Electronic supplementary information for

Synthesis of aminopyrazoles from sydnones and ynamides

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General Information

All reactions were conducted in flame-dried glassware under ambient conditions unless otherwise stated. THF and PhMe were dried before use over an alumina column. CH_2Cl_2 was distilled from calcium hydride. All commercially available solvents and reagents were used as supplied or purified using standard laboratory techniques according to methods described by Perrin and Armarego.[1]

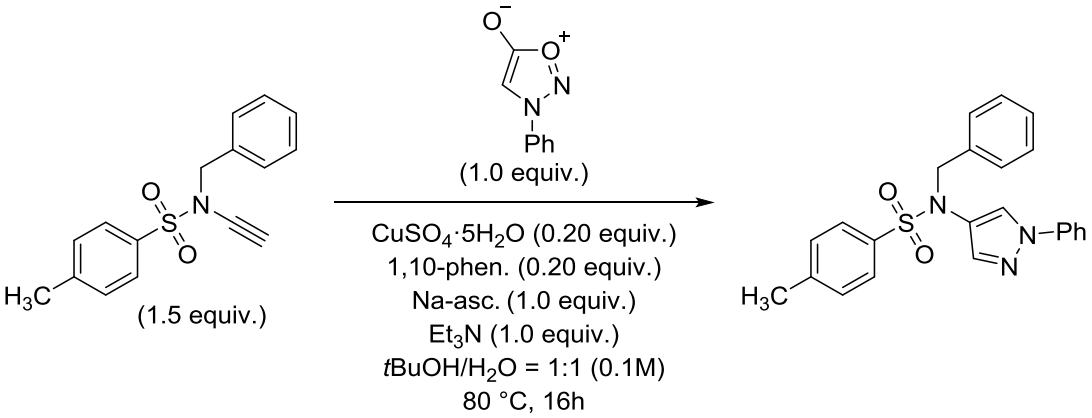
Thin layer chromatography was performed on aluminium-backed plates pre-coated with silica (Merck silica Kieselgel 60 F_{254}), which were developed using standard visualising agents: ultraviolet light, potassium permanganate or *para*-anisaldehyde. Flash chromatography was performed on silica gel (60 Å, mesh 40-63 µm). The solvent system used was graduated from 100% petroleum ether, increasing polarity towards the solvent mixture stated in the procedure. Melting points were obtained using a Gallenkamp apparatus, performed on recrystallised solids and are uncorrected. Optical rotation values were recorded on a Perkin Elmer 241 automatic polarimeter at 589 nm (Na-D line) with a path length of 1 dm, and are given in 10^{-1} deg cm^{-2} g^{-1} with concentrations (*c*) quoted in g 100 mL^{-1}.

^{1}H spectra were recorded on a Bruker AVII-500 (500 MHz), Bruker AVIII HD-400 (400 MHz), Bruker AVI-400 (400 MHz), Bruker AMX-400 (400 MHz), DPX-400 (400 MHz) or *Bruker* Avance 300 (300 MHz), *Bruker* Avance 400 (400 MHz) or a *Bruker* Avance DRX 500 (500 MHz) . Proton magnetic resonance chemical shifts are reported from tetramethylsilane with the residual protic solvent resonance as the internal standard ($CHCl_3$: δ = 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, br = broad, m = multiplet). ^{13}C NMR spectra were recorded on a Bruker AVII-500 (126 MHz), Bruker AVIII HD-400 (101 MHz), Bruker AVI-400 (101 MHz), Bruker AMX-400 (101 MHz), DPX-400 (101 MHz) or *Bruker* Avance 300 (75 MHz), *Bruker* Avance 400 (100 MHz) or a *Bruker* Avance DRX 500 (125 MHz). Carbon magnetic resonance chemical shifts are reported from tetramethylsilane with the solvent as the internal reference ($CHCl_3$: δ = 77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker AMX-400 (376

MHz) or Bruker AVIII HD-400 (376 MHz), and the chemical shifts are reported from trichlorofluoromethane. ^{11}B NMR spectra were recorded on a Bruker AVIII HD-400 (128 MHz), and the chemical shifts are reported from $BF_3 \cdot Et_2O$ as the internal standard (δ = 0.0 ppm). All chemical shifts are reported in ppm and the coupling constants (*J*) are quoted in Hz.

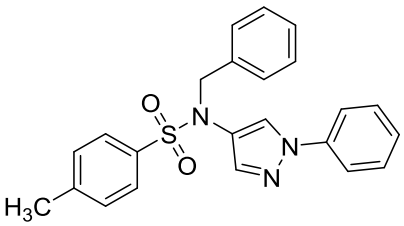
Infrared spectra were recorded on a Perkin-Elmer Paragon 100 FTIR spectrometer or Bruker IFS 88 using ATR (Attenuated Total Reflection). Spectra were analysed as thin films on a KBr disc or neat, and the most structurally relevant bands are quoted in cm^{-1}. Bands are characterised as broad (br), strong (s), medium (m) or weak (w). Mass spectra were recorded on a Finnigan MAT 95 using EI-MS (Electron ionization mass spectrometry) at 70 eV or FAB-MS (Fast Atom Bombardment Mass Spectroscopy) with 3-NBA as matrix or were performed on a MicroMass LCT operating in Electrospray mode (TOF ES+) or a MicroMass Prospec operating in FAB (FAB+), EI (EI+) or CI (CI+) modes. Ratios of pyrazole products were determined using 2D-NMR spectroscopic techniques (HSQC and HMBC).

General procedure GP1: 4-aminopyrazole synthesis using copper sulfate



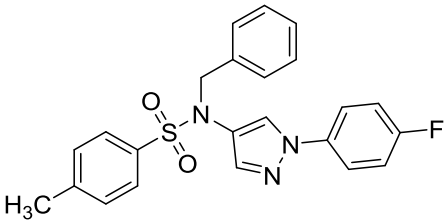
A 10 mL closed vial was charged with the respective sydnone (1.00 equiv., 0.200 mmol), *N*-benzyl-*N*-ethynyl-4-methylbenzenesulfonamide (86.0 mg, 1.50 equiv. 0.300 mmol), triethylamine (28 µl, 1.00 equiv., 0.200 mmol), sodium ascorbate (79.0 mg, 2.00 equiv., 0.400 mmol), 1,10-phenanthroline (7.2 mg, 0.20 equiv., 0.040 mmol) and copper(II) sulfate pentahydrate (10.0 mg, 0.200 equiv., 0.040 mmol) in a mixture of water (1.0 mL) and *t*BuOH (1.0 mL) to give an orange solution that was stirred at 80 °C for 16h. After TLC (*c*Hex/EtOAc mixtures) showed full conversion of the sydnone the reaction was quenched with a 0.05M aqueous solution of EDTA and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with water (1 × 10 mL), brine (1 × 10 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude products were purified by recrystallization from MeOH or by flash column chromatography.

***N*-benzyl-4-methyl-*N*-(1-phenyl-1H-pyrazol-4-yl)benzenesulfonamide (4a)**



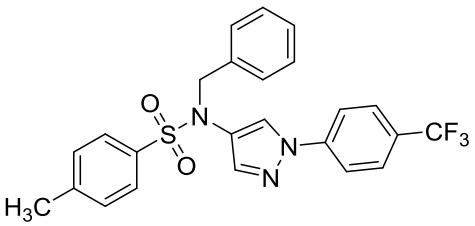
This compound was prepared according to general procedure GP1 using 3-phenyl-3H-1,2,3-oxadiazol-1-ium-5-olate (32.4 mg, 0.20 mmol) and was isolated after recrystallization from MeOH as colorless needles (52.0 mg, 0.129 mmol, 64%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.58 - 7.63 (m, 2H), 7.51 - 7.55 (m, 2H), 7.35 - 7.41 (m, 2H), 7.21 - 7.32 (m, 9H), 4.66 (s, 2H), 2.42 (s, 3H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 143.8 (C_q), 139.6 (C_q), 137.2 (s), 135.7 (C_q), 135.0 (C_q), 129.6 (+, 2 × CH_{Ar}), 129.3 (+, 2 × CH_{Ar}), 128.5 (+, 2 × CH_{Ar}), 128.2 (+, 2 × CH_{Ar}), 127.8 (+, CH_{Ar}), 127.5 (+, 2 × CH_{Ar}), 126.7 (+, CH_{Ar}), 124.5 (+, N*C*H), 123.6 (C_q), 118.7 (+, N*C*H), 54.7 (–, CH_2), 21.5 (+, CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 1597 (w), 1495 (m), 1453 (w), 1391 (w), 1364 (w), 1343 (m), 1200 (w), 1089 (m), 1050 (m), 978 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 403 (44) $[M]^+$, 316 (11), 248 (100). – **HRMS** (EI, $C_{23}H_{21}O_2N_3{}^{32}S$): calc. 403.1350; found 403.1349.

***N*-benzyl-*N*-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)-4-methylbenzenesulfonamide (5)**



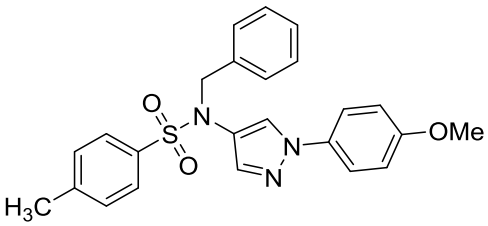
This compound was prepared according to general procedure GP1 using 3-(4-fluorophenyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (36.0 mg, 0.200 mmol) and was isolated after recrystallization from MeOH as colorless crystals (45.0 mg, 0.107 mmol, 53%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.68 (s, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.44 - 7.51 (m, 2H), 7.28 (s, 1H), 7.19 - 7.25 (m, 7H), 7.03 - 7.10 (m, 2H), 4.63 (s, 2H), 2.41 (s, 3H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 161.2 (d, C_{Ar}-F, *J* = 246 Hz), 143.9 (C_q), 137.1 (+, CH_{Ar}), 135.7 (C_q), 135.0 (C_q), 129.7 (+, CH_{Ar}), 128.5 (+, CH_{Ar}), 128.3 (+, CH_{Ar}), 127.9 (+, CH_{Ar}), 127.5 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 123.7 (C_q), 120.6 (+, CH_{Ar}), 120.5 (+, CH_{Ar}), 116.3 (+, CH_{Ar}), 116.1 (+, CH_{Ar}), 54.7 (−, CH_2), 21.6 (+, CH_3) ppm. – **IR** (ATR): ṽ = 3110 (vw), 1514 (m), 1454 (w), 1406 (w), 1364 (w), 1233 (w), 1162 (w), 1090 (m), 1027 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 422 (32) $[M+H]^+$, 307 (15), 266 (22), 154 (100). – **HRMS** (EI, $C_{23}H_{20}N_3O_2F^{32}S$): calc. 421.1255; found 421.1256.

***N*-benzyl-4-methyl-*N*-(1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-4-yl)benzenesulfonamide (6)**



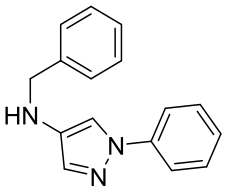
This compound was prepared according to general procedure GP1 using 3-(4-(trifluoromethyl)phenyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (46.0 mg, 0.200 mmol) and was isolated after flash column chromatography (*c*Hex/EtOAc = 9:1) as colorless crystals (54.0 mg, 0.115 mmol, 57%). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.84 (s, 1H), 7.67 (s, 4H), 7.62 (d, *J* = 8.1 Hz, 3H), 7.27 - 7.38 (m, 7H), 4.67 (s, 2H), 2.44 (s, 3H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 144.1 (C_q), 142.0 (C_q), 137.9 (+, CH_{Ar}), 135.5 (C_q), 135.0 (C_q), 129.7 (+, 2 × CH_{Ar}), 128.6 (+, CH_{Ar}), 128.6 (+, CH_{Ar}), 128.2 (+, 2 × CH_{Ar}), 128.0 (+, 2 × CH_{Ar}), 127.9 (+, CH_{Ar}), 127.7 (+, CH_{Ar}), 127.5 (+, 2 × CH_{Ar}), 126.7 (+, CH_{Ar}), 126.7 (+, q, CH_{Ar}, *J* = 4.2 Hz), 124.5 (C_q), 124.3 (+, CH_{Ar}), 123.8 (C_q, q, CF_3, *J* =272.2 Hz), 118.4 (+, NCH), 54.5 (−, CH_2), 21.6 (+, CH_3) ppm. – **^{19}F-NMR** (377 MHz, $CDCl_3$): δ −66.64 (s, 3F) ppm. – **IR** (ATR): ṽ = 3330 (vw), 1702 (vw), 1614 (w), 1523 (w), 1494 (w), 1440 (w), 1353 (w), 1321 (m), 1163 (m), 1110 (m), 1069 (w), 1020 (w), 943 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 471 (11) $[M]^+$, 315 (55), 238 (100). – **HRMS** (EI, $C_{24}H_{20}N_3O_2F_3{}^{32}S$): calc. 471.1223; found 471.1222.

***N*-benzyl-*N*-(1-(4-methoxyphenyl)-1H-pyrazol-4-yl)-4-methylbenzenesulfonamide (7)**



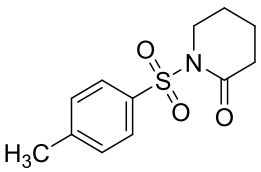
This compound was prepared according to general procedure GP1 using 3-(4-methoxybenzyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (38.0 mg, 0.200 mmol) and was isolated after recrystallization from MeOH as colorless crystals (49.0 mg, 0.113 mmol, 57%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.21 - 7.32 (m, 9H), 6.92 (m, 2H), 4.65 (s, 2H), 3.82 (s, 3H), 2.44 (s, 3H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 158.4 (C_q), 143.8 (C_q), 135.8 (C_q), 135.1 (C_q), 129.7 (+, CH_{Ar}), 128.5 (+, CH_{Ar}), 128.3 (+, CH_{Ar}), 127.8 (+, CH_{Ar}), 127.6 (+, CH_{Ar}), 120.4 (+, CH_{Ar}), 114.5 (+, CH_{Ar}), 55.6 (+, CH_3), 54.8 (–, CH_2), 21.6 (+, CH_3) ppm. – **IR** (ATR): ṽ = 2922 (vw), 1748 (w), 1700 (w), 1595 (w), 1514 (w), 1494 (w), 1452 (w) cm^{-1}. – **MS** (FAB), *m/z* (%): 434 (100) $[M+H]^+$, 278 (60), 153 (97). – **HRMS** (FAB, $C_{24}H_{24}N_3O_3{}^{32}S$): calc. 434.1533; found 434.1535.

***N*-benzyl-1-phenyl-1H-pyrazol-4-amine (8)**



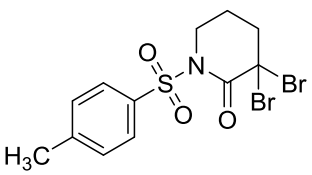
A 10 mL closed vial was charged with *N*-benzyl-4-methyl-*N*-(1-phenyl-1H-pyrazol-4-yl)benzenesulfonamide (30.0 mg, 0.074 mmol, 1.00 equiv.) in dry THF (1.0 mL) and stirred at 0 °C for 5 min before potassium diphenylphosphide (0.30 mL, 0.149 mmol, 2.00 equiv.) was added slowly. The reaction mixture was stirred at 0 °C for 2h and subsequently diluted with 1M HCl and stirred for 5 min. The suspension was quenched with sat. aq. $NaHCO_3$ and the aqueous layer extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Preparative TLC (*c*Hex/EtOAc/Et_3N = 90:5:1) yielded the pure product as white solid (9.0 mg, 0.036 mmol, 49%). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 7.7 Hz, 2H), 7.27 - 7.45 (m, 9H), 7.22 (m, 1H), 4.25 (s, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 140.3 (C_q), 131.9 (+, CH_{Ar}), 129.3 (+, CH_{Ar}), 128.7 (+, 2 × CH_{Ar}), 128.0 (+, 2 × CH_{Ar}), 127.6 (+, CH_{Ar}), 125.7 (+, CH_{Ar}), 118.2 (+, 2 × CH_{Ar}), 52.2 (–, CH_2) ppm. Two quaternary signals are missing due to low sensitivity. – **IR** (ATR): ṽ = 3307 (w), 3057 (vw), 2920 (w), 2848 (w), 1662 (w), 1594 (m), 1493 (m), 1393 (m), 1259 (w), 1170 (w), 1101 (w), 1073 (w), 1045 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 249.2 (100) $[M]^+$, 158.1 (45), 104.1 (71). – **HRMS** (EI, $C_{16}H_{15}N_3$): calc. 249.1260; found 249.1259.

1-Tosylpiperidin-2-one (9)



A 250 mL round-bottomed flask was charged with piperidin-2-one (6.00 g, 60.5 mmol, 1.00 equiv.) in dry THF (100 mL) to give a yellow solution. The reaction mixture was cooled to −78 °C and stirred for 10 min before *n*-butyllithium (29.1 mL, 2.5M in hexanes, 72.6 mmol, 1.20 equiv.) was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 1h before a solution of 4-methylbenzenesulfonyl chloride (12.69 g, 66.6 mmol, 1.10 equiv.) in dry THF (50 mL) was added via dropping funnel over 10 min. The reaction mixture was allowed to slowly reach room temperature over 1.5h and subsequently transferred to a separatory funnel and diluted with 100 mL of sat. aq. NH_4Cl solution and 50 mL of water. The aqueous layer was separated and extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with 200 mL of sat. aq. $NaHCO_3$ solution, dried over $MgSO_4$, filtered, and concentrated to give a white solid. Trituration with Et_2O (2 × 50 mL) afforded a white solid which was collected by removal of liquid (9.30 g, 36.7 mmol, 61%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.85 - 7.92 (m, 2H), 7.29 (m, 2H), 3.89 (t, *J* = 6.1 Hz, 2H), 2.40 (s, 3H), 2.37 - 2.40 (m, 2H), 1.84 - 1.93 (m, 2H), 1.71 - 1.80 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 170.1 (C_q), 144.6 (C_q), 136.0 (C_q), 129.2 (+, 2 × CH_{Ar}), 128.5 (+, 2 × CH_{Ar}), 46.8 (−, CH_2), 34.0 (−, CH_2), 23.2 (−, CH_2), 21.5 (+, CH_3), 20.3 (−, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2951 (vw), 1681 (m), 1594 (w), 1445 (w), 1382 (w), 1346 (m), 1280 (w), 1260 (w), 1151 (m), 1117 (m), 1088 (m), 1040 (m) cm^{-1}. – **MS** (FAB), *m/z* (%): 254 (100) $[M]^+$, 154.9 (14). – **HRMS** (FAB, $C_{12}H_{16}NO_3F_3{}^{32}S$): calc. 254.0845; found 254. 0847.

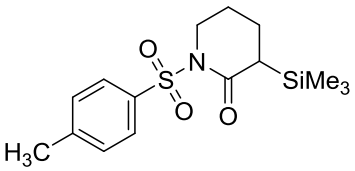
3,3-Dibromo-1-tosylpiperidin-2-one (S6)



A 250 mL three-neck round-bottomed flask was charged with 1-tosylpiperidin-2-one (3.00 g, 11.84 mmol, 1.00 equiv.) in dry THF (100 mL) and cooled to −78 °C. A solution of KHMDS (59.2 mL, 0.5M in toluene, 29.6 mmol, 2.50 equiv.) was added dropwise with the aid of a dropping funnel. Bromine (2.2 mL, 42.6 mmol, 3.60 equiv.) was added dropwise and the reaction was stirred for 25 min at −78 °C. The yellow reaction mixture was transferred to a separatory funnel and washed with sat. aq. sodium thiosulfate solution. The aqueous layer was extracted with Et_2O (2 × 150 mL) and the combined organic layers were washed with sat. aq. NaCl (1 × 50 mL) and subsequently dried over $MgSO_4$, filtered and concentrated under reduced pressure. Trituration with Et_2O (6 × 50 mL) afforded a white solid (2.99 g, 7.27 mmol, 61%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.88 - 7.95 (m, 2H), 7.35 – 7.33 (m, 2H), 4.04 (t, *J* = 6.2 Hz, 2H), 2.87 - 2.95 (m, 2H), 2.44 (s, 3H), 2.11 - 2.19 (m, 2H)

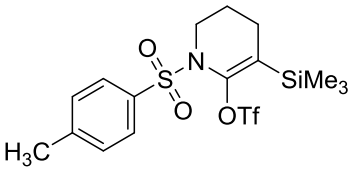
ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 162.9 (C_q), 145.4 (C_q), 134.3 (C_q), 129.5 (+, 2 × CH_{Ar}), 129.0 (+, 2 × CH_{Ar}), 58.9 (C_q), 46.7 (–, CH_2), 45.6 (–, CH_2), 21.9 (–, CH_2), 21.7 (+, CH_3) ppm. – **IR** (ATR): ṽ = 2914 (vw), 1699 (m), 1594 (w), 1483 (w), 1433 (w), 1360 (w), 1274 (w), 1163 (m), 1110 (m), 1085 (w) cm^{-1}. – **MS** (FAB), *m/z* (%): 410.0/411.9/413.9 (40/85/42) $[M+H]^+$, 154 (100). – **HRMS** (FAB, $C_{12}H_{14}NO_3{}^{79}Br^{81}Br^{32}S$): calc. 411.9035; found 411.9037.

1-Tosyl-3-(trimethylsilyl)piperidin-2-one (S7)



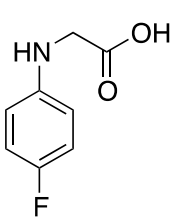
A 250 mL 3-neck round-bottomed flask was charged with 3,3-dibromo-1-tosylpiperidin-2-one (2.95 g, 7.18 mmol, 1.00 equiv.) and chlorotrimethylsilane (1.82 mL, 14.4 mmol, 2.00 equiv.) in dry THF (120 mL) and the reaction mixture was cooled to −78 °C. A solution of *n*-butyllithium (3.01 mL, 2.5M in hexanes, 7.53 mmol, 1.05 equiv.) was added dropwise over 5 min and the reaction mixture was stirred at −78 °C for 1h. A second equivalent of *n*-butyllithium (3.01 mL, 2.5M in hexanes, 7.53 mmol, 1.05 equiv.) was added dropwise over 5 min and the reaction mixture was stirred at −78 °C for another 2h. The reaction mixture was transferred to a separatory funnel and diluted with a solution of sat. aq. NH_4Cl.The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude oil was purified using flash chromatography using acetone-deactivated silica gel (e.g. silica gel is mixed with acetone (ca. 10 mL/g) and this slurry is used to pack the column. Before the crude is applied the column is flushed with two column volumes of *c*Hex) to yield a white crystalline solid (886 mg, 2.72 mmol, 38%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.88 - 7.93 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 3.77 - 3.97 (m, 2H), 2.41 (s, 3H), 2.08 - 2.14 (m, 1H), 1.83 - 2.00 (m, 2H), 1.62 - 1.78 (m, 2H), 0.04 (s, 9H). – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 172.7 (C_q), 144.3 (C_q), 136.7 (C_q), 129.1 (+, 2 × CH_{Ar}), 128.5 (+, 2 × CH_{Ar}), 47.6 (–, CH_2), 36.3 (+, CH), 23.7 (–, CH_2), 23.0 (–, CH_2), 21.6 (+, CH_3), -2.3 (+, 3 × CH_3) ppm. – **IR** (ATR): ṽ = 2952 (w), 1664 (w), 1596 (w), 1343 (w), 1276 (w), 1241 (w), cm^{-1}. – **MS** (FAB), *m/z* (%): 326.1 (100) $[M]^+$, 454.1 (26), 256.0 (35). – **HRMS** (FAB, $C_{15}H_{24}NO_3{}^{32}S^{28}Si$): calc. 326.1241; found 326.1242.

1-Tosyl-3-(trimethylsilyl)-1,4,5,6-tetrahydropyridin-2-yl trifluoromethanesulfonate (10)



A 250 mL three-neck round-bottomed flask was charged with Et_2O (40 mL) and cooled to −78 °C. A solution of KHMDS (5.44 mL, 0.5M in toluene, 2.72 mmol, 1.00 equiv.) was added rapidly. A solution of 1-tosyl-3-(trimethylsilyl)piperidin-2-one (886 mg, 2.72 mmol, 1.00 equiv.) in THF (20 mL) was added dropwise over 5 min and the reaction mixture was stirred for 1h at −78 °C. Trifluoromethanesulfonic anhydride (0.506 mL, 2.99 mmol, 1.10 equiv.) was added slowly over 1 min and after 5 min the reaction mixture turned to a colorless solution. After a total of 10 min the reaction mixture was transferred to a separatory funnel and diluted with a sat .aq. $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (2 × 150 mL). The combined organic layers were washed with sat. aq. NaCl (1 × 25 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified using flash chromatography using acetone-deactivated silica gel (e.g. silica gel is mixed with acetone (ca. 10 mL/g) and this slurry is used to pack the column. Before the crude is applied the column is flushed with two column volumes of *c*Hex, column ran isocratic *c*Hex/EtOAc = 20:1) to yield a clear oil (648 mg, 1.42 mmol, 52%). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 7.71 - 7.73 (d, *J* = 8.7 Hz, 2H), 7.31 - 7.33 (d, *J* = 7.9 Hz, 2H), 3.58 (m, 2H), 2.44 (s, 3H), 1.71 - 1.78 (m, 2H), 1.17 - 1.33 (m, 2H), 0.21 (s, 9H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 144.9 (C_q), 141.2 (C_q), 135.2 (C_q), 129.8 (+, 2 × CH_{Ar}), 128.0 (+, 2 × CH_{Ar}), 126.1 (C_q), 120.0 (C_q), 116.8 (C_q), 47.8 (−, CH_2), 26.9 (−, CH_2), 24.8 (−, CH_2), 21.7 (+, CH_3), 20.1 (−, CH_2), -1.4 (+, 3 × CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2956 (vw), 1627 (w), 1410 (m), 1367 (m), 1200 (m), 1172 (s), 1127 (s), 1049 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 457 (100) $[M]^+$, 286 (72). – **HRMS** (EI, $C_{22}H_{16}NO_5F_3{}^{32}S^{28}Si$): calc. 457.0655; found 457.0655.

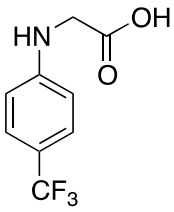
2-(4-(Fluorophenyl)amino)acetic acid (S1)



To a stirred solution of 4-fluoroaniline (10.00 g, 89.93 mmol) in anhydrous dimethylformamide at rt, DIPEA (18.8 mL, 107.92 mmol) and after, ethyl bromoacetate (10.9 mL, 98.92 mmol) were added dropwise. The reaction was left stirring at 60 °C for 16 hours. The crude mixture was extracted with EtOAc, washed with LiCl (5%), dried over $MgSO_4$ and the solvent was removed *in vacuo*. The obtained solid was dissolved in H_2O / EtOH (4.5:1) and NaOH (4.95 g, 123.80 mmol) was added. The reaction was left stirring for 1.5 hours under reflux. Upon cooling, the mixture was acidified to pH = 5 using 10% $HCl_{(aq)}$ until precipitation of a solid was observed. 2-(4-(Fluorophenyl)amino)acetic acid was isolated after filtration as a pale brown solid (4.56 g, 33% yield). **Melting point:** 134-136 °C (lit.[2]

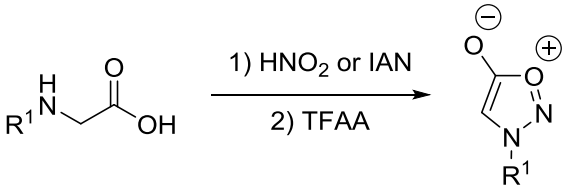
140 °C). **^{1}H NMR (*d*$_6$-DMSO, 400 MHz):** δ = 7.11 – 6.77 (m, 2H, Ph***H***), 6.70 – 6.41 (m, 2H, Ph***H***), 3.76 (s, 2H, -C***H***$_2$-). **^{19}F NMR (*d*$_6$-DMSO, 376 MHz):** δ = -129.5 (tt, *J* = 9.0, 4.5 Hz). **^{13}C NMR (*d*$_6$-DMSO, 100.6 MHz):** δ = 172.6, 154.5 (d, *J* = 231.0 Hz), 144.9, 115.2 (d, *J* = 22.0 Hz), 112.8 (d, *J* = 7.5 Hz), 45.1, 40.2.

