Development of antibiotics that dysregulate the *Neisserial* ClpP protease

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Supplementary Experimental Procedures – Characterization Data of ACP1 Analogs

General Chemistry

Tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl under nitrogen. Dichloromethane and acetonitrile were freshly distilled from calcium hydride under nitrogen. Anhydrous *N*,*N*-dimethylformamide, 1,4-dioxane, and methanol were obtained as ≥ 99.9 % pure and stored under argon. All other solvents were ACS grade or better from commercial suppliers and used as received. All reactions were performed under nitrogen in flame-dried glassware. 5-(trifluoromethyl)pyridine-2-thiol was purchased from TCI America. All other starting materials and reagents were purchased from Aldrich or VWR and were used as received. Flash chromatography on silica gel (60 Å, 230-400 mesh, obtained from Silicycle) was performed with reagent grade solvents. Analytical TLC was performed on Merck silica gel 60 F_{254} pre-coated plates and visualized with a UV lamp and $KMnO_4$ stain. IR spectra were obtained on a Shimadzu FTIR-8400S spectrometer for thin film (in CH_2Cl_2) or neat samples using NaCl plates; solid samples were obtained on a Perkin Elmer 100 Series FTIR spectrometer equipped with a diamond/ZnSe ATR accessory. Mass spectra were obtained by the University of Toronto AIMS mass spectrometry facility; HRMS were recorded on a ABI/Sciex QStar mass spectrometer (ESI) or a JEOL AccuTOF model JMS-T1000LC mass spectrometer equipped with an IONICS DART ion source. LRMS were recorded on an Agilent 1200 LC/MSD mass spectrometer (ESI). Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. All NMR spectra were obtained on 300, 400, 500 and 600 MHz spectrometers as solutions in deuterated solvents. Chemical shifts are reported in δ ppm values. ^{1}H chemical shifts were internally referenced to tetramethylsilane (δ 0.00) for $CDCl_3$ or to the residual proton resonance in CD_3OD (δ 3.31) and DMSO-d_6 (δ 2.49). Carbon chemical shifts were internally referenced to the solvent resonances in $CDCl_3$ (δ 77.16 ppm), CD_3OD (δ 49.15 ppm) or DMSO-d_6 (δ 39.51 ppm). Fluorine chemical shifts were recorded in the absence of an internal standard and remain uncorrected. Peak multiplicities are designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; *J*, coupling constant in Hz and rounded to the nearest 0.5 Hz.

General Procedures

General Procedure A: Synthesis of amides using PyBOP. To a solution of acid and PyBOP in DMF at 0 °C was sequentially added amine in DMF via cannula transfer followed by dropwise addition of Hünig's base. The reaction was then warmed to room temperature overnight. The reaction mixture was then diluted with water and extracted with two portions of EtOAc. The combined organic layers were then washed four times with brine, dried over $MgSO_4$, concentrated in vacuo and the crude product was then purified using flash chromatography to give the corresponding amide.

General Procedure B: Oxidation of sulfides to sulfones using MCPBA. To a solution of sulfide and $NaHCO_3$ in CH_2Cl_2 at 0 °C was added portionwise MCPBA. The reaction mixture was then warmed to room temperature overnight. After complete consumption of the starting material was

observed by TLC, the excess oxidant was quenched by portionwise addition of $Na_2S_2O_3$ (sat. aq). After stirring for 30 min the reaction mixture was diluted with water and extracted with three portions of CH_2Cl_2. The organic extracts were combined and washed with portion of $NaHCO_3$ (sat. aq), one portion of brine, dried over $MgSO_4$, concentrated in vacuo and the crude product was then purified using flash chromatography to give the corresponding sulfone.

General Procedure C: Synthesis of ureas, carbamates and *S*-thiocarbamates. To a stirred solution of **ACP1-11** in CH_2Cl_2 at room temperature was charged CDI and the reaction mixture was stirred overnight while minimizing exposure to light (reaction flask covered with aluminum foil). The reaction mixture was then cooled to 0 °C and amine/phenol/thiophenol was charged and stirred for 5 min. The crude reaction mixture was then purified by flash chromatography to give the corresponding urea/carbamate/*S*-thiocarbamate.

General Procedure D: Synthesis of acids by deprotection of benzyl esters using palladium-catalyzed hydrogenolysis. Palladium on activated carbon (10% by wt.) was added to a solution of benzyl ester in MeOH or THF. The reaction mixture was purged with nitrogen for 5 min then with hydrogen for 5 min using a balloon, and stirred under static hydrogen atmosphere overnight. After complete consumption of the starting material was observed by TLC, the reaction mixture was filtered over celite and rinsed with CH_2Cl_2. The filtrate was concentrated in vacuo to yield the corresponding crude acid. Residual MeOH/THF was removed by evaporation from $CHCl_3$ (performed 2−3 times) and drying under vacuum; the resultant crude acid was used without further purification.

General Procedure E: Synthesis of sulfides by alkylation of thiophenols with α-bromoacetate or α-bromoacetamide derivatives. To a solution of thiophenol and KOH in EtOH was added dropwise α-bromoacetate or α-bromoacetamide. After the addition was complete, the solution was heated to reflux and stirred overnight. The reaction mixture was then cooled to room temperature before being diluted with H_2O and extracted with three portions of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo and the crude product was then purified using flash chromatography to give the corresponding sulfide.

General Procedure F: Synthesis of acids via ester hydrolysis. Lithium hydroxide monohydrate was added to a vigorously stirring solution of ester in THF:H_2O. After complete consumption of the starting material by TLC, the reaction mixture was acidified with HCl (1.0 M, aq) until the resulting solution was acidic to pH paper (pH 2-3). The reaction mixture was diluted with water and extracted with three portions of $CHCl_3$. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo to yield corresponding crude acid product which was used without further purification.

General Procedure G: Synthesis of amines by alkylation of thiophenols with 2-bromoethylamine hydrobromide salt. To a stirred solution of thiophenol and K_2CO_3 in THF was added 2-bromoethylamine HBr salt. The solution was then heated to reflux and stirred overnight. The solution was then cooled to room temperature, diluted with water and extracted with three portions of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo to yield the corresponding amine which was used in its crude form without further purification unless stated otherwise. Note: in most cases the crude amine product was

contaminated with small amounts of unreacted thiophenol starting material (5−37 w/w % by ^{1}H NMR) or other unidentified impurities.

General Procedure H: Synthesis of benzyl esters by alkylation of acids with benzyl bromide. To a solution of acid and tetrabutylammonium iodide in THF at 0 °C was sequentially added benzyl bromide followed by dropwise addition of triethylamine. The reaction was then warmed to room temperature overnight. The reaction mixture was then diluted with water and extracted with two portions of $CHCl_3$. The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo and the crude product was then purified using flash chromatography to give the corresponding benzyl ester.

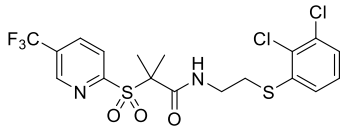
General Procedure I: Synthesis of carbocyclic ester derivatives by bis-alkylation of α-sulfonyl benzyl esters with dibromoalkanes. To a solution of α-sulfonyl benzyl ester in MeCN at room temperature was added K_2CO_3 and the mixture was stirred for 30 min. After this time, dibromoalkane was added dropwise and the mixture was then heated to reflux. After complete consumption of the starting material by TLC, the reaction mixture was cooled to room temperature, diluted with water and extracted with three portions of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo and the crude product was then purified using flash chromatography to give the corresponding cycloalkylated product.

Characterization Data for ACP1 Analogues

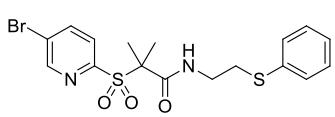
2-Methyl-*N*-(2-((2-(trifluoromethyl)phenyl)thio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-01). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (61.8 mg, 0.208 mmol, 1.0 equiv), PyBOP (132.8 mg, 0.2552 mmol, 1.2 equiv), DMF (2 mL), 2-((2-(trifluoromethyl)phenyl)thio)ethan-1-amine (85% by wt., 73.1 mg, 0.281 mmol, 1.3 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 1.1 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 73.2 mg of ACP1 analogue ACP1-01 as a yellow semisolid in 70% yield. R_f 0.21 (2:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3393, 3071, 2993, 2942, 1668, 1594, 1526, 1314, 1173, 1072, 1035, 855, 765, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96−8.91 (1H, m), 8.22 (1H, d, *J* = 8.0 Hz), 8.18 (1H, dd, *J* = 8.0, 2.0 Hz), 7.67 (1H, d, *J* = 7.5 Hz), 7.61 (1H, d, *J* = 7.5 Hz), 7.50 (1H, t, *J* = 7.5 Hz), 7.38−7.29 (2H, m), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.17 (2H, t, *J* = 6.5 Hz), 1.65 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 158.4 (q, *J* = 2.0 Hz), 147.2 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 134.8 (q, *J* = 1.0 Hz), 132.4 (q, *J* = 1.0 Hz), 131.9, 130.8 (q, *J* = 30.0 Hz), 130.4 (q, J = 34.0 Hz), 127.2 (q, *J* = 5.5 Hz), 126.7, 124.6, 123.9 (q, J = 273.5 Hz), 122.5 (q, J = 273.5 Hz), 67.9, 39.5, 33.7, 20.6; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.71 (3F, s), −62.75 (3F, s); HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{19}F_6N_2O_3S_2$ $[M + H]^+$: 501.0735, found 501.0713.

2-Methyl-*N*-(3-(4-sulfamoyl-2-(trifluoromethyl)phenyl)propyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-02). To a solution of 2-methyl-*N*-(3-(4-sulfamoyl-2-(trifluoromethyl)phenyl)prop-2-yn-1-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (37.3 mg, 0.0669 mmol, 1.0 equiv) in THF (3 mL) was added palladium on carbon (10% by wt., 12.0 mg, 0.0113 mmol, 17 mol %) and the reaction mixture was initially purged with nitrogen for 5 minutes and then with hydrogen for 5 minutes using a balloon and stirred under static hydrogen atmosphere. After complete consumption of the starting material by TLC (4 h), the reaction mixture was filtered off over a pad of celite with light suction and rinsed forward with CH_2Cl_2 (30 mL). Concentration of the filtrate afforded a crude product which was then purified using flash chromatography (1:1 hexanes:EtOAc) to afford 30.3 mg of ACP1-02 as a colorless oil in 80% yield. R_f 0.25 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3375, 3263, 3077, 2942, 1662, 1532, 1328, 1313, 1165, 1138, 1126, 1092, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.94–8.92 (1H, m), 8.24–8.19 (2H, m), 8.17 (1H, d, *J* = 2.0 Hz), 8.02 (1H, dd, *J* = 8.0, 2.0 Hz), 7.54 (1H, d, *J* = 8.0 Hz), 7.12 (1H, br t, *J* = 5.5 Hz), 5.13 (2H, s), 3.44–3.38 (2H, m), 2.96–2.88 (2H, m), 1.92 (2H, quintet, *J* = 7.0 Hz), 1.63 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 145.8 (q, *J* = 1.5 Hz), 140.6, 135.8 (q, *J* = 3.5 Hz), 132.2, 130.5 (q, *J* = 34.0 Hz), 129.9, 129.6 (q, *J* = 31.0 Hz), 123.7 (q, *J* = 274.5 Hz),124.77 (q, *J* = 6.0 Hz), 124.74, 122.4 (q, *J* = 273.5 Hz), 67.9, 40.1, 30.9, 30.1 (q, *J* = 2.0 Hz), 20.8; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.10 (3F, s), −62.75 (3F, s); HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{22}F_6N_3O_5S_2$ $[M + H]^+$: 562.0900, found 562.0900.

***N*-(2-((2,3-Dichlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-03).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (65.5 mg, 0.220 mmol, 1.0 equiv), PyBOP (162.4 mg, 0.3121 mmol, 1.4 equiv), DMF (3 mL), 2-((2,3-dichlorophenyl)thio)ethan-1-amine (93% by wt., 65.8 mg, 0.276 mmol, 1.3 equiv) in DMF (2 mL), Hünig's base (45.0 μL, 0.258 mmol, 1.2 equiv), 48 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 84.1 mg of ACP1-03 as a white solid in 76% yield. mp 144−145 °C (CH_2Cl_2); R_f 0.26 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3403, 3085, 3015, 2933, 1671, 1328, 1164, 1137, 1126, 1091, 1072, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.00−8.90 (1H, m), 8.23 (1H, d, *J* = 8.0 Hz), 8.19 (1H, dd, *J* = 8.0, 2.0 Hz), 7.42 (1H, br t, *J* = 6.0 Hz), 7.37−7.28 (2H, m), 7.18 (1H, t, *J* = 8.0 Hz), 3.56 (2H, td, *J* = 7.0, 6.0 Hz), 3.17 (2H, t, *J* = 7.0 Hz), 1.65 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 137.4, 135.8 (q, *J* = 3.5 Hz), 133.9, 131.7, 130.5 (q, *J* = 34.0 Hz), 127.78, 127.71, 126.4, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.7, 39.4, 31.7, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{18}Cl_2F_3N_2O_3S_2$ $[M + H]^+$: 501.0088, found 501.0102.



2-((5-Bromopyridin-2-yl)sulfonyl)-2-methyl-*N*-(2-(phenylthio)ethyl) propanamide (ACP1-04). Synthesized according to General Procedure A using 2-((5-bromopyridin-2-yl)sulfonyl)-2-methylpropanoic acid (58.0 mg, 0.188 mmol, 1.0 equiv), PyBOP (124.6 mg, 0.2394 mmol, 1.3 equiv), DMF (2 mL), 2-(phenylthio)ethan-1-amine (89% by wt., 35.6 mg, 0.207 mmol, 1.1 equiv) in DMF (2 mL), Hünig's base (45.0 μL, 0.258 mmol, 1.4 equiv), 19 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 74.6 mg of ACP1-04 as a colorless oil in 90% yield. R_f 0.33 (2:1 hexanes:EtOAc); IR (neat) ν_{max} 3385, 3053, 2992, 2940, 1664, 1521, 1439, 1308, 1162, 1087, 1006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.71 (1H, d, *J* = 2.0 Hz), 8.03 (1H, dd, *J* = 8.0, 2.0 Hz), 7.92 (1H, d, *J* = 8.0 Hz), 7.46−7.18 (6H, m), 3.49 (2H, dt, *J* = 6.5, 6.5 Hz), 3.11 (2H, t, *J* = 6.5 Hz), 1.61 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 153.2, 151.6, 140.7, 135.1, 130.0, 129.3, 126.8, 126.3, 126.1, 67.7, 39.7, 33.0, 20.6; HRMS ($DART^+$) *m*/*z* calcd for $C_{17}H_{20}BrN_2O_3S_2$ $[M + H]^+$: 443.0099, found 443.0095.



Benzyl (2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoyl) glycinate (ACP1-05). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (95.5 mg, 0.321 mmol, 1.0 equiv), PyBOP (197.3 mg, 0.3791 mmol, 1.2 equiv), DMF (5 mL), glycine benzyl ester hydrochloride (67.4 mg, 0.334 mmol, 1.0 equiv), Hünig's base (175.0 μL, 1.005 mmol, 3.1 equiv), 13 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 54.5 mg of ACP1-05 as a white solid in 38% yield. mp 110−112 °C (CH_2Cl_2); R_f 0.26 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3411, 3110, 3062, 3041, 2991, 2952, 1742, 1680, 1329, 1306, 1175, 1134, 1086, 1070 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97−8.92 (1H, m), 8.26 (1H, d, *J* = 8.0 Hz), 8.15 (1H, dd, *J* = 8.0, 2.0 Hz), 7.49 (1H, br t, *J* = 5.0 Hz), 7.42−7.30 (5H, m), 5.20 (2H, s), 4.11 (2H, d, *J* = 5.0 Hz), 1.69 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 167.9, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 135.2, 130.4 (q, *J* = 34.0 Hz), 128.79, 128.75, 128.6, 124.9, 122.5 (q, *J* = 273.5 Hz), 68.0, 67.5, 42.3, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{20}F_3N_2O_5S$ $[M + H]^+$: 445.1039, found 445.1037.

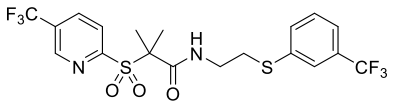
***N*-(2-((2-Chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-06[1]).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (52.9 mg, 0.178 mmol, 1.0 equiv), PyBOP (118.1 mg, 0.2269 mmol, 1.3 equiv), DMF (4 mL), 2-((2-chlorophenyl)thio)ethan-1-amine (37.9 mg, 0.202 mmol, 1.1 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 1.3 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 55.1 mg of ACP1 analogue ACP1-06 as a white solid in 66% yield. mp 78−80 °C (CH_2Cl_2); R_f 0.35 (2:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3391, 3065, 2991, 2943, 1674, 1593, 1577, 1526, 1454, 1433, 1386, 1326, 1172, 1143, 1092, 1073, 1015, 854, 749, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96−8.91 (1H, m), 8.22 (1H, d, *J* = 8.0 Hz), 8.16 (1H, dd, *J* = 8.0, 2.0 Hz), 7.48−7.35 (3H, m), 7.24 (1H, td, *J* = 8.0, 1.5 Hz), 7.16 (1H, td, *J* = 8.0, 1.5 Hz), 3.53 (2H, dt, *J* = 6.5, 6.5 Hz), 3.15 (2H, t, *J* = 6.5 Hz), 1.65 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 158.3 (q, *J* = 1.5 Hz), 147.2 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 134.6, 134.3, 130.4 (q, *J* = 34.0 Hz), 130.1, 129.9, 127.54, 127.51, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.8, 39.4, 32.0, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{19}ClF_3N_2O_3S_2$ $[M + H]^+$: 467.0472, found 467.0474.

***N*-(2-((3-Chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-07).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (38.1 mg, 0.128 mmol, 1.0 equiv), PyBOP (105.0 mg, 0.2018 mmol, 1.6 equiv), DMF (2 mL), 2-((3-chlorophenyl)thio)ethan-1-amine (85% by wt., 34.5 mg, 0.156 mmol, 1.2 equiv) in DMF (2 mL), Hünig's base (25.0 μL, 0.143 mmol, 1.1 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 51.3 mg of ACP1-07 as a white semisolid in 86% yield. R_f 0.34 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3386, 3068, 2926, 2853, 1670, 1577, 1523, 1463, 1324, 1136, 1089, 1071, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.94−8.89 (1H, m), 8.21 (1H, d, *J* = 8.0 Hz), 8.18 (1H, dd, *J* = 8.0, 2.0 Hz), 7.39 (1H, br t, *J* = 6.5 Hz), 7.37 (1H, t, *J* = 2.0 Hz), 7.37 (1H, dt, *J* = 7.5, 2.0 Hz), 7.23 (1H, t, *J* = 7.5 Hz), 7.18 (1H, dt, *J* = 7.5, 2.0 Hz), 3.53 (2H, dt, *J* = 6.5, 6.5 Hz), 3.14 (2H, t, *J* = 6.5 Hz), 1.63 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 137.4, 135.7 (q, *J* = 3.5 Hz), 135.0, 130.4 (q, *J* = 34.0 Hz), 130.3, 129.2, 127.6, 126.8, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.7, 39.6, 32.8, 20.6; HRMS ($DART^+$) *m*/*z* calcd for $C_{18}H_{19}ClF_3N_2O_3S_2$ $[M + H]^+$: 467.0478, found 467.0486.

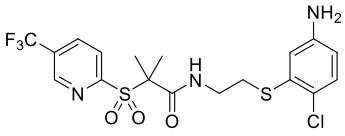
***N*-(2-((4-Amino-2-chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl) pyridin-2-yl)sulfonyl)propanamide (ACP1-08).** To a solution of ACP1-37 (149.1 mg, 0.2913 mmol, 1.0 equiv) in EtOAc (15 mL) was added stannous chloride dihydrate (689.2 mg, 3.055 mmol, 10.5 equiv) and the mixture was then heated to reflux. After complete consumption of the starting material was observed by TLC (19 h), the reaction mixture was treated with $NaHCO_3$ (sat. aq, 30 mL) and stirred for 5 minutes. The reaction mixture was then diluted with water (30 mL) and extracted with three portions of EtOAc (3 x 30 mL). The combined organic extracts were washed with two portions of brine (2 x 60 mL), concentrated in vacuo and the crude product was then purified using flash chromatography (1:1 hexanes:EtOAc) to afford ACP1-08 as a yellow foam in 84% yield. R_f 0.38 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2)

ν_{max} 3368, 3239, 2991, 2939, 1665, 1595, 1523, 1475, 1324, 1312, 1168, 1135, 1089, 1071, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.00−8.91 (1H, m), 8.22 (1H, d, *J* = 8.0 Hz), 8.18 (1H, dd, *J* = 8.0, 2.0 Hz), 7.41−7.31 (2H, m), 6.77 (1H, d, *J* = 2.5 Hz), 6.51 (1H, dd, *J* = 8.0, 2.5 Hz), 3.96 (2H, br s), 3.40 (2H, dt, *J* = 6.5, 6.5 Hz), 2.95 (2H, t, *J* = 6.5 Hz), 1.66 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 158.4 (q, *J* = 1.5 Hz), 148.0, 147.3 (q, *J* = 4.0 Hz), 139.2, 136.8, 135.6 (q, *J* = 3.5 Hz), 130.3 (q, *J* = 34.0 Hz), 124.7, 122.5 (q, *J* = 273.5 Hz), 119.6, 116.2, 114.2, 68.0, 39.3, 34.7, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{20}ClF_3N_3O_3S_2$ $[M + H]^+$: 482.0581, found 482.0589.

