Supporting Materials

Palladium-Catalyzed Intermolecular Coupling of Aryl Chlorides and Sulfonamides under Microwave Irradiation

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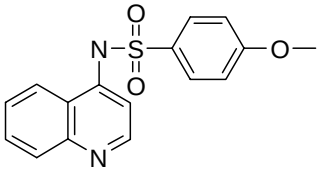
A. General procedures: All reactions and manipulations were performed under nitrogen or using standard Schlenk techniques. HPLC purification was performed using Gilson 210 using a YMC reverse phase column (50 x 20 mm I.D, s-5 μM, 12 nm) eluting with 10-90% acetonitrile/waterr containing 0.05% TFA. ^{1}H, ^{13}C and ^{31}P NMR were recorded on a Bruker DRX-500 spectrometers, chemical shifts are reported in ppm down field from tetramethylsilane with the solvent resonance as the internal standard. The OA LC/MS conditions used to recorded LC/MS spectra is: solutions containing the samples were injected using a HTS Pal (Leap Technologies) autosampler onto a 1 mm x 40 mm reversed-phase Aquasil C18 column applying a linear gradient from 4.5% to 90% CH_3CN (0.02 % TFA) in 3.2 min with a 0.4 min. hold, flowing at 300 μL/min. The MS data were acquired in positive ion mode on a Sciex API 150EX single quadrupole mass spectrometer with an electrospray ion source. UV data were acquired on a SPD 10Avp detector (Shimadzu) set at 214 nm, and the ELS data were acquired on a Sedex 75c (S.E.D.E.R.E.) operated at 45 °C.

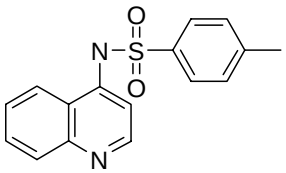
B. Materials: Aldrich dioxane in sure seal bottle was used as obtained. Phosphines **5, DPPF, Xantphos, 6, 7, BINAP** were purchased from Strem Chemicals a, **8** was purchased from Combiphos and **9, 10** were gifts from Johnson Matthey.

C. Experiments

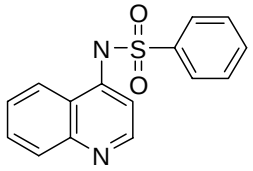


Typical experimental procedure for the synthesis of 4-Methoxy-*N*-quinolin-4-yl-benzenesulfonamide: A Smith Process Vial (0.5-2 mL) was charged with 1 mol% $Pd_2(dba)_3$ (4.6 mg, 5 umol), 3 mol% ligand (6.0 mg, 15 μmol) and Cs_2CO_3 (228 mg, 0.7 mmol). After sealing the cap, purging the vial twice with N_2, the vial was charged with 100 μL anhydrous 1,4-dioxane and stirred at room temperature for 10 minutes. A solution of 4-chloroquinoline (81.5 mg, 0.5 mmol) and 4-methoxybenzenesulfonamide (112.2 mg, 0.6 mmol) in 400 μL anhydrous 1,4 dioxane was introduced via a syringe. The resulting mixture was stirred at room temperature for 30 minutes, then irradiated at 180 ^{o}C for 10 minutes in Smith Synthesizer. After irradiation, the sample was cooled down to room temperature and dissolved in DMSO (5 mL). After filtration to remove the solid residue, the resulting solution was subjected to purification by reverse-phase HPLC to yield 88 mg (41% yield) of the desired product (as TFA salt) as a white solid. The synthesis of the other sulfonamides followed similar procedure.

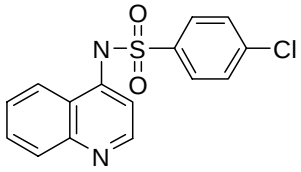
^{1}H NMR (500 MHz, DMSO-d^{6}) δ: 13.10 (s, br, 1H), 8.36 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.12 (d, *J* = 7.2 Hz, 1H), 7.79 (m, 3H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.58 (m, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.01 (m, 2H), 3.78 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d^{6}) δ: 161.29, 160.45, 140.17, 138.28, 135.78, 132.52, 128.03, 127.01, 125.35, 125.04, 123.16, 118.85, 113.82, 112.67, 104.26, 55.45. MS m/z: 315.2 [M^{+} + H].



