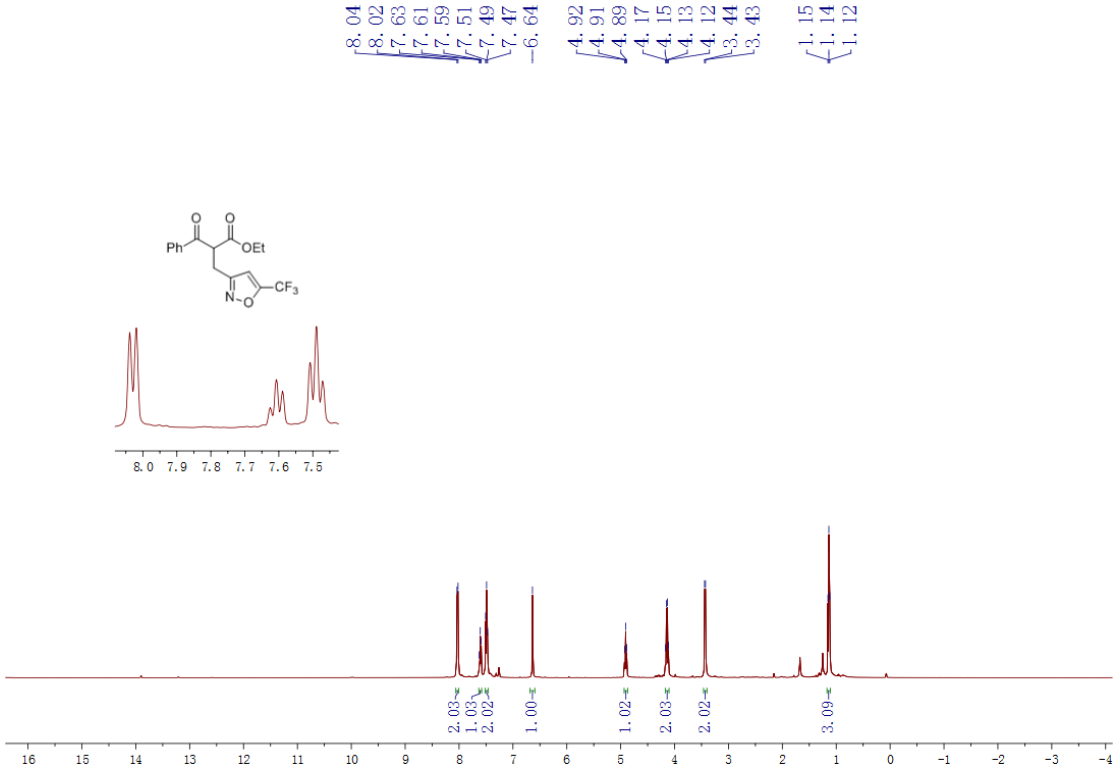
^{19}F NMR spectra of **4q** in $CDCl_3$



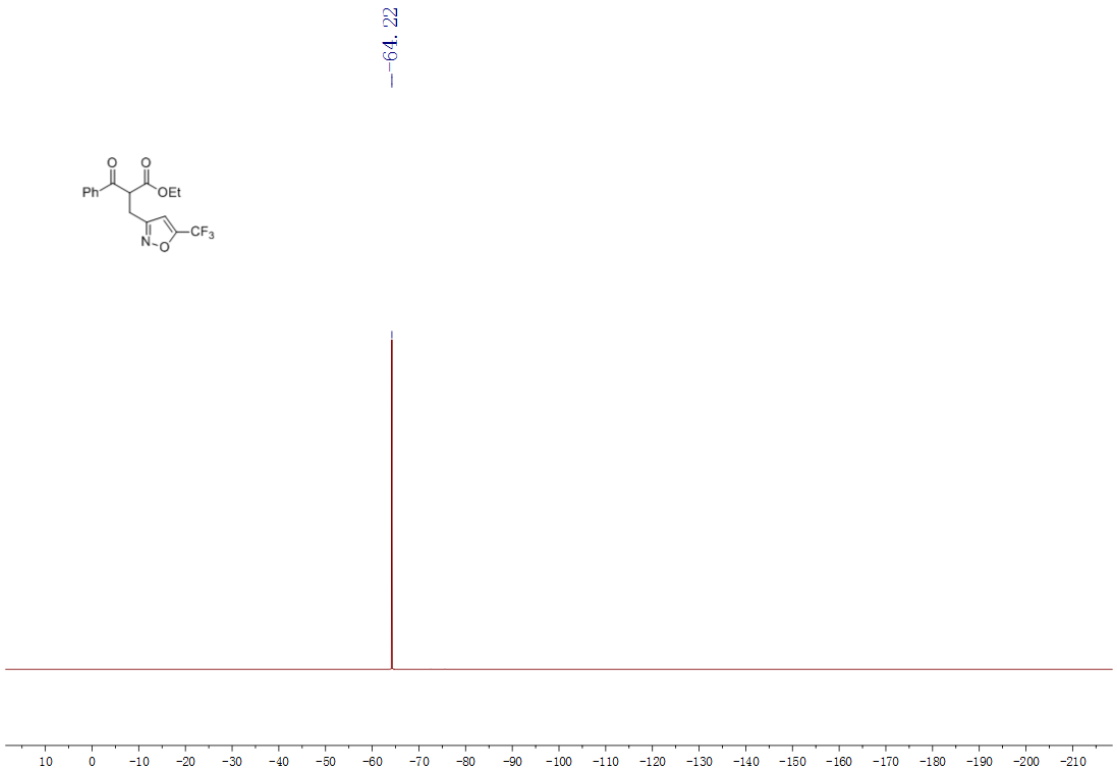
^{13}C NMR spectra of **4q** in $CDCl_3$



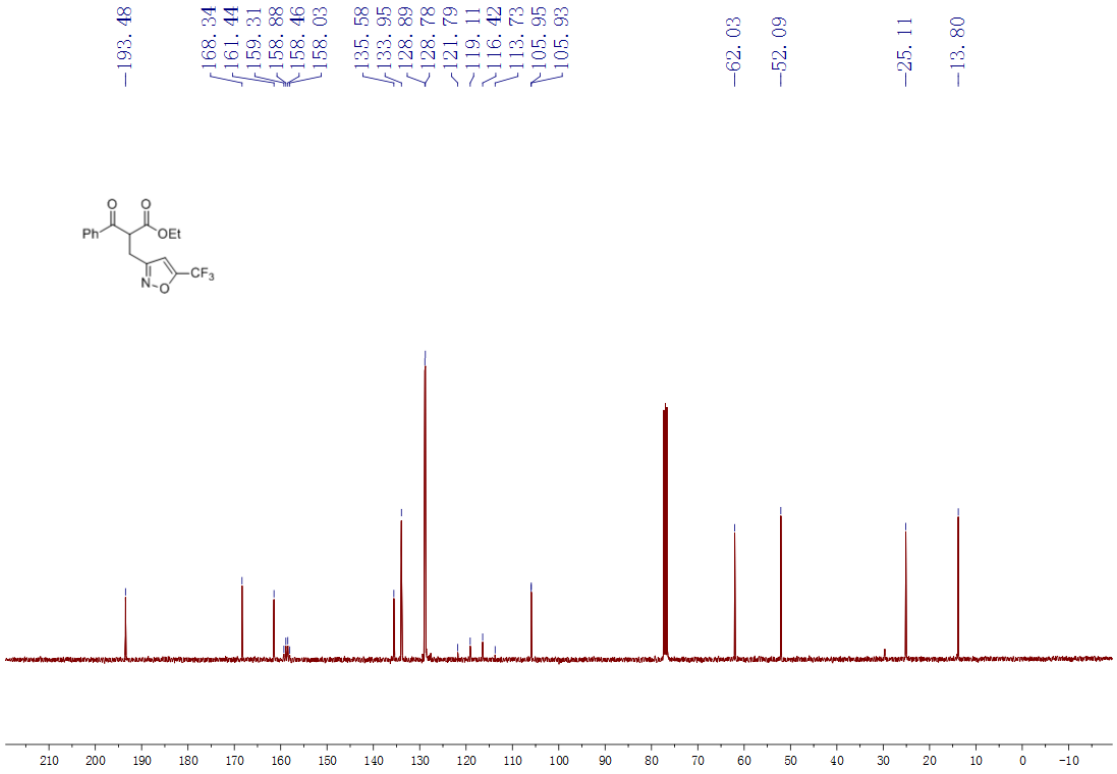
^{1}H NMR spectra of **4r** in $CDCl_3$



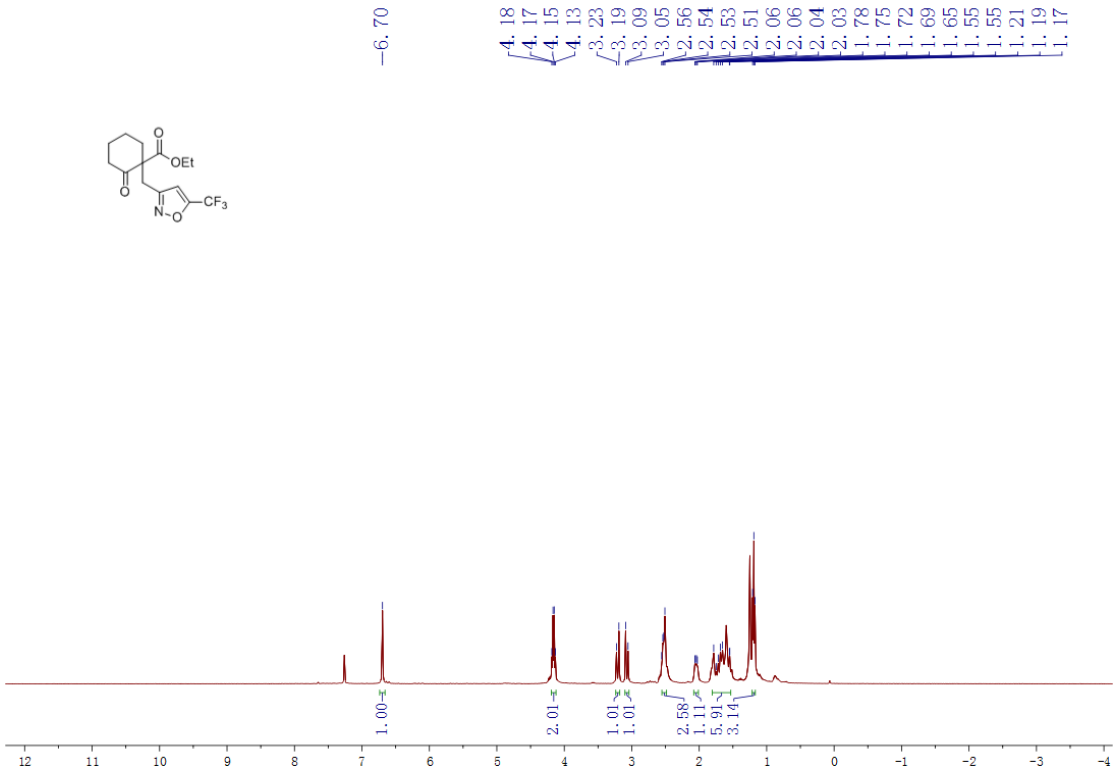
^{19}F NMR spectra of **4r** in $CDCl_3$



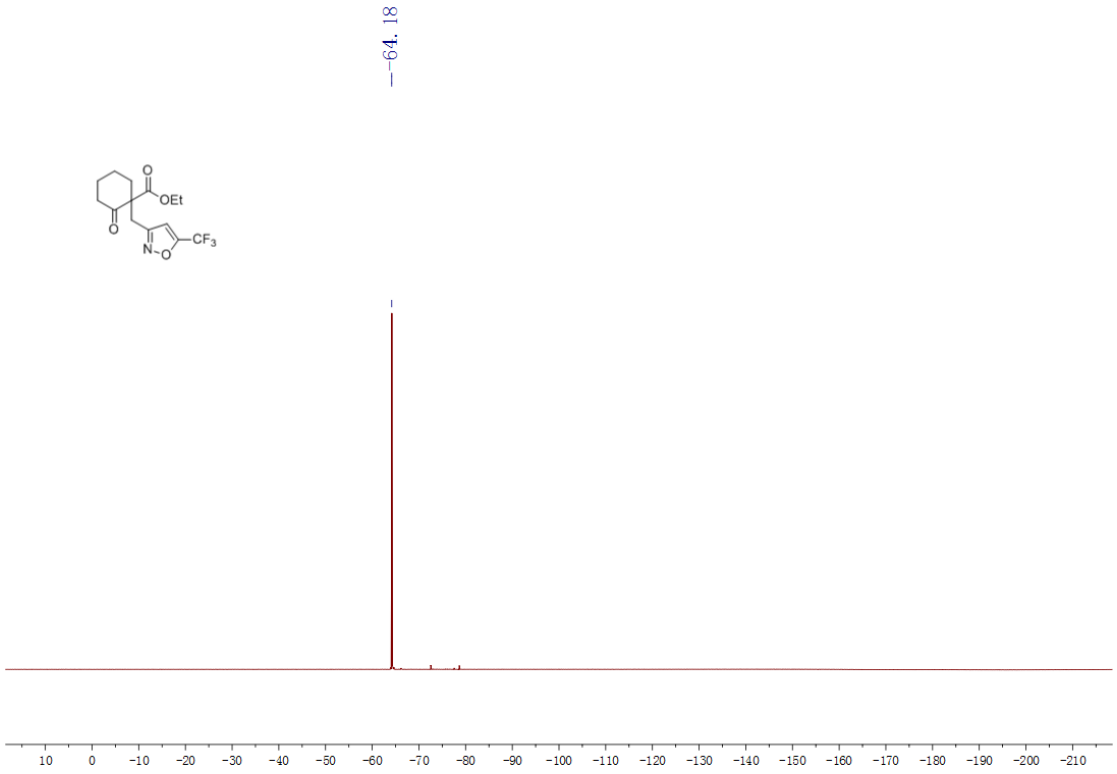
^{13}C NMR spectra of **4r** in $CDCl_3$



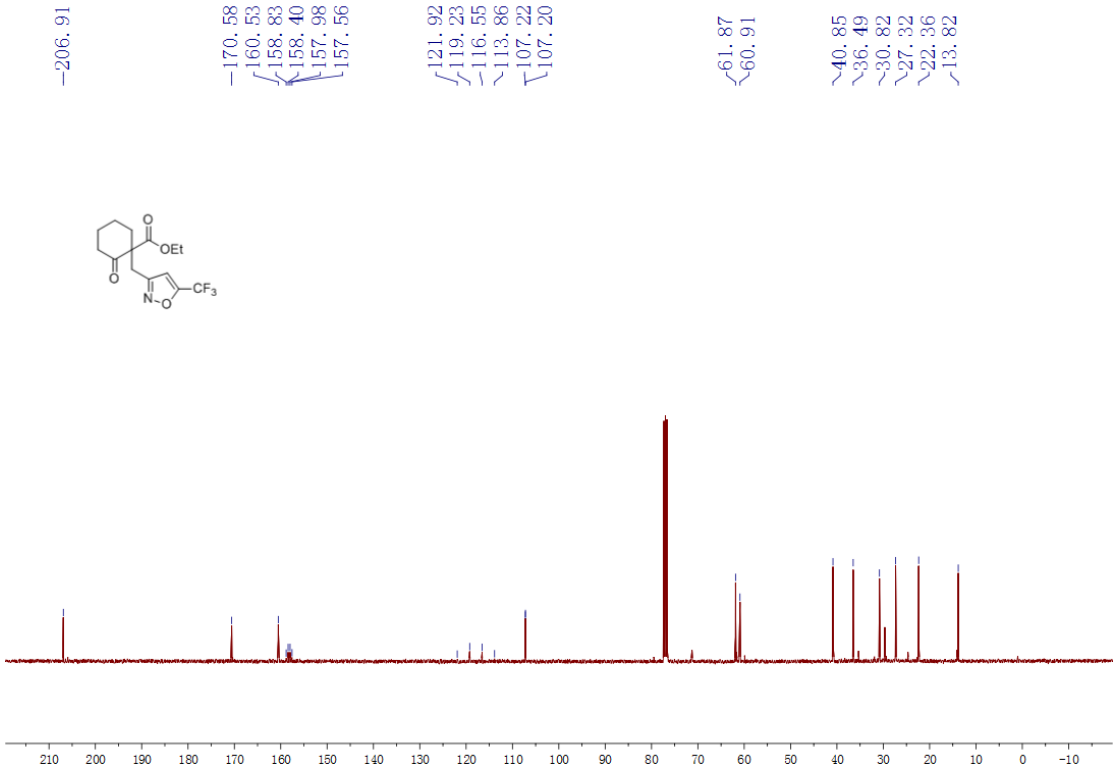
^{1}H NMR spectra of **4s** in $CDCl_3$



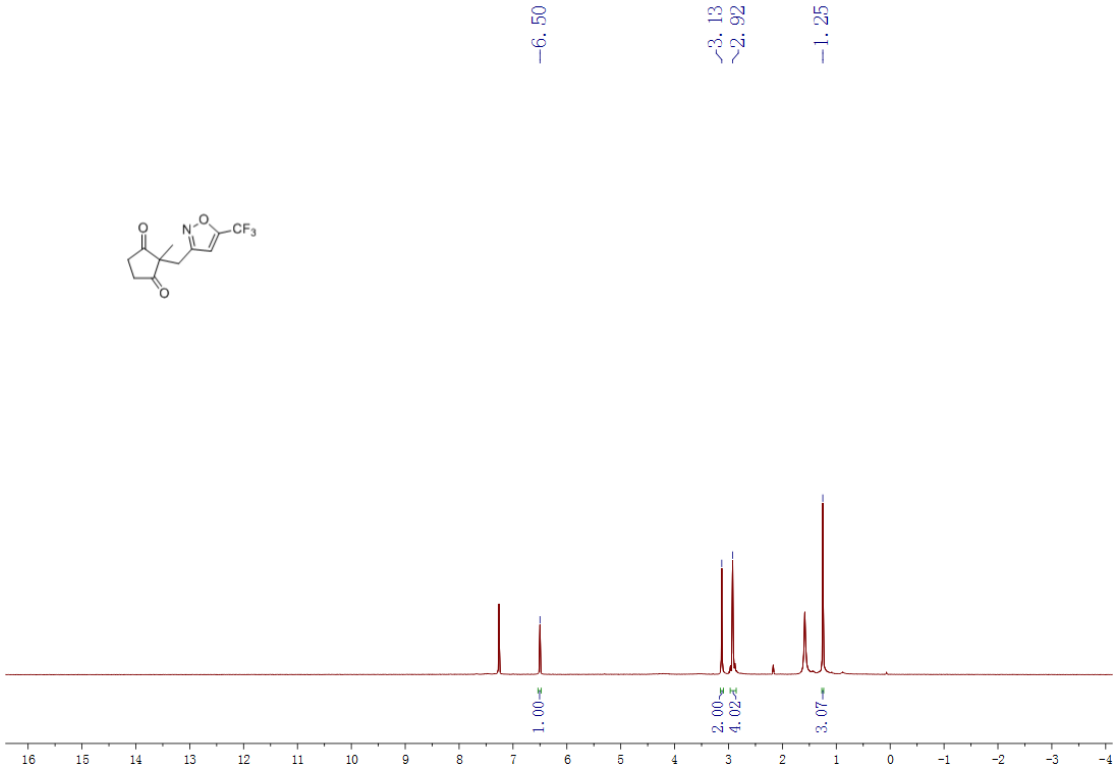
^{19}F NMR spectra of **4s** in $CDCl_3$



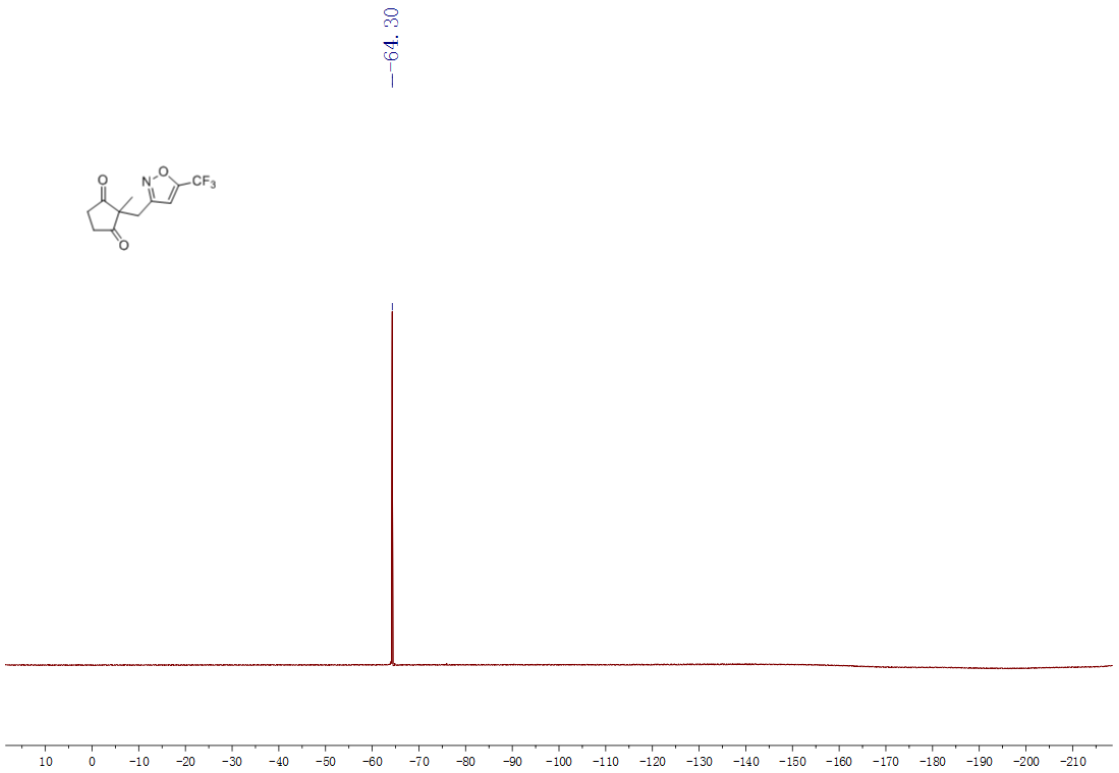
^{13}C NMR spectra of **4s** in $CDCl_3$



