Supporting Information

Combined STAT3 and BCR-ABL1 Inhibition Induces Synthetic Lethality in Therapy-Resistant Chronic Myeloid Leukemia

Anna M. Eiring[1,ξ], Brent D. G. Page[2,ξ], Ira L. Kraft[1,ξ], Clinton C. Mason[1], Nadeem A. Vellore[3], Diana Resetca[4], Matthew S. Zabriskie[1], Tian Y. Zhang[1], Jamshid S. Khorashad[1], Alexander J. Engar[1], Kimberly R. Reynolds[1], David J. Anderson[1], Anna Senina[1], Anthony D. Pomicter[1], Carolynn C. Arpin[2], Shazia Ahmad[3], William L. Heaton[1], Srinivas K. Tantravahi[1], Aleksandra Todic[2], Richard Moriggl[5], Derek J. Wilson[4,6], Riccardo Baron[3], Thomas O'Hare[1,7,ψ], Patrick T. Gunning[2,ψ], Michael W. Deininger[1,7,ψ,*]

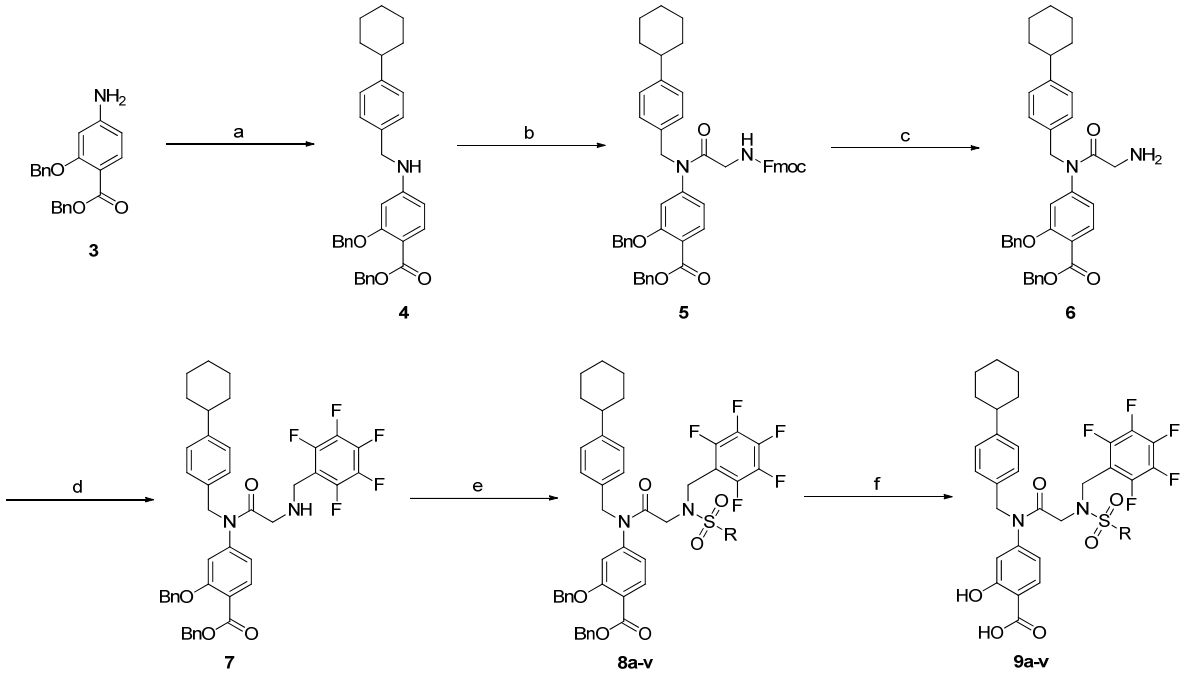
[1]Huntsman Cancer Institute, The University of Utah, Salt Lake City, Utah, USA; [2]Department of Chemical and Physical Sciences, University of Toronto Mississauga, Mississauga, Ontario, Canada; [3]Department of Medicinal Chemistry, College of Pharmacy, The University of Utah, Salt Lake City, Utah, USA; [4]York University Chemistry Department, Toronto, Ontario, Canada; [5]Ludwig Boltzmann Institute for Cancer Research, Vienna, Austria; [6]Center for Research in Mass Spectrometry, Department of Chemistry, York University, Toronto, Ontario, Canada; [7]Division of Hematology and Hematologic Malignancies, The University of Utah, Salt Lake City, Utah, USA. [ξ]Equal contributions. [ψ]Equal contributions. [*]Contact: Michael W. Deininger, MD, PhD; 2000 Circle of Hope, Room 4280, Salt Lake City, Utah 84112; Ph: 801-587-4640; E-Mail: michael.deininger@hci.utah.edu

