Supporting information

Synthesis and Structure-Activity Relationship Studies of 4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide Derivatives as Potent and Selective Inhibitors of 12-Lipoxygenase.

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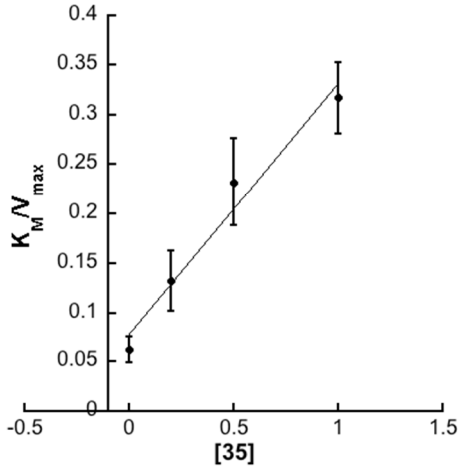


Figure S1. Steady-state kinetics data for the determination of K_i for 12-LOX with **35**. K_M/V_{max} (x-intercept, K_M/V_{max} units are μM/μmol/min/mg) versus [Inhibitor] (μM) is the secondary replot of the inhibition data, which yielded a K_i of 0.35 +/- 0.08 μM.

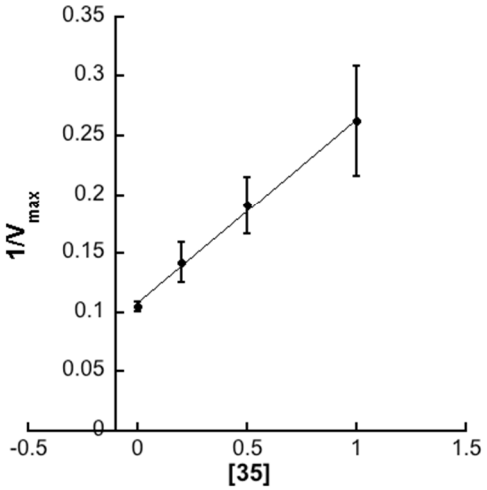


Figure S2. Steady-state kinetics data for the determination of K_i' for 12-LOX with **35**. $1/V_{max}$ (y-intercept, $1/V_{max}$ units are 1/μmol/min/mg) versus [Inhibitor] (μM) is the secondary replot of the inhibition data, which yielded a K_i of 0.72 +/- 0.1 μM.

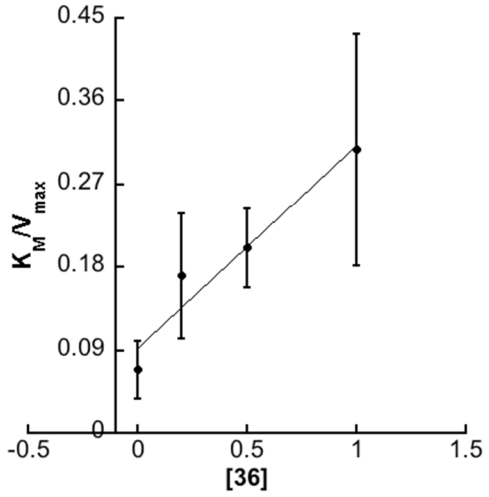


Figure S3. Steady-state kinetics data for the determination of K_i for 12-LOX with **36**. K_M/V_{max} (x-intercept, K_M/V_{max} units are μM/μmol/min/mg) versus [Inhibitor] (μM) is the secondary replot of the inhibition data, which yielded a K_i of 0.53 +/- 0.2 μM.

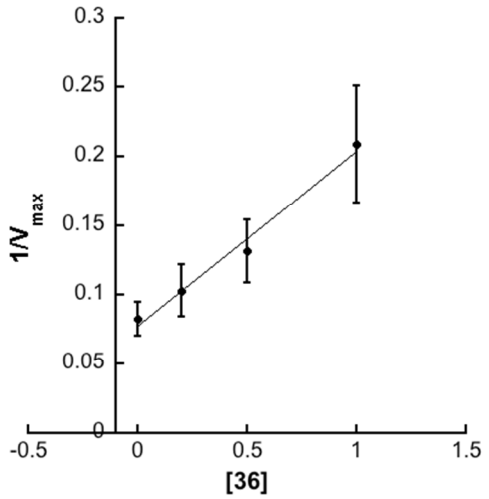


Figure S4. Steady-state kinetics data for the determination of K_i' for 12-LOX with **36**. $1/V_{max}$ (y-intercept, $1/V_{max}$ units are 1/μmol/min/mg) versus [Inhibitor] (μM) is the secondary replot of the inhibition data, which yielded a K_i of 0.63 +/- 0.1 μM.

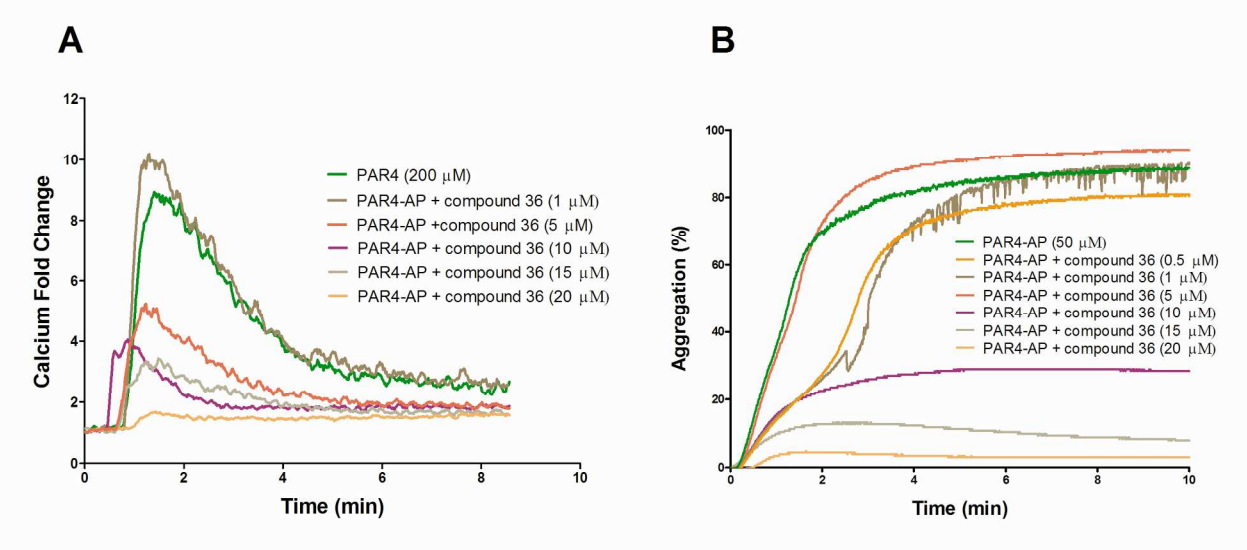


Figure S5. PAR4-AP-induced calcium mobilization (A) and platelet aggregation (B) in human platelets. For A: Washed human platelets (1 x 10^6 platelets/mL) were stimulated with 200 μM PAR4-AP in the absence or presence of increasing concentrations of compound **36**. Calcium mobilization was decreased as the concentration of compound **36** was increased. Calcium was measured in real time using a C6 Accuri flow cytometer. The experiments were done in triplicate. For B: Platelet aggregation of human platelets (3 x 10^8 platelets/mL) was measured in real-time using a Chronolog Lumi-Aggregometer (model 700D) following addition of PAR4-AP.

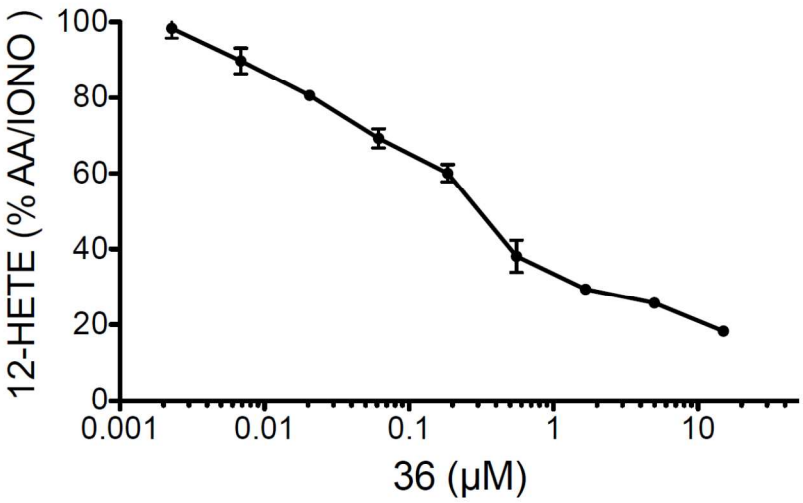


Figure S6. Inhibition of 12-HETE by compound **36** in mouse beta cells. Mouse beta cells (BTC3) were treated with arachidonic acid and calcium ionophore (AA/IONO) alone or in the presence of **36**. Graphed are the levels of 12-HETE expressed as a percentage of that detected in cells stimulated with AA/IONO alone. The data graphed in figure 3A is a representative experiment with each plotted data point being performed in triplicate. These plotted data are representative of four separate experimental determinations performed covering a lesser dose range. The graphed data are mean ± SEM, n=3. Error bars for some points are masked by the symbol. The data was analyzed by non-linear regression for dose-response curve inhibition, using variable or restricted hill slope, R^2>0.81. This analysis was facilitated with Prism 5 software. In addition to compound, DMSO (stock solvent) was included with each condition. DMSO is also the solvent for the calcium ionophore (stimulant).

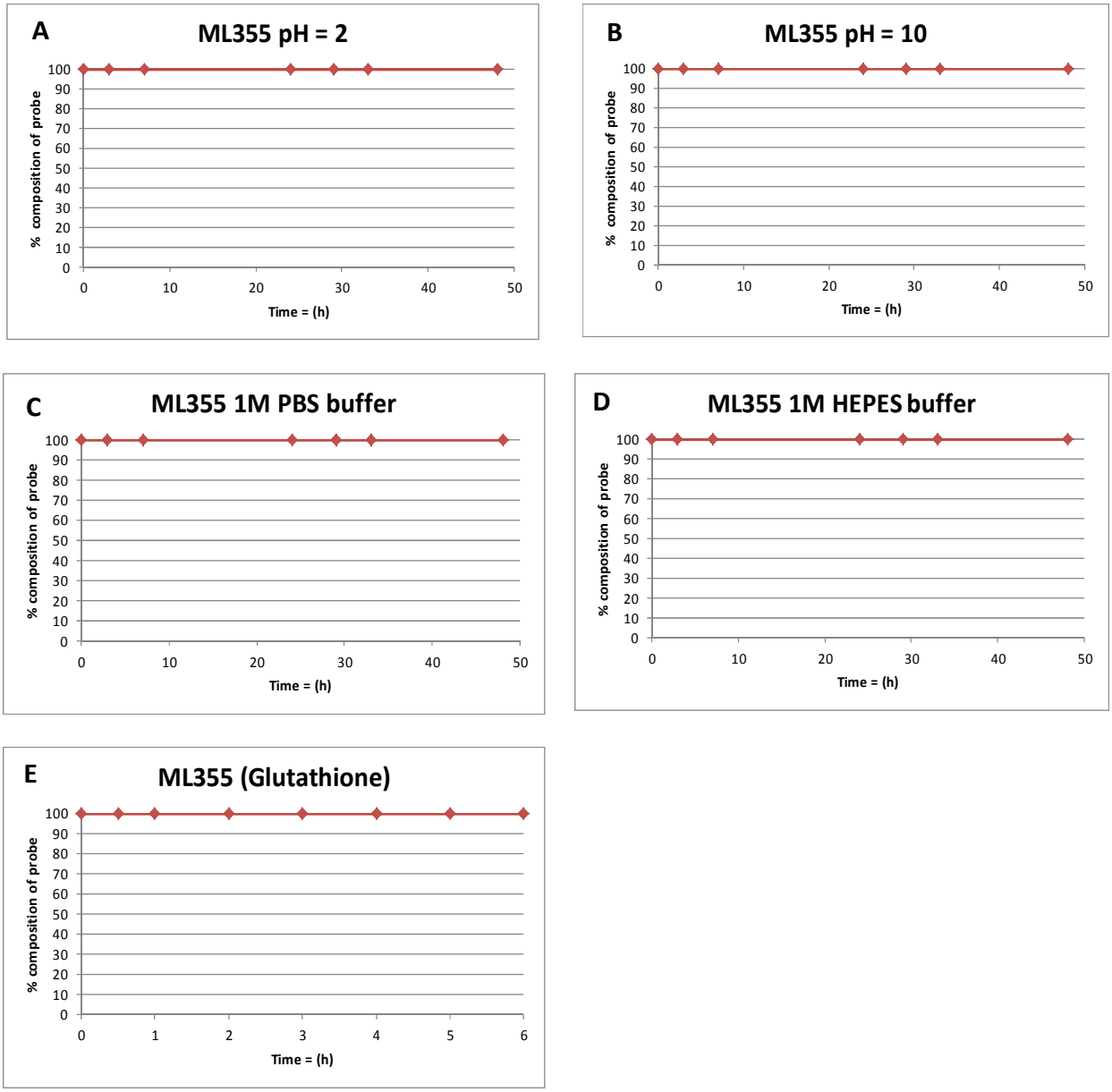
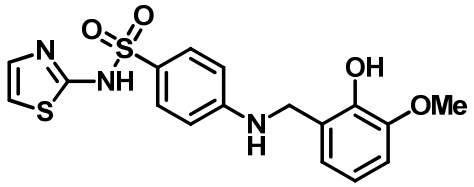
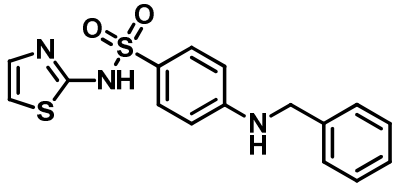


Figure S7. Stability of **35** (**ML355**) measured as percent composition of probe molecule in aqueous solution (contains 20 % acetonitrile) at r.t. over the indicated time period in (a) pH 2 buffer (pH 7.4) (b) pH 10 buffer (c) PBS buffer (pH 7.4) (d) Lipoxygenase UV-Vis assay buffer (1M HEPES buffer, pH 7.3) (e) in the presence of 5 mM glutathione (reduced form).

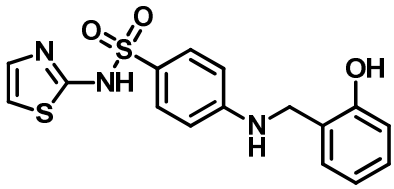
General Methods for Chemistry. All air or moisture sensitive reactions were performed under positive pressure of nitrogen with oven-dried glassware. Chemical reagents and anhydrous solvents were obtained from commercial sources and used as-is. Preparative purification was performed on a Waters semi-preparative HPLC. The column used was a Phenomenex Luna C18 (5 micron, 30 x 75 mm) at a flow rate of 45 mL/min. The mobile phase consisted of acetonitrile and water (each containing 0.1% trifluoroacetic acid). A gradient of 10% to 50% acetonitrile over 8 minutes was used during the purification. Fraction collection was triggered by UV detection (220 nm). Analytical analysis for purity was determined by two different methods denoted as Final QC Methods 1 and 2. Method 1: Analysis was performed on an Agilent 1290 Infinity Series HPLC. UHPLC Long Gradient Equivalent 4% to 100% acetonitrile (0.05% trifluoroacetic acid) in water over 3.5 minutes run time of 4 minutes with a flow rate of 0.8 mL/min. A Phenomenex Kinetex 1.7 micron C18 column (2.1 x 100 mm) was used at a temperature of 50 °C. Method 2: analysis was performed on an Agilent 1260 with a 7 minute gradient of 4% to 100% acetonitrile (containing 0.025% trifluoroacetic acid) in water (containing 0.05% trifluoroacetic acid) over 8 minute run time at a flow rate of 1 mL/min. A Phenomenex Luna C18 column (3 micron, 3 x 75 mm) was used at a temperature of 50 °C. Purity determination was performed using an Agilent Diode Array Detector for both Method 1 and Method 2. Mass determination was performed using an Agilent 6130 mass spectrometer with electrospray ionization in the positive mode. All of the analogs for assay have purity greater than 95% based on both analytical methods. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 (100) and 600 MHz spectrometers. High resolution mass spectrometry was recorded on Agilent 6210 Time-of-Flight LC/MS system.