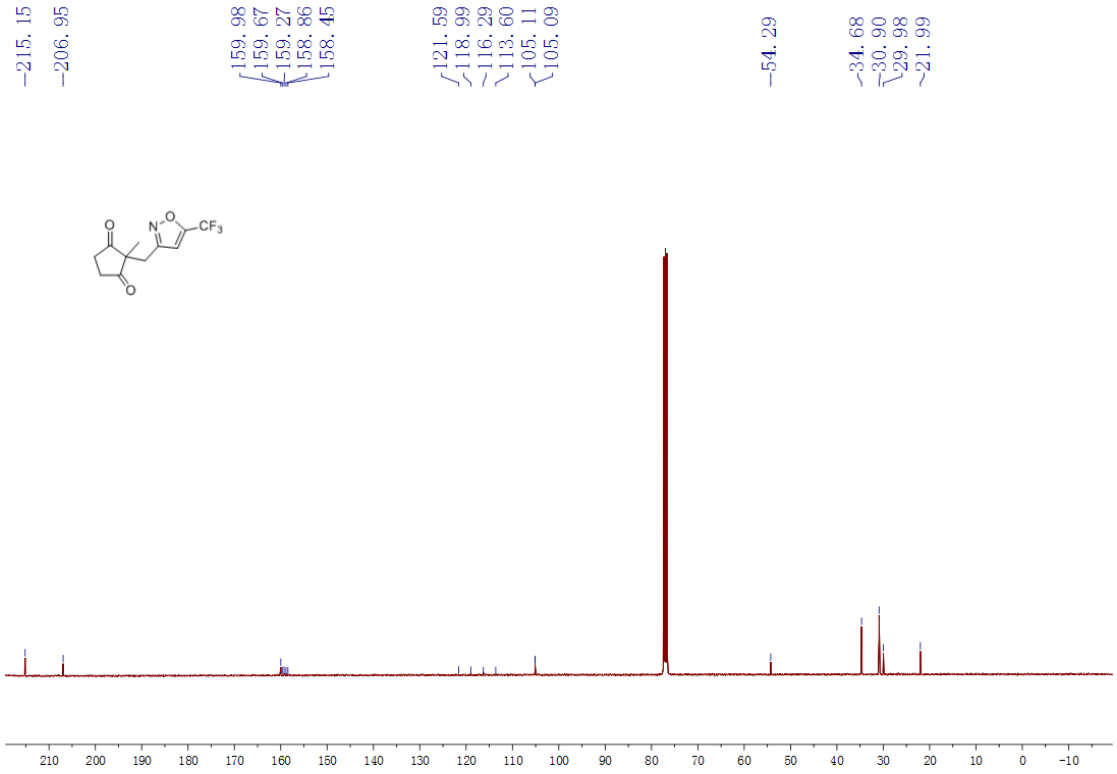
^{1}H NMR spectra of **4t** in $CDCl_3$



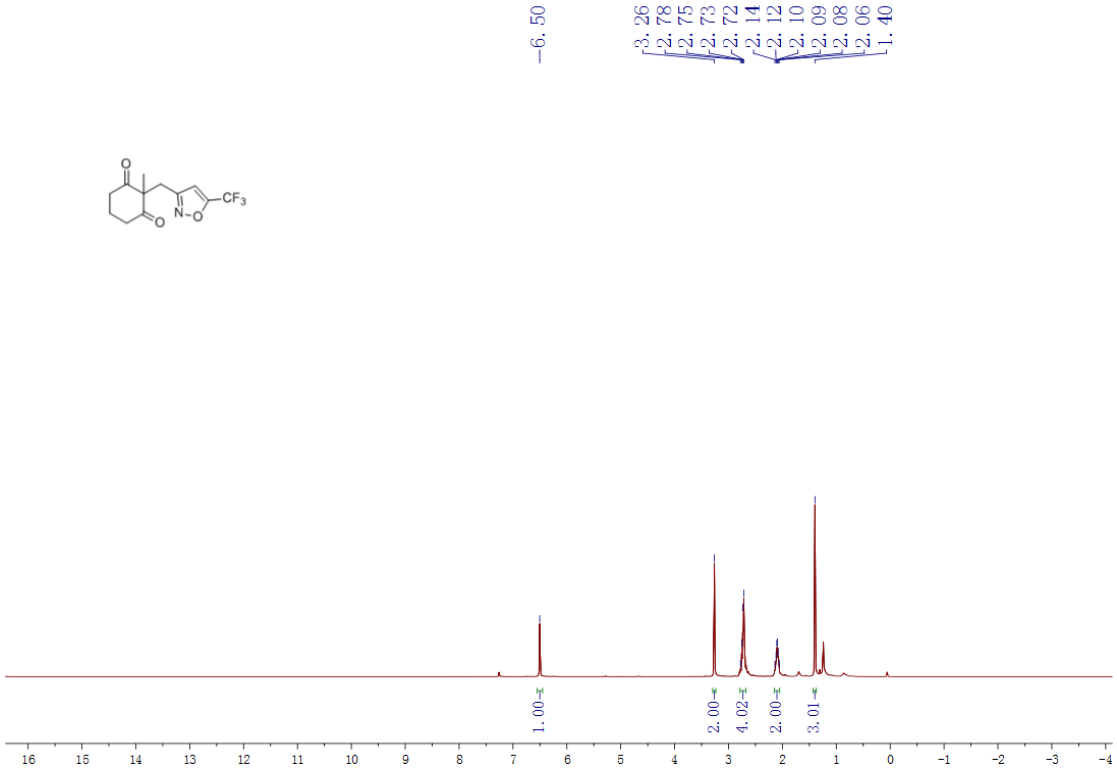
^{19}F NMR spectra of **4t** in $CDCl_3$



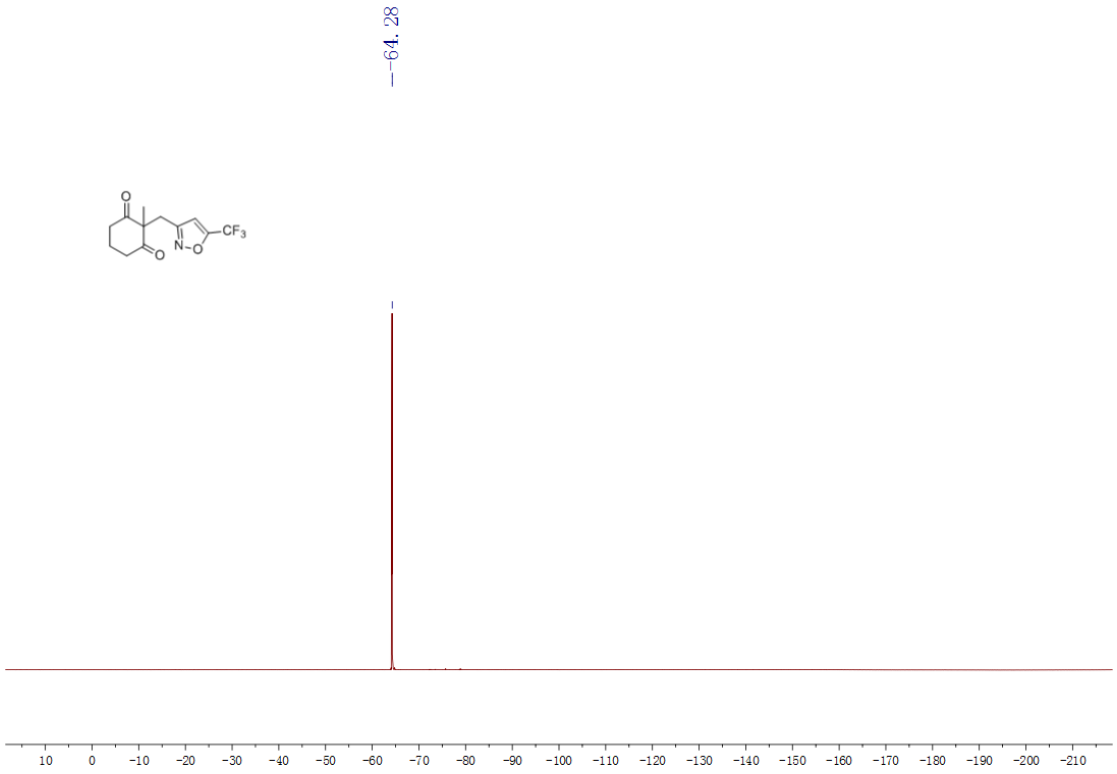
^{13}C NMR spectra of **4t** in $CDCl_3$



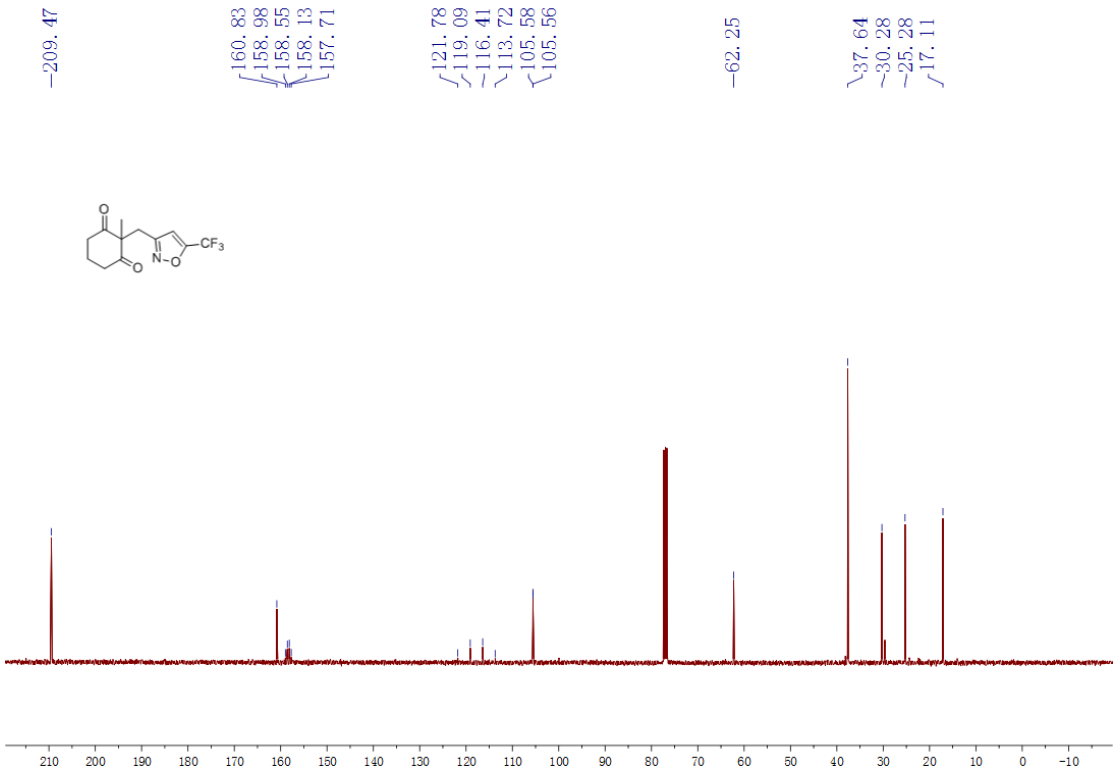
^{1}H NMR spectra of **4u** in $CDCl_3$



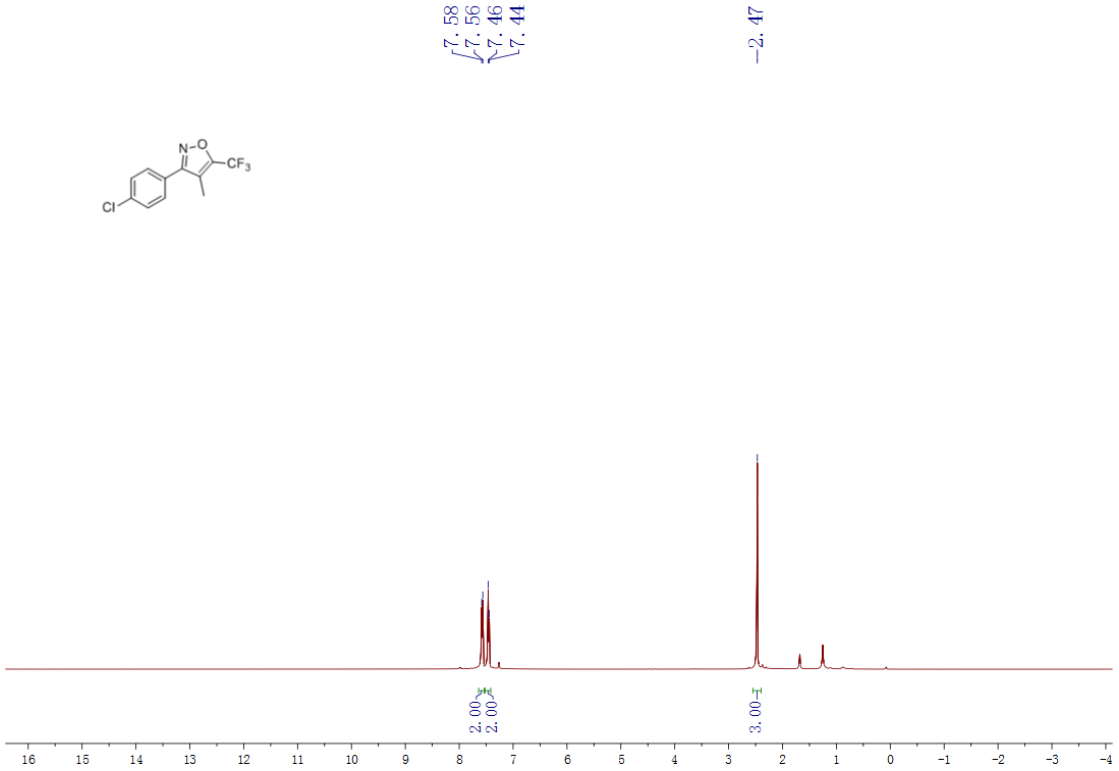
^{19}F NMR spectra of **4u** in $CDCl_3$



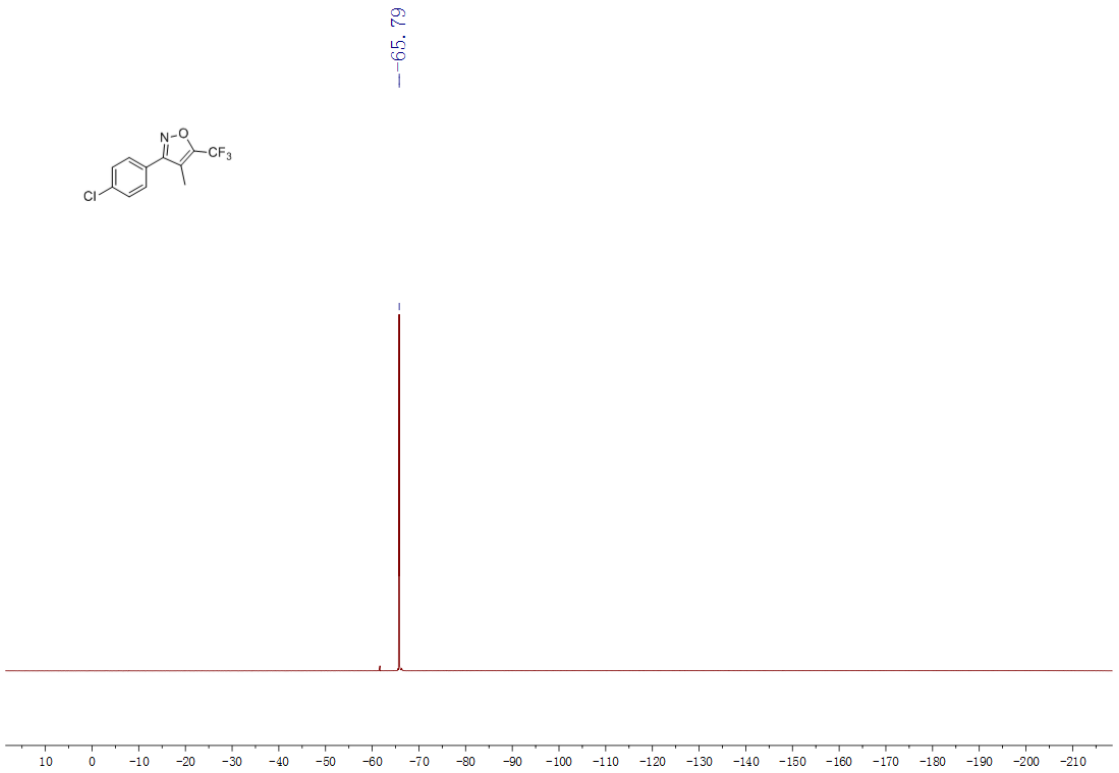
^{13}C NMR spectra of **4u** in $CDCl_3$



^{1}H NMR spectra of **5a** in $CDCl_3$



^{19}F NMR spectra of **5a** in $CDCl_3$



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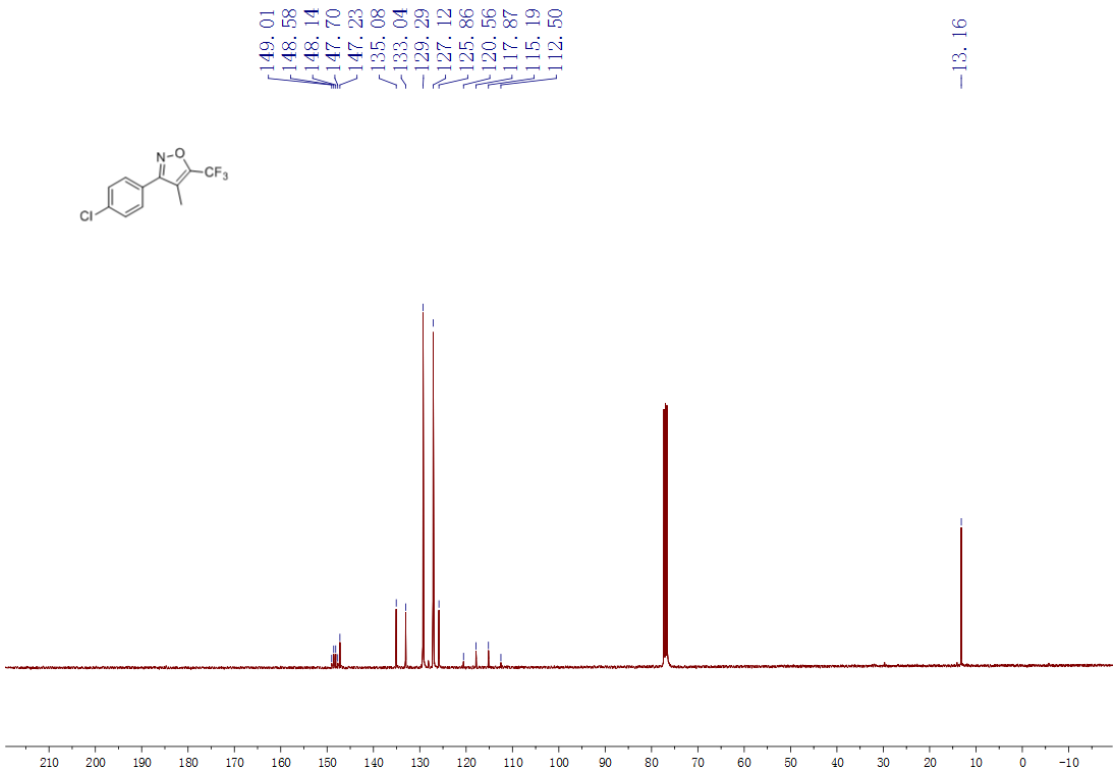

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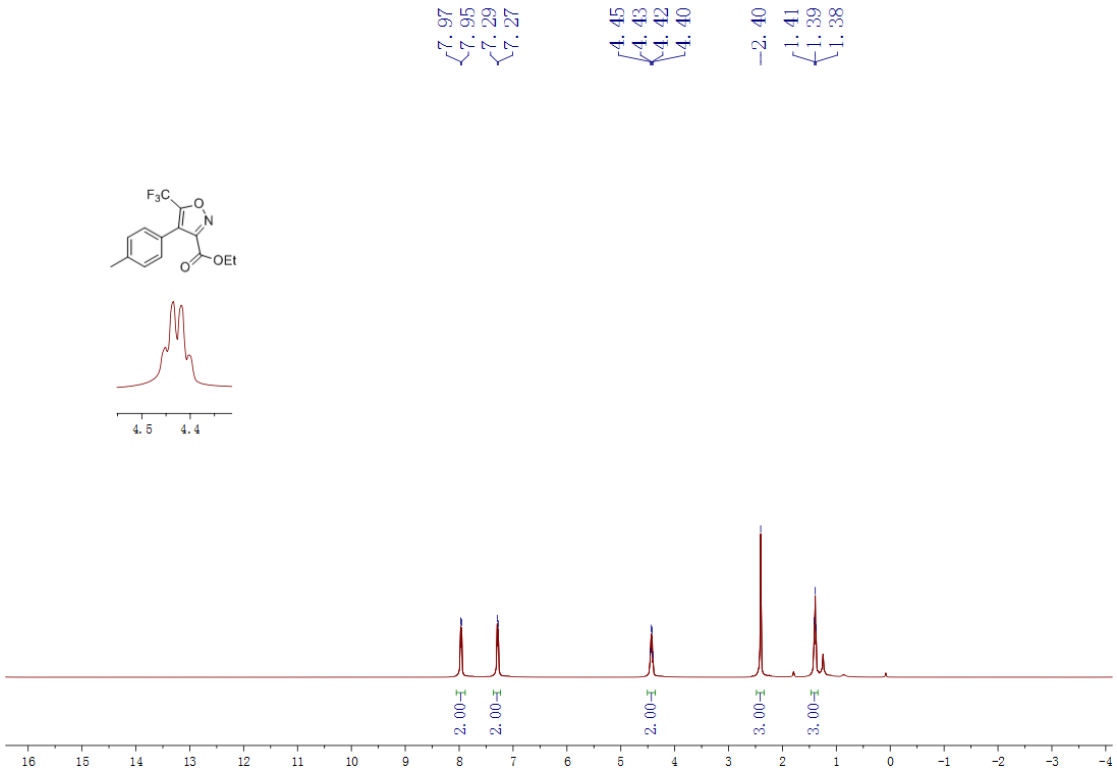

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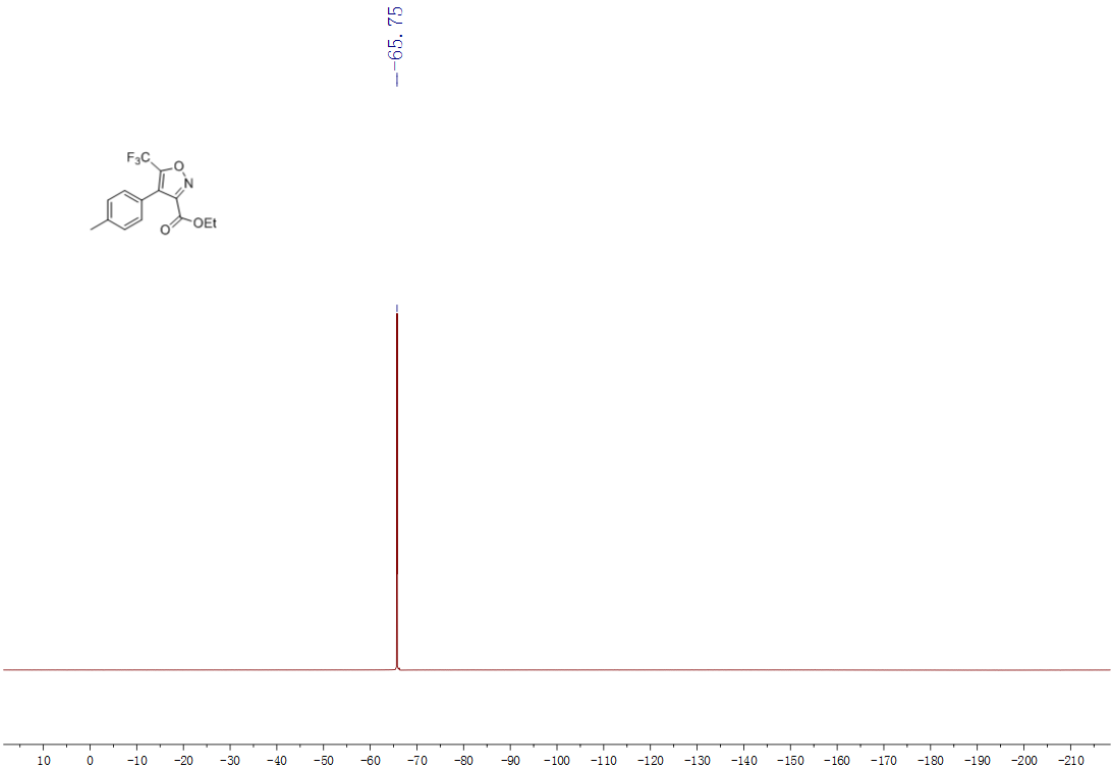