[ξ]Equal contributions

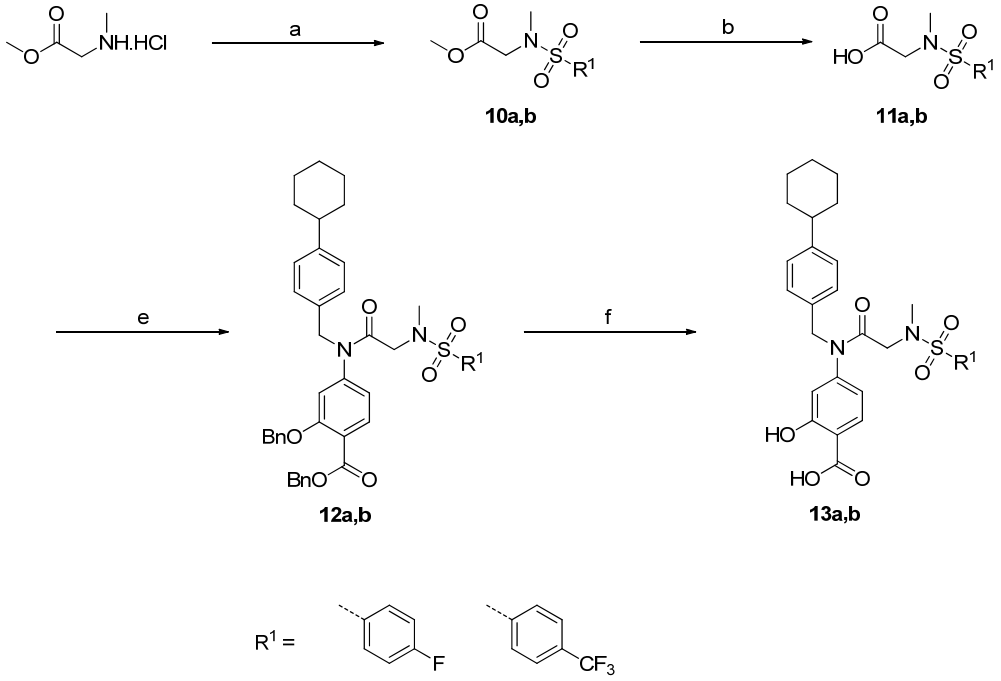
[ψ]Equal contributions

[*]Contact:
Michael W. Deininger, MD, PhD; Ph: 801-587-4640; E-Mail: michael.deininger@hci.utah.edu

