Electronic Supplementary Information

3,5-Isoxazoles from α-bromo pentafluorophenyl vinylsulfonates: Synthesis of sulfonates and sulfonamides

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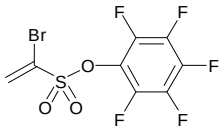
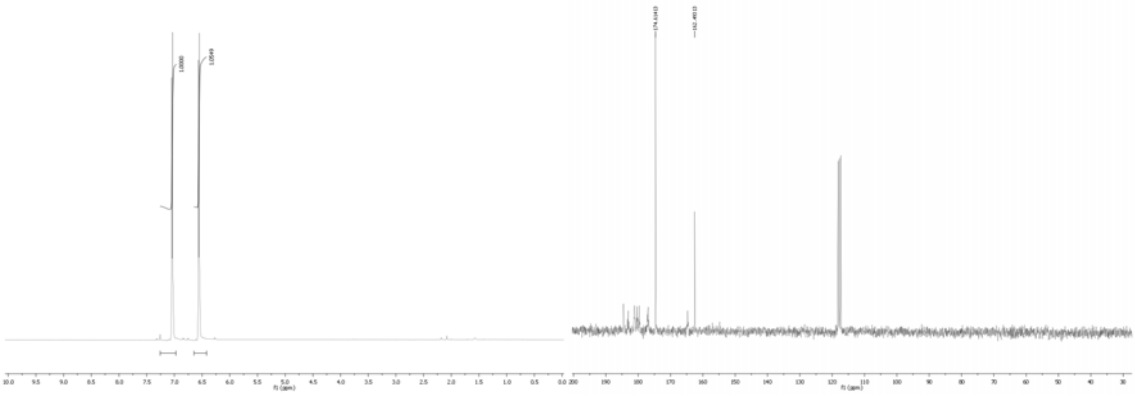
General Experimental

Chlorooximes were prepared according to literature procedures[1] and ethenesulfonic acid pentafluorophenyl ester was prepared as previously described.[2] All other chemicals were purchased from commercial sources and were used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates (254mm). Flash column chromatography was carried out with Kieselgel 60M 0.04/0.063mm (230-400 mesh) silica gel. All yields quoted are isolated yields. ^{1}H NMR spectra were recorded at 300 MHz and the chemical shift (δ) quoted in ppm relative to residual protonated signals of the solvent. ^{13}C NMR was recorded at 75 MHz on a Bruker AMX 300 or at 126 MHz on a Bruker AVANCE500 at ambient temperature and the chemical shift (δ) quoted in ppm relative to the signals of the solvent. In ^{13}C NMR pentafluorophenyl signals not observed due to C-F coupling. ^{19}F NMR was recorded at 286 MHz on a Bruker AMX 300 at ambient temperature and the chemical shift (δ) quoted in ppm relative to the signals of the solvent. Electron ionisation (EI) and fast atom bombardment (FAB) mass spectra were run on a VG70-SE mass spectrometer Infrared spectra were obtained on a Shimadzu FTIR 8700 Spectrophotometer. Melting points were measured with a Gallenkamp apparatus and are uncorrected.

1-Bromo-ethenesulfonic acid pentafluorophenyl ester



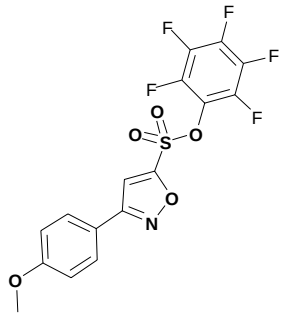
Br_2 (6 mL, 120 mmol, 2 eq.) was dissolved in CCl_4 (30 mL) and was added dropwise to the premixed solution of ethenesulfonic acid pentafluorophenyl ester (16.44 g, 60 mmol) and AIBN (0.6 g) in CCl_4 (200 mL) at 70°C. Additional AIBN was added after the addition of bromine solution and reaction was refluxed for 4h followed by 48h stirring at RT. Solvent was removed *in vacuo* and the residue was dissolved in benzene (200 mL). A premixed solution of NEt_3 (6.06 g, 60 mmol) in benzene (30 mL) was added to the 1,2-Dibromo-ethanesulfonic acid pentafluorophenyl ester solution and stirred at RT for 3h. Reaction mixture was washed with H_2O (x3) and brine (x1), dried ($MgSO_4$) and solvent was removed *in vacuo*. The residue was purified by flash chromatography (10% Et_2O/petroleum ether) to yield vinyl sulfonate (20.01 g, 57 mmol, 94%) and a white solid. R_f 0.51 (20% Et_2O/ petroleum ether); mp 37-39 °C; ν_{max}(film)/cm^{-1} 3120, 3032, 1651, 1606, 1510, 1355, 1140; δ_H($CDCl_3$; 300 MHz) 7.05 (1H, d, J = 3.5 Hz), 6.54 (1H, d, J = 3.5 Hz); δ_C($CDCl_3$; 75 MHz) 136.2 (s), 133.8 (t), 121.8 (s); *m/z* (CI) 352.8902 ($M^{+\bullet}$, $C_8H_2BrF_5O_3S$ requires 352.8906), 184 (100%) and 155 (36).



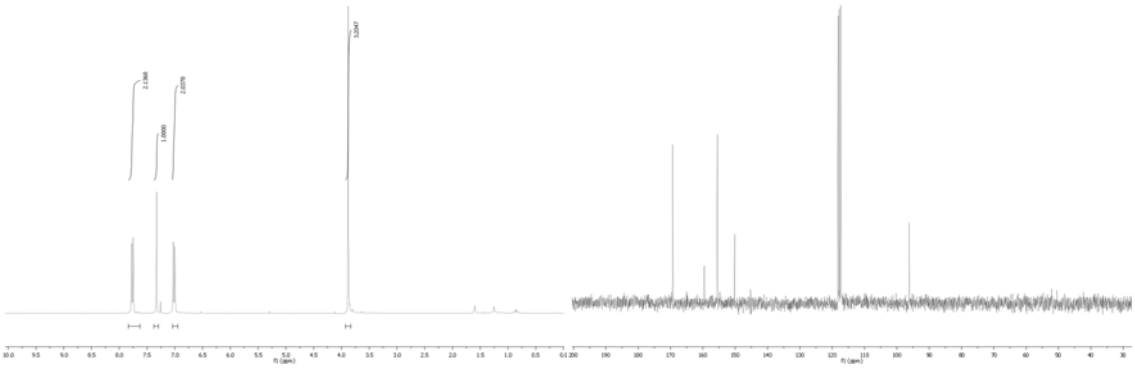
Preparation of isoxazole pentafluorophenylsulfonates

α-chloroaldoxime (1.5 eq.), 1-bromo-ethenesulfonic acid pentafluorophenyl ester (1 eq.) and NEt_3 (2.5 eq.) were mixed in MePh (~ 10 mL/mmol sulfonate) and stirred at room temperature for 2h. The solvent was removed *in vacuo* and crude product was purified by flash chromatography (Et_2O/petroleum ether). When required products were recrystallised from EtOAc/hexane.

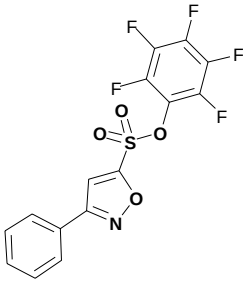
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



Yield: (0.11 g, 0.25 mmol, 92%) as a white solid. (Found: C, 45.5; H, 1.8; N, 3.1. $C_{16}H_8F_5NO_5S$ requires C, 45.6; H, 1.9; N, 3.3%); R_f 0.32 (10% Et_2O/petroleum ether); mp 133-135 °C; ν_{max}(film)/cm^{-1} 3055, 2987, 1612, 1612, 1309, 1130; δ_H($CDCl_3$, 300 MHz) 7.76 (2H, d, J = 8.9 Hz), 7.32 (1H, s), 7.01 (2H, d, J = 8.9 Hz), 3.87 (3H, s); δ_C($CDCl_3$, 75 MHz) 162.6 (s), 162.1 (s), 160.3 (s), 118.8 (s), 128.6 (d), 114.8 (d), 109.4 (d), 55.5 (q); δ_F($CDCl_3$, 282 MHz) -150.99, -153.60, -160.32; *m/z* (EI) 420.9989 ($M^{+\bullet}$, $C_{16}H_8F_5NO_5S$ requires 420.9988), 174 (51%), 146 (100) and 92 (39).

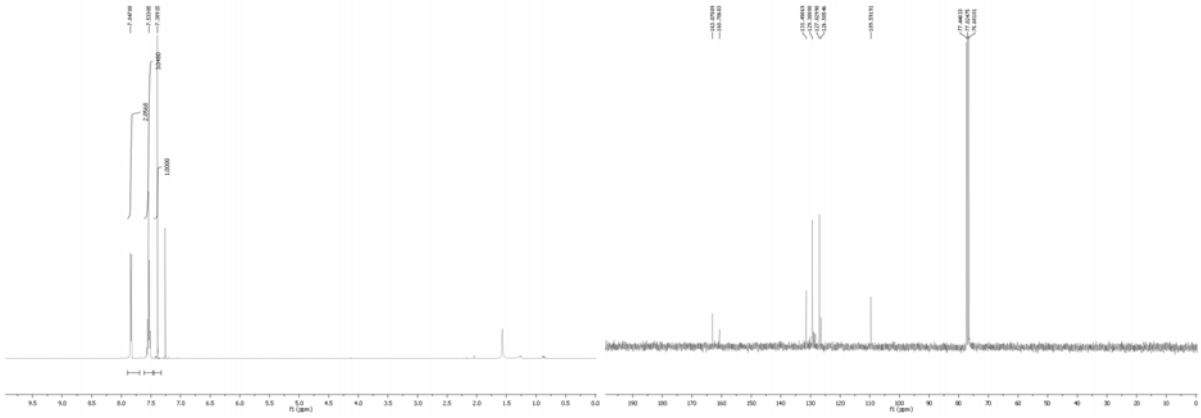


3-Phenyl-isoxazole-5-sulfonic acid pentafluorophenyl ester

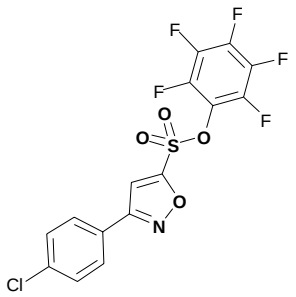


Yield: (2.01 g, 4.93 mmol, 86%) as a white solid. R_f 0.26 (10% Et_2O/petroleum ether); mp 105-107 °C; ν_{max}(film)/cm^{-1} 3055, 1593, 1506, 1130; δ_H($CDCl_3$, 300 MHz) 7.82-7.84 (2H, m), 7.38-7.53 (4H, m); δ_C($CDCl_3$, 75 MHz) 163.1 (s), 160.7 (s), 131.5 (d), 129.0 (d), 127.0

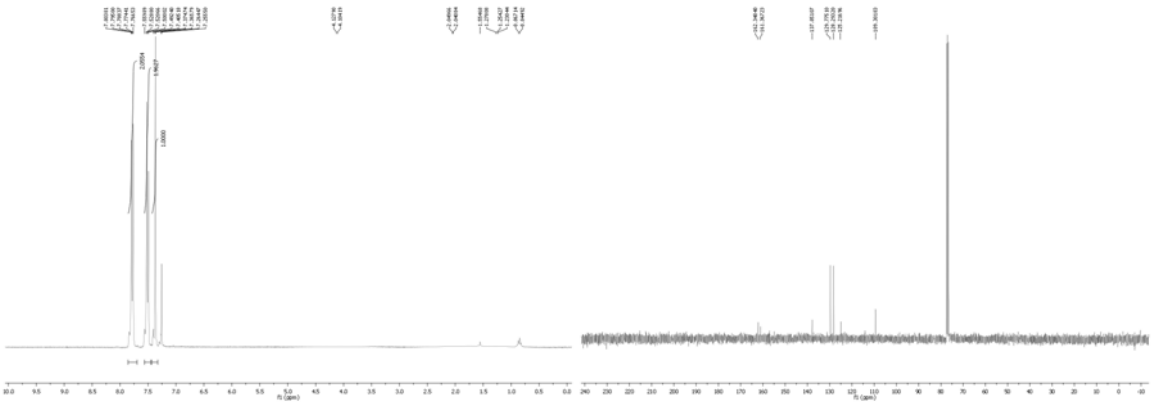
(d), 126.5 (s), 109.6 (d); δ_F($CDCl_3$, 282 MHz) -151.01, -153 67, -160.21; *m/z* (EI) 390.9934 ($M^{+\bullet}$, $C_{15}H_6F_5NO_4S$ requires 390.9932), 238 (31%) and 178 (100).



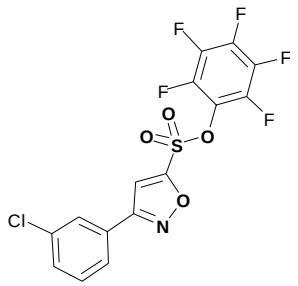
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



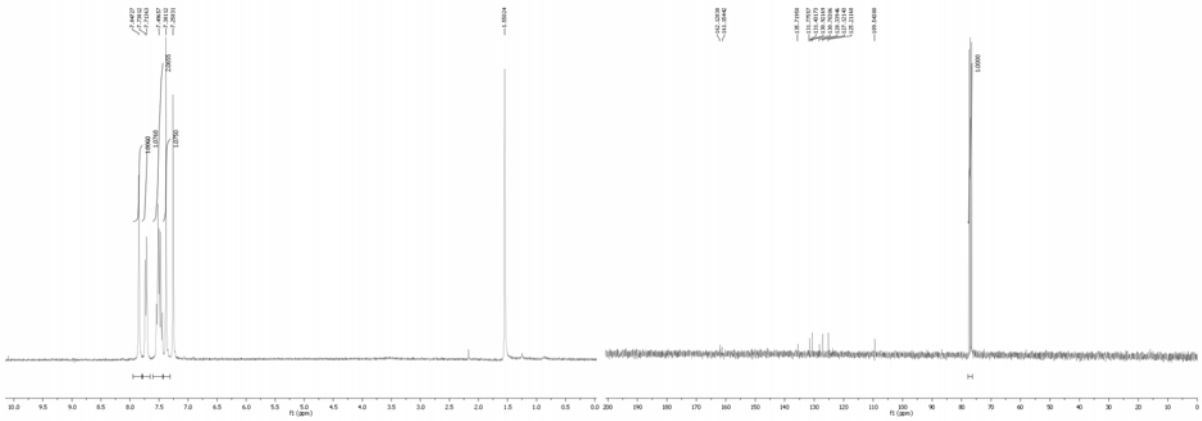
Yield: (2.252 g, 5.1 mmol, 88%) as a white solid. R_f 0.32 (10% Et_2O/petroleum ether); mp 106-107 °C; ν_{max}(film)/cm^{-1} 3055, 1519, 1199; δ_H($CDCl_3$, 300 MHz) 7.78 (2H, d, J = 8.5 Hz), 7.51 (2H, d, J = 8.5 Hz), 7.37 (1H, s); δ_C($CDCl_3$, 75 MHz) 162.1 (s), 161.4 (s), 137.8 (s), 129.7 (d), 128.3 (d), 125.0 (s), 109.4 (d); δ_F($CDCl_3$, 282 MHz) -150.95, -153.47, -160.06; *m/z* (EI) 427 (30%), 424.9483 ($M^{+\bullet}$, $C_{15}H_5ClF_5NO_4S$ requires 424.9493), 242 (67), 150 (100) and 111 (53).



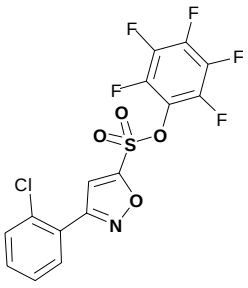
3-(3-Chloro-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



Yield: (1.72 g, 3.9 mmol, 75%) as a white solid. R_f 0.30 (10% Et_2O/petroleum ether); mp 93-95 °C; ν_{max}(film)/cm^{-1} 3055, 1525, 1136; δ_H($CDCl_3$, 300 MHz) 7.85 (1H, s), 7.72 (1H, dd, J = 7.3, 1.5 Hz), 7.45-7.54 (2H, m), 7.36 (1H, s); δ_C($CDCl_3$, 75 MHz) 135.6 (s), 131.6 (s), 130.7 (d), 130.5 (s), 128.2 (d) 127.2 (d), 125.1 (d), 124.31 (s), 109.4 (d); δ_F($CDCl_3$, 282 MHz) -150.95, -153.39, -160.06; *m/z* (EI) 427 (33%), 424.9543 ($M^{+\bullet}$, $C_{15}H_5ClF_5NO_4S$ requires 424.9542, 100), 242 (16).