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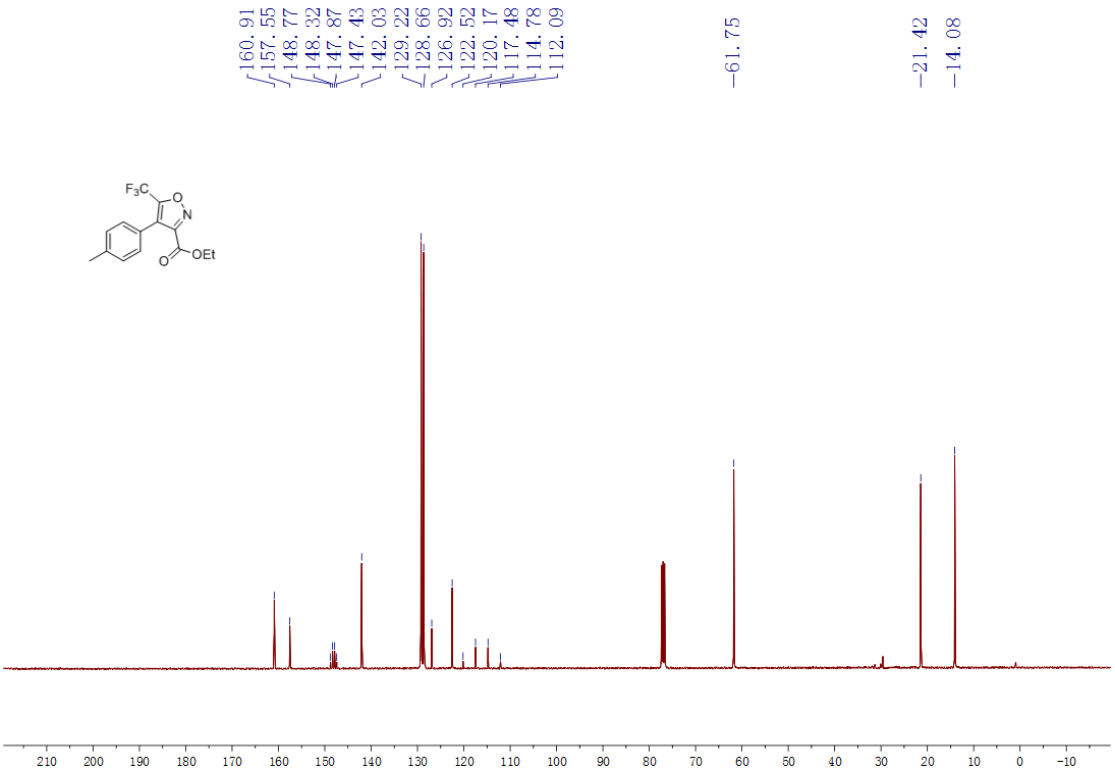

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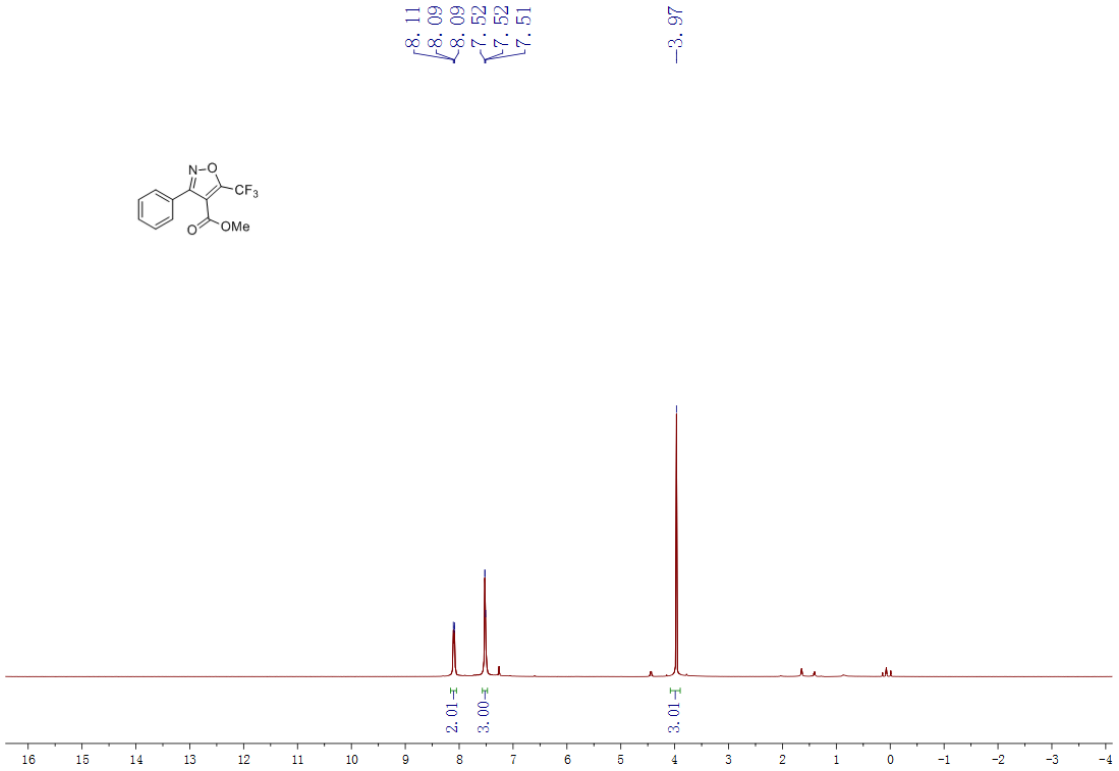

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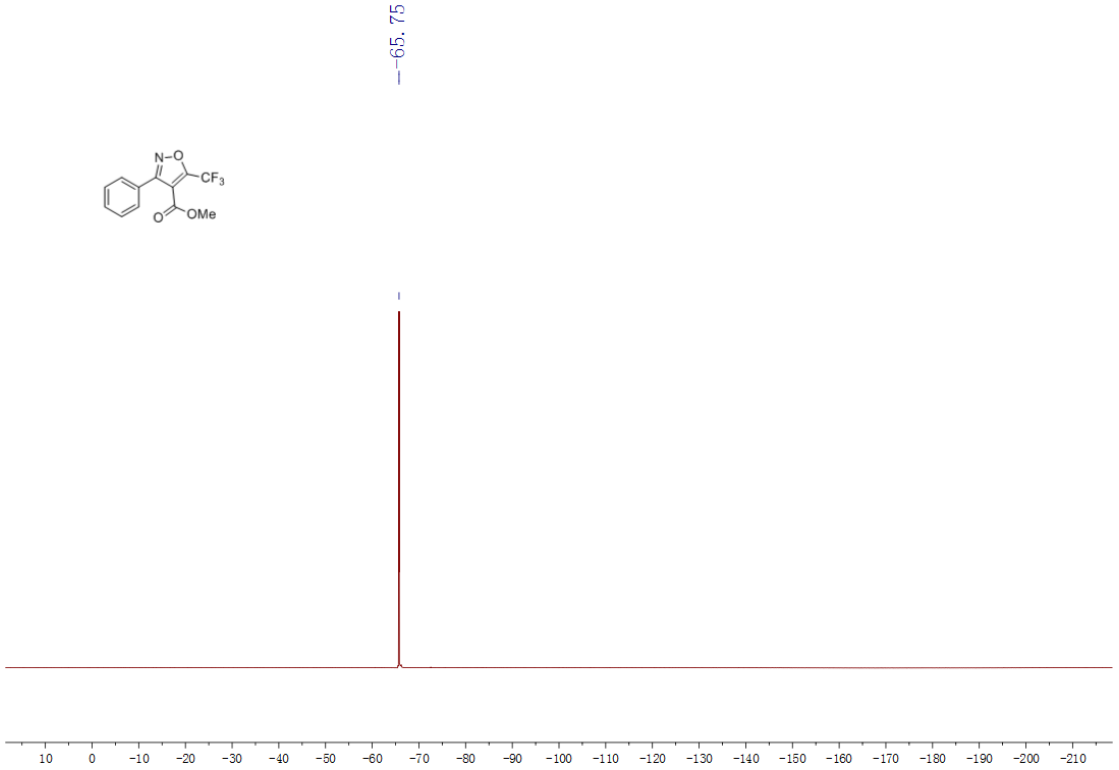

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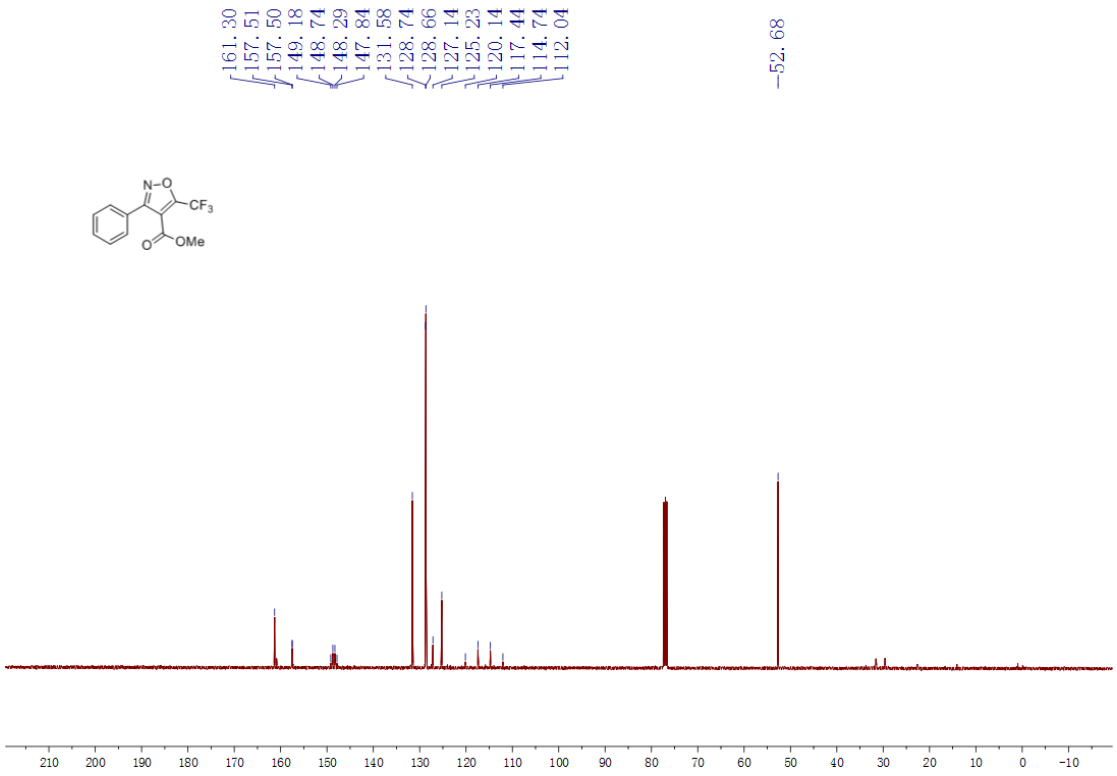

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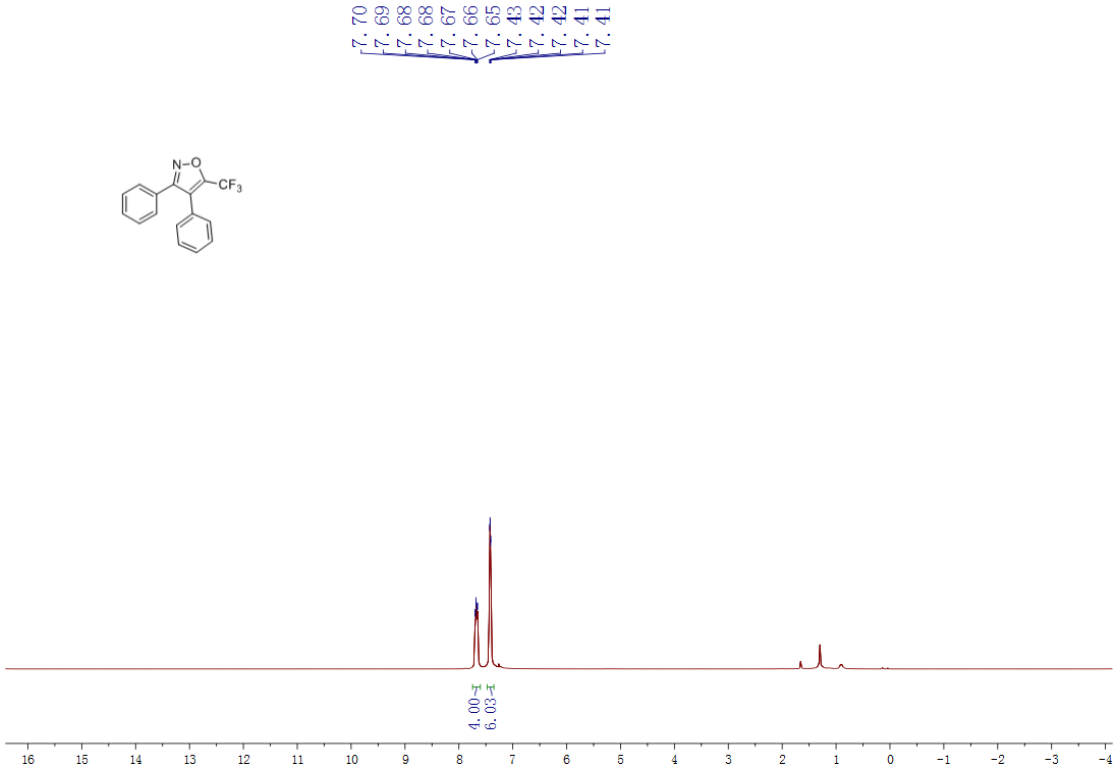

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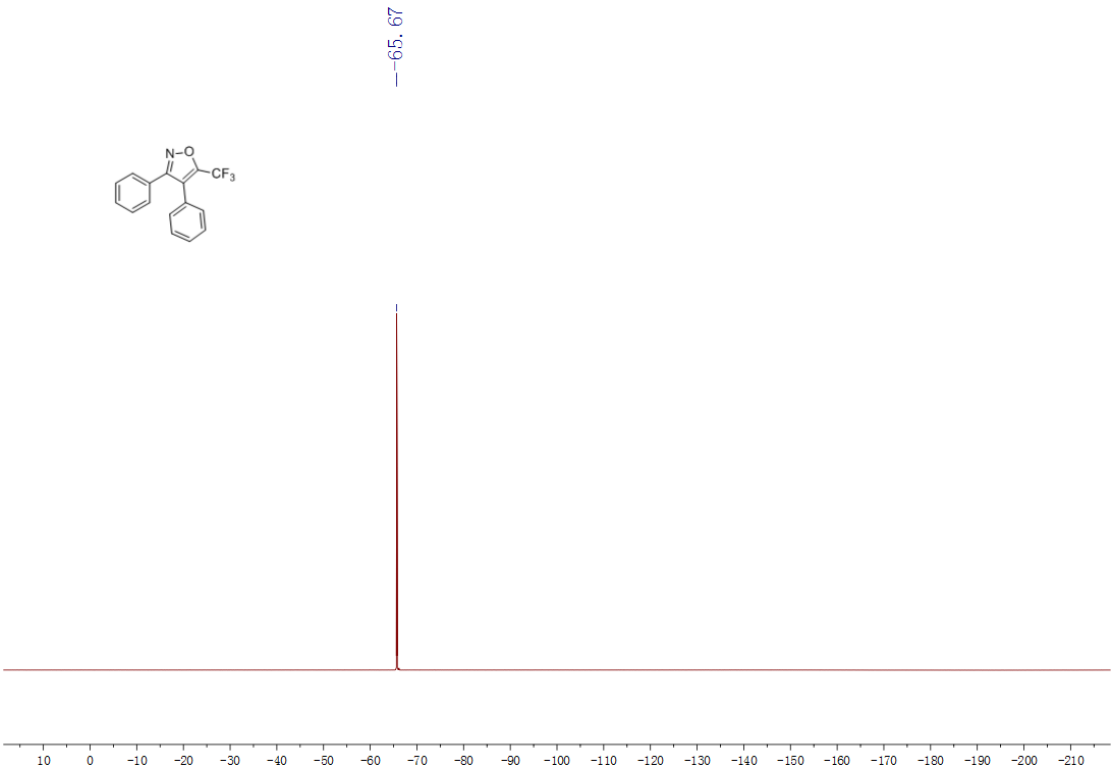

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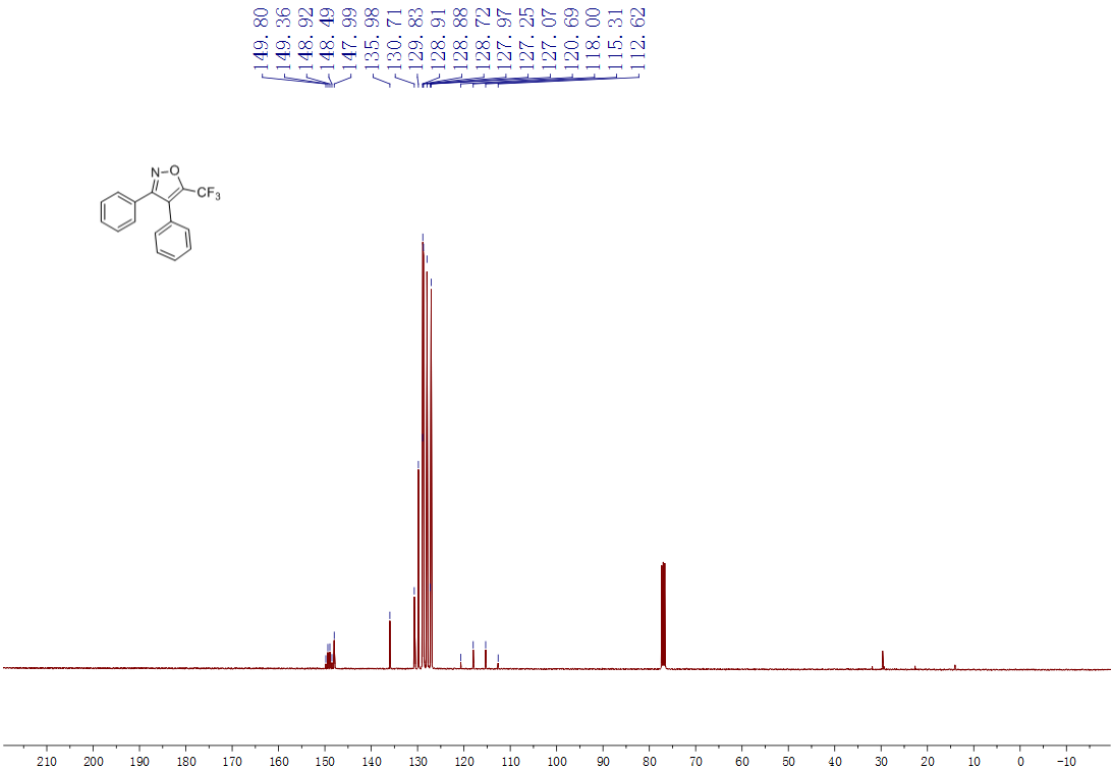
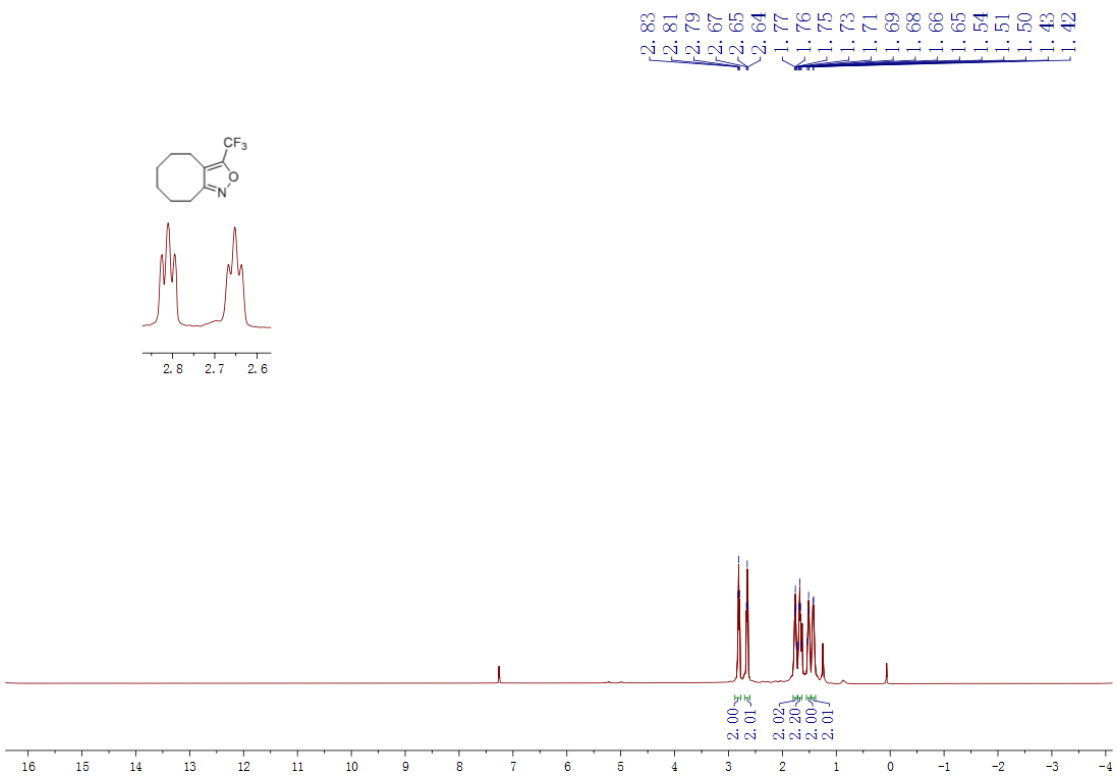