2-((4-(Trifluoromethyl)phenyl)amino)acetic acid[3] (S2)



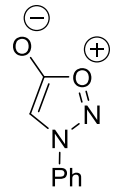
To a stirred solution of sodium acetate (1.31 g, 16.01 mmol), glacial acetic acid (1.80 mL, 32.02 mmol), glyoxylic acid monohydrate (1.11 g, 12.01 mmol) and sodium cyanoborohydride (0.50 g, 8.01 mmol) in methanol at 0 °C, was added 4-(trifluoromethyl)aniline (1 mL, 8.01 mmol). The reaction was left stirring under a N_2 atmosphere for 2 hours. After, the crude was filtrated through celite, washed with 1% AcOH in EtOAc and brine was added. The aqueous layer was extracted with EtOAc, the organic fractions dried over $MgSO_4$ and the solvent was removed *in vacuo*. 2-((4-(Trifluoromethyl)phenyl)amino)acetic acid was isolated as a pale yellow solid (1.54 g, 88% yield). **Melting point:** 130-132 °C (lit.[3] 141-143 °C). **^{1}H NMR (*d*$_6$-DMSO, 400 MHz):** δ = 7.37 (d, *J* = 8.5 Hz, 2H, Ph***H***), 6.66 (d, *J* = 8.5 Hz, 2H, Ph***H***), 3.83 (s, 2H, -C***H***$_2$-). **^{19}F NMR (*d*$_6$-DMSO, 376 MHz):** δ = -59.0. **^{13}C NMR (*d*$_6$-DMSO, 100.6 MHz):** δ = 172.1, 126.1 (q, *J* = 3.5 Hz), 125.4 (q, *J* = 270.0 Hz), 115.7 (q, *J* = 32.0 Hz), 111.6, 111.6, 44.4.

General Procedure GP2[4]: Synthesis of sydnones



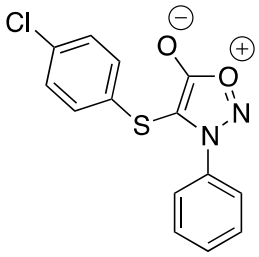
To a stirred solution of the corresponding amino acid (1 equiv.) in dimethoxyethane, was added isoamyl nitrite (1.1 equiv.). The mixture was left stirring at room temperature for 5 hours. The reaction was concentrated *in vacuo* and EtOAc / diethyl ether (1:20) was added until a solid precipitated. The resulting solid was dissolved in CH_2Cl_2 at 0 °C under N_2 atmosphere and trifluoroacetic anhydride (1.5 equiv.) was added dropwise. After 1.5 hours, the reaction was neutralized with saturated $NaHCO_{3\ (aq)}$. The organic layer was extracted with CH_2Cl_2, washed with brine, dried over $MgSO_4$ and the volatiles were removed *in vacuo*. The corresponding sydnone was isolated after recrystallisation from ethanol or CH_2Cl_2.

_N_-Phenylsydnone[1] (12)



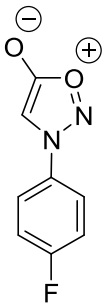
Following the general procedure GP2 using *N*-phenylglycine (20.00 g, 132.30 mmol), *N*-phenylsydnone was isolated as a golden brown solid after recrystallisation from ethanol (16.18 g, 75% yield). **Melting point:** 132-134 °C (lit.[5] 134 °C). **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 7.64-7.76 (m, 5H, Ph***H***), 6.74 (s, 1H, Syd***H***). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 169.1, 135.0, 132.6, 130.4, 121.5, 93.8.

4-((4-Chlorophenyl)thio)-3-phenyl-sydnone (13)



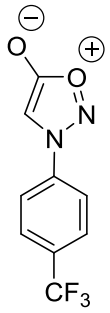
A solution of 4-chlorothiophenol (269 mg, 1.86 mmol) and *N*-chlorosuccinimide (166 mg, 1.24 mmol) in CH_2Cl_2 was stirred at rt under a N_2 atmosphere for 30 min. *N*-Phenylsydnone (150 mg, 0.93 mmol) was added and the mixture was left stirring for 5 h. The crude mixture was poured into a saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, dried over $MgSO_4$ and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluting solvent: 5% ethyl acetate in 60-40 petroleum ether) and the desired product was isolated as a pale brown solid (133 mg, 47% yield). **Melting point:** 76-80 °C. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 7.72 – 7.66 (m, 1H, Ph***H***), 7.64 – 7.57 (m, 2H, Ph***H***), 7.50 – 7.45 (m, 2H, Ph***H***), 7.26 – 7.21 (m, 2H, Ph***H***), 7.17 – 7.12 (m, 2H, Ph***H***). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 168.3, 134.4, 134.0, 132.7, 132.2, 130.6, 129.9, 129.9, 125.0, 100.0. **FTIR:** ν_{max} 3065 (w), 2922 (m), 2852 (w), 1759 (s), 1495 (m), 1475 (s), 1463 (m), 1388 (m), 1347 (w), 1242 (m), 1090 (m), 1042 (m), 1010 (m), 816 (m), 765 (m), 726 (m), 688 (m) cm^{-1}. **HRMS:** m/z [MH^+] calc. for $C_{14}H_9ClN_2O_2S$: 305.0152, found: 305.0161.

***N*-(4-Fluorophenyl)sydnone (S3)**



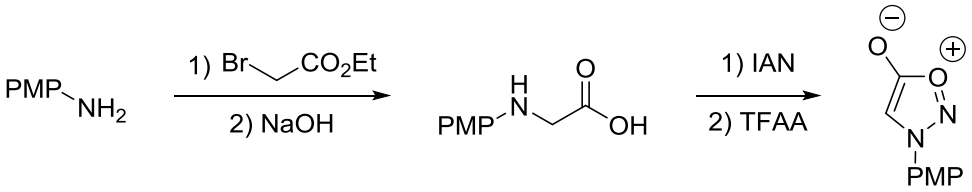
Following the general procedure GP2 using 2-(4-(fluorophenyl)amino)acetic acid **86** (4.00 g, 23.64 mmol), *N*-(4-fluorophenyl)sydnone was isolated as a golden brown solid after recrystallisation from CH_2Cl_2 (2.75 g, 65% yield). **Melting point:** 150-152 °C (lit.[6] 154 °C). **^{1}H NMR ($CDCl_3$, 400 MHz):** 7.81 – 7.70 (m, 2H, Ph***H***), 7.38 – 7.27 (m, 2H, Ph***H***), 6.72 (s, 1H, Syd***H***). **^{19}F NMR ($CDCl_3$, 377 MHz):** δ -105.4 (q, *J* = 6.0, 5.0 Hz). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ 168.9, 164.7 (d, *J* = 255.0 Hz), 131.1, 123.7 (d, *J* = 9.5 Hz), 117.7 (*J* = 24.0 Hz), 94.0.

***N*-(4-(Trifluoromethyl)phenyl)sydnone (S4)**



Following the general procedure GP2 using 2-((4-(trifluoromethyl)phenyl)amino)acetic acid **87** (1.50 g, 6.85 mmol), *N*-(4-(trifluoromethyl)phenyl)sydnone was isolated as a pale orange solid after recrystallisation from ethanol (548 mg, 35% yield). **Melting point:** 132-134 °C (lit.[7] 131-133 °C). **^{1}H NMR ($CDCl_3$, 400 MHz):** 7.98 – 7.85 (m, 4H, Ph***H***), 6.82 (s, 1H, Syd***H***). **^{19}F NMR ($CDCl_3$, 377 MHz):** δ -63.1. **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ 168.8, 137.3, 134.7 (q, *J* = 34.0 Hz), 127.8 (q, *J* = 3.5 Hz), 123.0 (*q* = 275.0 Hz), 122.1, 94.0.

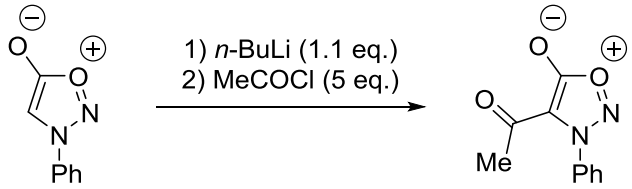
Synthesis of *N*-(4-methoxyphenyl)sydnone (14)



To a stirring solution of 4-methoxyaniline (10.00 g, 81.20 mmol) and sodium acetate (13.32 g, 162.40 mmol) in EtOH, ethyl bromoacetate (9.9 mL, 89.32 mmol) was added dropwise. The reaction was left stirring at reflux for 4 hours. The crude was concentrated *in vacuo*, dichloromethane was added and the resulting solid was filtered. The volatiles of the filtrate were removed *in vacuo* and the obtained solid was used without further purification. The crude solid was dissolved in H_2O / EtOH (4.5:1) and NaOH (4.87 g, 121.80 mmol) was added. The reaction was left stirring for 1 hour under reflux. Upon cooling, the mixture was acidified to pH = 4 using 10% $HCl_{(aq)}$ and the crude compound was directly used in the next step.

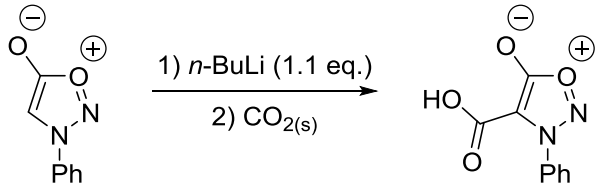
To a stirring solution of the obtained solid (8.00 g, 67.69 mmol) in dimethoxyethane, was added isoamyl nitrite (10.00 mL, 74.46 mmol). The mixture was left stirring at room temperature for 3 hours. The reaction was concentrated *in vacuo* and EtOAc / petroleum ether (1:20) was added until a pale brown solid precipitated. The resulting solid was dissolved in 40 mL of CH_2Cl_2 at 0 °C with stirring under a N_2 atmosphere. Trifluoroacetic anhydride (14.20 mL, 101.54 mmol) was added dropwise at 0 °C under N_2 atmosphere. After 1.5 hours, the reaction was neutralized with saturated $NaHCO_{3\ (aq)}$. The organic layer was extracted with CH_2Cl_2, dried over $MgSO_4$ and the volatiles were removed *in vacuo*. *N*-(4-Methoxyphenyl)sydnone was isolated as a brown solid after recrystallisation from ethanol (5.12 g, 39% yield). **Melting point:** 120-122 °C (lit.[8] 126 °C). **^{1}H NMR ($CDCl_3$, 400 MHz):** 7.64 (d, *J* = 9.0 Hz, 2H, PMP***H***), 7.07 (d, *J* = 9.0 Hz, 2H, PMP***H***), 6.67 (s, 1H, Syd***H***), 3.89 (s, 3H, -OC***H***$_3$). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ 169.2, 162.6, 127.9, 122.8, 115.4, 93.5, 96.0.

Synthesis of 4-acetyl-*N*-phenylsydnone (15)



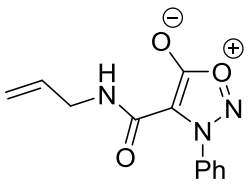
To a stirred solution of *N*-phenylsydnone (2.00 g, 12.33 mmol) in anhydrous THF at -78 °C under a N_2 atmosphere, *n*-BuLi (6.50 mL, 13.57 mmol) was added dropwise and the mixture was left to stir at -78 °C. After 30 min, the resulting intermediate was transferred *via* cannula to a flask containing acetyl chloride (4.40 mL, 61.67 mmol) at -78 °C under a N_2 atmosphere. The mixture was left to warm to rt and stirred for 24 hours. After that, the reaction was quenched with brine, extracted with CH_2Cl_2, dried over $MgSO_4$ and the volatiles were removed *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluting solvent: 30% EtOAc in petroleum ether). 4-Acetyl-*N*-phenylsydnone was isolated as a pale yellow solid after recrystallisation from CH_2Cl_2 / petroleum ether (912 mg, 36% yield). **Melting point:** 138-139 °C (lit.[9] 143-145 °C). **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 7.72 – 7.65 (m, 1H, Ph***H***), 7.64 – 7.57 (m, 2H, Ph***H***), 7.51 – 7.44 (m, 2H, Ph***H***), 2.53 (s, 3H, -C***H*****$_3$**). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 184.4, 166.4, 135.1, 132.5, 129.6, 125.0, 106.2, 28.3.

Synthesis of 4-carboxy-*N*-phenylsydnone[10] (S5)



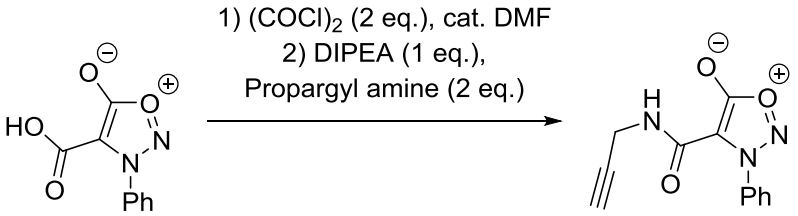
To a stirred solution of *N*-phenylsydnone (2.00 g, 12.33 mmol) in anhydrous THF at -78 °C under a N_2 atmosphere, *n*-BuLi (6.30 mL, 13.56 mmol) was added dropwise and the mixture was left to stir at -78 °C. After 30 min, the resulting intermediate was transferred *via* cannula to a flask containing a large excess of $CO_{2(s)}$ at -78 °C under a N_2 atmosphere. The mixture was left to stir at -78 °C for 20 min. After that, the reaction was extracted with EtOAc, and the aqueous layer was acidified with 10% HCl to pH = 2 until precipitation of a solid was observed. 4-Carboxy-*N*-phenylsydnone was isolated after filtration and recrystallisation from hot ethanol as a pale yellow solid (2.52 g, 99% yield). **Melting point:** 180-182 °C. **^{1}H NMR (d_6-DMSO, 400 MHz):** δ = 13.35 (s, 1H, -COO***H***), 7.79 – 7.74 (m, 2H, Ph***H***), 7.73 – 7.68 (m, 1H, Ph***H***), 7.66 – 7.60 (m, 2H, Ph***H***). **^{13}C NMR (d_6-DMSO, 100.6 MHz):** δ = 164.5, 157.6, 135.3, 132.0, 129.2, 125.6, 100.6.

4-(Allyllcarbamoyl)-3-phenylsydnone (16)



To a stirred solution of 4-carboxy-*3*-phenylsydnone (400 mg, 2.43 mmol) and a drop of DMF in dry dichloromethane at 0 °C, oxalyl chloride (0.31 mL, 3.66 mmol) was added dropwise. After 2.5 h stirring at rt, the volatiles were removed *in vacuo*, the crude mixture was dissolved in dry dichloromethane and added dropwise to a mixture of DIPEA (0.85 mL, 4.86 mmol) and allyl amine (0.37 mL, 4.86 mmol) at 0 °C. The reaction was left to stir at rt for 16 h and after, quenched with water, extracted with dichloromethane and dried over $MgSO_4$. The crude product was purified by filtration through a short pad of silica gel followed by recrystallisation from hot dichloromethane – petroleum ether affording the desired product as a pale orange solid (513 mg, 86% yield). **Melting point:** 108-110 °C. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 7.71 – 7.66 (m, 1H, -N***H***), 7.65 – 7.55 (m, 5H, Ph***H***), 5.84 (ddt, *J* = 17.0, 10.5, 5.5 Hz, 1H, H_2C=C***H***-CH_2-), 5.23 (ddd, *J* = 17.0, 3.0, 1.5 Hz, 1H, ***H***CH=CH-CH_2-), 5.16 (ddd, *J* = 10.5, 3.0, 1.5 Hz, 1H, HC***H***=CH-CH_2-), 3.96 (tt, *J* = 5.5, 1.5 Hz, 2H, HCH=CH-C***H$_2$***-). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 167.3, 155.3, 134.6, 133.4, 132.5, 129.4, 125.3, 117.0, 102.1, 41.4. **FTIR:** ν_{max} 3344 (m), 2926 (w), 1745 (s), 1660 (s), 1534 (s), 1468 (m), 1290 (m), 1264 (m), 1210 (s), 1069 (m), 906 (s), 726 (s), 689 (s), 647 (m), 634 (m) cm^{-1}. **HRMS:** m/z [MH^+] calc. for $C_{12}H_{11}N_3O_3$: 246.0873, found: 246.0874.

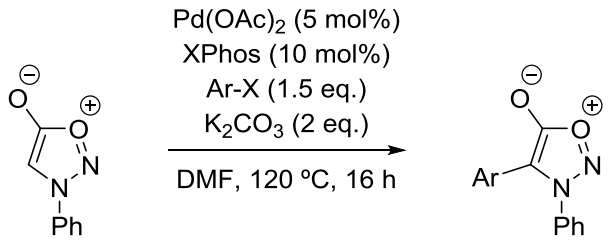
Synthesis of 3-phenyl-4-(prop-2-yn-1-ylcarbamoyl)sydnone (17)



To a stirred solution of 4-carboxy-*N*-phenylsydnone (1.00 g, 4.85 mmol) and a drop of DMF in dry dichloromethane at 0 °C, oxalyl chloride (0.82 mL, 9.70 mmol) was added dropwise. After 2 h stirring at rt, the volatiles were removed *in vacuo*, the crude mixture was dissolved in dry dichloromethane and added dropwise to a mixture of DIPEA (0.85 mL, 4.85 mmol) and propargylamine (0.62 mL, 9.70 mmol) at 0 °C. The reaction was left to stir at rt for 16 h and after, quenched with saturated $NaHCO_3$, extracted with dichloromethane and dried over $MgSO_4$. The crude product was purified by recrystallisation from dichloromethane / petroleum ether affording the desired product as a pale brown solid (936 mg, 79% yield). **Melting point:** 142-144 °C. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 7.75 – 7.66 (m, br, 2H, -N***H***- and Ph***H***), 7.64 – 7.53 (m, 4H, Ph***H***), 4.11 (dd, *J* = 5.5, 2.5 Hz, 2H, -C***H$_2$***-), 2.23 (t, *J* = 2.5 Hz, 1H, -C***H***). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 167.2, 155.1, 134.5, 132.6, 129.4, 125.3, 101.7,

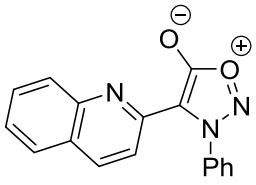
78.8, 72.0, 28.6. **FTIR:** ν_{max} 3429 (br), 3337 (m), 3291 (w), 1748 (s), 1666 (s), 1539 (m), 1492 (w), 1470 (w), 1451 (w), 1420 (w), 1291 (w), 1264 (w), 1208 (w), 1072 (w), 883 (w), 792 (w) cm^{-1}. **HRMS:** m/z [MH^+] calc. for $C_{12}H_9N_3O_3$: 244.0722, found: 244.0732.

General procedure GP3: Synthesis of 4-(heteroaryl)-*N*-phenylsydnone derivatives



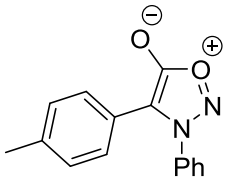
To a stirred solution of *N*-phenylsydnone (1 equiv.), $Pd(OAc)_2$ (5 mol%), XPhos (10 mol%) and K_2CO_3 (2 equiv.) in dry DMF, the corresponding aryl halide (1.5 equiv.) was added and the mixture was left to stir at 120 °C under a N_2 atmosphere. After 16 h, the reaction was quenched with brine, extracted with EtOAc, washed with 5% LiCl, dried over $MgSO_4$ and the volatiles were removed *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluting solvent: 20-40% EtOAc in petroleum ether). Further purification was achieved by recrystallisation from CH_2Cl_2 / petroleum ether.

***N*-Phenyl-4-(2-quinolinyl)sydnone (18)**



Following the general procedure GP3 using 2-bromoquinoline (387 mg, 1.86 mmol), the desired product was recrystallised as a bright yellow solid (556 mg, 62% yield). **Melting point:** 126-128 °C. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 8.29 (d, *J* = 8.5 Hz, 1H, Quin***H***), 8.18 (d, *J* = 8.5 Hz, 1H, Quin***H***), 7.75 (dd, *J* = 8.0, 1.0, 1H, Quin***H***), 7.72 – 7.67 (m, 1H, Quin***H***), 7.63 – 7.50 (m, 5H, Ph***H*** + Quin***H***), 7.48 – 7.42 (m, 1H, Ph***H***), 7.29 (d, *J* = 8.5 Hz, 1H, Quin***H***). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 167.1, 147.1, 144.7, 136.7, 136.5, 131.4, 129.8, 129.1, 129.0, 127.6, 127.0, 126.8, 125.6, 118.7, 107.1. **FTIR:** ν_{max} 3217 (w), 2923 (m), 2853 (w), 1745 (s), 1596 (m), 1510 (m), 1463 (w), 1446 (w), 1281 (w), 1037 (m), 832 (w) cm^{-1}. **HRMS:** m/z [MH^+] calc. for $C_{17}H_{11}N_3O_2$: 290.0924, found: 290.0918.

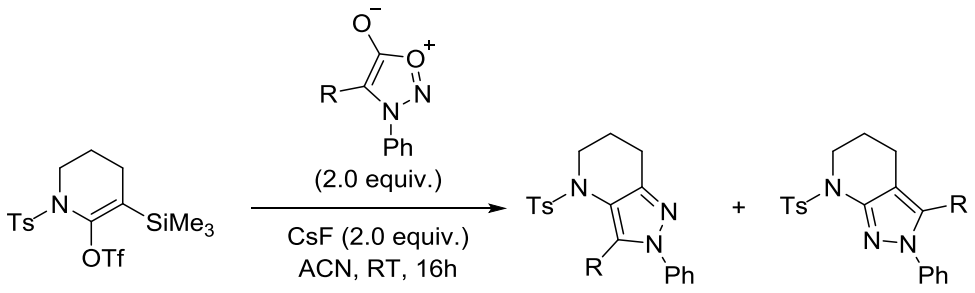
***N*-Phenyl-4-(*p*-tolyl)sydnone (19)**



Following the general procedure GP3 using *p*-chlorotoluene (1.10 mL, 9.26 mmol), the desired product was recrystallised as a pale brown solid (821 mg, 53% yield). **Melting point:** 136-138 °C (lit.[11] 141-143 °C). **^{1}H NMR ($CDCl_3$, 400**

MHz): δ = 7.69 – 7.62 (m, 1H, Ph***H***), 7.61 – 7.53 (m, 2H, Ph***H***), 7.53 – 7.44 (m, 2H, Ph***H***), 7.20 – 7.15 (m, 2H, Tol***H***), 7.09 (d, *J* = 8.0 Hz, 2H, Tol***H***), 2.31 (s, 3H, -C***H*****$_3$**). **^{13}C NMR ($CDCl_3$, 100.6 MHz):** δ = 167.3, 139.1, 134.9, 132.2, 130.3, 129.6, 127.4, 125.0, 121.6, 108.2, 21.5. **FTIR:** ν_{max} 3217 (w), 2923 (m), 2853 (w), 1745 (s), 1596 (m), 1510 (m), 1463 (w), 1446 (w), 1281 (w), 1037 (m), 832 (w) cm^{-1}. **HRMS:** m/z [MH^+] calc. for $C_{17}H_{11}N_3O_2$: 290.0924, found: 290.0918.

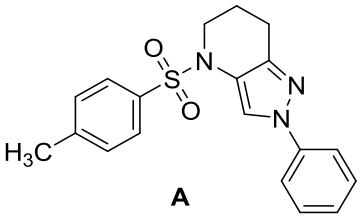
General procedure GP4: 4-aminopyrazole synthesis using strained ynamides



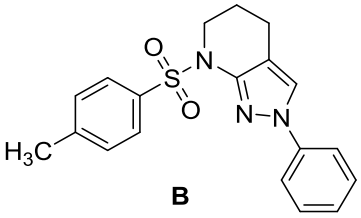
A 10 mL vial was charged with the respective sydnone (0.100 mmol, 2.00 equiv.) and 1-tosyl-3-(trimethylsilyl)-1,4,5,6-tetrahydropyridin-2-yl trifluoromethanesulfonate (22.9 mg, 0.050 mmol, 1.00 equiv.) in MeCN (0.05M) to give a colorless solution. After stirring for 5 minutes Caesium fluoride (15.2 mg, 0.100 mmol, 2.00 equiv.) was added rapidly in one portion. The reaction mixture was stirred at RT for 16h and the conversion was checked with ESI-MS. The crude reaction mixture was purified employing preparative TLC or flash column chromatography (*c*Hex/EtOAc mixtures).

2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (20a)

2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (20b)



A



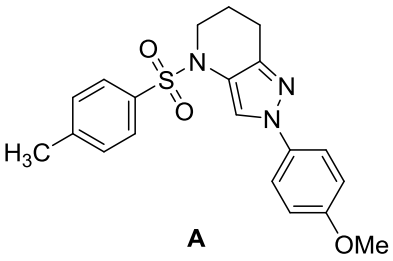
B

These compounds were prepared according to general procedure GP4 using 3-phenyl-3H-1,2,3-oxadiazol-1-ium-5-olate (16.0 mg, 0.10 mmol) and were isolated after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless crystals (15.0 mg, 0.042 mmol, 84%) Ratio by ^{1}H-NMR **A/B** = 4:1. **Isomer (B): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.20 (s, 1H), 7.63 - 7.69 (m, 3H), 7.43 - 7.48 (m, 2H), 7.17 - 7.23 (m, 4H), 3. 61 - 3.65 (m, 2H), 3.39 (t, *J* = 6.4 Hz, 1H), 2.86 (s, 1H), 2.67 (t, *J* = 6.4 Hz, 2H), 2.39 (s, 3H) ppm. – **Isomer (A): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.95 - 7.99 (m, 2H), 7.58 - 7.63 (m, 2H), 7.54 (s, 1H), 7.41 (m, 2H), 7.27 - 7.25 (m, 3H), 3.82 - 3.87 (m, 2H), 2.53 - 2.59 (m, 2H), 2.38 (s, 3H), 1.94 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 147.5 (C_q), 143.6 (C_q), 140.1 (C_q), 135.9 (C_q), 129.8 (+, CH_{Ar}), 129.5 (+, CH_{Ar}), 129.3 (+, CH_{Ar}), 129.2 (+, CH_{Ar}), 128.2 (+, CH_{Ar}), 127.2 (+, CH_{Ar}), 125.4 (+, CH_{Ar}), 123.3 (+, CH_{Ar}), 118.5 (+, CH_{Ar}), 117.9 (+, CH_{Ar}), 108.0 (C_q), 46.9 (–, CH_2), 46.2 (–, CH_2), 29.7 (–, CH_2), 22.8 (–, CH_2), 21.6 (+, CH_3), 21.4 (–, CH_2), 18.9 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2922 (vw), 2852 (vw), 1685 (w), 1596 (w), 1490 (m), 1459 (w), 1391 (w), 1349 (m), 1284 (m), 1222 (w), 1161 (m), 1088 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 353.2 (100) $[M]^+$, 198.1 (89). – **HRMS** (EI, $C_{19}H_{19}N_3O_2{}^{32}S$): calc.353.1193; found 353.1193.

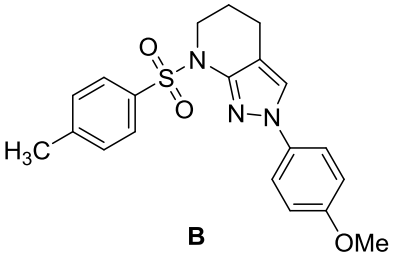
Product assignment was done on the basis of characteristic ^{1}H-NMR shifts, specifically of the pyrazole proton.