2-Methyl-*N*-(2-((3-(trifluoromethyl)phenyl)thio)ethyl)-2-((5-(trifluoromethyl) pyridin-2-yl)sulfonyl)propanamide (ACP1-09). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (62.4 mg, 0.210 mmol, 1.0 equiv), PyBOP (135.3 mg, 0.2600 mmol, 1.2 equiv), DMF (3 mL), 2-((3-(trifluoromethyl)phenyl)thio)ethan-1-amine (91% by wt., 59.6 mg, 0.250 mmol, 1.2 equiv) in DMF (2 mL), Hünig's base (45.0 μL, 0.258 mmol, 1.2 equiv), 15 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 84.7 mg of ACP1-09 as a white solid in 81% yield. mp 42−43 °C (CH_2Cl_2); R_f 0.36 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3403, 3083, 2937, 1673, 1521, 1167, 1138, 1321, 1315, 1117, 1091, 1071, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.95−8.86 (1H, m), 8.26−8.15 (2H, m), 7.66−7.53 (2H, m), 7.50−7.36 (3H, m), 3.54 (2H, dt, 6.5, 6.5 Hz), 3.19 (2H, t, *J* = 6.5 Hz), 1.62 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 136.9, 135.7 (q, *J* = 3.5 Hz), 132.4 (q, *J* = 1.5 Hz), 131.7 (q, *J* = 32.5 Hz), 130.5 (q, *J* = 34.0 Hz), 129.7, 126.0 (q, *J* = 4.0 Hz), 124.6, 123.8 (q, *J* = 272.5 Hz), 123.3 (q, *J* = 4.0 Hz), 122.5 (q, *J* = 273.0 Hz), 67.6, 39.6, 32.7, 20.6; ^{19}F NMR (564 MHz, $CDCl_3$) δ −62.77 (3F, s), −62.89 (3F, s); HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{19}F_6N_2O_3S_2$ $[M + H]^+$: 501.0741, found 501.0746.



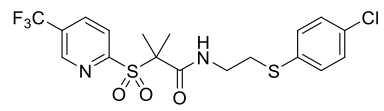
***N*-(3-Phenylpropyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)cyclopentane-1-carboxamide (ACP1-10).** Synthesized according to General Procedure A using 1-((4-(trifluoromethyl)phenyl)sulfonyl)cyclopentane-1-carboxylic acid (32.6 mg, 0.101 mmol, 1.0 equiv), PyBOP (69.7 mg, 0.134 mmol, 1.3 equiv), DMF (4 mL), 3-phenylpropylamine (20.0 μL, 0.140 mmol, 1.4 equiv), Hünig's base (20.0 μL, 0.115 mmol, 1.1 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 38.0 mg of ACP1-10 as a white solid in 86% yield. mp 56−57 °C (CH_2Cl_2); R_f 0.44 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 3335, 3029, 2947, 2924, 2874, 1654, 1538, 1403, 1317, 1306, 1296, 1168, 1144, 1134, 1108, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (2H, d, *J* = 8.0 Hz), 7.76 (2H, d, *J* = 8.0 Hz), 7.35−7.28 (2H, m), 7.25−7.16 (3H, m), 6.90 (1H, br t, *J* = 6.0 Hz), 3.32 (2H, td, *J* = 7.0, 6.0 Hz), 2.74−2.66 (2H, m), 2.46−2.35 (2H, m), 2.33−2.24 (2H, m), 1.97−1.77 (4H, m), 1.76−1.63 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 141.1, 140.3 (q, *J* = 1.0 Hz), 135.8 (q, *J* = 33.5 Hz), 130.2, 128.7, 128.5, 126.35 (q, *J* = 3.5 Hz), 126.32, 123.1 (q, *J* = 273.0 Hz), 78.6, 40.3, 33.4, 32.9, 30.9, 26.0; HRMS ($DART^+$) *m*/*z* calcd for $C_{22}H_{25}F_3NO_3S$ $[M + H]^+$: 440.1507, found 440.1516.



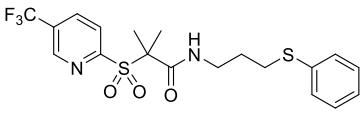
***N*-(2-((5-Amino-2-chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl) pyridin-2-yl)sulfonyl)propanamide (ACP1-11).** To a solution of ACP1-21 (455.0 mg, 0.8888 mmol, 1.0 equiv) in EtOAc (15 mL) was added stannous chloride dihydrate (2.11 g, 9.35 mmol, 10.5 equiv) and the

mixture was then heated to reflux. After complete consumption of the starting material was observed by TLC (4 h), the reaction mixture was treated with $NaHCO_3$ (sat. aq, 30 mL) and stirred for 5 minutes. The reaction mixture was then diluted with water (30 mL) and extracted with three portions of EtOAc (3 x 30 mL). The combined organic extracts were washed with two portions of brine (2 x 60 mL), concentrated in vacuo and the crude product was then purified using flash chromatography (1:1 hexanes:EtOAc) to afford ACP1-11 as a yellow foam in 92% yield. R_f 0.14 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3373, 3071, 2929, 1663, 1591, 1523, 1468, 1325, 1311, 1136, 1125, 1089, 1072, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.99−8.91 (1H, m), 8.22 (1H, d, *J* = 8.0 Hz), 8.17 (1H, dd, *J* = 8.0, 2.0 Hz), 7.37 (1H, br t, *J* = 6.5 Hz), 7.14 (1H, d, *J* = 8.5 Hz), 6.83 (1H, d, *J* = 2.5 Hz), 6.48 (1H, dd, *J* = 8.5, 2.5 Hz), 3.72 (2H, br s), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.10 (2H, t, *J* = 6.5 Hz), 1.66 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 146.0, 135.7 (q, *J* = 3.5 Hz), 134.3, 103.5, 130.4 (q, *J* = 34.0 Hz), 124.7, 123.5, 122.5 (q, *J* = 273.5 Hz), 116.4, 114.5, 68.0, 39.5, 31.9, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{20}ClF_3N_3O_3S_2$ $[M + H]^+$: 482.0581, found 482.0583.

***N*-(2-((4-Chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-12).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (69.3 mg, 0.233 mmol, 1.0 equiv), PyBOP (135.0 mg, 0.2594 mmol, 1.1 equiv), DMF (3 mL), 2-((4-chlorophenyl)thio)ethan-1-amine (94% by wt., 62.6 mg, 0.313 mmol, 1.3 equiv) in DMF (2 mL), Hünig's base (45.0 μL, 0.258 mmol, 1.1 equiv), 14 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 100.8 mg of ACP1-12 as a white solid in 93% yield. mp 69−70 °C (CH_2Cl_2); R_f 0.46 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3384, 3087, 3017, 2939, 1659, 1514, 1479, 1324, 1316, 1164, 1137, 1090, 1071 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.94−8.91 (1H, m), 8.23−8.17 (2H, m), 7.37 (1H, br t, *J* = 6.5 Hz), 7.36−7.32 (2H, m), 7.29−7.25 (2H, m), 3.50 (2H, dt, *J* = 6.5, 6.5 Hz), 3.10 (2H, t, *J* = 6.5 Hz), 1.63 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 133.5, 132.9, 131.4, 130.5 (q, *J* = 34.0 Hz), 129.4, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.7, 39.6, 33.2, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{19}ClF_3N_2O_3S_2$ $[M + H]^+$: 467.0472, found 467.0456.



2-Methyl-*N*-(3-(phenylthio)propyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-13). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (200 mg, 0.673 mmol, 1.0 equiv), PyBOP (525.1 mg, 1.01 mmol, 1.5 equiv), DMF (10 mL), 3-(phenylthio)propan-1-amine[2] (206 mg, 1.34 mmol, 2.0 equiv) in DMF (10 mL), Hünig's base (350 μL, 2.018 mmol, 3.0 equiv), 1 h. Flash chromatography (3:2 hexanes:EtOAc) of the concentrated reaction mixture afforded 98.11 mg of ACP1-13 as a white crystalline solid in 51 % yield. mp 74–78 °C (hexanes/EtOAc); R_f 0.22 (3:2 hexanes:EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.92 (1H, s), 8.18 (2H, s), 7.36–7.34 (2H, m), 7.33–7.26 (2H, m), 7.17 (1H, tt, *J* = 7.0, 1.5 Hz), 7.08 (1H, br s), 3.44 (2H, dt, *J* = 7.0, 7.0 Hz), 3.03 (2H, t, *J* = 7.0 Hz), 2.03–1.83 (2H, m), 1.62 (6H, s); HRMS (ESI^+) *m/z* calcd for $C_{19}H_{22}F_3N_2O_3S_2$ $[M + H]^+$: 447.1018, found 447.1008.



***N*-(2-((2-Chlorophenyl)thio)ethyl)-2-methyl-2-((4-(trifluoromethyl)phenyl) sulfonyl)propanamide (ACP1-14).** Synthesized according to General Procedure A using 2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanoic acid (46.1 mg, 0.156 mmol, 1.0 equiv), PyBOP (99.9 mg, 0.192 mmol, 1.2 equiv), DMF (3 mL), 2-((2-chlorophenyl)thio)ethan-1-amine (35.2 mg, 0.187 mmol, 1.2 equiv) in DMF (2 mL), Hünig's base (30.0 μL, 0.172 mmol, 1.1 equiv), 18 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 72.6 mg of ACP1-14 as a white solid in quantitative yield. mp 73−75 °C (CH_2Cl_2); R_f 0.33 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3393, 2928, 1664, 1523, 1404, 1319, 1292, 1159, 1125, 1107, 1060, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (2H, d, *J* = 8.0 Hz), 7.76 (2H, d, *J* = 8.0 Hz), 7.44 (1H, dd, *J* = 7.5, 1.5 Hz), 7.42 (1H, dd, *J* = 7.5, 1.5 Hz), 7.32−7.23 (2H, m), 7.19 (1H, td, *J* = 7.5, 1.5 Hz), 3.53 (2H, dt, *J* = 6.5, 6.5 Hz), 3.14 (2H, t, *J* = 6.5 Hz), 1.59 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 138.8 (q, *J* = 1.5 Hz), 136.1 (q, *J* = 33.0 Hz), 135.0, 134.0, 130.9, 130.27, 130.21, 127.8, 127.6, 126.3 (q, *J* = 3.5 Hz), 123.1 (q, *J* = 273.5 Hz), 68.5, 39.3, 32.4, 20.8; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{20}ClF_3NO_3S_2$ $[M + H]^+$: 466.0519, found 466.0512.

2-((5-Bromopyridin-2-yl)sulfonyl)-*N*-(2-((2-chlorophenyl)thio)ethyl)-2-methylpropanamide (ACP1-15). Synthesized according to General Procedure A using 2-((5-bromopyridin-2-yl)sulfonyl)-2-methylpropanoic acid (46.3 mg, 0.150 mmol, 1.0 equiv), PyBOP (106.0 mg, 0.2037 mmol, 1.3 equiv), DMF (2 mL), 2-((2-chlorophenyl)thio)ethan-1-amine (31.2 mg, 0.166 mmol, 1.1 equiv) in DMF (2 mL), Hünig's base (35.0 μL, 0.201 mmol, 1.3 equiv), 19 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 71.6 mg of ACP1-15 as a white solid in quantitative yield. mp 88−89 °C (CH_2Cl_2); R_f 0.29 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3343, 3076, 3009, 2962, 1668, 1511, 1305, 1087, 1006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.73 (1H, d, *J* = 2.0 Hz), 8.05 (1H, dd, *J* = 8.0, 2.0 Hz), 7.95 (1H, d, *J* = 8.0 Hz), 7.49−7.37 (3H, m), 7.25 (1H, td, *J* = 8.0, 2.0 Hz), 7.16 (1H, td, *J* = 8.0, 2.0 Hz), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.14 (2H, t, *J* = 6.5 Hz), 1.63 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 153.2, 151.6, 140.7, 134.6, 134.4, 130.1, 129.8, 127.53, 127.48, 126.3, 126.1, 67.7, 39.5, 31.9, 20.7; HRMS ($DART^+$) *m*/*z* calcd for $C_{17}H_{19}BrClN_2O_3S_2$ $[M + H]^+$: 476.9709, found 476.9712.

***N*-(2-((2-Bromophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-16).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (110.0 mg, 0.3701 mmol, 1.0 equiv), PyBOP (249.7 mg, 0.4798 mmol, 1.3 equiv), DMF (3 mL), 2-((2-bromophenyl)thio)ethan-1-amine (63% by wt., 137.0 mg, 0.3717 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (200.0 μL, 1.148 mmol, 3.1 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 21.3 mg of ACP1-16 as a yellow gel in 11% yield. R_f 0.34 (2:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3390, 2941, 1670, 1524, 1328, 1172, 1143, 1015, 749, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95−8.91 (1H, m), 8.23 (1H, d, *J* = 8.0 Hz), 8.16 (1H, dd, *J* = 8.0, 2.0 Hz), 7.57 (1H, dd, *J* = 8.0, 1.5 Hz), 7.45−7.37 (2H, m), 7.29 (1H, td, *J* = 8.0, 1.5 Hz), 7.08 (1H, td, *J* = 8.0, 1.5 Hz), 3.54 (2H, dt, *J* = 6.5, 6.5 Hz), 3.15 (2H, t, *J* = 6.5 Hz), 1.67 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 136.5, 135.7 (q, *J* = 3.5 Hz), 133.4, 130.1 (q, *J* = 34.0 Hz), 129.5, 128.2, 127.6, 124.8, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.8, 39.4, 32.4, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{19}BrF_3N_2O_3S_2$ $[M + H]^+$: 510.9967, found

510.9946.

2-Methyl-*N*-(2-(naphthalen-2-ylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-17). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (54.8 mg, 0.184 mmol, 1.0 equiv), PyBOP (137.0 mg, 0.2632 mmol, 1.4 equiv), DMF (3 mL), 2-(naphthalen-2-ylthio)ethan-1-amine (89% by wt., 61.0 mg, 0.267 mmol, 1.5 equiv) in DMF (2 mL), Hünig's base (35.0 μL, 0.201 mmol, 1.1 equiv), 12 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 51.8 mg of ACP1-17 as a light yellow oil in 58% yield. R_f 0.38 (2:1 hexanes:EtOAc); IR (neat) ν_{max} 3392, 3055, 2991, 2942, 1674, 1326, 1169, 1139, 1091, 1072, 1014 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.88–8.86 (1H, m), 8.17 (1H, d, *J* = 8.0 Hz), 8.09 (1H, dd, *J* = 8.0, 2.0 Hz), 7.88–7.86 (1H, m), 7.82–7.71 (3H, m), 7.51–7.43 (3H, m), 7.39 (1H, br t, *J* = 5.5 Hz), 3.59–3.51 (2H, m), 3.22 (2H, t, *J* = 6.5 Hz), 1.62 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 158.2 (q, *J* = 1.5 Hz), 147.2 (q, *J* = 4.0 Hz), 135.6 (q, *J* = 3.5 Hz), 133.8, 132.3, 132.1, 130.3 (q, *J* = 34.0 Hz), 128.9, 128.3, 127.84, 127.79, 127.3, 126.8, 126.2, 124.6, 122.4 (q, *J* = 273.5 Hz), 67.8, 39.6, 33.0, 20.5; HRMS (ESI^+) *m*/*z* calcd for $C_{22}H_{22}F_3N_2O_3S_2$ $[M + H]^+$: 483.0982, found 483.0982.

***N*-(2-((2,5-Dichlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-18).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (59.6 mg, 0.200 mmol, 1.0 equiv), PyBOP (162.8 mg, 0.3128 mmol, 1.5 equiv), DMF (3 mL), 2-((2,4-dichlorophenyl)thio)ethan-1-amine (70.2 mg, 0.317 mmol, 1.6 equiv) in DMF (2 mL), Hünig's base (45.0 μL, 0.258 mmol, 1.3 equiv), 48 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 71.6 mg of ACP1-18 as a white solid in 71% yield. mp 71−73 °C (CH_2Cl_2); R_f 0.44 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3382, 3063, 2982, 1663, 1306, 1163, 1136, 1123, 1086, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.92−8.84 (1H, m), 8.17 (1H, d, *J* = 8.0 Hz), 8.13 (1H, dd, *J* = 8.0, 2.0 Hz), 7.36 (1H, br t, *J* = 6.5 Hz), 7.32 (1H, d, *J* = 2.5 Hz), 7.22 (1H, d, *J* = 8.5 Hz), 7.06 (1H, dd, *J* = 8.5, 2.5 Hz), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.11 (2H, t, *J* = 6.5 Hz), 1.59 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 136.7, 135.7 (q, *J* = 3.5 Hz), 133.3, 132.3, 130.9, 130.5 (q, *J* = 34.0 Hz), 128.7, 127.2, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.7, 39.3, 31.9, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{18}Cl_2F_3N_2O_3S_2$ $[M + H]^+$: 501.0088, found 501.0083.

***N*-(2-((3,5-Dichlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-19).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (49.5 mg, 0.166 mmol, 1.0 equiv), PyBOP (113.4 mg, 0.2179 mmol, 1.3 equiv), DMF (3 mL), 2-((3,5-dichlorophenyl)thio)ethan-1-amine (95% by wt., 52.7 mg, 0.227 mmol, 1.4 equiv) in DMF (2 mL), Hünig's base (35.0 μL, 0.200 mmol, 1.2 equiv), 48 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 72.9 mg of ACP1-19 as a white solid in 88% yield. mp 74−75 °C (CH_2Cl_2); R_f 0.44 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3401, 3087, 2931, 2853, 1672, 1553, 1305, 1167, 1090, 1073, 1013 cm^{-1}; ^1H NMR (300 MHz,

$CDCl_3$) δ 8.92 (1H, s), 8.28−8.16 (2H, m), 7.41 (1H, br t, *J* = 6.5 Hz), 7.23 (2H, d, *J* = 1.5 Hz), 7.18 (1H, t, *J* = 1.5 Hz), 3.54 (2H, dt, *J* = 6.5, 6.5 Hz), 3.16 (2H, t, *J* = 6.5 Hz), 1.63 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 139.2, 135.8 (q, *J* = 3.5 Hz), 135.5, 130.5 (q, *J* = 34.0 Hz), 126.9, 126.5, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.6, 39.5, 32.4, 20.6; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{18}Cl_2F_3N_2O_3S_2$ [M + H]$^+$: 501.0088, found 501.0100.

***N*-(3-Phenylpropyl)-1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclopentane-1-carboxamide (ACP1-20).** Synthesized according to General Procedure A using 1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclopentane-1-carboxylic acid (29.1 mg, 0.0900 mmol, 1.0 equiv), PyBOP (54.7 mg, 0.105 mmol, 1.2 equiv), DMF (3 mL), 3-phenylpropylamine (15.0 μL, 0.105 mmol, 1.2 equiv), Hünig's base (35.0 μL, 0.200 mmol, 2.2 equiv), 12 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 23.7 mg of ACP1-20 as a light beige solid in 60% yield. mp 52−53 °C (CH_2Cl_2); R_f 0.39 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 3351, 3031, 2954, 2875, 1656, 1537, 1324, 1158, 1142, 1125, 1095, 1072, 1015 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90−8.87 (1H, m), 8.17−8.12 (2H, m), 7.32−7.25 (2H, m), 7.23−7.15 (3H, m), 7.10 (1H, br t, *J* = 6.0 Hz), 3.31 (2H, td, *J* = 7.0, 6.0 Hz), 2.72−2.64 (2H, m), 2.51−2.30 (4H, m), 1.95−1.68 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 159.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 141.4, 135.6 (q, *J* = 3.5 Hz), 130.2 (q, *J* = 34.0 Hz), 128.6, 128.5, 126.2, 123.7, 122.5 (q, *J* = 273.5 Hz), 76.7, 40.2, 33.2, 33.1, 30.7, 26.4; HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{24}F_3N_2O_3S$ [M + H]$^+$: 441.1454, found 441.1455.