^{1}H NMR spectra of **5e** in $CDCl_3$



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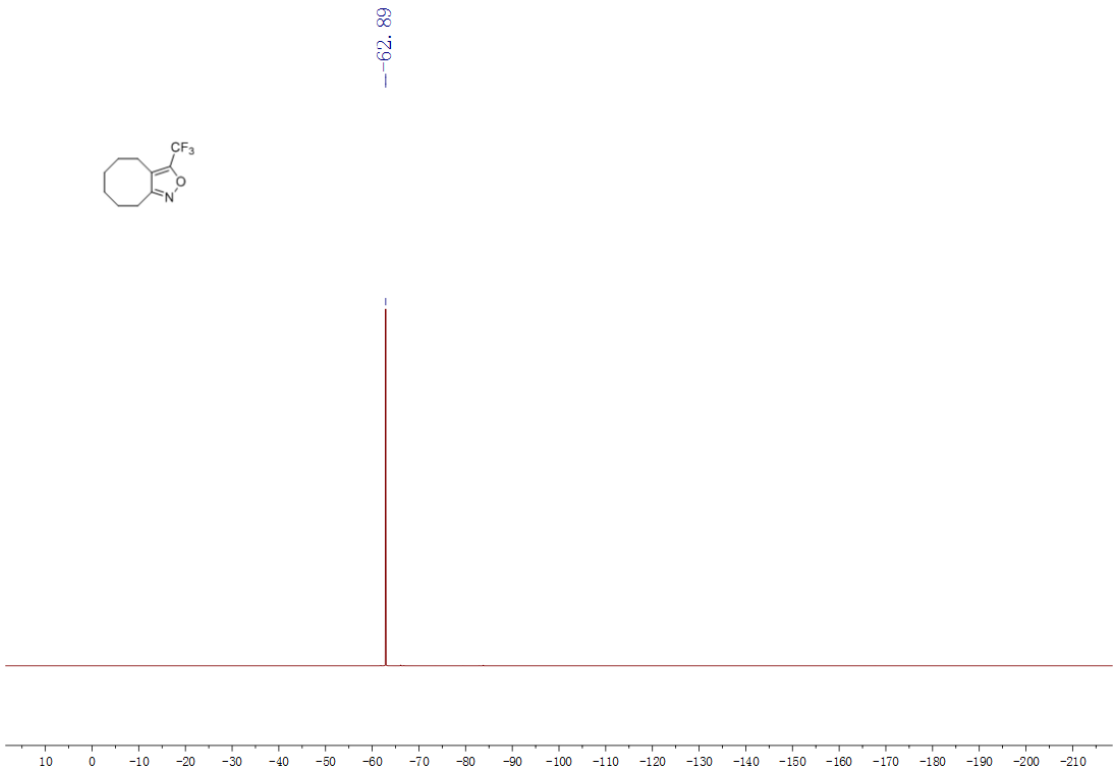
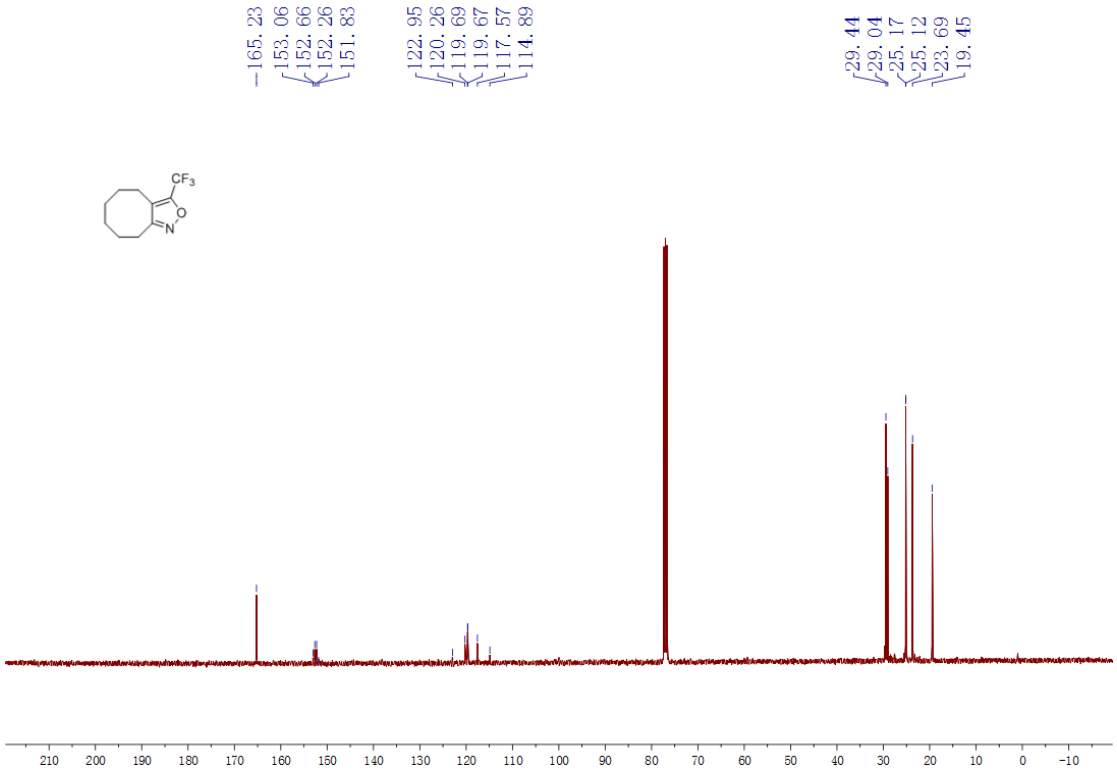
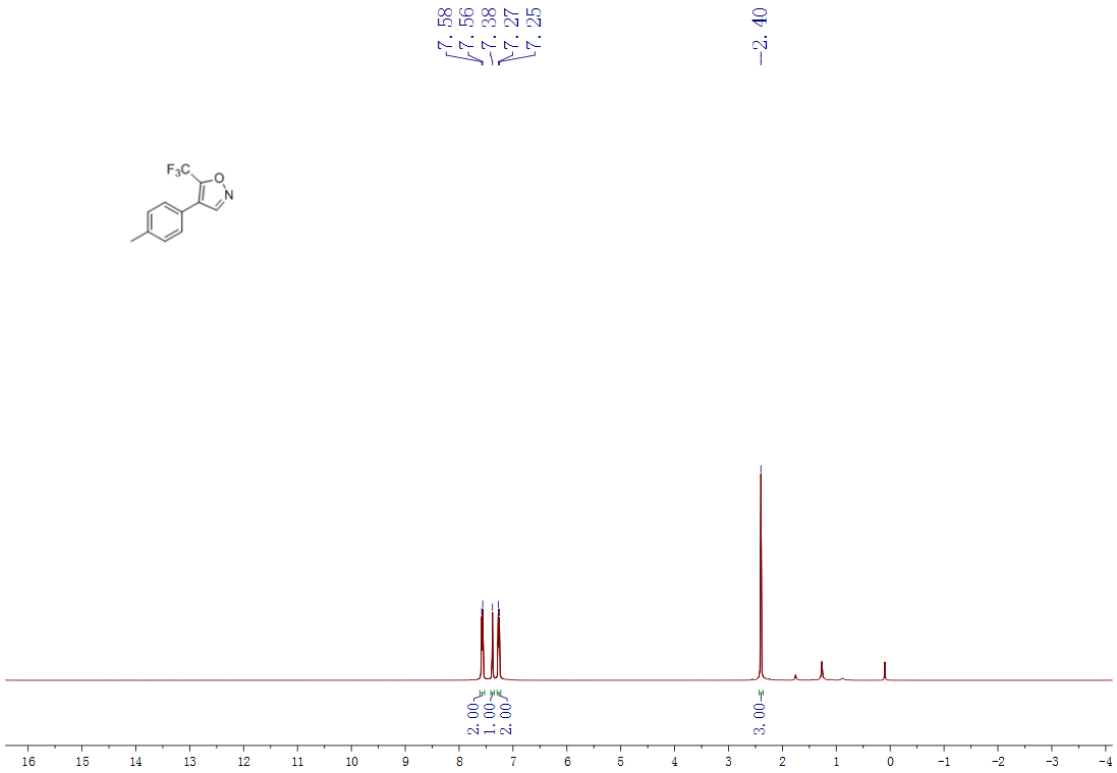


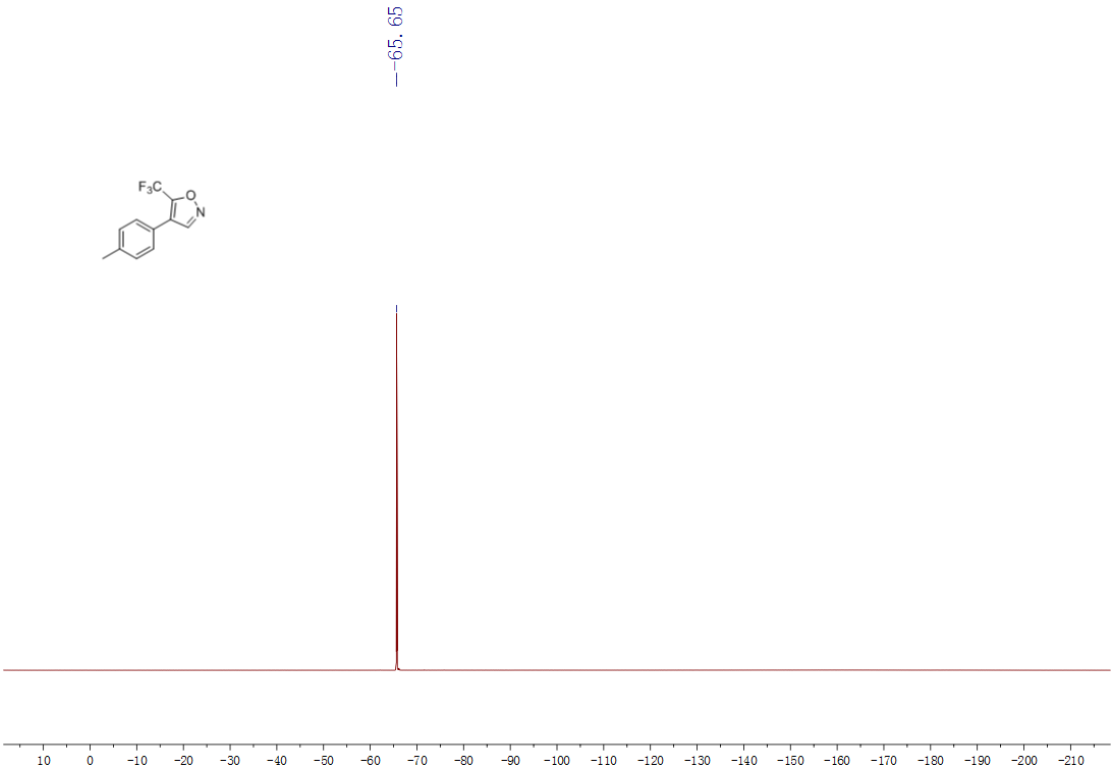
^{13}C NMR spectra of **5e** in $CDCl_3$



^{1}H NMR spectra of **6a** in $CDCl_3$



^{19}F NMR spectra of **6a** in $CDCl_3$



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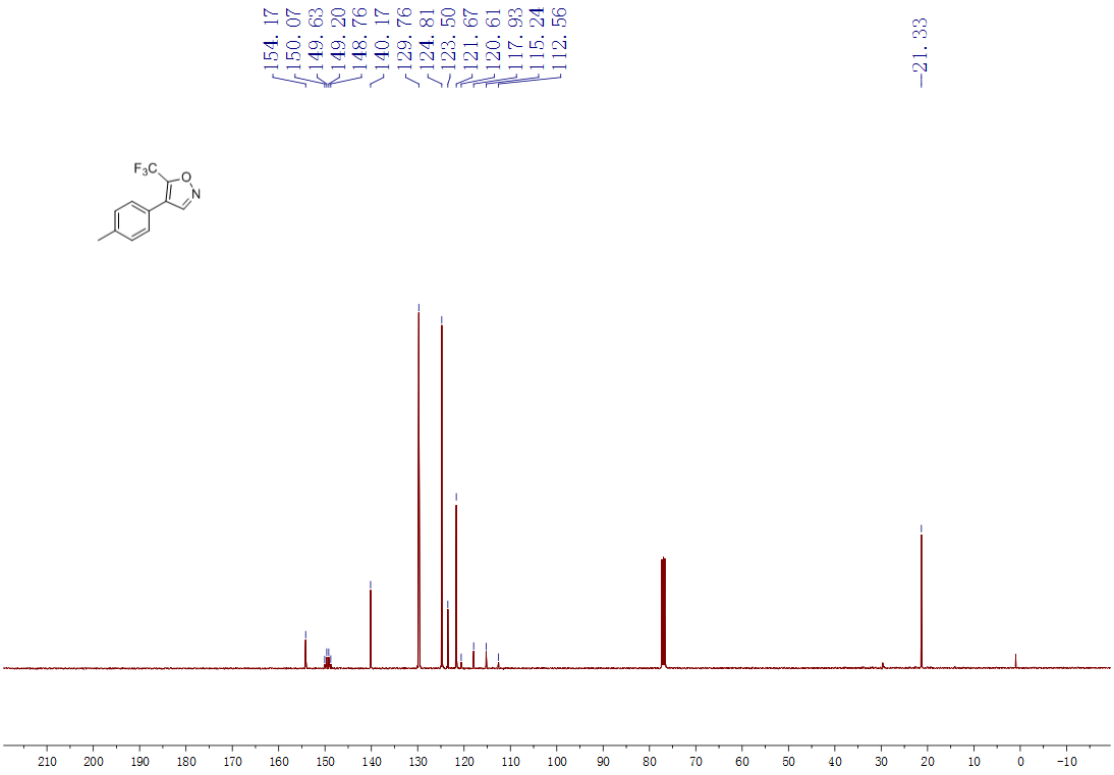

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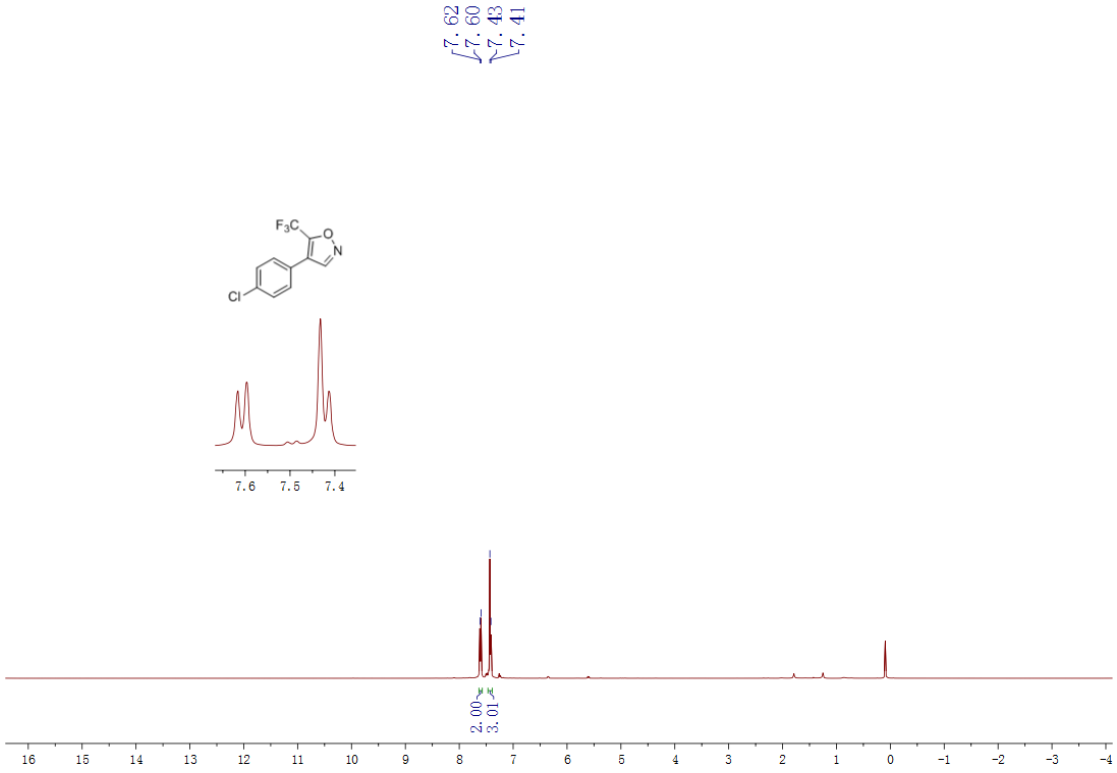

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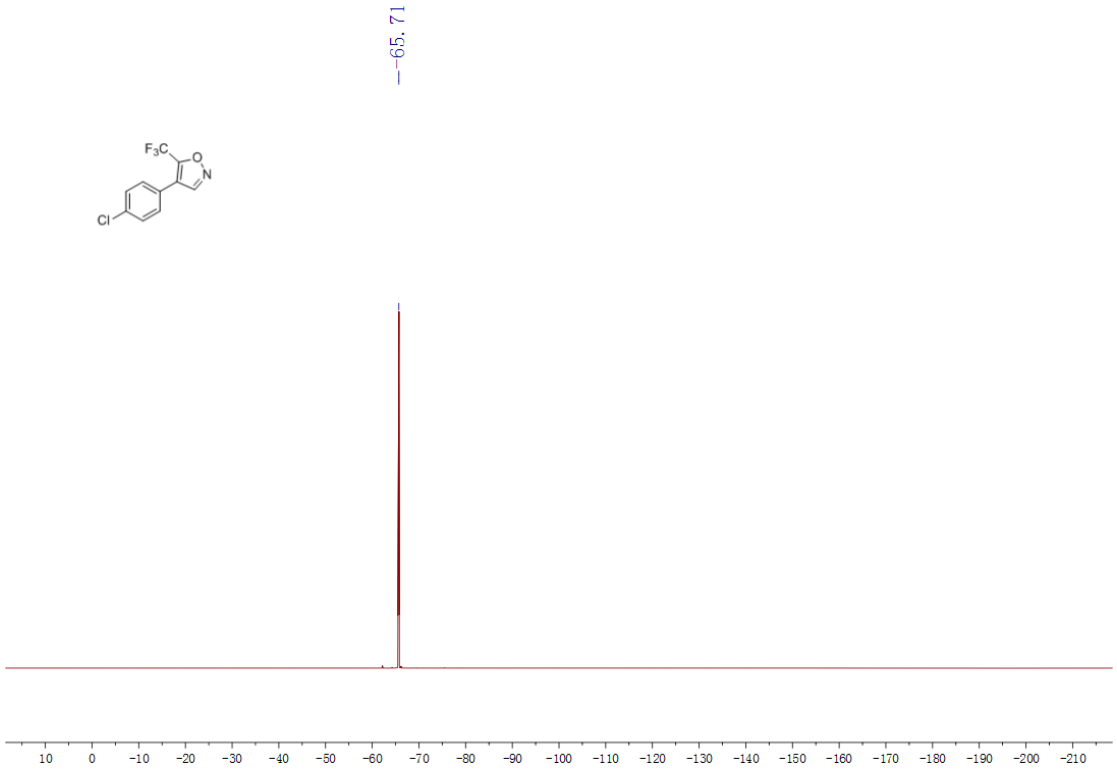

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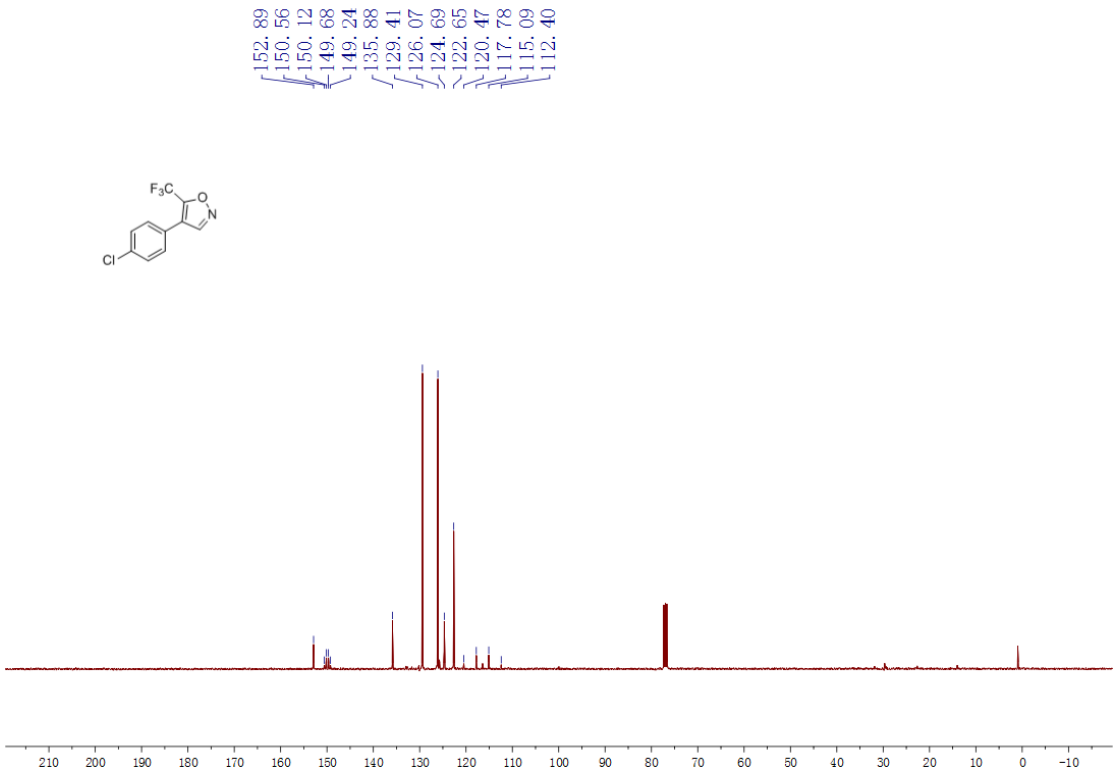