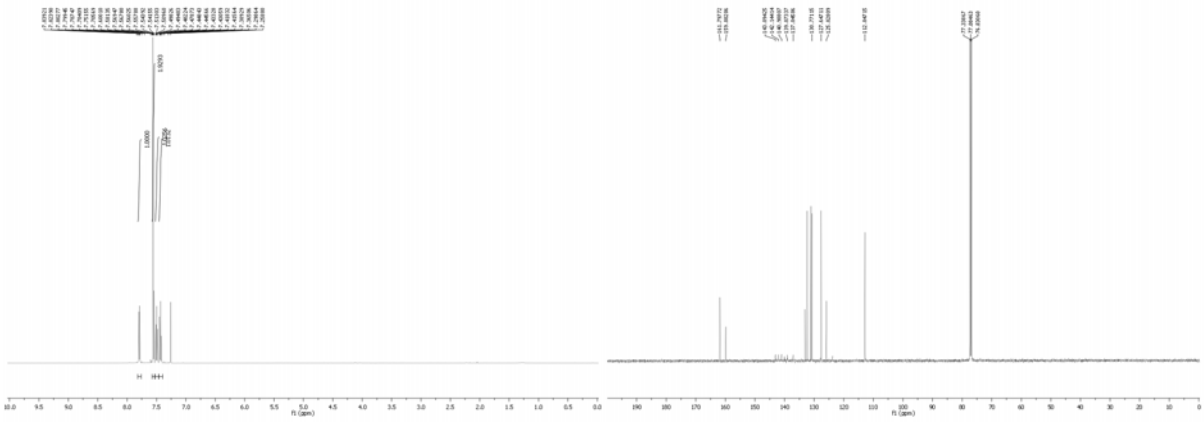


3-(2-Chloro-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester

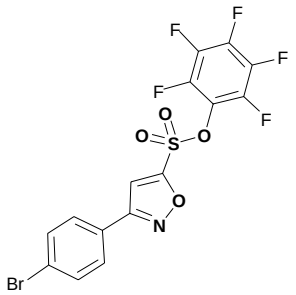


Yield: (2.21 g, 5.01 mmol, 87%) as a white solid. R_f 0.30 (10% Et_2O/petroleum ether); mp 89-90 °C; ν_{max}(film)/cm^{-1} 3055, 2985, 1596, 1517, 1132; δ_H($CDCl_3$, 300 MHz) 7.79 (1H, dd, J = 7.3, 1.8 Hz), 7.56 (1H, s), 7.40-7.54 (3H, m, ArH); δ_C($CDCl_3$, 75 MHz) 162.9 (s), 161.8 (s), 159.8 (s), 133.0 (s), 132.3 (d), 131.1 (d), 130.7 (d), 127.6 (d), 112.8 (d); δ_F($CDCl_3$, 282

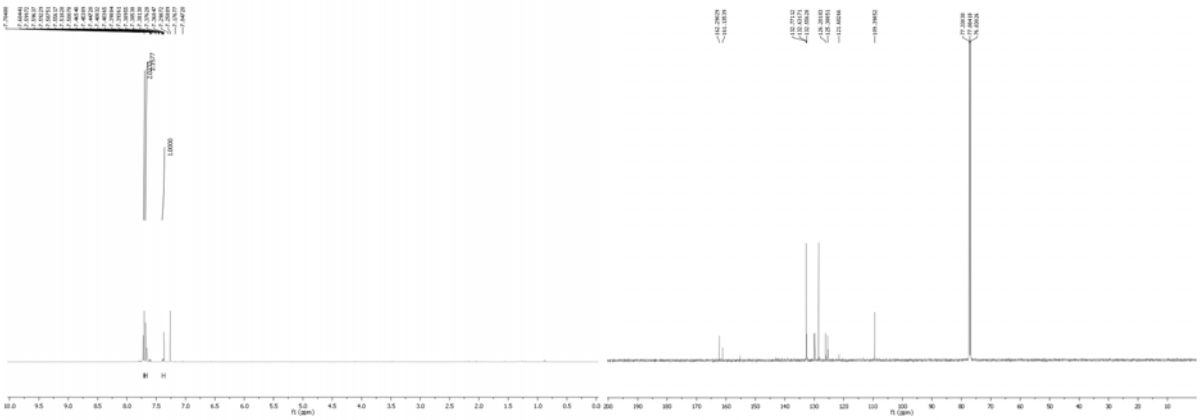
MHz) -151 05, -153.55, -160.15; *m/z* (EI) 427 (18%), 424.9546 ($M^{+\bullet}$, $C_{15}H_5ClF_5NO_4S$ requires 424.9542, 45), 242 (35), 178 (100), 155 (40) and 150 (79).



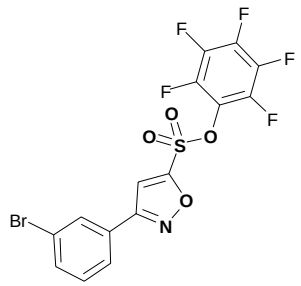
3-(4-Bromo-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



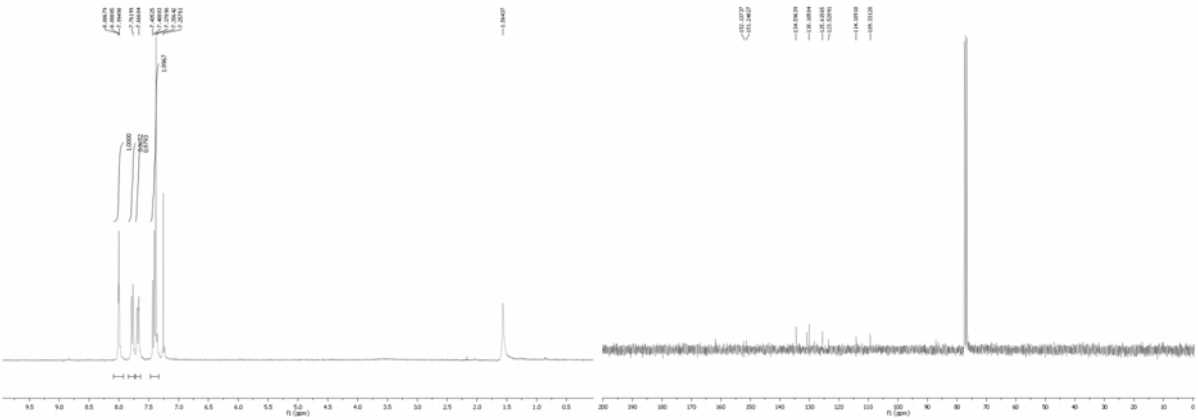
Yield: (2.45 g, 5.21 mmol, 87%) and a white solid. R_f 0.29 (10% Et_2O/petroleum ether); mp 110-113 °C; ν_{max}(film)/cm^{-1} 3055, 1596, 1519, 1199; δ_H($CDCl_3$, 300 MHz) 7.72 (2H, d, J = 8.6 Hz), 7.67 (2H, d, J = 8.4 Hz), 7.37 (1H, s); δ_C($CDCl_3$, 75 MHz) 162.2 (s), 161.1 (s), 132.7 (d), 128.5 (d), 126.1 (s), 125.4 (s), 109.33 (d); δ_F($CDCl_3$, 282 MHz) -151.02, -153.46, -160.12; *m/z* (EI) 471 (100%), 468.8990 ($M^{+\bullet}$, $C_{15}H_5BrF_5NO_4S$ requires 468.8987, 96), 336 (22), 288 (30), 186 (26), 224 (32), 196 (86), 194 (96) and 157 (42).



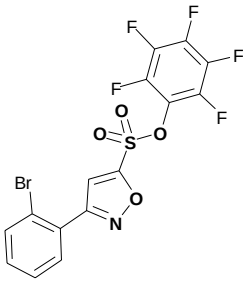
3-(3-Bromo-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



Yield (1.66 g, 3.53 mmol, 69%) off white solid. R_f 0.18 (10% Et_2O/petroleum ether); mp 106-107 °C; ν_{max}(film)/cm^{-1} 3055, 2987, 1525, 1367, 1134; δ_H($CDCl_3$, 300 MHz) 8.00 (1H, s,), 7.78 (1H, d, *J* = 7.7 Hz), 7.68 (1H, d, *J* = 7.2 Hz), 7.41 (1H, app t, *J* = 7.9 Hz), 7.38 (1H, s); δ_C($CDCl_3$, 75 MHz) 162.2 (s), 162 0 (s), 153.0 (s), 130.8 (s), 134.5 (d), 130.9 (d), 130.0 (d), 125.6 (d), 109.3 (d); δ_F($CDCl_3$, 282 MHz) -151.02, -153.41, -160.07; *m/z* (EI) 471 (70%), 468.9025 ($M^{+\bullet}$, $C_{15}H_5BrF_5NO_4S$ requires 468.9037, 67), 288 (62), 286 (61), 224 (63), 222 (64), 196 (42), 194 (44), 157 (62), 155 (100) and 102 (35).

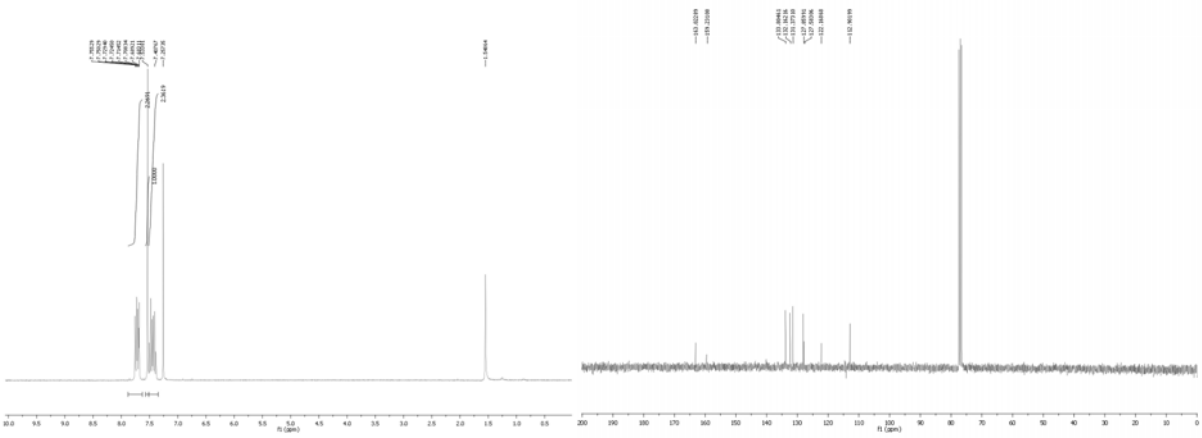


3-(2-Bromo-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester

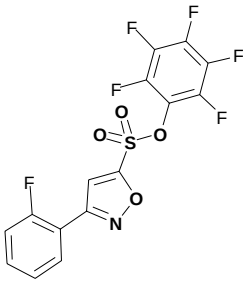


Yield: (2.08 g, 4.47 mmol, 86%) as a white solid. R_f 0.25 (10% Et_2O/petroleum ether); mp 100-102 °C; ν_{max}(film)/cm^{-1} 3055, 2985, 1519, 1199; δ_H($CDCl_3$, 300 MHz) 7.68-7.75 (2H, m), 7.53 (1H, s), 7.40-7.48 (2H, m); δ_C($CDCl_3$, 75 MHz) 163.1 (s), 159.6 (s), 133.9 (d), 132.4

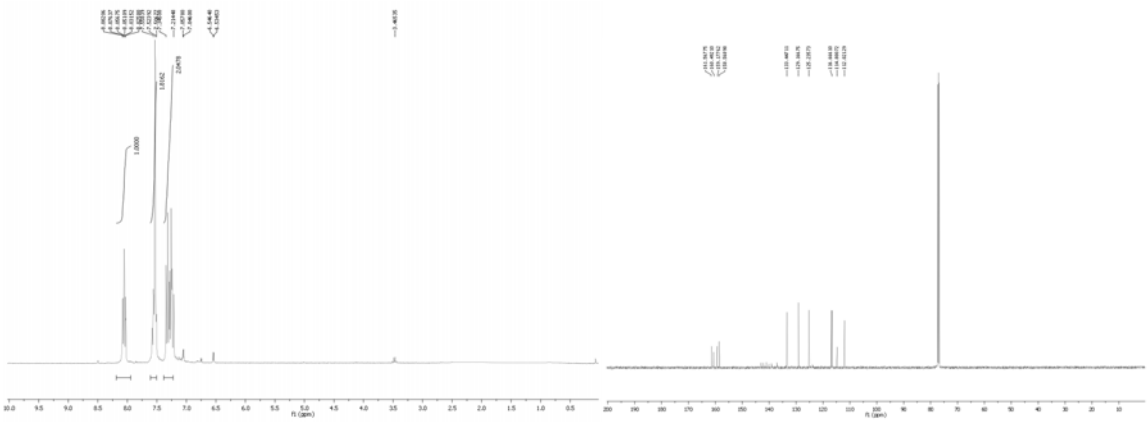
(d), 131.5 (d), 128.1 (d), 127.9 (s), 122.2 (s), 112.9 (d); δ_F($CDCl_3$, 282 MHz) -150.95, -153.48, -160.18; *m/z* (EI) 471 (9%), 468.8982 ($M^{+\bullet}$, $C_{15}H_5BrF_5NO_4S$ requires 468.8987, 8), 288 (7), 286 (7), 222 (15), 220 (17), 196 (24), 194 (27), 155 (25), 115 (100), and 88 (75).



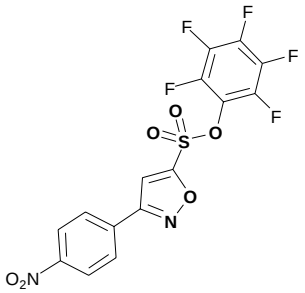
3-(2-Fluoro-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



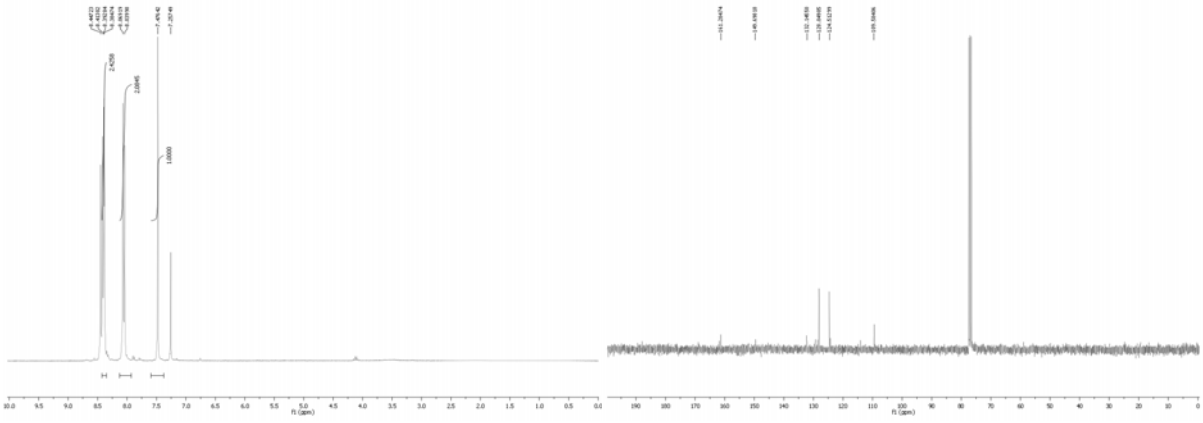
Yield: (1.65 g, 4.03 mmol, 68%) as a white solid. R_f 0.30 (10% Et_2O/petroleum ether); mp 76-77 °C; ν_{max}(film)/cm^{-1} 3055, 2987, 1519, 1197; δ_H($CDCl_3$, 300 MHz) 8.05 (1H, td, *J* = 7.6, 1.7 Hz), 7.54 (1H, s), 7.51-7.58 (1H, m), 7.23-7.34 (2H, m); δ_C($CDCl_3$, 126 MHz) 161.39 (s), 159.60 (s, J_{C-F} = 259.1 Hz), 159.38 (s), 133.41 (d, J_{C-F} = 8.6 Hz), 129.06 (d), 125.1 (d, J_{C-F} = 3.8 Hz)7, 116.75 (d, J_{C-F} = 22.1 Hz), 114.81 (s, J_{C-F} = 11.5 Hz), 112.06 (d, J_{C-F} = 11.5 Hz); δ_F($CDCl_3$, 282 MHz) -114.40, -150.95, -153.62, -160.35; *m/z* (EI) 408.9781 ($M^{+\bullet}$, $C_{15}H_5F_6NO_4S$ requires 408.9788, 100%), 226 (45), 162 (35), 134 (45) and 107 (19).