***N*-(2-((2-Chloro-5-nitrophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl) pyridin-2-yl)sulfonyl)propanamide (ACP1-21).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (410.7 mg, 1.382 mmol, 1.0 equiv), PyBOP (799.5 mg, 1.536 mmol, 1.1 equiv), DMF (6 mL), 2-((2-chloro-5-nitrophenyl)thio)ethan-1-amine (361.0 mg, 1.551 mmol, 1.0 equiv), Hünig's base (290.0 μL, 1.665 mmol, 1.2 equiv), 15 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 505.5 mg of ACP1-21 as a yellow solid in 71% yield. mp 103–105 °C (CH_2Cl_2); R_f 0.35 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3400, 3073, 2993, 2941, 1663, 1521, 1339, 1326, 1307, 1165, 1140, 1128, 1090, 1072 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97−8.93 (1H, m), 8.25−8.19 (3H, m), 7.97 (1H, dd, *J* = 8.5, 2.5 Hz), 7.54 (1H, d, *J* = 8.5 Hz), 7.46 (1H, br t, *J* = 6.5 Hz), 3.64 (2H, dt, *J* = 6.5, 6.5 Hz), 3.29 (2H, t, *J* = 6.5 Hz), 1.65 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 158.2 (q, *J* = 1.0 Hz), 147.3 (q, *J* = 4.0 Hz), 147.1, 139.8, 138.3, 135.8 (q, *J* = 3.5 Hz), 130.57, 130.53 (q, *J* = 34.0 Hz), 124.6, 122.5 (q, *J* = 273.5 Hz), 122.2, 121.3, 67.6, 39.1, 31.6, 20.6; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{18}ClF_3N_3O_5S_2$ [M + H]$^+$: 512.0329, found 512.0320.

***N*-(3-Phenylpropyl)-1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclohexane-1-carboxamide (ACP1-22).** Synthesized according to General Procedure A using 1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclohexane-1-carboxylic acid (51.7 mg, 0.153 mmol, 1.0 equiv), PyBOP (105.0 mg, 0.2018 mmol, 1.3 equiv), DMF (4 mL), 3-phenylpropylamine (25.0 μL, 0.175 mmol, 1.1 equiv), Hünig's base (60.0 μL, 0.344 mmol, 2.2 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 52.3 mg of ACP1-22 as a white solid in 75% yield. mp 108−110 °C (CH_2Cl_2); R_f 0.47 (3:1 hexanes:EtOAc);

IR (solid) ν_{max} 3348, 3069, 2949, 2934, 2862, 1650, 1546, 1324, 1165, 1144, 1125, 1096, 1072, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.93−8.89 (1H, m), 8.12 (1H, dd, *J* = 8.0, 2.0 Hz), 8.07 (1H, d, *J* = 8.0 Hz), 7.33−7.27 (2H, m), 7.24−7.17 (3H, m), 6.62 (1H, br t, *J* = 6.0 Hz), 3.33 (2H, td, *J* = 7.0, 6.0 Hz), 2.75−2.68 (2H, m), 2.25 (2H, br d, *J* = 13.0 Hz), 2.01 (2H, td, *J* = 13.0, 4.0 Hz), 1.92 (2H, quintet, *J* = 7.0 Hz), 1.83−1.74 (2H, br m), 1.71−1.62 (1H, br m), 1.41 (2H, dtt, *J* = 13.0, 13.0, 4.0 Hz), 1.25 (1H, tt, *J* = 13.0, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 157.7 (q, *J* = 1.5 Hz), 147.2 (q, *J* = 4.0 Hz), 141.4, 135.3 (q, *J* = 3.5 Hz), 130.2 (q, *J* = 34.0 Hz), 128.7, 128.5, 126.2, 125.1, 122.6 (q, *J* = 273.5 Hz), 72.9, 40.3, 33.4, 30.8, 28.3, 24.7, 22.6; HRMS (ESI^+) *m*/*z* calcd for $C_{22}H_{26}F_3N_2O_3S$ $[M + H]^+$: 455.1610, found 455.1602.

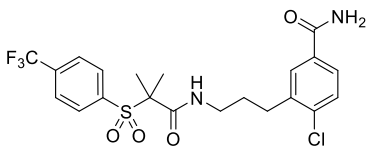
1-(4-Benzylpiperidin-1-yl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propan-1-one (ACP1-23). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (77.3 mg, 0.260 mmol, 1.0 equiv), PyBOP (152.3 mg, 0.2927 mmol, 1.1 equiv), DMF (4 mL), 4-benzylpiperidine (50.0 µL, 0.281 mmol, 1.1 equiv), Hünig's base (50.0 µL, 0.287 mmol, 1.1 equiv), 14 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 90.1 mg of ACP1-23 as a light yellow solid in 76% yield. mp 130−132 °C (CH_2Cl_2); R_f 0.50 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3053, 2937, 2861, 1630, 1326, 1306, 1167, 1134, 1091, 1072, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.94−8.87 (1H, m), 8.24 (1H, d, *J* = 8.0 Hz), 8.16 (1H, dd, *J* = 8.0, 2.0 Hz), 7.33−7.25 (2H, m), 7.23−7.17 (1H, m), 7.17−7.11 (2H, m), 4.45−4.34 (2H, br m), 2.78 (2H, br s), 2.56 (2H, d, *J* = 7.0 Hz), 1.95−1.59 (9H, m), 1.33−1.16 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.5 (q, *J* = 1.0 Hz), 146.5 (q, *J* = 4.0 Hz), 139.9, 135.3 (q, *J* = 3.5 Hz), 129.4 (q, *J* = 33.5 Hz), 129.2, 128.5, 126.3, 124.4, 122.8 (q, *J* = 273.0 Hz), 72.7, 46.1 (br), 43.0, 38.3, 32.2, 22.5; HRMS (ESI^+) *m*/*z* calcd for $C_{22}H_{26}F_3N_2O_3S$ $[M + H]^+$: 455.1610, found 455.1607.

***N*-(2-((2-Chlorophenyl)sulfonyl)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-24).** Synthesized according to General Procedure B using ACP1-06 (44.3 mg, 0.0945 mmol, 1.0 equiv), $NaHCO_3$ (60.0 mg, 0.750 mmol, 7.9 equiv), CH_2Cl_2 (4 mL), MCPBA (70% by wt., 55.0 mg, 0.245 mmol, 2.6 equiv), 12 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 47.2 mg of ACP1-24 as a white foam in quantitative yield. R_f 0.37 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3391, 3091, 3068, 2992, 2942, 1676, 1526, 1326, 1172, 1147, 1093, 1073, 1042, 1015 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.91 (1H, s), 8.23–8.15 (2H, m), 8.15 (1H, dd, *J* = 8.0, 1.5 Hz), 7.62–7.56 (2H, m), 7.53–7.47 (2H, m), 3.77–3.72 (2H, m), 3.71–3.67 (2H, m), 1.62 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 158.3, 147.2 (q, *J* = 4.0 Hz), 136.6, 135.7 (q, *J* = 3.5 Hz), 135.3, 132.9, 132.2, 131.8, 130.4 (q, *J* = 34.0 Hz), 127.8, 124.7, 122.5 (q, *J* = 274.0 Hz), 67.9, 53.4, 34.4, 20.4; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{19}ClF_3N_2O_5S_2$ $[M + H]^+$: 499.0371, found 499.0369.

2-Methyl-*N*-(2-(naphthalen-1-ylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-25). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (69.5 mg, 0.234 mmol, 1.0 equiv), PyBOP (146.0 mg, 0.2806 mmol, 1.2 equiv), DMF (4 mL), 2-(naphthalen-1-ylthio)ethan-1-amine (84% by wt., 62.6 mg, 0.259 mmol, 1.1 equiv) in DMF (2 mL), Hünig's

base (50.0 μL, 0.287 mmol, 1.2 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 93.5 mg of ACP1-25 as a light pink oil in 82% yield. R_f 0.17 (3:1 hexanes:EtOAc); IR (neat) ν_{max} 3390, 3058, 2991, 2939, 1674, 1652, 1387, 1326, 1173, 1140, 1092, 1072, 1015, 773, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.88−8.82 (1H, m), 8.47−8.43 (1H, m), 8.17 (1H, d, *J* = 8.5 Hz), 8.12−8.07 (1H, m), 7.86 (1H, dd, *J* = 8.5, 1.5 Hz), 7.79 (1H, d, *J* = 8.5 Hz), 7.70 (1H, dd, *J* = 7.0, 1.0 Hz), 7.60−7.55 (1H, m), 7.55−7.50 (1H, m), 7.42 (1H, dd, *J* = 8.5, 7.0 Hz), 7.38−7.32 (1H, br t, *J* = 6.5 Hz), 3.47 (2H, dt, *J* = 6.5, 6.5 Hz), 3.16 (2H, t, *J* = 6.5 Hz), 1.61 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 158.3, 147.2 (q, *J* = 4.0 Hz), 135.6 (q, *J* = 3.3 Hz), 134.2, 133.5, 131.9, 130.3 (q, *J* = 33.8 Hz), 129.9, 128.8, 128.3, 126.9, 126.5, 125.8, 125.2, 124.5, 122.5 (q, *J* = 272.3 Hz), 67.8, 39.6, 33.8, 20.5; HRMS (ESI^+) *m*/*z* calcd for $C_{22}H_{22}F_3N_2O_3S_2$ $[M + H]^+$: 483.1018, found 483.1006.

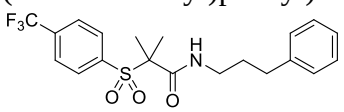
4-Chloro-3-(3-(2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamido)propyl)benzamide (ACP1-26). Synthesized according to modified version of General Procedure A using ACP1-41 (39.4 mg, 0.0801 mmol, 1.0 equiv), PyBOP (47.0 mg, 0.0903 mmol, 1.1 equiv), DMF (2 mL), hexamethyldisilazane (20.0 μL, 0.0922 mmol, 1.2 equiv), Hünig's base (35.0 μL, 0.201 mmol, 2.5 equiv), 15 h. For aqueous work-up, the mixture was diluted with HCl (1.0 M, aq, 10.0 mL) and extraxted with three portions of CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo and the crude product was then purified using flash chromatography (3:1 EtOAc:hexanes) to afford 39.3 mg of ACP1-26 as a white solid in quantitative yield. Decomposition temperature ~95 °C; R_f 0.25 (3:1 EtOAc:hexanes); IR (solid) ν_{max} 3642, 3572, 3398, 2926, 2854, 1660, 1607, 1534, 1321, 1132, 1062, 832 cm^{-1}; ^1H NMR (400 MHz, CD_3OD, note: benzamide proton resonance was not observed due to deuterium exchange) δ 8.09 (1H, br t, *J* = 6.0 Hz), 8.05 (2H, d, *J* = 8.5 Hz), 7.92 (2H, d, *J* = 8.5 Hz), 7.83 (1H, d, *J* = 2.0 Hz), 7.69 (1H, dd, *J* = 8.5, 2.0 Hz), 7.46 (1H, d, *J* = 8.5 Hz), 3.29–3.24 (2H, m), 2.87–2.80 (2H, m), 1.87 (2H, quintet, *J* = 7.5 Hz), 1.59 (6H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 171.4, 169.4, 140.9 (2C), 138.7, 136.7 (q, *J* = 33.0 Hz), 134.0, 132.5, 131.0, 130.8, 128.1, 127.2 (q, *J* = 4.0 Hz), 128.4 (q, *J* = 272.5 Hz), 70.3, 41.0, 31.9, 30.1, 20.8; HRMS (ESI^+) *m*/*z* calcd for $C_{21}H_{23}ClF_3N_2O_4S$ $[M + H]^+$: 491.1014, found 491.1008.



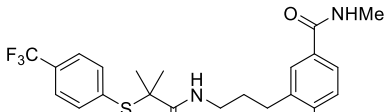
***N*-(2-((5-(3-(2-(1*H*-Imidazol-1-yl)ethyl)ureido)-2-chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-27).** Synthesized according to General Procedure C using ACP1-11 (81 mg, 0.168 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 32 mg, 10.176 mmol, 1.05 equiv), 16 h; 2-(1*H*-imidazol-1-yl)ethanamine (32 mg, 0.176 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (9:1 CH_2Cl_2:MeOH) of the crude reaction mixture, followed by reverse phase purification (MeOH) afforded 30.2 mg of ACP1-27 as a light yellow oil in 30% yield. Note: a pure sample used for characterization was obtained by semi-preparative reverse phase HPLC purification as a white semi-solid. R_f 0.23 (9:1 CH_2Cl_2:MeOH); IR (thin film in CH_2Cl_2) ν_{max} 3447, 3418, 3414, 3403, 3392, 3384, 3147, 2937, 2879, 1645, 1635, 1622, 1584, 1538, 1480, 1460, 1328 cm-1; ^1H NMR (500 MHz, $CDCl_3$) δ 8.95–8.94 (1H, m), 8.93 (1H, br s), 8.18–8.16 (2H, m), 7.64–7.60 (1H, m), 7.58 (2H, t, *J* = 6.0 Hz), 7.19–7.15 (1H, m), 7.06–7.01 (1H, m), 7.00–6.95 (2H, m),

6.40 (1H, br, s), 4.14–4.13 (2H, m), 3.66–3.56 (2H, m), 3.54–3.40 (2H, m), 3.10 (2H, t, *J* = 6.5 Hz), 1.66 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 158.3, 156.0, 147.3 (q, *J* = 4.0 Hz), 139.3, 137.1, 135.8 (q, *J* = 3.5 Hz), 134.8, 130.5 (q, *J* = 34.0 Hz), 130.0, 127.9, 126.7, 125.0, 122.5 (q, J = 273.5 Hz), 120.1, 118.7, 117.2, 68.5, 48.3, 40.5, 39.3, 31.7, 20.6; HRMS (ESI^+) *m/z* calcd for $C_{24}H_{27}ClF_3N_6O_4S_2$ [M + H]+: 619.1142, found 619.1170.

2-Methyl-*N*-(3-phenylpropyl)-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamide (ACP1-28). Synthesized according to General Procedure A using 2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanoic acid (47.9 mg, 0.161 mmol, 1.0 equiv), PyBOP (100.5 mg, 0.1931 mmol, 1.2 equiv), DMF (6 mL), 3-phenylpropylamine (30.0 μL, 0.210 mmol, 1.3 equiv), Hünig's base (30.0 μL, 0.172 mmol, 1.1 equiv), 18 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 64.4 mg of ACP1-28 as a white solid in 97% yield. mp 92−94 °C (CH_2Cl_2); R_f 0.44 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3358, 3024, 2939, 1680, 1650, 1537, 1321, 1132, 1107, 1082 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.91 (2H, m), 7.83−7.76 (2H, m), 7.35−7.28 (2H, m), 7.25−7.18 (3H, m), 6.86 (1H, br t, *J* = 6.0 Hz), 3.34 (2H, td, *J* = 7.0, 6.0 Hz), 2.76−2.67 (2H, m), 1.98−1.88 (2H, m), 1.56 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 141.2, 138.9 (q, *J* = 1.0 Hz), 136.0 (q, *J* = 33.0 Hz), 130.8, 128.7, 128.5, 126.31, 126.26 (q, *J* = 3.5 Hz), 123.1 (q, *J* = 273.0 Hz), 68.4, 40.2, 33.3, 30.9, 20.8; HRMS (ESI^+) *m/z* calcd for $C_{20}H_{23}F_3NO_3S$ $[M + H]^+$: 414.1345, found 414.1351.



4-Chloro-*N*-methyl-3-(3-(2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamido)propyl)benzamide (ACP1-29). Synthesized according to General Procedure A using 2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanoic acid (41.5 mg, 0.0844 mmol, 1.0 equiv), methylamine hydrochloride (8.1 mg, 0.093 mmol, 1.4 equiv), PyBOP (48.6 mg, 0.0934 mmol, 1.1 equiv), DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 2.7 equiv), 15 h. Flash chromatography (3:1 EtOAc:hexanes) of the organic extracts afforded 42.4 mg of ACP1-29 as a white solid in quantitative yield. mp 83–84 °C (CH_2Cl_2); R_f 0.71 (3:1 EtOAc:hexanes); IR (solid) ν_{max} 3446, 3056, 2942, 2867, 1652, 1536, 1320, 1130, 1062, 837 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD, note: the benzamide proton resonance was not observed due to deuterium exchange) δ 8.12 (1H, br t, *J* = 5.0 Hz), 8.05 (2H, d, *J* = 8.0 Hz), 7.93 (2H, d, *J* = 8.0 Hz), 7.77 (1H, d, *J* = 2.0 Hz), 7.63 (1H, dd, *J* = 8.0, 2.0 Hz), 7.45 (1H, d, *J* = 8.0 Hz), 3.29–3.24 (2H, m), 2.89 (3H, s), 2.87–2.80 (2H, m), 1.87 (2H, quintet, *J* = 7.5 Hz), 1.60 (6H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 169.8, 169.4, 140.97 (q, *J* = 1.0 Hz), 140.91, 138.4, 136.7 (q, *J* = 33.0 Hz), 134.6, 132.6, 130.8, 130.5, 127.6, 127.2 (q, *J* = 4.0 Hz), 124.9 (q, *J* = 272.5 Hz), 70.3, 40.9, 31.9, 30.1, 27.1, 20.8; HRMS (ESI^+) *m/z* calcd for $C_{22}H_{25}ClF_3N_2O_4S$ $[M + H]^+$: 505.1170, found 505.1161.



Methyl 3-chloro-4-((2-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamido)ethyl)thio)benzoate (ACP1-30). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (46.4 mg, 0.156 mmol, 1.0 equiv), PyBOP (92.8 mg, 0.179 mmol, 1.1 equiv), DMF (2 mL), methyl 4-((2-aminoethyl)thio)-3-chlorobenzoate (40.0 mg, 0.162 mmol, 1.0 equiv), Hünig's base (35.0 μL, 0.201 mmol, 1.3 equiv), 15 h. Flash

chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 69.5 mg of ACP1-30 as a white solid in 85% yield. mp 136–138 °C (CH_2Cl_2); R_f 0.35 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3407, 2953, 1704, 1677, 1525, 1432, 1385, 1325, 1310, 1293, 1244, 1174, 1143, 1130, 1090, 1073, 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.94−8.91 (1H, m), 8.24−8.22 (1H, m), 8.21−8.18 (1H, m), 8.01 (1H, dd, *J* = 2.0, 0.5 Hz), 7.90 (1H, dd, *J* = 8.5, 2.0 Hz), 7.45 (1H, br t, *J* = 6.5 Hz), 7.44 (1H, dd, *J* = 8.5, 0.5 Hz), 3.91 (3H, s), 3.60 (2H, td, *J* = 7.5, 6.5 Hz), 3.23 (2H, t, *J* = 7.5 Hz), 1.65 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 165.8, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 141.8, 135.8 (q, *J* = 3.5 Hz), 132.5, 130.7, 130.5 (q, *J* = 34.0 Hz), 128.4, 128.3, 126.2, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.7, 52.5, 39.4, 30.7, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{21}ClF_3N_2O_5S_2$ $[M + H]^+$: 525.0533, found 525.0534.

***N*-(2-((2-Fluorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-31).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (60.4 mg, 0.203 mmol, 1.0 equiv), PyBOP (125.5 mg, 0.2411 mmol, 1.2 equiv), DMF (3 mL), 2-((2-fluorophenyl)thio)ethan-1-amine (80% by wt., 54.2 mg, 0.253 mmol, 1.2 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 1.1 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 82.1 mg of ACP1-31 as a white solid in 90% yield. mp 68−69 °C (CH_2Cl_2); R_f 0.36 (2:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3391, 3070, 2943, 1676, 1526, 1473, 1326, 1173, 1143, 1092, 1015, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95−8.91 (1H, m), 8.24 (1H, d, *J* = 8.0 Hz), 8.18 (1H, dd, *J* = 8.0, 2.0 Hz), 7.47 (1H, td, *J* = 8.0, 2.0 Hz), 7.37 (1H, br t, *J* = 6.5 Hz), 7.30−7.23 (1H, m), 7.14−7.05 (2H, m), 3.47 (2H, dt, *J* = 6.5, 6.5 Hz), 3.10 (2H, t, *J* = 6.5 Hz), 1.65 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 162.1 (d, *J* = 245.5 Hz), 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 133.5 (d, *J* = 1.5 Hz), 130.4 (q, J = 34.0 Hz), 129.5 (d, J = 8.0 Hz), 124.8 (d, *J* = 3.5 Hz), 124.6, 122.5 (q, *J* = 273.5 Hz), 121.5 (d, J = 17.5 Hz), 116.1 (d, *J* = 22.5 Hz), 67.8, 39.7, 33.0, 20.6; ^{19}F NMR (564 MHz, $CDCl_3$) δ −62.73 (3F, s), −108.72 (1F, m); HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{19}F_4N_2O_3S_2$ $[M + H]^+$: 451.0767, found 451.0777.