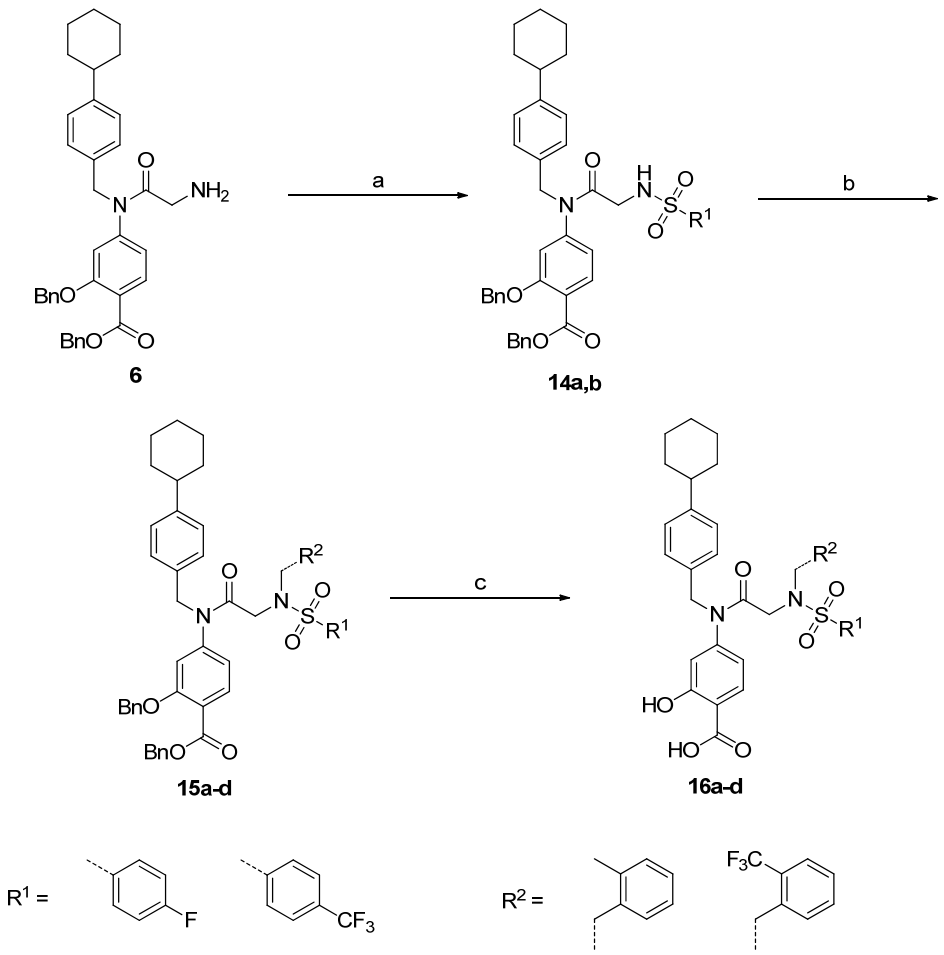
Chemical Synthesis and Characterization



Scheme 1. a) i. AcOH, 4-CyPhCHO, ii. $NaCNBH_3$, MeOH, 6h, 45 °C (83 %); b) FMOC-Gly-OH, PPh_3Cl_2, $CHCl_3$, 0.5, 110 °C (76 %); c) piperidine, DMF, 0.5 h, RT (62 %); d) F_5BnBr, Cs_2CO_3, DMF, RT (87 %); e) RSO_2Cl, DIPEA, DCM, 16 h, RT (48-100 %); f) H_2, 10 % Pd/C, THF:MeOH 1:1, RT, 1-6 h (85-100 %).



Scheme 2. Synthesis of N-methyl Analogs: a) R^1SO_2Cl, DIPEA, DCM, 16 h, RT (73-89 %); b) $LiOH.H_2O$, $THF:H_2O$, 3:1, 0.5 h, RT (96-100 %); c) **4**, PPh_3Cl_2, $CHCl_3$, 0.5, 110 °C (42-43 %); f) H_2, 10 % Pd/C, THF:MeOH 1:1, RT, 1-6 h (88-94 %).



Scheme 3. Synthesis of Top N-Alkyl Compounds: a) R^1SO_2Cl, K_2CO_3, MeCN, 16 h, 0 °C RT (48-83 %); b) R^2CH_2Br, Cs_2CO_3, DMF, RT (68-93 %); c) H_2, 10 % Pd/C, THF:MeOH 1:1, RT, 1-6 h (82-100 %).

General Procedures

General Procedure A: Secondary Sulfonamide Coupling

Secondary amine **5.1** (1.0 equiv.) was dissolved in anhydrous dichloromethane (DCM) with diisopropylethylamine (DIPEA) (1.3 equiv.). Sulfonyl chloride (1.2 equiv.) was added and the reaction mixture was stirred at RT for 16 hours. Upon completion, solvent was removed under reduced pressure and the crude product was then purified using flash column chromatography using a mixture of hexanes and ethyl acetate (EtOAc) as the eluent.

General Procedure B: Global deprotection of Benzylated Salicyclic Acid

The dibenzyl protected salicyclic acid (1 equiv.) was dissolved in a stirred solution of MeOH/THF (1:1) (0.1 M). The solution was degassed thoroughly before careful addition of 10% Pd/C (10 mg/mmol). H_2 gas was bubbled through the solvent for 5 mins before the solution was put under an atmosphere of H_2 gas and stirred continuously for 6 hours. The H_2 gas was evacuated and the reaction filtered (to remove the Pd catalyst) and concentrated under reduced pressure. Crude product was then purified using flash column chromatography using a mixture of DCM, MeOH and acetic acid (AcOH) as the eluent (generally 92 % DCM, 7 % MeOH and 1 % AcOH in a 1:2 ratio with DCM was utilized).

General Procedure C: Primary Sulfonamide Coupling

From primary amine **6** (1.0 equiv.) which was dissolved in anhydrous acetonitrile (MeCN) with K_2CO_3 (1.1 equiv.) and 4 Å molecular sieves and cooled to 0 °C. Sulfonyl chloride (1.0 equiv.) was added and the reaction mixture was allowed to warm to room temperature. After 6 hours the solution was filtered through cotton to remove molecular sieves and excess solvent was removed under reduced pressure. The concentrated mixture was diluted with DCM, then washed with 1M HCl, saturated $NaHCO_3$, H_2O and brine, then dried over Na_2SO_4. Crude product was then purified using flash column chromatography using a mixture of hexanes and EtOAc as the eluent.

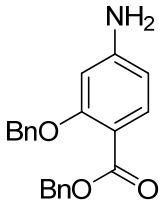
General Procedure D: Sulfonamide Alkylation

Activated alkyl halides (1.1 equiv.) were added to a stirred suspension of sulfonamide **13a-d** (1 equiv.) and Cs_2CO_3 (1.5 equiv.) in DMF. After 3 hours the mixture was diluted with H_2O then the product was extracted into EtOAc. Organics were combined and washed with 1 M HCl, saturated $NaHCO_3$, H_2O and brine, then dried over Na_2SO_4 and concentrated under reduced pressure. Crude products were purified using flash column chromatography using a mixture of hexanes and EtOAc as the eluent.