2-(4-methoxyphenyl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (21a)

2-(4-methoxyphenyl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (21b)



A



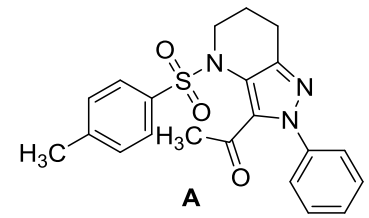
B

These compounds were prepared according to general procedure GP4 using 3-(4-methoxyphenyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (36.0 mg, 0.188 mmol) and were isolated as a mixture after flash column chromatography (*c*Hex/EtOAc = 9:1 → 1:1) as colorless solids (17.0 mg, 0.044 mmol, 47%) Ratio by ^{1}H-NMR **A/B** = 2:1. Another fraction yielded unreacted 1-tosyl-3-(trimethylsilyl)-1,4,5,6-tetrahydropyridin-2-yl trifluoromethanesulfonate (12.0 mg, 0.026 mmol, 28%) **Isomer (A): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.3 Hz, 2H), 7.48 - 7.53 (m, 2H), 7.43 (s, 1H), 7.23 - 7.26 (m, 2H), 6.89 - 6.95 (m, 2H), 3.83 (s, 3H), 3.59 - 3.66 (m, 2H), 2.54 (t, *J* = 6.4 Hz, 2H), 2.38 (s, 3H), 1.92 (dd, *J* = 6.2, 4.7 Hz, 2H) ppm. – **Isomer (B): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.54 - 7.59 (m, 2H), 7.22 - 7.25 (m, 2H), 6.95 - 6.99 (m, 2H), 3.85 (s, 3H), 3.79 - 3.82 (m, 2H), 2.65 (t, *J* = 6.4 Hz, 2H),), 2.39 (s, 3H), 1.63 - 1.72 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 158.1 (C_q), 157.5 (C_q), 147.1 (C_q), 144.0 (C_q), 143.6 (C_q), 141.1 (C_q), 136.0 (C_q), 134.6 (C_q), 134.0 (C_q), 129.8 (+, CH_{Ar}), 129.7 (+, CH_{Ar}), 129.2 (+, CH_{Ar}), 128.2 (+, CH_{Ar}), 127.2 (+, CH_{Ar}), 123.4 (+, CH_{Ar}), 121.6 (+, CH_{Ar}), 120.2 (+, CH_{Ar}), 119.6 (+, CH_{Ar}), 117.9 (+, CH_{Ar}), 114.5 (+, CH_{Ar}), 114.4 (+, CH_{Ar}), 107.5 (C_q), 55.6 (+, CH_3), 55.5 (+, CH_3), 46.9 (–, CH_2), 46.2 (–, CH_2), 29.7 (–, CH_2), 26.9 (–, CH_2), 22.8 (–, CH_2), 21.6 (–, CH_2), 21.3 (+, CH_3), 20.9 (–, CH_2), 18.9 (–, CH_2) ppm. – **IR** (ATR): ṽ = 2919 (m), 2849 (w), 1595 (w), 1513 (s), 1461 (m), 1336 (w), 1300 (w), 1242 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 383.3 (57) $[M]^+$, 228.2 (100). – **HRMS** (EI, $C_{20}H_{21}N_3O_3{}^{32}S$): calc. 383.1298; found 383.1299.

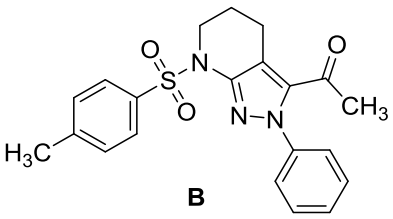
Product assignment was done on the basis of characteristic ^{1}H-NMR shifts, especially of the pyrazole proton.

1-(2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridin-3-yl)ethan-1-one (22a)

1-(2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridin-3-yl)ethan-1-one (22b)



A

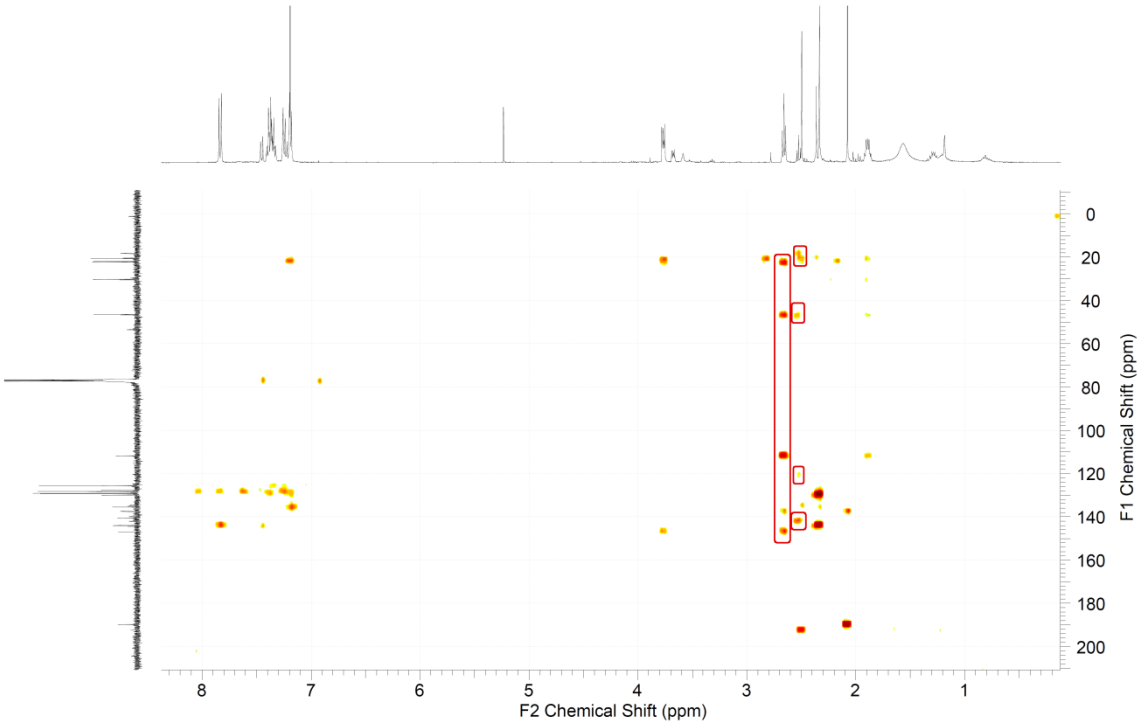


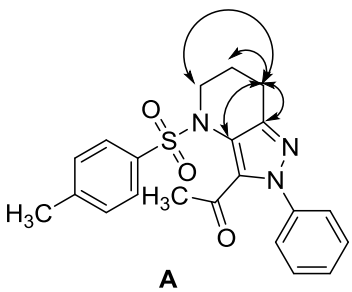
B

This inseparable mixture of compounds was prepared according to general procedure GP4 using 4-acetyl-3-phenyl-3H-1,2,3-oxadiazol-1-ium-5-olate (19.0 mg, 0.092 mmol) and was isolated after preparative TLC (*c*Hex/EtOAc = 5:1) as colorless solids (16.0 mg, 0.040 mmol, 88%) Ratio by ^{1}H-NMR: **A/B** = 2:5. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.3 Hz, 2H, major product), 7.52 (d, *J* = 8.3 Hz, 2H, minor product), 7.37 - 7.49 (m, 5H), 7.28 - 7.35 (m, 3H), 7.25 (m, 3H), 3.78 - 3.87 (m, 2H, major product), 3.70 - 3.78 (m, 2H, minor product), 2.73 (t, *J* = 6.4 Hz, 2H, major product), 2.57 - 2.63 (m, 2H, minor product), 2.56 (s, 3H, minor product), 2.43 (s, 3H, minor product), 2.40 (s, 3H, major product), 2.14 (s, 3H, major product), 1.90 - 2.01 (m, 2H, major product), 1.36 (m, 2H, minor product) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 189.8 (C_q), 146.9 (C_q), 143.9 (C_q), 140.5 (C_q), 137.6 (C_q), 135.6 (C_q), 129.9 (+, CH_{Ar}), 129.2 (+, CH_{Ar}), 129.0 (+, CH_{Ar}), 128.9 (+, CH_{Ar}), 128.5 (+, CH_{Ar}), 128.4 (+, CH_{Ar}), 128.3 (+, CH_{Ar}), 127.9 (+, CH_{Ar}), 125.7 (s+, CH_{Ar} 125.6 (+, CH_{Ar}), 111.8 (C_q), 46.7 (–, CH_2), 46.5 (–, CH_2), 30.6 (+, CH_3), 30.2 (+, CH_3), 22.3 (–, CH_2), 21.6 (+, CH_3), 21.6 (+, CH_3), 20.7 (–, CH_2), 20.4 (–, CH_2), 18.3 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2925 (w), 1674 (m), 1595 (w), 1552 (w), 1497 (m), 1459 (w), 1436 (w), 1355 (w), 1341 (m), 1301 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 395.3 (77) $[M]^+$, 240.2 (100). – **HRMS** (EI, $C_{21}H_{21}N_3O_3{}^{32}S$): calc. 395.1298; found 395.1300.

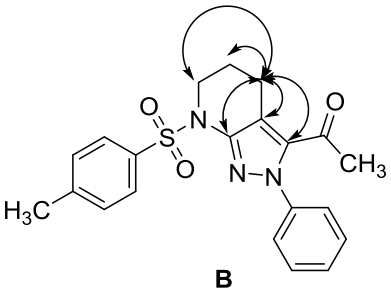
Determination of product ratios was done using integrals from ^{1}H-NMR. Determination of major isomer was determined by HMBC, as shown in spectrum below.

HMBC spectrum for compounds 22a&b





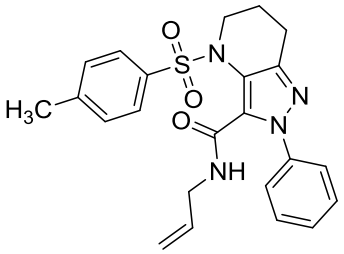
A
4 HMBC signals



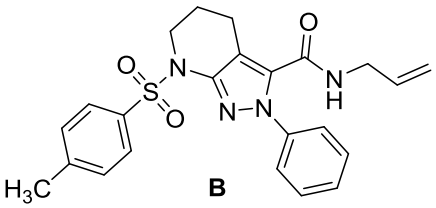
B
5 HMBC signals

***N*-allyl-2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine-3-carboxamide (23a)**

***N*-allyl-2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-3-carboxamide (23b)**



A

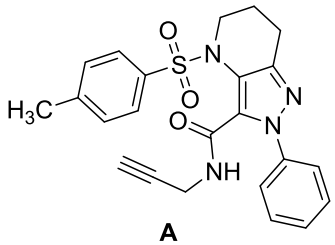


B

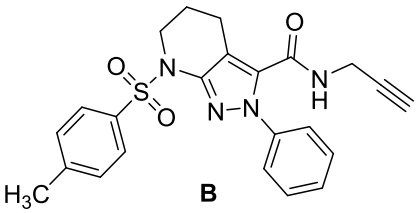
These compounds were prepared according to general procedure GP4 using 4-(allylcarbamoyl)-3-phenyl-3H-1,2,3-oxadiazol-1-ium-5-olate (20.0 mg, 0.083 mmol) and were isolated after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless solids (14.0 mg (B) and 4.0 mg (A), 0.040 mmol, 94%). **Isomer (A): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.3 Hz, 2H), 7.33 - 7.54 (m, 5H), 7.30 (d, *J* = 8.1 Hz, 2H), 5.93 (ddt, *J* = 17.1, 10.3, 5.7, 5.7 Hz, 1H), 5.27 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.17 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.04 (tt, *J* = 5.8, 1.5 Hz, 2H), 3.63 - 3.69 (m, 3H), 2.51 (t, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.45 - 1.55 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 159.4 (C_q), 144.7 (C_q), 143.3 (C_q), 140.3 (C_q), 135.0 (C_q), 133.6 (+, CH_{Ar}), 131.4 (+, CH_{Ar}), 129.9 (+, CH_{Ar}), 128.9 (+, CH_{Ar}), 128.1 (+, CH_{Ar}), 128.1 (+, CH_{Ar}), 124.5 (+, CH_{Ar}), 119.9 (C_q), 116.9 (–, CH_2), 47.3 (–, CH_2), 42.4 (–, CH_2), 29.7 (–, CH_2), 21.7 (+, CH_3), 19.8 (–, CH_2), 18.6 (–, CH_2) ppm. **Isomer (B): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.87 - 7.93 (m, 2H), 7.34 - 7.47 (m, 5H), 7.27 (s, 1H), 7.25 (s, 1H), 5.66 - 5.73 (m, 1H), 5.51 (app. t., 1H), 4.97 - 5.10 (m, 2H), 3.87 (tt, *J* = 5.7, 1.5 Hz, 2H), 3.78 - 3.85 (m, 2H), 2.68 (t, *J* = 6.4 Hz, 2H), 2.40 (s, 3H), 1.87 - 1.96 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 159.7 (C_q), 146.9 (C_q), 143.9 (C_q), 139.5 (C_q), 135.6 (C_q), 133.0 (C_q), 133.0 (+, CH), 129.3 (+, 2 × CH_{Ar}), 129.1 (+, 2 × CH_{Ar}), 128.2 (+, 2 × CH_{Ar}), 128.0 (+, CH_{Ar}), 124.5 (+, 2 × CH_{Ar}), 117.0 (–, CH_2), 110.1 (C_q), 46.7 (–, CH_2), 41.9 (–, CH_2), 22.3 (–, CH_2), 21.6 (+, CH_3), 19.7 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3394 (vw), 2923 (vw), 1662 (w), 1494 (w), 1354 (m), 1256 (m) cm^{-1}. – **MS** (FAB), *m/z* (%): 437.2 (8) $[M+H]^+$, 132.9 (100). – **HRMS** (FAB, $C_{23}H_{25}N_4O_3{}^{32}S$): calc. 437.1642; found 437.1640.

2-p1henyl-*N*-(prop-2-yn-1-yl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine-3-carboxamide (24a)

2-phenyl-*N*-(prop-2-yn-1-yl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-3-carboxamide (24b)



A

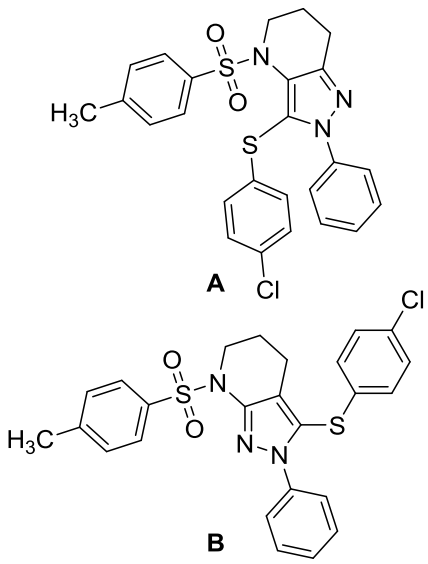


B

These compounds were prepared according to general procedure GP4 using 3-phenyl-4-(prop-2-yn-1-ylcarbamoyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (44.0 mg, 0.179 mmol) and were isolated as a mixture after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless solids (18.0 mg, 0.041 mmol, 46%) Ratio by ^{1}H-NMR **A/B** = 2:7. Another fraction yielded unreacted 1-tosyl-3-(trimethylsilyl)-1,4,5,6-tetrahydropyridin-2-yl trifluoromethane-sulfonate (22.0 mg, 0.048 mmol, 54%). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.3 Hz, 2H, major product), 7.62 (d, *J* = 8.3 Hz, 2H, minor product), 7.55 (t, *J* = 5.1 Hz, 1H, minor product), 7.34 - 7.52 (m, 7H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.25 (m, 2H), 5.65 (t, *J* = 5.1 Hz, 1H, major product), 4.19 (dd, *J* = 5.3, 2.5 Hz, 2H, minor product), 4.04 (dd, *J* = 5.4, 2.7 Hz, 2H, major product), 3.79 - 3.85 (m, 2H, major product), 3.62 - 3.68 (m, 2H, minor product), 2.68 (t, *J* = 6.4 Hz, 2H, major product), 2.51 (t, *J* = 7.2 Hz, 2H, minor product), 2.43 (s, 3H, minor product), 2.40 (s, 3H, major product), 2.26 (t, *J* = 2.7 Hz, 1H), 2.18 (t, *J* = 2.5 Hz, 1H, major product), 1.88 - 1.96 (m, 2H, major product), 1.46 - 1.54 (m, 1H, minor product) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 159.3 (C_q), 159.2 (C_q), 146.9 (C_q), 144.8 (C_q), 144.0 (C_q), 143.3 (C_q), 139.4 (C_q), 135.6 (C_q), 134.9 (C_q), 132.1 (C_q), 130.0 (+, CH_{Ar}), 129.3 (+, CH_{Ar}), 129.2 (+, CH_{Ar}), 128.9 (+, CH_{Ar}), 128.2 (+, CH_{Ar}), 128.1 (+, CH_{Ar}), 128.1 (+, CH_{Ar}), 124.5 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 120.1 (C_q), 110.6 (C_q), 79.0 (+, *C*H), 78.4 (+, *C*H), 72.0 (+, *C*H), 71.8 (+, *C*H), 47.4 (–, CH_2), 46.7 (–, CH_2), 29.7 (s), 29.2 (–, CH_2), 22.2 (–, CH_2), 21.6 (+, CH_3), 19.8 (–, CH_2), 19.7 (–, CH_2), 18.6 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3295 (w), 2923 (w), 1665 (w), 1595 (w), 1565 (m), 1494 (w), 1460 (w), 1339 (m), 1302 (w), 1165 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 434.3 (100) $[M]^+$, 280.2 (77), 279.2 (91). – **HRMS** (EI, $C_{23}H_{22}N_4O_3{}^{32}S$): calc. 434.1407; found 434.1406.

3-((4-chlorophenyl)thio)-2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (25a)

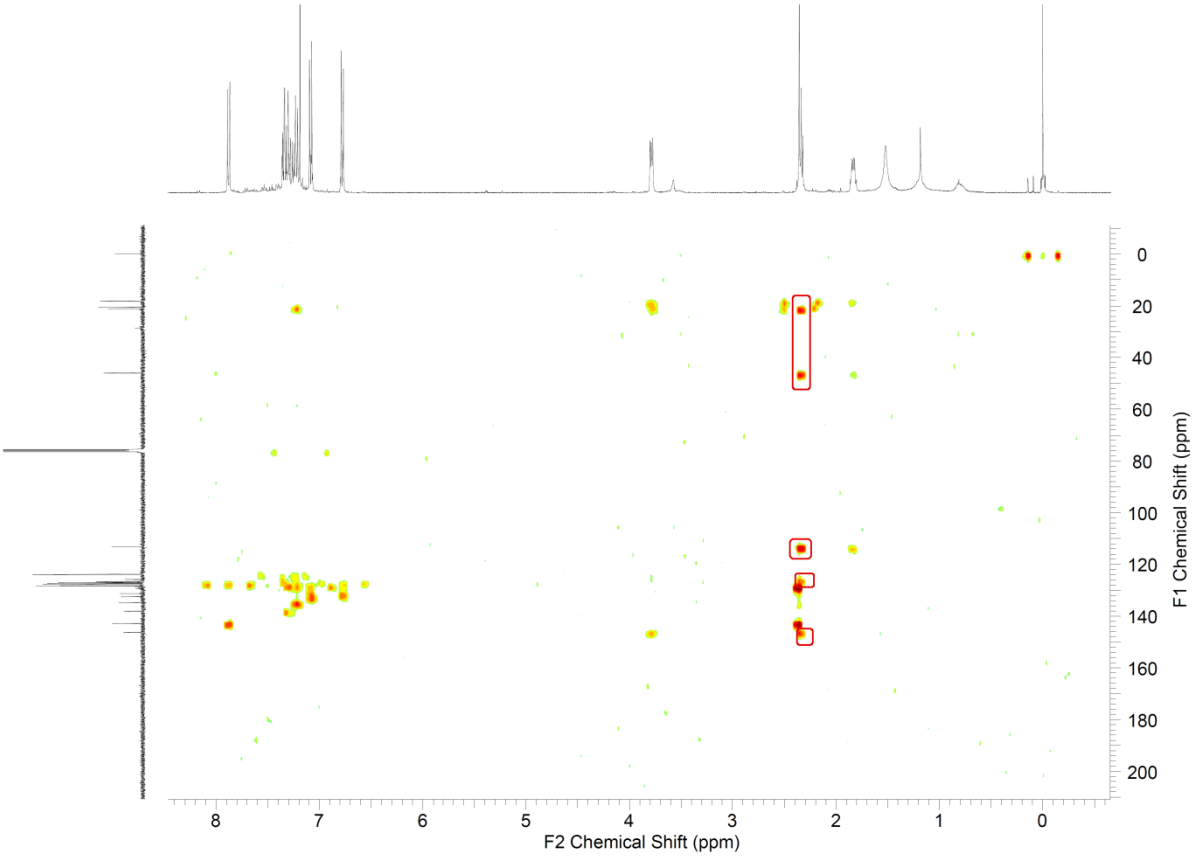
3-((4-chlorophenyl)thio)-2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (25b)

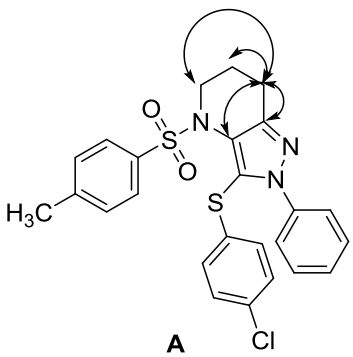


These compounds were prepared according to general procedure GP4 using 4-((4-chlorophenyl)thio)-3-phenyl-3H-1,2,3-oxadiazol-1-ium-5-olate (25.0 mg, 0.083 mmol) and were isolated after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless solids (9.0 mg (A) and 5.0 mg (B), 0.029 mmol, 68%). **Isomer (A): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.3 Hz, 2H), 7.29 - 7.43 (m, 7H), 6.97 - 7.03 (m, 2H), 6.72 - 6.77 (m, 2H), 3.62 - 3.67 (m, 2H), 2.70 (t, *J* = 6.9 Hz, 2H), 2.42 (s, 3H), 1.61 - 1.66 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 144.1 (C_q), 143.0 (C_q), 139.4 (C_q), 136.4 (C_q), 133.5 (C_q), 130.2 (C_q), 129.7 (+, CH_{Ar}), 129.4 (+, CH_{Ar}), 128.7 (+, CH_{Ar}), 128.6 (+, CH_{Ar}), 128.0 (+, CH_{Ar}), 127.9 (+, CH_{Ar}), 125.4 (+, CH_{Ar}), 121.3 (+, CH_{Ar}), 113.7 (C_q), 47.2 (–, CH_2), 29.7 (–, CH_2), 21.6 (+, CH_3), 20.6 (–, CH_2), 19.5 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2922 (w), 2852 (w), 1729 (w), 1596 (w), 1542 (m), 1497 (w), 1474 (w), 1357 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 495.3/497.3 (10/4) $[M]^+$, 340.2 (100) 246.1 (72). – **HRMS** (EI, $C_{25}H_{22}N_3O_2{}^{32}S_2{}^{35}Cl$): calc. 495.0837; found 495.0839. – **Isomer (B): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.95 (m, *J* = 8.3 Hz, 2H), 7.27 - 7.45 (m, 7H), 7.12 - 7.18 (m, 2H), 6.81 - 6.88 (m, 2H), 3.81 - 3.88 (m, 2H), 2.43 (s, 3H), 2.37 - 2.42 (m, 2H), 1.86 - 1.95 (m, 2H) ppm. – **^{13}C-NMR** ($CDCl_3$): δ = 147.3 (C_q), 143.9 (C_q), 139.1 (C_q), 135.9 (C_q), 133.5 (C_q), 132.3 (C_q), 129.4 (+, CH_{Ar}), 129.2 (+, CH_{Ar}), 128.6 (+, CH_{Ar}), 128.3 (+, CH_{Ar}), 128.0 (+, CH_{Ar}), 127.6 (+, CH_{Ar}), 126.9 (+, CH_{Ar}), 124.9 (+, CH_{Ar}), 114.1 (C_q), 47.0 (–, CH_2), 22.2 (–, CH_2), 21.6 (+, CH_3), 19.3 (–, CH_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2920 (w), 2850 (w), 1729 (w), 1595 (w), 1542 (m), 1497 (w), 1474 (w), 1357 (w) cm^{-1}. – **MS** (EI), *m/z* (%): 495.3/497.3 (77/34) $[M]^+$, 431.3 (21), 340.2 (100) 196.1 (49). – **HRMS** (EI, $C_{25}H_{22}N_3O_2{}^{32}S_2{}^{35}Cl$): calc. 495.0837; found 495.0837.

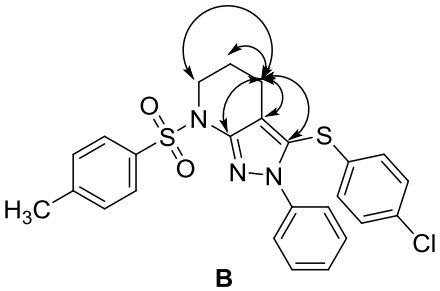
Determination of product ratios was done by chromatographic separation and isolation.
Determination of major isomer was determined by HMBC, as shown in spectrum below for compound B.

HMBC spectrum for compound 25b





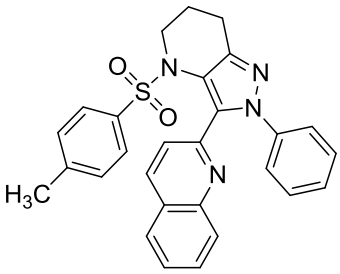
A
4 HMBC signals



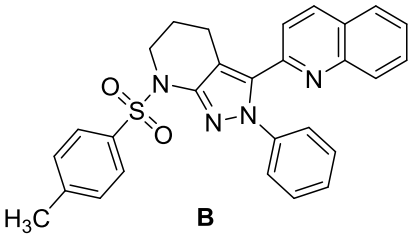
B
5 HMBC signals

2-(2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridin-3-yl)quinoline (26a)

2-(2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridin-3-yl)quinoline (26b)



A

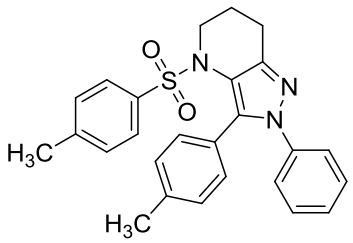


B

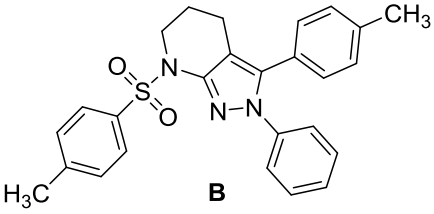
These compounds were prepared according to general procedure GP4 using 3-phenyl-4-(quinolin-2-yl)-3H-1,2,3-oxadiazol-1-ium-5-olate (28.0 mg, 0.096 mmol) and were isolated after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless solids (6.5 mg and 6.5 mg, 0.027 mmol, 56%). Due to low signal intensities in the NOESY and HSQC-NMR experiments it could not be determined which fraction was which isomer. **Isomer 1:** **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.20 (br. s., 1H), 7.84 (m, 1H), 7.76 (m, 1H), 7.61 (m, 3H), 7.43 - 7.52 (m, 1H), 7.26 (s, 5H), 7.12 - 7.22 (m, 2H), 3.74 - 3.83 (m, 2H), 2.79 (t, *J* = 6.8 Hz, 2H), 2.37 (s, 3H), 1.70 (br. s., 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 129.6 (+, *C*H_{Ar}), 128.8 (+, *C*H_{Ar}), 127.8 (+, *C*H_{Ar}), 125.6 (+, *C*H_{Ar}), 123.7 (+, *C*H_{Ar}), 47.0 (−, *C*H_2), 29.7 (−, *C*H_2), 21.5 (+, *C*H_3), 20.7 (−, *C*H_2) ppm. Due to low signal intensities several quaternary carbon were not detected. − **IR** (ATR): $\tilde{\nu}$ = 2920 (m), 2851 (w), 1730 (vw), 1597 (w), 1499 (w), 1458 (w), 1359 (w), 1344 (m), 1289 (w), 1259 (w), 1158 (m), 1088 (m), 1064 (m), 1002 (m) cm^{-1}. − **MS** (FAB), *m/z* (%): 481.2 (4) $[M+H]^+$, 325.0 (16), 132.8 (100). − **HRMS** (EI, $C_{28}H_{25}N_4O_2{}^{32}S$): calc. 481.1693; found 481.1692. **Isomer 2:** **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.8 Hz, 1H), 7.95 - 8.02 (m, 2H), 7.75 - 7.86 (m, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.27 - 7.31 (m, 7H), 7.26 (br. s., 2H), 7.06 (d, *J* = 8.5 Hz, 1H), 3.84 - 3.94 (m, 2H), 2.81 (br. s., 2H), 2.41 (s, 3H), 1.95 - 2.04 (m, 3H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 147.5 (*C*$_q$), 143.8 (*C*$_q$), 135.7 (*C*$_q$, 129.3 (*C*$_q$), 128.9 (*C*$_q$), 128.3 (+, *C*H_{Ar}), 127.6 (+, *C*H_{Ar}), 127.1 (+, *C*H_{Ar}), 126.9 (+, *C*H_{Ar}), 124.7 (+, *C*H_{Ar}), 122.3 (+, *C*H_{Ar}), 46.8 (−, *C*H_2), 29.7 (−, *C*H_2), 22.7 (−, *C*H_2), 21.6 (+, *C*H_3) ppm. − **IR** (ATR): $\tilde{\nu}$ = 2919 (w), 2850 (w), 1730 (vw), 1595 (w), 1493 (w), 1458 (w), 1359 (w), 1289 (w), 1259 (w), 1162 (m), 1088 (w), 1007 (m) cm^{-1}. − **MS** (FAB), *m/z* (%): 481.2 (23) $[M+H]^+$, 325.1 (18), 132.8 (100). − **HRMS** (EI, $C_{28}H_{25}N_4O_2{}^{32}S$): calc. 481.1693; found 481.1692.