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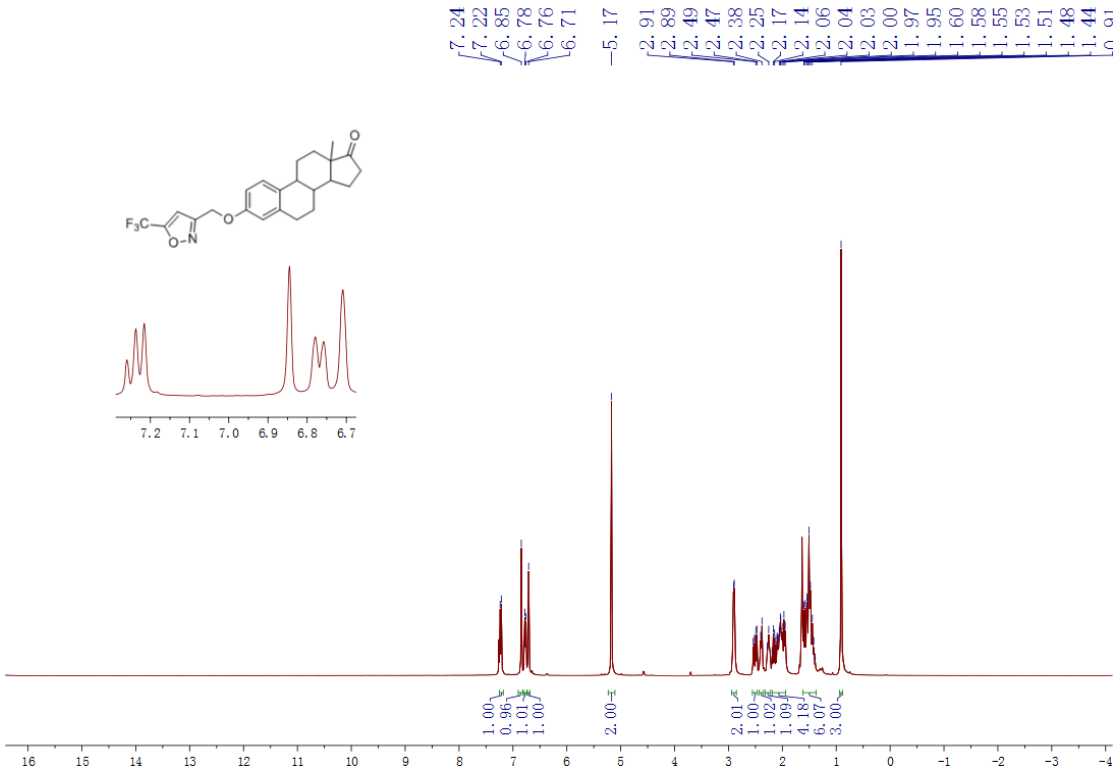
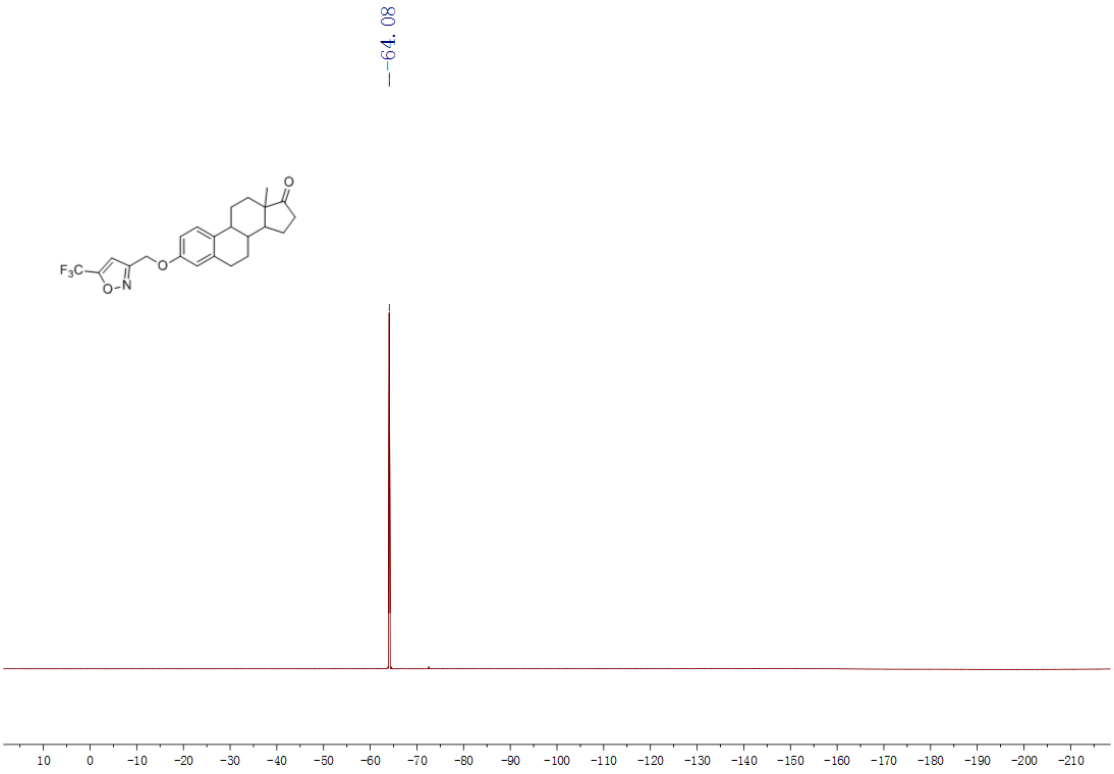


^{19}F NMR spectra of **7a** in $CDCl_3$



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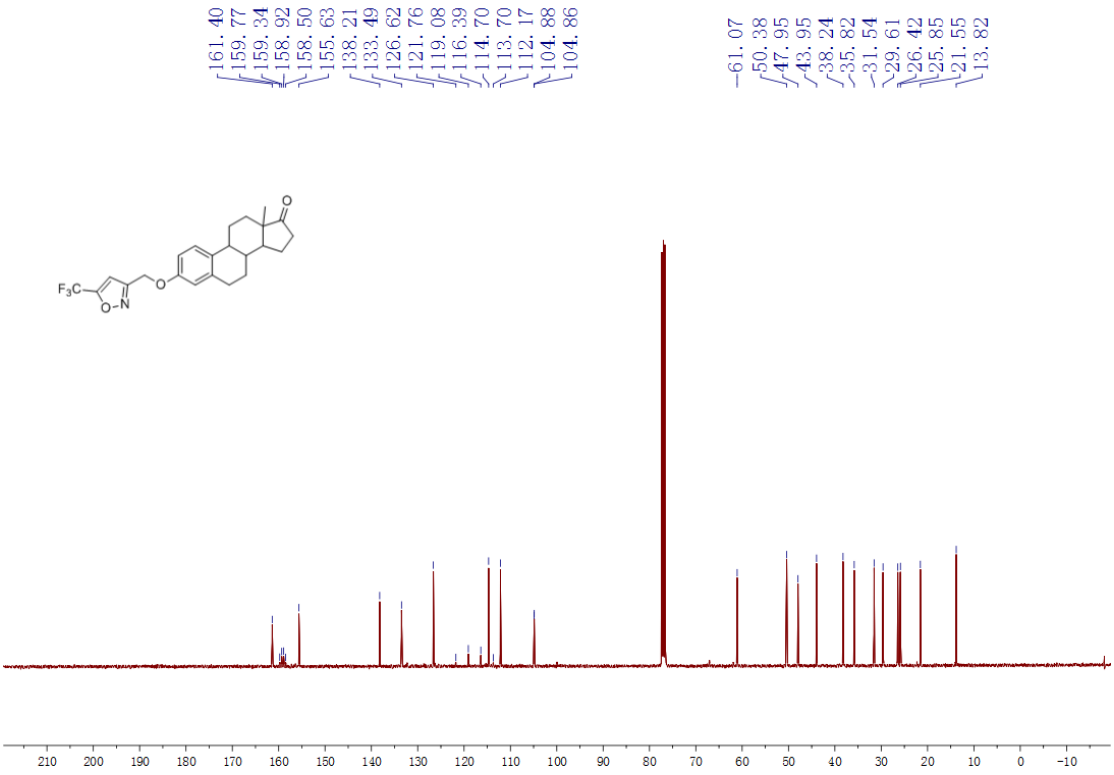

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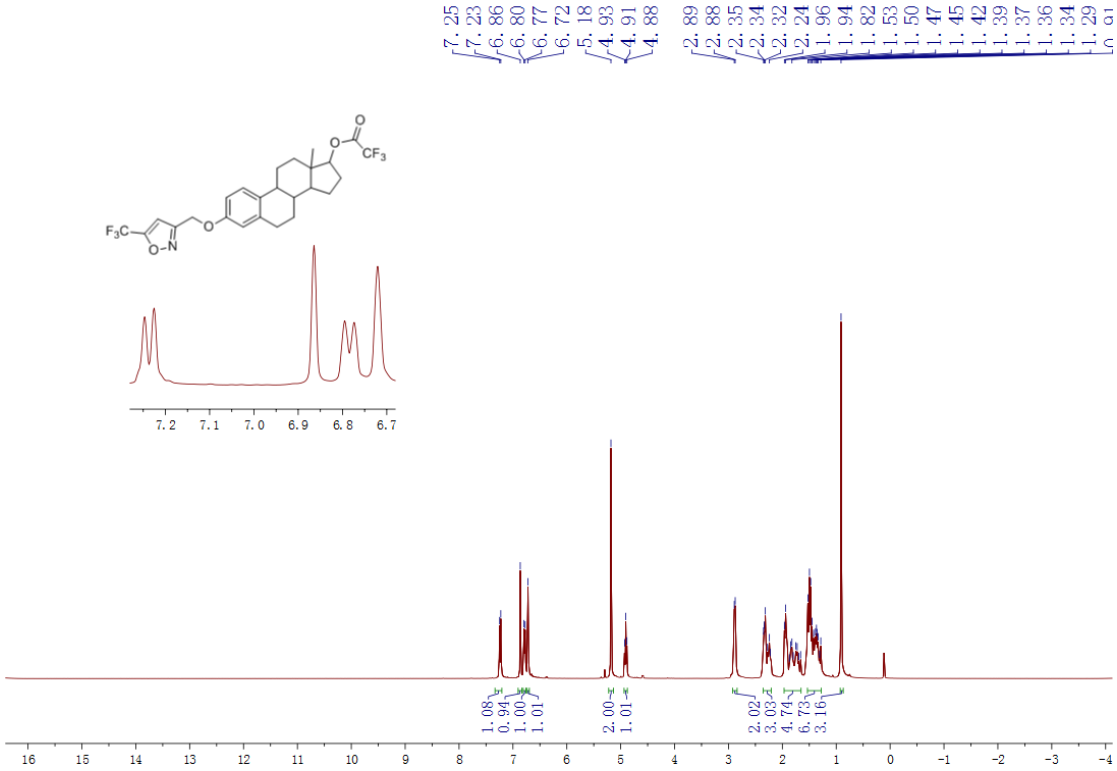

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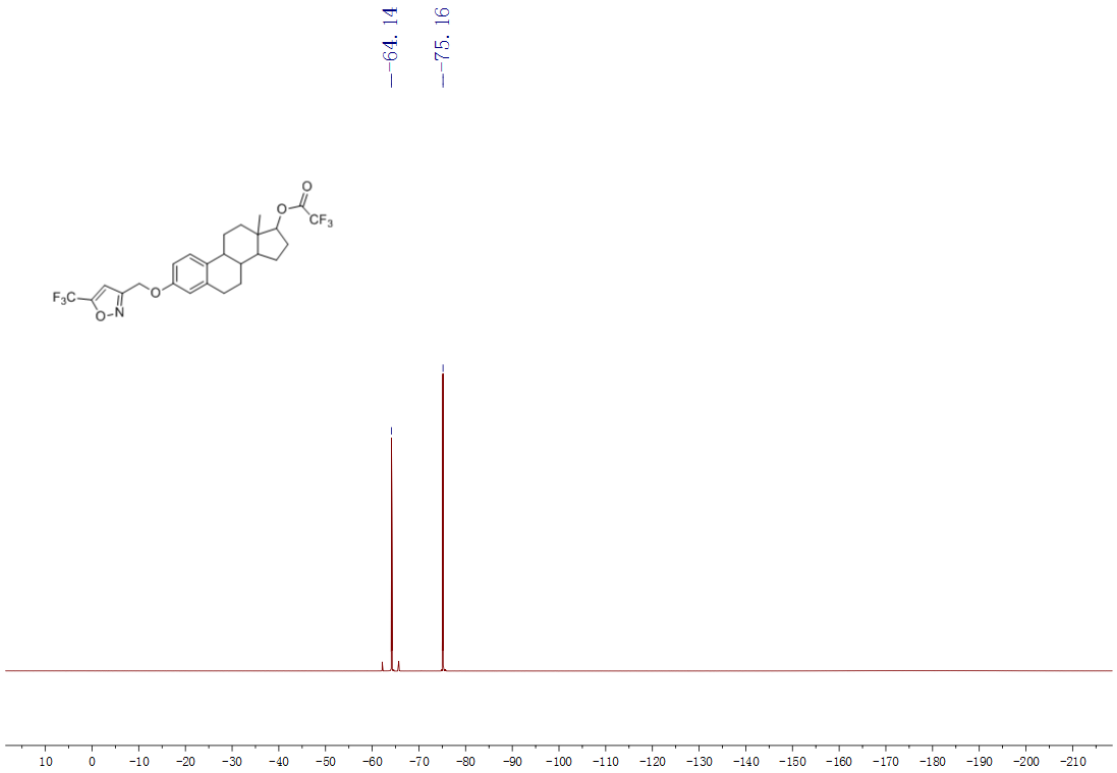

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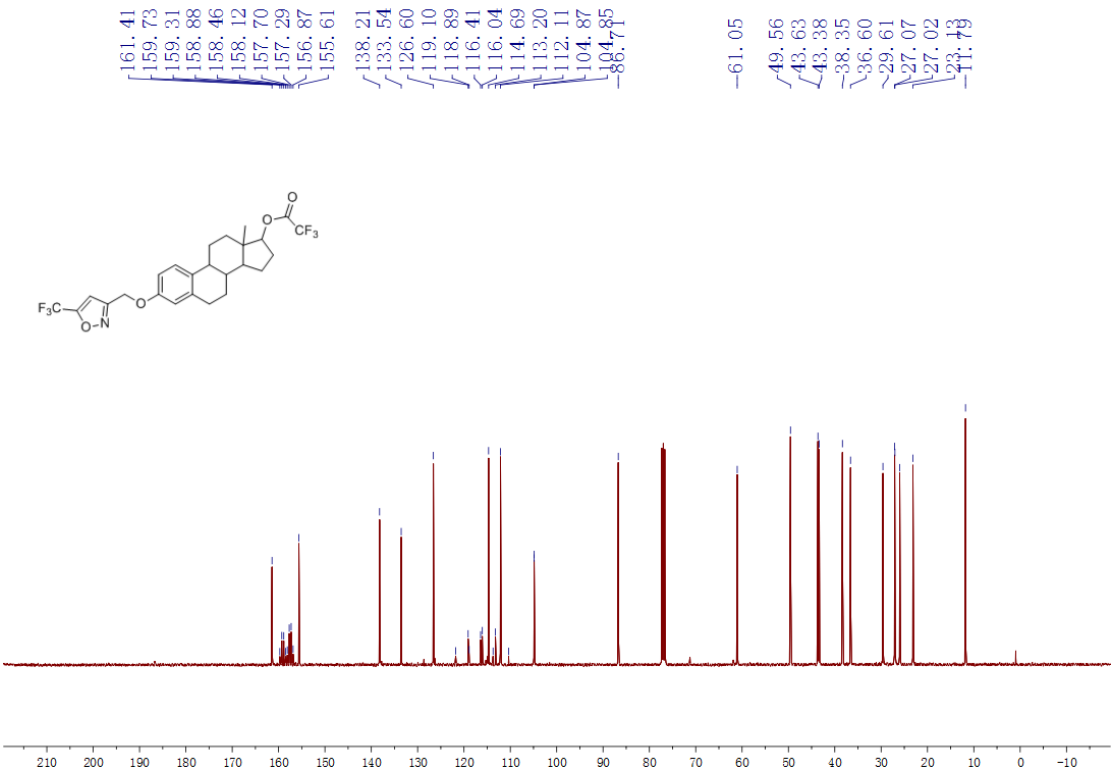
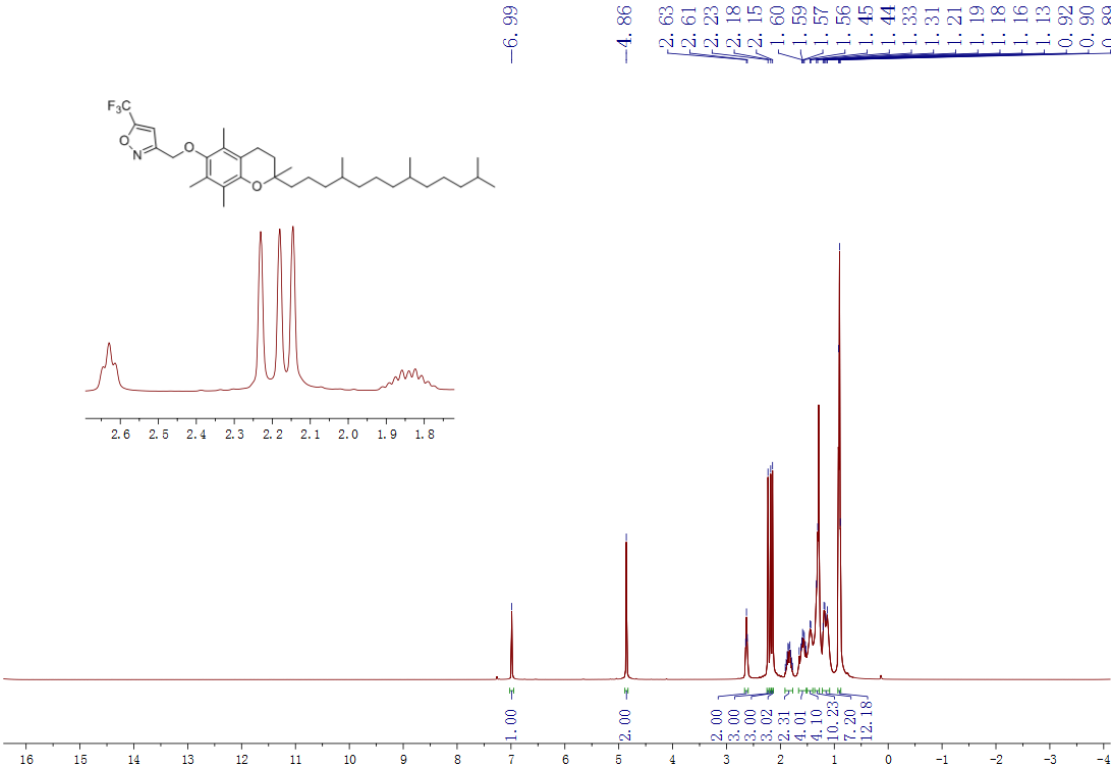


^{1}H NMR spectra of **7c** in $CDCl_3$



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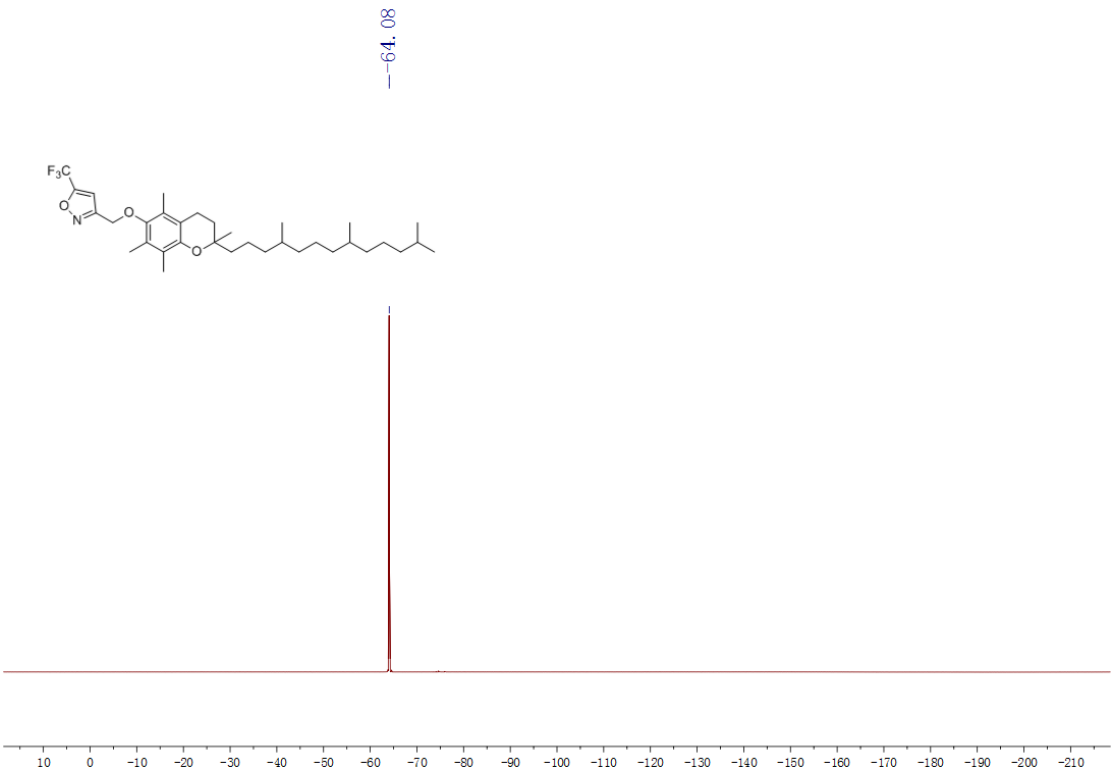

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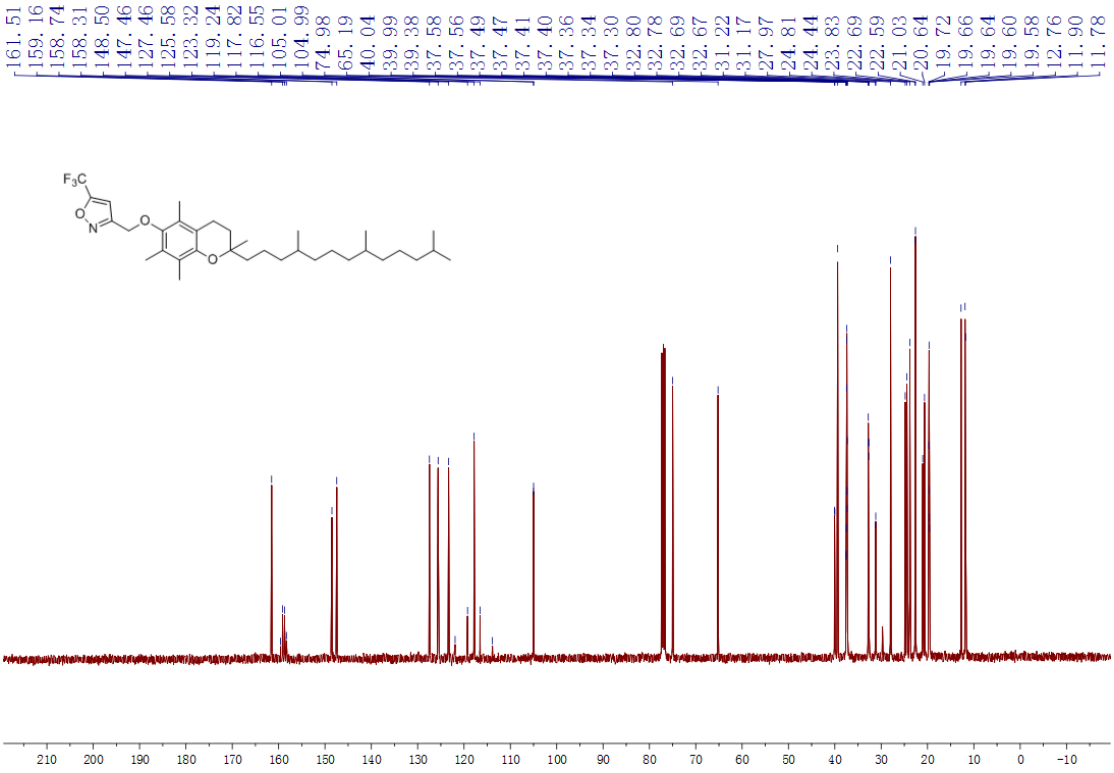

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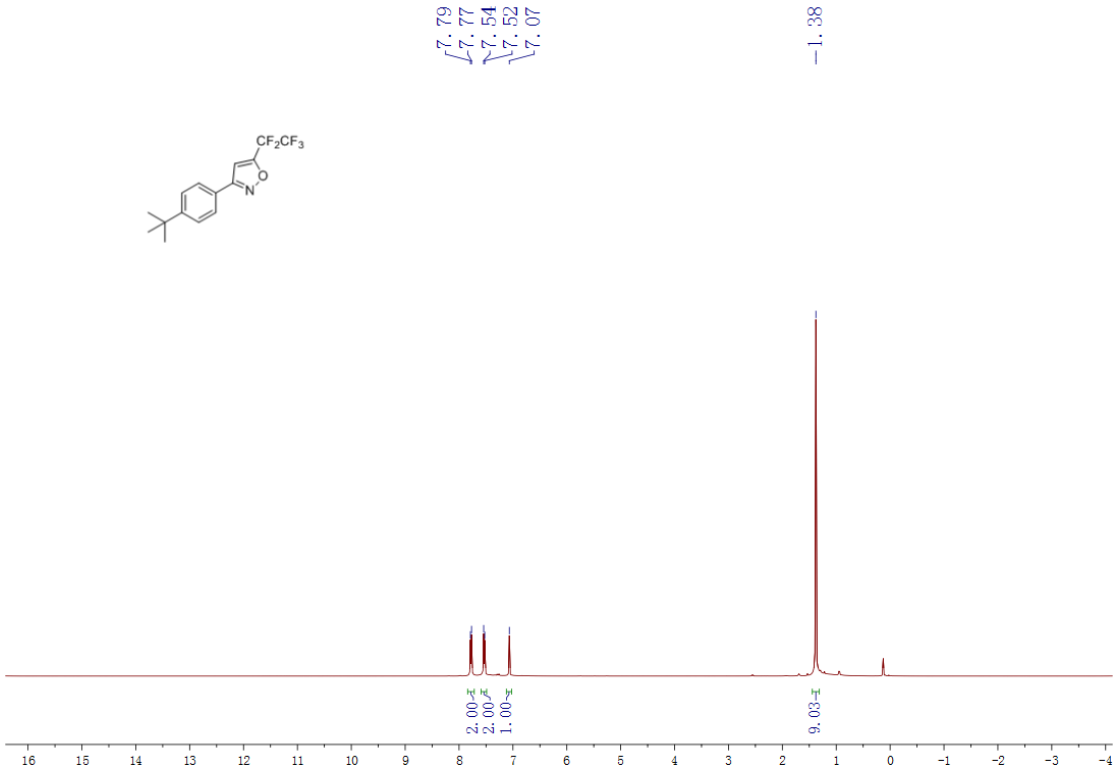