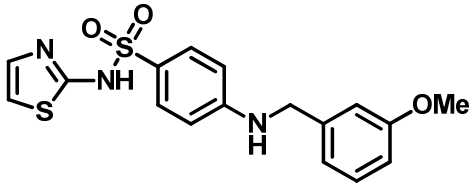
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (1): Method A: using 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 7.44–7.33 (m, 2H), 7.00 (d, J = 4.20 Hz, 1H), 6.85–6.62 (m, 3H), 6.60–6.45 (m, 4H), 4.19 (d, J = 5.91 Hz, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 2): 4.394 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_4S_2$ 392.0733) found, 392.0726.



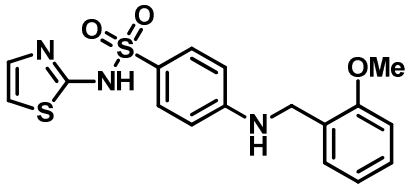
4-(benzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide TFA (8): Method A: using benzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (s, 1H), 7.48–7.39 (m, 2H), 7.35–7.13 (m, 6H), 6.99 (t, J = 6.00 Hz, 1H), 6.71 (d, J = 4.60 Hz, 1H), 6.62–6.54 (m, 2H), and 4.29 (d, J = 5.61 Hz, 2H); LC-MS retention time (Method 2): 4.780 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{16}N_3O_2S_2$ 346.0678) found, 346.0672.



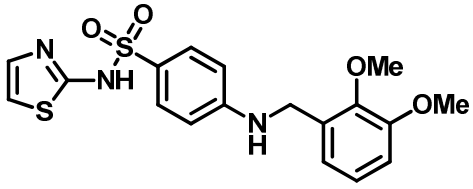
4-(2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide (9): Method A: using 2-hydroxybenzyaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.49 (s, 1H), 7.44–7.35 (m, 2H), 7.13 (dd, *J* = 1.65, and 7.55 Hz, 1H), 7.03 (ddd, *J* = 1.75, 7.32, and 8.01 Hz, 1H), 6.92–6.67 (m, 4H), 6.52–6.41 (m, 2H), 6.38–6.29 (m, 2H), and 4.17 (d, *J* = 5.68 Hz, 2H); LC-MS retention time (Method 2): 4.213 min; HRMS: *m/z* (M+H)$^+$ = (Calculated for $C_{16}H_{16}N_3O_3S_2$ 362.0628) found, 362.0620.



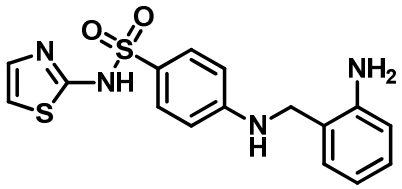
4-(3-methoxybenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide (10): Method B: using (3-dimethoxyphenyl)methanamine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48–7.41 (m, 2H), 7.27–7.19 (m, 1H), 7.18 (d, *J* = 4.63 Hz, 1H), 6.99 (t, *J* = 6.06 Hz, 1H), 6.93–6.85 (m, 2H), 6.79 (dd, *J* = 1.10, and 2.48 Hz, 1H), 6.73 (d, *J* = 4.60 Hz, 1H), 6.63–6.55 (m, 2H), 4.27 (d, *J* = 5.92 Hz, 2H), and 3.72 (s, 3H); LC-MS retention time (Method 2): 4.777 min; HRMS: *m/z* (M+Na)$^+$ = (Calculated for $C_{17}H_{17}N_3NaO_3S_2$ 398.0604) found, 398.0584.



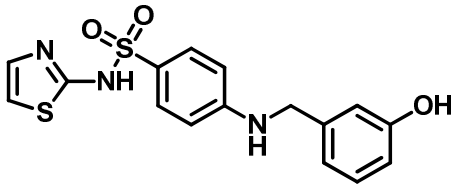
4-(2-methoxybenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide TFA (11): Method B: using 2-dimethoxyphenyl)methanamine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (s, 1H), 7.48–7.39 (m, 2H), 7.26–7.12 (m, 3H), 6.98 (dd, *J* = 1.03, and 8.26 Hz, 1H), 6.90–6.76 (m, 2H), 6.71 (d, *J* = 4.63 Hz, 1H), 6.59–6.50 (m, 2H), 4.23 (d, *J* = 5.89 Hz, 2H), and 3.81 (s, 3H); LC-MS retention time (Method 2): 4.888 min; HRMS: *m/z* (M+H)$^+$ = (Calculated for $C_{17}H_{18}N_3O_3S_2$ 376.0784) found, 376.0765.



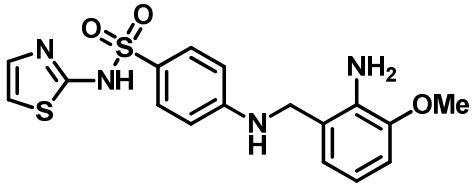
4-(2,3-dimethoxybenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide (12): Method B: using 2,3-dimethoxyphenyl)methanamine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46 (d, *J* = 8.78 Hz, 2H), 7.18 (d, *J* = 4.63 Hz, 1H), 7.06–6.90 (m, 2H), 6.87–6.79 (m, 2H), 6.73 (d, *J* = 4.58 Hz, 1H), 6.59 (d, *J* = 8.84 Hz, 2H), 4.28 (d, *J* = 5.90 Hz, 2H), and 3.78 (d, *J* = 13.99 Hz, 6H); LC-MS retention time (Method 2): 4.756 min; HRMS: *m/z* (M+H)$^+$ = (Calculated for $C_{18}H_{20}N_3O_4S_2$ 406.0890) found, 406.0885.



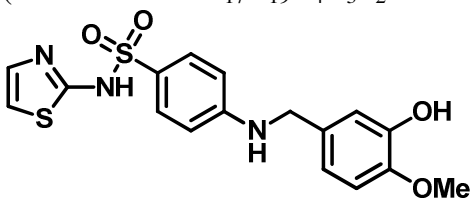
4-(2-aminobenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide (13): Method A: using tert-butyl (2-formylphenyl)carbamate and removing the subsequent carbamate with 4 M HCl in dioxane over 30 min. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54–7.37 (m, 3H), 7.24–7.06 (m, 3H), 6.96 (d, J = 7.86 Hz, 1H), 6.86 (h, J = 7.06 Hz, 1H), 6.74 (d, J = 4.61 Hz, 1H), 6.65–6.50 (m, 3H), and 4.23 (s, 2H); LC-MS retention time (Method 1): 1.863 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{17}N_4O_2S_2$ 361.0787) found, 361.0784.



4-(3-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzene sulfonamide (14): Method A: using 3-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.31 (s, 1H), 7.51–7.37 (m, 2H), 7.18 (d, J = 4.62 Hz, 1H), 7.10 (t, J = 7.77 Hz, 1H), 6.97 (t, J = 5.90 Hz, 1H), 6.79–6.68 (m, 3H), 6.66–6.49 (m, 3H), and 4.31–4.14 (m, 2H); LC-MS retention time (Method 1): 1.775 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{16}N_3O_3S_2$ 362.0628) found, 362.0614.

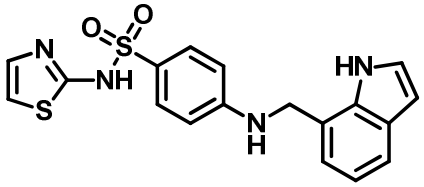


4-(2-amino-3-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide TFA (15): Method A: using 3-methoxy-2-nitrobenzaldehyde; A heterogeneous solution of 4-(3-methoxy-2-nitrobenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (0.075 g, 0.178 mmol) in MeOH (1.8 mL), AcOH (0.102 mL, 1.784 mmol) and zinc (0.023 g, 0.357 mmol) were stirred for 30 min, filtered through celite, and washed with MeOH. The filtrate was concentrated and purified using a prep-HPLC (gradient 10-100% acetonitrile w/ 0.1% TFA in water w/ 0.1% TFA) to give the desired product; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44 (d, J = 8.78 Hz, 2H), 7.17 (d, J = 4.61 Hz, 1H), 6.78 (dd, J = 1.23, and 7.81 Hz, 1H), 6.75–6.67 (m, 3H), 6.56 (d, J = 8.82 Hz, 2H), 4.16 (s, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 1): 2.775 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{19}N_4O_3S_2$ 391.0893) found, 391.0874.

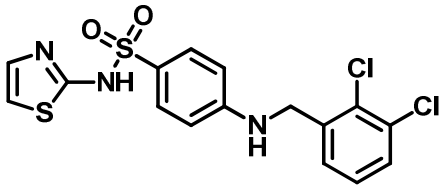


4-(3-hydroxy-4-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (16): Method A: using 3-hydroxy-4-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.86 (s, 1H), 7.52–7.32 (m, 2H), 7.15 (d, J = 4.61 Hz, 1H), 6.95–6.74 (m, 2H), 6.77–6.62 (m, 4H), 6.62–6.49 (m,

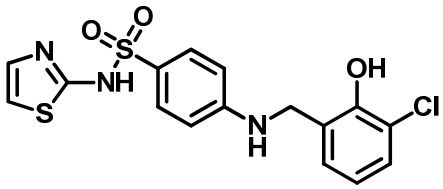
2H), 4.13 (d, J = 5.92 Hz, 2H), and 3.70 (s, 3H); LC-MS retention time (Method 2): 4.123 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_4S_2$ 392.0733) found, 392.0719.



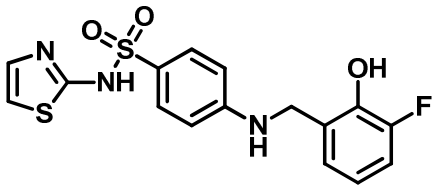
4-((1H-indol-7-yl)methylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (17): Method A: using 1H-indole-7-carbaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51–7.38 (m, 4H), 7.36–7.31 (m, 1H), 7.16 (t, J = 4.53 Hz, 1H), 6.95–6.85 (m, 2H), 6.70 (d, J = 4.62 Hz, 1H), 6.67–6.57 (m, 2H), 6.44 (dd, J = 1.83, and 3.08 Hz, 1H), and 4.53 (d, J = 5.67 Hz, 2H); LC-MS retention time (Method 2): 4.899 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{18}H_{17}N_4O_2S_2$ 385.0787) found, 385.0774.



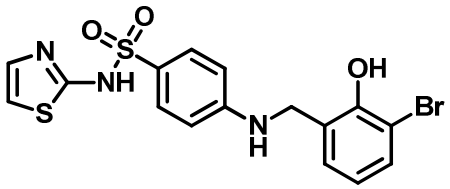
4-(2,3-dichlorobenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (18): Method A: using 2,3-dichlorobenzaldehyde; LC-MS retention time (Method 2): 5.786 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{14}Cl_2N_3O_2S_2$ 413.9899) found, 413.9907.



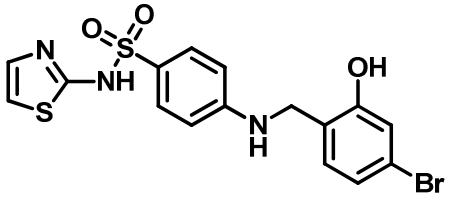
4-(3-chloro-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (19): Method A: using 3-chloro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48–7.35 (m, 2H), 7.21 (dd, J = 1.63, and 7.94 Hz, 1H), 7.13–7.02 (m, 1H), 6.87 (d, J = 3.82 Hz, 1H), 6.76 (t, J = 7.77 Hz, 1H), 6.51–6.43 (m, 2H), 6.35 (d, J = 3.82 Hz, 1H), and 4.25 (s, 2H); LC-MS retention time (Method 1): 2.076 min; HRMS: *m/z* $(M+Na)^+$ = (Calculated for $C_{16}H_{14}Cl\ N_3NaO_3S_2$ 419.0085) found, 419.0047.



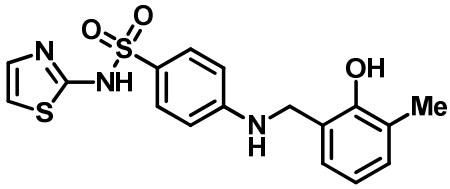
4-(3-fluoro-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (20): Method A: using 3-fluoro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.63 (s, 1H), 7.49–7.33 (m, 2H), 7.08–6.93 (m, 2H), 6.91–6.80 (m, 1H), 6.72 (t, J = 7.94 Hz, 1H), 6.51–6.38 (m, 3H), 6.34 (d, J = 3.80 Hz, 1H), and 4.23 (d, J = 3.52 Hz, 2H); LC-MS retention time (Method 1): 2.076 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}FN_3O_3S_2$ 380.0533) found, 380.0521.



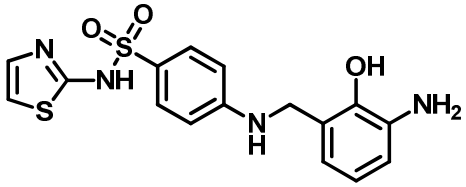
4-(3-bromo-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide, (21): Method A: using 3-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.64 (s, 1H), 8.16–8.02 (m, 1H), 7.86 (d, J = 8.75 Hz, 2H), 7.79 (dd, J = 1.59, and 7.90 Hz, 1H), 7.58 (d, J = 4.61 Hz, 1H), 7.52 (dd, J = 1.56, and 7.59 Hz, 1H), 7.28 (s, 1H), 7.14 (t, J = 7.78 Hz, 1H), 6.96 (d, J = 8.89 Hz, 2H), and 4.69 (d, J = 5.79 Hz, 2H); LC-MS retention time (Method 2): 4.777 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}BrN_3O_3S_2$ 441.9712) found, 441.9705.



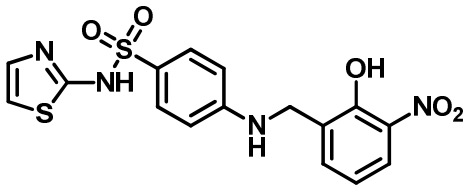
4-(4-bromo-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (22): Method A: using 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 7.47–7.34 (m, 2H), 7.03 (d, J = 8.13 Hz, 1H), 6.99–6.92 (m, 2H), 6.88 (dd, J = 1.97, and 8.10 Hz, 1H), 6.65–6.31 (m, 4H), and 4.12 (d, J = 5.91 Hz, 2H); LC-MS retention time (Method 1): 2.938 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}BrN_3O_3S_2$ 441.9712) found, 441.9704.