General Procedure E: PPh_3Cl_2 Peptide Coupling

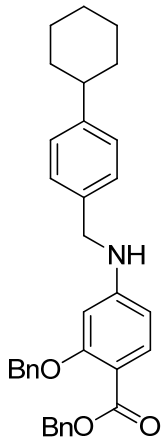
Carboxylic acid (1 equiv.) was stirred at room temperature with PPh_3Cl_2 in $CHCl_3$ for 15 minutes to form the activated acid. Aniline (1 equiv.) was added and the mixture was heated to 110 °C for 30 minutes using a Biotage Initiator microwave reactor. Upon completion, $CHCl_3$ was removed under reduced pressure and the crude product was purified using flash column chromatography using a mixture of hexanes and EtOAc as eluent.

Compounds **1**, **1a-d**, **2** and **2a-d** were prepared as previously reported.



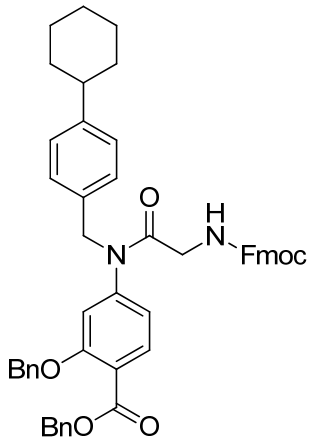
3, benzyl 4-amino-2-(benzyloxy)benzoate

Prepared as previously reported; δ_H (400 MHz, d_6-DMSO) 5.07 (s, 2H, CH_2), 5.21 (s, 2H, CH_2), 5.99 (br s, 2H, NH_2), 6.18 (d of d, J = 8.6 and 1.8 Hz, 1H, CH), 6.32 (d, J =1.7 Hz, 1H, CH), 7.28-7.38 (8H, m, CH), 7.47 (d, J = 7.2 Hz, 2H, CH), 7.60 (d, J = 8.6 Hz, 1H, CH); δ_C (100 MHz, d-$CDCl_3$) 65.8, 70.2, 99.1, 106.7, 109.0, 126.3, 126.8, 127.5, 127.7, 127.9, 128.1, 128.3, 128.4, 134.3, 136.6, 136.7, 152.2, 160.7, 165.7; LRMS (ESI+) Calcd for [$C_{21}H_{19}NO_3$ + H] 334.14 found 334.17.



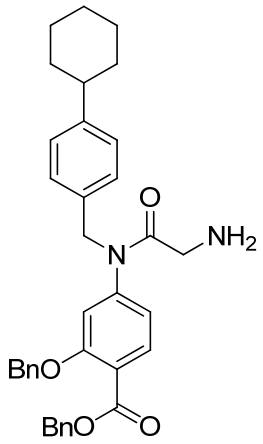
4, benzyl 2-(benzyloxy)-4-((4-cyclohexylbenzyl)amino)benzoate

To a solution of primary aniline (**3**) (2.65 g, 8.0 mmol) and acetic acid (0.26 g, 4.4 mmol) stirred in anhydrous MeOH (0.1 M) with activated 4 Å mol. sieves was added 4-cyclohexylbenzaldehyde (1.5 g, 8.0 mmol). The solution was then heated to 45 °C for 3 hr then $NaCNBH_3$ (0.75 g, 12.0 mmol) was added and the reaction was heated at 45 °C overnight. Crushed molecular sieves were filtered and washed thoroughly with CH_2Cl_2. The filtrate was collected and concentrated *in vacuo* then washed with saturated sodium bicarbonate, water, brine then dried over Na_2SO_4. Solvents were removed under reduced pressure to give compound **4** (3.3 g, 6.6 mmol, 83%); δ_H (400 MHz, *d*-$CDCl_3$) 1.25-1.48 (m, 5H, CH_2), 1.74 -1.95 (m, 5H, CH_2), 2.48-2.52 (m, 1H, CH), 4.28 (s, 2H, CH_2), 4.49 (br s, 1H, NH), 5.08 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.17 (d, J =2.0 Hz, 1H, CH), 6.21 (d of d, J = 8.6 and 2.0 Hz, 1H, CH), 7.19-7.27 (m, 4H, 4 CH), 7.28-7.37 (m, 6H, 6 CH), 7.40-7.49 (m, 4H, 4 CH), 7.85 (d, J = 8.6 Hz, 1H, 1 CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.3, 44.1, 47.3, 65.7, 70.3, 97.1, 104.8, 108.2, 126.8, 127.0, 127.4, 127.5, 127.6, 127.9, 128.2, 128.3, 134.2, 135.4, 136.7, 136.8, 147.4, 152.9, 160.8, 165.8; LRMS (ESI+) Calcd for [$C_{34}H_{35}NO_3$ + H] 506.27 found 506.22.