2-phenyl-3-(p-tolyl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (27a)

2-phenyl-3-(p-tolyl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (27b)



A

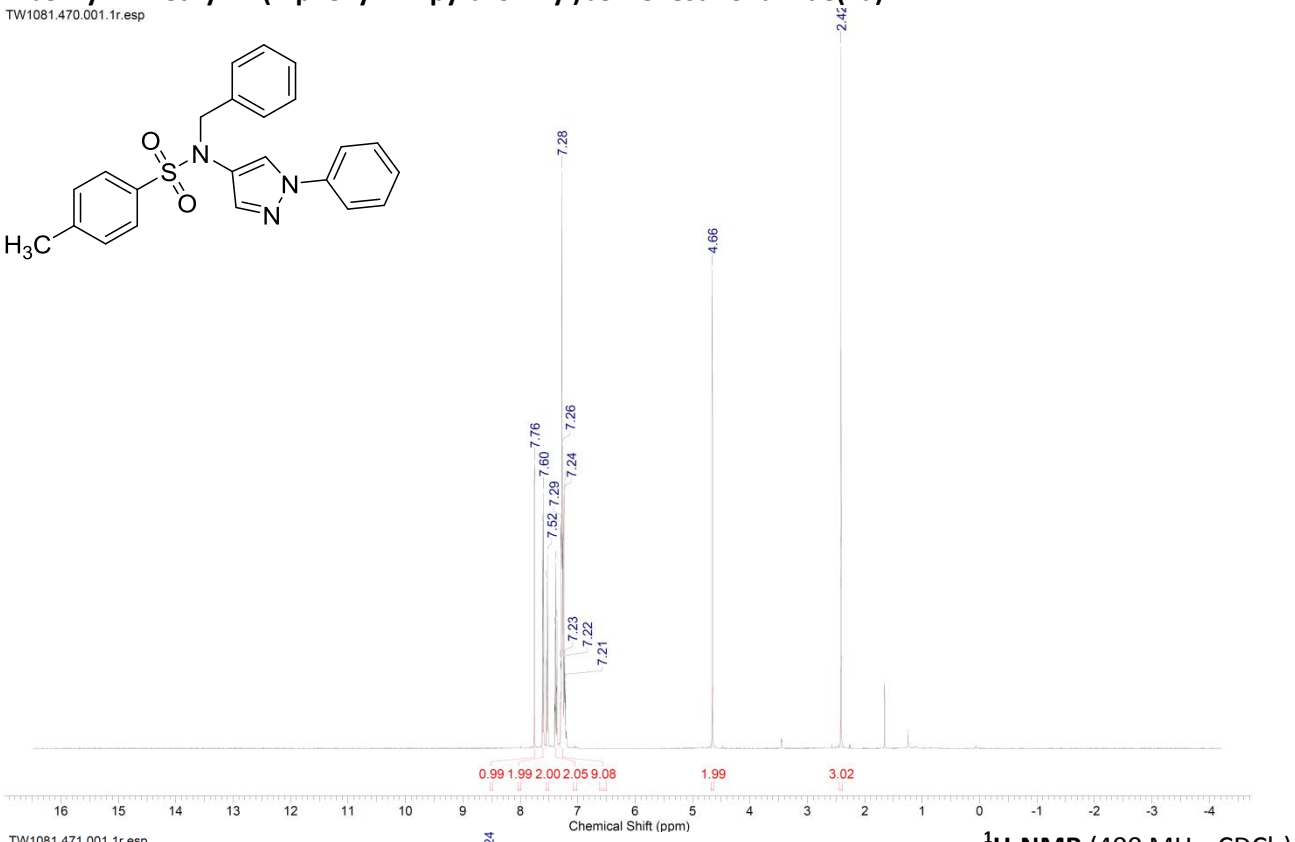


B

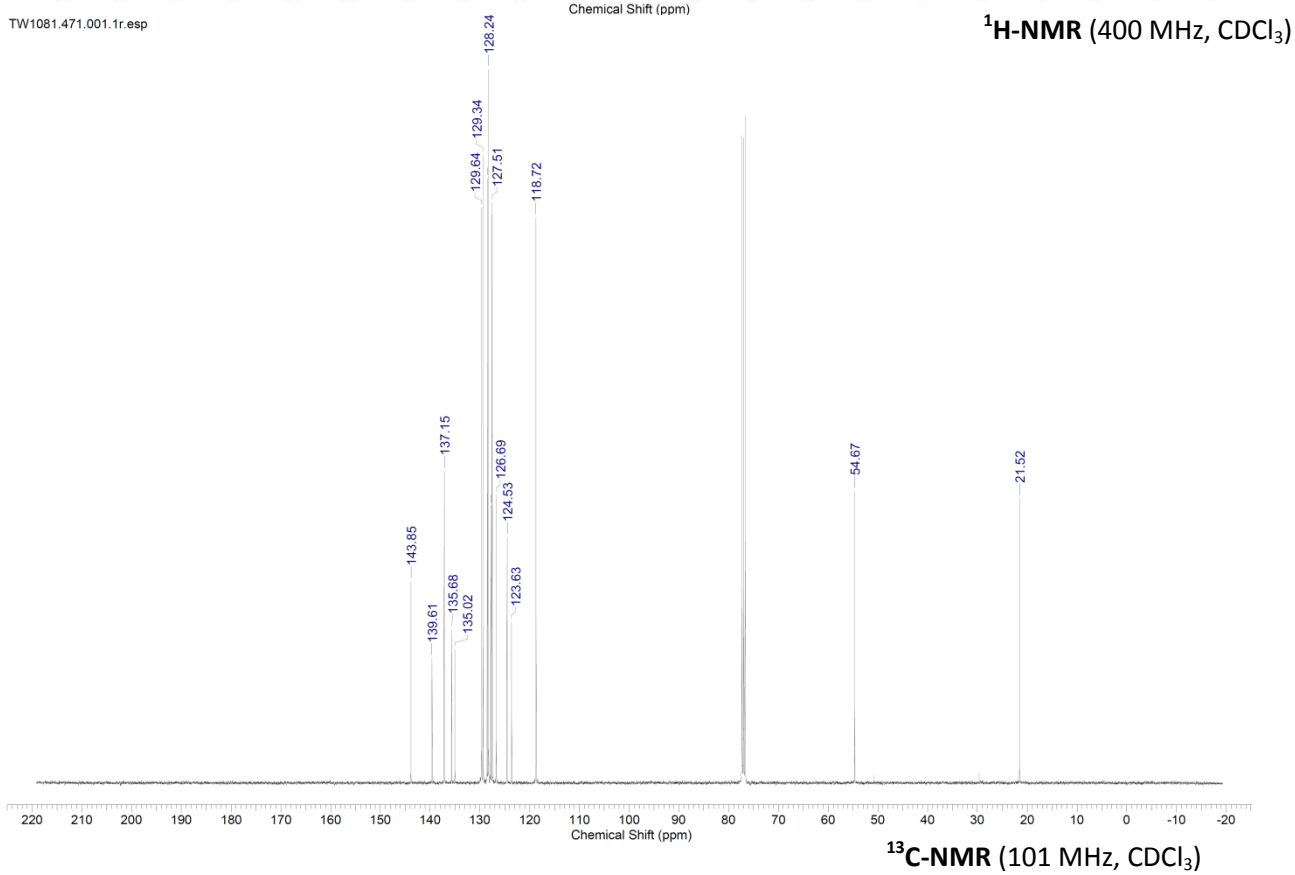
These compounds were prepared according to general procedure GP4 using 3-phenyl-4-(p-tolyl)-3H-1,2,3-oxadiazol-1-ium-5-olate (23.0 mg, 0.092 mmol) and were isolated after preparative TLC (*c*Hex/EtOAc = 4:1) as colorless solids (10.0 mg (A) and 8.0 mg (B), 0.041 mmol, 80%). **Isomer (A): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.3 Hz, 2H), 7.26 - 7.31 (m, 3H), 7.16 - 7.21 (m, 4H), 7.05 - 7.16 (m, 4H), 3.69 - 3.76 (m, 2H), 2.68 (t, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 2.34 (s, 3H), 1.59 - 1.68 (m, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 143.5 (C_q), 143.4 (C_q), 140.2 (C_q), 138.0 (C_q), 136.5 (C_q), 136.4 (C_q), 129.9 (+, CH_{Ar}), 129.4 (+, CH_{Ar}), 128.9 (+, CH_{Ar}), 128.6 (+, CH_{Ar}), 127.6 (+, CH_{Ar}), 127.3 (+, CH_{Ar}), 125.6 (+, CH_{Ar}), 119.0 (C_q), 47.5 (–, CH_2), 29.7 (–, CH_2), 21.6 (+, CH_3), 21.5 (+, CH_3), 20.4 (–, CH_2), 19.5 (–, CH_2) ppm. – **IR** (ATR): ṽ = 2918 (w), 2849 (w), 1692 (w), 1594 (w), 1519 (w), 1498 (m), 1448 (w), 1344 (m), 1286 (m), 1161 (w), 1161 (m), 1088 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 443.3 (7) $[M]^+$, 288.2 (50), 194.1 (100). – **HRMS** (EI, $C_{26}H_{25}N_3O_2{}^{32}S$): calc.443.1662; found 443.1660. – **Isomer (B): ^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 3H), 7.16 - 7.25 (m, 4H), 7.10 (m, *J* = 7.8 Hz, 2H), 6.99 (m, *J* = 8.1 Hz, 2H), 3.83 - 3.91 (m, 2H), 2.50 (t, *J* = 6.3 Hz, 2H), 2.40 (s, 3H), 2.33 (s, 3H), 1.92 (dt, *J* = 11.2, 5.9 Hz, 2H) ppm. – **^{13}C-NMR** (101 MHz, $CDCl_3$): δ = 146.8 (C_q), 143.5 (C_q), 140.1 (C_q), 138.4 (C_q), 138.2 (C_q), 136.2 (C_q), 129.2 (+, CH_{Ar}), 129.1 (+, CH_{Ar}), 129.0 (+, CH_{Ar}), 128.5 (+, CH_{Ar}), 128.4 (+, CH_{Ar}), 127.2 (+, CH_{Ar}), 126.2 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 106.3 (C_q), 46.8 (–, CH_2), 29.7 (–, CH_2), 22.9 (–, CH_2), 21.6 (+, CH_3), 21.3 (+, CH_3), 19.7 (–, CH_2) ppm. – **IR** (ATR): ṽ = 2918 (w), 2849 (w), 1693 (w), 1594 (w), 1519 (w), 1498 (m), 1448 (w), 1344 (m), 1286 (m), 1161 (w), 1161 (m), 1088 (m) cm^{-1}. – **MS** (EI), *m/z* (%): 443.3 (77) $[M]^+$, 288.2 (100). – **HRMS** (EI, $C_{26}H_{25}N_3O_2{}^{32}S$): calc.443.1662; found 443.1664.

Spectra

N-benzyl-4-methyl-*N*-(1-phenyl-1H-pyrazol-4-yl)benzenesulfonamide(4a)

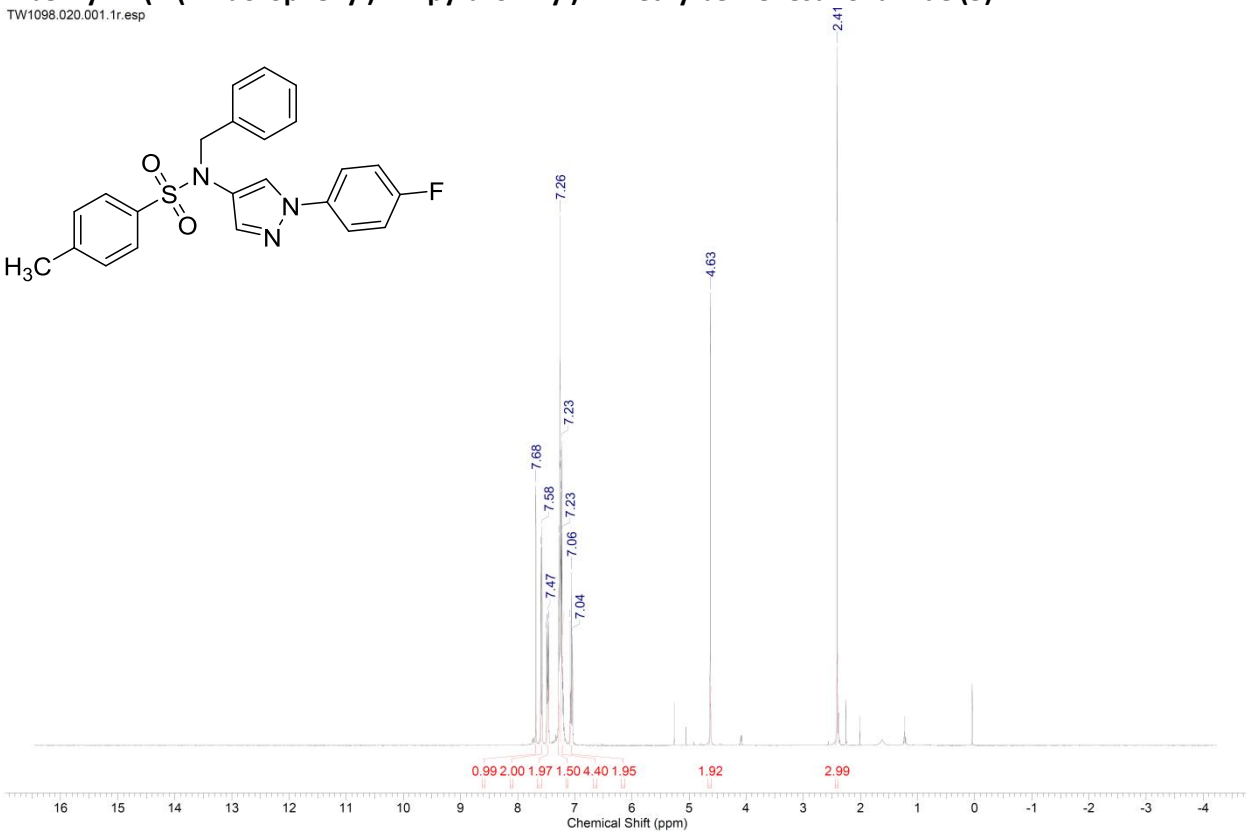


^{1}**H-NMR** (400 MHz, $CDCl_3$)

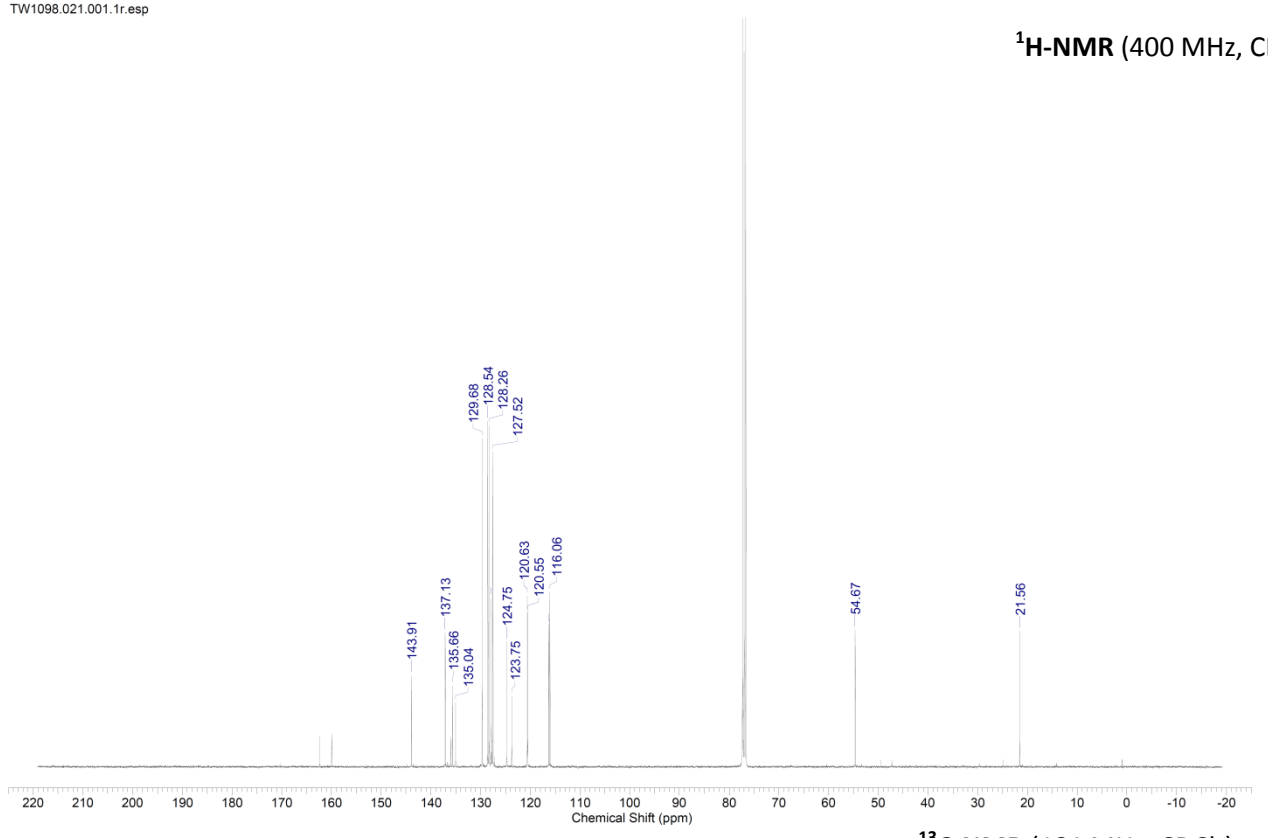


^{13}**C-NMR** (101 MHz, $CDCl_3$)

***N*-benzyl-*N*-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)-4-methylbenzenesulfonamide (5)**

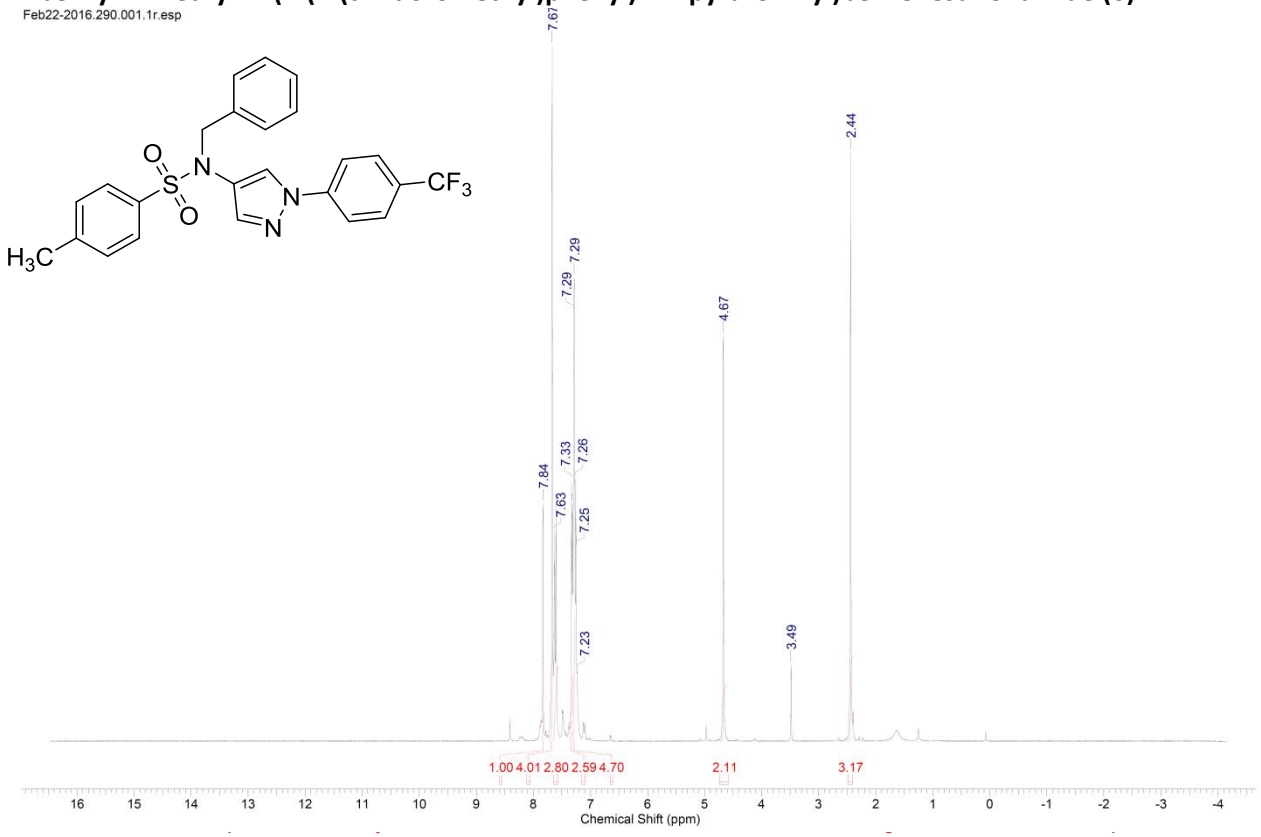


^{1}H-NMR (400 MHz, $CDCl_3$)

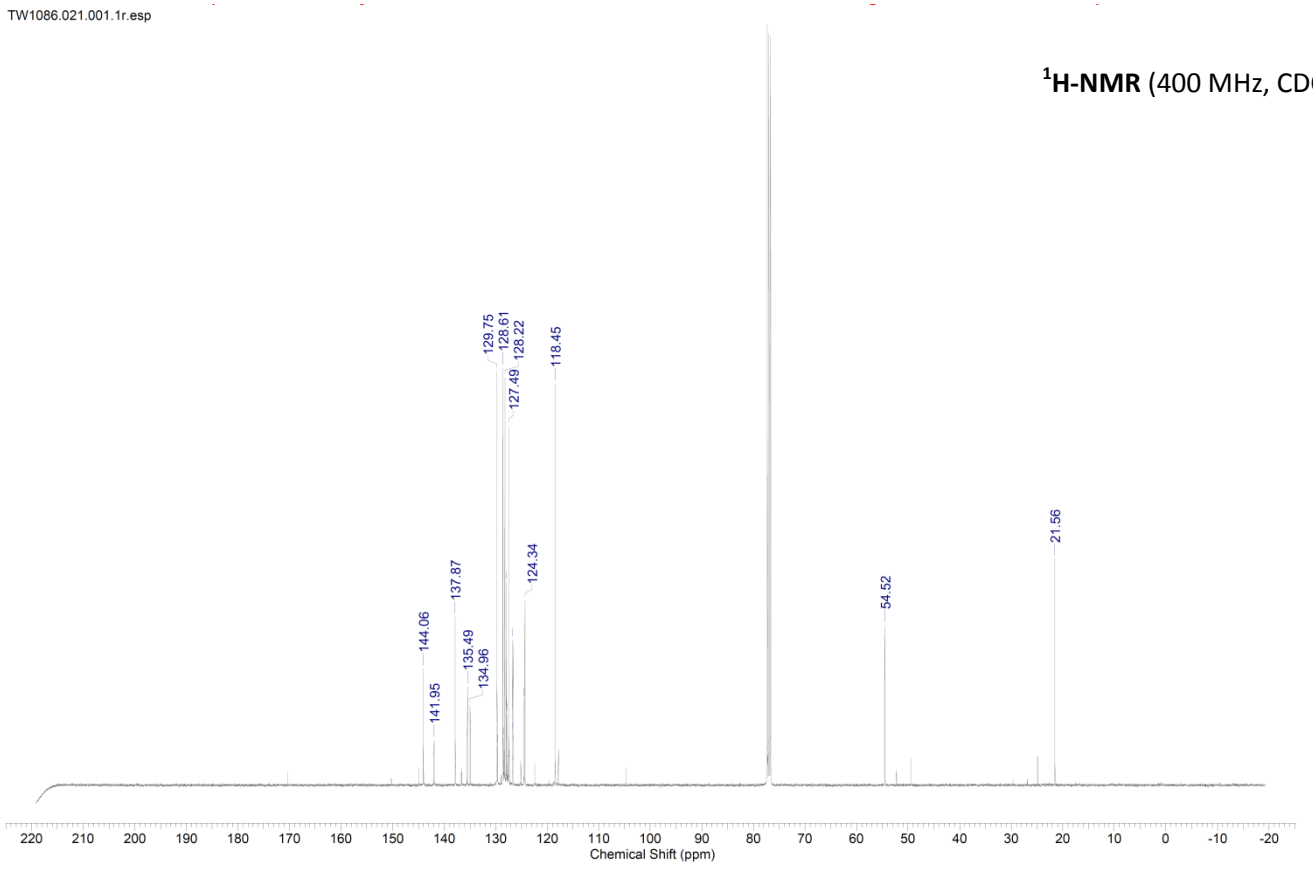


^{13}C-NMR (101 MHz, $CDCl_3$)