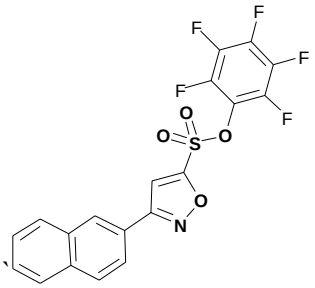
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid pentafluorophenyl ester



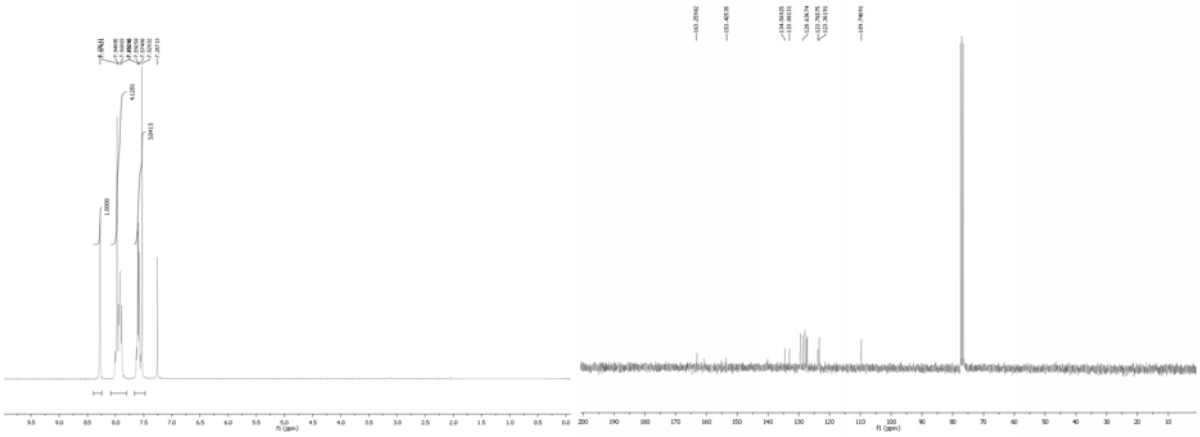
Yield: (1.13 g, 3.58 mmol, 50%) off white solid. R_f 0.20 (20% Et_2O/petroleum ether); mp 126-128 °C; ν_{max}(film)/cm^{-1} 3131, 1567, 1516, 1341, 1198; δ_H($CDCl_3$, 300 MHz) 8.40 (2H, d, J = 8.7 Hz), 8.06 (2H, d, J = 8.7 Hz), 7.48 (1H, s); δ_C($CDCl_3$, 75 MHz) 162.1 (s), 161.3 (s), 132.1 (s), 129.9 (s), 128.1 (d), 124.6 (d), 109.4 (d); δ_F($CDCl_3$, 282 MHz) -151.07, -153.15, -159.74; *m/z* (EI) 435.9798 ($M^{+\bullet}$, $C_{15}H_5F_5N_2O_6S$ requires 435.9783, 57%), 253 (79), 189 (36) and 143 (100).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid pentafluorophenyl ester



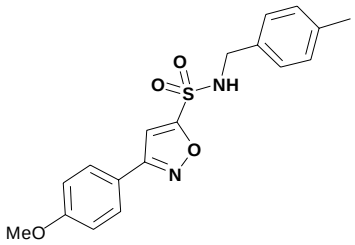
Yield: (2.12 g, 4.8 mmol, 80%) a as white solid. R_f 0.25 (10% Et_2O/petroleum ether); mp 120-121 °C; ν_{max}(film)/cm^{-1} 3055, 2987, 1517, 1136; δ_H($CDCl_3$, 300 MHz) 8.28 (1H, s), 7.89-8.01 (4H, m), 7.57-7.63 (2H, m), 7.53 (1H, s); δ_C($CDCl_3$, 75 MHz) 163.1 (s), 160.2 (s), 140.00 (d), 134.57 (s), 13.00 (s), 129.44 (d), 128.64 (d), 127.98 (d), 127.48 (d), 127.25 (d), 123.82 (s), 123.30 (d), 109.73 (d); δ_F($CDCl_3$, 282 MHz) -150.93, -153.59, -160.18; *m/z* (EI) 441.0084 ($M^{+\bullet}$, $C_{19}H_8F_5NO_4S$ requires 441.0088, 17%) and 184 (100).



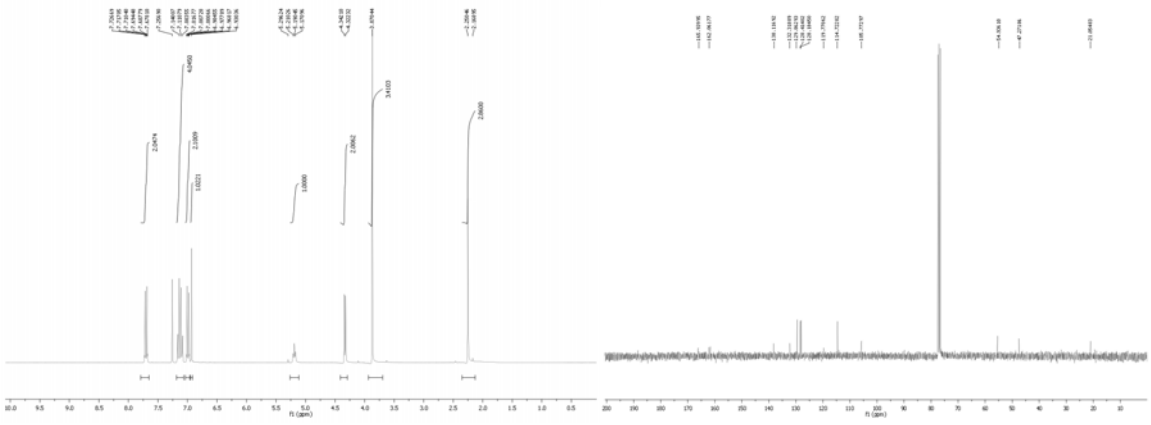
Preparation of sulfonic acid 4-methyl-benzylamides

To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added 4-methylbenzylamine (3 eq.) followed by NEt_3 (1.5 eq.) and the mixture was stirred at 66 °C for until complete by tlc (0.5~1 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x2), sat. $NaHCO_3$ (x2) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (20% Et_2O/petroleum ether).

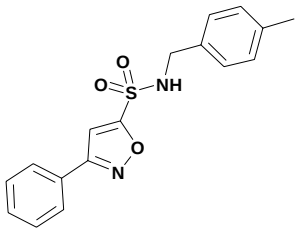
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid 4-methyl-benzylamide



Yield: (77 mg, 0.22 mmol, 71%) as a white solid. R_f 0.09 (20% Et_2O/petroleum ether); mp 135-137 °C; ν_{max}(film)/cm^{-1} 3369, 3055, 2985, 1612, 1527, 1170; δ_H($CDCl_3$, 300 MHz) 7.70 (2H, d, *J*= 8.7 Hz), 7.16 (2H, d, *J* = 8.1 Hz), 7.10 (2H, d, *J* = 8.1 Hz), 7.00 (2H, d, *J* = 8.7 Hz), 6.93 (1H, s), 5.19 (1H, t, *J* = 5.9 Hz), 4.33 (2H, d, *J* = 5.9 Hz), 3.87 (3H, s), 2.25 (3H, s); δ_C($CDCl_3$, 75 MHz) 165.5 (s), 162.4 (s), 162.3 (s), 138.3 (s), 132.2 (s), 119.9 (s), 129.5 (d), 128.4 (d), 128.1 (d), 114.6 (d), 105.8 (d), 55.5 (q), 47.5 (t), 21.1 (q); *m/z* (FAB) 359.1057 ([M+H]$^+$, $C_{18}H_{19}N_2O_4S$ requires 359.1065, 15%), 307 (27) and 154 (100).

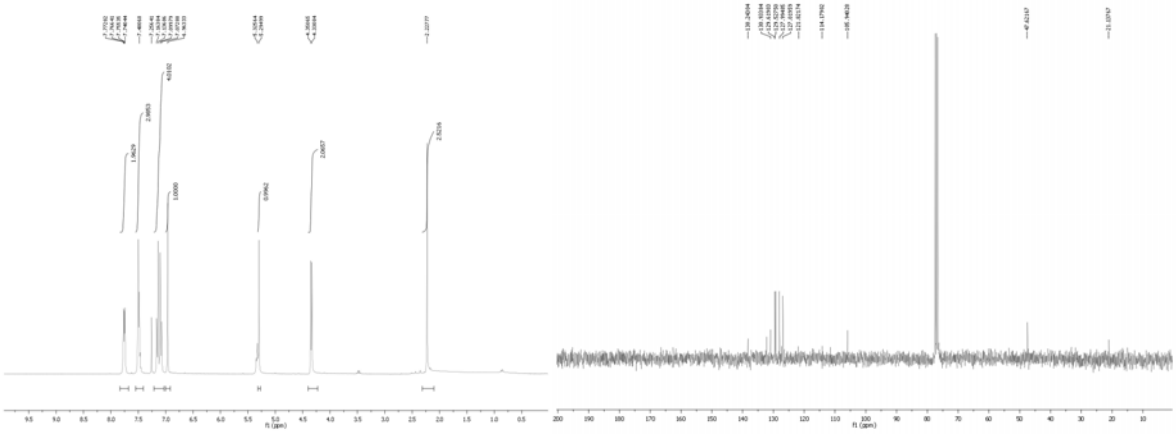


3-Phenyl-isoxazole-5-sulfonic acid 4-methyl-benzylamide

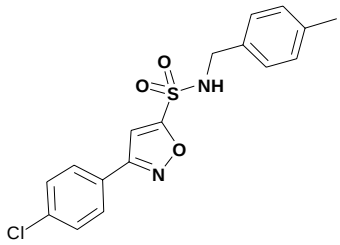


Yield (0.15 g, 0.48 mmol, 95%). R_f 0.06 (20% Et_2O/petroleum ether); mp 119-120 °C; ν_{max}(film)/cm^{-1} 3363, 3055, 2985, 1595, 1392; δ_H($CDCl_3$, 300 MHz) 7.74-7.77 (2H, m), 7.47-7.50 (3H, m), 7.15 (2H, d, *J* = 8.1 Hz), 7.08 (2H, d, *J* = 8.1 Hz), 6.96 (1H, s), 5.33 (1H, t, *J* = 5.8 Hz), 4.34 (2H, d, *J* = 5.8 Hz), 2.23 (3H, s); δ_C($CDCl_3$, 75 MHz) 162.4 (s), 161.9 (s), 147.5 (s), 138.3 (s), 132.2 (s), 130.9 (d), 129.5 (d), 129.2 (d), 128.1 (d), 126.9 (d), 105.9 (d), 47.5

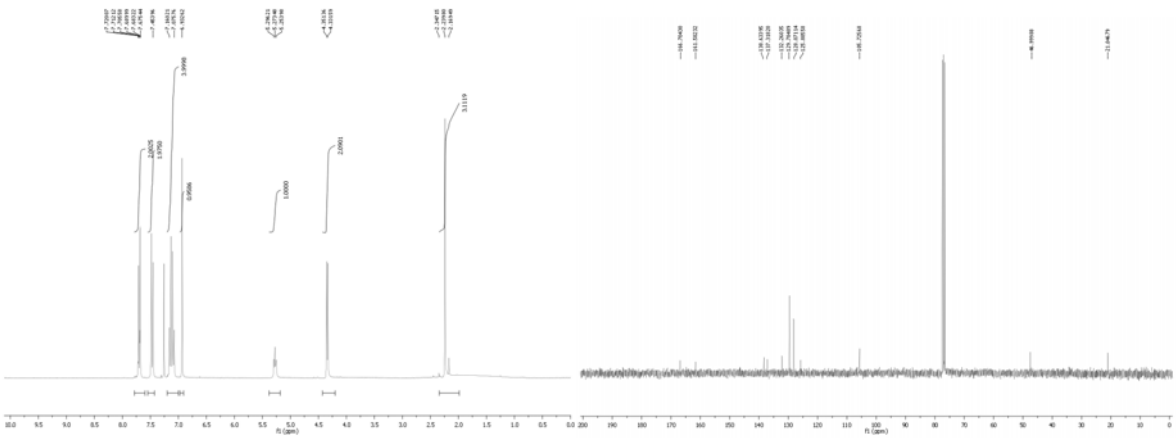
(t), 21.22 (q); *m/z* (FAB) 329.0951 ($[M+H]^+$, $C_{17}H_{17}N_2O_3S$ requires 329.0959, 100%) and 237 (8).



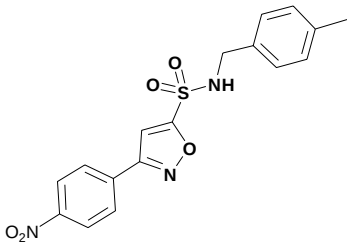
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid 4-methyl-benzylamide



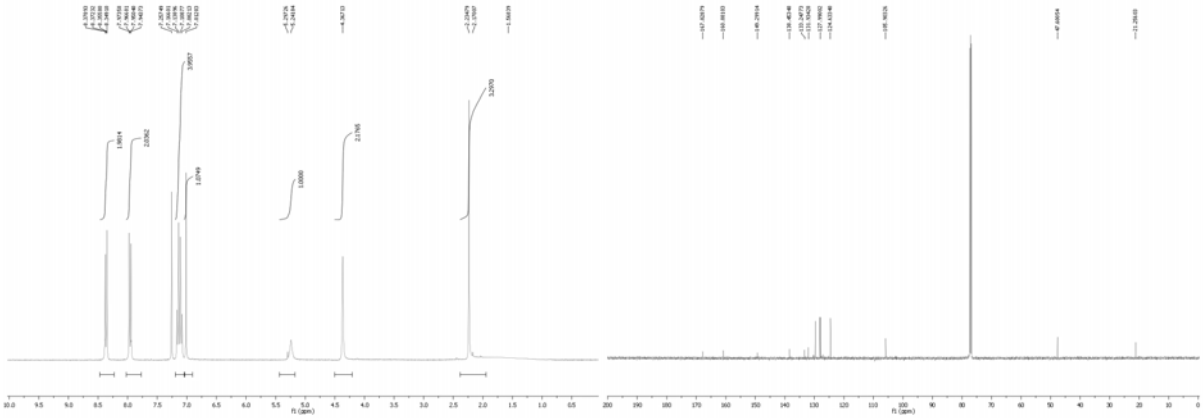
Yield: (0.15 g, 0.42 mmol, 83%) as a white solid. R_f 0.10 (20% Et_2O/petroleum ether); mp 153-155 °C; ν_{max}(film)/cm^{-1} 3375, 3053, 2985, 1170; δ_H($CDCl_3$, 300 MHz) 7.70 (2H, d, J = 8.6 Hz), 7.47 (2H, d, J = 8.6 Hz), 7.15 (2H, d, J = 8.0 Hz), 7.09 (2H, d, J = 8.0 Hz), 6.93 (1H, s), 5.27 (1H, br t, J = 5.8 Hz), 4.34 (2H, d, J = 5.9 Hz), 2.24 (3H, s); δ_C($CDCl_3$, 75 MHz) 166.9 (s), 161.6 (s), 138.3 (s), 137.1 (s), 132.1 (s), 129.5 (d), 128.2 (d), 128.1 (d), 125.9 (s), 105.7 (d), 47.5 (t), 21.1 (q); *m/z* (FAB) 365 (6%), 363.0579 ($[M+H]^+$, $C_{17}H_{16}ClN_2O_3S$ requires 363.0570, 18), 289 (10), 220 (6) and 154 (100).