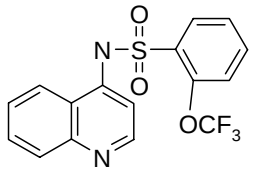
4-Methyl-*N*-quinolin-4-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, DMSO-d^{6}) δ: 13.07 (s, 1H), 8.37 (d, *J* = 7.8 Hz, 1H), 8.18 (m, 1H), 7.87 (m, 3H), 7.67 (m, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 7.2 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d^{6}) δ: 160.64, 141.30, 140.97, 140.20, 140.03, 138.22, 138.08, 132.60, 129.16, 126.07, 125.43, 125.05, 123.16, 118.83, 104.36, 20.89. MS m/z: 299.4 [M^{+} + H].



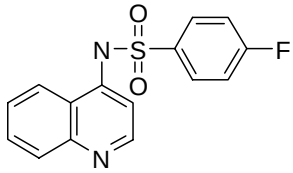
***N*-Quinolin-4-yl-benzenesulfonamide:** ^{1}H NMR (500 MHz, CD_3OD) δ: 8.57 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 7.1 Hz, 1H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.79 (m, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.52 (m, 4H), 7.26 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ: 162.79, 144.21, 141.27, 139.94, 134.14, 133.00, 129.89, 127.65, 127.09, 126.73, 125.02, 119.76, 106.39. MS m/z: 285.2 [M^+ + H].



4-Chloro-*N*-quinolin-4-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.55 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 2H), 7.79 (m, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.52 (m, 3H), 7.23 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ: 143.80, 141.68, 140.40, 139.39, 134.59, 130.50, 129.82, 127.49, 127.34, 125.74, 122.22, 120.15, 106.85. MS m/z: 319.2 [M^+ + H].

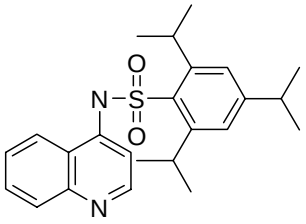


***N*-Quinolin-4-yl-2-trifluoromethoxy-benzenesulfonamide:** ^{1}H NMR (500 MHz, CD_3OD) δ: 8.54 (d, *J* = 8.4 Hz, 1H), 8.09 (dd, *J* = 1.6, 7.9 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.79 (dt, *J* = 7.2,1.2 Hz, 1H), 7.63 (m, 2H), 7.49 (m, 2H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.26 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ: 163.14, 147.59, 141.17, 139.92, 136.47, 134.79, 134.10, 131.19, 127.68, 126.98, 126.89, 125.16, 122.87, 121.75, 120.81, 119.58, 106.34. MS m/z: 369.0 [M^+ + H].

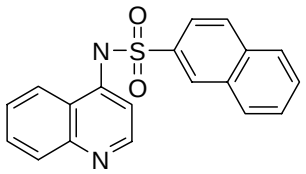


4-Fluoro-*N*-quinolin-4-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.55 (d, *J* = 8.2 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 8.02 (m, 2H), 7.79 (m, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* =

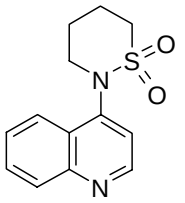
7.6 Hz, 1H), 7.23 (m, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ: 166.95, 164.96, 163.08, 141.22, 140.77, 139.93, 134.10, 130.46, 130.38, 127.00, 126.80, 125.17, 119.70, 116.85, 116.67, 106.31. MS m/z: 303.2 [M^+ + H].