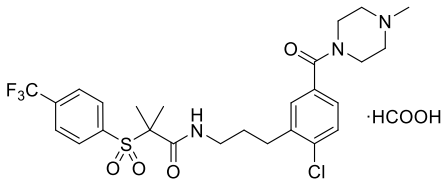
***N*-(3-phenylpropyl)-1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclobutane-1-carboxamide (ACP1-32).** Synthesized according to General Procedure A using 1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclobutane-1-carboxylic acid (52.4 mg, 0.169 mmol, 1.0 equiv), PyBOP (107.2 mg, 0.2060 mmol, 1.2 equiv), DMF (4 mL), 3-phenylpropylamine (35.0 μL, 0.245 mmol, 1.4 equiv), Hünig's base (70.0 μL, 0.402 mmol, 2.4 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 34.3 mg of ACP1-32 as a white solid in 48% yield. mp 54−55 °C (CH_2Cl_2); R_f 0.29 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 3323, 3067, 3027, 2959, 2868, 1650, 1545, 1314, 1295, 1162, 1141, 1070, 1093, 1012 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.91−8.87 (1H, m), 8.15−8.09 (2H, m), 7.31−7.25 (2H, m), 7.23−7.14 (3H, m), 6.71 (1H, br t, *J* = 6.0 Hz), 3.29 (2H, td, *J* = 7.0 Hz), 3.02−2.92 (2H, m), 2.74−2.62 (4H, m), 2.25−2.13 (1H, m), 2.12−2.00 (1H, m), 1.85 (2H, quintet, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 158.5 (q, *J* = 1.5 Hz), 147.4 (q, *J* = 4.0 Hz), 141.3, 135.6 (q, *J* = 3.5 Hz), 130.3 (q, *J* = 34.0 Hz), 128.6, 128.4, 126.2, 123.5, 122.5 (q, *J* = 273.5 Hz), 68.1, 40.1, 33.2, 30.8, 27.1, 16.2; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{22}F_3N_2O_3S$ $[M + H]^+$: 427.1297, found 427.1284.

2-Methyl-*N*-(2-(phenylthio)ethyl)-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamide (ACP1-33). Synthesized according to General Procedure A using 2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanoic acid (30.7 mg, 0.104 mmol, 1.0 equiv), PyBOP (65.7 mg, 0.126 mmol, 1.2 equiv), DMF (2 mL), 2-(phenylthio)ethan-1-amine (89% by wt., 26.5 mg, 0.153 mmol, 1.5 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 2.2 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 44.7 mg of ACP1-33 as a white solid in quantitative yield. mp 91−92 °C (CH_2Cl_2); R_f 0.29 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 3341, 3098, 3042, 3002, 2928, 1658, 1527, 1403, 1325, 1314, 1297, 1130, 1117, 1109, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (2H, d, J = 8.0 Hz), 7.74 (2H, d, J = 8.0 Hz), 7.45−7.40 (2H, m), 7.37−7.30 (2H, m), 7.29−7.22 (2H, m), 3.51 (2H, dt, J = 6.5, 6.5 Hz), 3.15−3.09 (2H, m), 1.57 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 138.7 (q, J = 1.0 Hz), 136.0 (q, J = 33.5 Hz), 134.6, 130.9, 130.1, 129.4, 127.0, 126.3 (q, J = 3.5 Hz), 123.1 (q, J = 273.5 Hz), 68.4, 39.4, 33.2, 20.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −63.33 (s); HRMS (ESI^+) m/z calcd for $C_{19}H_{21}F_3NO_3S_2$ $[M + H]^+$: 432.0909, found 432.0899.

2-((4-Chlorophenyl)sulfonyl)-2-methyl-*N*-(3-phenylpropyl)propanamide (ACP1-34). Synthesized according to General Procedure A using 2-((4-chlorophenyl)sulfonyl)-2-methylpropanoic acid (95.0 mg, 0.362 mmol, 1.0 equiv), PyBOP (213.3 mg, 0.4099 mmol, 1.1 equiv), DMF (4 mL), 3-phenylpropylamine (60.0 μL, 0.418 mmol, 1.2 equiv), Hünig's base (70.0 μL, 0.402 mmol, 1.1 equiv), 26 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 92.4 mg of ACP1-34 as a white solid in 67% yield. mp 73−75 °C (CH_2Cl_2); R_f 0.39 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3359, 3078, 3030, 2986, 2939, 2916, 2853, 1650, 1531, 1305, 1276, 1137, 1088, 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78−7.70 (2H, m), 7.54−7.47 (2H, m), 7.35−7.28 (2H, m), 7.25−7.18 (3H, m), 6.90 (1H, br t, J = 6.0 Hz), 3.33 (2H, td, J = 7.0, 6.0 Hz), 2.74−2.67 (2H, m), 1.92 (2H, quintet, J = 7.0 Hz), 1.54 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 141.4, 141.2, 133.6, 131.5, 129.5, 128.7, 128.5, 126.3, 68.3, 40.1, 33.3, 30.9, 20.9; HRMS (ESI^+) m/z calcd for $C_{19}H_{23}ClNO_3S$ $[M + H]^+$: 380.1081, found 380.1075.

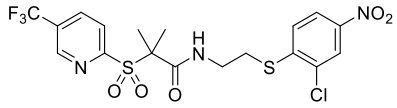
***N*-(2-((2-Chlorophenyl)thio)ethyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl) cyclopentane-1-carboxamide (ACP1-35).** Synthesized according to General Procedure A using 1-((4-(trifluoromethyl)phenyl)sulfonyl)cyclopentane-1-carboxylic acid (30.3 mg, 0.0940 mmol, 1.0 equiv), PyBOP (64.0 mg, 0.123 mmol, 1.3 equiv), DMF (3 mL), 2-((2-chlorophenyl)thio)ethan-1-amine (24.0 mg, 0.128 mmol, 1.4 equiv) in DMF (1 mL), Hünig's base (20.0 μL, 0.115 mmol, 1.2 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 43.8 mg of ACP1-35 as a white solid in 95% yield. mp 66−67 °C (CH_2Cl_2); R_f 0.61 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3390, 3100, 3074, 2958, 2935, 2875, 1666, 1514, 1319, 1306, 1297, 1146, 1130, 1124, 1107, 1087, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, d, J = 8.0 Hz), 7.72 (2H, d, J = 8.0 Hz), 7.42 (2H, dd, J = 7.5, 1.5 Hz), 7.31 (1H, br t, J = 6.5 Hz), 7.26 (1H, td, J = 7.5, 1.5 Hz), 7.19 (1H, td, 7.5, 1.5 Hz), 3.52 (2H, dt, J = 6.5, 6.5 Hz), 3.12 (2H, t, J = 6.5 Hz), 2.50−2.39 (2H, m), 2.38−2.27 (2H, m), 1.90−1.64 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 140.3 (q, J = 1.0 Hz), 135.9 (q, J = 33.0 Hz), 134.9, 134.0, 130.21, 130.15 (2C), 127.8, 127.6, 126.4 (q, J = 3.5 Hz), 123.1 (q, J = 273.5 Hz), 78.5, 39.4, 32.9, 32.4, 26.1; HRMS ($DART^+$) m/z calcd for $C_{21}H_{22}ClF_3NO_3S_2$ $[M + H]^+$: 492.0682, found 492.0676.

***N*-(3-(2-Chloro-5-(4-methylpiperazine-1-carbonyl)phenyl)propyl)-2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanamide formate (ACP1-36).** Synthesized according to



General Procedure A using ACP1-41 (44.3 mg, 0.0901 mmol, 1.0 equiv), PyBOP (54.2 mg, 0.104 mmol, 1.1 equiv), DMF (2 mL), 1-methylpiperazine (15.0 μL, 0.135 mmol, 1.5 equiv), Hünig's base (40.0 μL, 0.230 mmol, 2.5 equiv), 15 h. Flash chromatography (3:1 EtOAc:hexanes) of the organic extracts afforded 90.3 mg of an impure product whose composition by ^{1}H NMR was determined to be 61% w/w ACP1-36 and 39% w/w tri(pyrrolidin-1-yl)phosphine oxide (byproduct derived from the PyBOP coupling reagent). The product was then further purified using reversed phase HPLC (column: XTerra Prep C18 column (19.0 x 250 mm (10 μm)), acetonitrile/water with 0.1% formic acid 5:95 to 95:5 for 50 minutes, flow rate = 5.0 mL/min, 254 nm, 25 ºC). Analysis of the UV-active fractions by LRMS indicated that the product eluted between 27 and 30 min. Lyophillization of the product containing fractions afforded 31.8 mg of ACP1-36 as the corresponding formic acid salt as a light yellow oil in 57% yield. R_f 0.14 (3:1 EtOAc:hexanes); IR (thin film in CH_2Cl_2) ν_{max} 3371, 2942, 2866, 2799, 1665, 1625, 1322, 1133, 1062 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (1H, s), 7.96 (2H, d, *J* = 8.0 Hz), 7.82 (2H, d, *J* = 8.0 Hz), 7.39 (1H, d, *J* = 8.0 Hz), 7.32 (1H, d, *J* = 2.0 Hz), 7.19 (1H, dd, *J* = 8.0, 2.0 Hz), 6.96 (1H, br t, *J* = 5.5 Hz), 4.44 (1H, br s), 3.79 (2H, br s), 3.48 (2H, br s), 3.40–3.33 (2H, m), 2.86–2.79 (2H, m), 2.60–2.36 (4H, br m), 2.33 (3H, s), 1.92 (2H, quintet, *J* = 7.5 Hz), 1.57 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 169.4, 167.1, 139.5, 138.8 (q, *J* = 1.5 Hz), 136.1 (q, *J* = 33.5 Hz), 135.6, 134.5, 130.8, 129.8, 129.4, 126.5, 126.3 (q, *J* = 3.5 Hz), 123.1 (q, *J* = 273.5 Hz), 68.5, 54.7 (br), 47.4 (br), 45.7, 41.9 (br), 40.0, 31.0, 29.3, 20.9; LRMS (ESI$^+$, % base peak) *m*/*z* 596.2 (11, $[M + Na]^+$), 574.2 (100, $[M + H]^+$); HRMS (ESI$^+$) *m*/*z* calcd for $C_{26}H_{32}ClF_3N_3O_4S$ $[M – HCOO]^+$: 574.1749, found 574.1755.

***N*-(2-((2-Chloro-4-nitrophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl) pyridin-2-yl)sulfonyl)propanamide (ACP1-37).** Synthesized according to General Procedure A using 2-



methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (237.8 mg, 0.8000 mmol, 1.0 equiv), PyBOP (514.1 mg, 0.9879 mmol, 1.2 equiv), DMF (5 mL), 2-((2-chloro-4-nitrophenyl)thio)ethan-1-amine (242.9 mg, 1.044 mmol, 1.3 equiv), Hünig's base (170.0 μL, 0.9760 mmol, 1.2 equiv), 17 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 363.0 mg of ACP1-37 as a yellow solid in 89% yield. mp 124–126 °C (CH_2Cl_2); R_f 0.45 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3326, 3108, 3072, 2947, 1654, 1509, 1325, 1316, 1175, 1141, 1128, 1091, 1071, 1014 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (1H, s), 8.28−8.20 (3H, m), 8.13 (1H, dd, *J* = 9.0, 2.5 Hz), 7.58 (1H, d, *J* = 9.0 Hz), 7.52 (1H, br t, *J* = 6.0 Hz), 3.68−3.56 (2H, m), 3.34−3.24 (2H, m), 1.65 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 145.6, 145.3, 135.9 (q, *J* = 3.5 Hz), 132.2, 130.6 (q, *J* = 34.0 Hz), 125.5, 124.7, 124.6, 122.43 (q, *J* = 273.5 Hz), 122.42, 67.5, 39.3, 30.3, 20.7; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{18}ClF_3N_3O_5S_2$ $[M + H]^+$: 512.0329, found 512.0333.

4-Chloro-3-(3-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamido)propyl)benzoic acid (ACP1-38). Synthesized according to General Procedure D using benzyl 4-chloro-3-(3-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamido)prop-1-yn-1-yl)benzoate (308.1 mg, 0.5312 mmol, 1.0 equiv), THF (8 mL), palladium on carbon (10% by wt., 66.0 mg, 0.0620 mmol, 12 mol %), 15 h. Concentration of the filtrate afforded 259.1 mg of ACP1-38 as a beige crystalline solid in 99% yield. mp 50–51 °C ($CHCl_3$); IR (thin film in CH_2Cl_2) ν_{max} 3389, 3066, 2989, 2940, 1720, 1693, 1534, 1328, 1174, 1145, 1092, 1073, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, note: carboxylic acid proton resonance was not observed due to deuterium exchange) δ 8.95–8.90 (1H, m), 8.23–8.18 (2H, m), 7.96 (1H, d, *J* = 1.5 Hz), 7.87 (1H, dd, *J* = 8.0, 1.5 Hz), 7.44 (1H, d, *J* = 8.0 Hz), 7.15 (1H, br t, *J* = 6.0 Hz), 3.44–3.32 (2H, m), 2.92–2.75 (2H, m), 1.95 (2H, quintet, *J* = 7.5 Hz), 1.66 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 167.7, 158.2 (q, *J* = 1.5 Hz), 147.4 (q, *J* = 4.0 Hz), 139.9, 139.6, 135.7 (q, *J* = 3.5 Hz), 132.0, 130.4 (q, *J* = 34.0 Hz), 130.0, 129.4, 128.4, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.8, 40.1, 30.9, 29.1, 20.7; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{21}ClF_3N_2O_5S$ $[M + H]^+$: 493.0806, found 493.0806.

***N*-Cinnamyl-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamide (ACP1-39).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (75.4 mg, 0.254 mmol, 1.0 equiv), PyBOP (160.0 mg, 0.3074 mmol, 1.2 equiv), DMF (3 mL), cinnamyl amine[3] (38.5 mg, 0.289 mmol, 1.1 equiv) in DMF (1 mL), Hünig's base (55.0 μL, 0.316 mmol, 1.2 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 87.3 mg of ACP1-39 as a light yellow solid in 83% yield. mp 62−63 °C (CH_2Cl_2); R_f 0.70 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3313, 3091, 3060, 3035, 2928, 1655, 1532, 1319, 1165, 1132, 1091, 1070, 1014, 964 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.92−8.88 (1H, m), 8.17−8.13 (1H, m), 8.09−8.03 (1H, m), 7.39−7.30 (4H, m), 7.26 (1H, tt, *J* = 6.0, 1.5 Hz), 7.15 (1H, br t, *J* = 6.5 Hz), 6.61 (1H, d, *J* = 16.0 Hz), 6.21 (1H, dt, *J* = 16.0, 6.5 Hz), 4.07 (2H, td, *J* = 6.5, 1.5 Hz), 1.69 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 158.1 (q, *J* = 1.5 Hz), 147.4 (q, *J* = 4.0 Hz), 136.6, 135.6 (q, *J* = 3.5 Hz), 132.9, 130.4 (q, *J* = 34.0 Hz), 128.8, 128.1, 126.5, 124.70, 124.67, 122.5 (q, *J* = 273.5 Hz), 68.0, 42.6, 20.7; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{20}F_3N_2O_3S$ $[M + H]^+$: 413.1141, found 413.1155.

***N*-(3-(2-Chloro-5-(morpholine-4-carbonyl)phenyl)propyl)-2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanamide (ACP1-40).** Synthesized according to General Procedure A using ACP1-41 (41.3 mg, 0.0840 mmol, 1.0 equiv), PyBOP (53.3 mg, 0.102 mmol, 1.2 equiv), DMF (2 mL), morpholine (15.0 μL, 0.173 mmol, 2.1 equiv), Hünig's base (40.0 μL, 0.230 mmol, 2.7 equiv), 15 h. Flash chromatography (3:1 EtOAc:hexanes) of the organic extracts afforded 26.3 mg of **ACP1-40** as a white crystalline solid in 56% yield. mp 53–55 °C (CH_2Cl_2); R_f 0.36 (3:1 EtOAc:hexanes); IR (thin film in CH_2Cl_2) ν_{max} 3367, 2963, 2927, 2859, 1668, 1627, 1322, 1133, 1110, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, d, *J* = 8.0 Hz), 7.82 (2H, d, *J* = 8.0 Hz), 7.40 (1H, d, *J* = 8.0 Hz), 7.33 (1H, d, *J* = 2.0 Hz), 7.20 (1H, dd, *J* = 8.0, 2.0 Hz), 6.96 (1H, br t, *J* = 6.0 Hz), 3.90–3.30 (10H, m), 2.86–2.80 (2H, m), 1.92 (2H, quintet, *J* = 7.5 Hz), 1.57 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 167.1, 139.6, 138.8, 136.1 (q, *J* = 33.0 Hz), 135.7, 134.3,

130.8, 129.9, 129.4, 126.5, 126.3 (q, J = 4.0 Hz), 123.1 (q, J = 273.5 Hz), 68.5, 67.0, 48.3 (br), 42.8 (br), 40.0, 31.0, 29.3, 21.0; HRMS (ESI^+) m/z calcd for $C_{25}H_{29}ClF_3N_2O_5S$ $[M + H]^+$: 561.1432, found 561.1437.

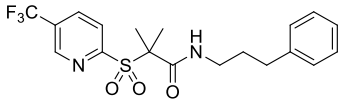
4-Chloro-3-(3-(2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamido)propyl)benzoic acid (ACP1-41). Synthesized according to General Procedure D using benzyl 4-chloro-3-(3-(2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl) propanamido)prop-1-yn-1-yl)benzoate (520.4 mg, 0.8988 mmol, 1.0 equiv), THF (10 mL), palladium on carbon (10% by wt., 99.0 mg, 0.0930 mmol, 10 mol %), 17 h. Concentration of the filtrate afforded 428.0 mg of ACP1-41 as a beige solid in 97% yield. mp 149–150 °C ($CHCl_3$); IR (solid) ν_{max} 3377, 2945, 1715, 1639, 1548, 1317, 1168, 1160, 1132, 1079, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, note: carboxylic acid proton resonance was not observed due to deuterium exchange) δ 8.00–7.94 (3H, m), 7.89 (1H, dd, J = 8.0, 1.0 Hz), 7.82 (2H, d, J = 8.5 Hz), 7.46 (1H, d, J = 8.0 Hz), 7.01 (1H, br t, J = 5.5 Hz), 3.44–3.33 (2H, m), 2.92–2.74 (2H, m), 1.95 (2H, quintet, J = 7.5 Hz), 1.59 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 167.3, 140.0, 139.4, 138.8, 136.1 (q, J = 33.0 Hz), 132.0, 130.8, 130.1, 129.5, 128.4, 126.3 (q, J = 4.0 Hz), 123.1 (q, J = 273.5 Hz), 68.5, 40.1, 31.0, 29.3, 20.9; HRMS (ESI^+) m/z calcd for $C_{21}H_{22}ClF_3NO_5S$ $[M + H]^+$: 492.0854, found 492.0854.

2-Methyl-1-(4-phenylpiperidin-1-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propan-1-one (ACP1-42). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (85.3 mg, 0.287 mmol, 1.0 equiv), PyBOP (174.6 mg, 0.3355 mmol, 1.2 equiv), DMF (6 mL), 4-phenylpiperidine (52.8 mg, 0.327 mmol, 1.1 equiv), Hünig's base (60.0 μL, 0.344 mmol, 1.2 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 111.3 mg of ACP1-42 as a white solid in 88% yield. mp 55−57 °C (CH_2Cl_2); R_f 0.37 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3099, 3031, 2998, 2945, 2919, 2873, 1644, 1331, 1306, 1126, 1087, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96−8.93 (1H, m), 8.30−8.25 (1H, m), 8.21−8.16 (1H, m), 7.36−7.28 (2H, m), 7.26−7.18 (3H, m), 4.63−4.53 (2H, br m), 3.09−2.87 (2H, br m), 2.80 (1H, tt, J = 12.0, 4.0 Hz), 2.04−1.86 (8H, m), 1.80−1.66 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 161.3 (q, J = 1.5 Hz), 146.6 (q, J = 4.0 Hz), 144.9, 135.3 (q, J = 3.5 Hz), 129.5 (q, J = 33.5 Hz), 128.8, 126.81, 126.77, 124.4, 122.8 (q, J = 273.5 Hz), 72.6, 46.5 (br), 42.7, 33.4, 22.7; HRMS (ESI^+) m/z calcd for $C_{21}H_{24}F_3N_2O_3S$ $[M + H]^+$: 441.1454, found 441.1450.