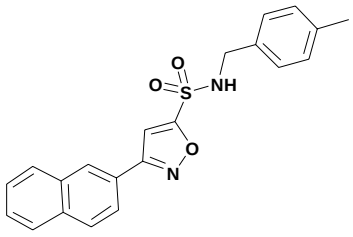
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid 4-methyl-benzylamide



Yield: (0.13 g, 0.36 mmol, 72%) as a white solid. R_f 0.10 (40% Et_2O/petroleum ether); mp 183-184 °C; ν_{max}(film)/cm^{-1} 3274, 3055, 1521, 1164; δ_H($CDCl_3$, 300 MHz) 8.37 (2H, d, *J* = 8.9 Hz), 7.96 (2H, d, *J* = 8.9 Hz), 7.16 (2H, d, *J* = 8.0 Hz), 7.10 (2H, d, *J* = 8.0 Hz), 7.01 (1H, s), 5.24 (1H, br s), 4.37 (2H, s), 2.24 (3H, s); δ_C($CDCl_3$, 126 MHz) 167.83 (s), 160.80 (s), 149.30 (s), 138.42 (s), 133.40 (s), 132.07 (s), 129.63 (d), 128.15 (d), 127.95 (d), 124.52 (d), 105.85 (d), 47.60 (t), 21.12 (q); *m/z* (FAB) 374.0806 ($[M+H]^+$, $C_{17}H_{16}N_3O_5S$ requires 374.0810, 6%), 307 (24), 289 (14) and 154 (100).

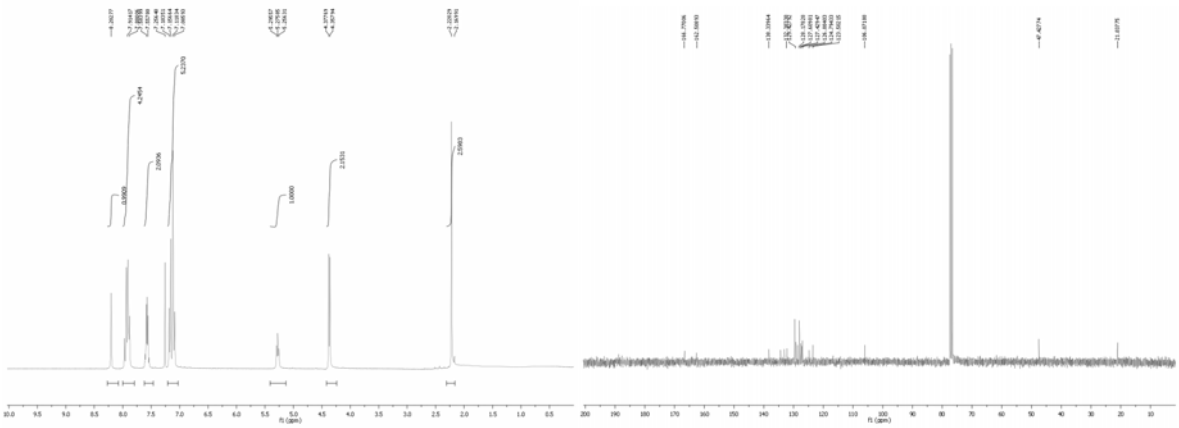


3-Naphthalen-2-yl-isoxazole-5-sulfonic acid 4-methyl-benzylamide



Yield: (0.15 g, 0.41 mmol, 83%) a white solid. R_f 0.06 (20% Et_2O/petroleum ether); mp 131-133 °C; ν_{max}(film)/cm^{-1} 3365, 3307, 3055, 2985, 1170; δ_H($CDCl_3$, 300 MHz) 8.20 (1H, s), 7.88-7.97 (4H, m), 7.54-7.61 (2H, m), 7.17 (2H, d, *J* = 8.1 Hz), 7.12 (1H, s), 7.10 (2H, d, *J* = 8.1 Hz), 5.28 (1H, t, *J* = 5.8 Hz), 4.37 (2H, d, *J* = 5.8 Hz), 2.22 (3H, s); δ_C($CDCl_3$, 75 MHz) 166.6 (s), 162.5 (s), 138.3 (s), 134.4 (s), 133.1 (s), 132.2 (s), 129.6 (d), 129.2 (d), 128.6 (d),

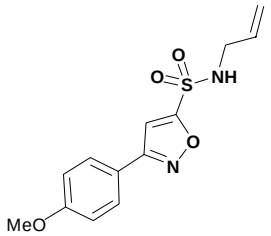
128.1 (d), 127.9 (d), 127.6 (d), 127.2 (d), 127.0 (d), 124.7 (s), 123.5 (d), 106.1 (d), 47.5 (t), 21.0 (q); *m/z* (FAB) 379.1107 ([M+H]$^+$, $C_{21}H_{19}N_2O_3S$ requires 379.1116, 100%), 307 (11), 194 (18) and 154 (83).



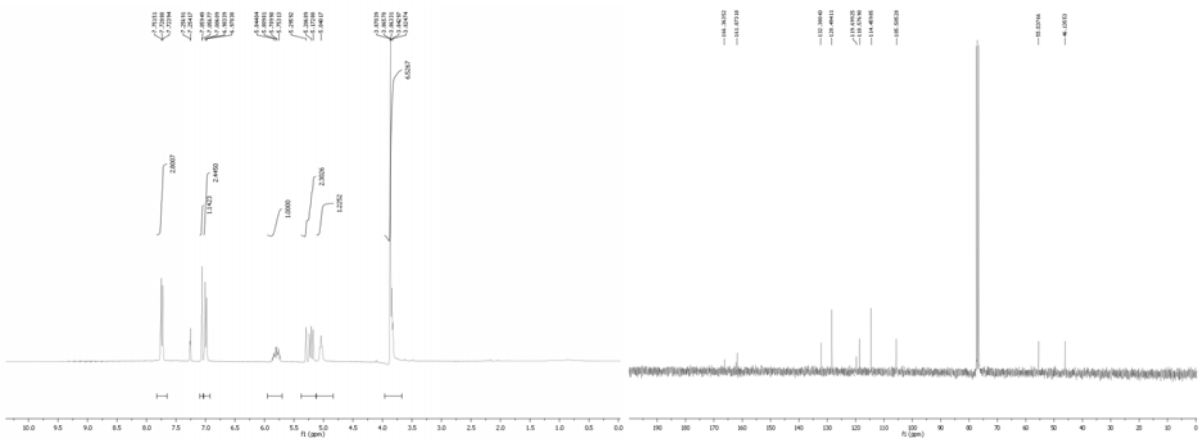
Preparation of sulfonic acid allylamides

To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added allylamine (3 eq.) followed by NEt_3 (1.5 eq.) and the mixture was stirred at 66 °C for until complete by tlc (1.5~2 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x2), sat. $NaHCO_3$ (x2) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (10% EtOAc/petroleum ether).

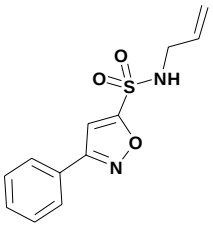
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid allylamide



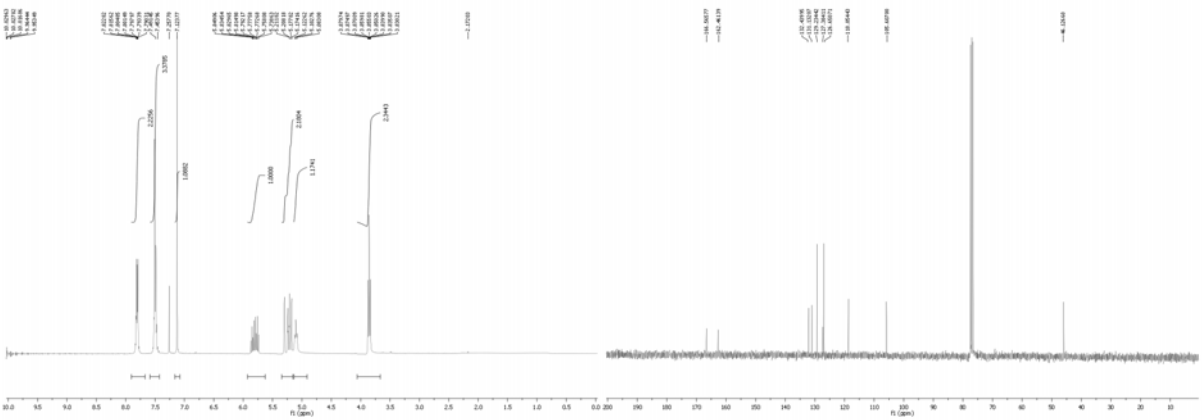
Yield: (92 mg, 0.31 mmol, 66%) as an off white solid. R_f 0.1 (20% EtOAc/petroleum ether); mp 106-108 °C; ν_{max}(film)/cm^{-1} 3277, 1606, 1589, 1344, 1162; δ_H($CDCl_3$, 300 MHz) 7.73 (2H, d, *J* = 8.9 Hz), 7.06 (1H, s), 6.99 (2H, d, *J* = 8.9 Hz), 5.80 (1H, m), 5.26 (1H, dd, *J* = 7.1, 0.9 Hz), 5.19 (1H, dd, *J* = 10.2, 0.9 Hz), 5.04 (1H, app t, *J* = 5.0 Hz)3.86 (3H, s), 3.80-3.87 (2H, m); δ_C($CDCl_3$, 75 MHz) 161.7 (s), 132.1 (s), 128.4 (d), 119.4 (s), 118.6 (s), 114.6 (d), 105.7 (d), 68.2 (d), 65.24 (t), 55.5 (q), 46.1 (t); *m/z* (EI) 294.0673 (M^+, $C_{13}H_{15}N_2O_4S$ requires 294.0668, 46%), 174 (85) and 146 (100).



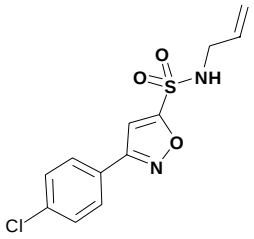
3-Phenyl-isoxazole-5-sulfonic acid allylamide



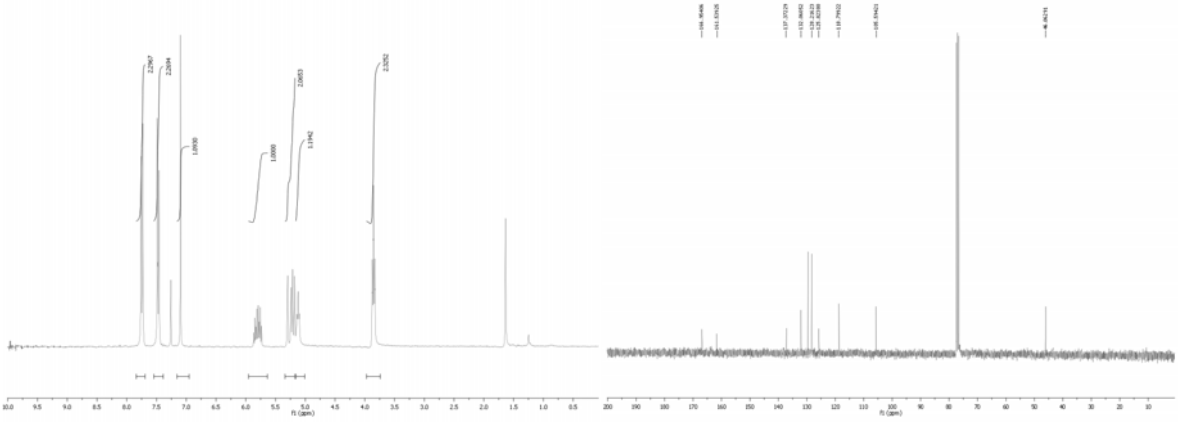
Yield: (85 mg, 0.32 mmol, 64%) off white solid. R_f 0.10 (20% EtOAc/petroleum ether); mp 74-76 °C; ν_{max}(film)/cm^{-1} 3256, 1352, 1169; δ_H($CDCl_3$, 300 MHz) 7.81 (2H, m), 7.50 (3H, m), 7.12 (1H, s), 5.80 (1H, m), 5.27 (1H, dd, *J* = 17.1, 1.0 Hz), 5.19 (1H, dd, *J* = 10.2, 1.0 Hz), 5.10 (1H, t, *J* = 5.9 Hz), 3.86 (2H, app tt, *J* = 5.9, 1.4 Hz); δ_C($CDCl_3$, 75 MHz) 166.6 (s), 162.6 (s), 132.1 (s), 131.0 (d), 129.2 (d), 127.3 (d), 127.0 (d), 118.6 (t), 105.9 (d), 46.1 (t); *m/z* (EI) 264.0570 (M^+, $C_{12}H_{13}N_2O_3S$ requires 264.0563, 12), 144 (100), 116 (74) and 103 (25).



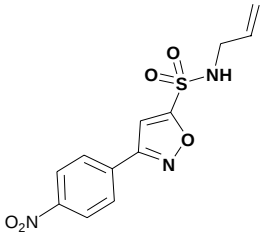
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid allylamide



Yield: (90 mg, 0.3 mmol, 60%) as a white solid. R_f 0.13 (20% EtOAc/petroleum ether); mp 123-125 °C; ν_{max}(film)/cm^{-1} 3273, 1601, 1329, 1159; δ_H($CDCl_3$, 300 MHz) 7.75 (2H, d, *J* = 8.7 Hz), 7.47 (2H, d, *J* = 8.7 Hz), 7.10 (1H, s), 5.74-5.87 (1H, m), 5.27 (1H, dd, *J* = 17.1, 1.0 Hz), 5.19 (1H, dd, *J* = 10.2, 1.0 Hz), 5.12 (1H, t, *J* = 6.0 Hz), 3.85 (2H, app tt, *J* = 6.0, 1.4 Hz); δ_C($CDCl_3$, 75 MHz) 166.9 (s), 161.7 (s), 137.2 (s), 132.1 (d), 129.6 (d), 128.2 (d), 125.8 (s), 118.7 (t), 105.64 (d), 46.06 (t); *m/z* (EI) 300 (9%), 298.0169 ($M^{+\bullet}$, $C_{12}H_{11}ClN_2O_3S$ requires 298.0173, 24), 178 (100), 152 (40), 150 (98), 123 (34) and 111 (60).