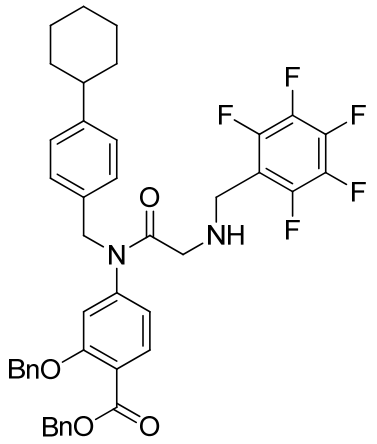
5, benzyl 4-(2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-N-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate

Fmoc-glycine-OH (1.13g, 3.80 mmol) was stirred at room temperature with PPh_3Cl_2 (2.76 g, 8.30 mmol) in $CHCl_3$ for 15 minutes to form the activated acid. Aniline **4** (1.75g, 3.46 mmol) was added and the solution was heated to 110 °C for 30 minutes using a Biotage Initiator microwave reactor. Upon completion, $CHCl_3$ was removed under reduced pressure and the crude product was purified using flash column chromatography using a mixture of hexanes and EtOAc as eluent (**5**, 2.08 g, 76 %) ; δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.54 (m, 5H, CH_2), 1.70-1.90 (m, 5H, CH_2), 2.17 (s, 2H, CH_2), 2.40-2.55 (m, 1H, CH), 3.68 (s, 2H, CH_2), 4.23 (t, J = 7.0 Hz, 1H, CH), 4.36 (d, J = 7.0 Hz, 2H, CH_2), 4.83 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 5.71 (s (br), 1H, NH), 6.52 (s, 1H, CH), 6.70 (d, J = 8.0 Hz, 1H, CH), 7.07 (d, J = 8.0 Hz, 2H, CH), 7.13 (d, J = 8.0 Hz, 2H, CH), 7.27-7.43 (m, 14H, CH), 7.61 (d, J = 7.4 Hz, 2H, CH), 7.77 (d, J = 7.4 Hz, 2H, CH), 7.84 (d, J = 8.0 Hz, 1H, CH).



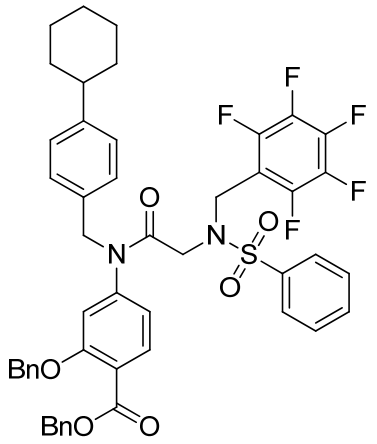
6, benzyl 4-(2-amino-N-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate

Compound **5** was dissolved in a 5 % solution of piperidine in DMF and stirred for 30 minutes at room temperature. Upon completion the reaction mixture was diluted with H_2O and organics were extracted into EtOAc. Combined organics were then washed with saturated $NaHCO_3$, H_2O and brine, then dried over Na_2SO_4. Crude product was purified using flash column chromatography in a mixture of 92 % DCM, 7 % MeOH, 1 % NH_4OH, and DCM in a 1:1 ratio (**6**, 62 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.43 (m, 5H, CH_2), 1.66-1.88 (m, 5H, CH_2), 2.17 (s, 2H, CH_2), 2.38-2.51 (m, 1H, CH), 3.06 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.50 (s, 1H, CH), 6.64 (d, J = 8.0 Hz, 1H, CH), 7.05-7.12 (m, 4H, CH), 7.22-7.41 (m, 10H, CH), 7.81 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 25.7, 26.4, 34.0, 43.8, 43.9, 52.3, 66.5, 70.2, 113.8, 119.7, 120.0, 126.5, 126.6, 127.6, 127.8, 127.8, 128.1, 128.2, 128.4, 132.6, 134.0, 135.4, 135.4, 145.1, 147.1, 158.2, 164.9, 171.9.



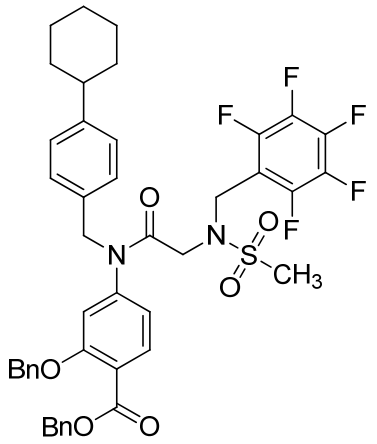
7, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(((perfluorophenyl)methyl)amino)acetamido)benzoate