2-Methyl-*N*-(2-(phenylamino)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-43). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (55.5 mg, 0.187 mmol, 1.0 equiv), PyBOP (112.0 mg, 0.2152 mmol, 1.1 equiv), DMF (2 mL), *N*-phenylethylenediamine (25.0 μL, 0.192 mmol, 1.0 equiv), Hünig's base (35.0 μL, 0.201 mmol, 1.1 equiv), 11 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 81.0 mg of ACP1-43 as a light yellow crystalline solid in quantitative yield. mp 92–93 °C (CH_2Cl_2); R_f 0.49 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3387, 3057, 2990, 2942, 1669, 1604, 1513, 1327, 1173, 1139, 1092, 1072, 1014 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.83–8.81 (1H, m), 8.18 (1H, d, J = 8.0 Hz), 8.07

(1H, dd *J* = 8.0, 2.0 Hz), 7.23 (1H, br t, *J* = 5.5 Hz), 7.20–7.16 (2H, m), 6.73 (1H, tt, *J* = 7.5, 1.0 Hz), 6.66–6.62 (2H, m), 4.43 (1H, br s), 3.57–3.52 (2H, m), 3.43–3.39 (2H, m), 1.63 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 157.8, 147.8, 147.4 (q, *J* = 4.0 Hz), 135.8 (q, *J* = 3.5 Hz), 130.4 (q, *J* = 34.0 Hz), 129.5, 124.9, 122.4 (q, *J* = 274.0 Hz), 117.9, 113.2, 67.7, 42.9, 39.8, 20.4; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{21}F_3N_3O_3S$ [M + H]$^+$: 416.1250, found 416.1246.

2-Methyl-*N*-(3-phenylpropyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamide (ACP1-44[1]). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (381.9 mg, 1.285 mmol, 1.0 equiv), PyBOP



(741.4 mg, 1.425 mmol, 1.1 equiv), DMF (8 mL), 3-phenylpropylamine (190.0 µL, 1.331 mmol, 1.0 equiv), Hünig's base (250.0 µL, 1.435 mmol, 1.1 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 467.7 mg of ACP1-44 as a white solid in 88% yield. mp 83–86 °C (CH_2Cl_2); R_f 0.26 (3:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3394, 3063, 3028, 2939, 2862, 1670, 1531, 1327 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (1H, s), 8.20–8.16 (2H, m), 7.35–7.25 (2H, m), 7.25–7.15 (3H, m), 6.99 (1H, br m), 3.38–3.28 (2H, m), 2.71 (2H, t, *J* = 7.5 Hz), 1.92 (2H, quintet, *J* = 7.5 Hz), 1.62 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 141.4, 135.6 (q, *J* = 3.5 Hz), 130.3 (q, *J* = 34.0 Hz), 128.6, 128.5, 126.2, 124.6, 122.5 (q, *J* = 273.0 Hz), 67.9, 40.1, 33.2, 30.7, 20.6; HRMS (ESI$^+$) *m*/*z* calcd for $C_{19}H_{22}F_3N_2O_3S$ [M + H]$^+$: 415.1297, found 415.1296.

2-Methyl-*N*-(2-(phenylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-45[1]). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (372.2 mg, 1.252 mmol, 1.0 equiv), PyBOP (718.8 mg, 1.381 mmol, 1.1 equiv), DMF (6 mL), 2-(phenylthio)ethan-1-amine (89% by wt., 217.8 mg, 1.265 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (250.0 µL, 1.435 mmol, 1.1 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 285.7 mg of ACP1-45 as a light yellow oil in 53% yield. R_f 0.42 (2:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3390, 3063, 3028, 2992, 2942, 1667, 1526, 1327, 1171, 1142, 1092, 1072, 1015 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92−8.90 (1H, m), 8.21–8.18 (1H, m), 8.17–8.13 (1H, m), 7.42–7.38 (2H, m), 7.35 (1H, br t, *J* = 5.5 Hz), 7.33–7.28 (2H, m), 7.24–7.20 (1H, m), 3.51 (2H, td, *J* = 6.5, 5.5 Hz), 3.12 (2H, t, *J* = 6.5 Hz), 1.63 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 135.7 (q, *J* = 3.5 Hz), 135.0, 130.4 (q, *J* = 34.0 Hz), 130.1, 129.3, 126.8, 124.6, 122.5 (q, *J* = 273.5 Hz), 67.8, 39.7, 33.1, 20.6; ^{19}F NMR (564 MHz, $CDCl_3$) δ −62.72 (s); HRMS (ESI$^+$) *m/z* calcd for $C_{18}H_{20}N_2O_3F_3S_2$ [M + H]$^+$: 433.0861, found 433.0856.

2-Methyl-*N*-(2-(*o*-tolylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-46). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (85.3 mg, 0.287 mmol, 1.0 equiv), PyBOP (213.9 mg, 0.4110 mmol, 1.4 equiv), DMF (3 mL), 2-(*o*-tolylthio)ethan-1-amine (74% by wt., 101.4 mg, 0.4483 mmol, 1.6 equiv) in DMF (2 mL), Hünig's base (150.0 µL, 0.8612 mmol, 3.0 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 48.2 mg of ACP1-46 as a beige solid in 38% yield. mp 67–68 °C (CH_2Cl_2); R_f 0.46 (2:1 hexanes:EtOAc); IR (thin film

in CH_2Cl_2) ν_{max} 3392, 3063, 2987, 2939, 1674, 1591, 1576, 1525, 1471, 1387, 1322, 1172, 1141, 1092, 1072, 1015, 854, 747, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.91−8.87 (1H, s), 8.18 (1H, d, *J* = 8.0 Hz), 8.11 (1H, dd, *J* = 8.0, 2.0 Hz), 7.42−7.32 (2H, m), 7.21−7.09 (3H, m), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.10 (2H, t, *J* = 6.5 Hz), 2.39 (3H, s), 1.64 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 158.2 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 138.4, 135.6 (q, *J* = 3.5 Hz), 134.2, 130.5, 130.3 (q, *J* = 34.0 Hz), 128.9, 126.7, 126.5, 124.5, 122.5 (q, *J* = 273.5 Hz), 67.8, 39.5, 32.2, 20.5 (2C); HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{22}F_3N_2O_3S_2$ $[M + H]^+$: 447.1018, found 447.1012.

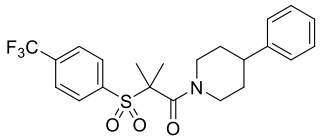
***N*-(2-((4-Methoxyphenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-47).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (49.3 mg, 0.166 mmol, 1.0 equiv), PyBOP (109.0 mg, 0.2094 mmol, 1.3 equiv), DMF (3 mL), 2-((4-methoxyphenyl)thio)ethan-1-amine (83% by wt., 36.7 mg, 0.166 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 1.4 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 62.3 mg of ACP1-47 as a white solid in 81% yield. mp 56−57 °C (CH_2Cl_2); R_f 0.61 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3389, 3097, 3067, 2993, 2942, 2838, 1672, 1592, 1526, 1497, 1328, 1247, 1173, 1142, 1092, 1072, 1014, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.96−8.90 (1H, m), 8.21 (1H, d, *J* = 8.0 Hz), 8.17 (1H, dd, *J* = 8.0, 2.0 Hz), 7.45−7.37 (2H, m), 7.33 (1H, br t, *J* = 6.5 Hz), 6.90−6.79 (2H, m), 3.80 (3H, s), 3.44 (2H, dt, *J* = 6.5, 6.5 Hz), 2.99 (2H, t, *J* = 6.5 Hz), 1.64 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 159.5, 158.3 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 3.9 Hz), 135.6 (q, *J* = 3.5 Hz), 134.0, 130.3 (q, *J* = 34.0 Hz), 124.8, 124.6, 122.5 (q, *J* = 273.5 Hz), 114.9, 67.9, 55.5, 39.5, 35.0, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{22}F_3N_2O_4S_2$ $[M + H]^+$: 463.0967, found 463.0956.

2-Methyl-1-(4-phenylpiperazin-1-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propan-1-one (ACP1-48). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (85.0 mg, 0.286 mmol, 1.0 equiv), PyBOP (166.1 mg, 0.3192 mmol, 1.1 equiv), DMF (4 mL), 1-phenylpiperazine (45.0 μL, 0.295 mmol, 1.0 equiv), Hünig's base (60.0 μL, 0.344 mmol, 1.2 equiv), 14 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 84.7 mg of ACP1-48 as a light yellow solid in 67% yield. mp 155−157 °C (CH_2Cl_2); R_f 0.23 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3099, 3065, 3008, 2977, 2852, 1629, 1328, 1319, 1242, 1160, 1139, 1126, 1092, 1072, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97−8.92 (1H, m), 8.23 (1H, d, *J* = 8.0 Hz), 8.18 (1H, dd, *J* = 8.0, 2.0 Hz), 7.33−7.25 (2H, m), 6.98−6.88 (3H, m), 3.91 (4H, br s), 3.30−3.21 (4H, m), 1.87 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 160.1 (q, *J* = 1.5 Hz), 150.8, 146.8 (q, *J* = 4.0 Hz), 135.4 (q, *J* = 3.5 Hz), 129.8 (q, *J* = 33.5 Hz), 129.4, 124.6, 122.7 (q, *J* = 273.5 Hz), 120.7, 116.6, 71.6, 49.5, 45.8 (br), 22.9; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{23}F_3N_3O_3S$ $[M + H]^+$: 442.1406, found 442.1409.

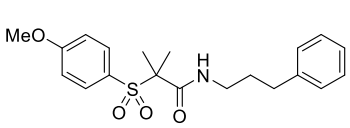
(4-Phenylpiperidin-1-yl)(1-((4-(trifluoromethyl)phenyl)sulfonyl)cyclopentyl)methanone (ACP1-49). Synthesized according to General Procedure A using 1-((4-(trifluoromethyl)phenyl)sulfonyl)cyclopentane-1-carboxylic acid (38.2 mg, 0.118 mmol, 1.0 equiv), PyBOP (72.2 mg, 0.139 mmol, 1.2 equiv), DMF (3 mL), 4-phenylpiperidine (24.2 mg, 0.150 mmol, 1.3 equiv) in DMF (1 mL), Hünig's base (25.0 μL, 0.143 mmol, 1.2 equiv), 24 h.

Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 49.5 mg of ACP1-49 as a white solid in 90% yield. mp 95−96 °C (CH_2Cl_2); R_f 0.44 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 2964, 2937, 2847, 1618, 1426, 1318, 1312, 1305, 1174, 1137, 1106, 1085, 1060, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J* = 8.5 Hz), 7.79 (2H, d, *J* = 8.5 Hz), 7.37−7.29 (2H, m), 7.28−7.20 (3H, m), 4.66 (2H, br d, *J* = 13.0 Hz), 3.40−2.65 (3H, m), 2.61−2.47 (2H, m), 2.46−2.30 (2H, m), 2.12−1.50 (8H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 145.0, 140.4 (q, *J* = 1.0 Hz), 135.6 (q, *J* = 33.0 Hz), 130.4, 128.8, 126.8, 126.7, 125.9 (q, *J* = 3.5 Hz), 123.3 (q, *J* = 273.0 Hz), 80.3, 48.5 (br), 45.6 (br), 42.6, 35.1, 33.5, 26.5; HRMS ($DART^+$) *m/z* calcd for $C_{24}H_{27}F_3NO_3S$ $[M + H]^+$: 466.1664, found 466.1670.

2-Methyl-1-(4-phenylpiperidin-1-yl)-2-((4-(trifluoromethyl)phenyl)sulfonyl)propan-1-one (ACP1-50). Synthesized according to General Procedure A using 2-methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)propanoic acid (50.6 mg, 0.171 mmol, 1.0 equiv), PyBOP (155 mg, 0.298 mmol, 1.7 equiv), DMF (5 mL), 4-phenylpiperidine (29.9 mg, 0.185 mmol, 1.1 equiv) in DMF (1 mL), Hünig's base (35 μL , 0.200 mmol, 1.2 equiv), 18 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 71.3 mg of ACP1-50 as a white solid in 95% yield. mp 136−138 °C (CH_2Cl_2); R_f 0.44 (2:1 hexanes:EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (2H, d, *J* = 8.0 Hz), 7.81 (2H, d, *J* = 8.0 Hz), 7.37−7.30 (2H, m), 7.28−7.20 (3H, m), 4.79−4.70 (2H, br m), 3.13−2.90 (2H, br m), 2.83 (1H, tt, *J* = 12.0, 4.0 Hz), 2.04−1.94 (2H, br m), 1.82−1.65 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 145.0, 140.1 (q, *J* = 1.5 Hz), 136.1 (q, *J* = 33.0 Hz), 130.8, 128.8, 126.81, 126.74, 125.9 (q, *J* = 3.5 Hz), 123.3 (q, *J* = 273.0 Hz), 70.8, 47.1, 42.6, 33.6, 23.5; HRMS (ESI^+) *m/z* calcd for $C_{22}H_{25}F_3NO_3S$ $[M + H]^+$: 440.1501, found 440.1515.



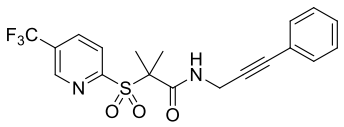
2-Methyl-*N*-(2-phenoxyethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamide (ACP1-51). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (94.3 mg, 0.317 mmol, 1.0 equiv), PyBOP (165 mg, 0.317 mmol, 1.0 equiv), DMF (3 mL), 2-phenoxyethan-1-amine[4] (43.5 mg, 0.317 mmol, 1.0 equiv) in DMF (3 mL), Hünig's base (165 μL, 0.951 mmol, 3.0 equiv), 1 h. Flash chromatography (3:2 hexanes:EtOAc) of the concentrated reaction mixture afforded 86.18 mg of ACP1-51 as a white crystalline solid in 65 % yield. mp 108–109 °C (hexanes/EtOAc); R_f 0.25 (3:2 hexanes:EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.76–8.75 (1H, m), 8.11 (1H, d, *J* = 8.0 Hz), 7.81 (1H, dd, *J* = 8.0, 2.0 Hz), 7.53–7.51 (1H, br m), 7.31–7.27 (2H, m), 6.97 (1H, tt, *J* = 7.0, 1.0 Hz), 6.89–6.87 (2H, m), 4.02 (2H, t, *J* = 5.5 Hz), 3.69 (2H, app. q, *J* = 5.5 Hz), 1.67 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 158.6, 147.3, 144.9, 135.6, 130.2 (q, *J* = 34.0 Hz), 129.9, 123.9, 122.5 (q, *J* = 273.0 Hz), 121.1, 114.7, 68.0, 66.2, 40.2, 20.8; IR (thin film in CH_2Cl_2) ν_{max} 3394, 2924, 2854, 1670, 1597, 1531 cm^{-1}; HRMS (ESI^+) *m/z* calcd for $C_{18}H_{20}F_3N_2O_4S$ $[M + H]^+$: 417.1096, found 417.1090.



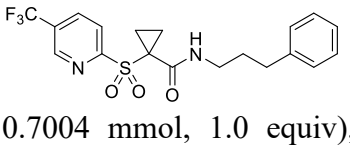
2-((4-Methoxyphenyl)sulfonyl)-2-methyl-*N*-(3-phenylpropyl)propanamide (ACP1-52). Synthesized according to General Procedure B using 2-((4-methoxyphenyl)thio)-2-methyl-*N*-(3-phenylpropyl)propanamide (323.2 mg, 0.9410 mmol, 1.0 equiv), $NaHCO_3$ (516.7 mg, 6.151 mmol, 6.5 equiv), CH_2Cl_2 (40 mL), MCPBA (70% by wt., 536.0 mg, 2.174 mmol, 2.3 equiv), 24 h. Flash

chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 299.7 mg of ACP1-52 as a white solid in 85% yield. mp 75−77 °C (CH_2Cl_2); R_f 0.50 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3362, 3028, 3010, 2936, 2909, 1657, 1526, 1294, 1259, 1125, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80−7.69 (2H, m), 7.35−7.25 (2H, m), 7.24−7.16 (3H, m), 7.06 (1H, br t, *J* = 7.0 Hz), 7.01−6.92 (2H, m), 3.86 (3H, s), 3.32 (2H, dt, *J* = 7.0, 7.0 Hz), 2.75−2.65 (2H, m), 1.92 (2H, quintet, *J* = 7.0 Hz), 1.53 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 164.4, 141.3, 132.3, 128.6, 128.5, 126.4, 126.2, 114.4, 68.1, 55.8, 40.0, 33.3, 30.9, 21.1; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{26}NO_4S$ $[M + H]^+$: 376.1577, found 376.1578.

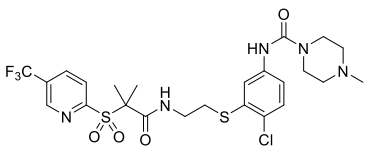
2-Methyl-*N*-(3-phenylprop-2-yn-1-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-53). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (72.3 mg, 0.243 mmol, 1.0 equiv), PyBOP (200.1 mg, 0.4229 mmol, 1.7 equiv), DMF (3 mL), 3-phenylprop-2-yn-1-amine[5] (41.6 mg, 0.317 mmol, 1.3 equiv) in DMF (2 mL), Hünig's base (50.0 μL, 0.287 mmol, 1.2 equiv), 28 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 57.3 mg of ACP1-53 as a light yellow solid in 57% yield. mp 104–105 °C (CH_2Cl_2); R_f 0.44 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3356, 2990, 1658, 1526, 1327, 1313, 1154, 1091, 1071, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95–8.93 (1H, m), 8.21 (1H, d, *J* = 8.0 Hz), 8.07–8.03 (1H, m), 7.45–7.40 (2H, m), 7.37–7.25 (4H, m), 4.30 (2H, d, *J* = 5.5 Hz), 1.70 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 158.0 (q, *J* = 1.5 Hz), 147.4 (q, *J* = 4.0 Hz), 135.6 (q, *J* = 3.5 Hz), 131.9, 130.4 (q, *J* = 34.0 Hz), 128.8, 128.5, 124.6, 122.5, 122.4 (q, *J* = 143.5 Hz), 84.3, 83.7, 67.9, 31.0, 20.5; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{18}F_3N_2O_3S$ $[M + H]^+$: 411.0984, found 411.1000.



***N*-(3-Phenylpropyl)-1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclopropane-1-carboxamide (ACP1-54).** Synthesized according to General Procedure A using 1-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)cyclopropane-1-carboxylic acid (200.3 mg, 0.6784 mmol, 1.0 equiv), PyBOP (441.2 mg, 0.8478 mmol, 1.2 equiv), DMF (6 mL), 3-phenylpropylamine (100.0 μL, 0.7004 mmol, 1.0 equiv), Hünig's base (250.0 μL, 1.435 mmol, 2.1 equiv), 18 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 104.3 mg of ACP1-54 as a beige solid in 37% yield. mp 69−71 °C (CH_2Cl_2); R_f 0.50 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3410, 3089, 3054, 3030, 2954, 2853, 1660, 1552, 1332, 1169, 1159, 1131, 1097, 1073, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95−8.91 (1H, m), 8.22−8.17 (1H, m), 8.14−8.10 (1H, m), 7.89 (1H, br t, *J* = 5.5 Hz), 7.32−7.26 (2H, m), 7.23−7.14 (3H, m), 3.34 (2H, td, *J* = 7.0, 6.0 Hz), 2.73−2.63 (2H, m), 1.94−1.84 (2H, m), 1.82−1.74 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 160.4 (q, *J* = 1.5 Hz), 147.5 (q, *J* = 4.0 Hz), 141.3, 136.0 (q, *J* = 3.5 Hz), 130.4 (q, *J* = 34.0 Hz), 128.6, 128.4, 126.2, 122.5 (q, *J* = 273.5 Hz), 122.1, 42.5, 40.0, 33.1, 30.9, 15.6; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{20}F_3N_2O_3S$ $[M + H]^+$: 413.1141, found 413.1150.