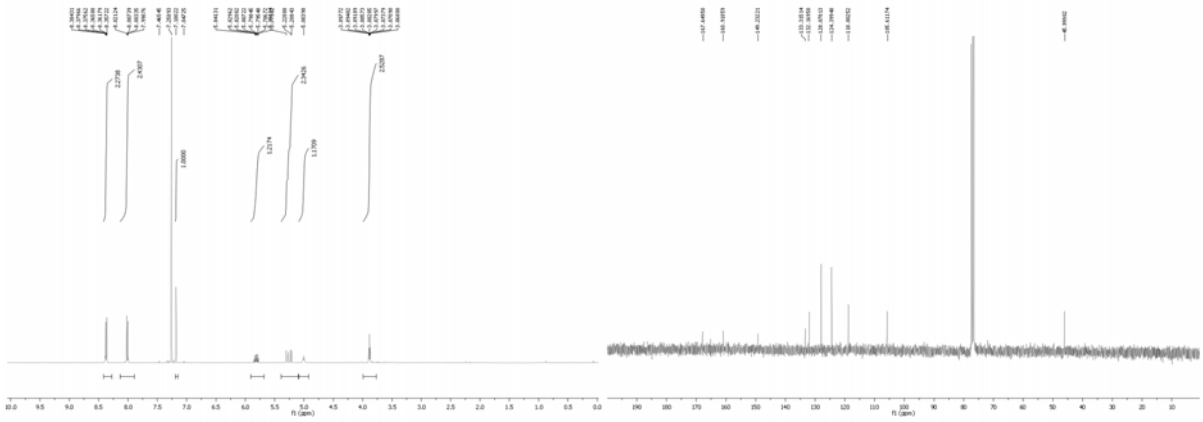


3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid allylamide

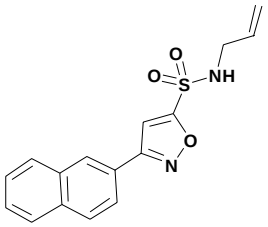


Yield: (105 mg, 0.34 mmol, 69%) as an off white solid. R_f 0.10 (20% EtOAc/petroleum ether); mp 131-133 °C; ν_{max}(film)/cm^{-1} 3247, 1613, 1536, 1343, 1160; δ_H($CDCl_3$, 300 MHz) 8.36 (2H, d, *J* = 8.5 Hz), 8.00 (2H, d, *J* = 8.5 Hz), 7.19 (1H, s), 5.72-5.88 (1H, m), 5.27 (1H, d, *J* = 14.1 Hz), 5.20 (1H, d, *J* = 9.9 Hz), 3.88 (2H, d, *J* = 5.4 Hz); δ_C($CDCl_3$, 75 MHz) 167.8 (s), 160.9 (s), 149.1 (s), 133.3 (s), 132.0 (d), 128.0 (d), 124.5 (d), 118.8 (t), 105.7 (d), 46.1 (t);

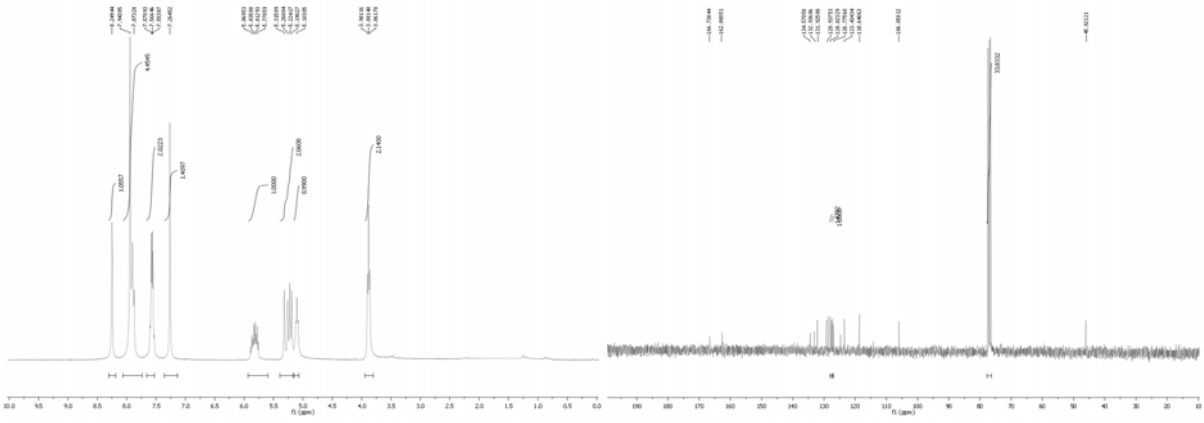
LRMS (EI+) 310 (M+, 100), 248 (27), 216 (26), 189 (48); *m/z* (EI) 310.0501 ($M^{+\bullet}$, $C_{12}H_{11}N_3O_5S$ requires 310.0497, 100%).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid allylamide



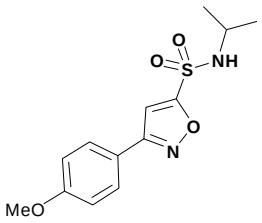
Yield: (105 mg, 0.33 mmol, 69%) as a white solid. R_f 0.20 (20% EtOAc/petroleum ether); mp 112-114 °C; ν_{max}(film)/cm^{-1} 3280, 1347, 1166; δ_H($CDCl_3$, 300 MHz) 8.25 (1H, s), 7.91 (4H, m), 7.56 (2H, m), 7.25 (1H, s), 5.81 (1H, ddt, *J* = 13.9, 10.3, 5.8 Hz), 5.29 (1H, d, *J* = 16.9 Hz), 5.20 (1H, d, *J* = 10.4 Hz), 5.10 (1H, t, *J* = 5.8 Hz), 3.88 (2H, app t, *J* = 5.8 Hz); δ_C($CDCl_3$, 75 MHz) 167.4 (s), 162.7 (s), 134.4 (s), 133.1 (s), 132.1 (d), 129.2 (d), 128.6 (d), 127.9 (d), 127.6 (d), 127.2 (d), 127.0 (d), 124.7 (s), 123.5 (d), 118.6 (t), 105.98 (d), 46.10 (t); *m/z* (EI) 314.0720 ($M^{+\bullet}$, $C_{16}H_{14}N_2O_3S$ requires 314.0719, 73), 194 (94), 166 (45) and 127 (100).



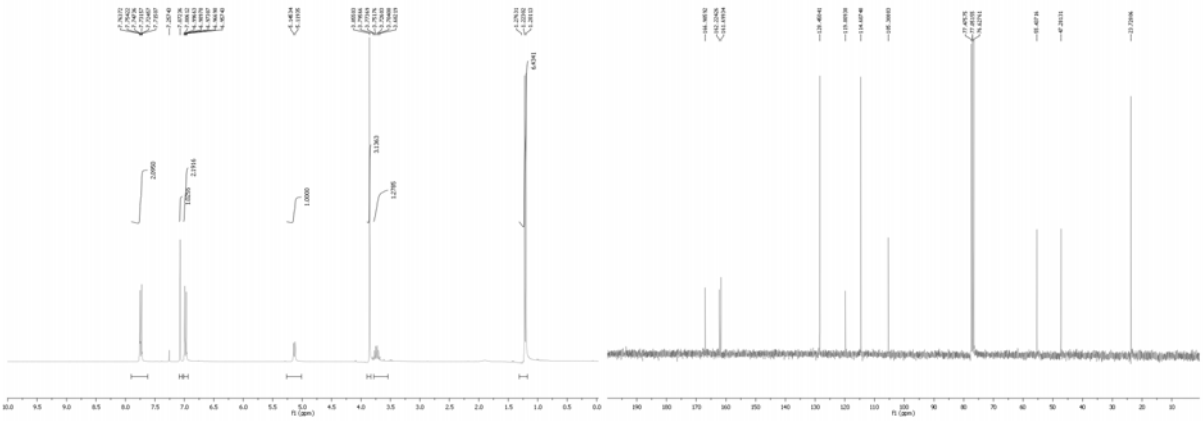
Preparation of sulfonic acid isopropylamides

To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added *iso*-propylamine (3 eq.) and tetrabutylammonium chloride (2 eq.) followed by NEt_3 (1.5 eq.) and the mixture was stirred at 66 °C for until complete by tlc (1~3 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x3), sat. $NaHCO_3$ (x3) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (20% EtOAc/petroleum ether).

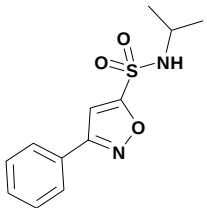
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid isopropylamide



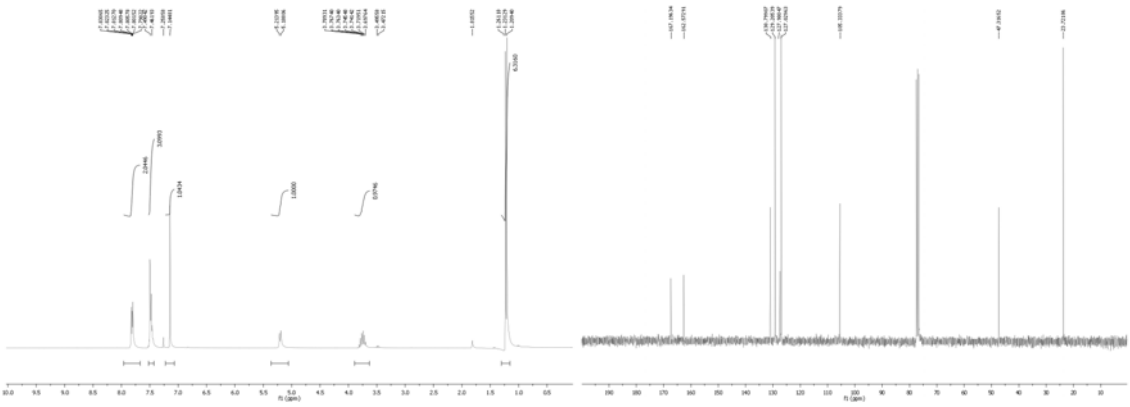
Yield: (131 mg, 0.44 mmol, 89%) as an off white solid. (Found: C, 52.5; H, 5.4; N, 9.8. $C_{13}H_{16}N_2O_4S$ requires C, 52.7; H, 5.4; N, 9.5%); R_f 0.15 (20% EtOAc/petroleum ether); mp 98-101 °C; ν_{max}(film)/cm^{-1} 3155, 1610, 1520, 1346, 1176; δ_H($CDCl_3$, 300 MHz) 7.73 (2H, d, J = 8.8 Hz), 7.07 (1H, s), 6.97 (2H, d, J = 8.8 Hz), 5.13 (1H, d, J = 7.5 Hz), 3.85 (3H, s), 3.73 (1H, app octet, J = 6.7 Hz), 1.21 (6H, d, J = 6.7 Hz); δ_C($CDCl_3$, 75 MHz) 167.0 (s), 162.2 (s), 161.8 (s), 128.5 (d), 119.8 (s), 114.6 (d), 105.3 (d), 55.4 (q), 47.3 (d), 23.7 (q); *m/z* (EI) 296.0823 ($M^{+\bullet}$, $C_{13}H_{16}N_2O_4S$ requires 296.0825, 50%), 174 (100) and 146 (79)



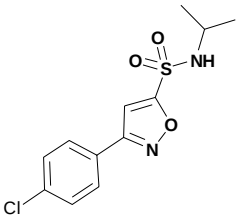
3-Phenyl-isoxazole-5-sulfonic acid isopropylamide



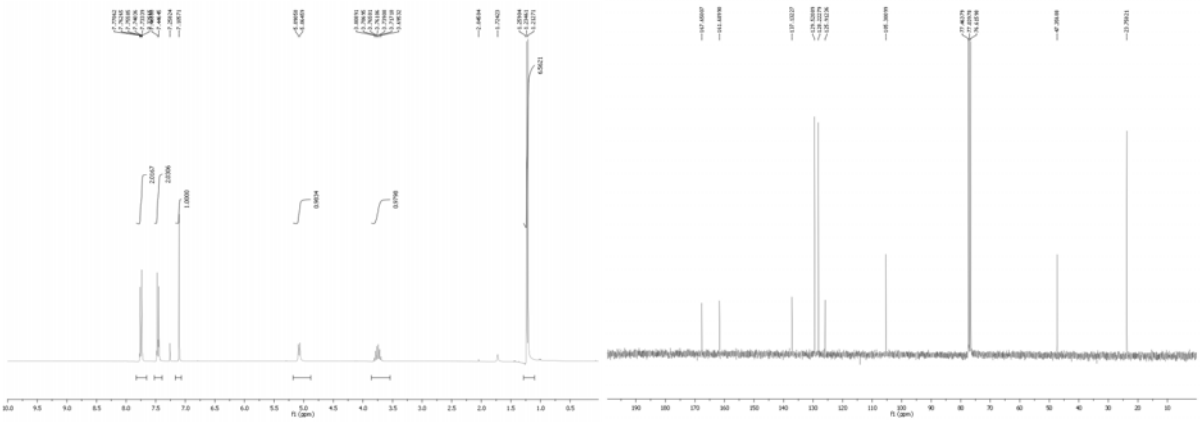
Yield: (105 mg, 0.39 mmol, 79%) as a white solid. R_f 0.24 (20% EtOAc/petroleum ether); mp 117-120 °C; ν_{max}(film)/cm^{-1} 3272, 1605, 1351, 1171; δ_H($CDCl_3$, 300 MHz) 7.79-7.84 (2H, m), 7.46-7.51 (3H, m), 7.14 (1H, s), 5.19 (1H, d, *J* = 7.2 Hz), 3.75 (1H, app octet, *J* = 6.4 Hz), 1.21 (6H, d, *J* = 6.4 Hz); δ_C($CDCl_3$, 75 MHz) 167.3 (s), 162.7 (s), 130.9 (d), 129.2 (d), 127.4 (s), 127.0 (d), 105.5 (d), 47.32 (d), 23.72 (q); *m/z* (EI) 266.0712 ($M^{+\bullet}$, $C_{12}H_{14}N_2O_3S$ requires 266.0719, 28%), 251 (100) and 144 (75).



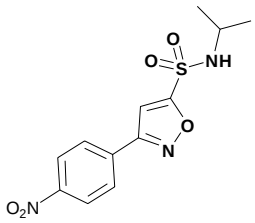
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid isopropylamide



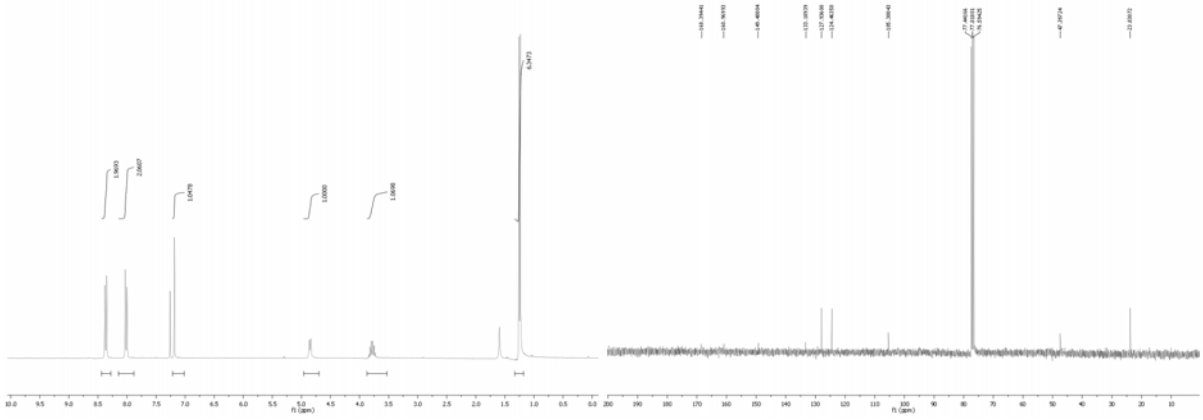
Yield: (111 mg, 0.37 mmol, 74%) to yield a white solid. R_f 0.28 (20% EtOAc/petroleum ether); mp 121-124 °C; ν_{max}(film)/cm^{-1} 3150, 1601, 1507, 1353, 1179; δ_H($CDCl_3$, 300 MHz) 7.74 (2H, d, *J* = 8.8 Hz), 7.45 (2H, d, *J* = 8.8 Hz), 7.10 (1H, s), 5.07 (1H, d, *J* = 7.8 Hz), 3.75 (1H, app octet, *J* = 6.7 Hz), 1.22 (6H, d, *J* = 6.7 Hz); δ_C($CDCl_3$, 75 MHz) 167.7 (s), 161.7 (s), 137.1 (s), 129.5 (d), 128.2 (d), 125.9 (s), 105.3 (d), 47.4 (d), 23.8 (q); *m/z* (EI) 365 (34%), 363.0643 ($M^{+\bullet}$, $C_{12}H_{13}ClN_2O_3S$ requires 363.0641, 100), 287 (18) and 285 (53).