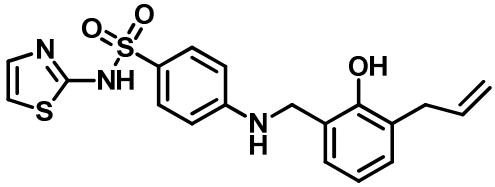
4-(2-hydroxy-3-methylbenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (23): Method A: using 2-hydroxy-3-methylbenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (s, 1H), 7.34–7.21 (m, 2H), 7.00 (d, J = 4.62 Hz, 1H), 6.84–6.75 (m, 2H), 6.64–6.48 (m, 3H), 6.44–6.31 (m, 2H), 4.08 (d, J = 5.76 Hz, 2H), and 2.01 (s, 3H); LC-MS retention time (Method 1): 2.083 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_3S_2$ 376.0784) found, 376.0779.



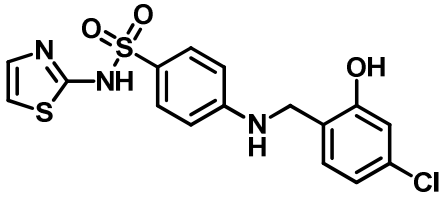
4-(3-amino-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (24): Method A: using 2-hydroxy-3-nitrobenzaldehyde and reducing the nitro-group with zinc and acetic acid conditions (see compound **15** for details). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49–7.39 (m, 2H), 7.17 (d, J = 4.65 Hz, 1H), 6.92 (t, J = 8.63 Hz, 2H), 6.85–6.69 (m, 3H), 6.60–6.50 (m, 2H), and 4.28 (s, 2H); LC-MS retention time (Method 1): 2.263 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{17}N_4O_3S_2$ 377.0737) found, 377.0730.



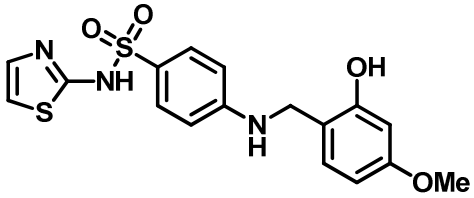
4-(2-hydroxy-3-nitrobenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (25): Method 1A: using 2-hydroxy-3-nitrobenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (dd, J = 1.65, and 8.43 Hz, 1H), 7.58–7.24 (m, 3H), 7.17 (d, J = 4.66 Hz, 1H), 7.05–6.88 (m, 2H), 6.72 (d, J = 4.61 Hz, 1H), 6.67–6.34 (m, 2H), and 4.33 (d, J = 4.46 Hz, 2H); LC-MS retention time (Method 2): 4.742 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}N_4O_5S_2$ 407.0478) found, 407.0465.



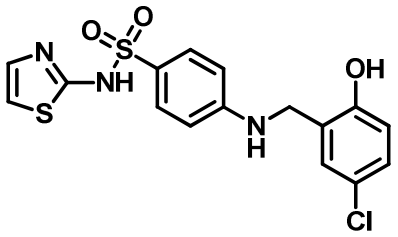
4-(3-allyl-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide TFA (26): Method A: using 3-allyl-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.47 (s, 1H), 7.49–7.38 (m, 2H), 7.17 (d, J = 4.61 Hz, 1H), 6.96 (ddd, J = 1.73, 7.52, and 22.52 Hz, 2H), 6.80–6.65 (m, 3H), 6.61–6.50 (m, 2H), 5.93 (ddt, J = 6.63, 10.04, and 16.79 Hz, 1H), 5.08–4.95 (m, 2H), 4.25 (s, 2H), and 3.34 (dt, J = 1.44, and 6.58 Hz, 2H); LC-MS retention time (Method 1): 3.155 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{19}H_{20}N_3O_3S_2$ 402.0941) found, 402.0926.



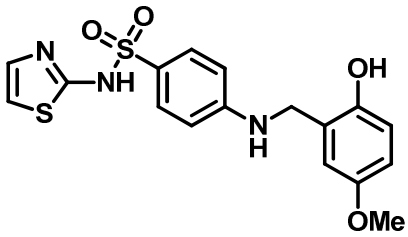
4-(4-chloro-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (27): Method A: using 4-chloro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.38 (d, J = 8.6 Hz, 2 H), 7.07 (d, J = 8.2 Hz, 1 H), 6.92–6.61 (m, 3 H), 6.49–6.20 (m, 4 H), and 4.12 (s, 2 H); LC-MS retention time (Method 2): 4.700 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}ClN_3O_3S_2$ 396.0238) found, 396.0220.



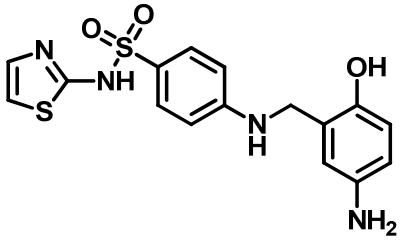
4-(2-hydroxy-4-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (28): Method A: using 2-hydroxy-4-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 7.41–7.32 (m, 2H), 7.00 (d, J = 8.37 Hz, 1H), 6.87–6.80 (m, 1H), 6.49–6.39 (m, 2H), 6.36 (d, J = 2.47 Hz, 1H), 6.34–6.26 (m, 2H), 6.21 (t, J = 5.86 Hz, 1H), 4.07 (d, J = 5.77 Hz, 2H), and 3.63 (s, 3H); LC-MS retention time (Method 1): 3.155 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_4S_2$ 392.0733) found, 392.0715.



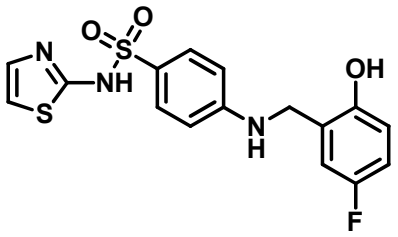
4-(5-chloro-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (29): Method A: using 5-chloro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 7.48–7.37 (m, 2H), 7.13–7.00 (m, 3H), 6.89–6.76 (m, 2H), 6.64 (d, J = 4.44 Hz, 1H), 6.58–6.48 (m, 2H), and 4.17 (d, J = 5.97 Hz, 2H); LC-MS retention time (Method 2): 4.610 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}ClN_3O_3S_2$ 396.0238) found, 396.0233.



4-(2-hydroxy-5-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (30): Method A: using 2-hydroxy-5-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (s, 1H), 7.47–7.38 (m, 2H), 7.08 (d, J = 4.44 Hz, 1H), 6.77–6.65 (m, 3H), 6.65–6.48 (m, 4H), 4.15 (d, J = 5.91 Hz, 2H), and 3.56 (s, 3H); LC-MS retention time (Method 2): 4.137 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_4S_2$ 392.0733) found, 392.0725.

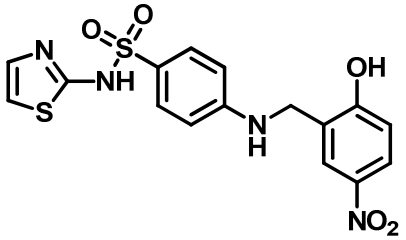


4-(5-amino-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (31): Method A: using 2-hydroxy-5-nitrobenzylaldehyde and reducing the nitro-group with zinc and acetic acid conditions (see compound **15** for details). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.92 (s, 1H), 7.46 (d, J = 8.83 Hz, 2H), 7.18 (d, J = 4.64 Hz, 1H), 7.04–6.92 (m, 2H), 6.86 (d, J = 8.23 Hz, 1H), 6.73 (d, J = 4.66 Hz, 1H), 6.53 (d, J = 8.83 Hz, 2H), and 4.22 (d, J = 5.77 Hz, 2H); LC-MS retention time (Method 1): 2.165 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{17}N_4O_3S_2$ 377.0737) found, 377.0719.

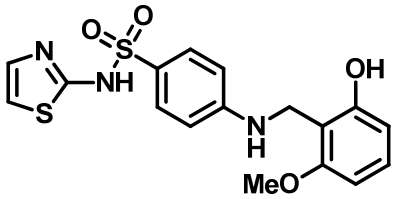


4-(5-fluoro-2-hydroxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (32): Method A: using 5-fluoro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.63–9.54 (m, 1H),

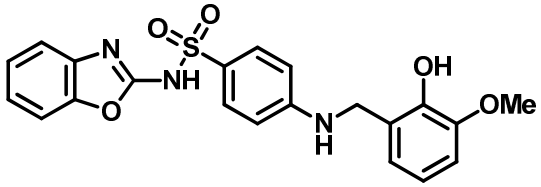
7.44–7.33 (m, 2H), 6.92–6.73 (m, 4H), 6.51–6.36 (m, 3H), 6.36–6.29 (m, 1H), and 4.14 (d, J = 6.00 Hz, 2H); LC-MS retention time (Method 1): 3.017 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}FN_3O_3S_2$ 380.0533) found, 380.0526.



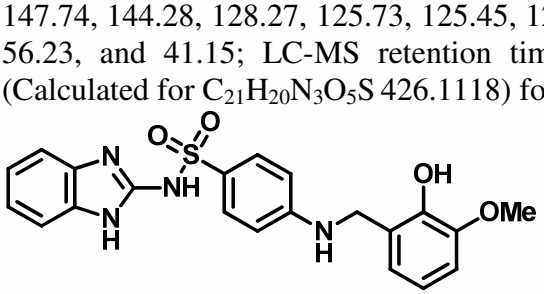
4-(2-hydroxy-5-nitrobenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (33): Method A: using 2-hydroxy-5-nitrobenzylaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.92–7.76 (m, 2 H), 7.41 (d, J = 9.0 Hz, 2 H), 6.97 (d, J = 4.3 Hz, 1 H), 6.56–6.40 (m, 4 H), 5.74 (s, 1 H), and 4.10 (s, 2 H); LC-MS retention time (Method 2): 4.273 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{16}H_{15}N_4O_5S_2$ 407.0478) found, 407.0470.



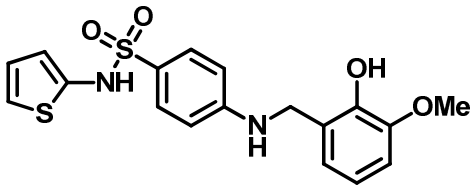
4-(2-hydroxy-6-methoxybenzylamino)-*N*-(thiazol-2-yl)benzenesulfonamide (34): Method B: using 2-hydroxy-6-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.59 (s, 1H), 7.74–7.54 (m, 1H), 7.42 (d, J = 8.79 Hz, 2H), 7.24–7.05 (m, 1H), 6.68 (d, J = 8.87 Hz, 2H), 6.46 (ddd, J = 0.93, 7.08, and 8.22 Hz, 2H), 6.22 (d, J = 5.51 Hz, 1H), 4.12 (d, J = 5.21 Hz, 2H), and 3.74 (s, 3H); LC-MS retention time (Method 1): 2.960 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{17}H_{18}N_3O_4S_2$ 392.0733) found, 392.0716.



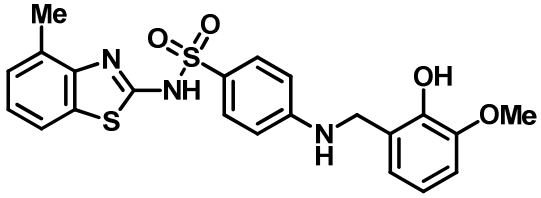
***N*-(benzo[d]oxazol-2-yl)-4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide (36):** Method C: using 2-bromobenzoxazole; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.40 (s, 1H), 8.71 (s, 1H), 7.55 (dd, J = 2.60, and 9.29 Hz, 2H), 7.43 (d, J = 7.93 Hz, 1H), 7.31–7.25 (m, 1H), 7.26–7.20 (m, 1H), 7.16 (td, J = 1.42, and 7.82 Hz, 1H), 6.86 (t, J = 5.64 Hz, 1H), 6.81 (dd, J = 1.72, and 7.88 Hz, 1H), 6.75–6.69 (m, 1H), 6.66 (t, J = 7.85 Hz, 1H), 6.61–6.54 (m, 2H), 4.21 (d, J = 5.58 Hz, 2H), and 3.76 (d, J = 2.79 Hz, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.01, 152.37, 147.74, 144.28, 128.27, 125.73, 125.45, 123.67, 120.40, 119.06, 112.19, 111.31, 110.88, 110.59, 56.23, and 41.15; LC-MS retention time (Method 2): 4.848 min; HRMS: *m/z* $(M+H)^+$ = (Calculated for $C_{21}H_{20}N_3O_5S$ 426.1118) found, 426.1098.



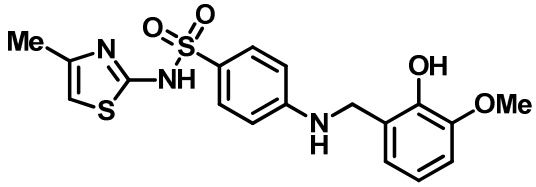
***N*-(1H-benzo[*d*]imidazol-2-yl)-4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide (37):** Method D: using 2-aminobenzimidazole and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.68 (s, 2H), 7.56–7.49 (m, 2H), 7.22 (dt, J = 3.37, and 5.83 Hz, 2H), 7.06 (dt, J = 3.34, and 5.73 Hz, 2H), 6.79 (dd, J = 1.71, and 7.99 Hz, 1H), 6.71 (dd, J = 1.59, and 7.73 Hz, 1H), 6.65 (t, J = 7.83 Hz, 1H), 6.58–6.50 (m, 2H), 4.19 (s, 2H), and 3.75 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 151.47, 150.22, 147.72, 144.26, 130.61, 129.89, 127.61, 125.79, 122.59, 120.44, 119.05, 111.46, 111.09, 110.86, 56.23, and 41.32; LC-MS retention time (Method 2): 4.454min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{21}H_{20}N_4O_4S$, 424.1205) found 424.1202.



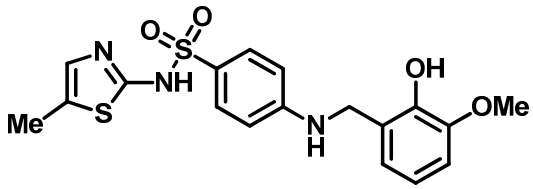
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(thiophen-2-yl)benzenesulfonamide (38): Method C: using 2-bromothiophene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (s, 1 H), 7.38−7.28 (m, 1 H), 7.05−6.98 (m, 1 H), 6.91 (t, J = 6.1 Hz, 1 H), 6.83 (dd, J = 2.0, and 7.8 Hz, 1 H), 6.78−6.64 (m, 3 H), 6.61−6.52 (m, 2 H), 6.51−6.43 (m, 1 H), 4.25 (s, 2 H), and 3.80 (s, 3 H); LC-MS retention time (Method 1): 2.435 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{18}H_{19}N_2O_4S_2$, 391.0781) found 391.0773.



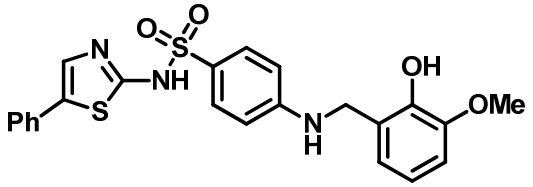
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(4-methylbenzo[d]thiazol-2-yl)benzenesulfonamide TFA (39): Method D: using 2-amino-4-methylbenzthiazole and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.76 (s, 1H), 8.71 (s, 1H), 7.58–7.45 (m, 3H), 7.18–7.05 (m, 2H), 6.81 (dd, J = 1.73, and 7.89 Hz, 1H), 6.76–6.54 (m, 4H), 4.21 (s, 2H), 3.76 (s, 3H), and 2.34 (s, 3H); LC-MS retention time (Method 2): 5.522 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{22}N_3O_4S_2$, 456.1046) found 456.1037.