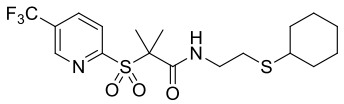


***N*-(4-Chloro-3-((2-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamido)ethyl)thio)phenyl)-4-methylpiperazine-1-carboxamide (ACP1-55).** Synthesized according to General Procedure C using ACP1-11 (30.0 mg, 0.0622 mmol, 1.0 eq), CH_2Cl_2 (1 mL), CDI (90% by wt., 11.2 mg, 0.0654 mmol, 1.05 equiv), 20 h; *N*-methylpiperazine (7.2 μL, 0.065 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography

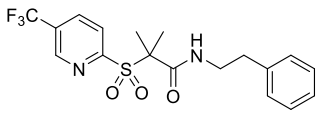


(4:1 EtOAc:CH_2Cl_2) of the crude reaction mixture afforded 8.6 mg of ACP1-55 as a white semi-solid in 22% yield. R_f 0.38 (EtOAc/CH_2Cl_2); IR (thin film in CH_2Cl_2) ν_{max} 3345, 3096, 3067, 2926, 2853, 1647, 1593, 1522, 1468, 1439, 1387, 1327, 1296, 1260, 1236 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.95 (1H, s), 8.21 (2H, m), 7.55 (1H, d, *J* = 2.5 Hz), 7.48 (1H, t, *J* = 6.0 Hz), 7.40 (1H, dd, *J* = 8.5, 2.5 Hz), 7.28 (1H, s), 6.87 (1H, br s), 3.53–3.51 (6H, m), 3.12 (2H, t, *J* = 7.0 Hz), 2.47–2.46 (4H, m), 2.34 (3H, s), 1.66 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 168.3, 158.4, 155.8, 146.6 (q, *J* = 4.0 Hz), 139.1, 135.9 (q, *J* = 3.5 Hz), 134.9, 129.8 (q, *J* = 33.5 Hz), 129.2, 126.3, 125.2, 119.7, 118.4, 68.8, 54.1, 44.5, 43.2, 39.0, 30.3, 19.2; HRMS (ESI^+) *m/z* calcd for $C_{24}H_{30}ClF_3N_5O_4S_2$ $[M + H]^+$: 608.1359, found 608.1374.

***N*-(2-(Cyclohexylthio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-56).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (72.1 mg, 0.243 mmol, 1.0 equiv), PyBOP (154.7 mg, 0.2973 mmol, 1.2 equiv), DMF (4 mL), 2-(cyclohexylthio)ethan-1-amine[6] (65.2 mg, 0.409 mmol, 1.7 equiv) in DMF (2 mL), Hünig's base (100.0 μL, 0.5741 mmol, 2.4 equiv), 16 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 47.3 mg of ACP1-56 as a white solid in 44% yield. mp 89−91 °C (CH_2Cl_2); R_f 0.35 (3:1 hexanes:EtOAc); IR (solid) ν_{max} 3413, 3059, 2933, 2857, 1679, 1526, 1326, 1303, 1172, 1162, 1141, 1088, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.01−8.95 (1H, m), 8.25−8.18 (2H, m), 7.30 (1H, br t, *J* = 6.0 Hz), 3.46 (2H, td, *J* = 7.0, 6.0 Hz), 2.77−2.63 (3H, m), 2.05−1.89 (2H, m), 1.85−1.54 (9H, m), 1.42−1.17 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 158.4 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 135.6 (q, *J* = 3.5 Hz), 130.4 (q, *J* = 34.0 Hz), 124.7, 122.5 (q, *J* = 273.5 Hz), 68.0, 43.6, 40.4, 33.9, 29.3, 26.2, 25.9, 20.7; HRMS (ESI^+) *m/z* calcd for $C_{18}H_{26}F_3N_2O_3S_2$ $[M + H]^+$: 439.1331, found 439.1324.



2-Methyl-*N*-phenethyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-57). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (20 mg, 0.0673 mmol, 1.0 equiv), PyBOP (38.5 mg, 0.074 mmol, 1.0 equiv), DMF (2 mL), phenethylamine (12.7 μL, 0.1009 mmol, 1.0 equiv) in DMF (1 mL), Hünig's base (35 μL, 0.2019 mmol, 3.0 equiv), 1 h. Flash chromatography (3:2 hexanes:EtOAc) of the concentrated reaction mixture afforded 29.9 mg of ACP1-57 as a grey solid in quantitative yield. mp 82–83 °C (hexanes/EtOAc); R_f 0.30 (3:2 hexanes:EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H, s), 8.17–8.14 (1H, m), 8.08–8.06 (1H, m), 7.34–7.30 (2H, m), 7.25–7.22 (3H, m), 7.22 (1H, br s), 3.55 (2H, dt, *J* = 7.0, 7.0 Hz), 2.89 (2H, t, *J* = 7.0 Hz), 1.61 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 158.4, 147.3, 138.8, 129.0, 128.9, 126.9, 124.7, 68.0, 41.9, 35.4, 20.7; HRMS (ESI^+) *m/z* calcd for $C_{18}H_{20}F_3N_2O_3S$ $[M + H]^+$: 401.1141, found 401.1153.



2-Methyl-*N*-(3-phenylpropyl)-2-(pyrimidin-2-ylsulfonyl)propanamide (ACP1-58). Synthesized according to General Procedure B using 2-methyl-*N*-(3-phenylpropyl)-2-(pyrimidin-2-ylthio)propanamide (97.7 mg, 0.310 mmol, 1.0 equiv), $NaHCO_3$ (152.3 mg, 1.813 mmol, 5.8 equiv), CH_2Cl_2 (17 mL), MCPBA (70% by wt., 173.2 mg, 0.7026 mmol, 2.3 equiv), 24 h. Flash chromatography (EtOAc) of the organic extracts afforded 95.6 mg of ACP1-58 as a colorless oil in 89% yield. R_f 0.54 (EtOAc); IR (neat) ν_{max} 3388, 3060, 3027, 2940, 2863, 1661, 1563, 1530, 1383,

1311, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.89 (2H, d, *J* = 5.0 Hz), 7.53 (1H, t, *J* = 5.0 Hz), 7.31−7.24 (2H, m), 7.22−7.14 (3H, m), 7.11 (1H, br t, *J* = 5.0 Hz), 3.34−3.25 (2H, m), 2.69−2.61 (2H, m), 1.92−1.80 (2H, m), 1.70 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 164.1, 158.7, 141.4, 128.6, 128.4, 126.1, 124.1, 67.6, 40.0, 33.1, 30.6, 20.7; HRMS (ESI^+) *m*/*z* calcd for $C_{17}H_{22}N_3O_3S$ $[M + H]^+$: 348.1376, found 348.1384.

***N*-(2-((2-Chlorophenyl)amino)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-59).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (59.2 mg, 0.199 mmol, 1.0 equiv), PyBOP (117.6 mg, 0.2260 mmol, 1.1 equiv), DMF (2 mL), N^1-(2-chlorophenyl)ethane-1,2-diamine (34.7 mg, 0.201 mmol, 1.0 equiv), Hünig's base (40.0 μL, 0.230 mmol, 1.1 equiv), 24 h. Flash chromatography (3:1 hexanes:EtOAc) of the organic extracts afforded 85.1 mg of ACP1-59 as a white solid in 95% yield. mp 102–103 °C (CH_2Cl_2); R_f 0.12 (3:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3388, 3068, 2990, 2942, 1669, 1599, 1518, 1327, 1173, 1143, 1092, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.82–8.79 (1H, m), 8.17 (1H, d, *J* = 8.0 Hz), 8.09–8.04 (1H, m), 7.38 (1H, br t, *J* = 6.0 Hz), 7.23 (1H, dd, *J* = 8.0, 1.5 Hz), 7.19–7.13 (1H, m), 6.70 (1H, dd, *J* = 8.0, 1.5 Hz), 6.66 (1H, ddd, *J* = 8.0, 8.0, 1.5 Hz), 4.84 (1H, br s), 3.62–3.55 (2H, m), 3.48–3.41 (2H, br m), 1.65 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 158.0 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 143.7, 135.7 (q, *J* = 3.5 Hz), 130.4 (q, *J* = 34.0 Hz), 129.5, 128.0, 124.7, 122.4 (q, *J* = 273.5 Hz), 119.5, 117.7, 111.0, 67.7, 42.9, 39.8, 20.5; HRMS (ESI^+) *m*/*z* calcd for $C_{18}H_{20}ClF_3N_3O_3S$ $[M + H]^+$: 450.0861, found 450.0868.

***N*-(2-((2-Methoxyphenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-60).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (61.4 mg, 0.206 mmol, 1.0 equiv), PyBOP (128.2 mg, 0.2463 mmol, 1.2 equiv), DMF (3 mL), 2-((2-methoxyphenyl)thio)ethan-1-amine (72% by wt., 52.5 mg, 0.206 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (50.0 μL, 0.287 mmol, 1.4 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 43.0 mg of ACP1-60 as a white solid in 45% yield. mp 115−117 °C (CH_2Cl_2); R_f 0.64 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3393, 3097, 3065, 2942, 2838, 1669, 1327, 1172, 1139, 1092, 1072 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.96−8.90 (1H, m), 8.21 (1H, d, *J* = 8.0 Hz), 8.14 (1H, dd, *J* = 8.0, 2.0 Hz), 7.48−7.32 (2H, m), 7.25 (1H, td, *J* = 8.0, 2.0 Hz), 6.98−6.85 (2H, m), 3.91 (3H, s), 3.44 (2H, dt, *J* = 6.5, 6.5 Hz), 3.04 (2H, t, *J* = 6.5 Hz), 1.65 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 158.6, 158.3 (q, *J* = 1.5 Hz), 147.2 (q, *J* = 4.0 Hz), 135.6 (q, *J* = 3.5 Hz), 132.3, 130.3 (q, *J* = 34.0 Hz), 128.7, 124.7, 122.5 (q, *J* = 273.5 Hz), 122.3, 121.4, 111.1, 68.0, 56.0, 39.5, 32.3, 20.6; HRMS (ESI^+) *m*/*z* calcd for $C_{19}H_{22}F_3N_2O_4S_2$ $[M + H]^+$: 463.0967, found 463.0955.

2-Methyl-*N*-(3-phenylpropyl)-2-((3-(trifluoromethyl)phenyl)sulfonyl) propanamide (ACP1-61). Synthesized according to General Procedure B using 2-methyl-*N*-(3-phenylpropyl)-2-((3-(trifluoromethyl)phenyl)thio) propanamide (158.0 mg, 0.4142 mmol, 1.0 equiv), $NaHCO_3$ (445.0 mg, 5.298 mmol, 12.7 equiv), CH_2Cl_2 (30 mL), MCPBA (70% by wt., 284.0 mg, 1.152 mmol, 2.7 equiv), 24 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 154.7 mg of ACP1-

61 as a white solid in 90% yield. mp 91−92 °C (CH_2Cl_2); R_f 0.15 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3396, 3080, 3031, 2941, 2928, 2861, 1667, 1534, 1324, 1294, 1124, 1068 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (1H, s), 8.01 (1H, d, *J* = 8.0 Hz), 7.93 (1H, d, *J* = 8.0 Hz), 7.69 (1H, t, *J* = 8.0 Hz), 7.35−7.27 (2H, m), 7.25−7.17 (3H, m), 6.86 (1H, br t, *J* = 6.0 Hz), 3.32 (2H, td, *J* = 7.0, 6.0 Hz), 2.76−2.66 (2H, m), 1.93 (2H, quintet, *J* = 7.0 Hz), 1.56 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 141.2, 136.5, 133.4 (q, *J* = 1.0 Hz), 132.0 (q, *J* = 33.5 Hz), 131.1 (q, *J* = 3.5 Hz), 129.9, 128.7, 128.5, 127.2 (q, *J* = 4.0 Hz), 126.8 (q, *J* = 273.0 Hz), 126.3, 68.5, 40.1, 33.4, 30.8, 20.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −62.89 (3F, s); HRMS (ESI^+) *m/z* calcd for $C_{20}H_{23}F_3NO_3S$ $[M + H]^+$: 414.1351, found 414.1336.

***N*,2-Dimethyl-*N*-(2-(phenylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamide (ACP1-62).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (61.9 mg, 0.208 mmol, 1.0 equiv), PyBOP (136.2 mg, 0.2617 mmol, 1.2 equiv), DMF (4 mL), *N*-methyl-2-(phenylthio)ethan-1-amine[7] (39.2 mg, 0.234 mmol, 1.1 equiv) in DMF (2 mL), Hünig's base (50.0 μL, 0.287 mmol, 1.4 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 57.6 mg of ACP1-62 as a white solid in 62% yield. mp 53−55 °C (CH_2Cl_2); R_f 0.64 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3122, 3058, 2927, 2887, 1639, 1385, 1325, 1292, 1115, 1091, 1071, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95−8.90 (1H, m), 8.21 (1H, d, *J* = 8.0 Hz), 8.14 (1H, dd, *J* = 8.0, 2.0 Hz), 7.36 (2H, d, *J* = 7.5 Hz), 7.29 (2H, t, *J* = 7.5 Hz), 7.21 (1H, t, *J* = 7.5 Hz), 3.55 (2H, br s), 3.30 (3H, br s), 3.12−3.05 (2H, m), 1.80 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 160.1, 146.6 (q, *J* = 4.0 Hz), 135.3 (2C), 129.7 (q, *J* = 34.0 Hz), 129.2 (2C), 126.6 (br), 124.6, 122.7 (q, *J* = 273.5 Hz), 72.0, 51.3 (br), 38.1 (br), 30.3 (br), 22.4; HRMS (ESI^+) *m/z* calcd for $C_{19}H_{22}F_3N_2O_3S_2$ $[M + H]^+$: 447.1018, found 447.1010.

***N*-(4-Chloro-3-((2-(2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl) propanamido)ethyl)thio)phenyl)-morpholine-4-carboxamide (ACP1-63).** Synthesized according to General Procedure C using ACP1-11 (50 mg, 0.104 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 20 mg, 0.123 mmol, 1.05 equiv), 16 h; morpholine (9 μL, 0.104 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (EtOAc) of the crude reaction mixture afforded 18.3 mg of ACP1-63 as a yellow oil in 30% yield. R_f 0.36 (EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3721, 3368, 3175, 3096, 3063, 3003, 2963, 2955, 2924, 2901, 2857, 2855, 1647, 1593, 1580, 1468, 1464, 1424, 1418, 1387, 1327, 1275, 1250, 1244 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, note: amide proton resonances were not observed due to deuterium exchange) δ 9.05 (1H, m), 8.40 (1H, dd, *J* = 8.0, 2.5 Hz), 8.26 (1H, d, *J* = 8.5 Hz), 7.56 (1H, d, *J* = 2.5 Hz), 7.26 (1H, d, *J* = 9.0 Hz), 7.20 (1H, dd, *J* = 9.0, 2.5 Hz), 3.67–3.65 (4H, m, *J* = 5 Hz), 3.45–3.42 (4H, m, *J* = 5 Hz), 3.42 (2H, app. t, *J* = 7.0 Hz), 3.08 (2H, app. t, *J* = 8.0 Hz), 1.69 (6H, s); ^{13}C NMR (125 MHz, CD_3OD) δ 169.7, 159.8, 157.5, 148.1 (q, *J* = 4.0 Hz), 140.5, 137.4 (q, *J* = 3.5 Hz), 136.3, 130.1 (q, *J* = 33.5 Hz), 130.6, 127.7, 126.6, 121.1, 119.8, 125.2 (q, *J* = 272.5 Hz), 70.2, 67.6, 45.6, 40.4, 31.7, 20.6; HRMS (DART+) *m/z* calcd for $C_{23}H_{27}ClF_3N_4O_5S_2$ $[M + H]$+: 595.1081, found 595.1064.

2-Methyl-2-((4-nitrophenyl)sulfonyl)-*N*-(3-phenylpropyl)propanamide (ACP1-64). Synthesized according to General Procedure A using 2-methyl-2-((4-nitrophenyl)sulfonyl)propanoic acid (91.7 mg, 0.335 mmol, 1.0 equiv), PyBOP (221.0 mg, 0.4247 mmol, 1.3 equiv), DMF (5 mL), 3-phenylpropylamine (50.0 μL, 0.350 mmol, 1.0 equiv), Hünig's base (70.0 μL, 0.402 mmol, 1.2 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 130.7 mg of ACP1-64 as a light yellow solid in quantitative yield. mp 50−51 °C (CH_2Cl_2); R_f 0.56 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3374, 3026, 3010, 2937, 2864, 1652, 1528, 1350, 1310, 1300, 1160, 1128, 1079 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39−8.32 (2H, m), 8.03−7.97 (2H, m), 7.35−7.29 (2H, m), 7.25−7.19 (3H, m), 6.72 (1H, br t, *J* = 6.0 Hz), 3.33 (2H, td, *J* = 7.0, 6.0 Hz), 2.77−2.67 (2H, m), 1.93 (2H, quintet, *J* = 7.0 Hz), 1.56 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 151.2, 141.08, 140.99, 131.6, 128.8, 128.5, 126.4, 124.1, 68.8, 40.2, 33.3, 30.8, 20.6; HRMS (ESI^+) *m/z* calcd for $C_{19}H_{23}N_2O_5S$ $[M + H]^+$: 391.1322, found 391.1339.

***N*-(2-((2-Chloro-5-(3,3-diethylureido)phenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-65).** Synthesized according to General Procedure C using ACP1-11 (50 mg, 0.104 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 19 mg, 0.117 mmol, 1.05 equiv), 16 h; diethylamine (11.9 μL, 0.114 mmol, 1.1 equiv), 0 °C, 5 min. Flash chromatography (7:3 hexanes:EtOAc) of the crude reaction mixture afforded 8.3 mg of ACP1-65 as a yellow oil in 14% yield. R_f 0.30 (7:3 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3376, 3354, 3308, 2972, 2930, 2872, 2855, 1636, 1593, 1464, 1447, 1435, 1385, 1327 cm-1; 1H NMR (500 MHz, $CDCl_3$) δ 8.96–8.95 (1H, m), 8.21–8.19 (2H, m), 7.64 (1H, d, *J* = 2.5 Hz), 7.49 (1H, t, *J* = 6.0 Hz), 7.35 (1H, dd, *J* = 8.5, 2.5 Hz), 7.25 (1H, d, *J* = 8.5 Hz), 6.53 (1H, br s), 3.51 (2H, dt, *J* = 6.5, 6.5 Hz), 3.35 (4H, q, *J* = 7.0 Hz), 3.13 (2H, t, *J* = 7.0 Hz), 1.67 (6H, s), 1.18 (6H, t, *J* = 7.0 Hz); 13C NMR (125 MHz, $CDCl_3$) δ 169.8, 159.8, 157.0, 148.5 (q, *J* = 4.0 Hz), 140.7, 137.3 (q, *J* = 3.5 Hz), 136.1, 131.2 (q, *J* = 33.5 Hz), 130.5, 127.7, 126.7, 125.2 (q, *J* = 274.5 Hz), 121.6, 120.3, 70.2, 42.5, 40.4, 31.7, 20.6, 14.1; HRMS (ESI+) *m/z* calcd for $C_{23}H_{29}ClF_3N_4O_4S_2$ [M + H]+: 581.1262, found 581.1265.

2-Methyl-*N*-(2-(phenylthio)ethyl)-2-(pyridin-2-ylsulfonyl)propanamide (ACP1-66). Synthesized according to General Procedure A using 2-methyl-2-(pyridin-2-ylsulfonyl)propanoic acid (230 mg, 1.0033 mmol, 1.0 equiv), PyBOP (522.1 mg, 1.0033 mmol, 1.0 equiv), DMF (10 mL), 2-(phenylthio)ethan-1-amine (230.6 mg, 1.505 mmol, 1.5 equiv) in DMF (0.5 mL), Hünig's base (524 μL, 3.01 mmol, 3.0 equiv), 16 h. Flash chromatography (4:3 hexanes:EtOAc) of the concentrated reaction mixture afforded 226.6 mg of ACP1-66 as a grey solid in 62% yield. mp 65–67 °C; R_f 0.39 (hexanes/EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3387, 3055, 2993, 2939, 1662, 1577, 1519, 1473 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (1H, d, *J* = 3.5 Hz), 8.06 (1H, d, *J* = 7.5 Hz), 7.92 (1H, td, *J* = 7.5, 1.5 Hz), 7.56–7.51 (2H, m), 7.40 (2H, dd, *J* = 7.5, 1.5 Hz), 7.30 (2H, t, *J* = 7.5 Hz), 7.21 (1H, t, *J* = 7.5 Hz), 3.50 (2H, dt, *J* = 6.5, 6.5 Hz), 3.12 (2H, t, *J* = 6.5 Hz), 1.61 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 155.0, 150.4, 138.2, 135.3, 129.8, 129.4, 128.0, 126.7, 124.9, 67.6, 39.8, 32.9, 20.8; HRMS (ESI^+) *m/z* calcd for $C_{17}H_{21}N_2O_3S_2$ $[M + H]^+$: 365.0988, found 365.0991.