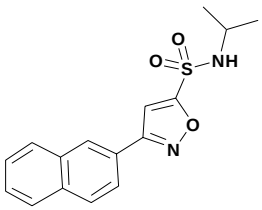
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid isopropylamide



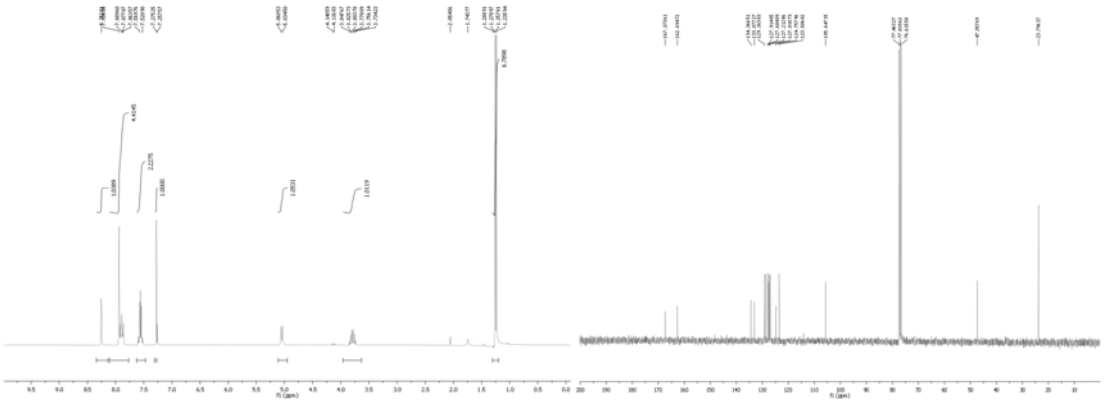
Yield: (126 mg, 0.41 mmol, 81%) as an off white solid. R_f 0.16 (20% EtOAc/petroleum ether); mp 150-152 °C; ν_{max}(film)/cm^{-1} 3337, 1606, 1560, 1353, 1114; δ_H($CDCl_3$, 300 MHz) 8.36 (2H, d, *J* = 8.8 Hz), 8.01 (2H, d, *J* = 8.8 Hz), 7.18 (1H, s), 4.85 (1H, d, *J* = 7.2 Hz), 3.78 (1H, app octet, *J* = 6.4 Hz), 1.24 (6H, d, *J* = 6.7 Hz); δ_C($CDCl_3$, 75 MHz) 169.8 (s), 167.0 (s), 149.4 (s), 144.7 (s), 127.9 (d), 124.5 (d), 105.4 (d), 47.5 (d), 23.9 (q); *m/z* (EI) 312.0654 ($M^{+\bullet}$, $C_{12}H_{13}N_3O_5S$ requires 312.0654, 100) and 147 (19).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid isopropylamide



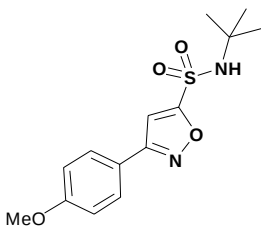
Yield: (129 mg, 0.41 mmol, 82%) as a white solid. R_f 0.20 (20% EtOAc/petroleum ether); mp 163-165 °C; ν_{max}(film)/cm^{-1} 3288, 1349, 1126; δ_H($CDCl_3$, 300 MHz) 8.25 (1H, s), 7.85-7.95 (4H, m), 7.52-7.60 (2H, m), 7.27 (1H, s), 5.04 (1H, d, *J* = 6.8 Hz), 3.79 (1H, app octet, *J* = 6.7 Hz), 1.24 (6H, d, *J* = 6.7 Hz); δ_C($CDCl_3$, 75 MHz) 167.4 (s), 162.7 (s), 134.4 (s), 133.1 (s), 129.2 (d), 128.6 (d), 127.9 (d), 127.6 (d), 127.2 (d), 127.0 (d), 124.8 (s), 105.7 (d), 47.4 (q), 23.8 (q); *m/z* (EI) 316.0880 ($M^{+\bullet}$, $C_{16}H_{16}N_2O_3S$ requires 316.0876, 70), 194 (100) and 127 (49)



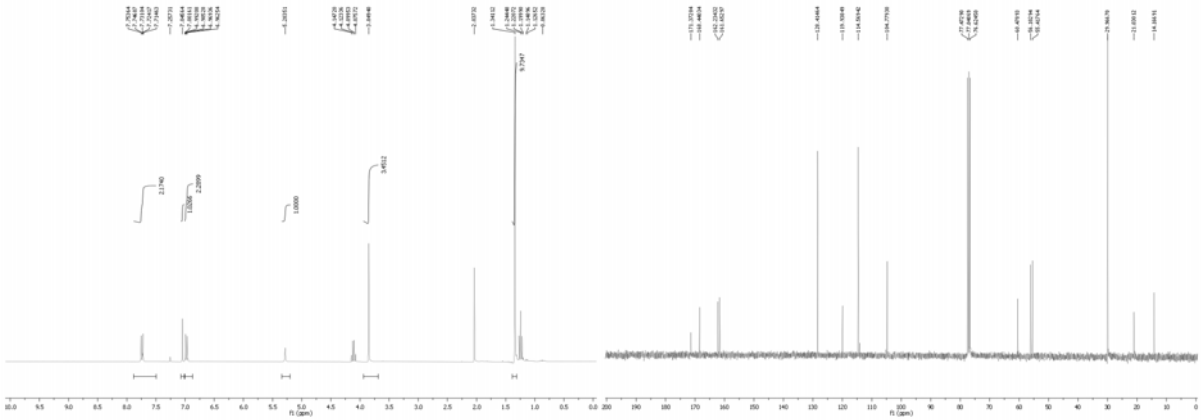
4.2.10 Preparation of isoxazole-5-sulfonic-acid-*tert*-butylsulfonamide

To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added *tert*-butylamine (3 eq.) and tetrabutylammonium chloride (2 eq.) followed by NEt_3 (1.5 eq.) and the mixture was stirred at 66 °C for until complete by tlc (1~3 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x3), sat. $NaHCO_3$ (x3) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (20% EtOAc/petroleum ether).

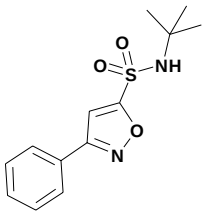
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid tert-butylamide



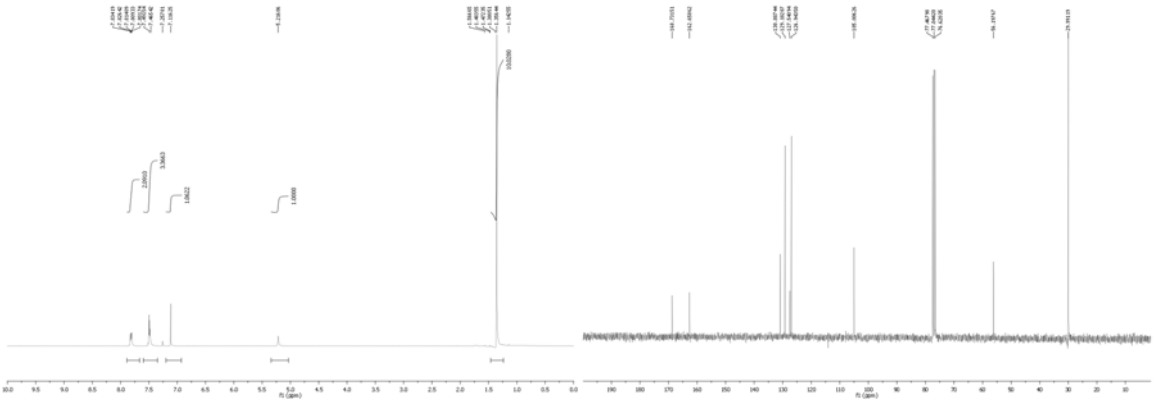
Yield: (89 mg, 0.28 mmol, 63%) as an off white solid. (Found: C, 54.2; H, 5.8; N, 9.0. $C_{14}H_{18}N_2O_4S$ requires C, 54.2; H, 5.9; N, 9.0%); R_f 0.18 (20% EtOAc/petroleum ether); mp 143-146 °C; ν_{max}(film)/cm^{-1} 3281, 1346, 1154; δ_H($CDCl_3$, 300 MHz) 7.73 (2H, d, J = 8.8 Hz), 7.04 (1H, s), 6.97 (2H, d, J = 8.8 Hz), 5.28 (1H, s), 3.85 (3H, s), 1.34 (9H, s); δ_C($CDCl_3$, 75 MHz) 168.4 (s), 162.2 (s), 161.7 (s), 128.4 (d), 119.9 (s), 114.6 (d), 104.8 (d), 56.1 (q), 55.4 (s), 29.8 (q); *m/z* (EI) 310.0985 ($M^{+\bullet}$, $C_{14}H_{18}N_2O_4S$ requires 310.0981, 47), 174 (100), 146 (60) and 92 (14).



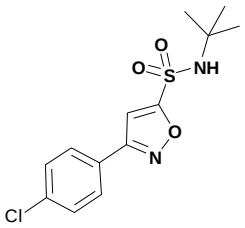
3-Phenyl-isoxazole-5-sulfonic acid tert-butylamide



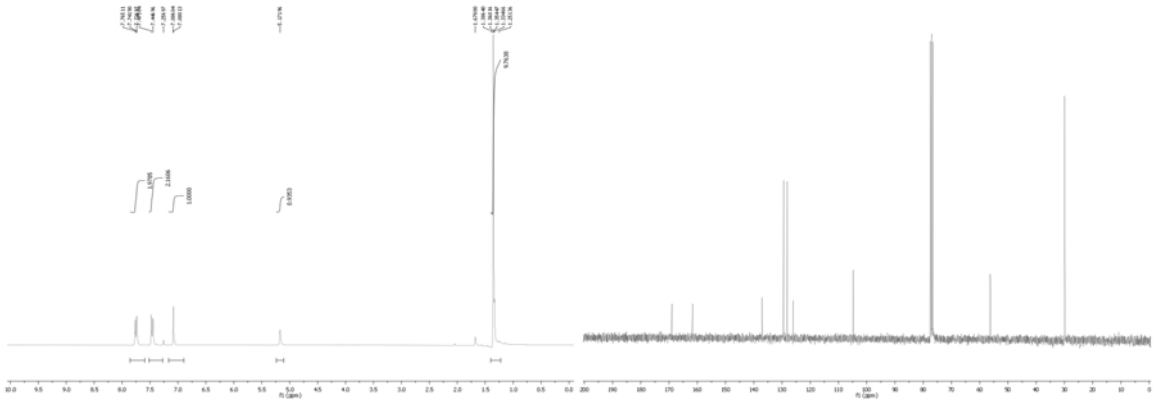
Yield: (69 mg, 0.25 mmol, 49%) as a white solid. R_f 0.19 (20% EtOAc/petroleum ether); mp 121-124 °C; ν_{max}(film)/cm^{-1} 3282, 3158, 1345, 1156; δ_H($CDCl_3$, 300 MHz) 7.82 (2H, m), 7.48 (3H, m), 7.11 (1H, s), 5.21 (1H, s), 1.35 (9H, s); δ_C($CDCl_3$, 75 MHz) 168.7 (s), 162.7 (s), 130.9 (d), 129.2 (d), 127.5 (s), 127.0 (d), 105.0 (d), 56.21 (s), 30.0 (q); *m/z* (EI) 280.0868 ($M^{+\bullet}$, $C_{13}H_{16}N_2O_3S$ requires 280.0876, 6%), 265 (58), 144 (100) and 116 (15).



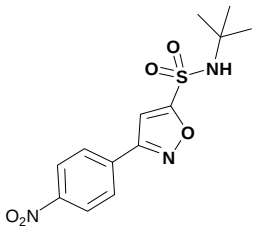
3-(4-chlorophenyl)-isoxazole-5-sulfonic-acid-*tert*-butylamide (91)



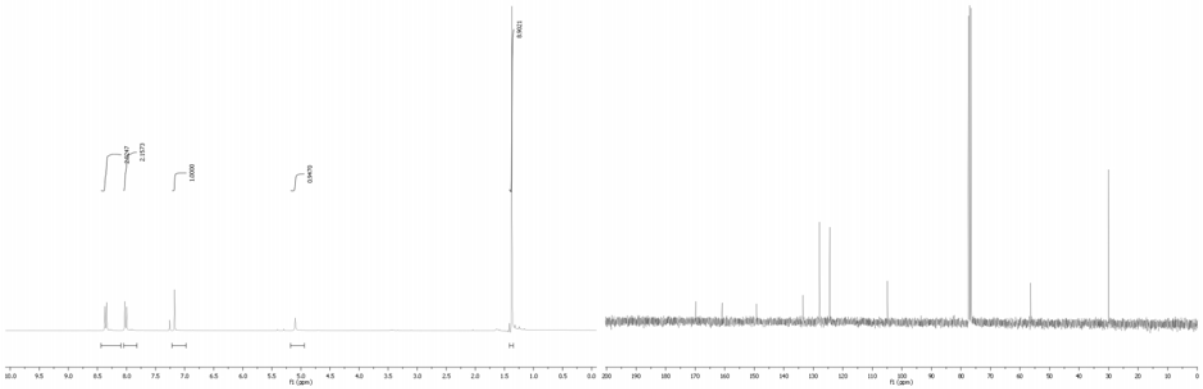
Yield: (74 mg, 0.23 mmol, 47%) as a white solid. R_f 0.26 (20% EtOAc/petroleum ether); mp 153-156 °C; ν_{max}(film)/cm^{-1} 3295, 3153, 1602, 1346, 1160; δ_H($CDCl_3$, 300 MHz) 7.75 (2H, d, *J* = 8.8 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.08 (1H, s), 5.17 (1H, s), 1.35 (9H, s); δ_C($CDCl_3$, 75 MHz) 169.1 (s), 161.7 (s), 137.1 (s), 129.5 (d), 128.2 (d), 126.0 (s), 104.8 (d), 56.3 (s), 30.0 (CH_3); *m/z* (EI) 316 (6%), 314.0480 ($M^{+\bullet}$, $C_{13}H_{15}ClN_2O_3S$ requires 314.0486, 15), 301 (18), 299 (54), 180 (36), 178 (100%)



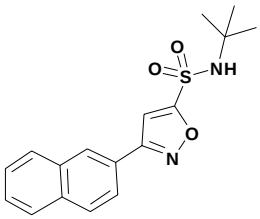
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid tert-butylamide



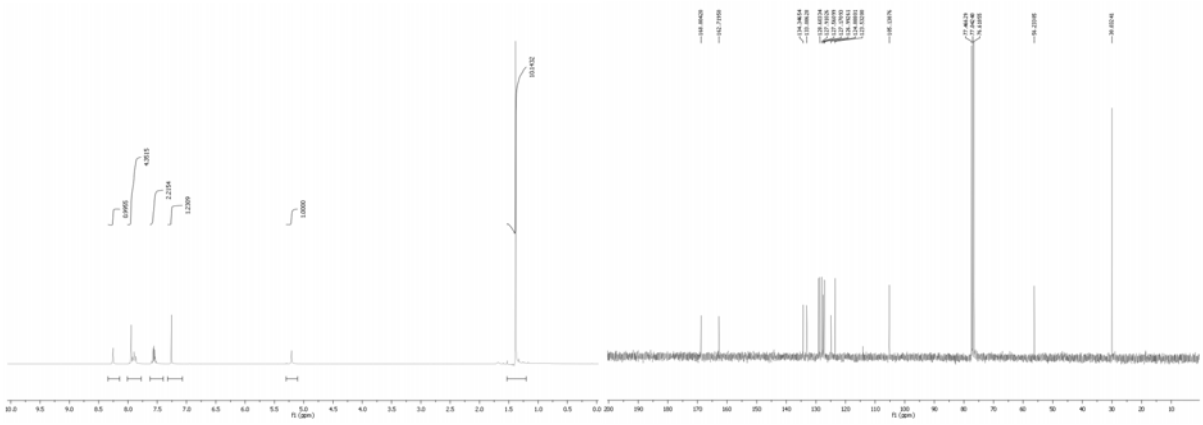
Yield: (60 mg, 0.18 mmol, 37%) as an off white solid. R_f 0.20 (20% EtOAc/petroleum ether); mp 167-168 °C; ν_{max}(film)/cm^{-1} 3203, 3148, 1343, 1157; δ_H($CDCl_3$, 300 MHz) 8.26 (2H, d, *J* = 8.8 Hz), 8.01 (2H, d, *J* = 8.8 Hz), 7.17 (1H, s), 5.09 (1H, s), 1.37 (9H, s); δ_C($CDCl_3$, 75 MHz) 169.9 (s), 160.9 (s), 149.2 (s), 133.5 (s), 127.9 (d), 124.4 (d), 104.9 (d), 56.5 (s), 30.0 (q); *m/z* (CI) 326.0813 ($M^{+\bullet}$, $C_{13}H_{16}N_3O_5S$ requires 326.0810, 7%), 310 (80), 189 (100), 143 (96) and 115 (40).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid tert-butylamide



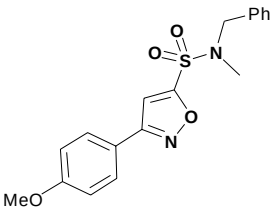
Yield: (70 mg, 0.21 mmol, 42%) and off white solid. R_f 0.30 (20% EtOAc/petroleum ether); mp 143-148 °C; ν_{max}(film)/cm^{-1} 3285, 1604, 1514, 1334, 1154; δ_H($CDCl_3$, 300 MHz) 8.25 (1H, s),, 7.86-7.96 (4H, m), 7.25 (2H, m), 7.25 (1H, s), 5.20 (1H, s), 1.38 (9H, s); δ_C($CDCl_3$, 75 MHz) 168.8 (s), 162.7 (s), 134.3 (s), 133.1 (s), 129.1 (d), 128.6 (d), 127.9 (d), 127.6 (d), 127.1 (d), 127.0 (d), 124.9 (s), 123.5 (d), 105.1 (d), 56.2 (s), 30.0 (q); LRMS (EI+) 330 (M+, 45), 194 (100), 166 (27), 127 (65); *m/z* (EI) 330.1026 ($M^{+\bullet}$, $C_{17}H_{18}N_2O_3S$ requires 330.1032, 100%).