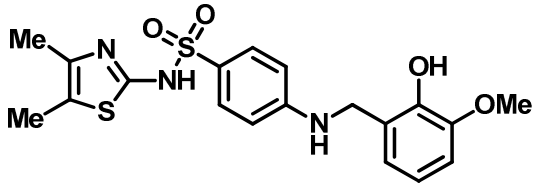
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(4-methylthiazol-2-yl)benzenesulfonamide TFA (40): Method C: using 2-bromo-4-methylthiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1 H), 8.70 (s, 1 H), 7.48−7.32 (m, 3 H), 6.89−6.72 (m, 6 H), 6.61−6.47 (m, 3 H), 6.27 (s, 1 H), 4.20 (d, J = 5.90 Hz, 2 H), 3.76 (s, 3 H), and 1.95 (s, 3 H); LC-MS retention time (Method 1): 1.962 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{18}H_{20}N_3O_4S_2$, 406.0890) found 406.0875.



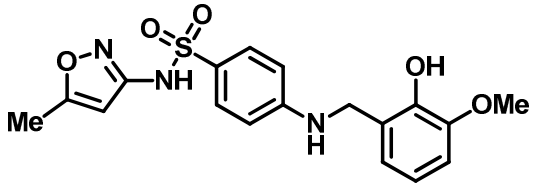
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(5-methylthiazol-2-yl)benzenesulfonamide TFA (41): Method D: using 2-amino-5-methylthiazole and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 8.73 (s, 1H), 7.46–7.38 (m, 2H), 6.91–6.63 (m, 5H), 6.59–6.51 (m, 2H), 4.20 (d, J = 5.86 Hz, 2H), 3.77 (s, 3H), and 2.13 (d, J = 1.39 Hz, 3H); LC-MS retention time (Method 1): 3.182 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{18}H_{20}N_3O_4S_2$, 406.0890) found 406.0889.



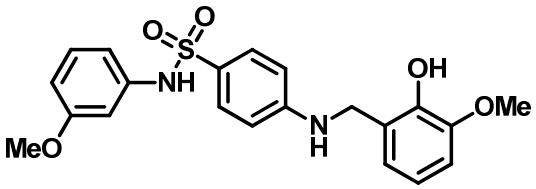
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(5-phenylthiazol-2-yl)benzenesulfonamide TFA (42): Method D: using 2-amino-5-phenylthiazole and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.70 (s, 1H), 7.68 (s, 1H), 7.56–7.25 (m, 8H), 6.87–6.78 (m, 2H), 6.79–6.62(m, 2H), 6.61–6.53 (m, 2H), 4.21 (d, J = 5.8 Hz, 2H), and 3.76 (s, 3H); LC-MS retention time (Method 2): 5.417 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{22}N_3O_4S_2$, 468.1046) found 468.1028.



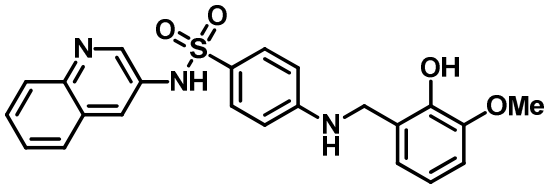
***N*-(4,5-dimethylthiazol-2-yl)-4-(2-hydroxy-3-methoxybenzylamino)benzenesulfonamide TFA (43):** Method C: using 2-bromo-4,5-dimethylthiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.25 (s, 1H), 8.94 (d, J = 0.71 Hz, 1H), 7.73–7.45 (m, 2H), 7.13–6.80 (m, 4H), 6.83–6.62 (m, 2H), 4.53–4.25 (m, 2H), 3.98 (d, J = 0.60 Hz, 3H), ad 2.35–1.95 (m, 6H); LC-MS retention time (Method 2): 4.859 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{19}H_{21}N_3O_4S_2$, 420.1046) found 420.1037.



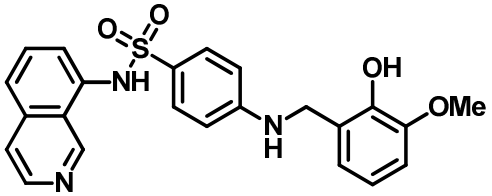
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide TFA (44): Method D: using 3-amino-5-methylisoxazole and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.91 (d, J = 1.25 Hz, 1H), 8.76 (d, J = 3.84 Hz, 1H), 7.77–7.55 (m, 1H), 7.52–7.28 (m, 2H), 7.02 (t, J = 5.41 Hz, 1H), 6.77–6.64 (m, 2H), 6.63–6.51 (m, 2H), 6.11–6.02 (m, 1H), 4.27–4.14 (m, 2H), 3.77 (d, J = 1.18 Hz, 3H), and 2.26 (s, 3H); LC-MS retention time (Method 2): 4.804 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{18}H_{20}N_3O_5S$, 390.1118) found 390.1109.



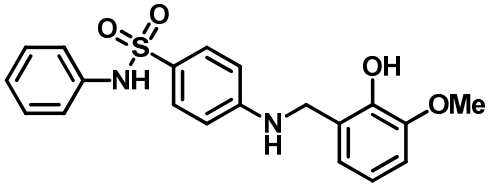
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(3-methoxyphenyl)benzenesulfonamide (45): Method C: using 1-bromo-3-methoxybenzene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 8.73 (d, J = 0.5 Hz, 1H), 7.48–7.36 (m, 2H), 7.13–7.03 (m, 1H), 6.95–6.80 (m, 2H), 6.77–6.47 (m, 7H), 4.20 (d, J = 5.8 Hz, 2H), 3.78 (s, 3H), and 3.64 (s, 3H); LC-MS retention time (Method 2): 5.437 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{21}H_{23}N_2O_5S$, 415.1322) found 415.1302.



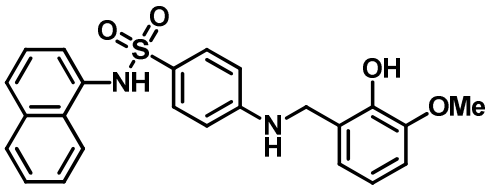
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(quinolin-3-yl)benzenesulfonamide TFA (46): Method C: using 3-bromoquinoline; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (d, J = 1.27 Hz, 1H), 8.20 (dd, J = 0.78, and 2.71 Hz, 1H), 7.60–7.33 (m, 3H), 7.17 (dddd, J = 1.31, 6.90, 8.19, and 31.70 Hz, 2H), 7.09–7.04 (m, 2H), 6.41 (dd, J = 1.94, 7.69 Hz, 1H), 6.30–6.20 (m, 2H), 6.17–6.10 (m, 2H), 3.76 (s, 2H), and 3.36 (s, 3H); LC-MS retention time (Method 1): 2.304 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{22}N_3O_4S$, 436.1326) found 436.1316.



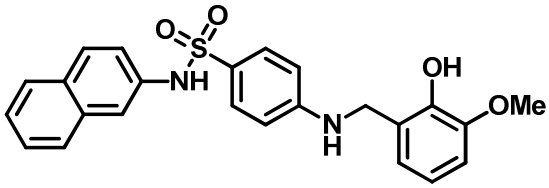
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(isoquinolin-8-yl)benzenesulfonamide (47): Method C: using 8-bromoisoquinoline; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34–10.24 (s, 1H), 9.56 (s, 1H), 8.74 (s, 1H), 8.54 (d, J = 5.95 Hz, 1H), 8.02 (d, J = 5.96 Hz, 1H), 7.91–7.73 (m, 2H), 7.44–7.29 (m, 3H), 6.85 (t, J = 4.80 Hz, 1H), 6.76–6.62 (m, 2H), 6.61–6.44 (m, 2H), 4.19 (s, 2H), and 3.79 (s, 3H); LC-MS retention time (Method 1): 1.914 min; HRMS: *m/z* $(M+Na)^+$ (Calculated for $C_{23}H_{21}NaN_3O_4S$, 458.1145) found 458.1129.



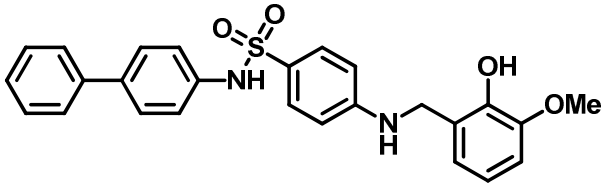
4-(2-hydroxy-3-methoxybenzylamino)-*N*-phenylbenzenesulfonamide TFA (48): Method C: using bromobenzene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 8.73 (d, J = 2.23 Hz, 1H), 7.42–7.34 (m, 2H), 7.21–7.12 (m, 2H), 7.06–6.99 (m, 2H), 6.98–6.91 (m, 1H), 6.82 (dd, J = 1.86, and 7.72 Hz, 1H), 6.74–6.64 (m, 2H), 6.57–6.49 (m, 2H), 4.31–3.99 (m, 2H), and 3.76 (s, 3H); LC-MS retention time (Method 1): 2.750 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{20}H_{21}N_2O_4S$, 385.1217) found 385.1223.



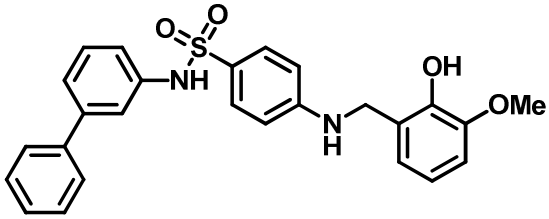
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(naphthalen-1-yl)benzenesulfonamide (49): Method D: using naphthalen-1-amine and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.74 (s, 1H), 8.73 (s, 1H), 8.06 (ddd, *J* = 0.74, 1.48, and 8.45 Hz, 1H), 7.89–7.82 (m, 1H), 7.72 (d, *J* = 8.15 Hz, 1H), 7.54–7.27 (m, 5H), 7.15 (dd, *J* = 1.05, and 7.45 Hz, 1H), 6.85 (q, *J* = 4.87 Hz, 2H), 6.75–6.66 (m, 2H), 6.57–6.47 (m, 2H), 4.19 (d, *J* = 5.65 Hz, 2H), and 3.79 (s, 3H); LC-MS retention time (Method 1): 2.744 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{23}N_2O_4S$, 435.1373) found 435.1392.



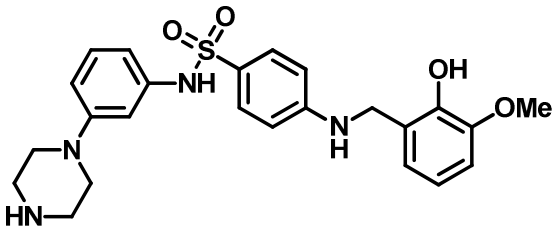
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(naphthalen-2-yl)benzenesulfonamide (50): Method D: using naphthalen-2-amine and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (d, *J* = 1.4 Hz, 1H), 8.71 (s, 1H), 7.81–7.67 (m, 3H), 7.54–7.30 (m, 5H), 7.27 (dt, *J* = 1.9, and 8.8 Hz, 1H), 6.94–6.76 (m, 2H), 6.76–6.61 (m, 2H), 6.53 (dd, *J* = 8.8, 1.7 Hz, 2H), 4.16 (s, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 1): 3.281 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{23}N_2O_4S$, 435.1373) found 435.1373.



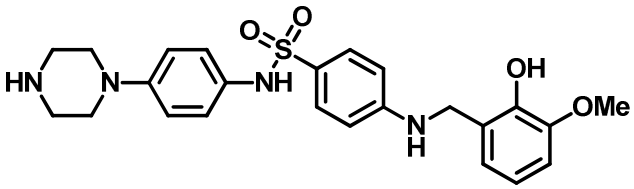
***N*-([1,1'-biphenyl]-4-yl)-4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide (51):** Method D: using biphenyl-4-amine and 2-hydroxy-3-methoxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 8.72 (s, 1H), 7.60–7.35 (m, 8H), 7.34–7.24 (m, 1H), 7.18–7.09 (m, 2H), 6.90 (t, *J* = 5.9, Hz, 1H), 6.82 (dd, *J* = 1.7, and 7.8 Hz, 1H), 6.76–6.62 (m, 2H), 6.61–6.52 (m, 2H), 4.19 (d, *J* = 5.8 Hz, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 2): 6.433 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{26}H_{25}N_2O_4S$, 461.1530) found 461.1529.



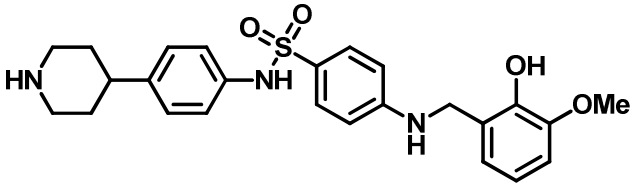
***N*-([1,1'-biphenyl]-3-yl)-4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide (52):** Method C: using 3-bromo-1,1'-biphenyl; ^{1}H NMR (400 MHz, DMSO-d_6) δ9.98 (s, 1H), 8.72 (s, 1H), 7.55–7.19 (m, 11H), 7.06 (ddd, *J* = 1.5, 2.2, and 7.6 Hz, 1H), 6.96–6.73 (m, 2H), 6.75–6.49 (m, 4H), 4.20 (d, *J* = 5.8 Hz, 2H), and 3.78 (s, 3H); LC-MS retention time (Method 2): 6.131 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{26}H_{25}N_2O_4S$, 461.1530) found 461.1521.



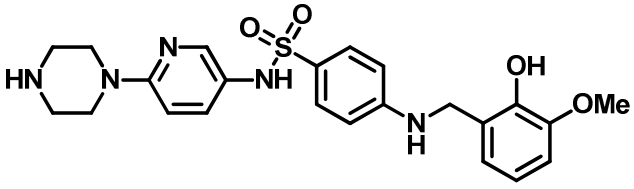
4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(3-(piperazin-1-yl)phenyl)benzenesulfonamide (53): Method 1C: using tert-butyl 4-(3-bromophenyl)piperazine-1-carboxylate and the Boc group was removed after the reductive amination with 4 M HCl in dioxanes over a 30 min period. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.75 (s, 1H), 7.47–7.38 (m, 2H), 7.05 (t, J = 8.12 Hz, 1H), 6.95–6.81 (m, 2H), 6.77–6.65 (m, 3H), 6.64–6.51 (m, 4H), 4.20 (d, J = 5.58 Hz, 2H), 3.79 (s, 3H), 3.21 (s, 8H), and 0.88–0.76 (m, 1H); LC-MS retention time (Method 1): 1.660 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{29}N_4O_4S$, 469.1904) found 469.1897.



4-(2-hydroxy-3-methoxybenzylamino)-*N*-(4-(piperazin-1-yl)phenyl)benzenesulfonamide (54): Method D: using tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate and 2-hydroxy-3-methoxybenzaldehyde. The Boc group was removed after the reductive amination with 4 M HCl/dioxanes for 1 h at rt. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.50 (s, 1H), 8.74 (d, J = 0.47 Hz, 1H), 7.39–7.30 (m, 2H), 6.98–6.79 (m, 6H), 6.78–6.65 (m, 2H), 6.59–6.50 (m, 2H), 4.20 (d, J = 5.63 Hz, 2H), 3.79 (s, 3H), and 3.19 (s, 8H); LC-MS retention time (Method 1): 1.648 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{29}N_4O_4S$, 469.1904) found 469.1900.