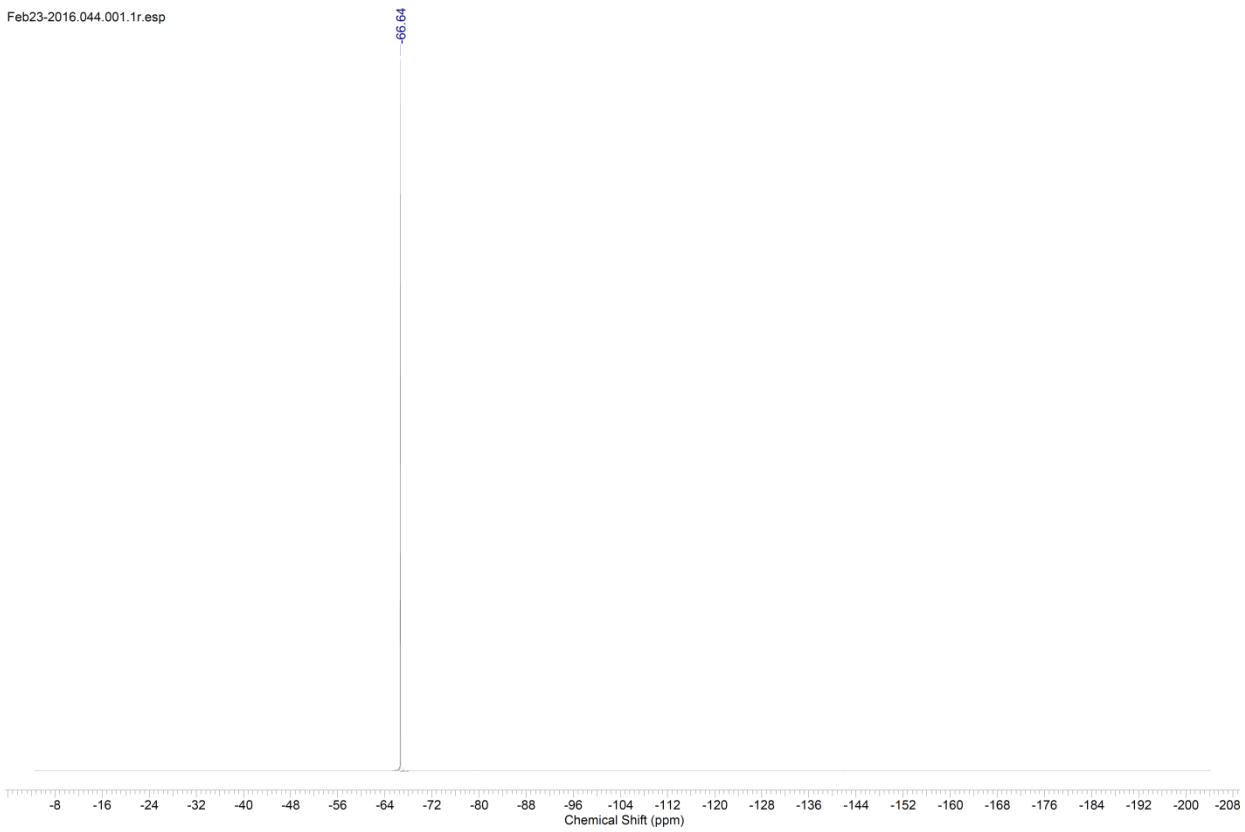
***N*-benzyl-4-methyl-*N*-(1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-4-yl)benzenesulfonamide (6)**



^{1}H-NMR (400 MHz, $CDCl_3$)

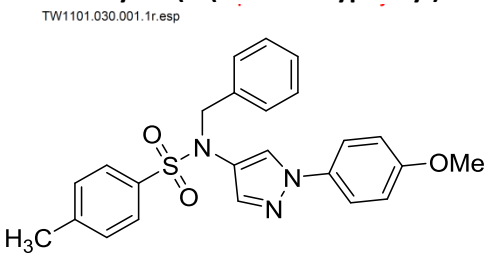


^{13}C-NMR (101 MHz, $CDCl_3$)

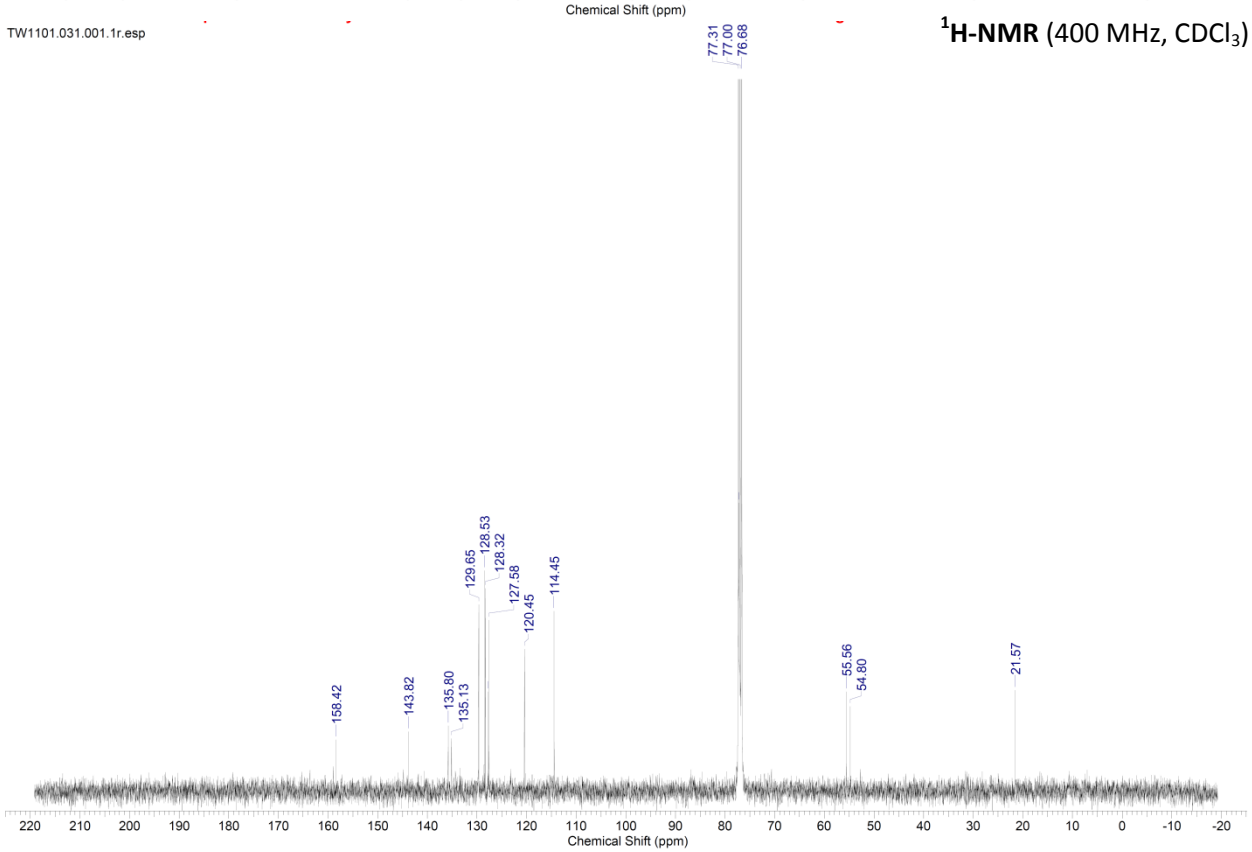


^{19}F-NMR (377 MHz, $CDCl_3$)

***N*-benzyl-*N*-(1-(4-methoxyphenyl)-1H-pyrazol-4-yl)-4-methylbenzenesulfonamide (7)**

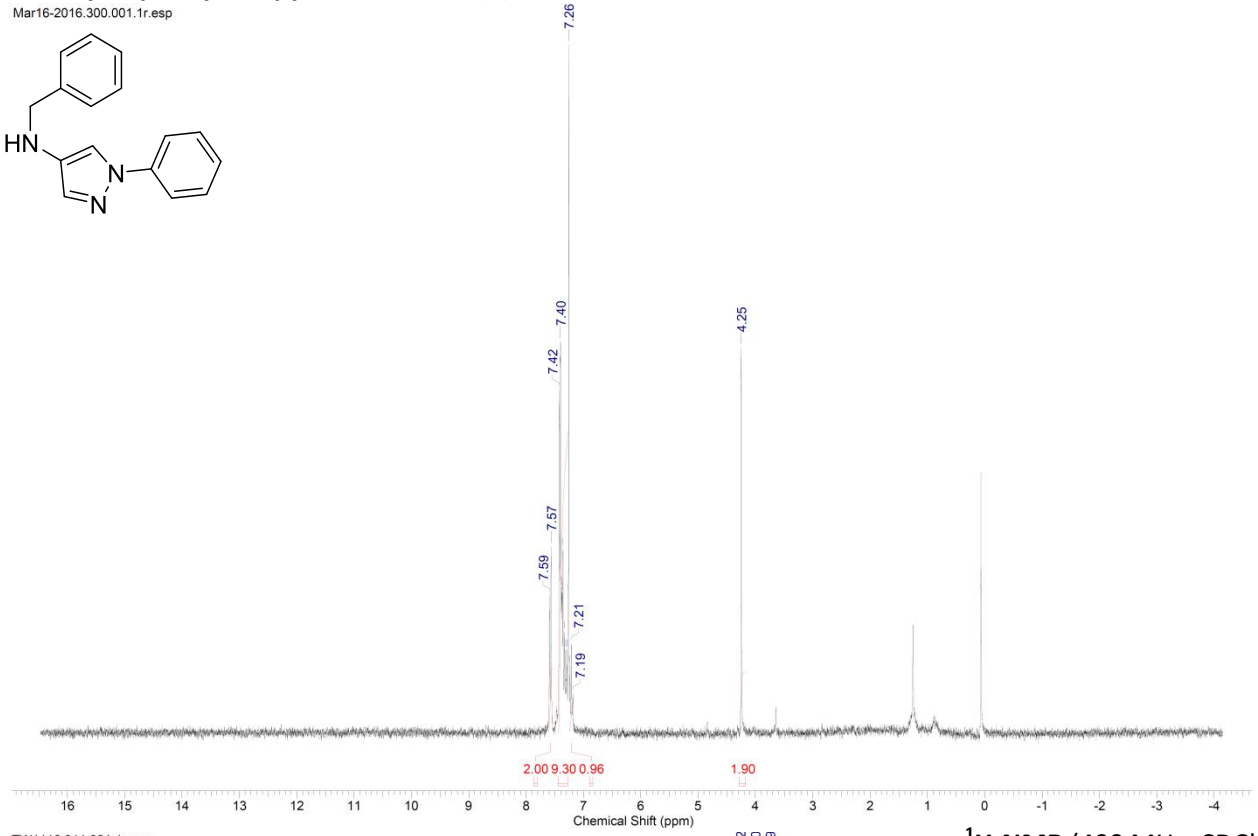


^{1}H-NMR (400 MHz, $CDCl_3$)

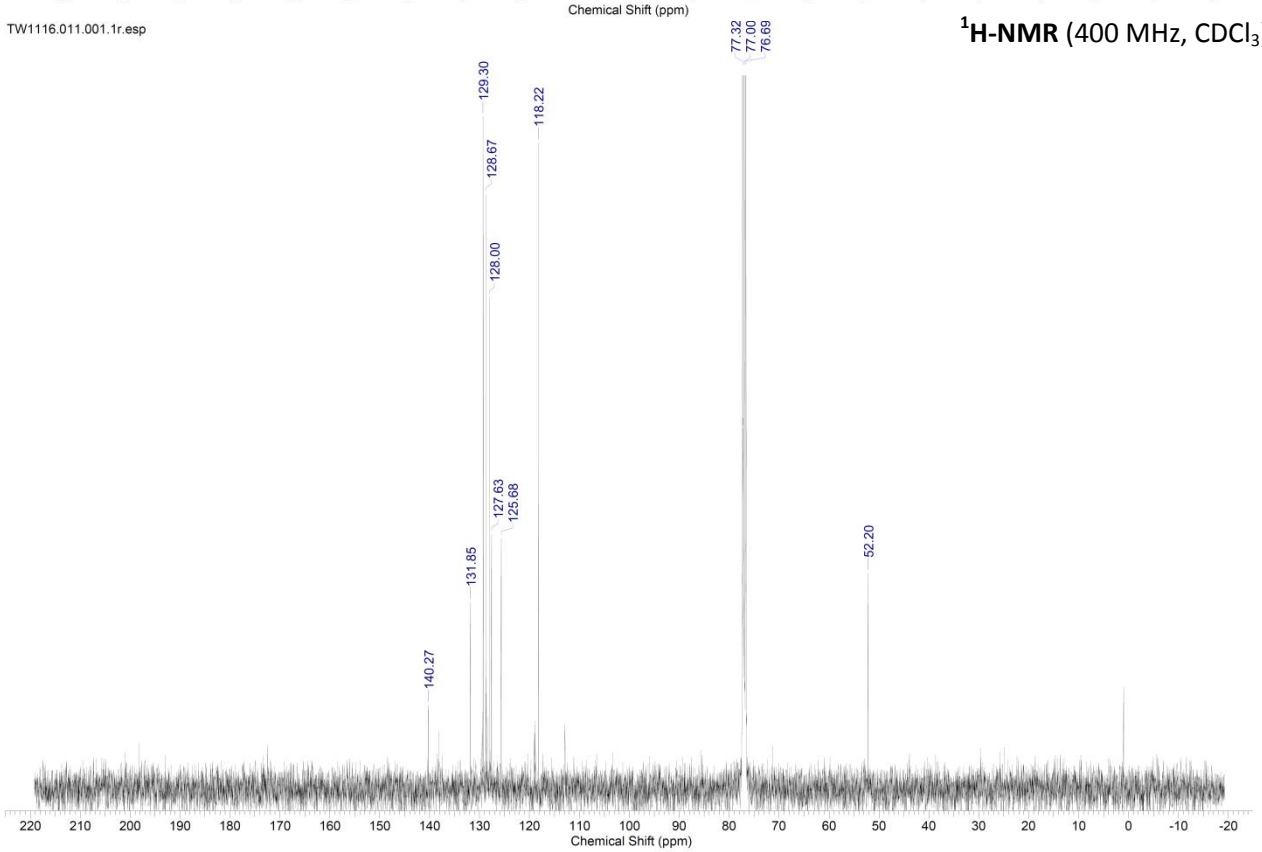


^{13}C-NMR (101 MHz, $CDCl_3$)

***N*-benzyl-1-phenyl-1H-pyrazol-4-amine (8)**

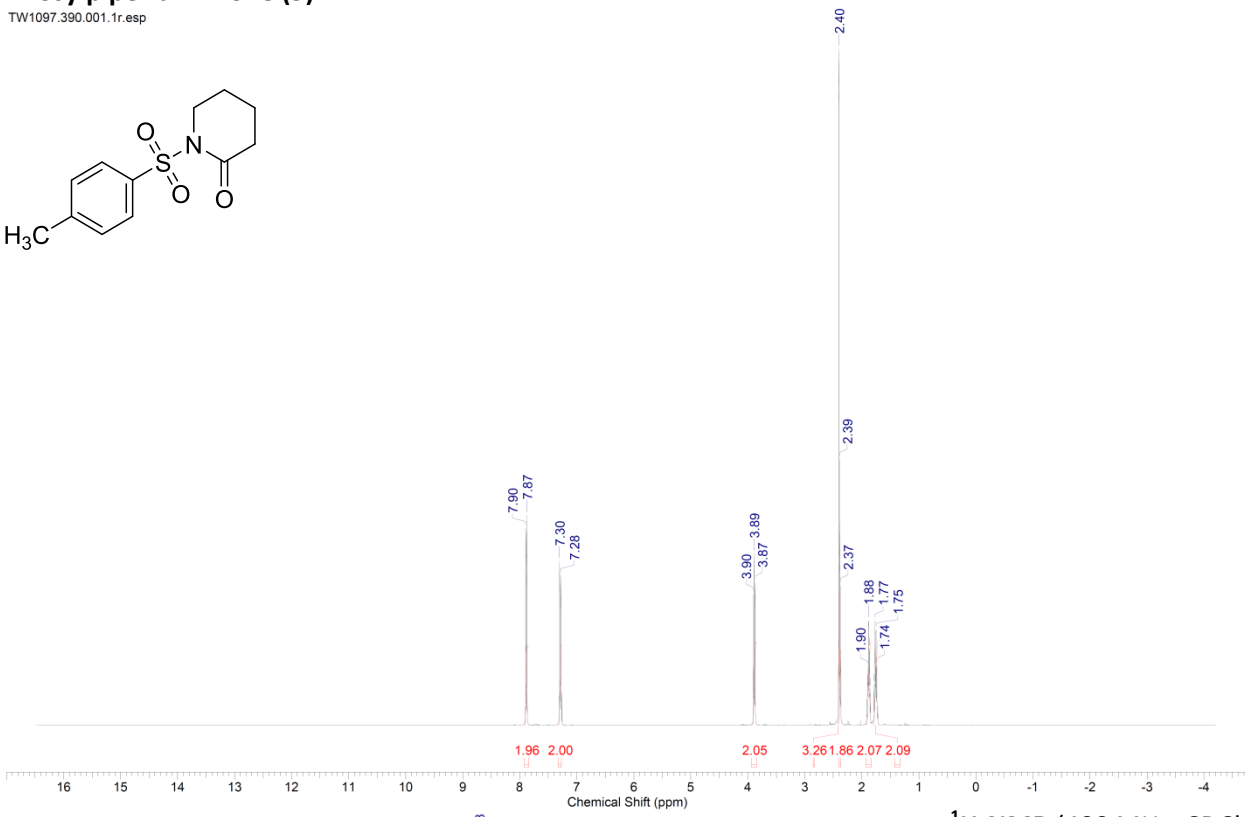


^{1}H-NMR (400 MHz, $CDCl_3$)

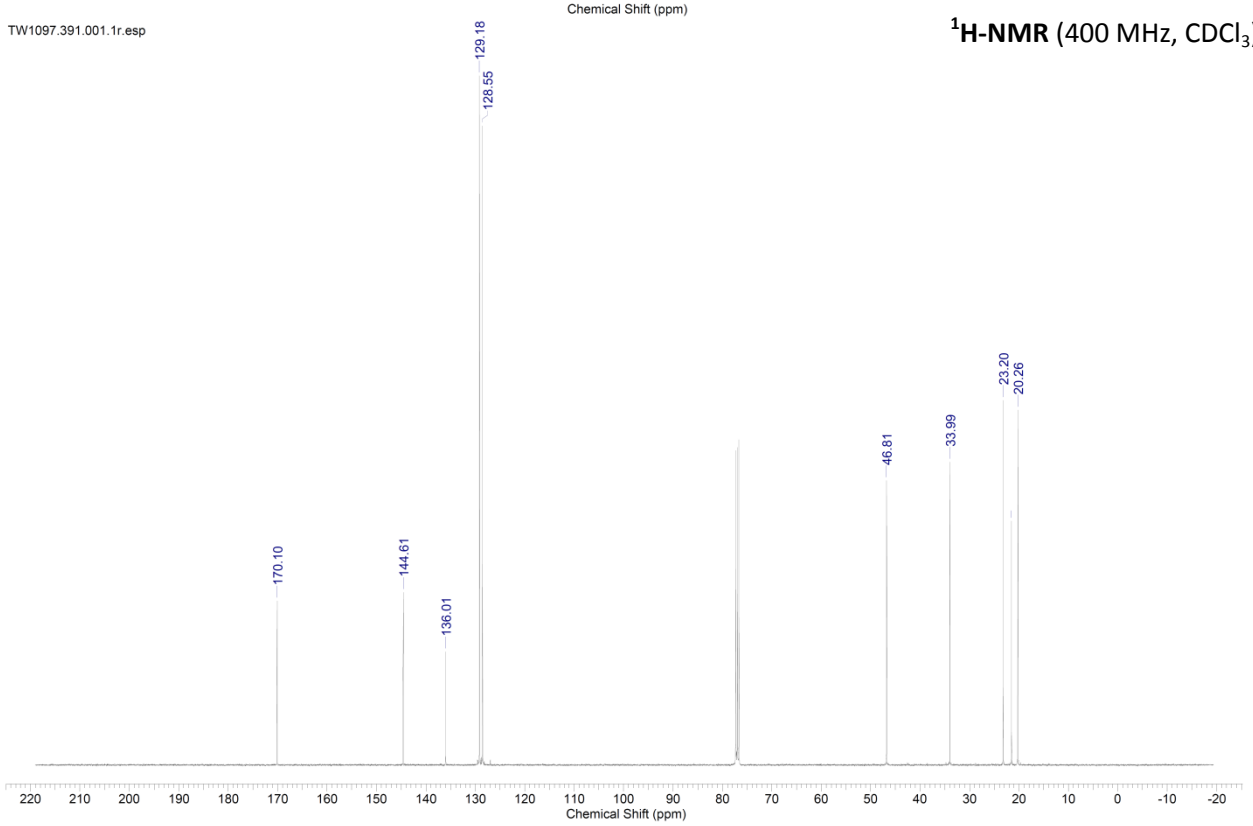


^{13}C-NMR (101 MHz, $CDCl_3$)

1-Tosylpiperidin-2-one (9)



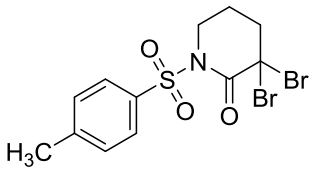
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)

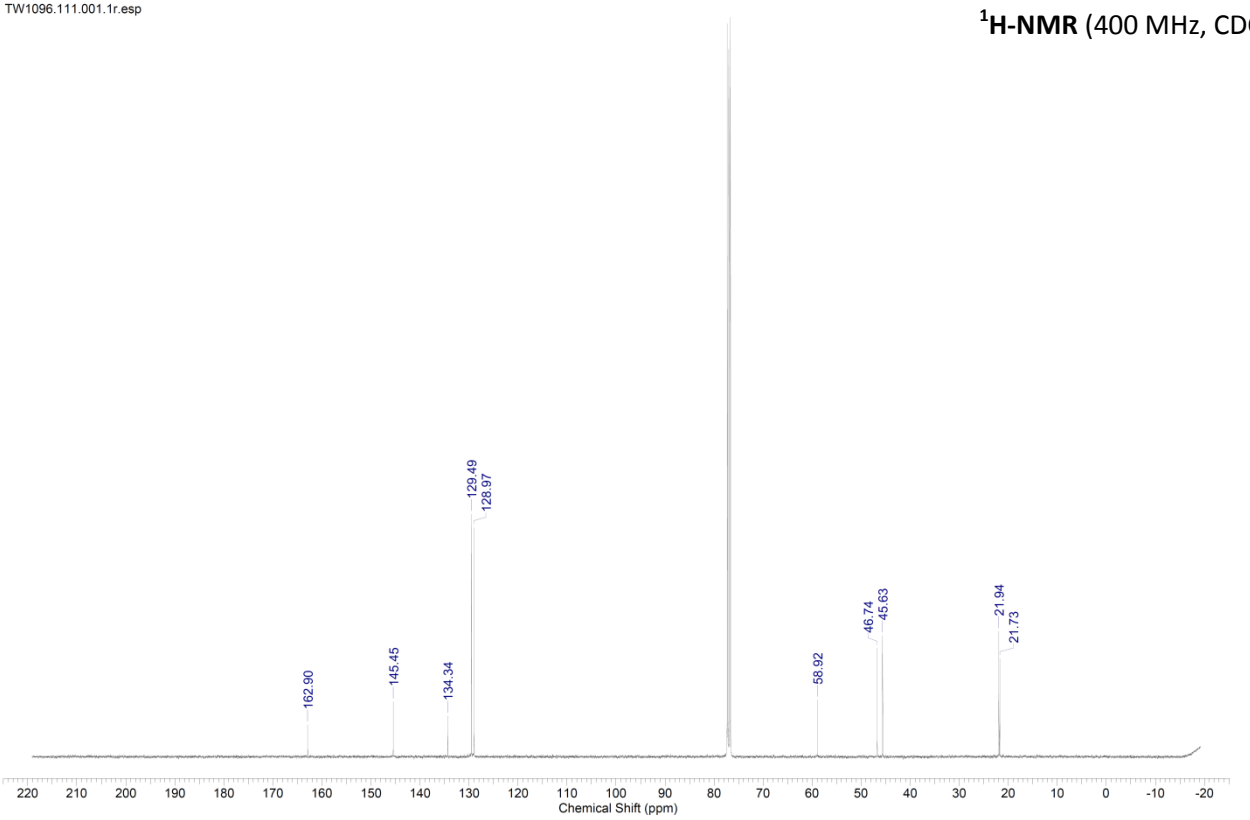
3,3-Dibromo-1-tosylpiperidin-2-one (S6)

TW1096.110.001.1r.esp



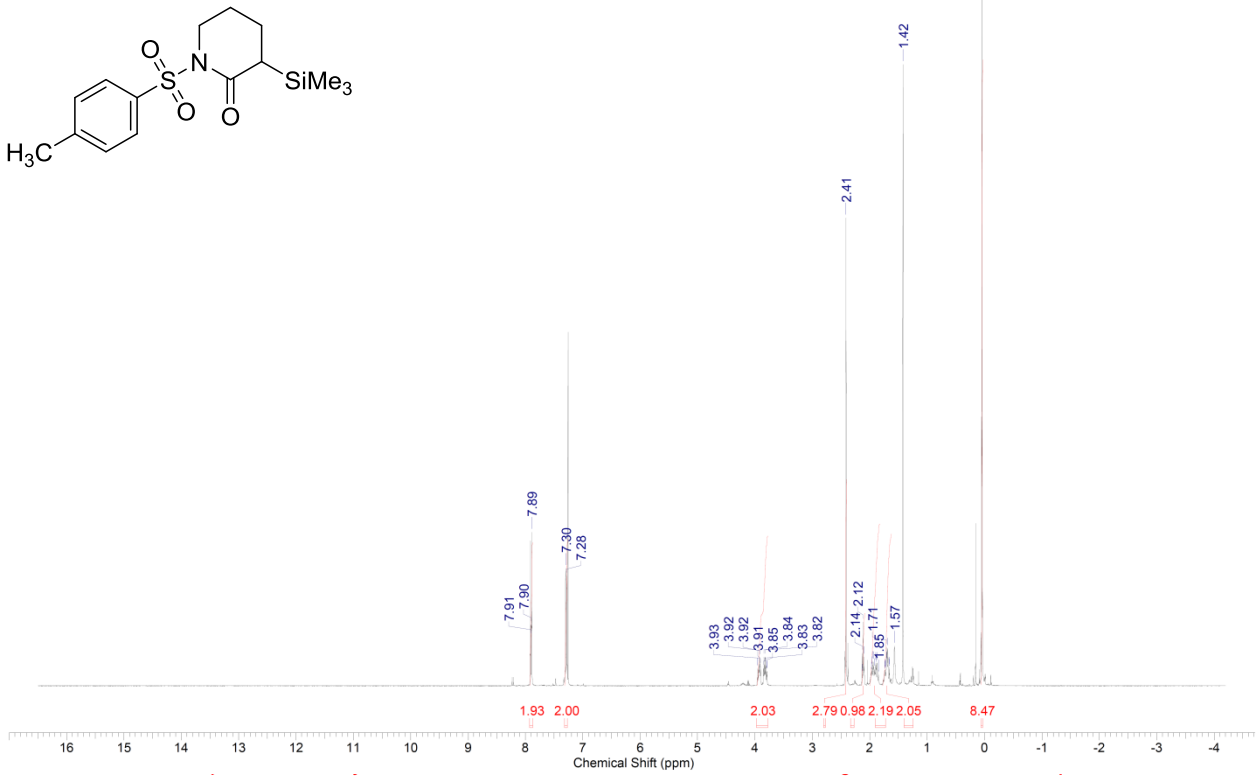
^{1}H-NMR (400 MHz, $CDCl_3$)

TW1096.111.001.1r.esp

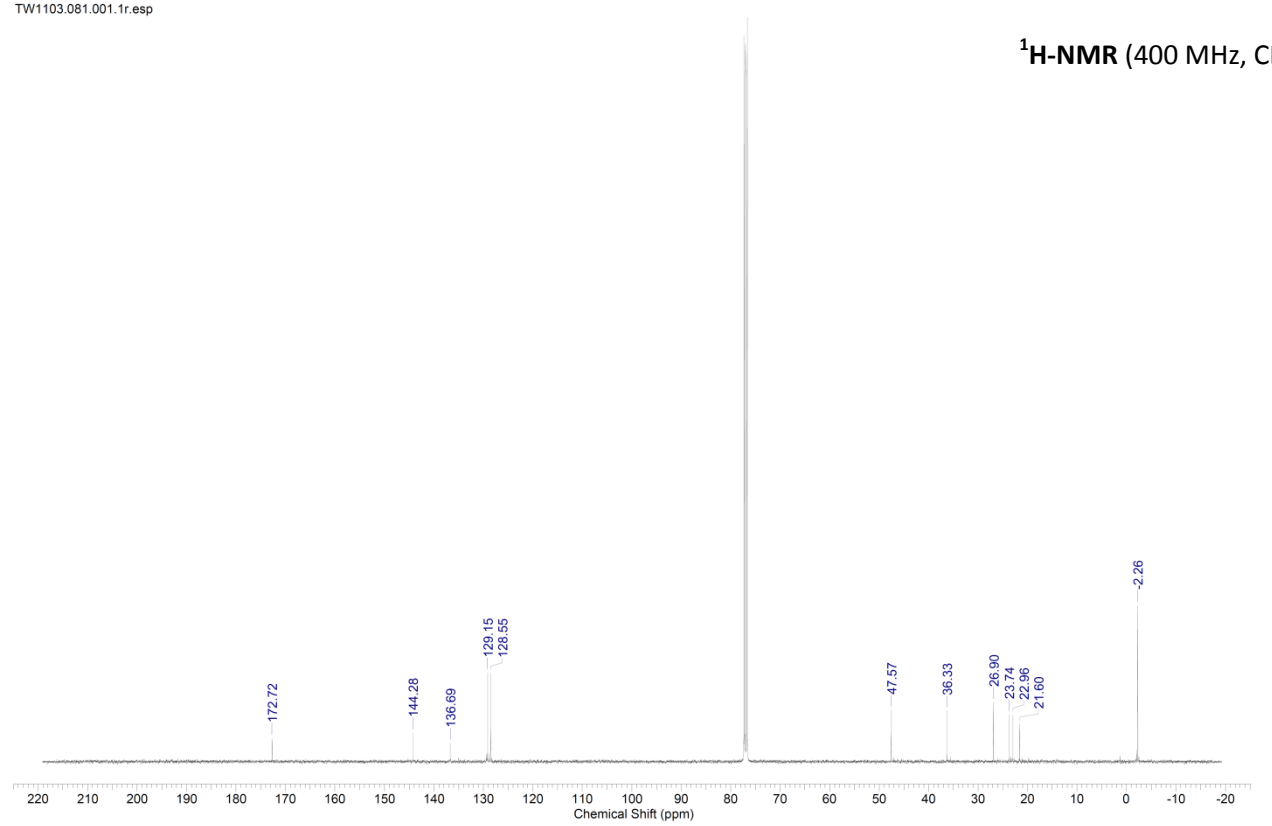


^{13}C-NMR (101 MHz, $CDCl_3$)