2,4,6-Triisopropyl-*N*-quinolin-4-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.53 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 7.3 Hz, 1H), 7.75 (dt, *J* = 1.2, 8.4 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.49 (m, 1H), 7.18 (d, *J* = 9.5 Hz, 2H), 6.91 (d, *J* = 7.2 Hz 1H) 4.61 (m, 2H), 2.87 (m, 1H), 1.22 (m, 18H). ^{13}C NMR (125 MHz, CD_3OD) δ:162.21, 153.05, 150.84, 140.53, 139.92, 137.38, 133.85, 127.92, 126.85, 126.64, 124.98, 124.47, 119.52, 105.34, 35.38, 30.68, 25.14, 24.08. MS m/z: 411.2 [M^+ + H].

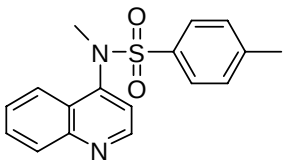


Naphthalene-2-sulfonic acid quinolin-4-ylamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.61 (d, *J* = 8.1 Hz, 1H), 8.56 (s, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.95 (m, 4H), 7.80 (m, 1H), 7.62 (m, 4H), 7.31 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR(125 MHz, CD_3OD) δ: 141.31, 141.14, 139.94, 136.00, 134.14, 133.61, 130.16, 130.13, 129.44, 128.92, 128.43, 128.13, 127.12, 126.76, 125.06, 123.80, 119.77, 106.37. MS m/z: 335.2 [M^+ + H].

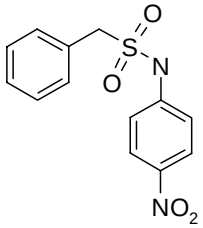


4-(1,1-Dioxo-1-l^6-[1,2]thiazinan-2-yl)-quinoline: ^{1}H NMR (500 MHz, CD_3OD)δ: 8.95 (d, *J* = 5.1 Hz, 1H), 8.34 (d, *J* =8.4 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.91 (m, 1H), 7.77 (m, 2H), 3.87 (s, 2H), 3.47 (s, 2H), 2.41 (m, 2H), 2.03 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ: 150.77, 150.12,

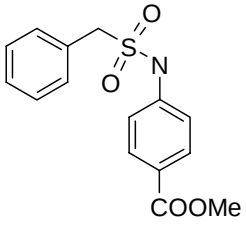
147.92, 132.94, 129.28, 128.22, 127.47, 125.74, 120.24, 55.91, 52.06, 25.38, 25.23. MS m/z: 263.2 [M^+ + H].



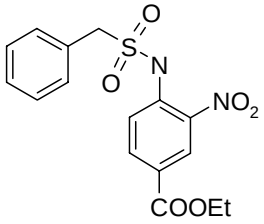
4,*N*-Dimethyl-*N*-quinolin-4-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.84 (d, *J* = 5.1 Hz, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.91 (m, 1H), 7.75 (m, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 5.1 Hz, 1H), 3.31 (s, 3H), 2.46 (s, 3H) . ^{13}C NMR (100 MHz, CD_3OD)δ: 151.62, 150.28, 148.35, 146.33, 134.38, 132.87, 131.06, 130.71, 130.45, 129.45, 129.06, 128.23, 127.57, 126.29, 120.43, 39.82, 21.57. MS m/z: 313.0 [M^+ + H].



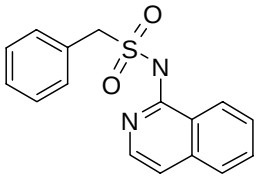
***N*-(4-Nitro-phenyl)-1-phenyl-methanesulfonamide:** ^{1}H NMR (500 MHz, CD_3OD) δ: 8.13 (m, 2H), 7.32-7.22 (m, 7H), 4.54 (s, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ: 146.44, 144.20, 132.19, 130.32, 129.82, 129.69, 126.20, 118.46, 59.30. MS m/z: 293.2 [M^+ + H].



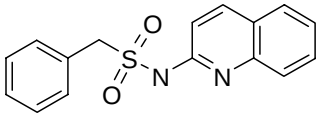
4-Phenylmethanesulfonylamino-benzoic acid methyl ester. ^{1}H NMR (500 MHz, CD_3OD) δ: 7.92 (m, 2H), 7.30-7.25 (m, 5H), 7.19 (m, 2H), 4.47 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ: 168.08, 144.59, 132.09, 132.01, 130.42, 129.67, 129.59, 125.78, 118.49, 58.77, 52.49. MS m/z: 306.2 [M^+ + H].