***N*-(2-((4-Acetamidophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-67).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (70.0 mg, 0.235 mmol, 1.0 equiv), PyBOP (137.0 mg, 0.2632 mmol, 1.1 equiv), DMF (5 mL), *N*-(4-((2-aminoethyl)thio)phenyl)acetamide (76% by wt., 65.1 mg, 0.235 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (50.0 μL, 0.287 mmol, 1.2 equiv), 24 h. Flash chromatography (EtOAc) of the organic extracts afforded 82.2 mg of ACP1-67 as a white solid in 71% yield. mp 52−54 °C ($CHCl_3$); R_f 0.54 (EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3321, 3181, 3103, 3061, 2991, 2940, 1668, 1591, 1525, 1496, 1328, 1173, 1143, 1093, 1072, 1014, 848, 720 cm^{-1}; ^1H NMR (300 MHz, CD_3OD, note: amide proton resonances were not observed due to deuterium exchange) δ 9.04−8.99 (1H, m), 8.41 (1H, dd, *J* = 8.5, 2.0 Hz), 8.23 (1H, d, *J* = 8.5 Hz), 7.54−7.44 (2H, m), 7.39−7.29 (2H, m), 3.38−3.24 (2H, m), 2.98 (2H, t, *J* = 6.5 Hz), 2.11 (3H, s), 1.64 (6H, s); ^{13}C NMR (75 MHz, CD_3OD) δ 171.7, 169.8, 159.9 (q, *J* = 1.5 Hz), 148.1 (q, *J* = 4.0 Hz), 138.9, 137.4 (q, *J* = 4.0 Hz), 132.1, 131.5, 131.2 (q, *J* = 33.5 Hz), 126.7, 124.3 (q, *J* = 272.5 Hz), 121.8, 70.3, 41.1, 33.9, 23.9, 20.7; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{23}F_3N_3O_4S_2$ $[M + H]^+$: 490.1082, found 490.1073.

2-Methyl-*N*-(3-phenylpropyl)-2-tosylpropanamide (ACP1-68). Synthesized according to General Procedure A using 2-methyl-2-tosylpropanoic acid (141.5 mg, 0.5840 mmol, 1.0 equiv), PyBOP (335.9 mg, 0.6455 mmol, 1.1 equiv), DMF (6 mL), 3-phenylpropylamine (85.0 μL, 0.595 mmol, 1.0 equiv), Hünig's base (110.0 μL, 0.6315 mmol, 1.1 equiv), 23 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 191.8 mg of ACP1-68 as a white solid in 91% yield. mp 76−78 °C (CH_2Cl_2); R_f 0.40 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3339, 3062, 3024, 2945, 2922, 1657, 1529, 1309, 1290, 1129, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (2H, d, *J* = 8.5 Hz), 7.37−7.26 (4H, m), 7.25−7.16 (3H, m), 7.07 (1H, br t, *J* = 6.0 Hz), 3.32 (2H, td, *J* = 7.0, 6.0 Hz), 2.75−2.65 (2H, m), 2.43 (3H, s), 1.92 (2H, quintet, *J* = 7.0 Hz), 1.53 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 145.6, 141.3, 132.1, 130.1, 129.8, 128.6, 128.5, 126.2, 68.1, 40.0, 33.3, 30.9, 21.8, 21.0; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{26}NO_3S$ $[M + H]^+$: 360.1627, found 360.1632.

***S*-Phenyl (4-chloro-3-((2-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamido)ethyl)thio)phenyl)carbamothioate (ACP1-69).** Synthesized according to General Procedure C using ACP1-11 (56.4 mg, 0.117 mmol, 1.0 equiv), CH_2Cl_2 (1.5 mL), CDI (90% by wt., 22 mg, 0.136 mmol, 1.05 equiv), 16 h; thiophenol (12 μL, 0.117 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (7:3 hexanes:EtOAc) of the crude reaction mixture afforded 28.7 mg of ACP1-69 as a yellow oil in 40% yield. R_f 0.40 (7:3 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3383, 3291, 3003, 2955, 2930, 2855, 1663, 1593, 1582, 1526, 1468, 1464, 1441, 1418, 1387, 1327, 1296, 1250, 1236 cm-1; 1H NMR (500 MHz, $CDCl_3$) δ 8.94 (1H, m), 8.23–8.21 (1H, m), 8.18–8.16 (1H, m), 7.61 (1H, d, *J* = 2.5 Hz), 7.56–7.54 (2H, m), 7.50–7.48 (1H, m), 7.46–7.40 (3H, m), 7.37 (1H, t, *J* = 6.0 Hz), 7.28–7.26 (1H, m), 7.20 (1H, dd, *J* = 9.0, 2.5 Hz), 3.51 (2H, dt, *J* = 6.0, 6.0 Hz), 3.13 (2H, t, *J* = 7.0 Hz), 1.65 (6H, s); 13C

NMR (125 MHz, $CDCl_3$) δ 168.1, 164.8, 158.3, 147.3 (q, *J* = 3.5 Hz), 137.3, 135.8 (q, *J* = 4.0 Hz), 135.7, 135.3, 130.5 (q, *J* = 34.0 Hz), 130.6, 130.4, 130.2, 129.7, 127.6, 124.8, 122.5 (q, *J* = 273.5 Hz), 119.3, 118.0, 68.2, 39.3, 31.6, 20.6; HRMS (ESI+) *m/z* calcd for $C_{25}H_{24}ClF_3N_3O_4S_3$ [M + H]+: 618.0575, found 618.0564.

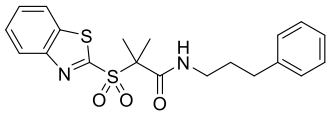
2-Methyl-*N*-(3-phenylpropyl)-2-(pyridin-4-ylsulfonyl)propanamide (ACP1-70). Synthesized according to General Procedure B using 2-methyl-*N*-(3-phenylpropyl)-2-(pyridin-4-ylthio)propanamide (90.2 mg, 0.287 mmol, 1.0 equiv), $NaHCO_3$ (84.2 mg, 1.00 mmol, 3.5 equiv), CH_2Cl_2 (25 mL), MCPBA (70% by wt., 156.2 mg, 0.6336 mmol, 2.2 equiv), 29 h. Flash chromatography (EtOAc) of the organic extracts afforded 59.8 mg of ACP1-70 as a colorless oil in 60% yield (note: following flash chromatography, 31.6 mg of the corresponding pyridine *N*-oxide analogue of ACP1-70 was also isolated in 30% yield). R_f 0.50 (EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3388, 3026, 2940, 2862, 1667, 1529, 1404, 1311, 1160, 1132, 1090, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.90−8.84 (2H, m), 7.68−7.63 (2H, m), 7.33−7.27 (2H, m), 7.24−7.17 (3H, m), 6.85−6.76 (1H, br m), 3.34 (2H, td, *J* = 7.0, 6.0 Hz), 2.73−2.68 (2H, m), 1.97−1.88 (2H, m), 1.57−1.53 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 151.1, 143.6, 141.1, 128.7, 128.4, 126.3, 123.1, 68.4, 40.1, 33.3, 30.8, 20.6; HRMS (ESI^+) *m/z* calcd for $C_{18}H_{23}N_2O_3S$ $[M + H]^+$: 347.1423, found 347.1429.

***N*-(4-Chloro-3-((2-(2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanamido)ethyl)thio)phenyl)-piperidine-1-carboxamide (ACP1-72).** Synthesized according to General Procedure C using ACP1-11 (40.7 mg, 0.084 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 16 mg, 0.099 mmol, 1.05 equiv), 16 h; piperidine (8.3 μL, 0.084 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (EtOAc) of the crude reaction mixture afforded 15.8 mg of ACP1-72 as a yellow oil in 32% yield. R_f 0.40 (EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3368, 3098, 3067, 3003, 2955, 2938, 2857, 2855, 1645, 1636, 1593, 1578, 1520, 1468, 1464, 1433, 1418, 1386, 1387, 1356, 1258, 1254, 1231 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, note: amide proton resonances were not observed due to deuterium exchange) δ 9.04 (1H, d, *J* = 2.5 Hz), 8.39 (1H, dd, *J* = 8.0, 2.5 Hz), 8.25 (1H, d, *J* = 8.0 Hz), 7.54 (1H, d, *J* = 2.5 Hz), 7.24 (1H, d, *J* = 9.0 Hz), 7.18 (1H, dd, *J* = 9.0, 2.5 Hz), 3.48–3.46 (4H, m), 3.43–3.40 (2H, m), 3.08–3.05 (2H, m), 1.66 (6H, s), 1.66–1.57 (6H, m); ^{13}C NMR (125 MHz, CD_3OD) δ 169.7, 159.7, 157.3, 148.1 (q, *J* = 4.0 Hz), 140.8, 137.3 (q, *J* = 3.5 Hz), 136.2, 131.1 (q, *J* = 33.5 Hz), 130.6, 127.5, 126.6, 125.2 (q, *J* = 272.5 Hz), 121.1, 119.8, 70.2, 46.3, 40.4, 31.7, 27.0, 25.5, 20.6; HRMS (ESI^+) *m/z* calcd for $C_{24}H_{29}ClF_3N_4O_4S_2$ $[M + H]^+$: 593.1258, found 593.1265.

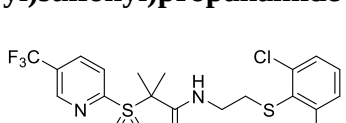
2-Methyl-*N*-(2-(phenylthio)ethyl)-2-((5-(trifluoromethyl)pyridin-2-yl)thio)propanamide (ACP1-73). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)thio)propanoic acid (85 mg, 0.32 mmol, 1.0 equiv), PyBOP (166 mg, 0.32 mmol, 1.0 equiv), DMF (5 mL), 2-(phenylthio)ethan-1-amine (49 mg, 0.32 mmol, 1.0 equiv) in DMF (1 mL), Hünig's base (167 μL, 0.96 mmol, 3.0 equiv), 1 h. Flash chromatography (3:2 hexanes:EtOAc) of the concentrated reaction mixture afforded 39.8 mg of ACP1-73 as a yellow oil in 31% yield. R_f 0.43 (3:2 hexanes:EtOAc); ^1H NMR (400 MHz,

$CDCl_3$) δ 8.64 (1H, s), 7.72 7.68 (2H, m), 7.29–7.22 (5H, m), 7.16–7.14 (1H, m), 3.44 (2H, dt, *J* = 6.5, 6.5 Hz), 2.99 (2H, t, *J* = 6.5 Hz), 1.68 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 162.4, 146.2, 135.2, 133.2 (q, J = 3.0 Hz), 129.6, 129.3, 126.6, 123.7 (q, *J* = 272.0 Hz), 123.4 (q, *J* = 33.5 Hz), 122.9, 52.8, 39.0, 33.5, 26.7; LRMS (ESI^+, % base peak) *m/z* 401 (100, $C_{18}H_{20}F_3N_2OS_2$ [M + H]$^+$), 365 (90).

2-(Benzo[*d*]thiazol-2-ylsulfonyl)-2-methyl-*N*-(3-phenylpropyl)propanamide (ACP1-78). Synthesized according to General Procedure B using 2-(benzo[*d*]thiazol-2-ylthio)-2-methyl-*N*-(3-phenylpropyl) propanamide (96.6 mg, 0.261 mmol, 1.0 equiv), $NaHCO_3$ (170.0 mg, 2.024 mmol, 7.7 equiv), CH_2Cl_2 (15 mL), MCPBA (70% by wt., 141.7 mg, 0.5748 mmol, 2.2 equiv), 24 h. Flash chromatography (2:1 EtOAc:hexanes) of the organic extracts afforded 75.1 mg of ACP1-78 as a white solid in 71% yield. mp 94−95 °C (CH_2Cl_2); R_f 0.45 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3341, 3062, 3029, 3002, 3945, 2921, 2854, 1661, 1538, 1468, 1319, 1122 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15−8.08 (1H, m), 8.02−7.94 (1H, m), 7.64−7.55 (2H, m), 7.34−7.27 (2H, m), 7.24−7.18 (3H, m), 7.09 (1H, br t, *J* = 6.0 Hz), 3.36 (2H, td, *J* = 7.0, 6.0 Hz), 2.76−2.69 (2H, m), 2.00−1.91 (2H, m), 1.74 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 162.4, 152.8, 141.4, 137.4, 128.61, 128.55, 128.4, 127.8, 126.1, 126.0, 122.2, 69.5, 40.3, 33.3, 30.8, 20.8; HRMS (ESI^+) *m/z* calcd for $C_{20}H_{23}N_2O_3S_2$ [M + H]$^+$: 403.1151, found 403.1148.



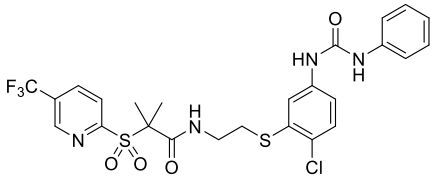
***N*-(2-((2,6-Dichlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-79).** Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (56.8 mg, 0.191 mmol, 1.0 equiv), PyBOP (125.8 mg, 0.2417 mmol, 1.3 equiv), DMF (2 mL), 2-((2,6-dichlorophenyl)thio)ethan-1-amine (59.6 mg, 0.268 mmol, 1.4 equiv) in DMF (2 mL), Hünig's base (40.0 μL, 0.230 mmol, 1.2 equiv), 15 h. Flash chromatography (2:1 hexanes:EtOAc) of the organic extracts afforded 88.9 mg of ACP1-79 as a white solid in 93% yield. mp 106−107 °C (CH_2Cl_2); R_f 0.30 (2:1 hexanes:EtOAc); IR (solid) ν_{max} 3385, 3351, 1655, 1534, 1323, 1315, 1135, 1093, 1072, 1014 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.98−8.96 (1H, m), 8.24−8.22 (1H, m), 8.21−8.18 (1H, m), 7.45 (1H, br t, *J* = 5.5 Hz), 7.42−7.40 (2H, m), 7.22 (1H, dd, *J* = 8.5, 7.5 Hz), 3.39 (2H, td, *J* = 6.5, 5.5 Hz), 3.10−3.04 (2H, m), 1.66 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 158.4 (q, *J* = 1.5 Hz), 147.3 (q, *J* = 4.0 Hz), 141.8, 135.6 (q, *J* = 3.5 Hz), 131.8, 130.6, 130.4 (q, *J* = 34.0 Hz), 129.0, 124.7, 122.5 (q, *J* = 273.5 Hz), 68.0, 39.7, 34.8, 20.6; HRMS (ESI^+) *m/z* calcd for $C_{18}H_{18}Cl_2F_3N_2O_3S_2$ [M + H]$^+$: 501.0088, found 501.0108.



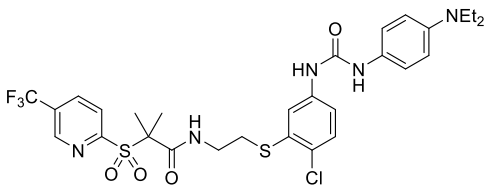
***N*-(2-((2-Chloro-5-ureidophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-80).** Trimethylsilyl isocyanate (22.0 μL, 0.140 mmol, 1.4 equiv) was charged to a solution of ACP1-11 (48 mg, 0.1 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) at room temperature for 16 h. Flash chromatography (1:1 hexanes:EtOAc) of the crude reaction mixture afforded 9.5 mg of ACP1-80 as a yellow oil in 20% yield. R_f 0.40 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3367, 2926, 2855, 1662, 1576, 1538, 1469, 1464, 1326 cm-1; 1H NMR (500 MHz, $CDCl_3$) δ 8.94 (1H, s), 8.19–8.18 (2H, m), 7.78 (1H, s), 7.47 (1H, t, *J* = 6.0 Hz), 7.42 (1H, d, *J* = 2.5 Hz), 7.18 (1H, d, *J* = 8.5 Hz), 7.11 (1H, dd, *J* = 8.5, 2.5 Hz), 5.26 (2H, br, s), 3.49 (2H, dt, *J* = 6.5, 6.5 Hz), 3.07

(2H, t, *J* = 6.5 Hz), 1.66 (6H, s); 13C NMR (125 MHz, $CDCl_3$) δ 168.0, 158.0, 156.9, 147.16 (q, *J* = 3.5 Hz), 138.3, 135.7 (q, *J* = 3.5 Hz), 134.7, 130.4 (q, *J* = 34.0 Hz), 130.0, 127.4, 124.8, 122.5 (q, *J* = 273.5 Hz), 119.6, 118.2, 68.3, 39.3, 31.4, 20.5; HRMS (ESI+) *m/z* calcd for $C_{19}H_{21}ClF_3N_4O_4S_2$ [M + H]+: 525.0614, found 525.0639.

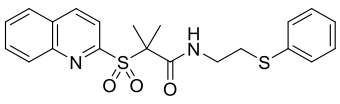
***N*-(2-((2-Chloro-5-(3-phenylureido)phenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-81).** Phenyl isocyanate (136.0 μL, 0.124 mmol, 1.2 equiv) was charged to a solution of ACP1-11 (50.0 mg, 0.104 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) at room temperature for 5 h. Flash chromatography (1:1 hexanes:EtOAc) of the crude reaction mixture afforded 21.8 mg of ACP1-81 as a yellow oil in 35% yield. R_f 0.33 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3354, 3003, 2955, 2855, 1651, 1595, 1537, 1501, 1478, 1464, 1443, 1418, 1387, 1327, 1294, 1250, 1231 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.91 (1H, m), 8.19 (1H, d, *J* = 8.0 Hz), 8.15 (1H, dd, *J* = 8.0, 2.0 Hz), 7.43 (1H, m), 7.30–7.28 (3H, m), 7.25–7.22 (2H, m), 7.16 (2H, m), 7.02 (1H, tt, *J* = 7.0 Hz), 3.50 (2H, t, *J* = 7.0 Hz), 3.08 (2H, t, *J* = 7.0 Hz), 1.66 (6H, s), 1.22 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$ δ 168.1, 158.2, 153.3, 147.3 (q, *J* = 4.0 Hz), 138.3, 138.2, 135.8 (q, *J* = 3.0 Hz), 134.8, 130.3, 130.0 (q, *J* = 34.0 Hz), 129.3, 127.5, 124.8 123.9, 123.0 (q, *J* = 273.5 Hz), 120.4, 119.4, 118.2, 68.4, 39.4, 31.4, 20.7, 18.3; HRMS (ESI^+) *m/z* calcd for $C_{25}H_{25}ClF_3N_4O_4S_2$ [M + H]$^+$: 601.0973, found 601.0992.



***N*-(2-((2-Chloro-5-(3-(4-(diethylamino)phenyl)ureido)phenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-82).** Synthesized according to General Procedure I using ACP1-11 (97.1 mg, 0.0977 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 19 mg, 0.117 mmol, 1.05 equiv), 16 h; N^1,N^1-diethylbenzene-1,4-diamine (16.2 μL, 0.0977 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (4:1 hexanes:EtOAc) of the crude reaction mixture afforded 15.7 mg of ACP1-82 as a yellow oil in 24% yield. R_f 0.50 (4:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3337, 3325, 3069, 3031, 2972, 2970, 2910, 2848, 1697, 1664, 1649, 1591, 1577, 1520, 1449, 1448, 1436, 1421, 1386, 1357, 1326 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, note: amide proton resonances were not observed due to deuterium exchange) δ 9.02 (1H, m), 8.35 (1H, dd, *J* = 8.0, 3.5 Hz), 8.23 (1H, d, *J* = 8.0 Hz), 7.64 (1H, d, *J* = 2.5 Hz), 7.22 (1H, m), 7.19–7.10 (2H, m), 7.08 (1H, dd, *J* = 8.5, 2.5 Hz), 6.70–6.68 (2H, m), 3.42 (2H, t, *J* = 6.5 Hz), 3.32–3.27 (4H, m), 3.06 (2H, t, *J* = 7.5 Hz), 1.65 (6H, s), 1.15 (6H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ 169.8, 159.7, 155.9, 148.0 (q, *J* = 4.0 Hz), 146.1, 140.4, 137.3 (q, *J* = 3.5 Hz), 136.6, 131.3 (q, *J* = 33.5 Hz), 130.8, 129.1, 127.0, 126.6, 124.0 (q, *J* = 272.5 Hz), 123.9, 119.3, 118.3, 114.9, 70.2, 46.0, 40.4, 31.6, 20.6, 12.8; HRMS (ESI^+) *m/z* calcd for $C_{29}H_{34}ClF_3N_5O_4S_2$ [M + H]$^+$: 672.1712, found 672.1687.