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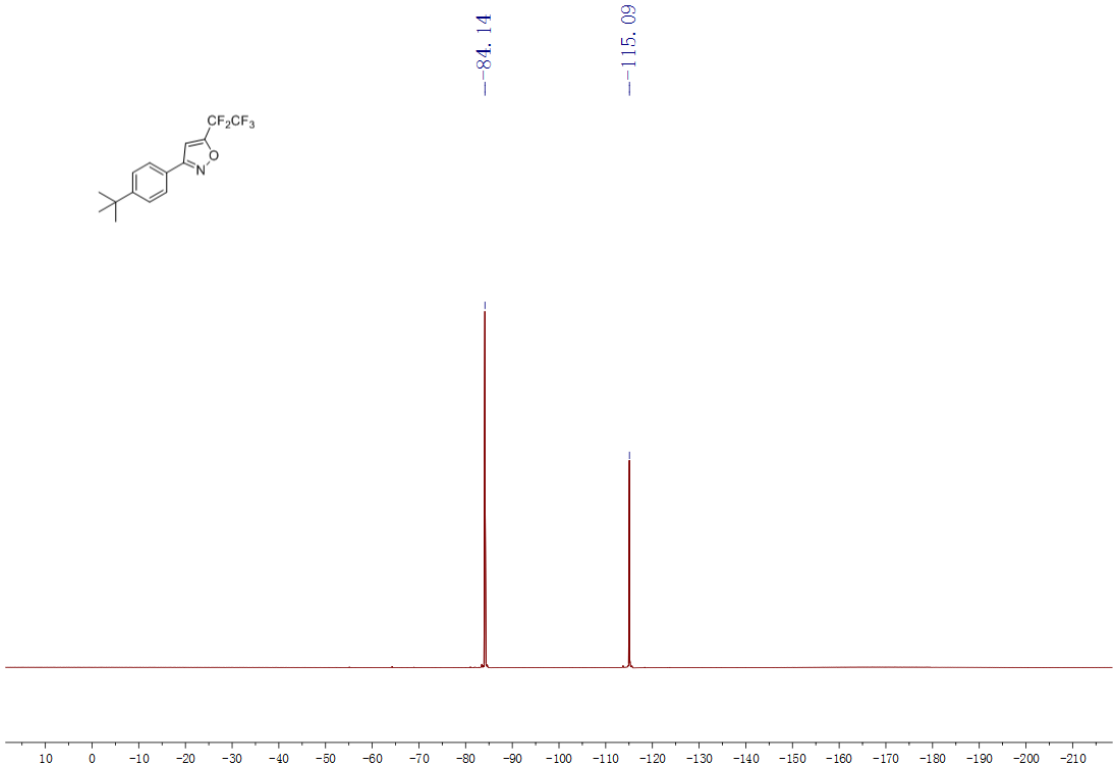
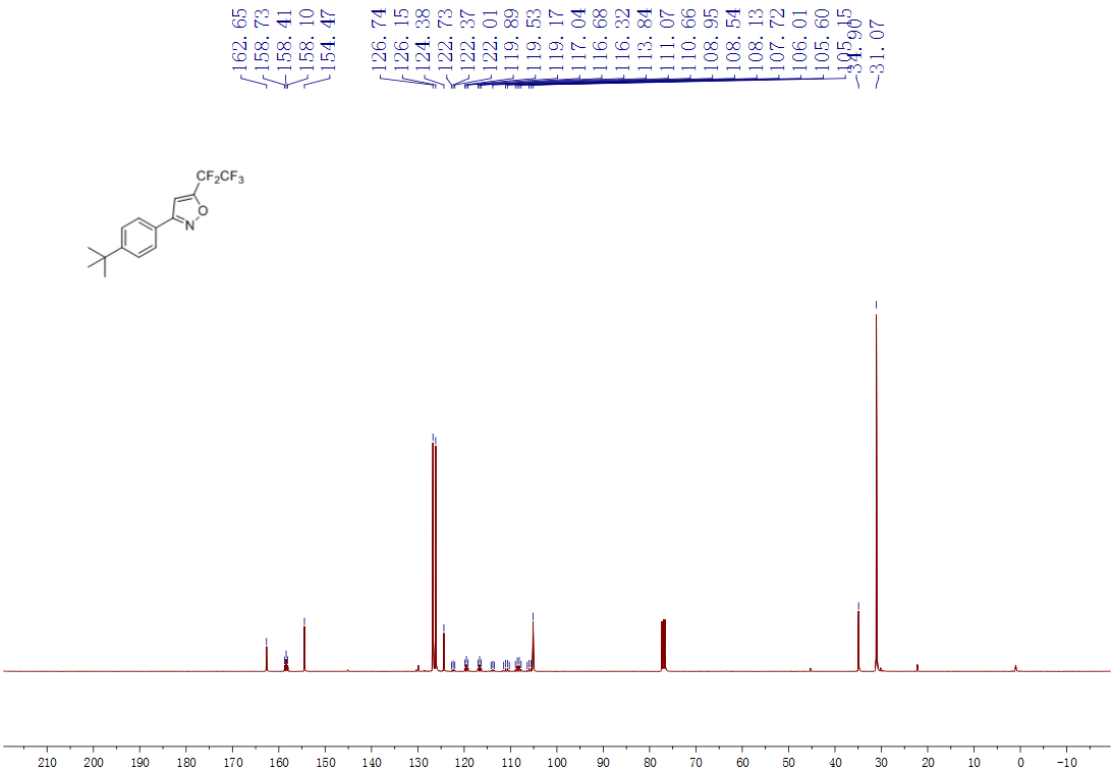


^{13}C NMR spectra of **8a** in $CDCl_3$



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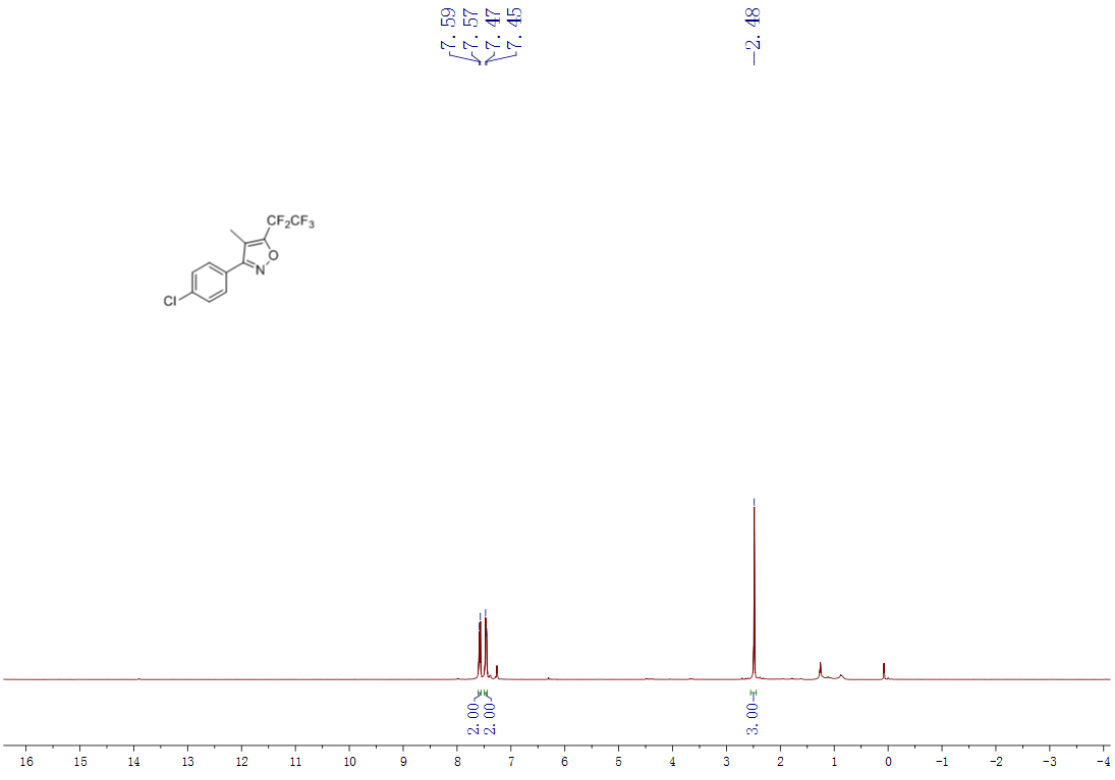

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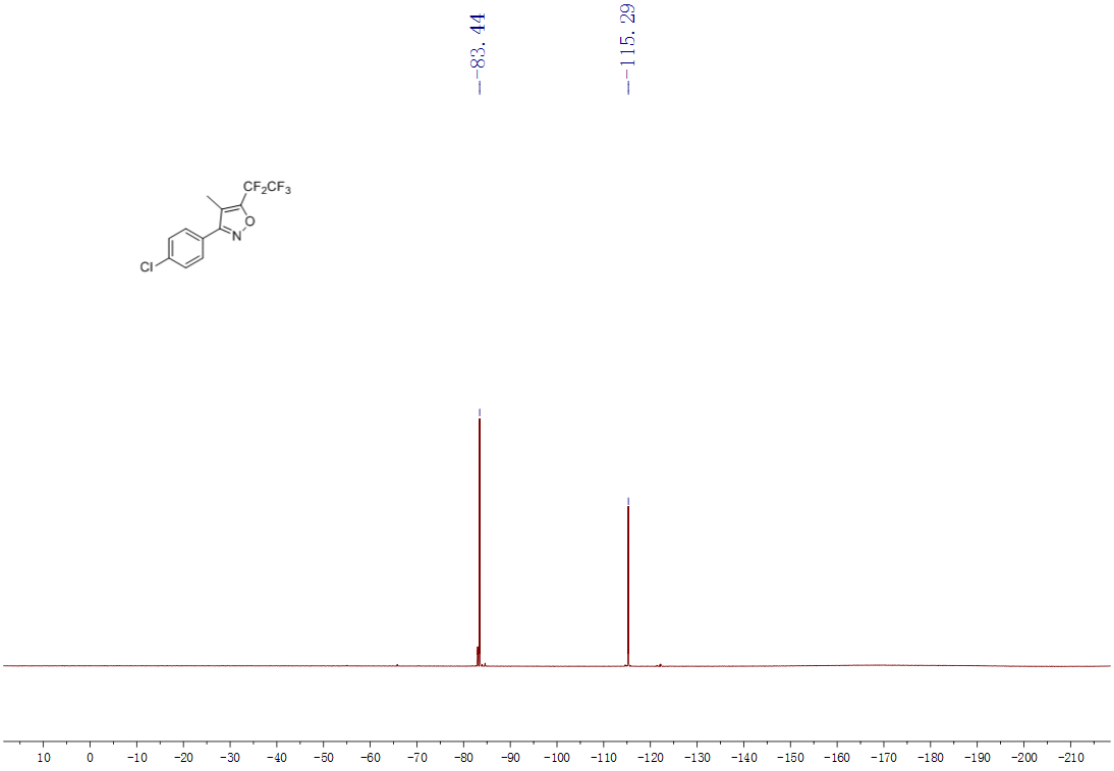

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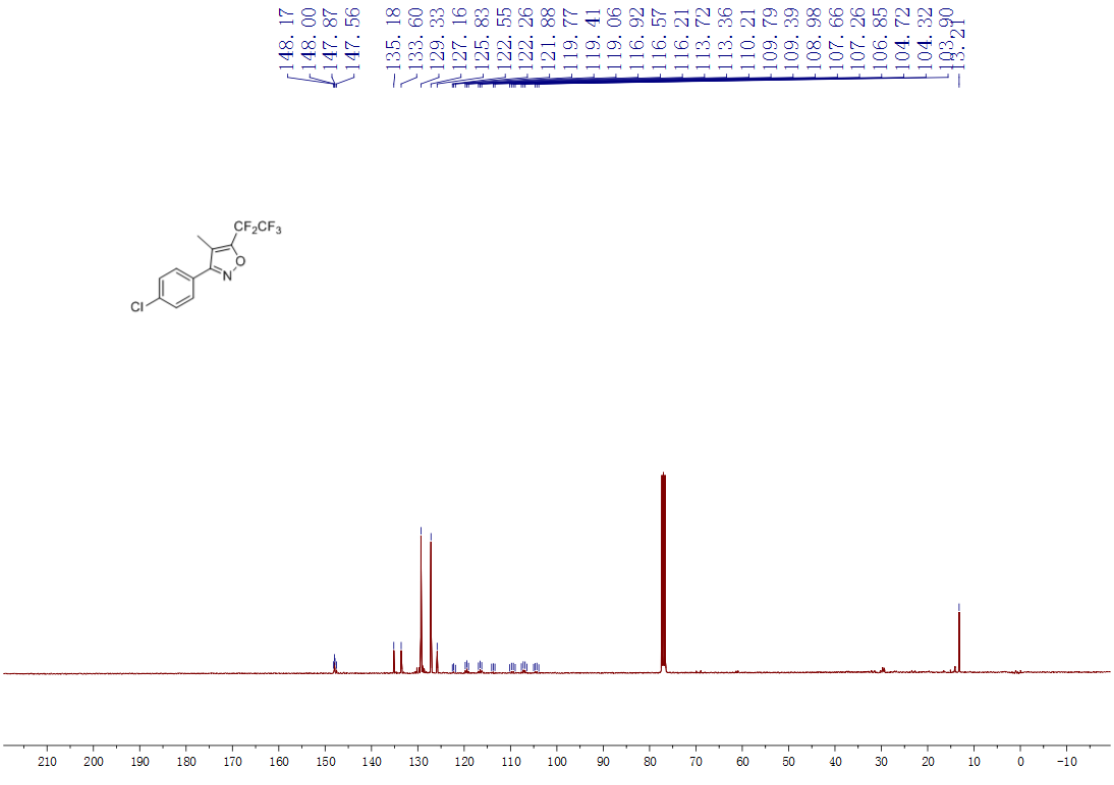

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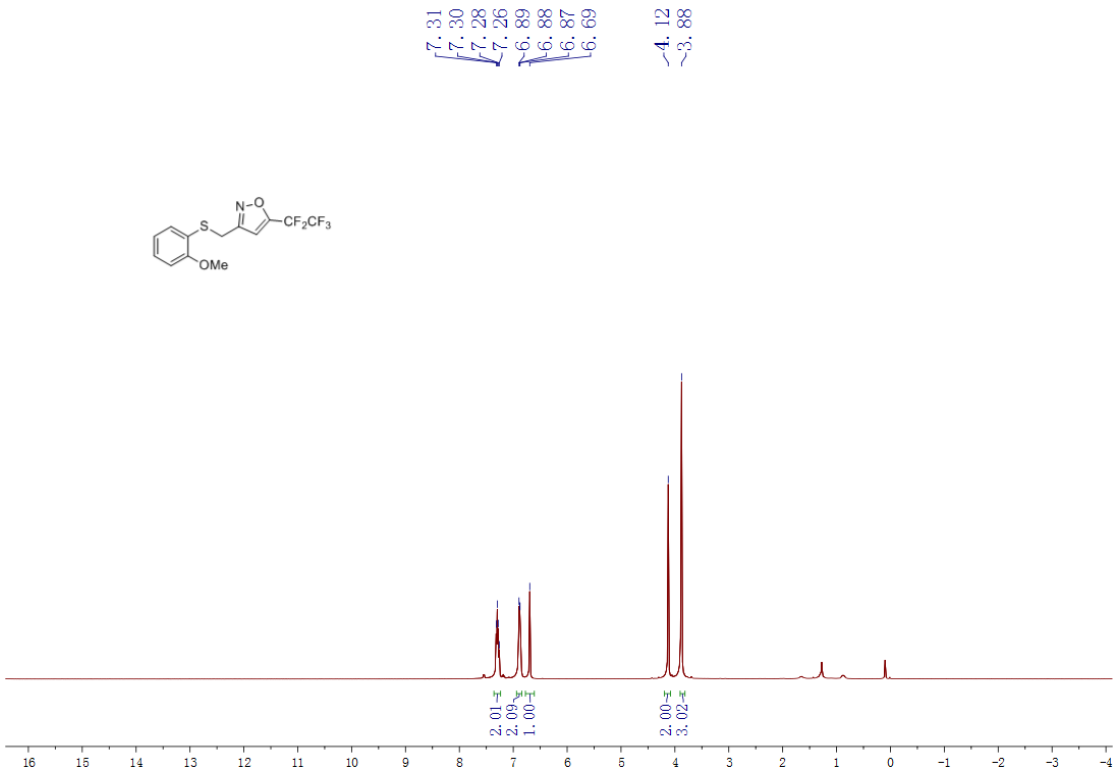

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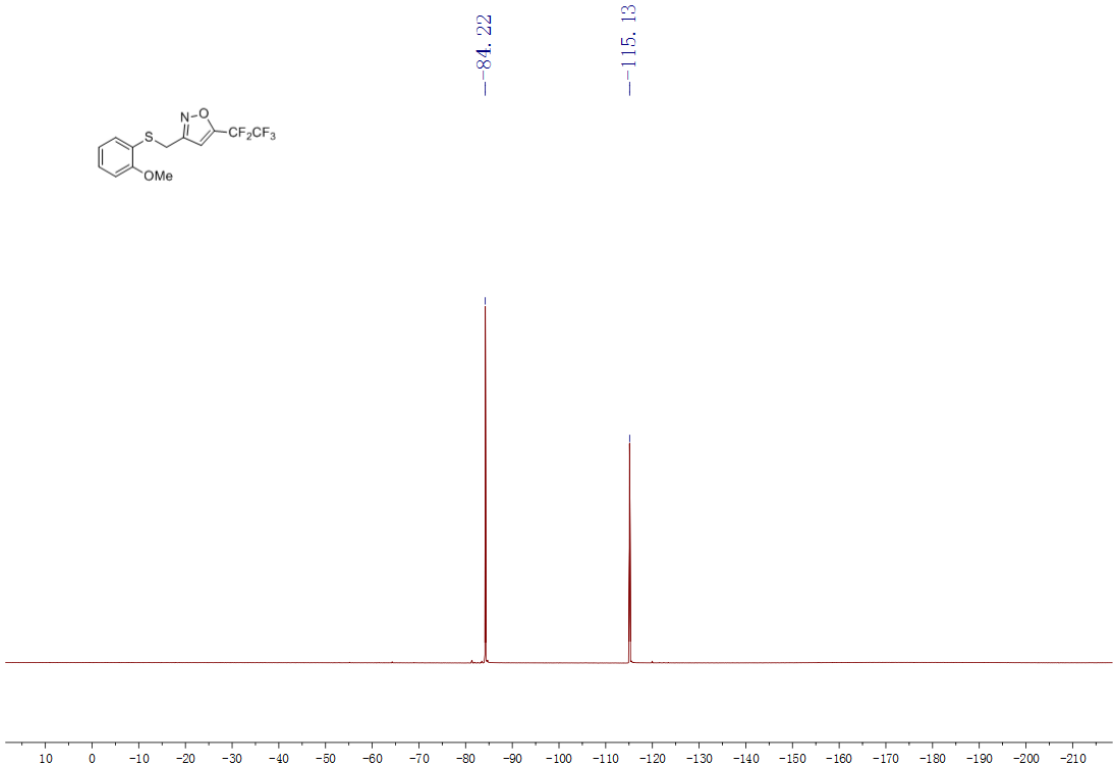

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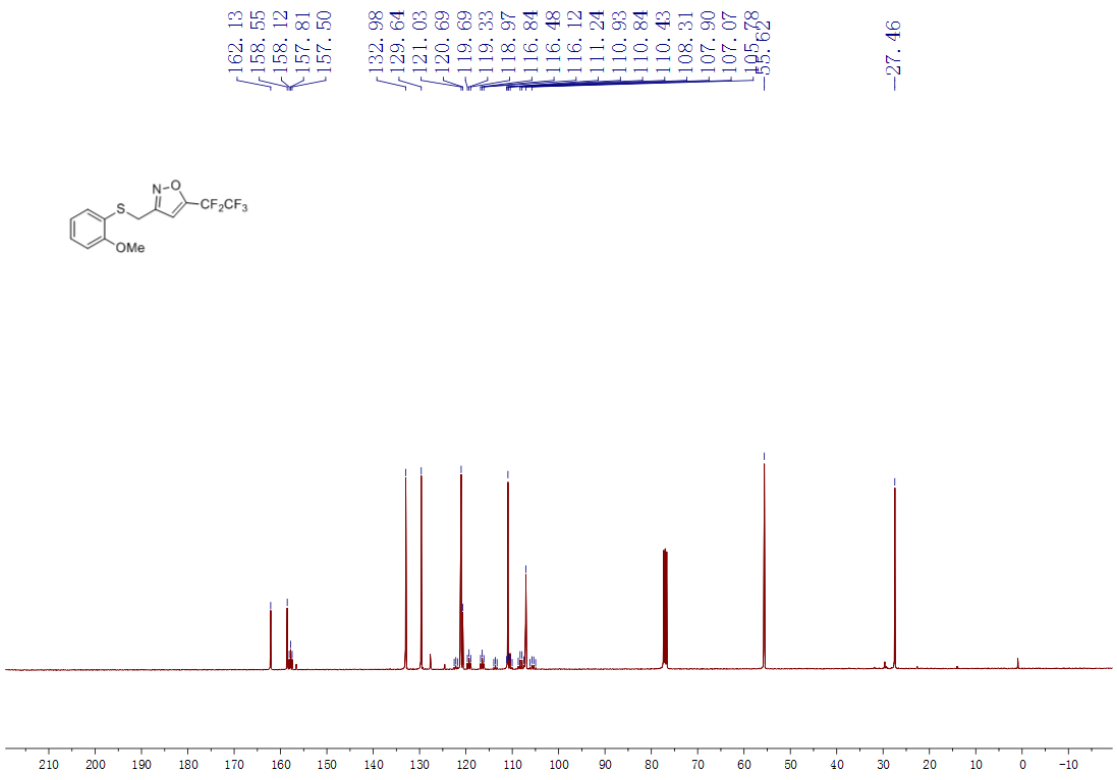