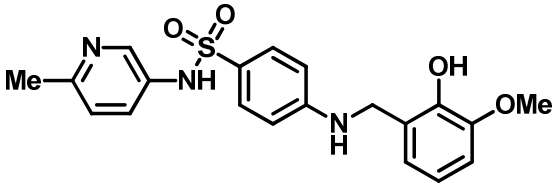


4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(4-(piperidin-4-yl)phenyl)benzenesulfonamide (55): Method D: using tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate and 2-hydroxy-3-methoxybenzaldehyde. The Boc group was removed after the reductive amination with 4 M HCl in dioxane for 1 h at rt. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 8.92 (d, J = 0.5 Hz, 1H), 7.63–7.56 (m, 2H), 7.32–7.15 (m, 6H), 6.95–6.82 (m, 2H), 6.78–6.68 (m, 2H), 4.37 (d, J = 5.7 Hz, 2H), 3.96 (s, 3H), 3.57–3.42 (m, 4H), 3.14-3.01 (m, 4H), and 2.90 (d, J = 11.4 Hz, 1H); LC-MS retention time (Method 1): 1.710 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{25}H_{30}N_3O_4S$, 468.1952) found 468.1935.

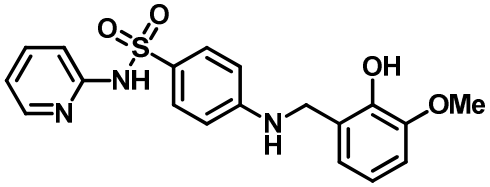


4-(2-hydroxy-3-methoxybenzylamino)-*N*-(6-(piperazin-1-yl)pyridin-3-yl)benzenesulfonamide (56): Method C: using tert-butyl 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate, and the Boc group was removed after the reductive amination with 4 M

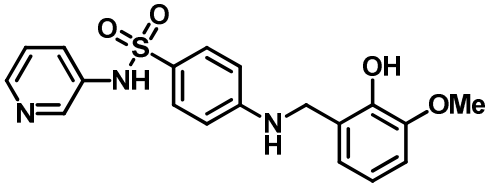
HCl/dioxanes over a 1 h. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.57 (s, 1H), 9.12 (d, J = 7.21 Hz, 2H), 7.74 (d, J = 2.65 Hz, 1H), 7.31 (dd, J = 4.87, and 7.36 Hz, 2H), 7.07 (s, 1H), 6.89–6.80 (m, 2H), 6.76–6.59 (m, 2H), 6.60–6.51 (m, 2H), 4.19 (s, 2H), 3.77 (s, 3H), 3.75–3.53 (m, 4H), and 3.17–3.07 (m, 4H); LC-MS retention time (Method 1): 1.993 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{28}N_5O_4S$, 470.1857) found 470.1848.



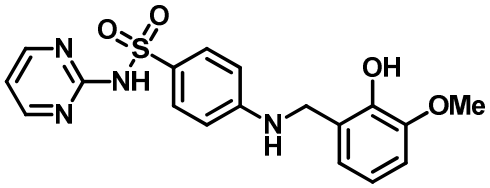
4-(2-hydroxy-3-methoxybenzylamino)-*N*-(6-methylpyridin-3-yl)benzenesulfonamide (57): Method C: using 5-bromo-2-methylpyridine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 8.61 (s, 1H), 8.02 (dd, J = 0.68, 2.63 Hz, 1H), 7.47–7.39 (m, 1H), 7.32–7.23 (m, 2H), 7.18 (d, J = 8.47 Hz, 1H), 6.70 (dd, J = 1.92, and 7.68 Hz, 1H), 6.63–6.50 (m, 2H), 6.48–6.40 (m, 2H), 4.06 (s, 2H), 3.64 (s, 3H), and 2.28 (s, 3H); LC-MS retention time (Method 1): 1.840 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{20}H_{22}N_3O_4S$, 400.1326) found 400.1315.



4-(2-hydroxy-3-methoxybenzylamino)-*N*-(pyridin-2-yl)benzenesulfonamide (58): Method C: using 2-bromopyridine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (d, J = 0.54 Hz, 1H), 8.11–7.96 (m, 1H), 7.65–7.58 (m, 1H), 7.52 (d, J = 8.70 Hz, 2H), 7.09–6.98 (m, 1H), 6.92–6.79 (m, 3H), 6.76–6.63 (m, 2H), 6.58–6.50 (m, 2H), 4.19 (d, J = 5.83 Hz, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 2): 4.540 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{19}H_{20}N_3O_4S$, 386.1169) found 386.1158.

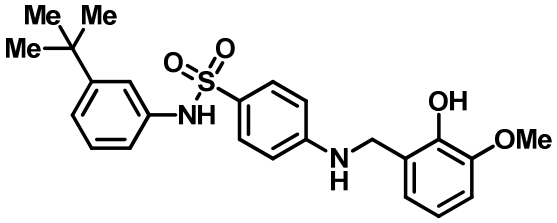


4-(2-hydroxy-3-methoxybenzylamino)-*N*-(pyridin-3-yl)benzenesulfonamide (59): Method C: using 3-bromopyridine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.30 (s, 1H), 8.73 (s, 1H), 8.31–8.21 (m, 2H), 7.57 (ddd, J = 1.38, 2.63, and 8.37 Hz, 1H), 7.46–7.32 (m, 3H), 6.83 (dd, J = 1.92, and 7.71 Hz, 1H), 6.75–6.62 (m, 2H), 6.61–6.51 (m, 2H), 4.19 (s, 2H), 3.77 (s, 3H); LC-MS retention time (Method 1): 1.804 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{19}H_{20}N_3O_4S$, 386.1169) found 386.1166.

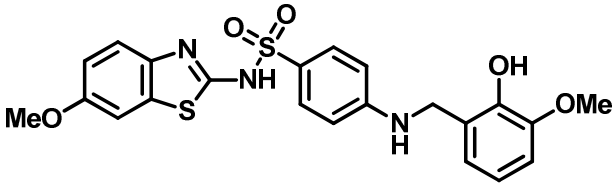


4-(2-hydroxy-3-methoxybenzylamino)-*N*-(pyrimidin-2-yl)benzenesulfonamide TFA (60): Method C: using 2-bromopyrimidine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.25 (s, 1H), 8.77 (s, 1H), 8.48 (d, J = 4.83 Hz, 2H), 7.72–7.50 (m, 2H), 6.99 (dt, J = 5.43, and 15.84 Hz, 2H), 6.85

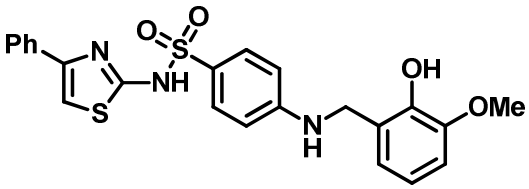
(dd, J = 1.69, and 7.85 Hz, 1H), 6.77–6.66 (m, 2H), 6.62–6.56 (m, 2H), 4.23 (d, J = 5.65 Hz, 2H), and 3.79 (s, 3H); LC-MS retention time (Method 2): 4.266 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{18}H_{19}N_4O_4S$, 387.1122) found 387.1115.



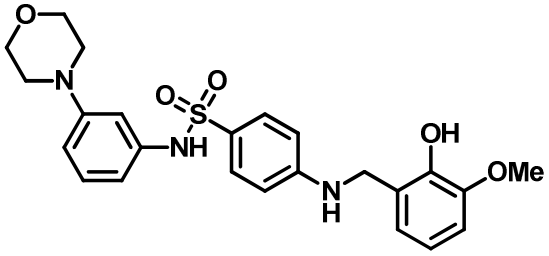
***N*-(3-(tert-butyl)phenyl)-4-((2-hydroxy-3-methoxybenzyl)amino)benzenesulfonamide, TFA (61):** Method C: using 1-bromo-3-(tert-butyl)benzene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 1H), 8.71 (s, 1H), 7.42–7.32 (m, 2H), 7.14–6.93 (m, 3H), 6.93–6.78 (m, 3H), 6.73–6.60 (m, 2H), 6.58–6.47 (m, 2H), 4.18 (s, 2H), 3.76 (s, 3H), and 1.14 (s, 9H); LC-MS retention time (Method 2): 6.184 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{29}N_2O_4S$, 441.0843) found 441.1844.



4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(6-methoxybenzo[d]thiazol-2-yl)benzenesulfonamide, TFA (62): Method C: using 2-bromo-6-methoxybenzo[d]thiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.71 (d, J = 0.47 Hz, 1H), 7.51–7.41 (m, 2H), 7.38 (d, J = 2.54 Hz, 1H), 7.14 (d, J = 8.76 Hz, 1H), 6.96–6.78 (m, 3H), 6.76–6.62 (m, 2H), 6.61–6.53 (m, 2H), 4.21 (d, J = 5.89 Hz, 2H), 3.75 (s, 3H), and 3.73 (s, 3H); LC-MS retention time (Method 2): 5.278 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{22}N_3O_5S_2$, 472.0995) found 472.0998.

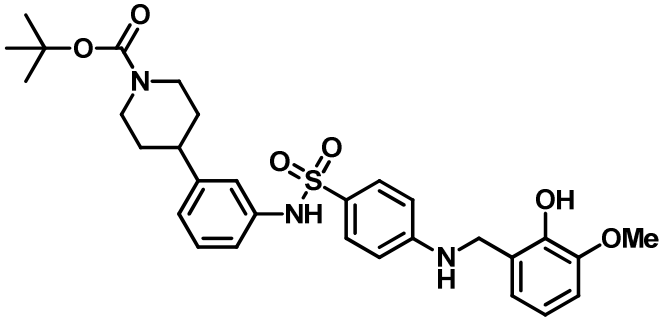


4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(4-phenylthiazol-2-yl)benzenesulfonamide, TFA (63): Method C: using 2-bromo-4-phenylthiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 7.67 (d, J = 7.47 Hz, 2H), 7.53–7.24 (m, 6H), 7.08 (d, J = 19.97 Hz, 1H), 6.92–6.45 (m, 6H), 4.21 (d, J = 5.55 Hz, 2H), and 3.77 (s, 3H); LC-MS retention time (Method 2): 5.200 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{22}N_3O_4S$, 468.1046) found 468.1066.

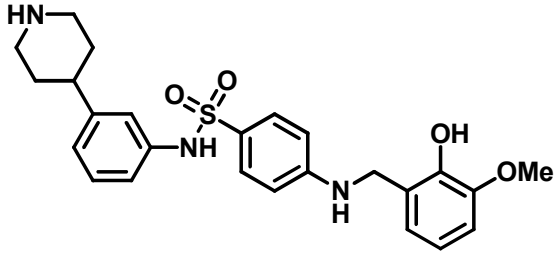


4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(3-morpholinophenyl)benzenesulfonamide, TFA (64): Method C: using 4-(3-bromophenyl)morpholine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.70 (s, 1H), 8.72 (s, 1H), 7.46–7.34 (m, 2H), 7.00 (t, J = 8.09 Hz, 1H), 6.82 (dd, J = 1.86, and 7.75 Hz,

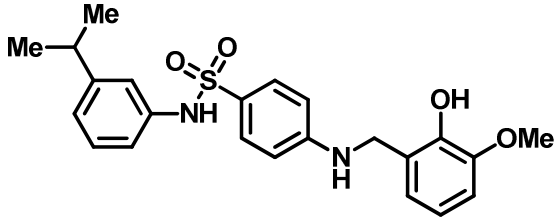
2H), 6.76–6.43 (m, 7H), 4.19 (s, 2H), 3.77 (s, 3H), 3.71–3.59 (m, 4H), and 2.98–2.86 (m, 4H); LC-MS retention time (Method 2): 4.961 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{24}H_{28}N_3O_5S$, 470.1744) found 470.1753.



***tert*-butyl4-(3-(4-((2-hydroxy-3-methoxybenzyl)amino)phenylsulfonamido)phenyl)piperidine-1-carboxylate (65):** Method C: using *tert*-butyl-4-(3-bromophenyl)piperidine-1-carboxylate; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (s, 1H), 7.46–7.28 (m, 2H), 7.08 (t, *J* = 7.74 Hz, 1H), 6.94–6.75 (m, 6H), 6.75–6.59 (m, 2H), 6.59–6.44 (m, 2H), 4.18 (d, *J* = 5.82 Hz, 2H), 4.00 (d, *J* = 12.83 Hz, 2H), 3.76 (s, 3H), 2.59–2.50 (m, 1H), 1.62 (d, *J* = 12.87 Hz, 2H), 1.39 (s, 9H), and 1.31 (m, 4H); LC-MS retention time (Method 2): 6.322 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{30}H_{38}N_3O_6S$, 568.2476) found 568.2461.

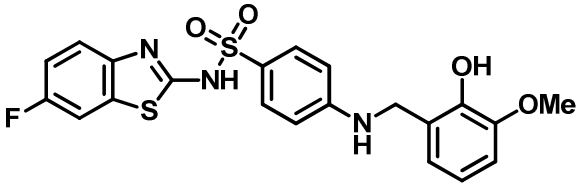


4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(3-(piperidin-4-yl)phenyl)benzenesulfonamide, TFA (66): Method 1C: using tert-butyl-4-(3-bromophenyl)piperidine-1-carboxylate the Boc group was removed after the reductive amination with 4 M HCl/dioxanes over a 30 min period. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (s, 1H), 7.53–7.24 (m, 2H), 7.12 (t, *J* = 7.85 Hz, 1H), 6.99 (t, *J* = 1.96 Hz, 1H), 6.93–6.77 (m, 4H), 6.73–6.61 (m, 2H), 6.57–6.48 (m, 2H), 4.33–4.01 (m, 2H), 3.77 (s, 3H), 3.33 (s, 1H), 2.95 (t, *J* = 12.62 Hz, 2H), 2.83–2.55 (m, 1H), and 1.94–1.43 (m, 4H); LC-MS retention time (Method 2): 4.079 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{25}H_{30}N_4O_4S$, 468.1952) found 468.1948.

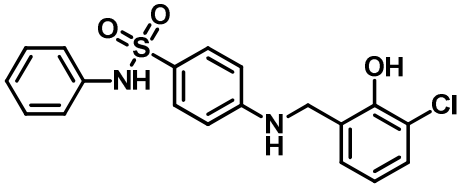


4-((2-hydroxy-3-methoxybenzyl)amino)-*N*-(3-isopropylphenyl)benzenesulfonamide, TFA (67): Method C: using 1-bromo-3-isopropylbenzene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 1H), 8.70 (s, 1H), 7.42–7.32 (m, 2H), 7.07 (t, *J* = 7.77 Hz, 1H), 6.98–6.75 (m, 4H), 6.73–6.61 (m, 2H), 6.58–6.45 (m, 2H), 4.18 (s, 2H), 3.76 (d, *J* = 0.87 Hz, 3H), 2.72 (h, *J* = 6.82 Hz, 1H),

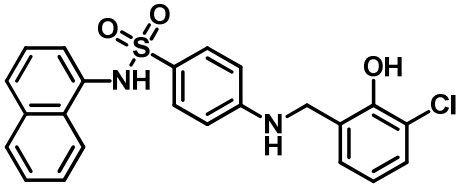
and 1.07 (dd, J = 0.91, and 6.94 Hz, 6H); LC-MS retention time (Method 2): 6.040 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{27}N_2O_4S$, 427.1686) found 427.1680.