1-Tosyl-3-(trimethylsilyl)piperidin-2-one (S7)

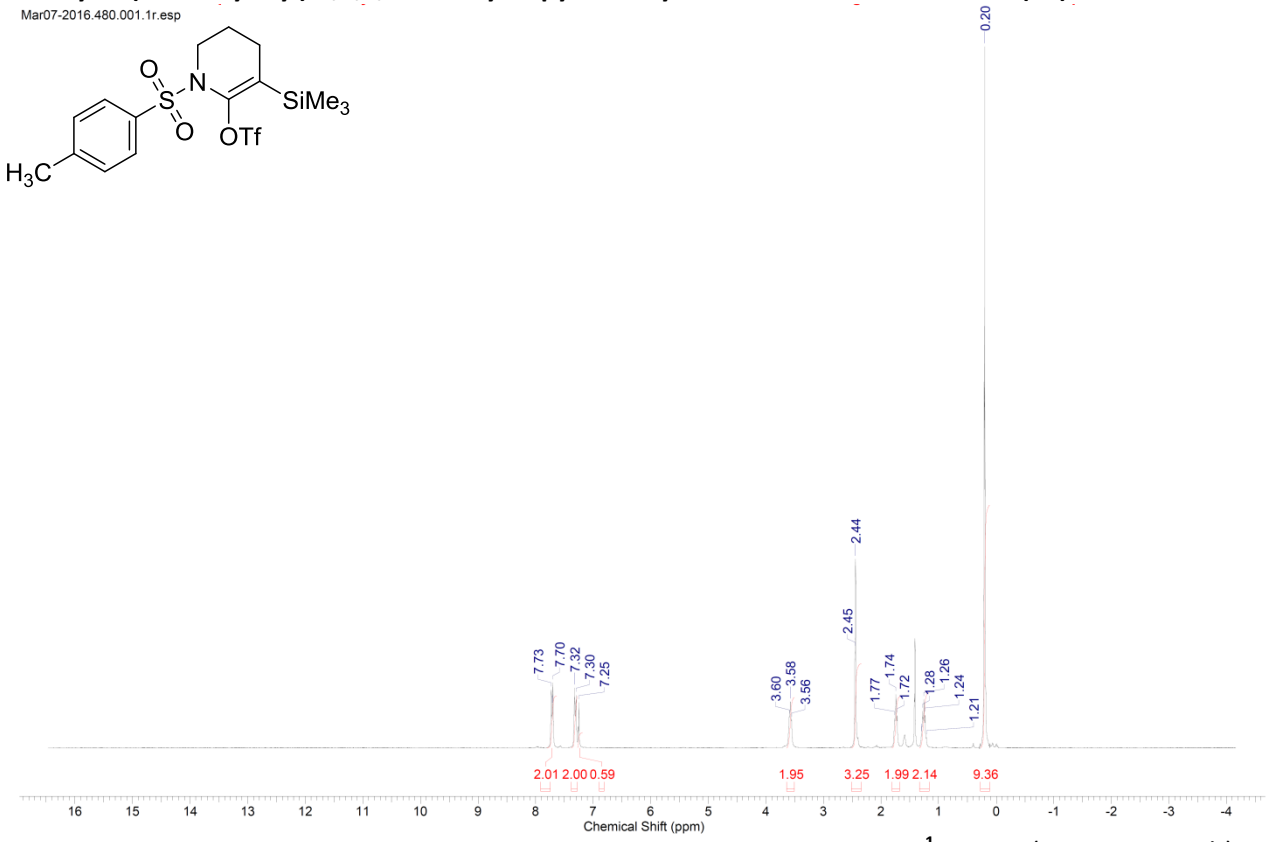


^{1}H-NMR (400 MHz, $CDCl_3$)

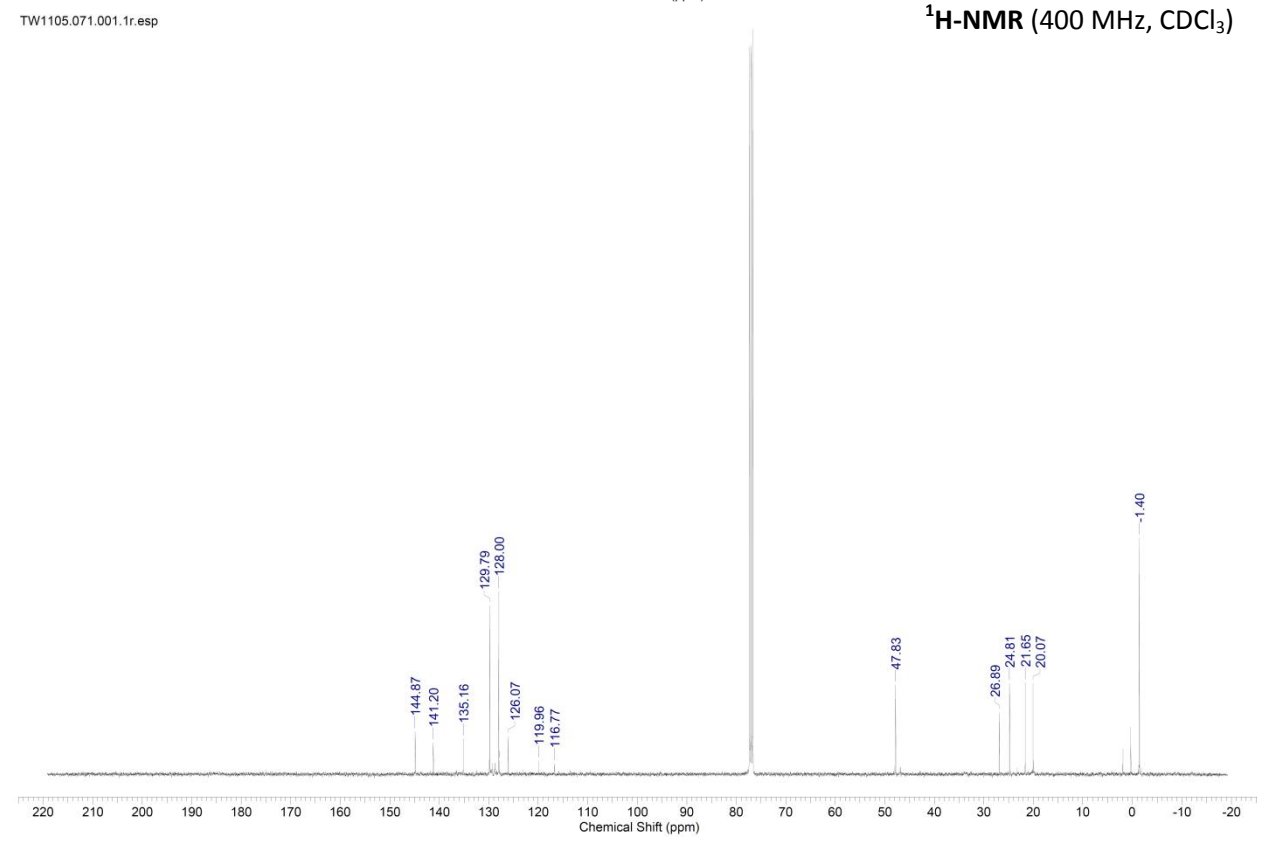


^{13}C-NMR (101 MHz, $CDCl_3$)

1-Tosyl-3-(trimethylsilyl)-1,4,5,6-tetrahydropyridin-2-yl trifluoromethanesulfonate (10)

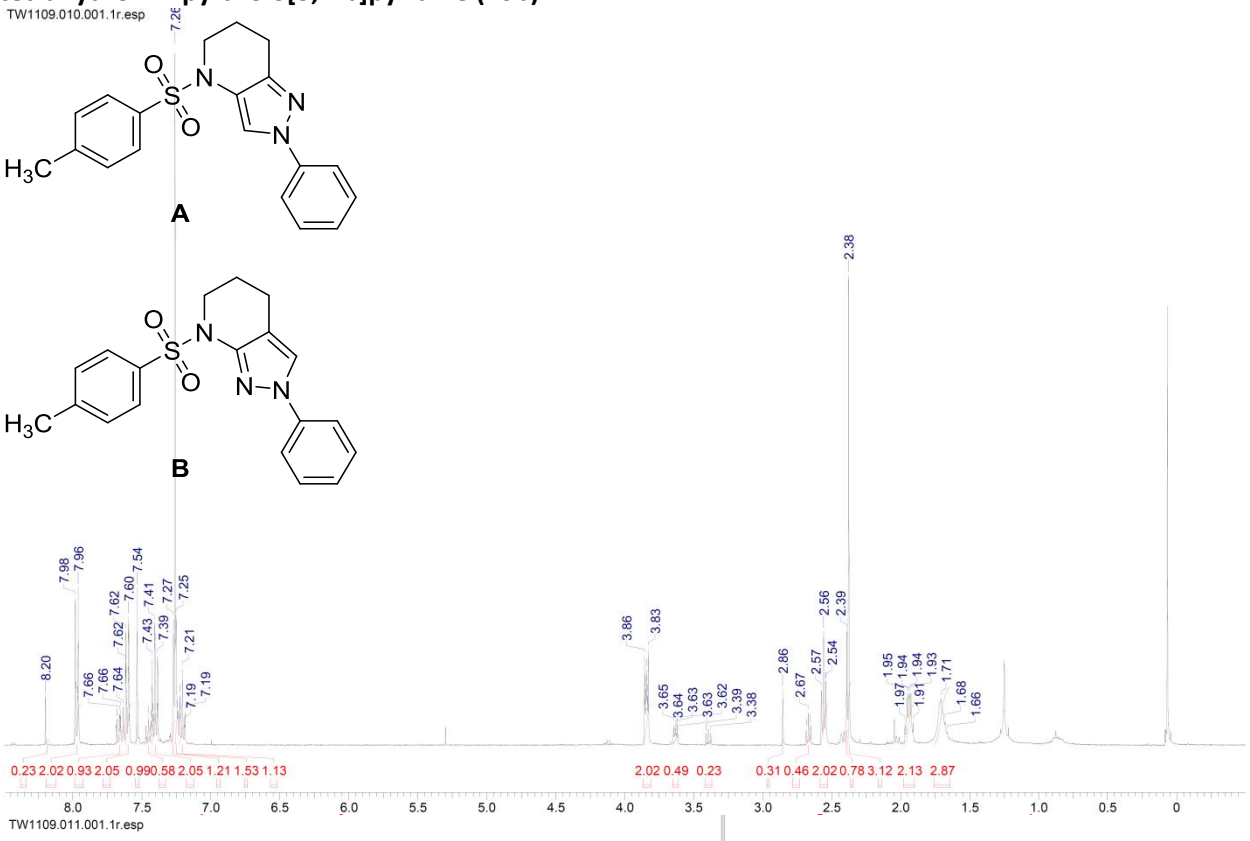


^{1}H-NMR (400 MHz, $CDCl_3$)

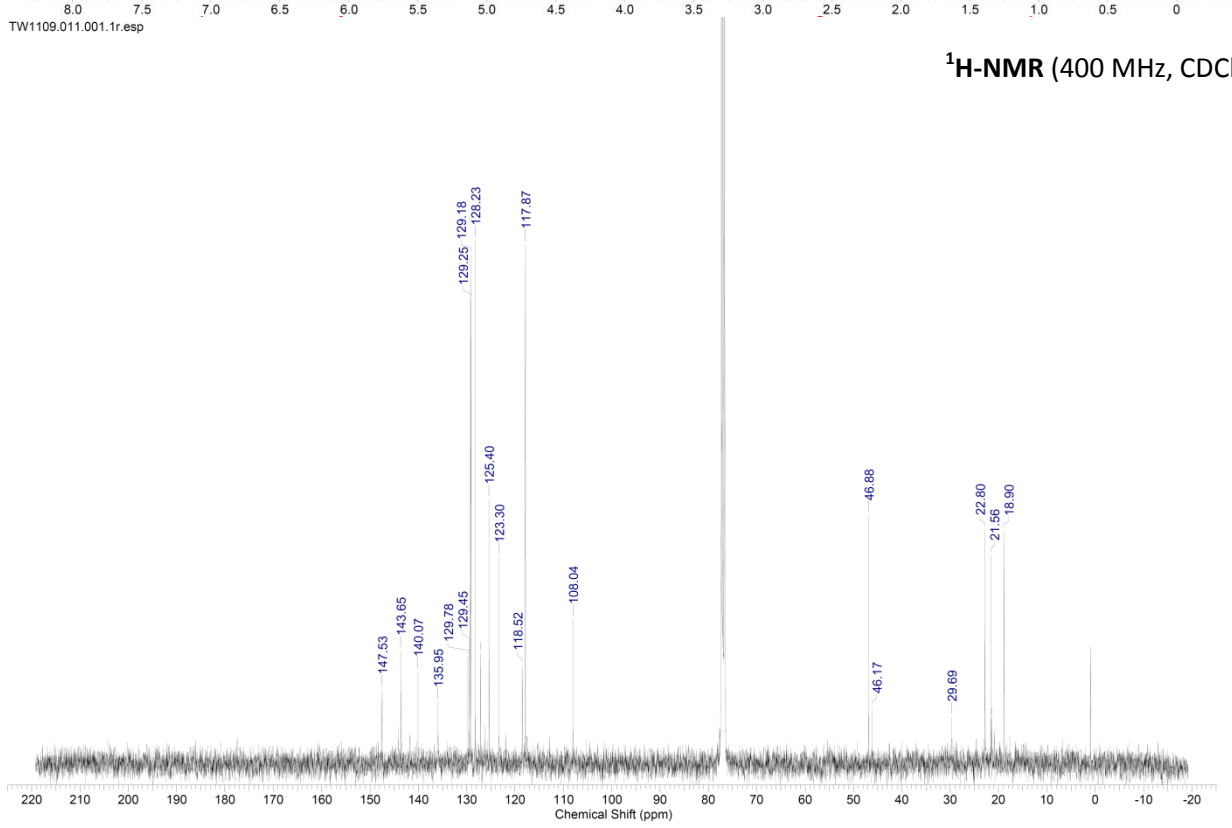


^{13}C-NMR (101 MHz, $CDCl_3$)

2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (20a) and 2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (20b)

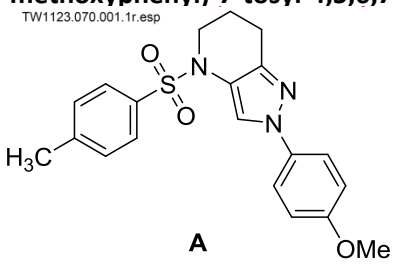


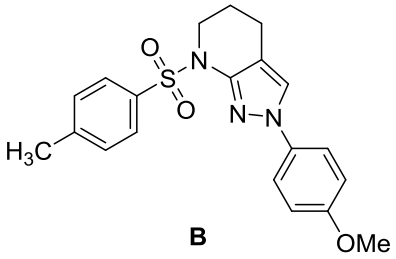
^{1}H-NMR (400 MHz, $CDCl_3$)



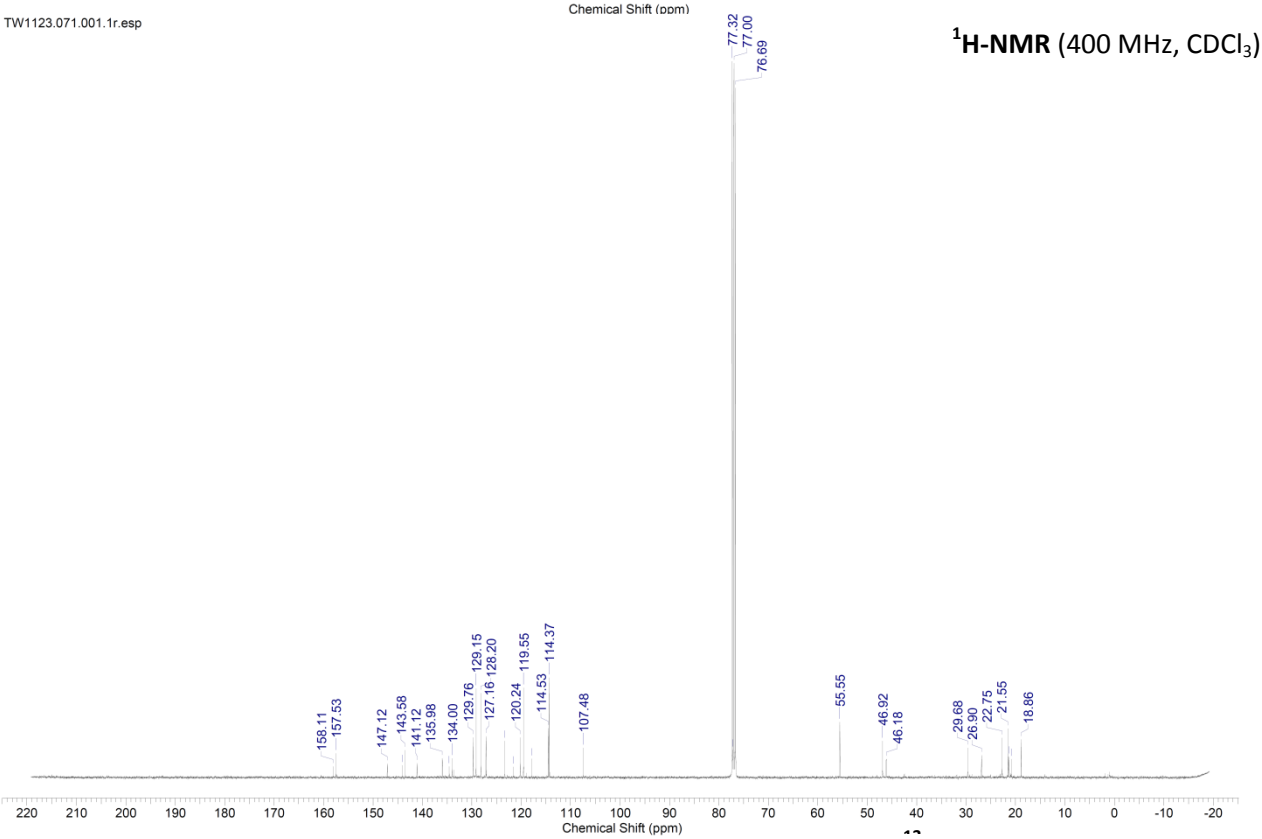
^{13}C-NMR (101 MHz, $CDCl_3$)

2-(4-methoxyphenyl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (21a) and 2-(4-methoxyphenyl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (21b)



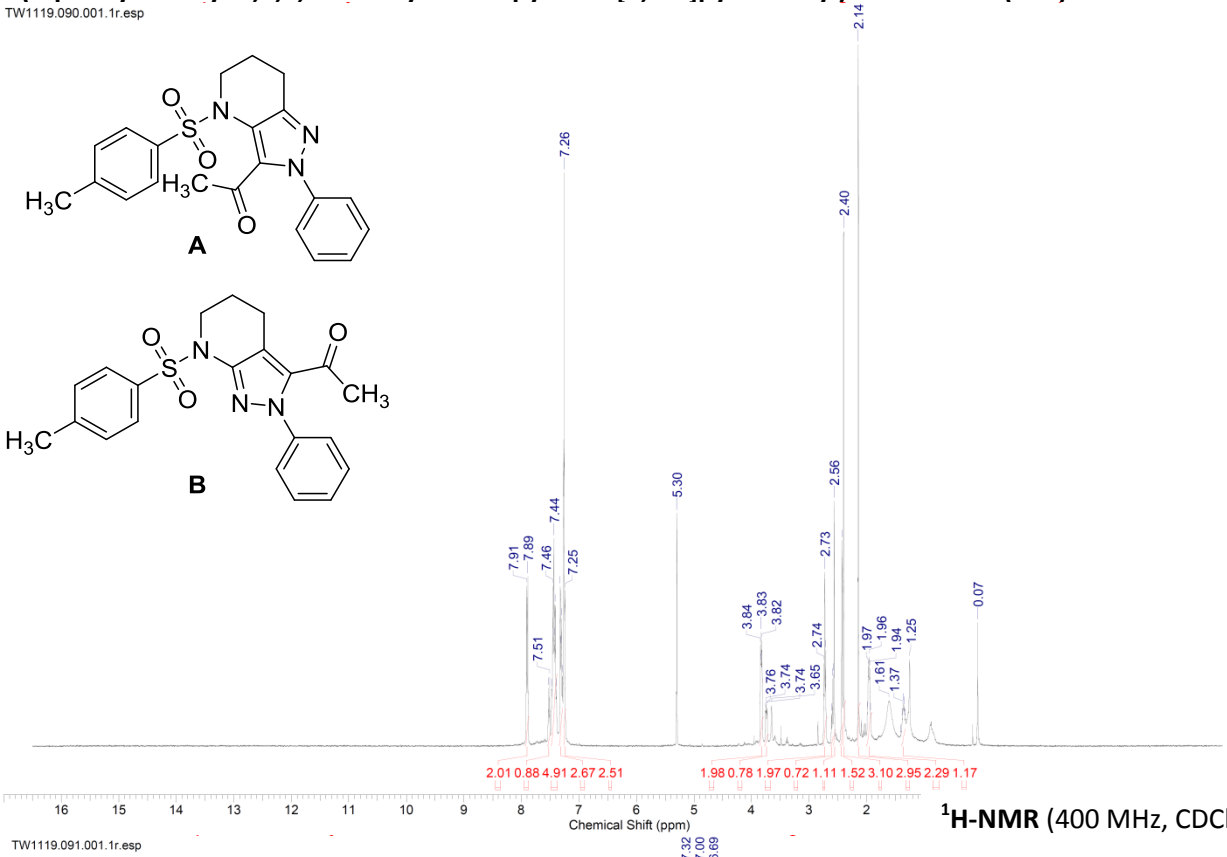


^{1}**H-NMR** (400 MHz, $CDCl_3$)

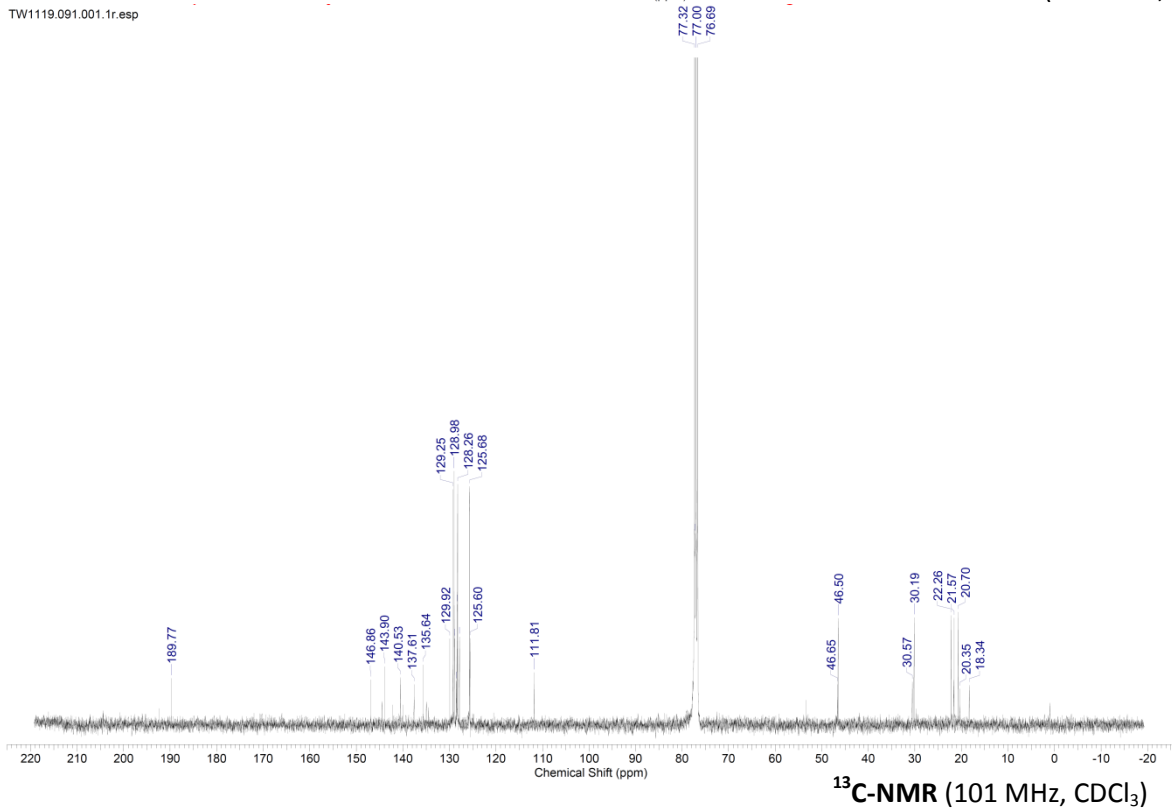


^{13}**C-NMR** (101 MHz, $CDCl_3$)

1-(2-phenyl-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridin-3-yl)ethan-1-one (22a)
1-(2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridin-3-yl)ethan-1-one (22b)

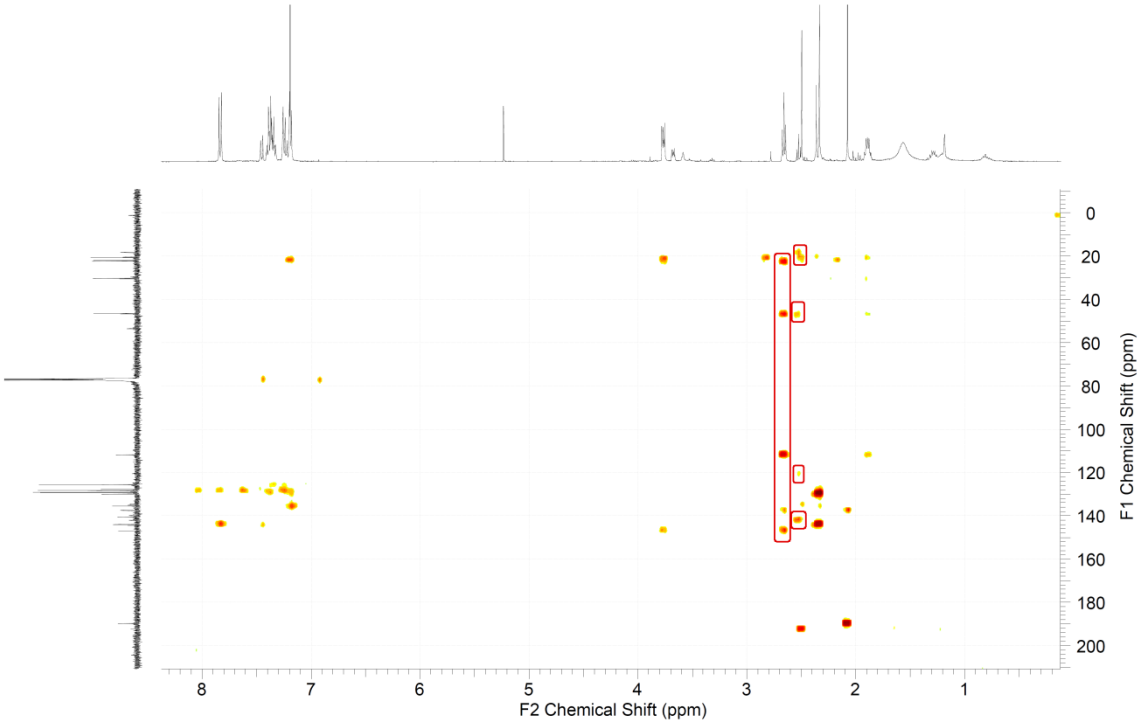


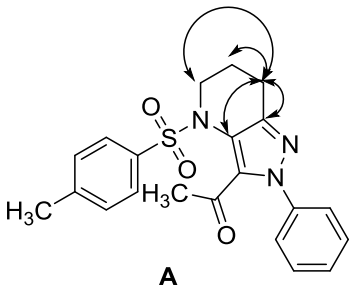
^{1}H-NMR (400 MHz, $CDCl_3$)