To a stirred solution of primary amine **6** (900 mg, 1.6 mmol) and Cs_2CO_3 (630 mg, 1.9 mmol), was added 2,3,4,5,6-pentafluorobenzyl bromide (420 mg, 1.6 mmol). The mixture was stirred at RT for 1 h, then diluted with H_2O and organics were extracted into EtOAc. Combined organic layers were washed with saturated $NaHCO_3$, H_2O and brine and dried over Na_2SO_4. Solvents were removed under reduced pressure and the crude product was purified using flash column chromatography with a gradient mixture of hexanes and EtOAc to give **7** (1.03g, 87 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.15-1.50 (m, 5H, CH_2), 1.67-1.96 (m, 5H, CH_2), 2.18-2.40 (m, 1H, NH), 2.41-2.59 (m, 1H, CH), 3.08 (s, 3H, C_3), 3.81 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 4.93 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.47 (s, 1H, CH), 6.67 (d, J = 8.0 Hz, 1H, CH), 7.03 (d, J = 7.8 Hz, 2H, CH), 7.12 (d, J = 7.9 Hz, 2H, CH), 7.28-7.48 (m, 10H, CH) 7.85 (d, J = 8.2 Hz, 1H, CH).



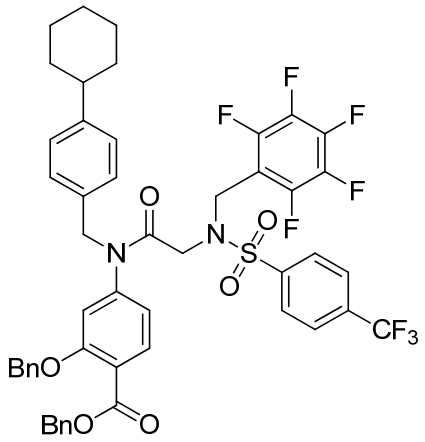
8a, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8a** (18.2 mg, 74 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.48 (m, 5H, CH_2), 1.68-1.92 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 83 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.48 (s, 1H, CH), 6.66 (d, J = 8.2 Hz, 1H, CH), 6.97 (d, J = 7.6 Hz, 2H, CH), 7.10 (d, J = 8.0 Hz, 2H, CH), 7.27-7.42 (m, 10H, CH) 7.45-7.52 (m, 2H, CH), 7.54-7.61 (m, 1H, CH), 7.77 (d, J = 7.7 Hz, 2H, CH), 7.82 (d, J = 8.2 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 39.9, 44.4, 49.5, 53.0, 67.2, 70.9,113.8, 120.1, 121.5, 127.1, 127.2, 127.7, 128.2, 128.4, 128.5, 128.7, 128.8, 129.0, 129.1, 129.8, 133.1, 133.4, 133.9, 135.8, 135.8, 139.5, 148.0, 159.0, 165.5, 166.5.



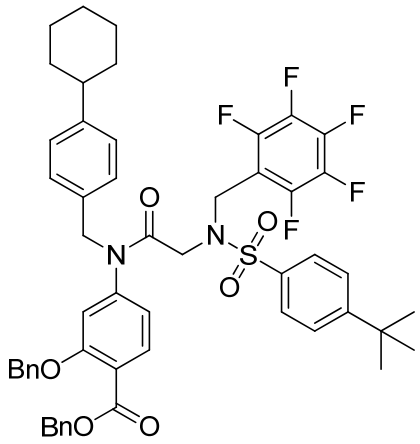
8b, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)methylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8b** (22.9 mg, 80.6 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.74-2.15 (m, 5H, CH_2), 2.32-2.63 (m, 1H, CH), 3.17 (s, 3H, C_3), 3.80 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.44 (s, 1H, CH), 6.63 (d, J = 7.7 Hz, 1H, CH), 6.98 (d, J = 7.6 Hz, 2H, CH), 7.11 (d, J = 7.7 Hz, 2H, CH), 7.23-7.41 (m, 10H, CH) 7.80 (d, J = 8.1 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.4, 40.7, 44.4, 49.7, 53.1, 67.2, 70.8,113.8, 120.1, 121.5, 127.2, 127.3, 128.3, 128.4, 128.5, 128.7, 128.8, 129.0, 133.4, 133.7, 135.7, 135.8, 144.5, 148.2, 159.0, 165.4, 167.0.