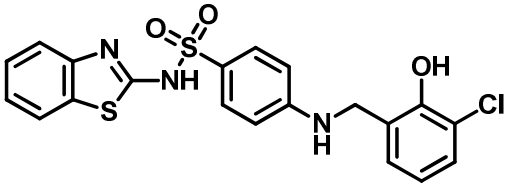
***N*-(6-fluorobenzo[d]thiazol-2-yl)-4-((2-hydroxy-3-methoxybenzyl)amino) benzenesulfonamide, TFA (68):** Method C: using 2-bromo-6-fluorobenzo[d]thiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 7.69 (dd, J = 2.43, and 8.51 Hz, 1H), 7.54–7.39 (m, 2H), 7.19 (qd, J = 3.40, 8.25, and 8.85 Hz, 3H), 6.88 (t, J = 5.68 Hz, 1H), 6.81 (dd, J = 1.71, and 7.87 Hz, 1H), 6.74–6.63 (m, 2H), 6.60–6.54 (m, 2H), 4.21 (d, J = 5.90 Hz, 2H), and 3.76 (s, 3H); LC-MS retention time (Method 2): 5.164 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{21}H_{19}FN_3O_4S_2$, 460.0796) found 460.0797.



4-(3-chloro-2-hydroxybenzylamino)-*N*-phenylbenzenesulfonamide, TFA (69): Method C: using 3-chloro-2-hydroxybenzaldehyde and bromobenzene; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.38 (s, 1H), 7.47–7.34 (m, 2H), 7.28–7.14 (m, 3H), 7.11–7.01 (m, 3H), 7.01– 6.88 (m, 2H), 6.79 (t, J = 7.78 Hz, 1H), 6.60–6.50 (m, 2H), and 4.29–4.23 (m, 2H); LC-MS retention time (Method 2): 5.442 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{19}H_{18}ClN_2O_3S$, 389.0721) found 389.0702.

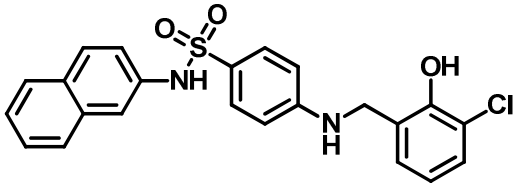


4-(3-chloro-2-hydroxybenzylamino)-*N*-(naphthalen-1-yl)benzenesulfonamide, TFA (70): Method D: using naphthalen-1-amine and 3-chloro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 9.36 (s, 1H), 8.03 (dd, J = 1.20, and 8.53 Hz, 1H), 7.90–7.80 (m, 1H), 7.70 (d, J = 8.22 Hz, 1H), 7.54–7.28 (m, 3H), 7.23 (dd, J = 1.58, and 8.01 Hz, 1H), 7.15 (dd, J = 1.08, and 7.40 Hz, 1H), 7.02 (dd, J = 1.58, and 7.65 Hz, 1H), 6.90 (t, J = 5.82 Hz, 1H), 6.78 (t, J = 7.79 Hz, 1H), 6.57–6.42 (m, 2H), and 4.24 (d, J = 4.97 Hz, 2H); LC-MS retention time (Method 1): 2.755 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{20}ClN_2O_3S$, 439.0878) found 439.0862.

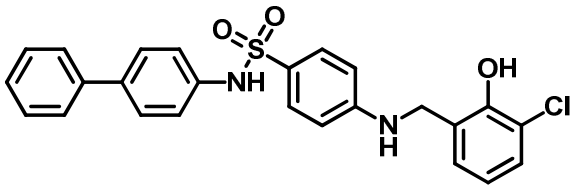


***N*-(benzo[d]thiazol-2-yl)-4-(3-chloro-2-hydroxybenzylamino)benzenesulfonamide, TFA (71):** Method C: using 3-chloro-2-hydroxybenzaldehyde and 2-bromobenzthiazole; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.88 (s, 1H), 9.38 (s, 1H), 7.80–7.69 (m, 1H), 7.59–7.46 (m, 2H), 7.35

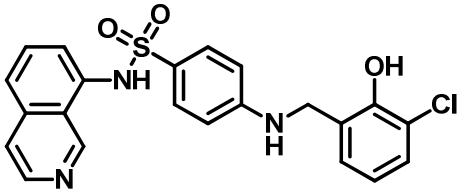
(ddd, J = 1.24, 7.44, and 8.26 Hz, 1H), 7.31–7.13 (m, 3H), 7.12–7.02 (m, 1H), 6.95 (t, J = 5.93 Hz, 1H), 6.78 (t, J = 7.79 Hz, 1H), 6.69–6.52 (m, 2H), and 4.28 (d, J = 5.72 Hz, 2H); LC-MS retention time (Method 2): 5.258 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{20}H_{17}ClN_3O_3S_2$, 446.0390) found 446.0379.



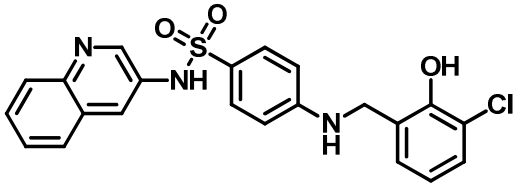
4-(3-chloro-2-hydroxybenzylamino)-*N*-(naphthalen-2-yl)benzenesulfonamide, TFA (72): Method D: using naphthalen-2-amine and 3-chloro-2-hydroxybenzaldehyde; LC-MS retention time (Method 1): 2.637 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{20}ClN_2O_3S$, 439.0878) found 439.0867.



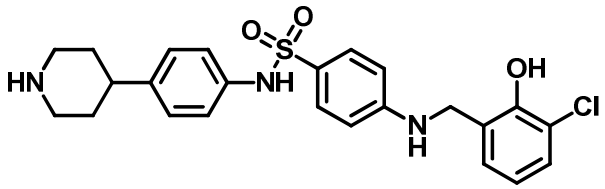
***N*-([1,1'-biphenyl]-4-yl)-4-((3-chloro-2-hydroxybenzyl)amino)benzenesulfonamide, TFA (73):** Method D: using biphenyl-4-amine and 3-chloro-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 9.37 (s, 1H), 7.61–7.36 (m, 9H), 7.35–7.04 (m, 5H), 6.97 (t, J = 5.8 Hz, 1H), 6.78 (t, J = 7.8 Hz, 1H), 6.62–6.52 (m, 2H), and 4.26 (d, J = 5.7 Hz, 2H); LC-MS retention time (Method 2): 6.592 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{25}H_{22}ClN_2O_3S$, 465.1034) found 465.1021.



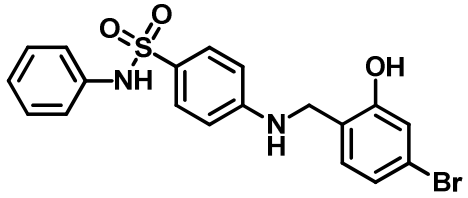
4-(3-chloro-2-hydroxybenzylamino)-*N*-(isoquinolin-8-yl)benzenesulfonamide, TFA (74): Method C: using 3-chloro-2-hydroxybenzaldehyde and 8-bromoisoquinoline; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.60 (s, 1H), 8.55 (d, J = 6.0 Hz, 1H),8.09 (d, J = 6.0 Hz, 1H), 7.99–7.71 (m, 2H), 7.46–7.29 (m, 3H), 7.23 (dd, J = 1.6, and 7.9 Hz, 1H), 7.11–6.93 (m, 1H), 6.78 (t, J = 7.8 Hz, 1H), 6.64–6.39 (m, 2H), and 4.24 (s, 2H); LC-MS retention time (Method 1): 1.669 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{19}ClN_3O_3S$, 440.0830) found 440.0811.



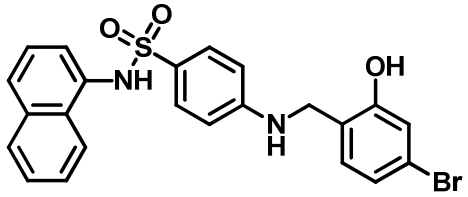
4-(3-chloro-2-hydroxybenzylamino)-*N*-(quinolin-3-yl)benzenesulfonamide, TFA (75): Method C: using 3-chloro-2-hydroxybenzaldehyde and 3-bromoquinoline; LC-MS retention time (Method 1): 2.346 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{19}ClN_3O_3S$, 440.0830) found 440.0824.



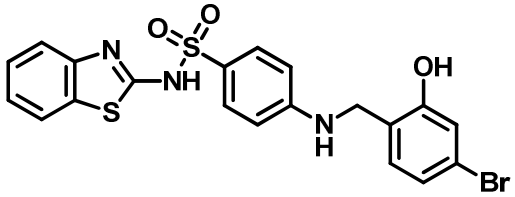
4-(3-chloro-2-hydroxybenzylamino)-*N*-(4-(piperidin-4-yl)phenyl)benzenesulfonamide, TFA (76): Method D: using *tert*-butyl-4-(4-aminophenyl)piperidine-1-carboxylate and 3-chloro-2-hydroxybenzaldehyde. The Boc group was removed after the reductive amination with 4 M HCl in dioxane over a 30 min period. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.20 (s, 1H), 9.71 (s, 1H), 7.87–7.59 (m, 2H), 7.57 (dd, J = 1.64, and 7.96 Hz, 1H), 7.48–7.15 (m, 6H), 7.21–7.02 (m, 1H), 6.96–6.69 (m, 2H), 4.59 (d, J = 5.77 Hz, 2H), 3.64 (s, 2H), 3.27 (t, J = 12.85 Hz, 3H), 3.10–2.93 (m, 1H), 2.18 (d, J = 13.73 Hz, 2H), and 1.98 (qd, J = 4.00, and 13.16 Hz, 2H); LC-MS retention time (Method 1): 2.884 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{20}ClN_2O_3S$, 472.1456) found 472.1442.



4-(4-bromo-2-hydroxybenzylamino)-*N*-phenylbenzenesulfonamide, TFA (77): Method D: using 4-bromo-2-hydroxybenzaldehyde and benzylamine; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 9.85 (s, 1H), 7.52–7.28 (m, 2H), 7.28–7.12 (m, 2H), 7.12–6.78 (m, 7H), 6.63–6.41 (m, 2H), 4.12 (d, J = 2.80 Hz, 2H); LC-MS retention time (Method 2): 5.501 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{19}H_{18}BrN_2O_3S$, 434.0246) found 434.0239.

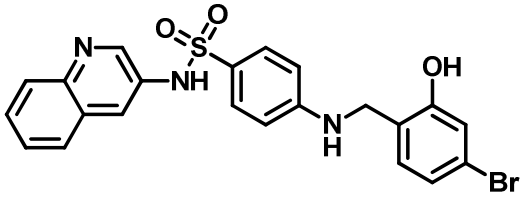


4-(4-bromo-2-hydroxybenzylamino)-*N*-(naphthalen-1-yl)benzenesulfonamide (78): Method D: using 1-amino-naphthalene and 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (d, J = 1.50 Hz, 1H), 9.74 (s, 1H), 8.03 (dd, J = 1.23, and 8.56 Hz, 1H), 7.87–7.80 (m, 1H), 7.70 (d, J = 8.24 Hz, 1H), 7.45 (ddd, J = 1.23, 6.81,and 8.11 Hz, 1H), 7.41–7.28 (m, 4H), 7.17–7.09 (m, 1H), 7.01–6.94 (m, 2H), 6.92–6.81 (m, 2H), 6.53–6.42 (m, 2H), and 4.12 (s, 2H); LC-MS retention time (Method 2): 6.282 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{20}BrN_2O_3S$, 483.0373) found 483.0367.

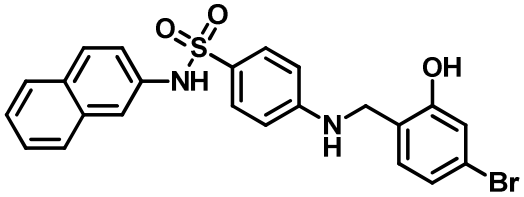


***N*-(benzo[d]thiazol-2-yl)-4-(4-bromo-2-hydroxybenzylamino)benzenesulfonamide, TFA (79):** Method D: using 2-aminobenzothiazole and 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.15 (s, 1H), 10.38 (s, 1H), 8.07–7.95 (m, 1H), 7.85–7.68 (m, 2H), 7.62 (ddd, J = 1.22, 7.36, and 8.30 Hz, 1H), 7.54–7.40 (m, 2H), 7.37–7.04 (m, 5H), 6.93–6.67

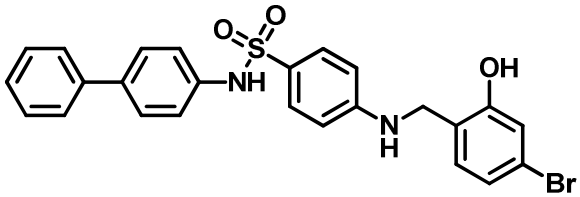
(m, 2H), and 4.43 (d, J = 5.75 Hz, 2H); LC-MS retention time (Method 1): 2.505 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{20}H_{17}BrN_3O_3S_2$, 491.9869) found 491.9855.



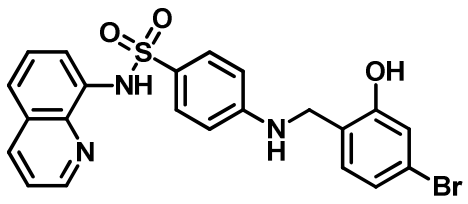
4-(4-bromo-2-hydroxybenzylamino)-*N*-(quinolin-3-yl)benzenesulfonamide, TFA (80): Method D: using 3-amino-quinoline and 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d6) δ 10.41 (d, J = 2.1 Hz, 1H), 10.08 (s, 1H), 8.59 (d, J = 2.6 Hz, 1H), 7.94–7.83 (m, 3H), 7.61 (tt, J = 2.43, and 6.74 Hz, 1H), 7.59–7.41 (m, 3H), 7.01–6.88 (m, 2H), 6.85 (dt, J = 2.11, and 8.10 Hz, 1H), 6.53 (dd, J = 2.22, and 9.01 Hz, 2H), and 4.10 (s, 2H); LC-MS retention time (Method 1): 2.166 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{19}BrN_3O_3S$, 485.0355) found 485.0331.



4-(4-bromo-2-hydroxybenzylamino)-*N*-(naphthalen-2-yl)benzenesulfonamide, TFA (81): Method D: using 2-amino-naphthalene and 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 10.07 (s, 1H), 7.79–7.66 (m, 3H), 7.51–7.30 (m, 5H), 7.25 (dd, J = 2.19, and 8.81 Hz, 1H), 7.00–6.92 (m, 2H), 6.91–6.81 (m, 2H), 6.61–6.25 (m, 2H), and 4.09 (d, J = 2.95 Hz, 2H); LC-MS retention time (Method 1): 2.856 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{23}H_{20}BrN_2O_3S$, 483.0373) found 483.0372.