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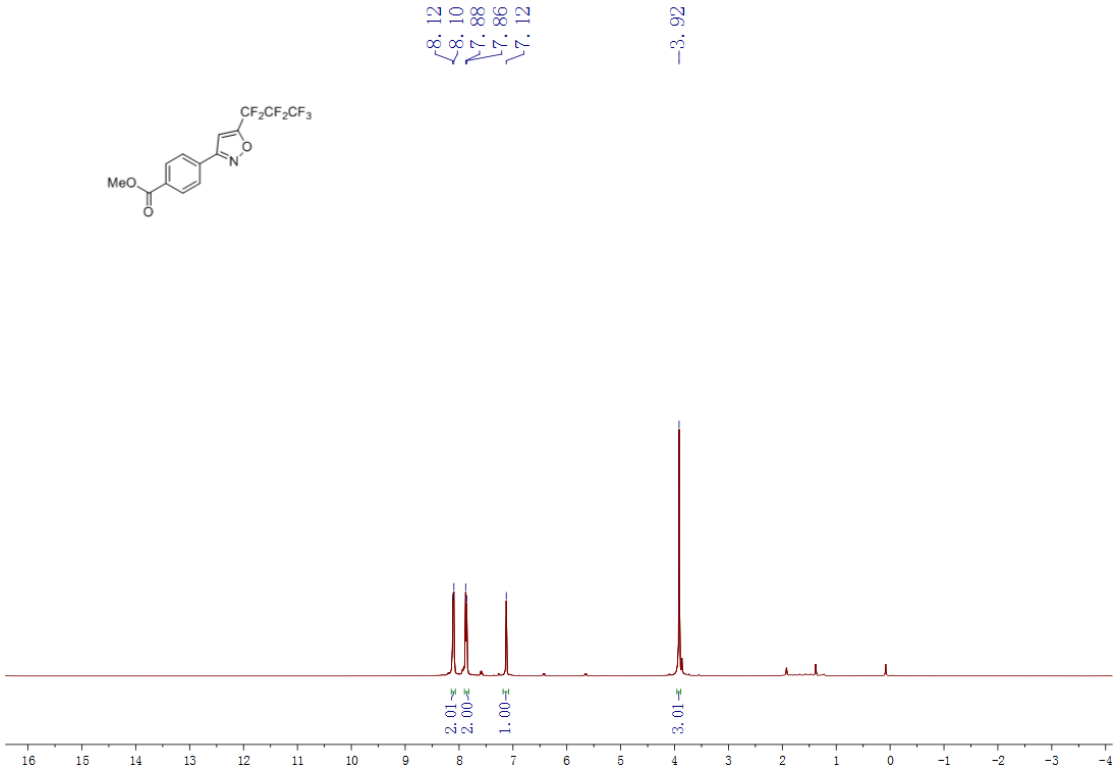

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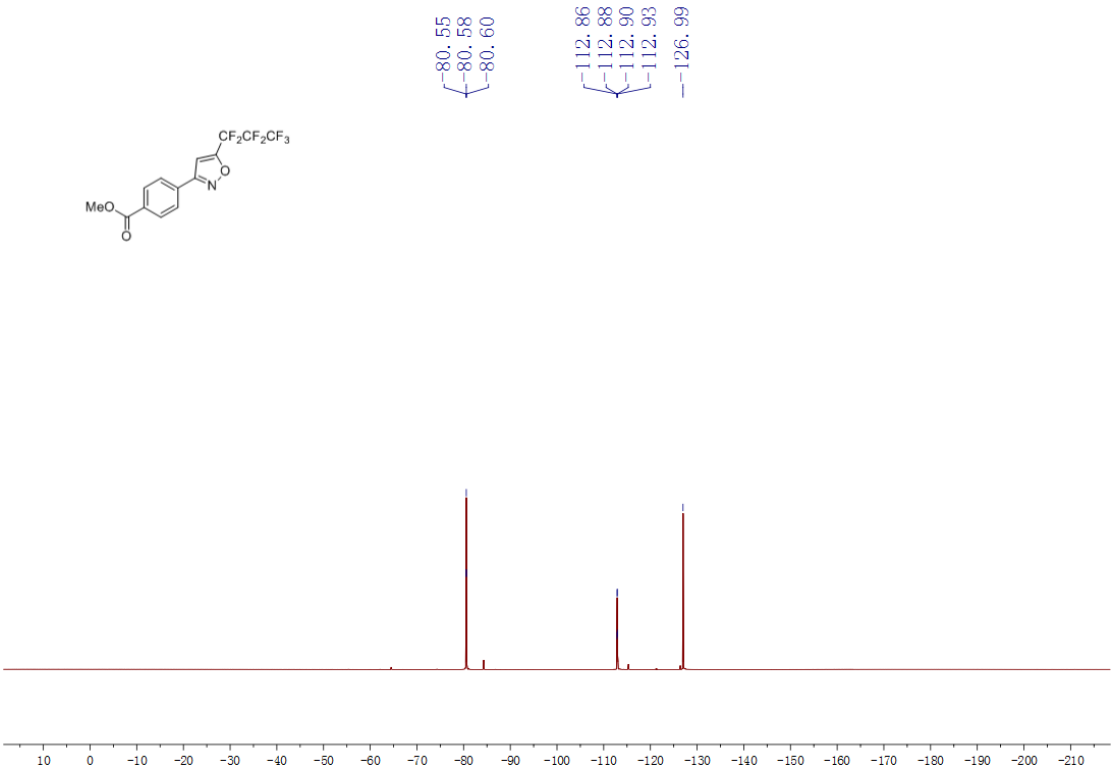

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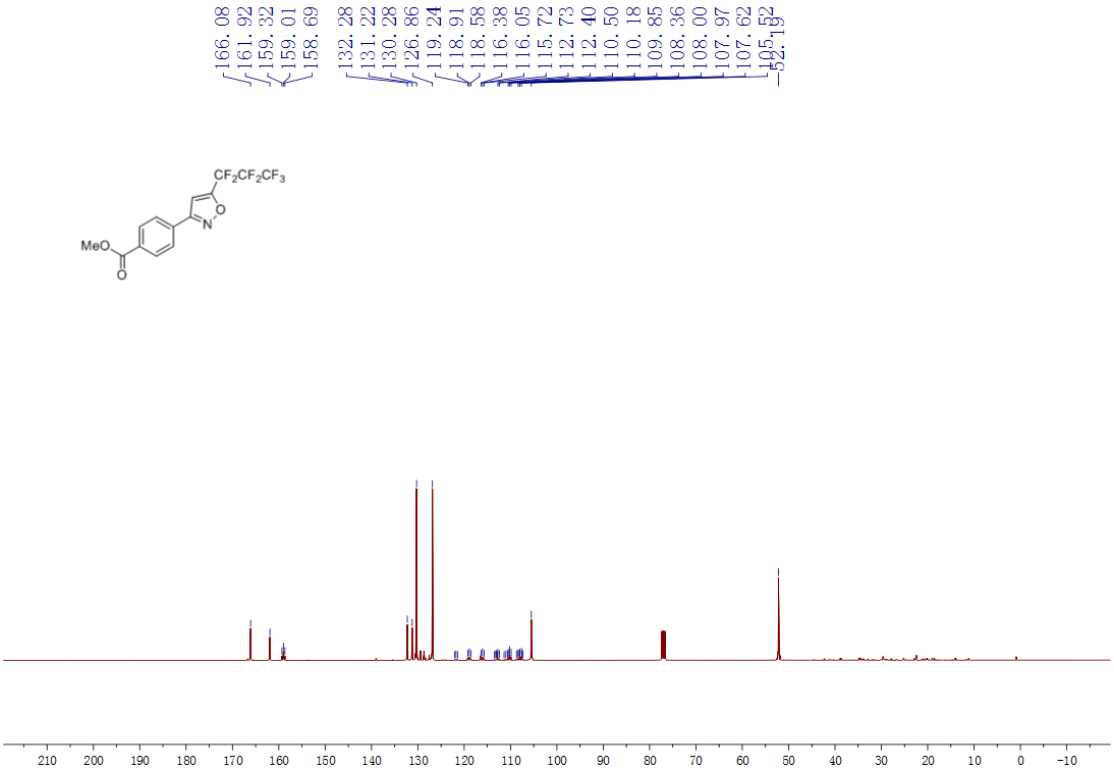

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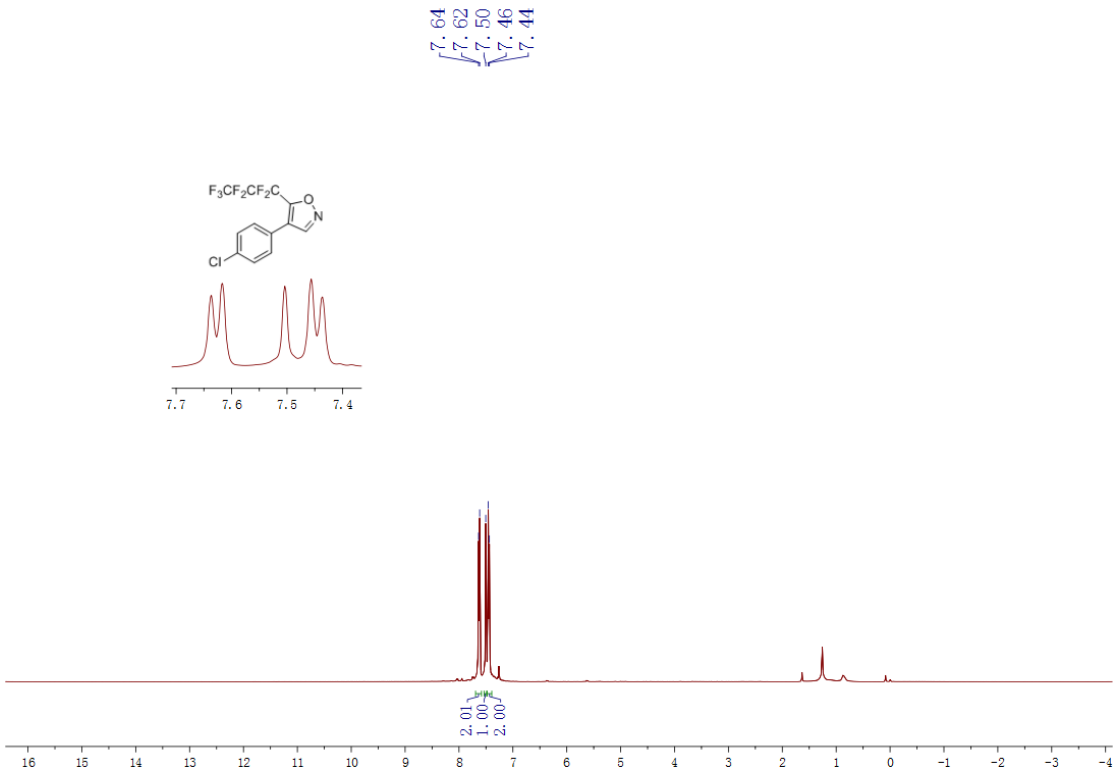

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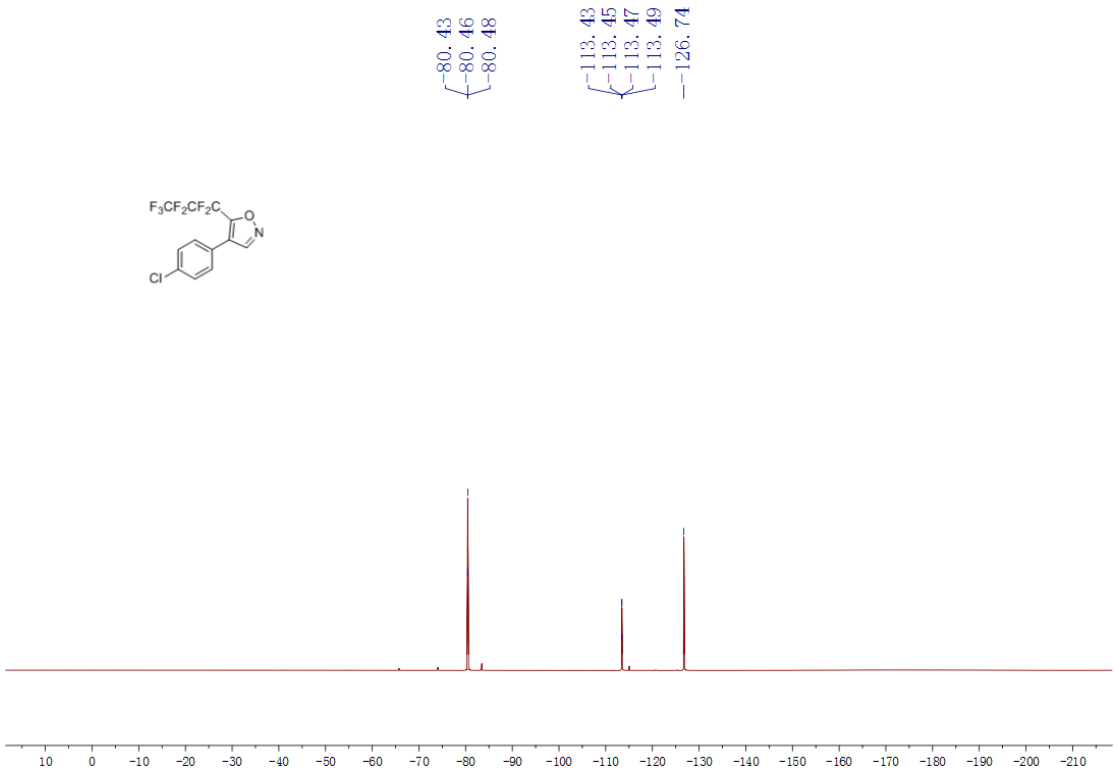

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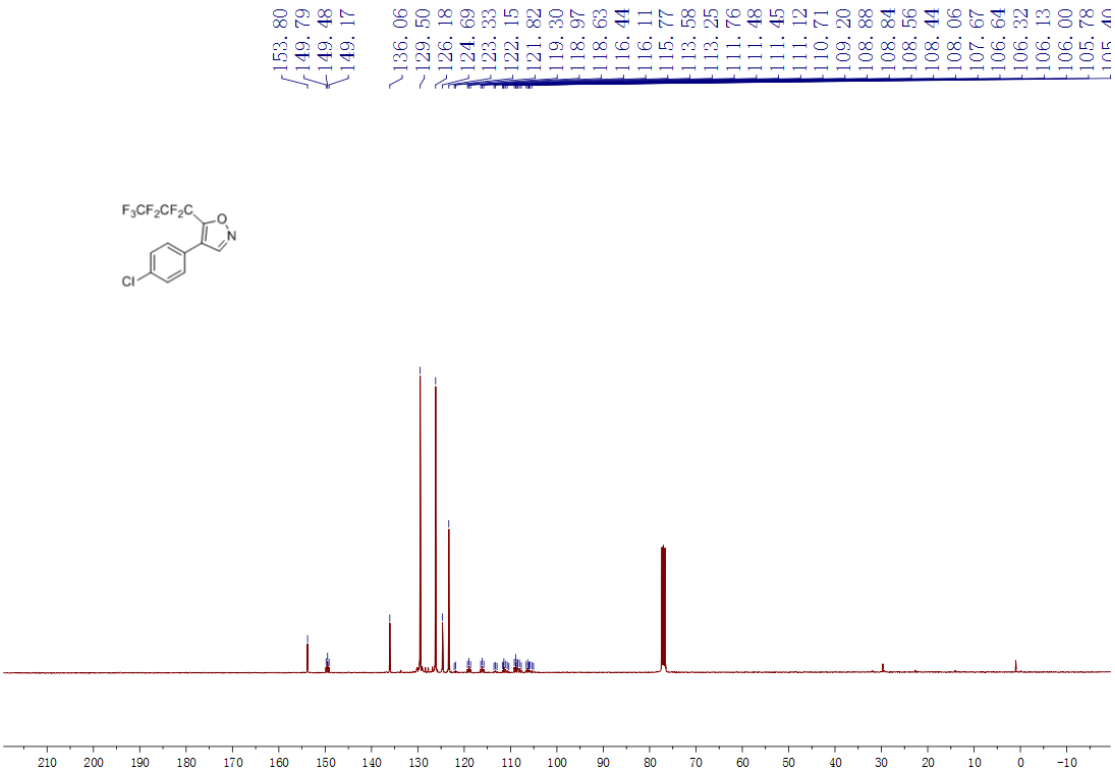
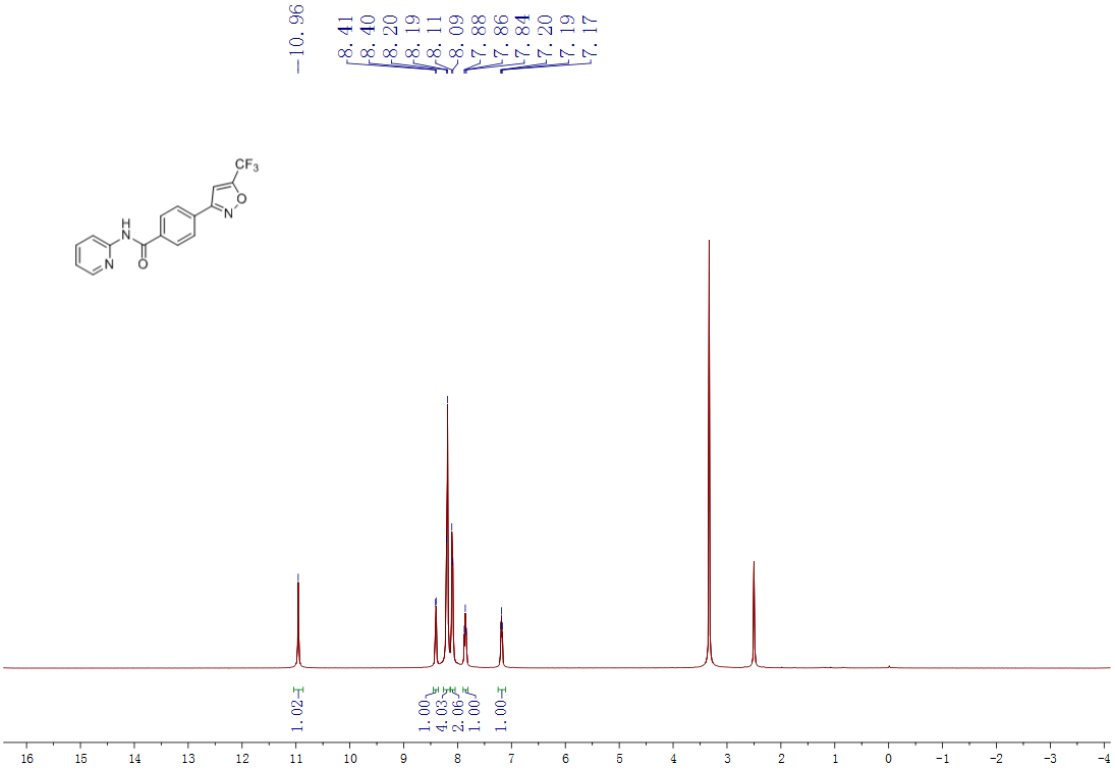
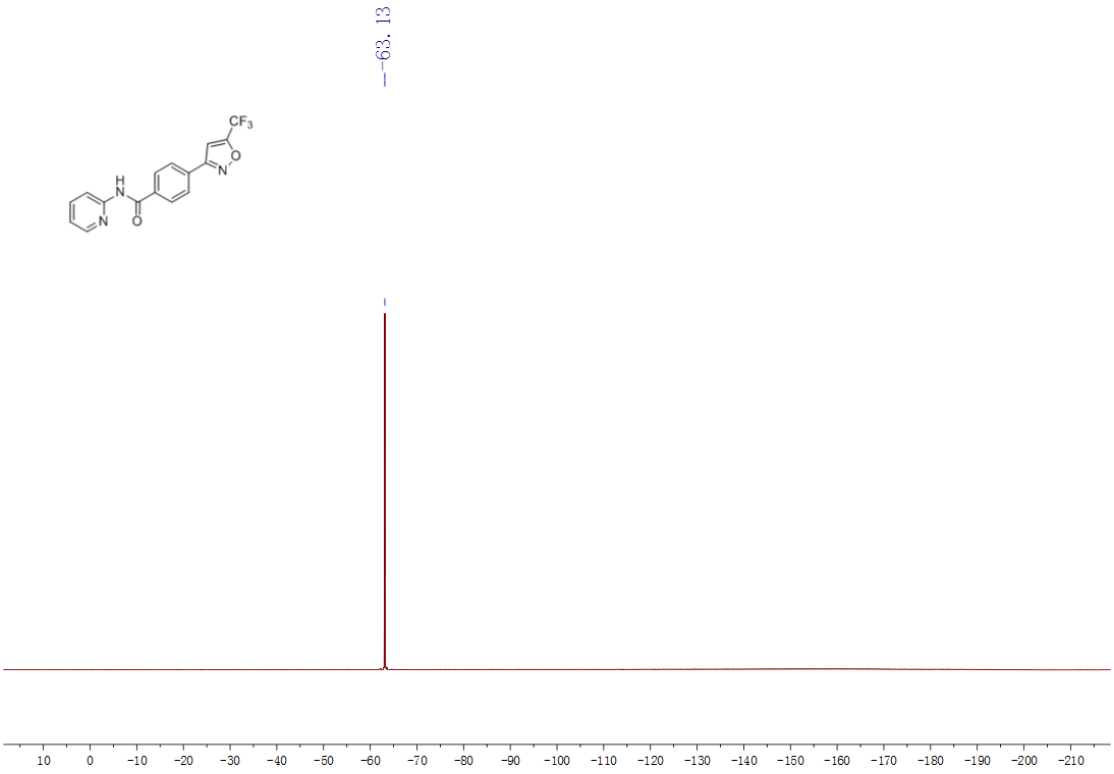


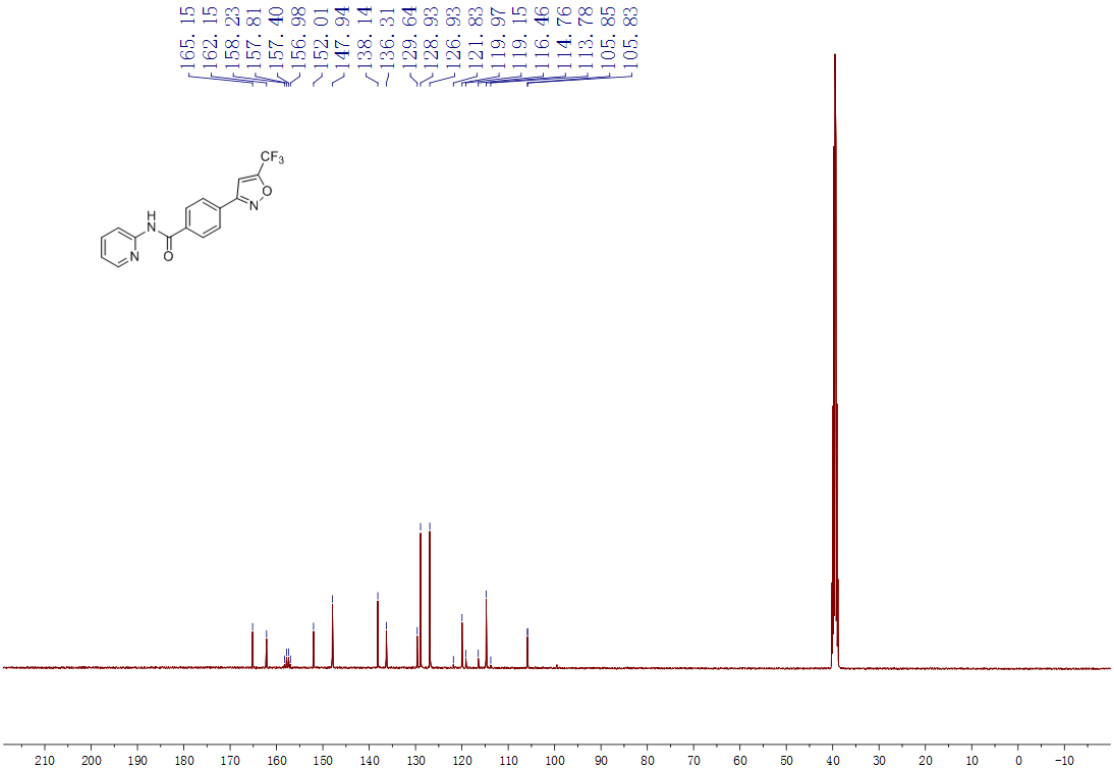
^{1}H NMR spectra of **11a** in DMSO-d_6