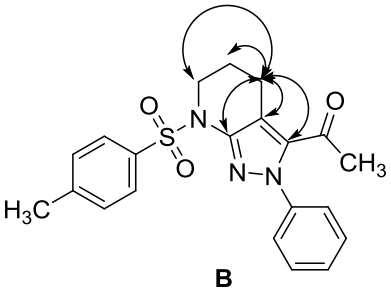
^{13}C-NMR (101 MHz, $CDCl_3$)

HMBC spectrum for compounds 22a&b



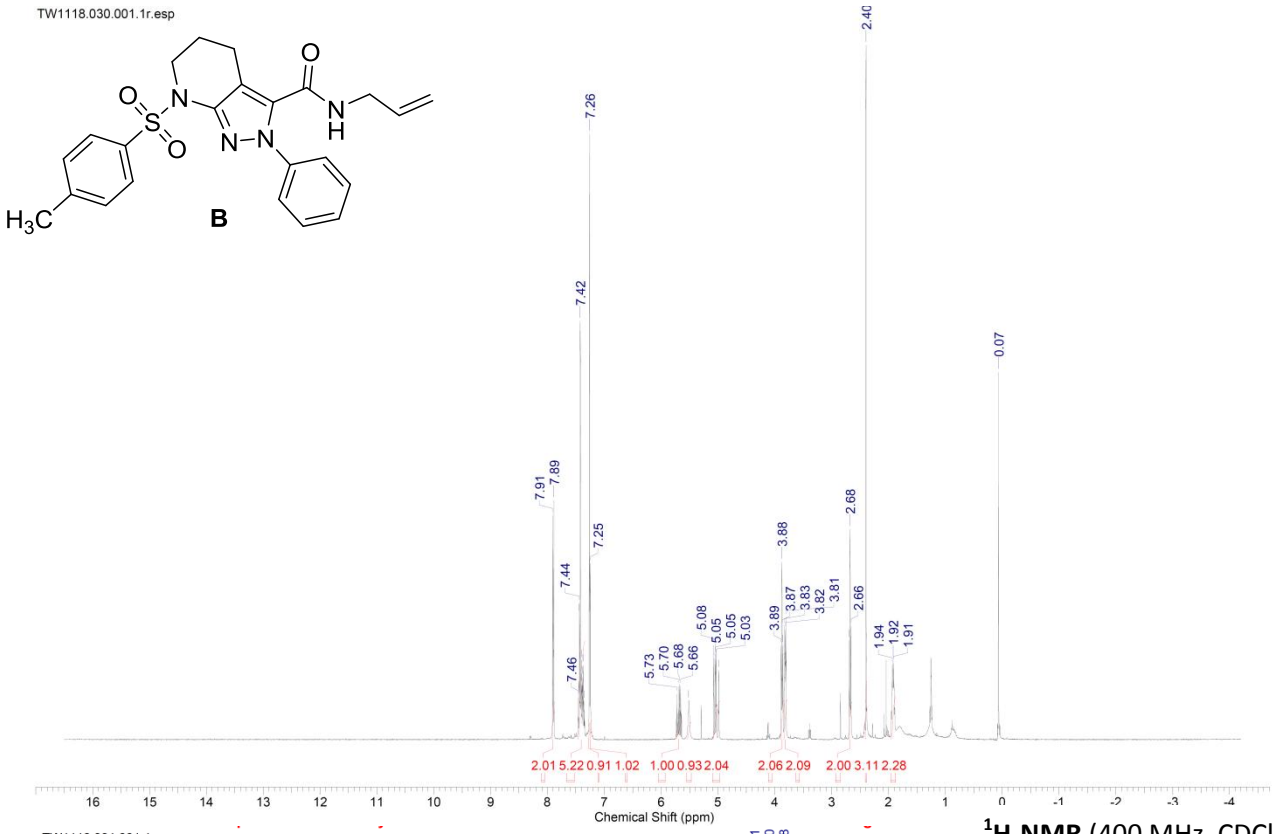


A
4 HMBC signals

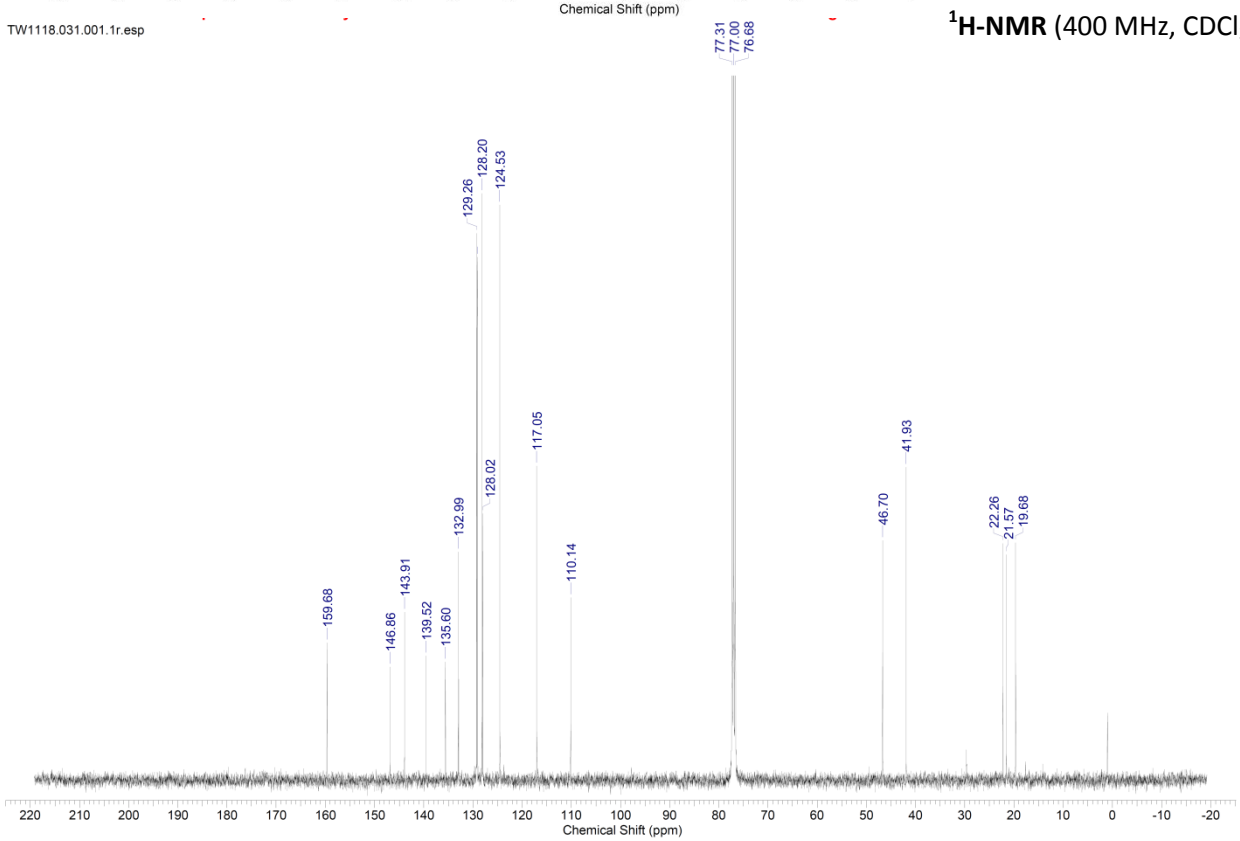


B
5 HMBC signals

***N*-allyl-2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-3-carboxamide (23b)**

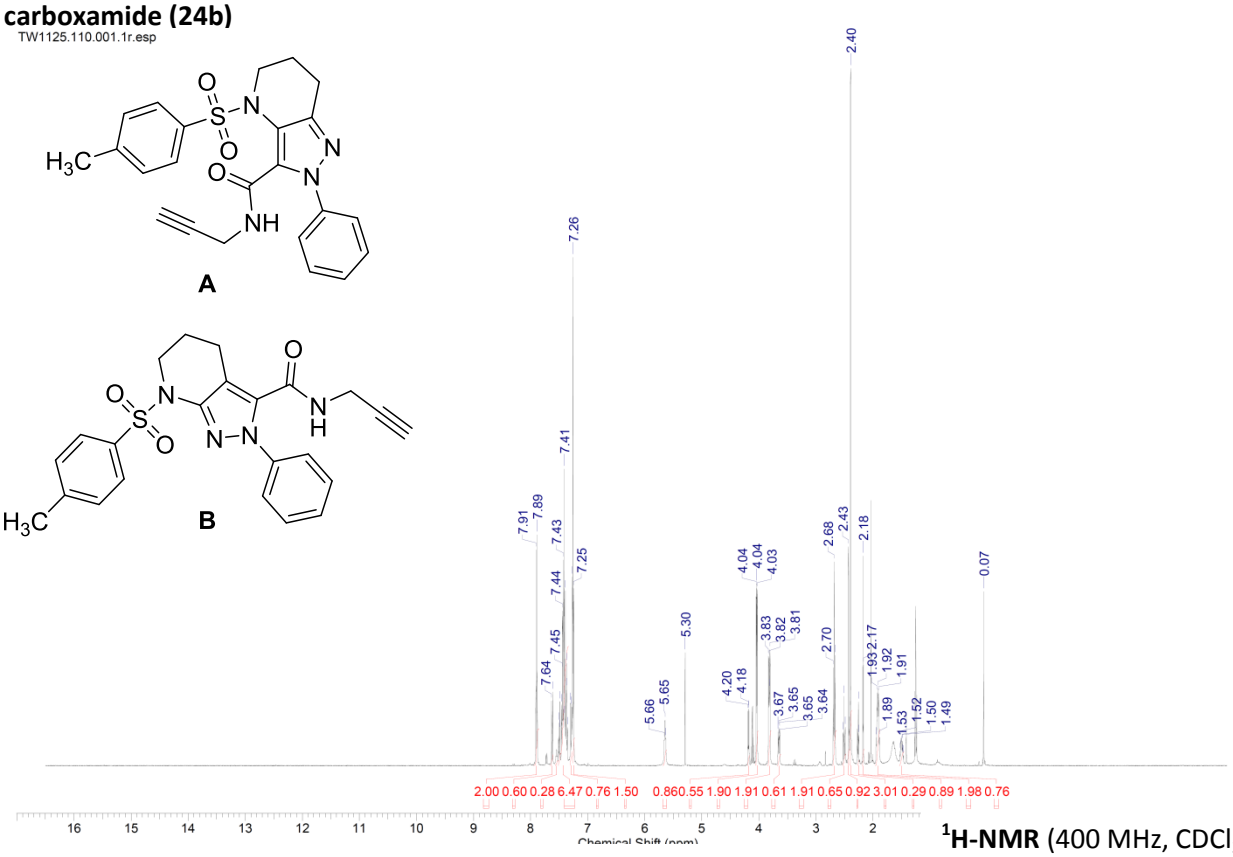


^{1}H-NMR (400 MHz, $CDCl_3$)

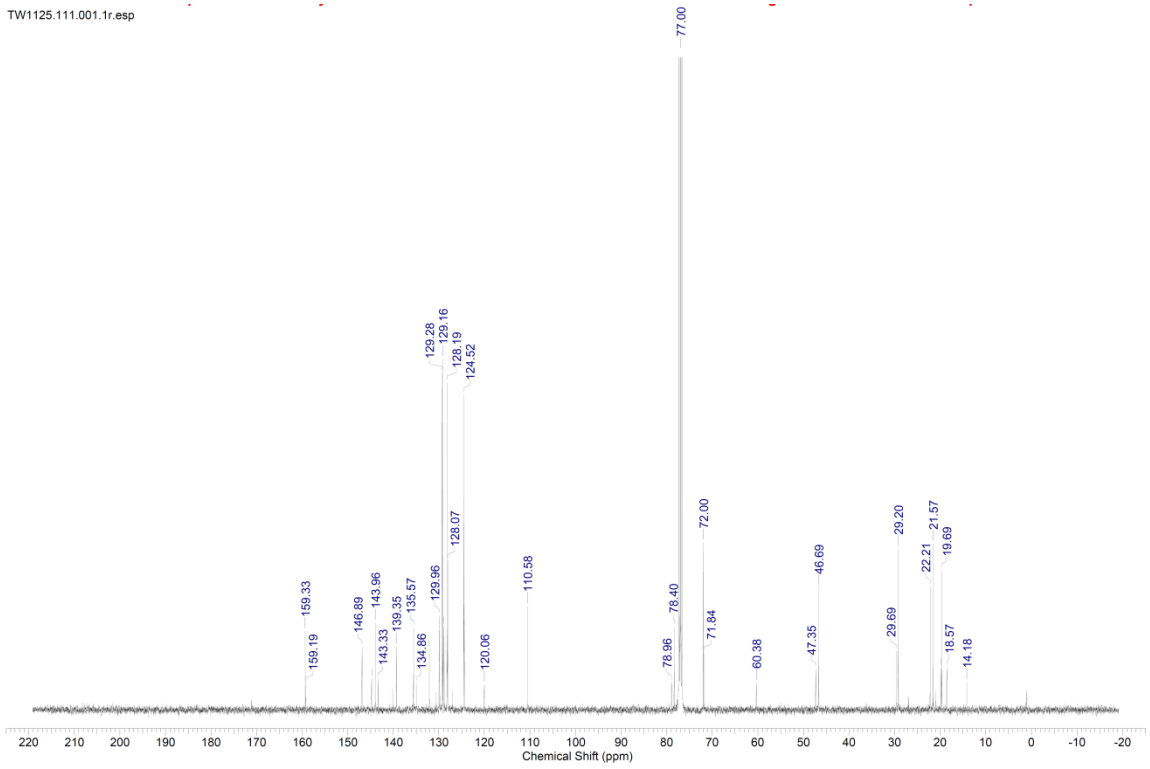


^{13}C-NMR (101 MHz, $CDCl_3$)

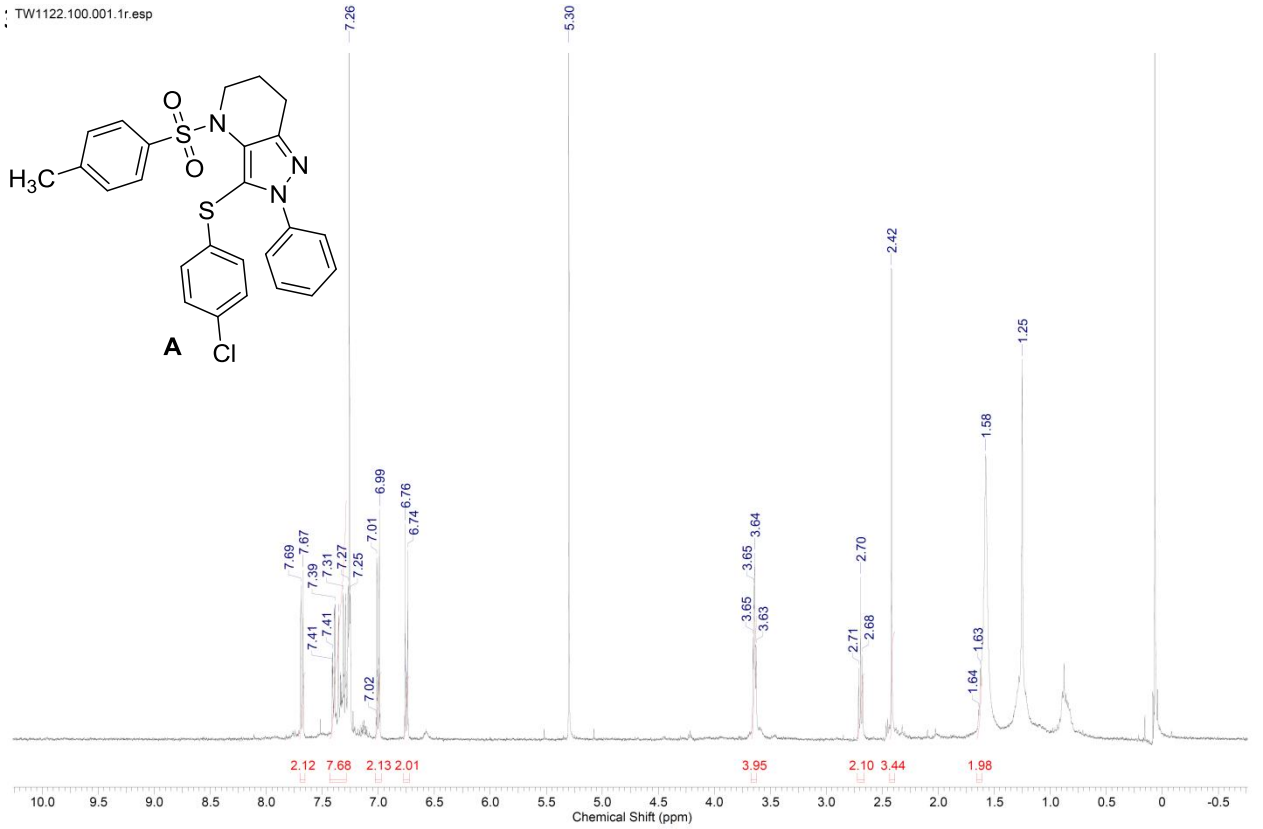
2-p1henyl-*N*-(prop-2-yn-1-yl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine-3-carboxamide (24a) and 2-phenyl-*N*-(prop-2-yn-1-yl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-3-carboxamide (24b)



^{1}H-NMR (400 MHz, $CDCl_3$)

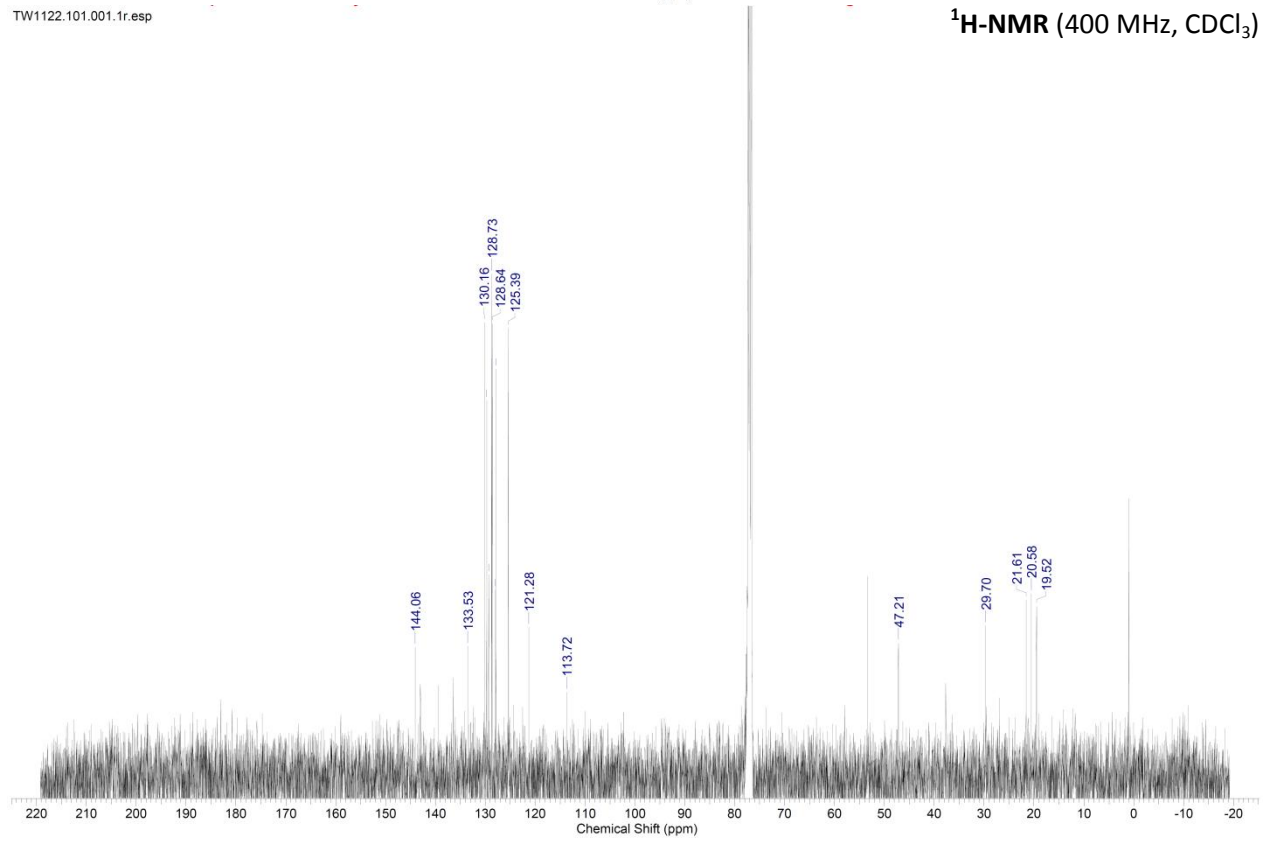


^{13}C-NMR (101 MHz, $CDCl_3$)



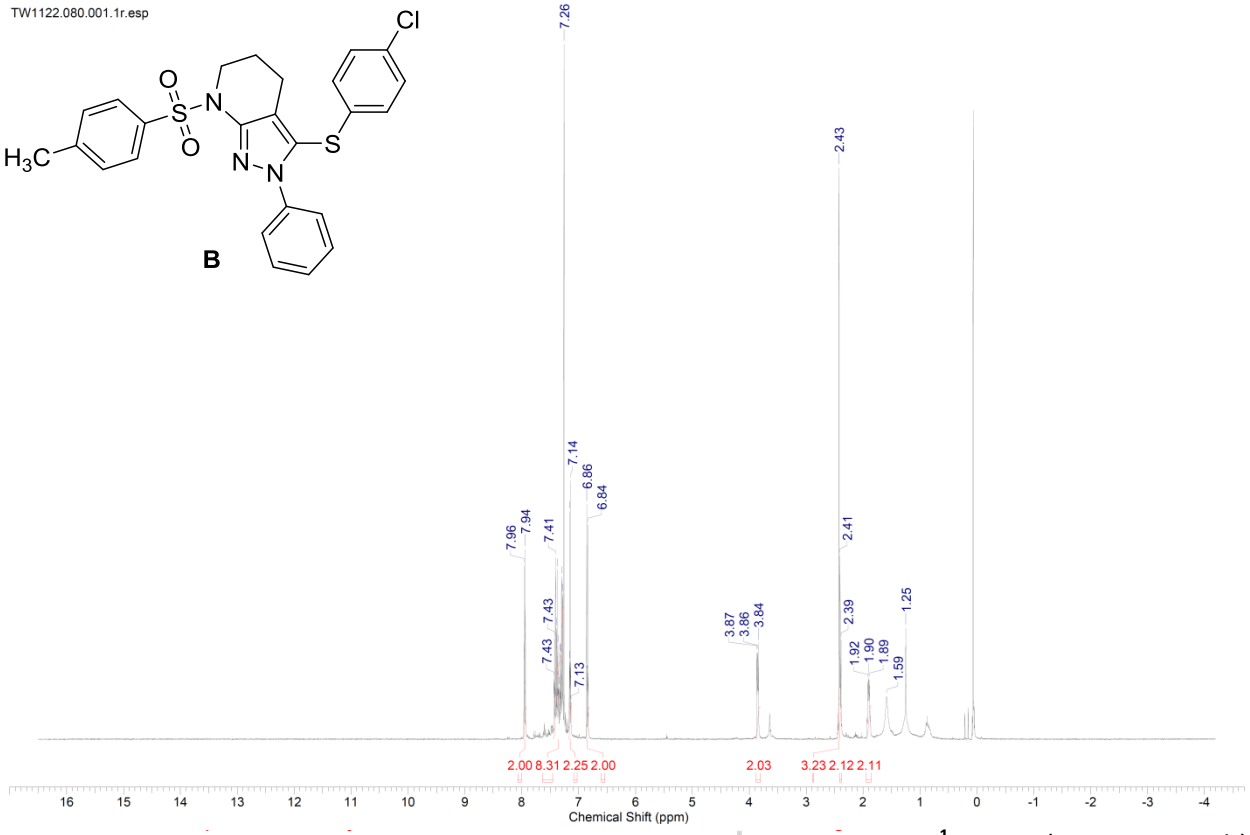
A

^{1}H-NMR (400 MHz, $CDCl_3$)

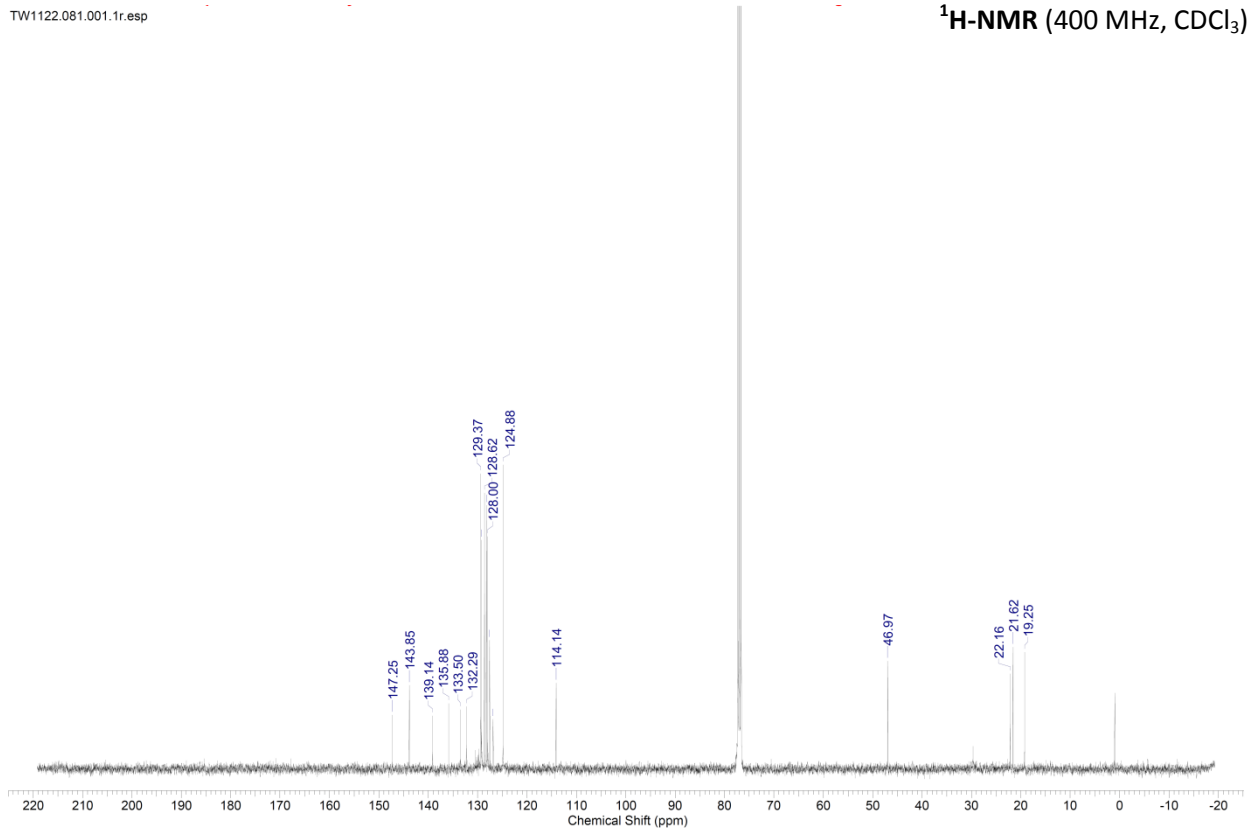


^{13}C-NMR (101 MHz, $CDCl_3$)