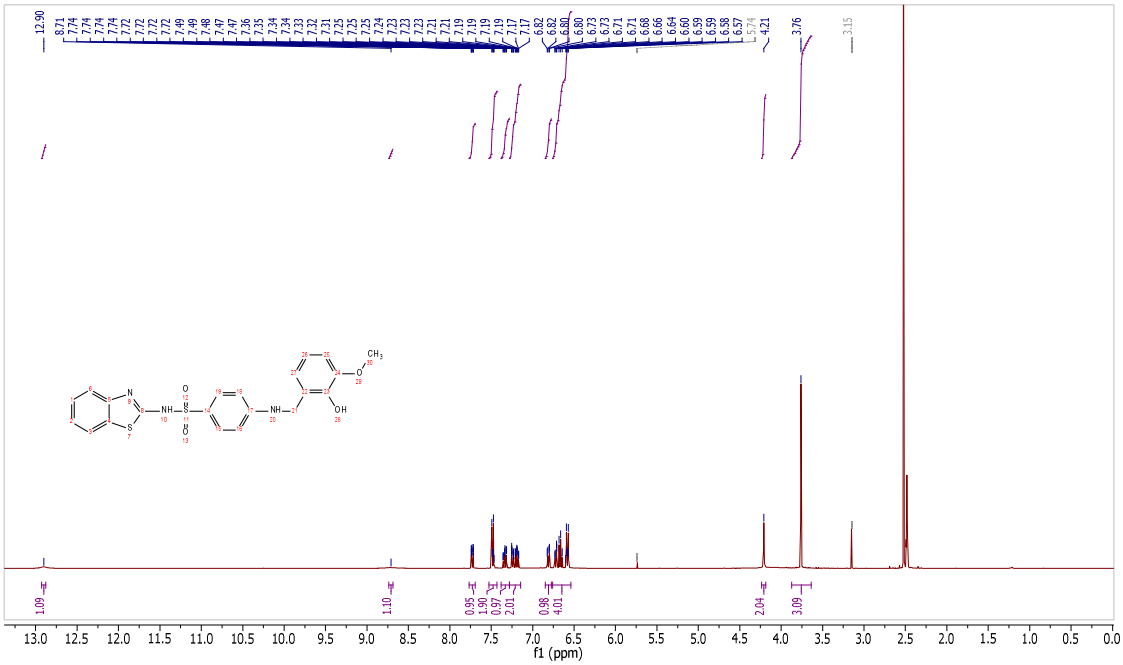


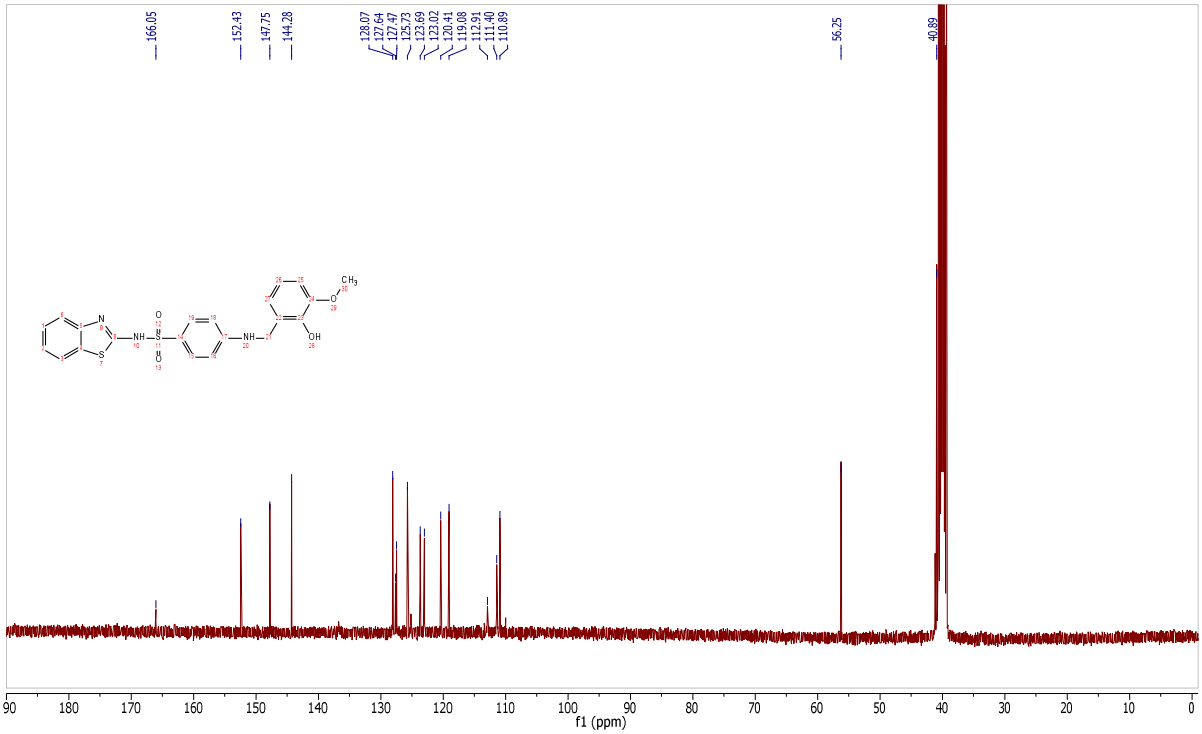
***N*-([1,1'-biphenyl]-4-yl)-4-((4-bromo-2-hydroxybenzyl)amino)benzenesulfonamide, TFA (82):** Method D: using 4-amino-biphenyl and 4-bromo-2-hydroxybenzaldehyde; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 9.37 (s, 1H), 7.61–7.36 (m, 8H), 7.35–7.04 (m, 5H), 6.97 (t, J = 5.8 Hz, 1H), 6.78 (t, J = 7.8 Hz, 1H), 6.62–6.52 (m, 2H), 4.26 (d, J = 5.7 Hz, 2H); LC-MS retention time (Method 2): 6.592 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{25}H_{22}BrN_2O_3S$, 510.0560) found 510.0549.



4-(4-bromo-2-hydroxybenzylamino)-*N*-(quinolin-8-yl)benzenesulfonamide, TFA (83): Method D: using 8-amino-isoquinoline and 4-bromo-2-hydroxybenzaldehyde; LC-MS retention time (Method 1): 2.524 min; HRMS: *m/z* $(M+H)^+$ (Calculated for $C_{22}H_{19}BrN_3O_3S$, 485.0355) found 485.0345.

Spectra for compound **35** [^{1}H NMR (top) and ^{13}C NMR (bottom):





LC/MS characterization for compound **35** [detection at 220 nm (top) and 254 nm (bottom)]

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File ..W\MSCHEM\11-12\141112-FINAL_GRAD_NP-16190.D Tgt Mass (EZX): 441.00
Injection Date    : 14 Nov 12   8:57 am -0500          Seq. Line : 0
Sample Name       : DKL13-092                    Location  : P2-A-02
Acq. Operator     : M. S. Chemist                          Inj : 1
Spec. Reported    : UV Integration                 Inj Volume : 0.5 ul
Acq. Method       : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Analysis Method   : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Sample Info : Easy-Access Method: 'SUBMISSION'  441.00
Method Info : UHPLC Long Gradient Equivalent 4% to 100%Acetonitrile (0.05% TFA) over 4 minutes
              enomenex Kinetex 1.7 micron column
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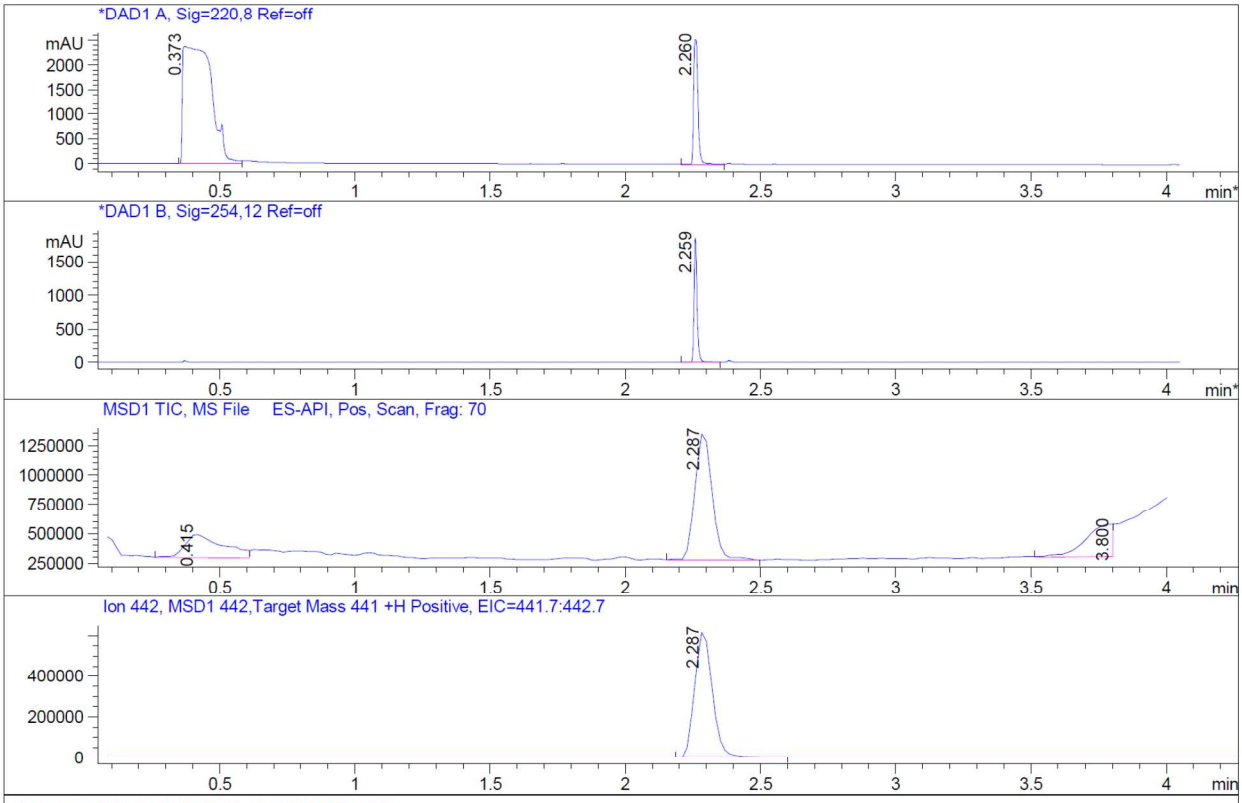


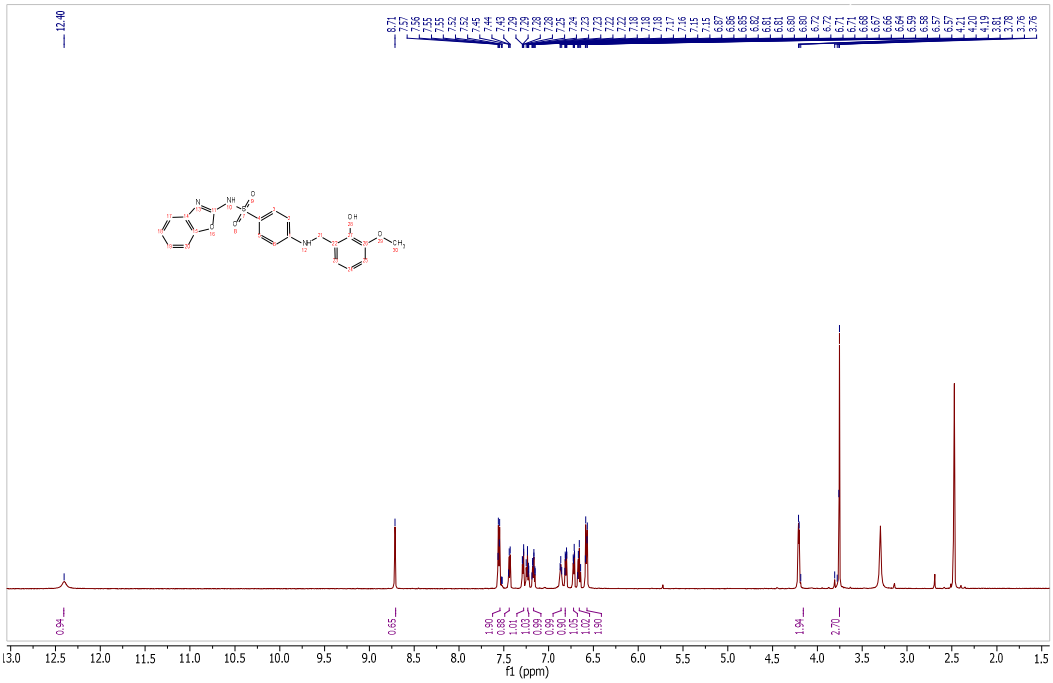
Integration Results for DAD1 A, Sig=220,8 Ref=off

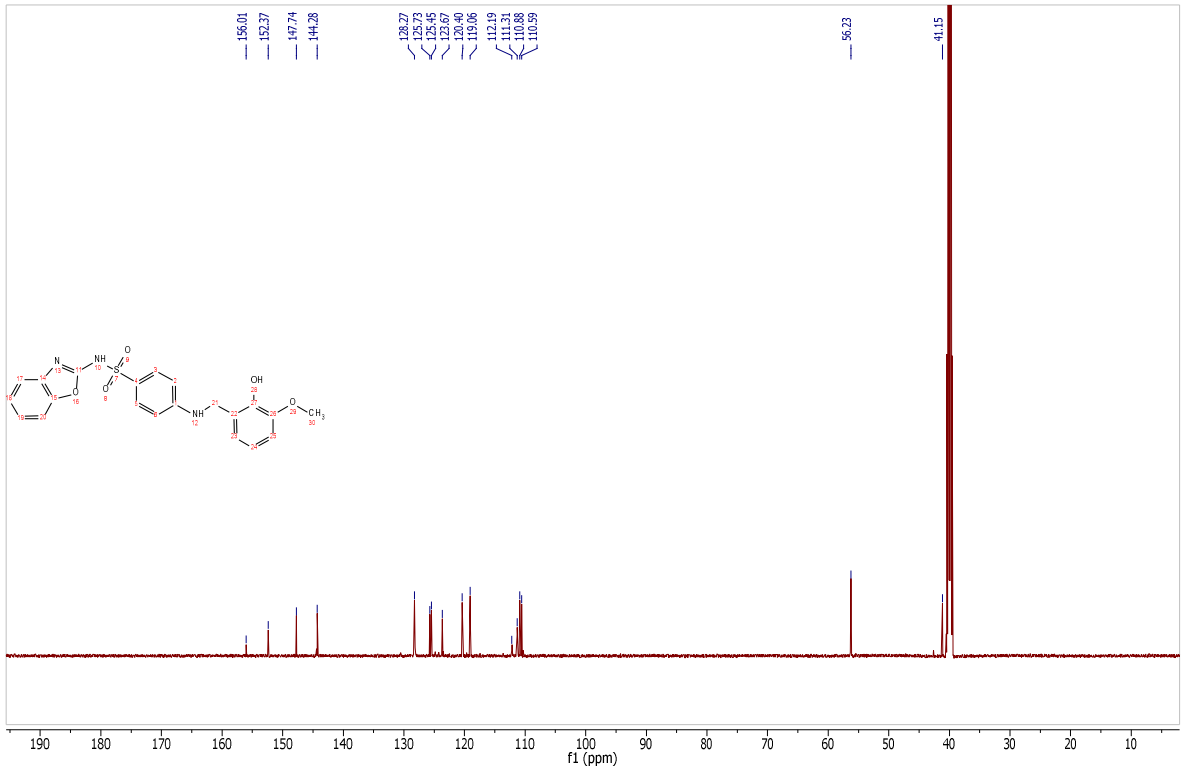
RetTim	Width	Area	Height	Area%	MS(+)
0.37	0.09	17532.57	2379.63	86.26	179
2.26	0.02	2792.64	2538.06	13.74	186