2-Methyl-*N*-(2-(phenylthio)ethyl)-2-(quinolin-2-ylsulfonyl)propanamide (ACP1-83). Synthesized according to General Procedure A using 2-methyl-2-(quinolin-2-ylsulfonyl)propanoic acid (68.3 mg, 0.244 mmol, 1.0 equiv), PyBOP (140.9 mg, 0.2707 mmol, 1.3 equiv), DMF (3 mL), 2-(phenylthio)ethan-1-amine (89%



by wt., 42.0 mg, 0.244 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (50.0 μL, 0.287 mmol, 1.2 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 59.7 mg of ACP1-83 as a white solid in 59% yield. mp 125−127 °C (CH_2Cl_2); R_f 0.55 (1:1 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3387, 3054, 2989, 2941, 1667, 1522, 1309, 1167, 1118, 1088, 832, 752, 739, 692, 650, 616 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.38 (1H, d, *J* = 8.5 Hz), 8.16−8.06 (2H, m), 7.92 (1H, dd, *J* = 8.5, 1.0 Hz), 7.88−7.77 (1H, m), 7.76−7.68 (1H, m), 7.67−7.58 (1H, br m), 7.46−7.36 (2H, m), 7.34−7.24 (2H, m), 7.24−7.16 (1H, m), 3.55 (2H, dt, *J* = 7.0, 7.0 Hz), 3.14 (2H, t, *J* = 7.0 Hz), 1.66 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 154.4, 147.3, 138.7, 135.1, 131.5, 130.5, 130.0, 129.8, 129.31, 129.25, 128.0, 126.7, 119.5, 67.7, 39.7, 33.1, 20.8; HRMS (ESI^+) *m*/*z* calcd for $C_{21}H_{23}N_2O_3S_2$ $[M + H]^+$: 415.1144, found 415.1135.

Methyl 2-((2-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamido) ethyl)thio)benzoate (ACP1-84). Synthesized according to General Procedure A using 2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanoic acid (75.2 mg, 0.253 mmol, 1.0 equiv), PyBOP (150.1 mg, 0.2884 mmol, 1.1 equiv), DMF (6 mL), methyl 2-((2-aminoethyl)thio)benzoate (81% by wt., 66.0 mg, 0.253 mmol, 1.0 equiv) in DMF (2 mL), Hünig's base (60.0 μL, 0.344 mmol, 1.4 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 36.3 mg of ACP1-84 as a light yellow solid in 29% yield. mp 126−127 °C (CH_2Cl_2); R_f 0.60 (1:1 hexnaes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3389, 3067, 2993, 2952, 1716, 1669, 1635, 1526, 1328, 1253, 1172, 1143, 1092, 1072, 744, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (1H, s), 8.22 (1H, d, *J* = 8.5 Hz), 8.16 (1H, dd, *J* = 8.5, 2.0 Hz), 7.92 (1H, d, *J* = 7.5 Hz), 7.63−7.39 (3H, m), 7.24−7.14 (1H, m), 3.91 (3H, s), 3.56 (2H, dt, *J* = 6.5, 6.5 Hz), 3.14 (2H, t, *J* = 6.5 Hz), 1.66 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.2, 158.3 (q, *J* = 1.5 Hz), 147.2 (q, *J* = 4.0 Hz), 139.4, 135.7 (q, *J* = 4.0 Hz), 132.6, 131.3, 130.3 (q, *J* = 33.5 Hz), 129.3, 127.0, 124.9, 124.7, 122.5 (q, *J* = 274.0 Hz), 68.0, 52.3, 39.3, 31.6, 20.5; HRMS (ESI^+) *m*/*z* calcd for $C_{20}H_{22}F_3N_2O_5S_2$ $[M + H]^+$: 491.0916, found 491.0910.

***N*-(2-((5-(3-(3-(2-(2-(3-Aminopropoxy)ethoxy)ethoxy)propyl)ureido)-2-chlorophenyl)thio)ethyl)-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl) sulfonyl)propanamide (ACP1-85).** Synthesized according to General Procedure C using ACP1-11 (47.1 mg, 0.0977 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 18 mg, 0.103 mmol, 1.05 equiv), 16 h; 4,7,10-trioxa-1,13-tridecanediamine (13 μL, 0.0586 mmol, 0.6 equiv), 0 °C, 5 min. Flash chromatography (9:1 CH_2Cl_2:MeOH) of the crude reaction mixture afforded 18.3 mg of ACP1-85 as a yellow oil in 26% yield. R_f 0.30 (9:1 CH_2Cl_2:MeOH); IR (thin film in CH_2Cl_2) ν_{max} 3361, 3069, 2972, 2926, 2910, 2848, 1697, 1593, 1576, 1533, 1516, 1496, 1456, 1436, 1326, 1316 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.95–8.94 (1H, m), 8.21–8.18 (2H, m), 7.63–7.61 (2H, m), 7.49 (1H, t, *J* = 6.0 Hz), 7.18 (1H, d, *J* = 8.5 Hz), 7.06 (1H, dd, *J* = 8.5, 2.0 Hz), 5.81–5.80 (1H, m), 3.73–3.63 (6H, m), 3.59 (2H, t, *J* = 6.0 Hz), 3.49 (2H, dt, *J* = 6.0, 6.0 Hz), 3.30 (2H, m), 3.09 (2H, t, *J* = 6.5 Hz), 1.76–1.60 (10H, m), 1.25 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 158.4, 156.1, 147.3 (q, *J* = 4.0 Hz), 139.3, 135.8 (q, *J* = 4.0 Hz), 134.6, 130.3 (q, *J* = 3.5 Hz), 130.1 (q, *J* = 34.0 Hz), 129.9, 126.8, 125.0, 122.5 (q, *J* = 273.5 Hz), 119.4, 117.6, 70.4, 70.0, 69.4, 68.7, 39.4, 38.5, 31.9, 29.2, 20.6, 20.0; LRMS (ESI^+, % base peak) *m/z* 728 (7, $C_{29}H_{42}ClF_3N_5O_7S_2$ $[M + H]^+$), 671

(7), 618 (7), 560 (7), 532 (36), 504 (15), 482 (100), 418 (7).

***N*-((2-((2-Chlorophenyl)thio)ethyl)carbamoyl)-4-(trifluoromethyl) benzenesulfonamide (ACP1-86).** A solution of ethyl ((4-(trifluoromethyl)phenyl)sulfonyl)carbamate (58.8 mg, 0.198 mmol, 1.0 equiv) and 2-((2-chlorophenyl)thio)ethan-1-amine (40.1 mg, 0.214 mmol, 1.1 equiv) in toluene (10 mL) was heated to reflux. After 24 h the crude reaction mixture was concentrated in vacuo to give a crude residue which was then purified using flash chromatography (1:1 hexanes:EtOAc) to afford 42.6 mg of ACP1-86 as a white solid in 49% yield. mp 160–162 °C (MeOH); R_f 0.45 (1:1 hexanes:EtOAc); IR (solid) ν_{max} 3332, 3187, 3117, 2925, 1663, 1550, 1319, 1161, 1121, 1107, 1091, 1061, 1037, 1004 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2SO$) δ 11.10 (1H, br s), 8.10 (2H, d, *J* = 8.0 Hz), 7.98 (2H, d, *J* = 8.0 Hz), 7.42 (1H, dd, *J* = 8.0, 1.5 Hz), 7.40 (1H, br d, *J* = 8.0 Hz), 7.29 (1H, td, *J* = 8.0, 1.5 Hz), 7.19−7.14 (1H, m), 3.23−3.16 (2H, m), 6.88 (1H, br t, *J* = 5.5 Hz), 3.04−2.97 (2H, m); ^{13}C NMR (125 MHz, $(CD_3)_2SO$) δ 151.7, 144.3, 135.0, 132.6 (q, *J* = 32.0 Hz), 131.1, 129.5, 128.2, 127.8, 127.1, 126.4, 126.3 (q, *J* = 3.5 Hz), 123.4 (q, *J* = 273.0 Hz), 38.3, 30.4; HRMS (DART$^+$) *m*/*z* calcd for $C_{16}H_{15}ClF_3N_2O_3S_2$ $[M + H]^+$: 439.0165, found 439.0169.

2-((1,3,4-Thiadiazol-2-yl)sulfonyl)-2-methyl-*N*-(3-phenylpropyl)propanamide (ACP1-87). Synthesized according to General Procedure B using 2-((1,3,4-thiadiazol-2-yl)thio)-2-methyl-*N*-(3-phenylpropyl)propanamide (222.9 mg, 0.6934 mmol, 1.0 equiv), $NaHCO_3$ (450.0 mg, 5.357 mmol, 7.7 equiv), CH_2Cl_2 (25 mL), MCPBA (70% by wt., 393.0 mg, 1.594 mmol, 2.3 equiv), 24 h. Flash chromatography (1:1 hexanes:EtOAc) of the organic extracts afforded 136.6 mg of ACP1-87 as a colorless oil in 56% yield. R_f 0.24 (1:1 hexanes:EtOAc); IR (neat) ν_{max} 3379, 3085, 3029, 2923, 2853, 1659, 1527, 1324, 1162, 1126, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.41 (1H, s), 7.34−7.26 (2H, m), 7.23−7.17 (3H, m), 6.80−6.67 (1H, br m), 3.32 (2H, td, *J* = 7.0, 6.0 Hz), 2.73−2.65 (2H, m), 1.95−1.85 (2H, m), 1.71 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.8, 157.1, 141.3, 128.7, 128.5, 126.2, 70.4, 40.3, 33.3, 30.7, 20.5; HRMS (ESI$^+$) *m*/*z* calcd for $C_{15}H_{20}N_3O_3S_2$ $[M + H]^+$: 354.0940, found 354.0928.

2-Methyl-2-((1-methyl-1*H*-imidazol-2-yl)sulfonyl)-*N*-(3-phenylpropyl) propanamide (ACP1-88). Synthesized according to General Procedure B using 2-methyl-2-((1-methyl-1*H*-imidazol-2-yl)thio)-*N*-(3-phenylpropyl) propanamide (391.5 mg, 1.233 mmol, 1.0 equiv), $NaHCO_3$ (517.0 mg, 6.155 mmol, 5.0 equiv), CH_2Cl_2 (50 mL), MCPBA (70% by wt., 707.0 mg, 2.868 mmol, 2.3 equiv), 24 h. Flash chromatography (EtOAc) of the organic extracts afforded 421.0 mg of ACP1-88 as a white solid in 98% yield. mp 69−70 °C (CH_2Cl_2); R_f 0.38 (EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3396, 2938, 1663, 1529, 1319, 1280, 1186, 1109, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.24 (2H, m), 7.23−7.15 (4H, m), 7.05−7.02 (1H, m), 7.01−6.94 (1H, br m), 3.95 (3H, s), 3.32 (2H, td, *J* = 7.0, 5.9 Hz), 2.74−2.63 (2H, m), 1.89 (2H, quintet, *J* = 7.0 Hz), 1.61 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 141.5, 138.7, 130.2, 128.67, 128.51, 126.7, 126.1, 69.8, 40.1, 35.8, 33.3, 30.8, 20.7; HRMS (ESI$^+$) *m*/*z* calcd for $C_{17}H_{24}N_3O_3S$ $[M + H]^+$: 350.1532, found 350.1538.

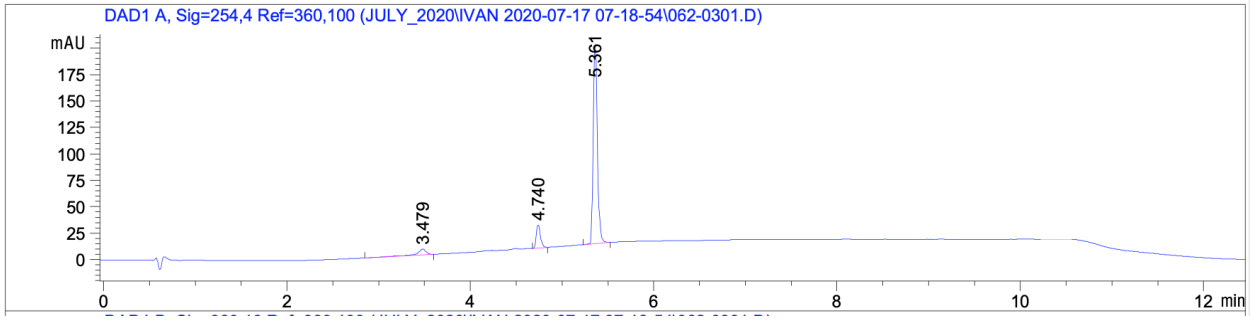
***N*-Butyl-2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl)propanamide (ACP1-89).** Synthesized according to General Procedure A 2-methyl-2-((5-(trifluoromethyl)pyridine-2-yl)sulfonyl)propanoic acid (100 mg, 0.336 mmol, 1.0 equiv), PyBOP (175 mg, 0.336 mmol, 1.0 equiv), DMF (8 mL), *n*-butylamine (67 μL , 0.673 mmol, 1.0 equiv) in DMF (1 mL), Hünig's base (176 μL, 1.01 mmol, 3.0 equiv), 1 h. Flash chromatography (3:2 hexanes:EtOAc) of the concentrated reaction mixture afforded 49.4 mg of ACP1-89 as a grey solid in 42% yield. mp 63–65 °C (hexanes/EtOAc); R_f 0.36 (3:2 hexanes:EtOAc); IR (thin film in CH_2Cl_2) ν_{max} 3356, 2958, 2935, 1662, 1531, 1315 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.98 (1H, s), 8.22–8.18 (2H, m), 6.95 (1H, br s), 3.30 (2H, app. q, *J* = 7.0 Hz), 1.65 (6H, s), 1.55 (2H, app. pentet, *J* = 7.0 Hz), 1.38 (2H, qt, *J* = 7.0, 7.0 Hz), 0.94 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 158.5, 147.4, 135.7, 130.4 (q, *J* = 34.0 Hz), 124.7, 122.6 (q, *J* = 273.5 Hz), 68.0, 40.2, 31.3, 20.8, 20.3, 13.9; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{20}N_2O_3F_3S$ $[M + H]^+$: 353.1141, found 353.1127.

((4-Chloro-3-((2-(2-methyl-2-((5-(trifluoromethyl)pyridin-2-yl)sulfonyl) propanamido)ethyl)thio)phenyl)carbamoyl)proline (ACP1-90). Synthesized according to General Procedure C using ACP1-11 (47.1 mg, 0.0977 mmol, 1.0 equiv), CH_2Cl_2 (1 mL), CDI (90% by wt., 19 mg, 0.117 mmol, 1.05 equiv), 16 h; DL-proline (11.3 mg, 0.0977 mmol, 1.05 equiv), 0 °C, 5 min. Flash chromatography (4:1 CH_2Cl_2:MeOH) of the crude reaction mixture afforded 8.7 mg of ACP1-90 as a yellow oil in 14% yield. R_f 0.10 (4:1 CH_2Cl_2:MeOH); IR (thin film in CH_2Cl_2) ν_{max} 3363, 3069, 3031, 2972, 2926, 2910, 2848, 1657, 1645, 1635, 1623, 1593, 1576, 1516, 1496, 1469, 1456, 1441, 1436, 1404, 1398, 1387, 1356, 1327 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, note: carboxylic acid and amide proton resonances were not observed due to deuterium exchange) δ 9.05–9.04 (1H, m), 8.42 (1H, dd, *J* = 8.0, 2.0 Hz), 8.27 (1H, d, *J* = 8.0 Hz), 7.61–7.60 (1H, m), 7.21–7.17 (2H, m), 4.35–4.25 (1H, m), 3.54–3.50 (2H, m), 3.42 (2H, t, *J* = 7.0 Hz), 3.05 (2H, t, *J* = 7.0 Hz), 2.25–1.80 (4H, m), 1.67 (6H, s); ^{13}C NMR (125 MHz, CD_3OD) δ 169.8, 159.8, 146.7 (q, *J* = 4.0 Hz), 140.6, 139.0, 137.0 (q, *J* = 3.5 Hz), 136.2, 130.5, 130.2 (q, *J* = 33.5 Hz), 126.6, 125.3, 124.0 (q, *J* = 272.5 Hz), 122.7, 120.8, 119.7, 70.3, 64.2, 47.7, 40.4, 31.7, 20.7, 20.6, 19.9; HRMS (ESI^+) *m/z* calcd for $C_{24}H_{25}ClF_3N_4O_6S_2$ $[M + H]^+$: 621.0840, found 621.0861.

HPLC Chromatograms

Method Information:
Analytical HPLC analyses were carried out on an Agilent 1100 series instrument equipped with a Phenomenex KINETEX® C18 column (2.6 µm, 50x4.6 mm). A linear gradient starting from acetonitrile/water 20:80 (0.1% formic acid) to 95:5 (0.1% formic acid) over 15 minutes followed by 5 minutes of elution at 95% acetonitrile and 5% water (0.1% formic acid) was employed. The column was then equilibrated back to the starting acetonitrile/water 20:80 (0.1% formic acid) mixture over 2 minutes. The flow rate was 2.0 mL/min, and UV detection was set to 254 nm. HPLC analyses were conducted at room temperature, unthermostatted.

ACP1-01



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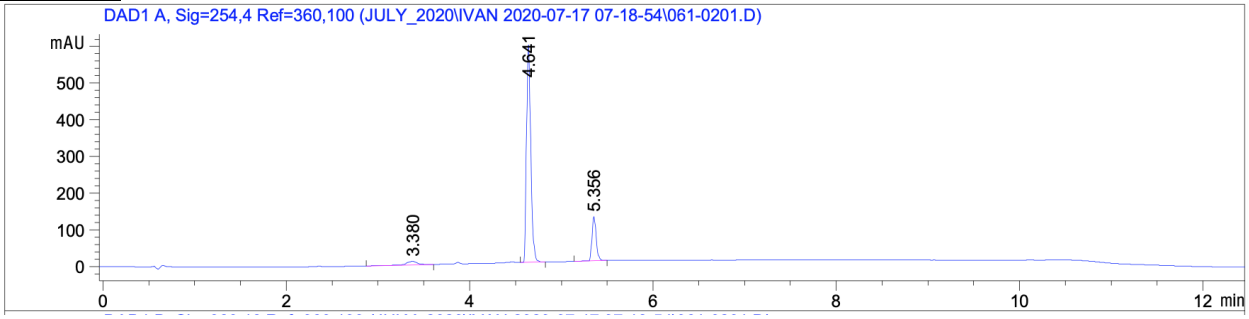
ACP1-06



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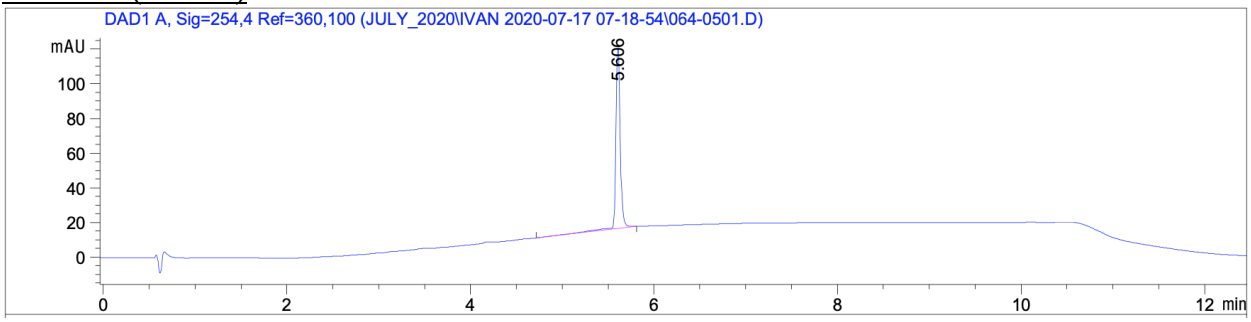

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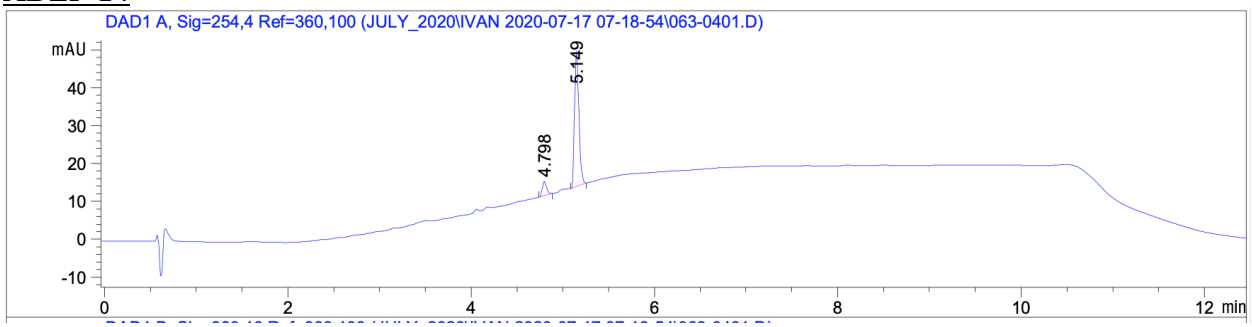
ADEP-14



t_R = 5.149 min

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