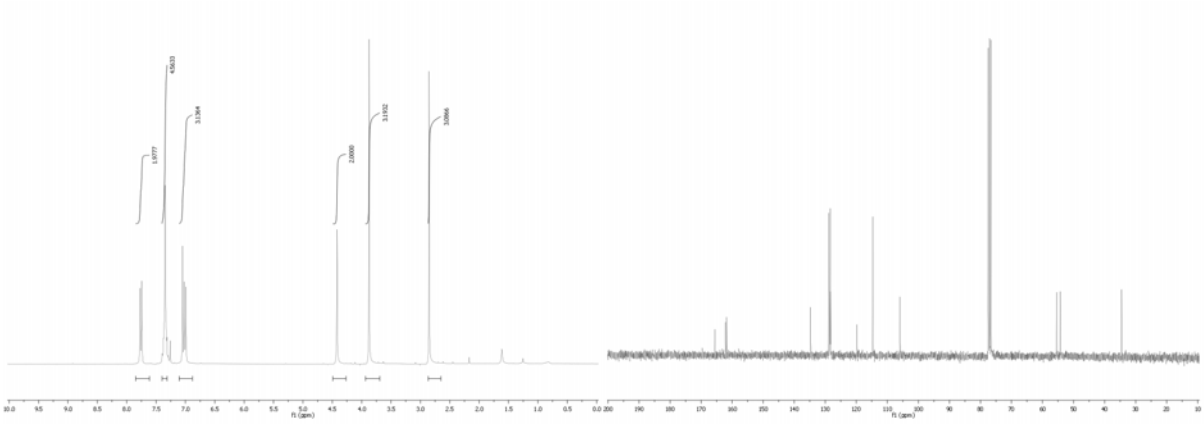
Preparation of sulfonic acid benzyl-methyl-amides

To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added *N*-methyl-*N*-benzylamine (3 eq.) and tetrabutylammonium chloride (2 eq.) followed by NEt_3 (1.5 eq.) and the mixture was stirred at 66 °C for until complete by tlc (16~24 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x3), sat. $NaHCO_3$ (x3) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (10% EtOAc/petroleum ether).

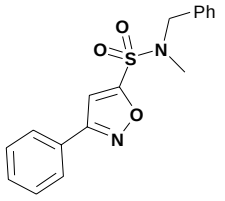
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid benzyl-methyl-amide



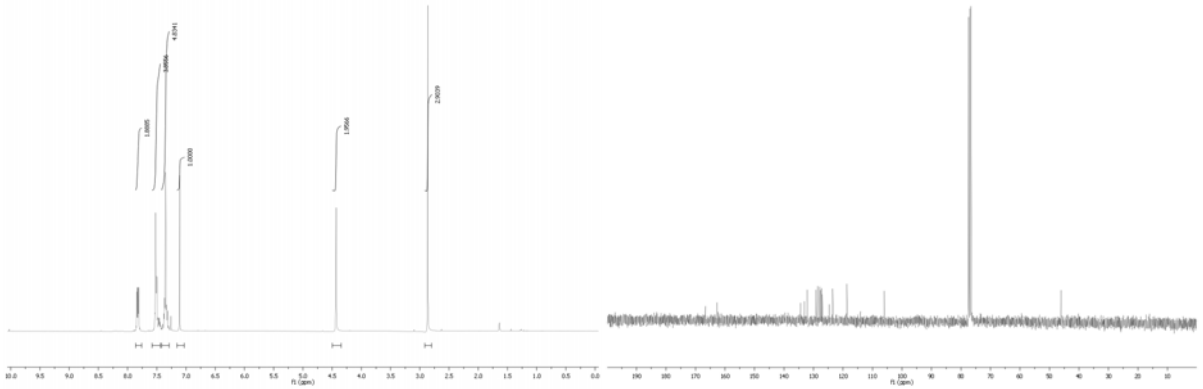
Yield: (151 mg, 0.42 mmol, 84%) as an off white solid. R_f 0.19 (20% EtOAc/petroleum ether); mp 98-100 °C; ν_{max}(film)/cm^{-1} 3132, 1610, 1589, 1495, 1350, 1163; δ_H($CDCl_3$, 300 MHz) 7.75 (2H, d, J = 8.6 Hz), 7.29-7.41 (5H, m), 7.04 (1H, s), 7.00 (2H, d, J = 8.6 Hz), 4.41 (2H, s), 3.87 (3H, s), 2.85 (3H, s); δ_C($CDCl_3$, 75 MHz) 165.6 (IsoxC), 162.1 (IsoxC), 161.7 (ArC), 134.7 (ArC), 128.9 (ArCH), 128.5 (ArCH), 128.4 (ArCH), 128.3 (ArCH), 119.8 (ArC), 114.6 (ArCH), 105.9 (IsoxCH), 55.5 (OCH_3), 54.3 (CH_2), 34.5 (NCH_3); *m/z* (EI) 358.0976 ($M^{+\bullet}$, $C_{18}H_{18}N_2O_4S$ requires 358.0982, 45%), 239 (100), 174 (65), 146 (70), 118 (37).



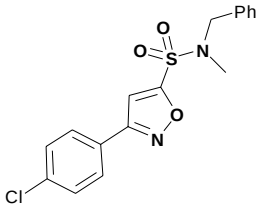
3-Phenyl-isoxazole-5-sulfonic acid benzyl-methyl-amide



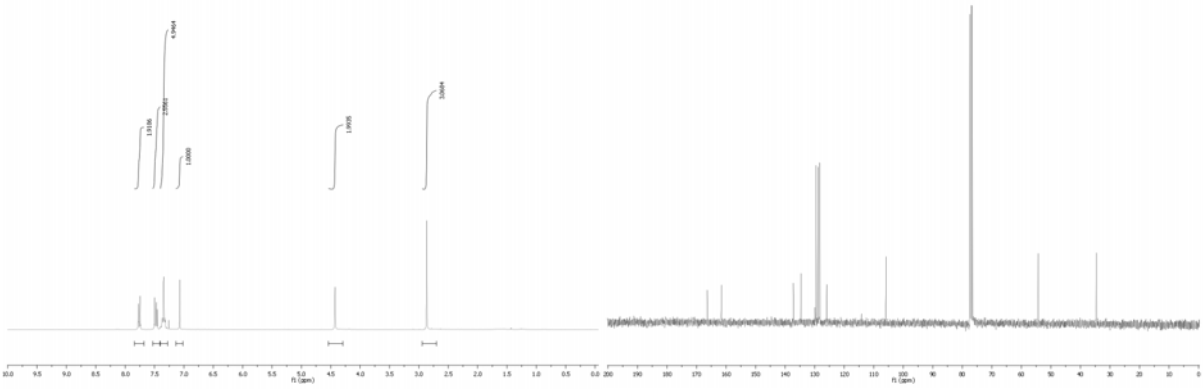
Yield: (113 mg, 0.34 mmol, 69%) as an off white solid. R_f 0.31 (20% EtOAc/petroleum ether); mp 86-89 °C; ν_{max}(film)/cm^{-1} 3153, 1350, 1153; δ_H($CDCl_3$, 300 MHz) 7.83 (1H, d, J = 2.4 Hz), 7.81 (1H, d, J = 2.7 Hz), 7.51-7.54 (3H, m), 7.49-7.51 (1H, m), 7.31-7.39 (4H, m), 7.11 (1H, s), 4.43 (2H, s), 2.86 (3H, s); δ_C($CDCl_3$, 75 MHz) 165.9 (s), 162.5 (s), 134.7 (s), 131.0 (d), 130.6 (s), 129.3 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.4 (d), 106.1 (d), 54.3 (t), 34.6 (q); *m/z* (EI) 328.0868 ($M^{+\bullet}$, $C_{17}H_{16}N_2O_3S$ requires 328.0876, 15%), 263 (26), 178 (100) and 119 (78).



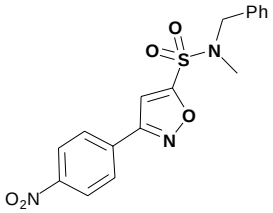
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid benzyl-methyl-amide



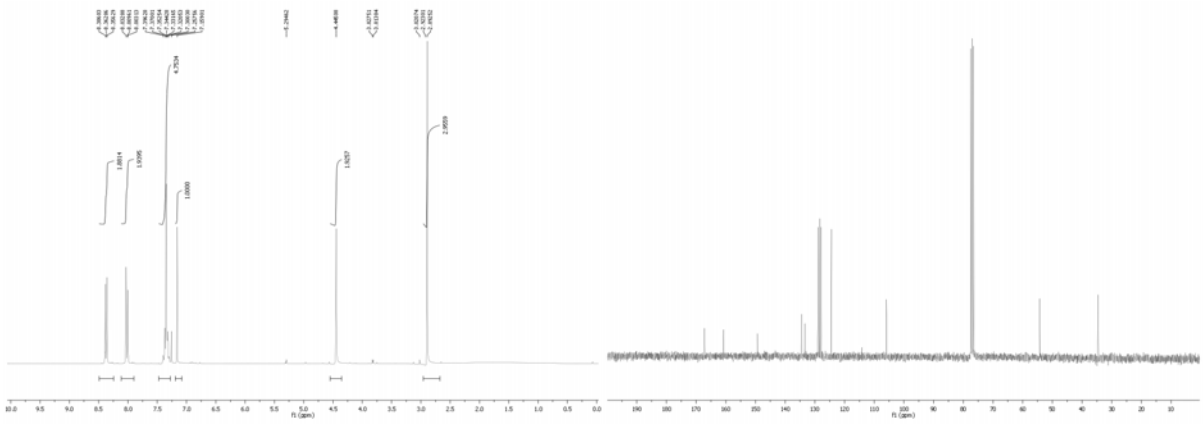
Yield: (107 mg, 0.29 mmol, 62%) as an off white solid. R_f 0.34 (20% EtOAc/petroleum ether); mp 124-127 °C; ν_{max}(film)/cm^{-1} 1600, 1504, 1361, 1161; δ_H($CDCl_3$, 300 MHz) 7.76 (2H, d, *J* = 8.6 Hz), 7.48 (2H, d, *J* = 8.6 Hz), 7.31-7.40 (5H, m), 7.07 (1H, s), 4.42 (2H, s), 2.86 (3H, s); δ_C($CDCl_3$, 75 MHz) 166.3 (s), 161.6 (s), 137.2 (s), 134.6 (s), 129.9 (d), 128.9 (d), 128.4 (d), 128.4 (d), 128.2 (d), 125.9 (s), 105.9 (d), 54.3 (t), 34.6 (q); *m/z* (EI) 364 (3%), 362.0491 ($M^{+\bullet}$, $C_{17}H_{15}ClN_2O_3S$ requires 362.0486, 8), 196 (5), 194 (19), 120 (38) and 118 (100).



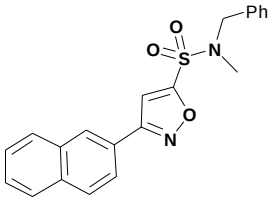
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid benzyl-methyl-amide



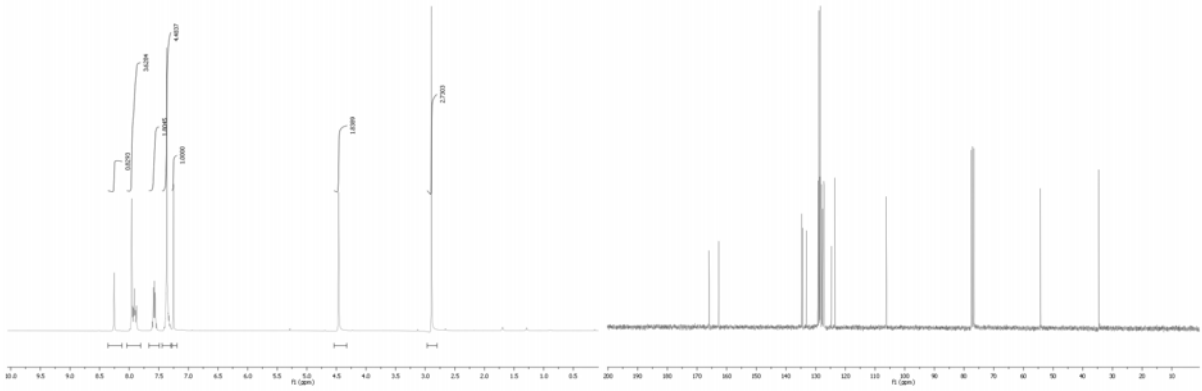
Yield: (42 mg, 0.11 mmol, 23%) as an off white solid. R_f 0.19 (20% EtOAc/petroleum ether); mp 163-167 °C; ν_{max}(film)/cm^{-1} 1609, 1560, 1495, 1361, 1164; δ_H($CDCl_3$, 300 MHz) 8.37 (2H, d, *J* = 9.0 Hz), 8.01 (2H, d, *J* = 9.0 Hz), 7.31-7.38 (5H, m), 7.15 (1H, s), 4.44 (2H, s), 2.88 (3H, s); δ_C($CDCl_3$, 75 MHz) 167.2 (s), 160.8 (s), 149.3 (s), 134.4 (s), 133.4 (s), 128.9 (d), 128.4 (d), 128.4 (d), 127.9 (d), 124.5 (d), 105.9 (d), 54.3 (t), 34.6 (q); *m/z* (EI) 373.0733 ($M^{+\bullet}$, $C_{17}H_{15}N_3O_5S$ requires 373.0727, 100), 343 (24), 189 (91) and 143 (39).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid benzyl-methyl-amide



Yield: (138 mg, 0.36 mmol, 73%) an off white solid. R_f 0.36 (20% EtOAc/petroleum ether); mp 105-110 °C; ν_{max}(film)/cm^{-1} 3156, 1605, 1515, 1362, 1165; δ_H($CDCl_3$, 300 MHz) 8.25 (1H, s), 7.87-7.97 (4H, m), 7.55-7.60 (2H, m), 7.32-7.39 (5H, m), 7.25 (1H, s), 4.46 (2H, s), 2.89 (3H, s); δ_C($CDCl_3$, 75 MHz) 166.0 (s), 162.6 (s), 134.7 (s), 134.4 (s), 133.1 (s), 129.2 (d), 128.9 (d), 128.6 (d), 128.4 (d), 128.4 (d), 128.0 (d), 127.7 (d), 127.3 (d), 127.1 (d), 124.8 (s), 123.5 (d), 106.3 (d), 54.3 (t), 34.6 (q); *m/z* (EI) 378.1043 ($M^{+\bullet}$, $C_{21}H_{18}N_2O_3S$ requires 378.1032, 100%), 259 (57), 194 (36), 119 (100).