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
2.26	0.01	1404.64	1792.23	100.00	442

Spectra for compound **36** [^{1}H NMR (top) and ^{13}C NMR (bottom):





LC/MS characterization for compound **36** [detection at 220 nm (top) and 254 nm (bottom)]

Instrument: Agilent02 Datafile: S:\PurGroup\Instr\Ag02Raw\mschem\10-13\211013-DKL019-0391-06914.D

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File ..RAW\MSCHEM\10-13\211013-DKL019-0391-06914.D Tgt Mass (EZX): 425.00
Injection Date    : 21 Oct 13   2:47 pm -0500          Seq. Line : 0
Sample Name       : DKL019-039                    Location  : P2-A-08
Acq. Operator     : M. S. Chemist                       Inj : 1
Spec. Reported    : UV Integration                 Inj Volume : 3 ul
Acq. Method       : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Analysis Method   : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Sample Info : Easy-Access Method: 'SUBMISSION'  425.00
Method Info : Standard Gradient 4% to 100% Acetonitrile (0.05% TFA) over 7 minutes
              Luna C18 3 micron 3 x 75mm
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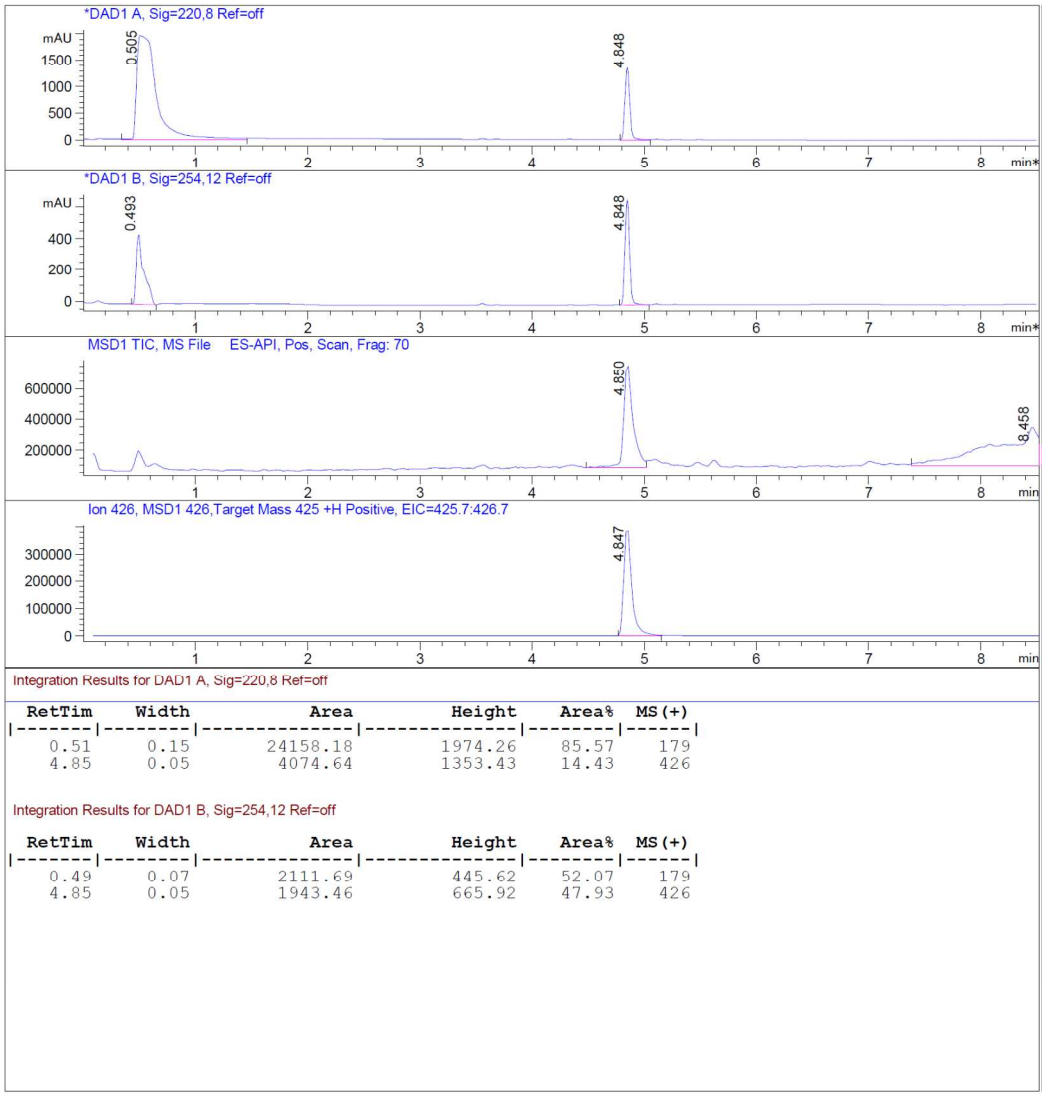


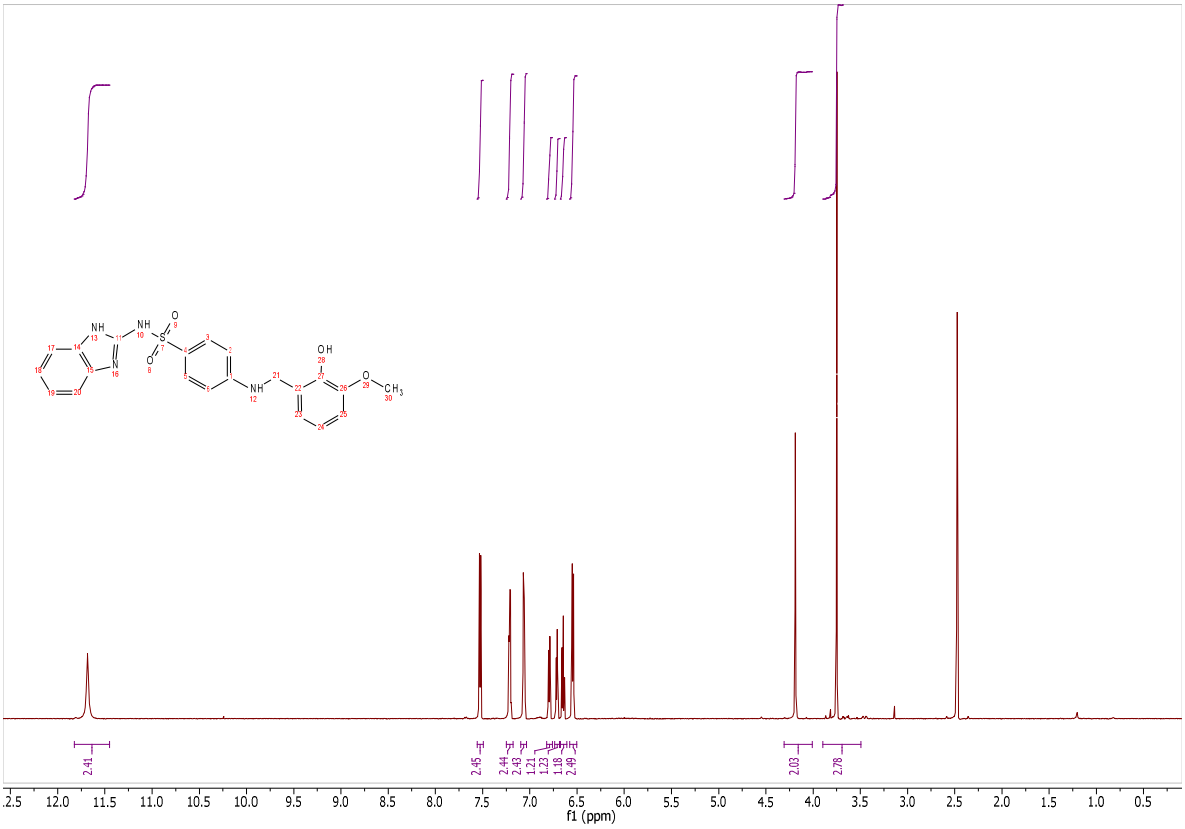
Integration Results for DAD1 A, Sig=220,8 Ref=off

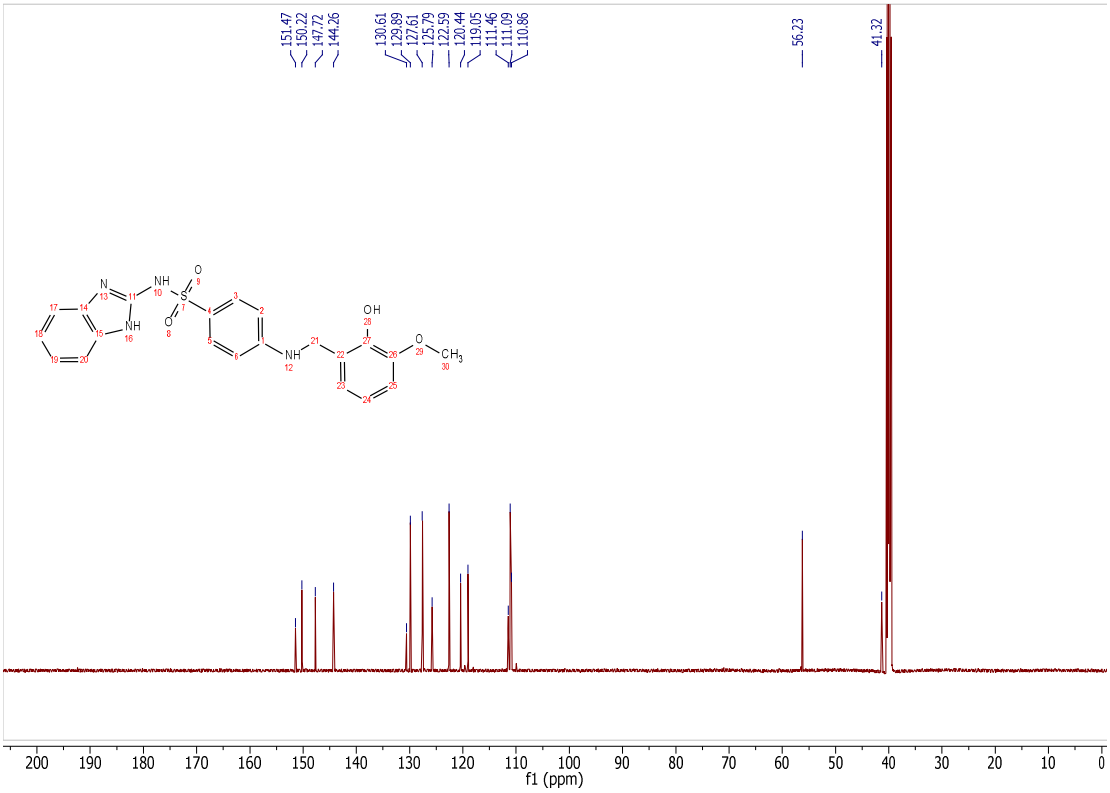
RetTim	Width	Area	Height	Area%	MS(+)
0.51	0.15	24158.18	1974.26	85.57	179
4.85	0.05	4074.64	1353.43	14.43	426

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
0.49	0.07	2111.69	445.62	52.07	179
4.85	0.05	1943.46	665.92	47.93	426

Spectra for compound **37** [^{1}H NMR (top) and ^{13}C NMR (bottom):





LC/MS characterization for compound **37** [detection at 220 nm (top) and 254 nm (bottom)]

Instrument: Agilent02 Datafile: Z:\PurGroup\Instr\Ag02Raw\mschem\11-13\151113-DKL019-0811-07671.D

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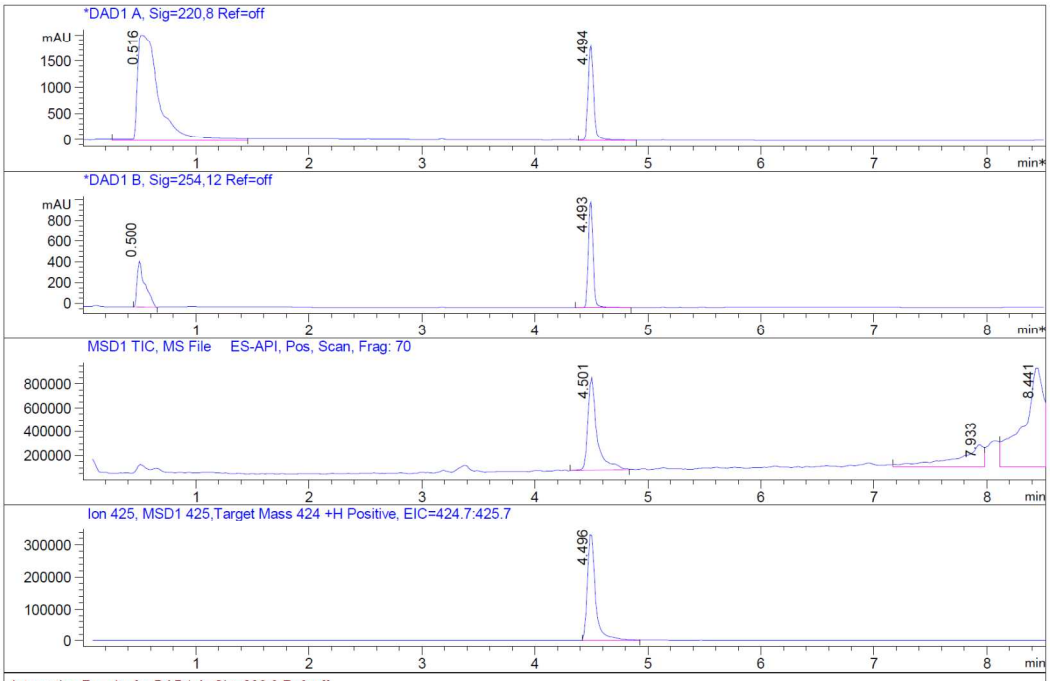
File ..RAW\MSCHEM\11-13\151113-DKL019-0811-07671.D Tgt Mass (EZX): 424.00
Injection Date    : 15 Nov 13   8:08 am -0500          Seq. Line : 0
Sample Name       : DKL019-081                   Location  : P2-A-03
Acq. Operator     : M. S. Chemist                          Inj : 1
Spec. Reported    : UV Integration                 Inj Volume : 3 ul
Acq. Method       : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Analysis Method   : C:\Chem32\1\METHODS\FINAL_GRAD_NP.M
Sample Info : Easy-Access Method: 'SUBMISSION'  424.00
Method Info : Standard Gradient 4% to 100% Acetonitrile (0.05% TFA) over 7 minutes
              Luna C18 3 micron 3 x 75mm
```



Integration Results for DAD1 A, Sig=220,8 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
0.52	0.16	26032.12	2006.01	80.88	179
4.49	0.05	6154.19	1798.66	19.12	425

Integration Results for DAD1 B, Sig=254,12 Ref=off

RetTim	Width	Area	Height	Area%	MS(+)
0.50	0.07	2131.25	439.73	41.23	179
4.49	0.05	3037.89	1026.59	58.77	425