^{19}F NMR spectra of **11a** in DMSO-d_6



^{13}C NMR spectra of **11a** in DMSO-d_6



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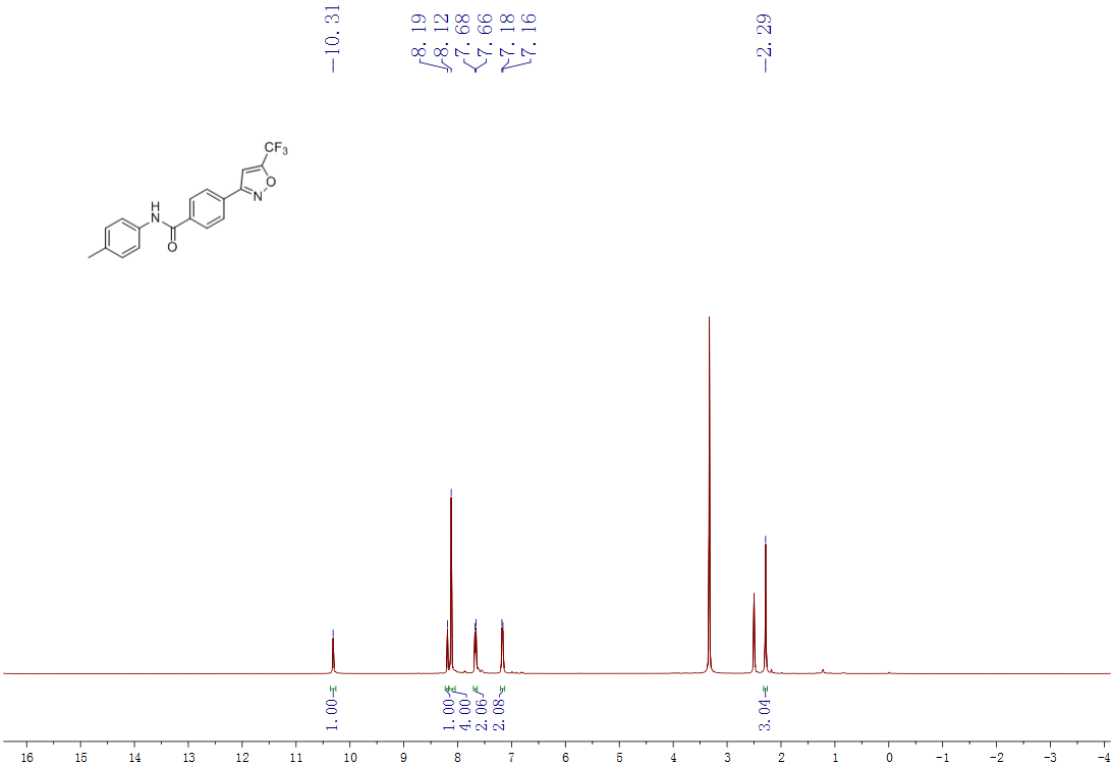
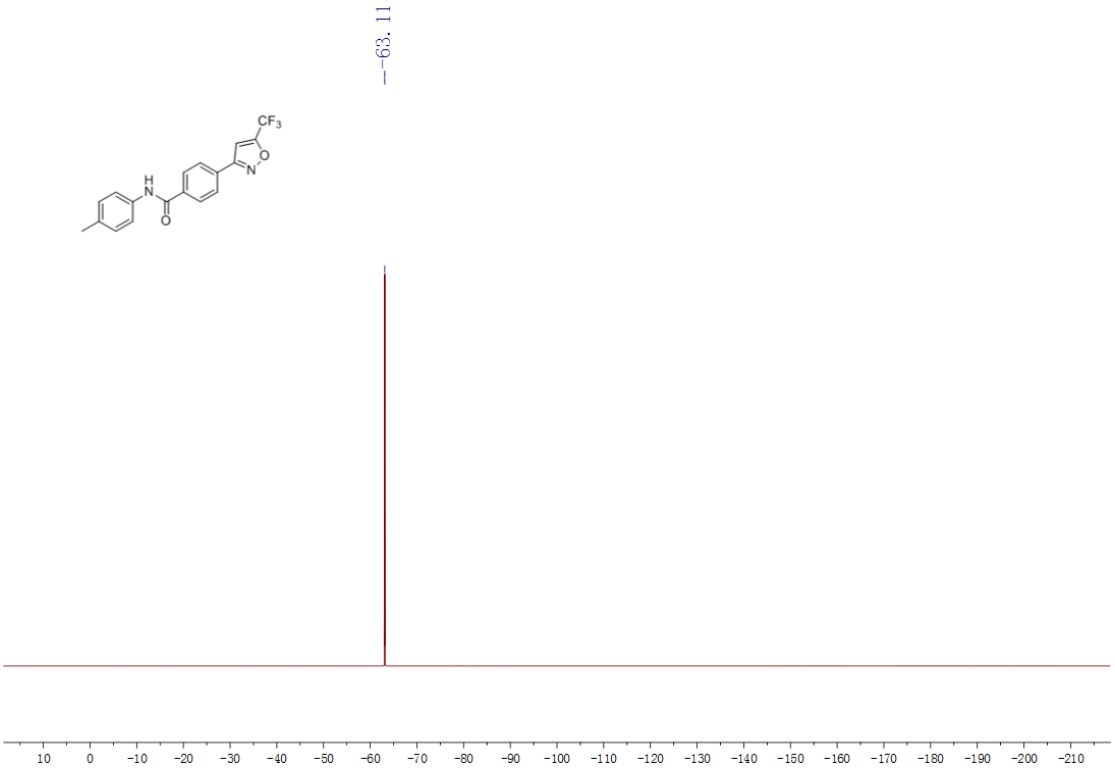
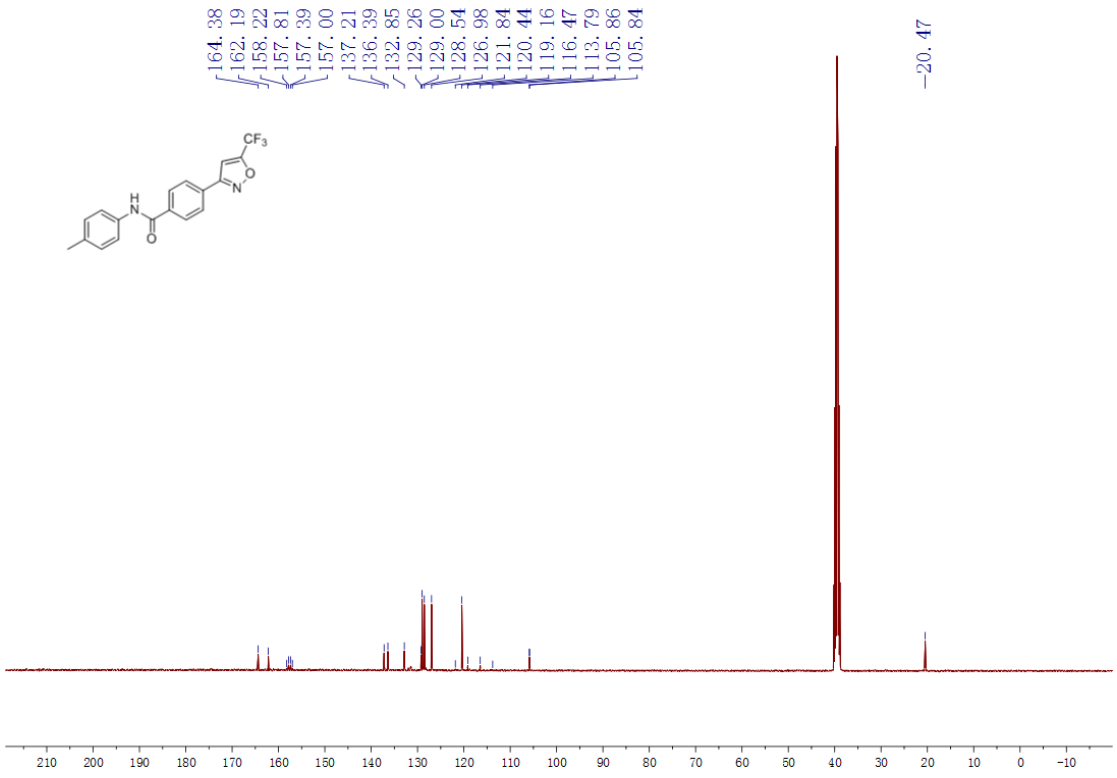


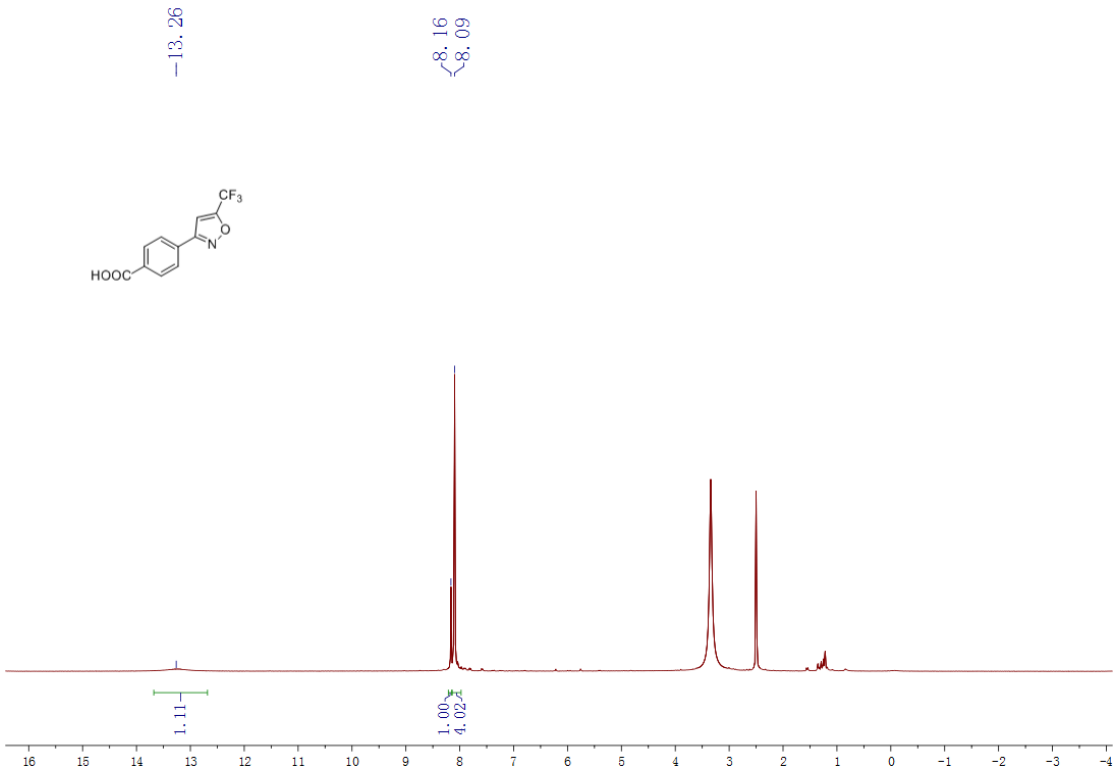
^{19}F NMR spectra of **11b** in DMSO-d_6



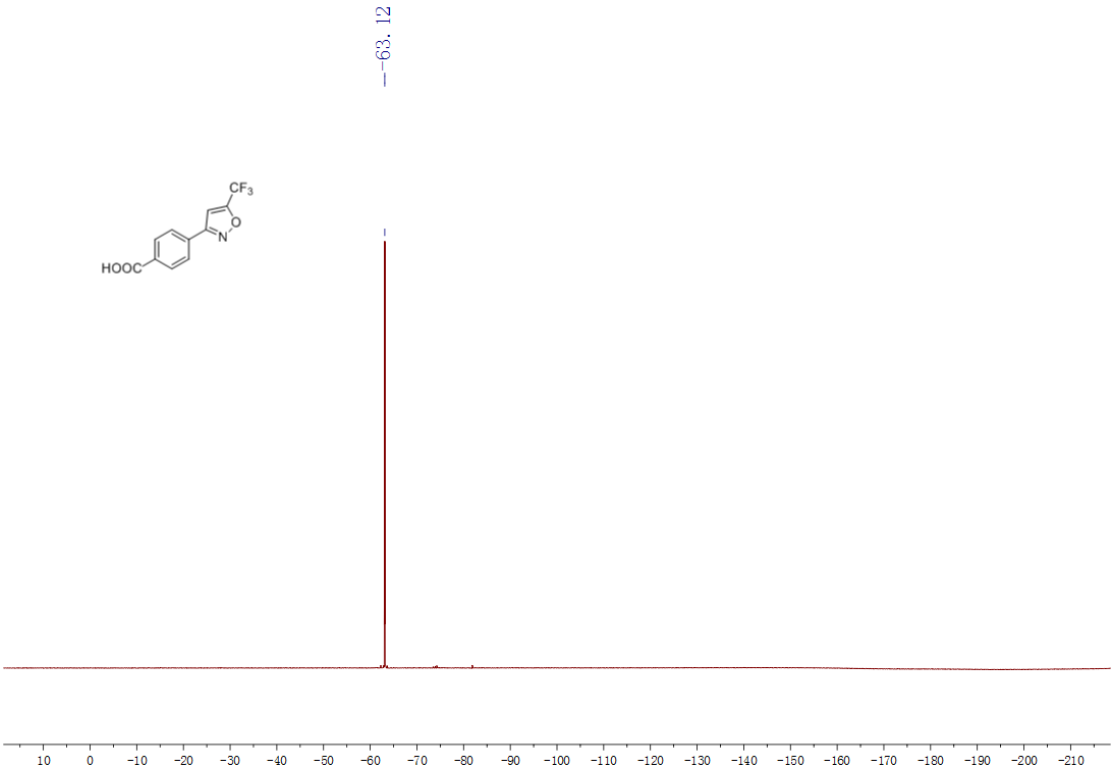
^{13}C NMR spectra of **11b** in DMSO-d_6



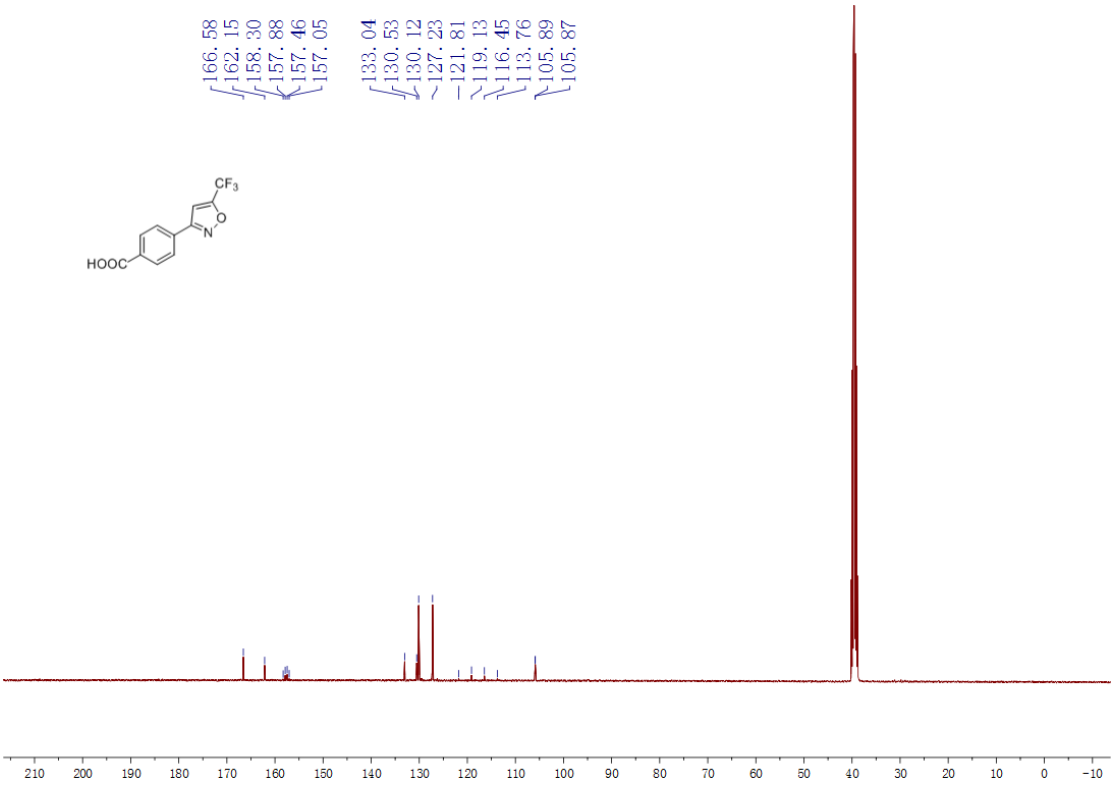
^{1}H NMR spectra of **12** in DMSO-d_6



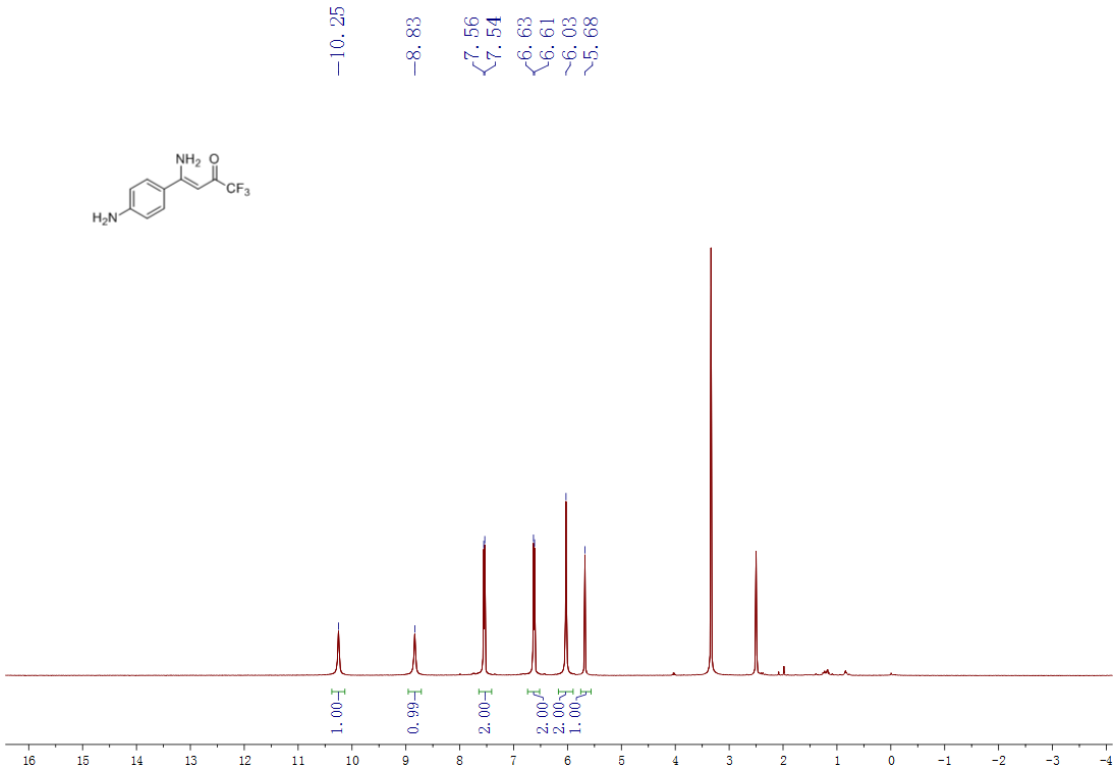
^{19}F NMR spectra of **12** in DMSO-d_6



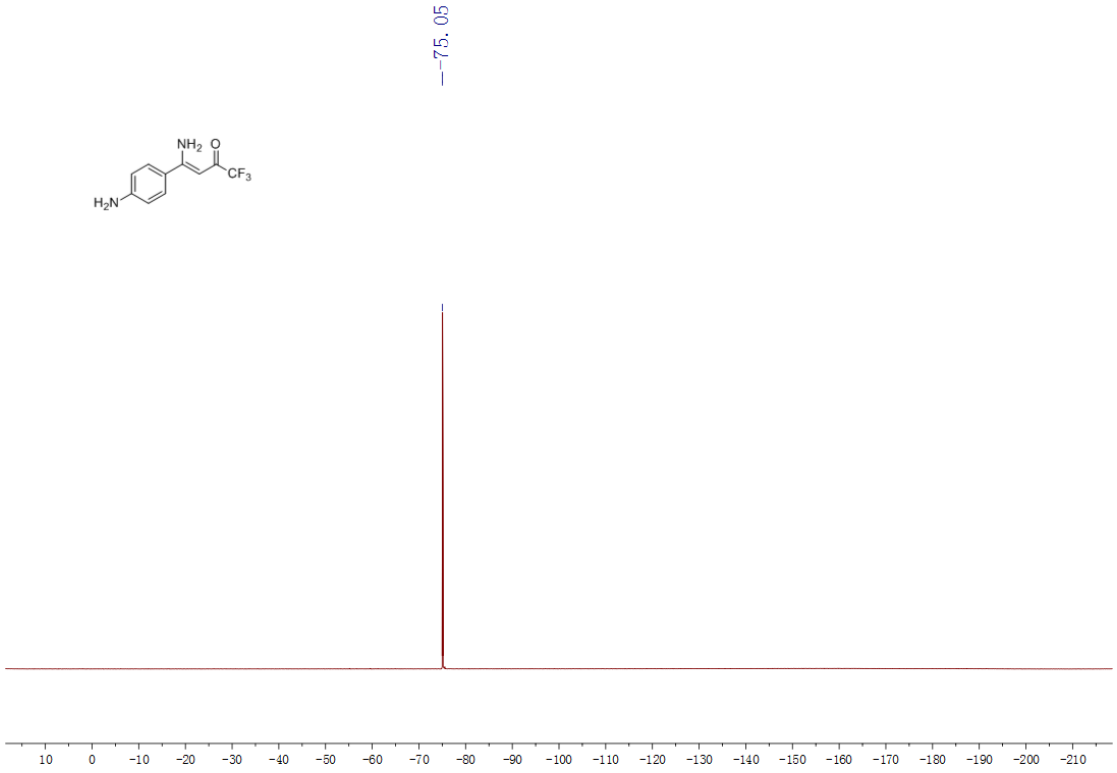
^{13}C NMR spectra of **12** in DMSO-d_6



^{1}H NMR spectra of **13** in DMSO-d_6



^{19}F NMR spectra of **13** in DMSO-d_6



^{13}C NMR spectra of **13** in DMSO-d_6