3-((4-chlorophenyl)thio)-2-phenyl-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (25b)

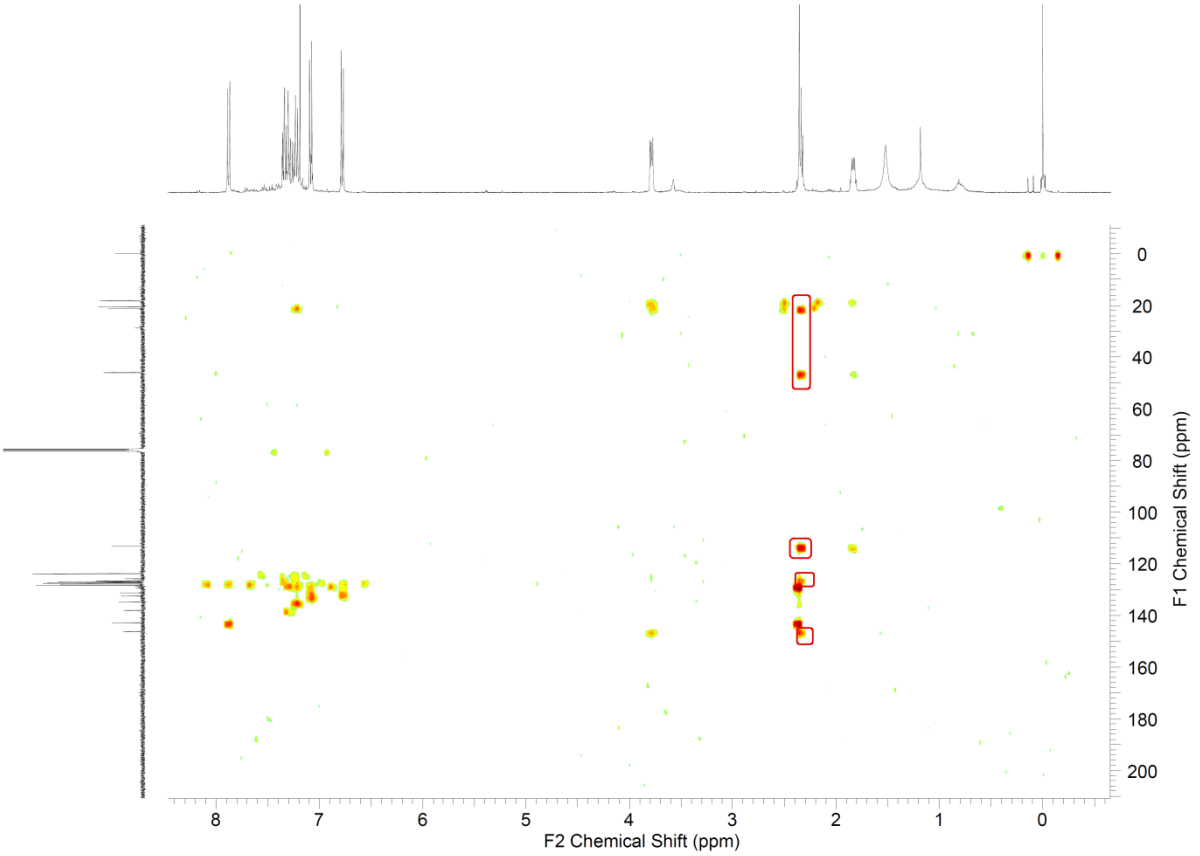


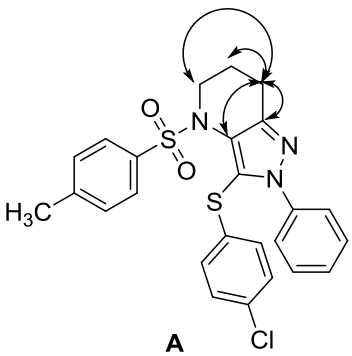
^{1}H-NMR (400 MHz, $CDCl_3$)



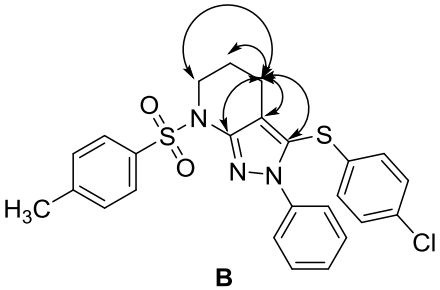
^{13}C-NMR (101 MHz, $CDCl_3$)

HMBC spectrum for compound 25b



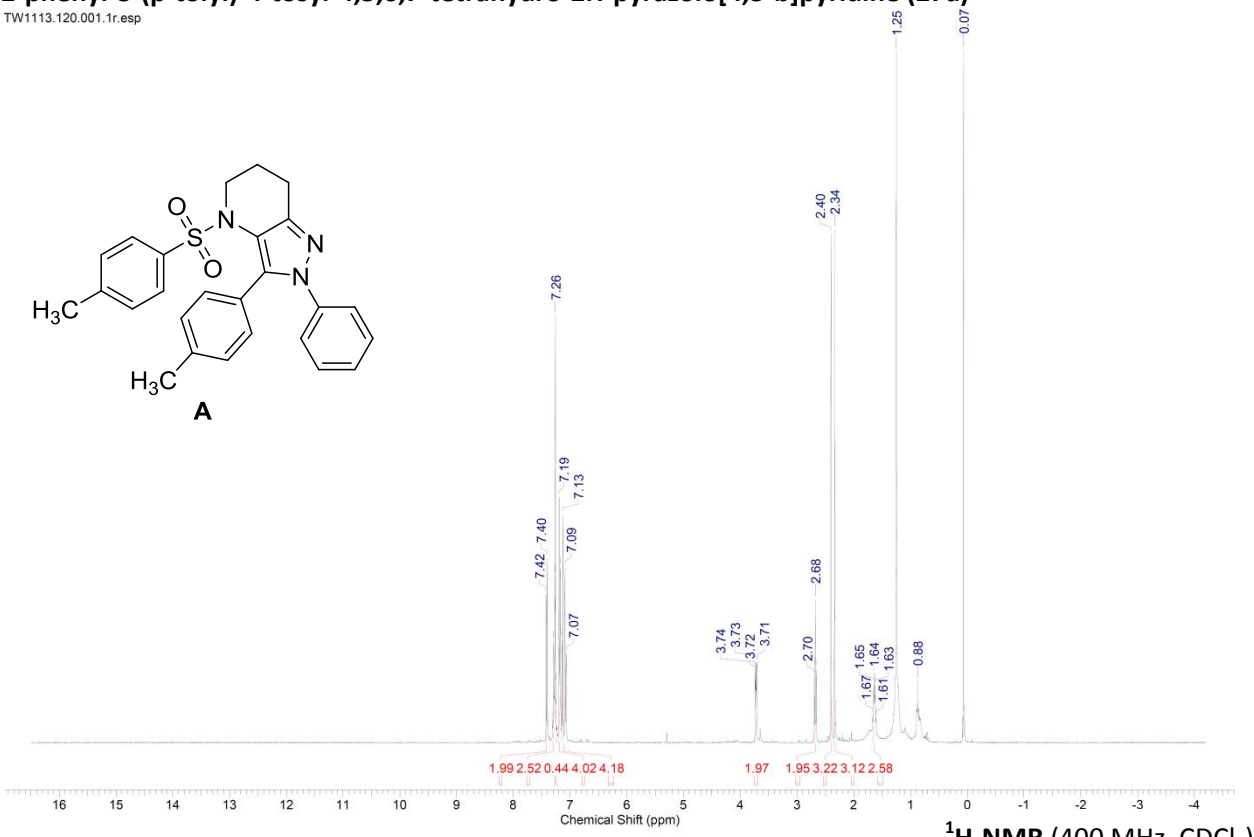


A
4 HMBC signals

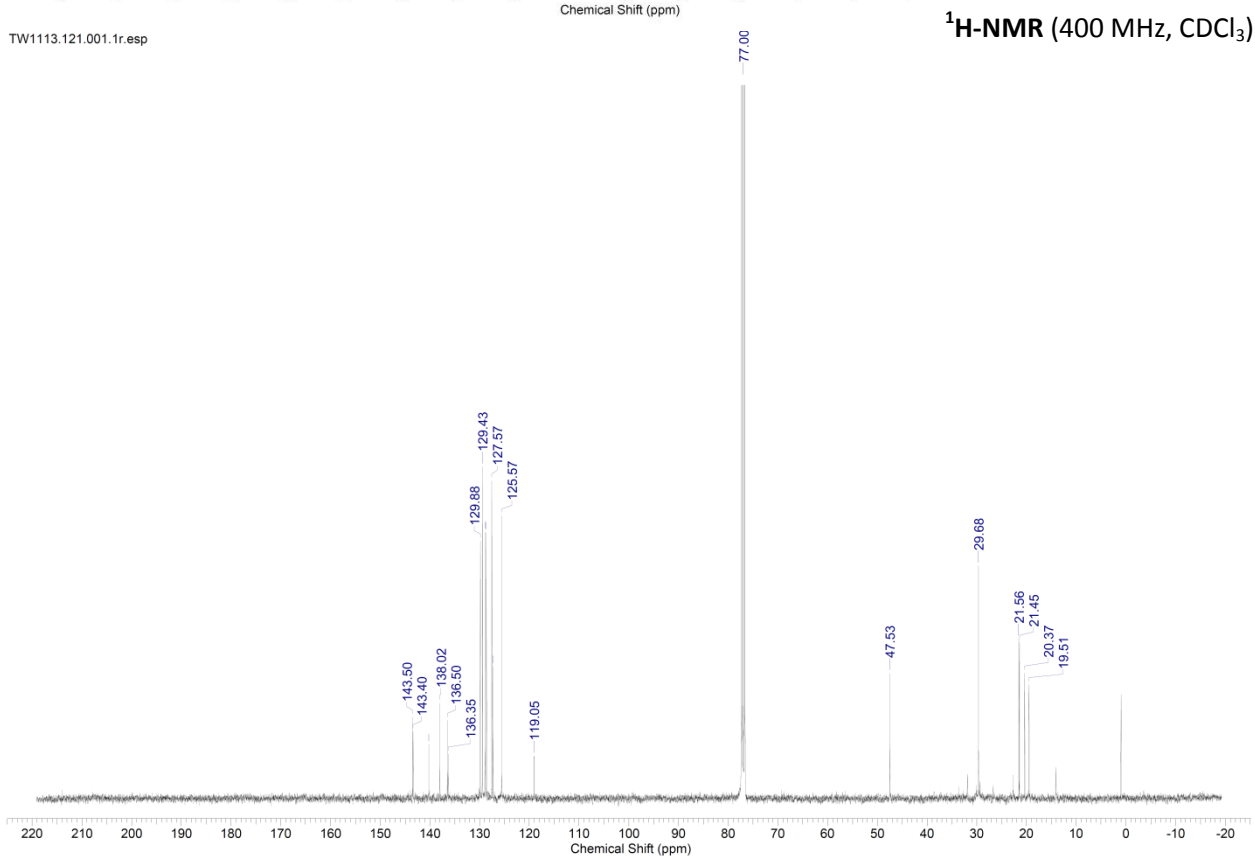


B
5 HMBC signals

2-phenyl-3-(p-tolyl)-4-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-b]pyridine (27a)

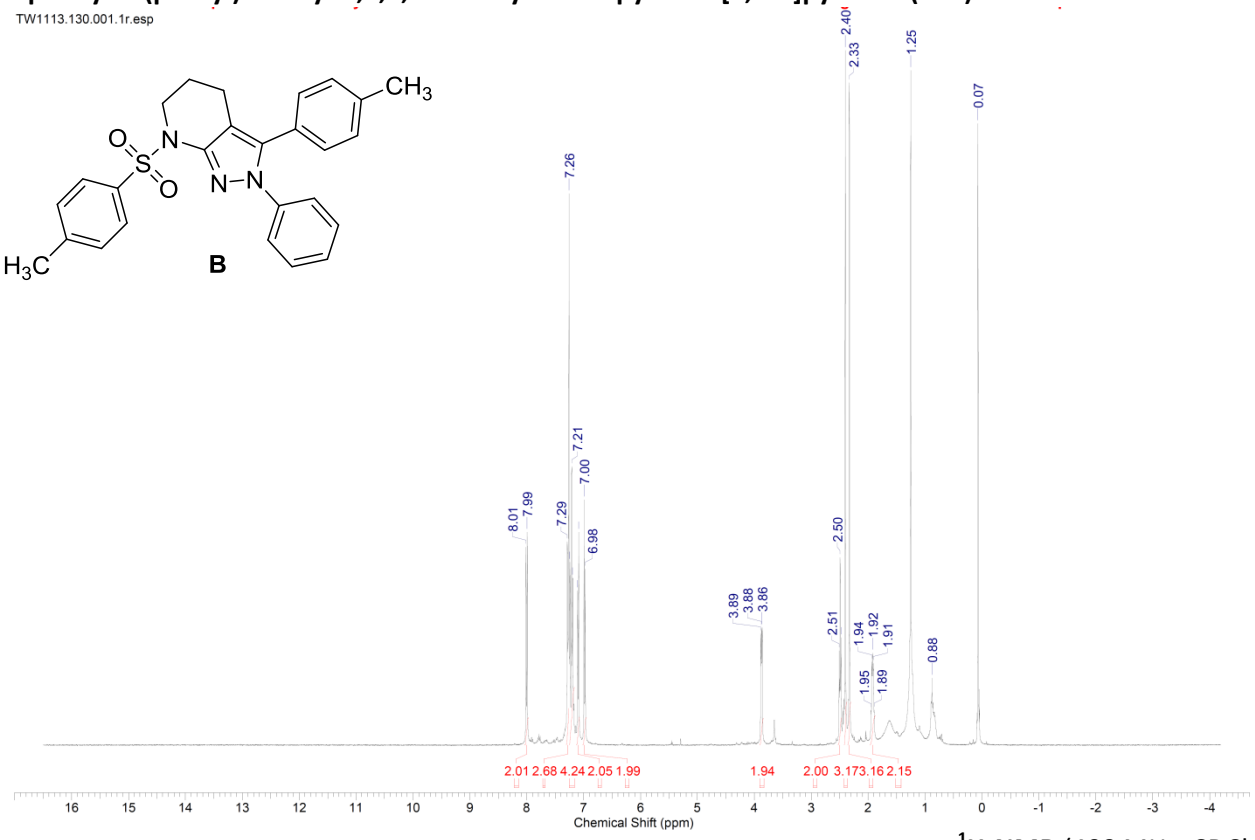


^{1}H-NMR (400 MHz, $CDCl_3$)

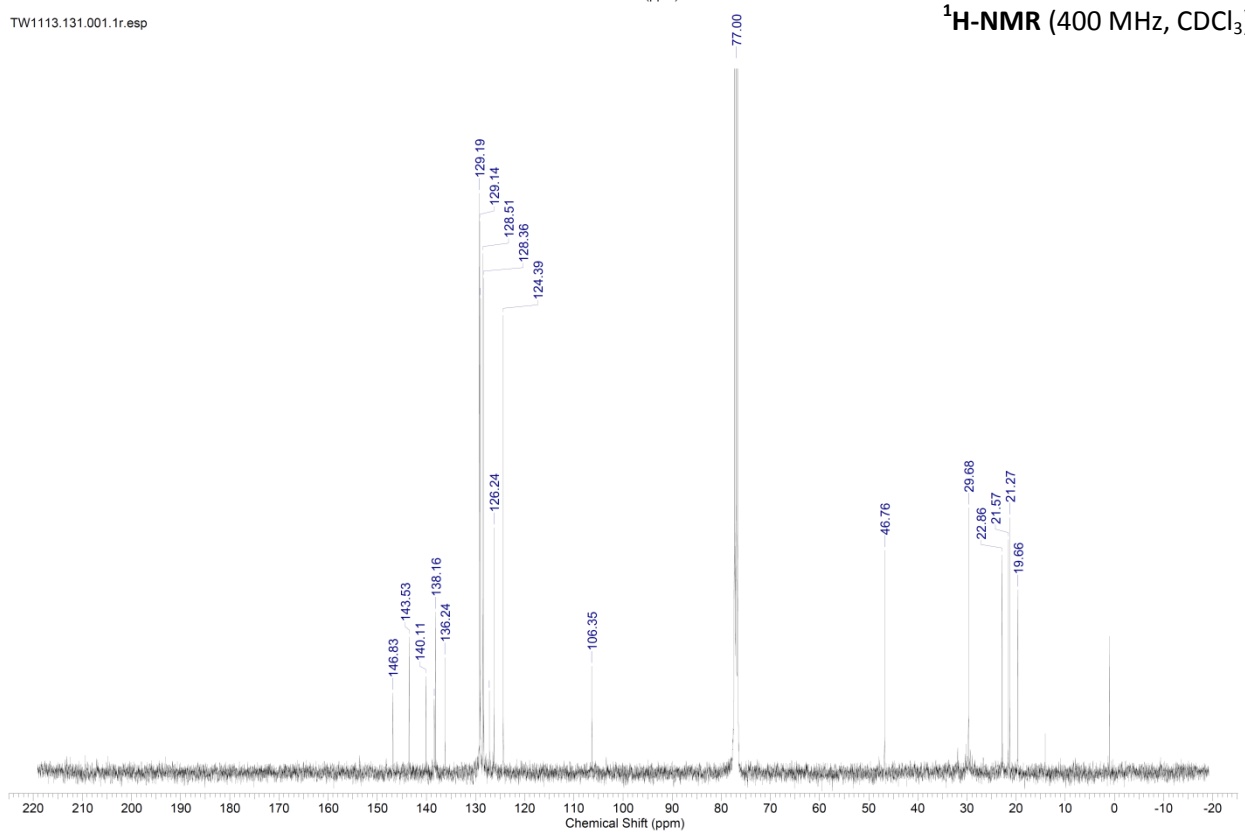


^{13}C-NMR (101 MHz, $CDCl_3$)

2-phenyl-3-(p-tolyl)-7-tosyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine (27b)



^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)

Crystallographic Data

Crystal Structure Determinations

The single-crystal X-ray diffraction study were carried out on a Bruker D8 Venture diffractometer with Photon100 detector at 123(2) K using Cu-Kα radiation (λ = 1.54178 Å). Direct Methods (SHELXS-97) [G. M. Sheldrick, *Acta Crystallogr.* 2008, **A64**, 112-122] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **C71**, 3-8]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model. Semi-empirical absorption corrections were applied. For **4a** an extinction correction was applied. In **6** the phenyl ring of the p-CF_3-phenylgroup is disordered.

4a: colourless crystals, $C_{23}H_{21}N_3O_2S$, M_r = 403.49, crystal size 0.20 × 0.04 × 0.02 mm, monoclinic, space group $P2_1/n$ (No. 14), a = 16.8632(5) Å, b = 5.6827(2) Å, c = 20.8486(6) Å, β = 100.486(1)°, V = 1964.52(11) Å^3, Z = 4, ρ = 1.364 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 1.665 mm^{-1}, F(000) = 848, $2\theta_{max}$ = 144.0°, 20213 reflections, of which 3835 were independent (R_{int} = 0.039), 264 parameters, R_1 = 0.035 (for 3333 I > 2σ(I)), wR_2 = 0.087 (all data), S = 1.04, largest diff. peak / hole = 0.242 / -0.369 e Å^{-3}.

6: colourless crystals, $C_{24}H_{20}F_3N_3O_2S$, M_r = 471.49, crystal size 0.20 × 0.09 × 0.03 mm, triclinic, space group *P-1* (No. 2), a = 5.9736(3) Å, b = 9.6554(5) Å, c = 19.0149(9) Å, α = 83.760(2)°, β = 86.840(2)°, γ = 77.757(2)°, V = 1064.86(9) Å^3, Z = 2, ρ = 1.470 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 1.883 mm^{-1}, F(000) = 488, $2\theta_{max}$ = 144.2°, 11969 reflections, of which 4112 were independent (R_{int} = 0.029), 292 parameters, 40 restraints, R_1 = 0.038 (for 3650 I > 2σ(I)), wR_2 = 0.094 (all data), S = 1.03, largest diff. peak / hole = 0.360 / -0.401 e Å^{-3}.

CCDC 1484278 (**4a**), and 1484279 (**6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

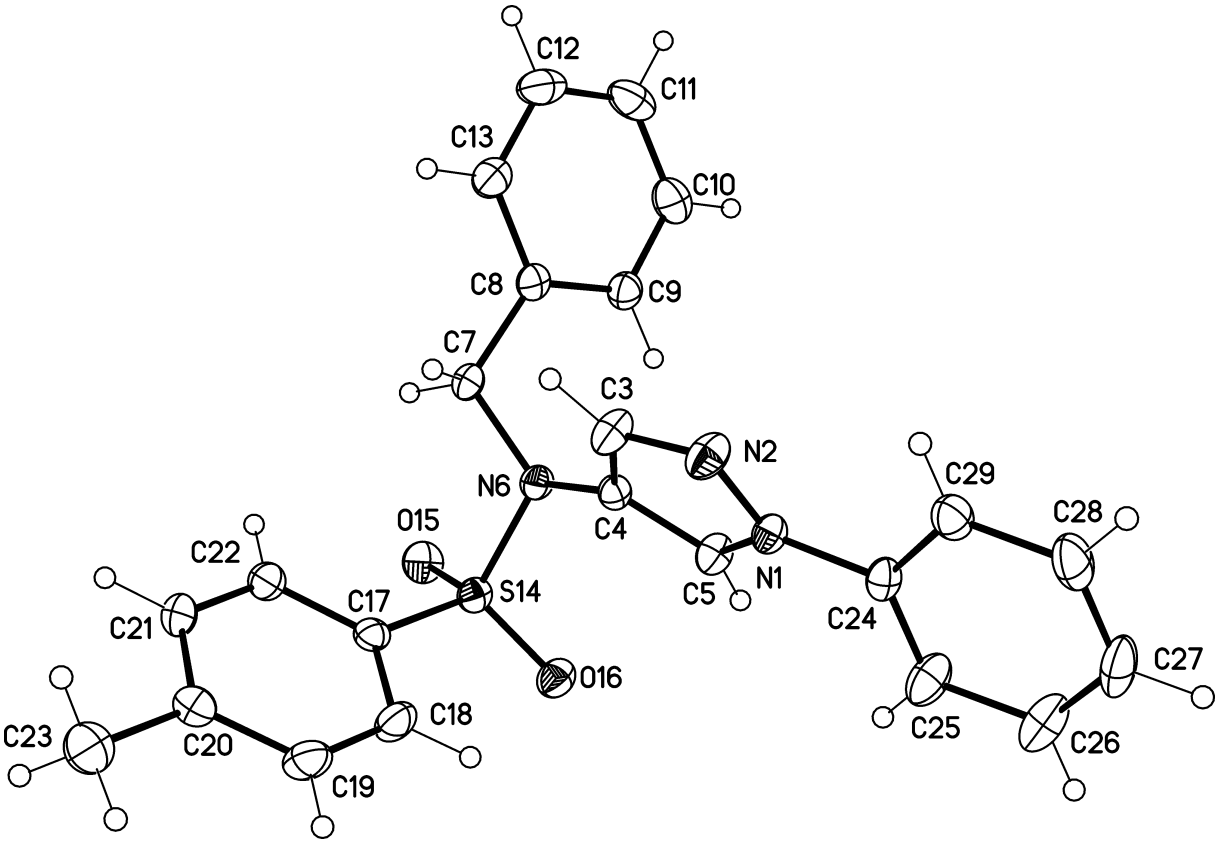


Fig. S1. Molecular structure of **4a** (displacement parameters are drawn at 50 % probability level).

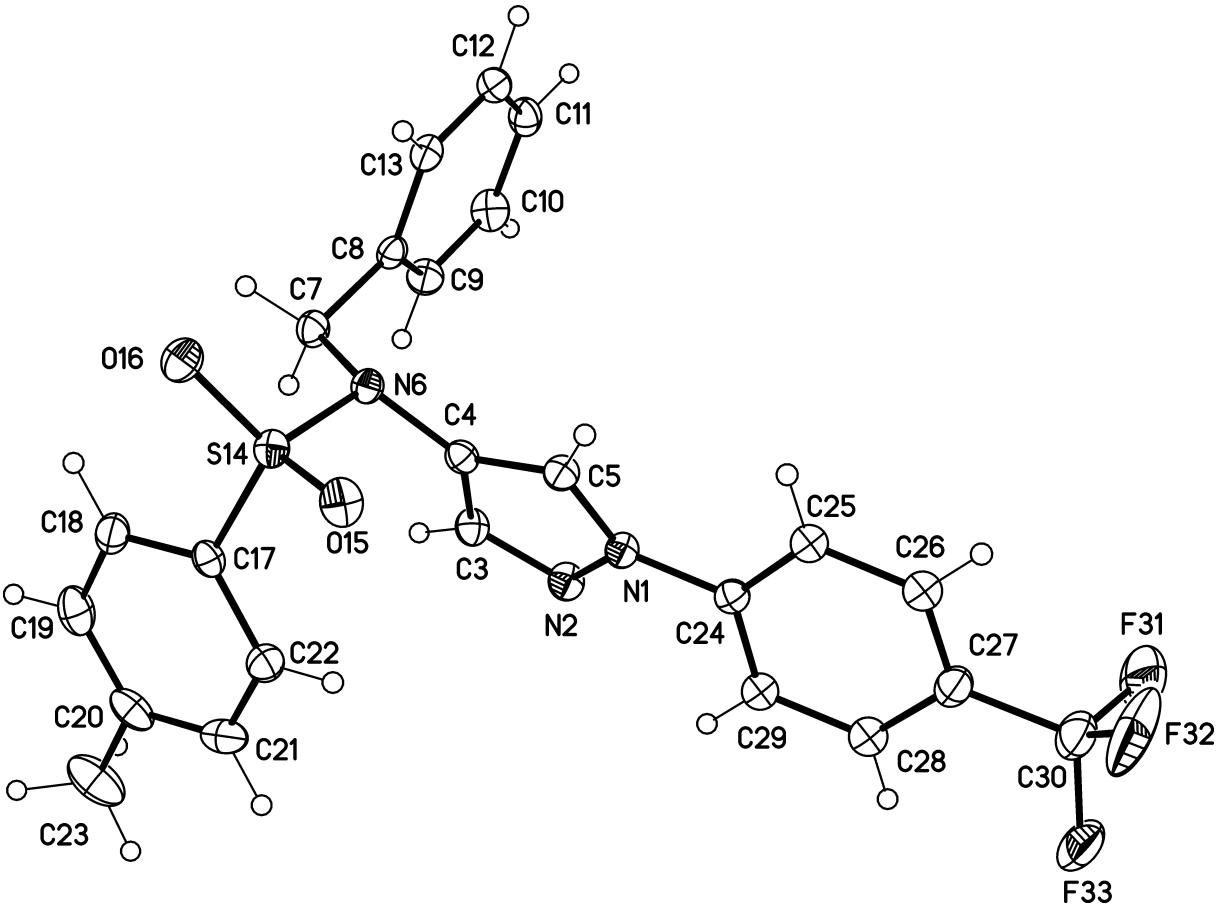


Fig. S2. Molecular structure of **6** (displacement parameters are drawn at 50 % probability level, minor disordered part omitted for clarity).

References

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