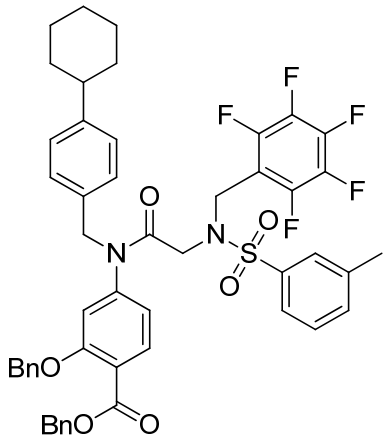
8c, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-4-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8c** (20.7 mg, 64 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.43 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.43-2.53 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.47 (s, 1H, CH), 6.65 (d, J = 8.0 Hz, 1H, CH), 6.95 (d, J = 8.0 Hz, 2H, CH), 7.12 (d, J = 8.0 Hz, 2H, CH), 7.27-7.41 (m, 10H, CH), 7.74 (d, J = 8.2 Hz, 2H, CH), 7.83 (d, J = 8.0 Hz, 1H, CH), 7.92 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 40.0, 44.4, 49.6, 53.1, 67.3, 70.9, 114.0, 120.2, 121.4, 126.1, 126.1, 127.2, 127.2, 128.3, 128.4, 128.5, 128.5, 128.7, 128.8, 129.1, 129.1, 133.4, 133.8, 135.8, 135.8, 143.0, 148.2, 159.0, 165.5, 166.2.



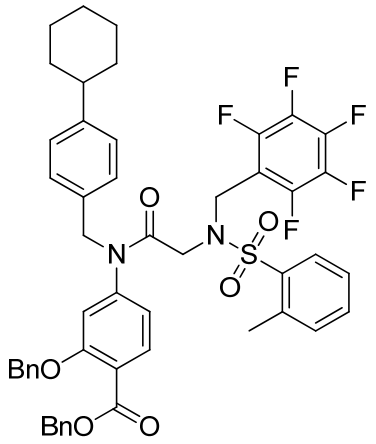
8d, benzyl 2-(benzyloxy)-4-(2-(4-(tert-butyl)-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8d** (26.9 mg, 83 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.34-1.44 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.39-2.54 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.68 (d, J = 8.1 Hz, 1H, CH), 7.00 (d, J = 8.0 Hz, 1H, CH), 7.11 (d, J = 8.0 Hz, 2H, CH), 7.26-7.41 (m, 10H, CH), 7.45 (d, J = 8.5 Hz, 2H, CH), 7.65 (d, J = 7.9 Hz, 2H, CH), 7.83 (d, J = 8.2 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 31.2, 34.6, 35.3, 40.0, 44.4, 49.8, 53.0, 67.2, 70.9, 107.31, 114.1, 120.3, 121.1, 125.9, 127.1, 127.3, 127.5, 128.2, 128.4, 128.5, 128.7, 128.7, 129.1, 130.4, 133.3, 134.0, 135.8, 148.0, 156.9, 159.0, 165.5, 166.8.



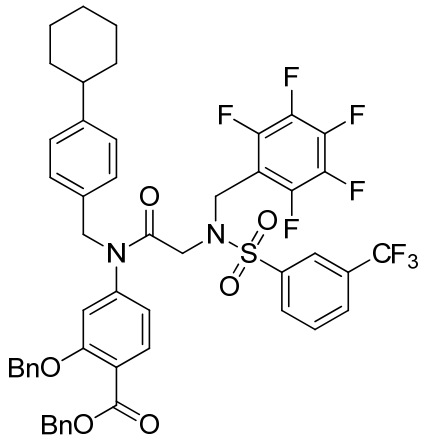
8e, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(3-methyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8e** (21.4 mg, 68 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.90 (m, 5H, CH_2), 2.39 (s, 3H, CH_3), 2.41-2.54 (m, 1H, CH), 3.84 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.68 (d, J = 8.2 Hz, 1H, CH), 7.00 (d, J = 8.0 Hz, 2H, CH), 7.12 (d, J = 8.0 Hz, 2H, CH), 7.27-7.42 (m, 12H, CH), 7.55 (d, J = 7.6 Hz, 1H, CH), 7.57 (s, 1H, CH), 7.84 (d, J = 8.2 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.4, 26.2, 27.0, 34.6, 40.0, 44.4, 49.6, 53.0, 67.2, 70.9, 110.3, 114.1, 120.3, 124.7, 127.1, 127.1, 127.3, 128.0, 128.2, 128.4, 128.5, 128.7, 128.7, 128.8, 129.1, 133.3, 133.8, 133.9, 135.8, 135.8, 139.1, 139.4, 148.0, 159.0, 165.5, 166.6.