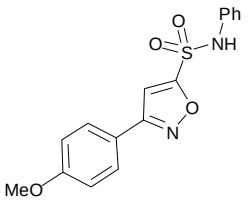


Preparation of sulfonic acid phenylamides

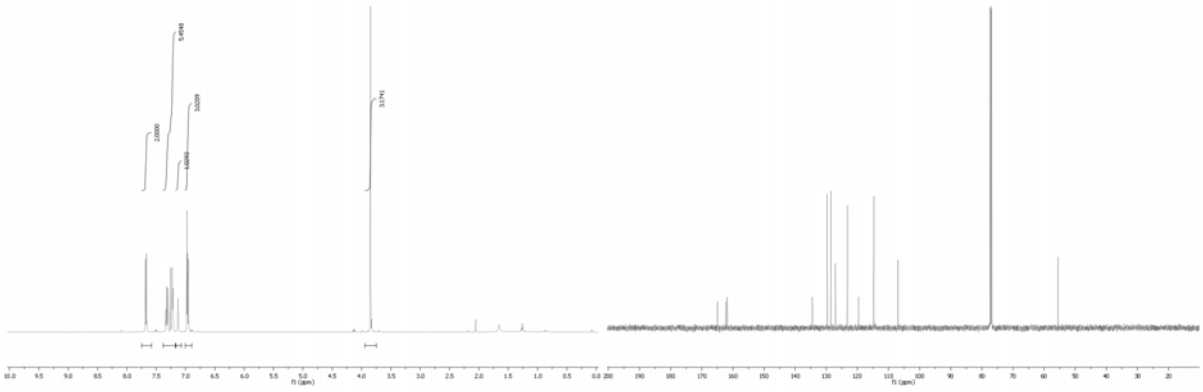
To a stirring solution of the pentafluorophenyl ester (1 eq.) in dry THF (~12 mL/mmol ester) was added analine (3 eq.) and tetrabutylammonium chloride (2 eq.) followed by NEt_3 (1.5

eq.) and the mixture was stirred at 66 °C for until complete by tlc (16~24 h). The mixture was diluted with CH_2Cl_2 and washed with 2M HCl (x3), sat. $NaHCO_3$ (x3) and water (x2), dried ($MgSO_4$) and solvent removed *in vacuo*. The crude residue was purified by flash chromatography (10% EtOAc/petroleum ether).

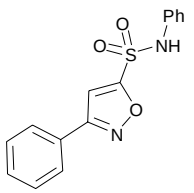
3-(4-Methoxy-phenyl)-isoxazole-5-sulfonic acid phenylamide



Yield: (153 mg, 0.46 mmol, 93%) as a white solid. R_f 0.13 (10% EtOAc/petroleum ether); mp 116-117 °C; ν_{max}(film)/cm^{-1} 3167, 2968, 1608, 1512, 1351, 1162; δ_H($CDCl_3$, 300 MHz) 7.65 (2H, d, *J* = 8.8 Hz), 7.32 (2H, app t, *J* = 7.88 Hz), 7.20-7.24 (3H, m), 7.12 (1H, s), 6.97 (1H, s), 6.95 (2H, d, *J* = 8.8 Hz); δ_C($CDCl_3$, 75 MHz) 165.0 (s), 162.3 (s), 161.8 (s), 134.5 (s), 129.7 (d), 128.5 (d), 127.0 (d), 123.2 (d), 119.6 (s), 114.7 (d), 107.0 (d), 55.5 (q); *m/z* (EI) 330.0653 ($M^{+\bullet}$, $C_{16}H_{14}N_2O_4S$ requires 330.0668, 14%), 174 (63) and 146 (100).

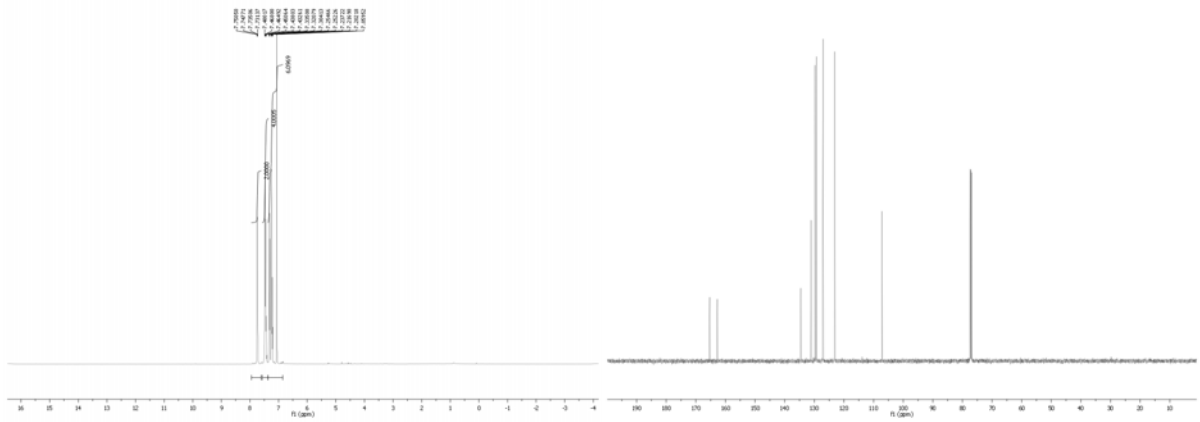


3-Phenyl-isoxazole-5-sulfonic acid phenylamide

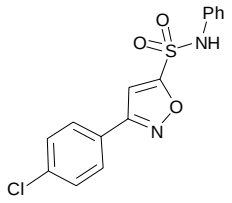


Yield: (102 mg, 0.34 mmol, 68%) as an off white solid. R_f 0.13 (10% EtOAc/petroleum ether); mp 114-116 °C; ν_{max}(film)/cm^{-1} 3290, 3067, 1599, 1498, 1353, 1159; δ_H($CDCl_3$, 300 MHz) 7.74 (2H, dd, *J* = 8.2, 1.4 Hz), 7.46 (3H, m), 7.32 (2H, dd, *J* = 7.2, 1.6 Hz, ArH), 7.20-

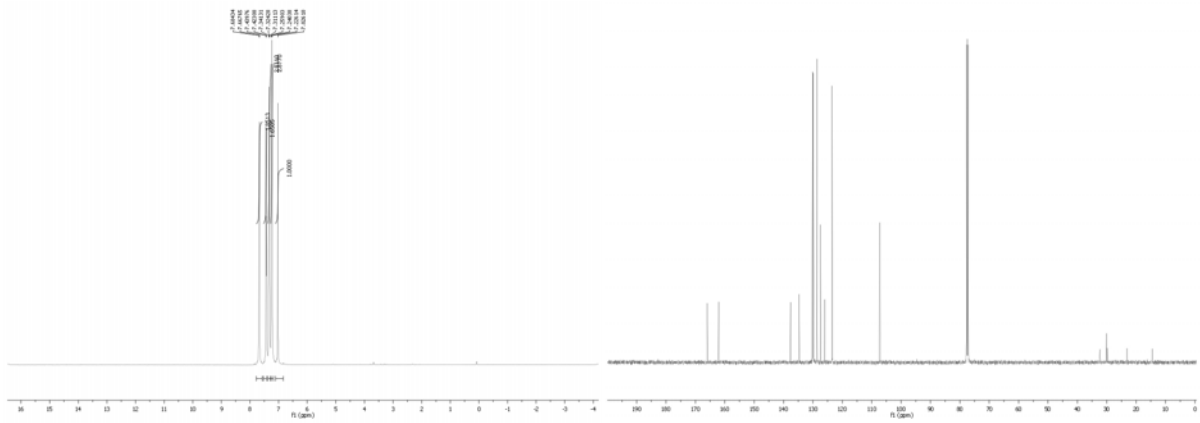
7.25 (3H, m), 7.04 (1H, s); δ_C($CDCl_3$, 75 MHz) 165.3 (s), 162.7 (s), 134.5 (s), 131.1 (d), 129.8 (d), 129.3 (d), 127.2 (s), 127.0 (d), 127.0 (d), 123.2 (d), 107.2 (d); *m/z* (EI) 300.0574 ($M^{+\bullet}$, $C_{15}H_{12}N_2O_3S$ requires 300.0563, 13%), 236 (54), 144 (87), 116 (100) and 105 (63).



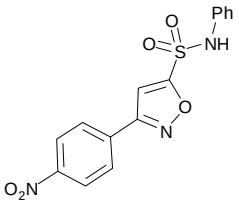
3-(4-Chloro-phenyl)-isoxazole-5-sulfonic acid phenylamide



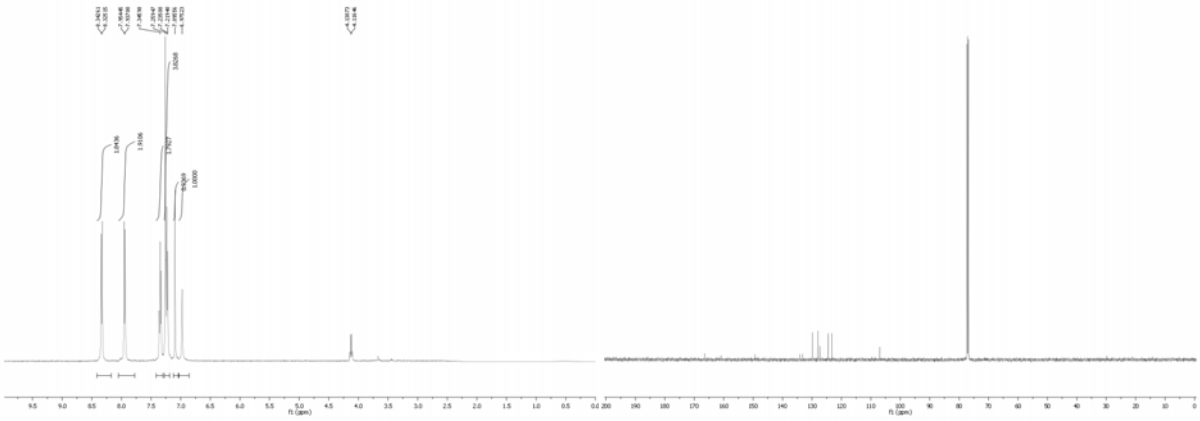
Yield: (114 mg, 0.34 mmol, 68%) as an off white solid. R_f 0.10 (20% EtOAc/petroleum ether); mp 153-155 °C; ν_{max}(film)/cm^{-1} 3238, 3152, 1601m, 1492, 1351, 1169; δ_H($CDCl_3$, 300 MHz) 7.66 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz), 7.32 (2H, app t, *J* = 7.2 Hz), 7.20-7.25 (3H, m), 7.10 (1H, s), 7.01 (1H, s); δ_C($CDCl_3$, 75 MHz) 165.73 (s), 161.67 (s), 137.24 (s), 134.05 (s), 129.71 (d), 129.52 (d), 128.19 (d), 127.10 (d), 125.65 (s), 123.15 (d), 106.87 (d); *m/z* (EI) 336 (9%), 334.0176 ($M^{+\bullet}$, $C_{15}H_{11}ClN_2O_3S$ requires 334.0173, 26), 272 (24), 270 (63), 152 (35) and 150 (100).



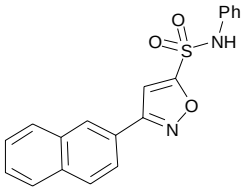
3-(4-Nitro-phenyl)-isoxazole-5-sulfonic acid phenylamide



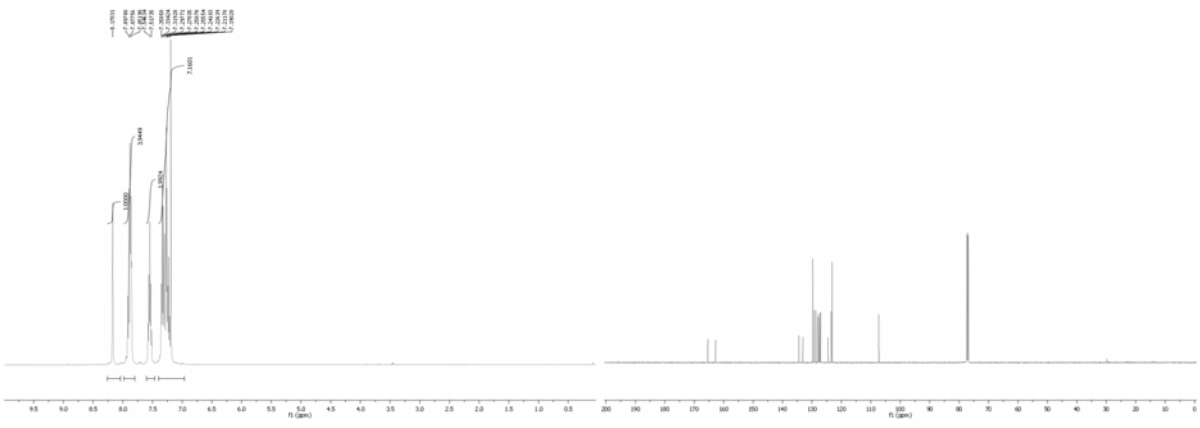
Yield: (76 mg, 0.22 mmol, 44%) as an off white solid. R_f 0.09 (10% EtOAc/petroleum ether); mp 168-171 °C; ν_{max}(film)/cm^{-1} 3283, 3103, 1611, 1562, 1491, 1355, 1338s, 1174; δ_H($CDCl_3$, 300 MHz) 8.33 (2H, d, *J* = 8.8 Hz), 7.94 (2H, d, *J* = 8.8 Hz), 7.34 (2H, app t, *J* = 7.9 Hz), 7.20-7.25 (3H, m), 7.09 (1H, m), 6.97 (1H, s); δ_C($CDCl_3$, 75 MHz) 166.5 (s), 160.9 (s), 149.3 (s), 134.1 (s), 133.2 (s), 129.8 (d), 128.0 (d), 127.3 (d), 124.5 (d), 123.3 (d), 107.0 (d); *m/z* (EI) 345.0414 ($M^{+\bullet}$, $C_{15}H_{11}N_3O_5S$ requires 345.041, 100), 281 (62), 189 (71) and 163 (22).



3-Naphthalen-2-yl-isoxazole-5-sulfonic acid phenylamide



Yield: (80 mg, 0.25 mmol, 46%) as and off white solid. R_f 0.08 (10% EtOAc/petroleum ether); mp 139-141 °C; ν_{max}(film)/cm^{-1} 3220, 3051, 1595, 1494, 1352, 1170; δ_H($CDCl_3$, 300 MHz) 8.17 (1H, s), 7.89 (1H, t, *J* = 8.5 Hz), 7.84-7.87 (3H, m), 7.54 (2H, app. qd, *J* = 7.9, 1.7 Hz), 7.33 (2H, t, *J* = 7.3 Hz), 7.20-7.25 (3H, m), 7.19 (1H, s); δ_C($CDCl_3$, 75 MHz) 165.4 (s), 162.8 (s), 134.5 (s), 134.4 (s), 133.1 (s), 129.8 (d), 129.2 (d), 128.7 (d), 128.0 (d), 127.7 (d), 127.3 (d), 127.1 (d), 127.1 (d), 124.5 (s), 123.5 (d), 123.2 (d), 107.3 (d); *m/z* (EI) 350.0707 ($M^{+\bullet}$, $C_{19}H_{14}N_2O_3S$ requires 350.0719, 30%), 286 (23), 194 (100), 166 (61) and 127 (65).



References

1. K. C. Liu, B. R. Shelton and R. K. Howe, *J. Org. Chem.*, 1980, **45**, 3916-3918.
2. R. J. Fitzmaurice, J. M. Ahern and S. Caddick, *Org. Biomol. Chem.*, 2009, **7**, 235-237.