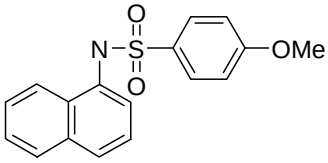
3-Nitro-4-phenylmethanesulfonylamino-benzoic acid ethyl ester: ^{1}H NMR (500 MHz, CD_3OD) δ: 8.71 (d, *J* = 1.8 Hz, 1H), 8.08 (dd, *J* = 1.9, 8.8 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.28 (m, 6H), 4.64 (s, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ: 165.15, 138.73, 137.05, 136.43, 131.55, 129.97, 129.67, 128.72, 128.25, 126.20, 120.66, 62.61, 60.26, 14.49. MS m/z: 365.2 [M^+ + H].



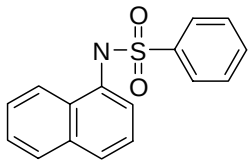
***N*-Isoquinolin-1-yl-1-phenyl-methanesulfonamide:** ^{1}H NMR (500 MHz, DMSO-d6) δ: 11.64 (s, 1H), 8.37 (d, *J* = 8.2 Hz, 1H), 7.81 (m, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.61 (m, 1H), 7.40 (m, 3H), 7.22 (m, 3H), 6.92 (d, *J* = 7.0 Hz, 1H), 4.44 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ: 153.00, 136.64, 133.50, 130.99, 130.86, 128.22, 127.93, 127.77, 126.69, 126.62, 123.74, 109.37, 59.55. MS m/z: 299.2 [M^+ + H].



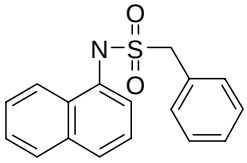
1-Phenyl-*N*-quinolin-2-yl-methanesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 7.93 (d, *J* = 9.4 Hz, 1H), 7.69 (d, *J* =8.0 Hz, 1H), 7.62 (m, 1H), 7.33 (m, 4H), 7.17 (m, 4H), 4.42 (s, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ: 142.03, 132.77, 132.13, 131.36, 129.25, 129.17, 129.07, 125.54, 61.17. MS m/z: 299.2 [M^+ + H].



4-Methoxy-*N*-naphthalen-1-yl-benzenesulfonamide: ^{1}H NMR (500 MHz, CD_3OD) δ: 7.93 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.59 (m, 2H), 7.44-7.33 (m, 3H), 7.23 (dd, *J* = 0.9, 7.4 Hz, 1H), 6.89 (m, 2H), 3.76 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD)δ: 164.54, 135.84, 133.86, 132.90, 131.35, 130.41, 129.09, 128.14, 127.14, 127.09, 126.31, 125.05, 124.02, 115.03, 56.11. MS m/z: 314.2 [M^+ + H].



***N*-Naphthalen-1-yl-benzenesulfonamide:** ^{1}H NMR (500 MHz, CD_3OD) δ: 7.88 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.66 (m, 2H), 7.51 (m, 1H), 7.35 (m, 5H), 7.23 (dd, *J* = 0.8, 7.3 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ: 141.46, 135.82, 133.74, 133.63, 131.32, 129.96, 129.10, 128.28, 128.23, 127.16, 127.13, 126.30, 125.20, 123.89. MS m/z: 284 [M^+ + H].



***N*-Naphthalen-1-yl-1-phenyl-methanesulfonamide:** ^{1}H NMR (500 MHz, CD_3OD) δ: 8.09 (m, 1H), 7.88 (m, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.51 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.29 (m, 5H), 4.43 (s, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ: 135.96, 134.09, 132.16, 130.77, 130.61, 129.53, 129.50, 129.32, 127.72, 127.41, 127.37, 126.61, 123.94, 123.20, 59.24. MS m/z: 298 [M^+ + H].