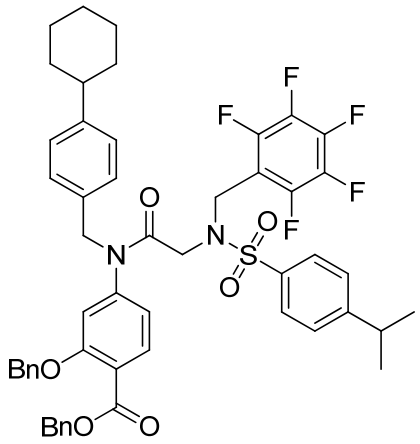
8f, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(2-methyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8f** (20.4 mg, 66 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.71-1.92 (m, 5H, CH_2), 2.41-2.52 (m, 1H, CH), 2.52 (s, 3H, CH_3), 3.83 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.45 (s, 1H, CH), 6.62 (d, J = 8.1 Hz, 1H, CH), 7.98 (d, J = 8.0 Hz, 2H, CH), 7.11 (d, J = 8.0 Hz, 2H, CH), 7.24-7.41 (m, 12H, CH), 7.45 (t, J = 6.8 Hz, 1H, CH), 7.82 (d, J = 8.1 Hz, 1H, CH), 7.96 (d, J = 7.8 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 20.4, 26.2, 27.0, 34.6, 39.5, 44.4, 48.9, 53.0, 67.2, 70.9, 114.0, 120.2, 121.3, 125.9, 127.1, 127.2, 128.2, 128.4, 128.5, 128.7, 128.8, 129.2, 129.3, 130.3, 132.7, 133.2, 133.4, 133.9, 135.8, 135.8, 137.5, 138.4, 148.0, 159.0, 165.5, 166.4.



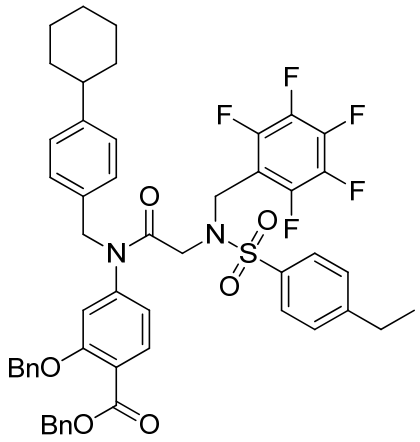
8g, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-3-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8g** (19.8 mg, 52 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.70-1.95 (m, 5H, CH_2), 2.36-2.61 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.48 (s, 1H, CH), 6.67 (d, J = 8.1 Hz, 1H, CH), 6.98 (d, J = 7.7 Hz, 2H, CH), 7.12 (d, J = 7.7 Hz, 2H, CH), 7.30-7.48 (m, 10H, CH), 7.66 (t, 1H, CH), 7.86 (t,2H, CH), 7.92 (d, J = 8.0 Hz, 1H, CH), 8.09 (s, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 39.9, 44.4, 49.6, 53.0, 67.3, 70.9, 114.0, 120.2, 121.5, 124.9, 127.2, 127.3, 128.3, 128.4, 128.5, 128.7, 128.8, 129.1, 129.8, 131.1, 133.4, 133.7, 135.7, 135.8, 140.7, 144.5, 148.1, 159.0, 165.5, 166.1.



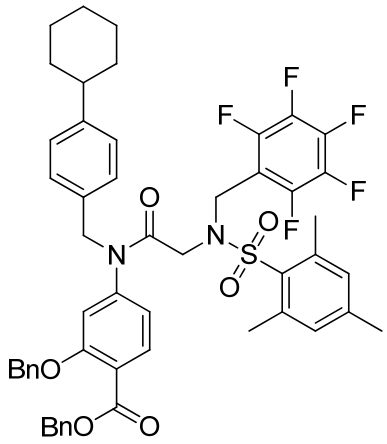
8h, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-isopropyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8h** (29.8 mg, 94 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.27 (d, J = 7.6 Hz, 6H, CH_3), 1.32-1.49 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.42-2.55 (m, 1H, CH), 2.98 (m, 1H, CH), 3.88 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 5.37 (s, 2H, CH_2), 6.54 (s, 1H, CH), 6.70 (d, J = 8.0 Hz, 1H, CH), 7.03 (d, J = 8.0 Hz, 2H, CH), 7.14 (d, J = 8.0 Hz, 2H, CH), 7.28-7.43 (m, 12H, CH), 7.69 (d, J = 8.0 Hz, 2H, CH), 7.86 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 23.7, 26.2, 26.9, 34.3, 34.6, 40.0, 44.4, 49.7, 53.0, 67.2, 70.8, 110.3, 114.1, 120.3, 127.0, 127.1, 127.2, 127.8, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 133.3, 133.9, 135.8, 136.9, 147.9, 154.6, 159.0, 165.5, 166.8.



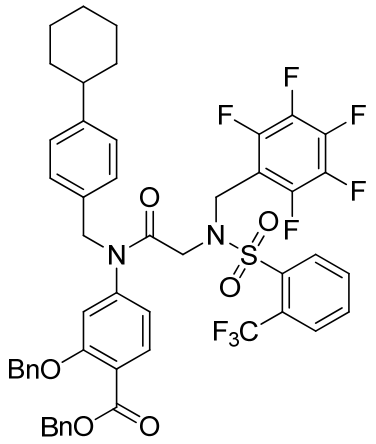
8i, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-ethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8i** (25.9 mg, 94 %); δ_H (400 MHz, *d*-$CDCl_3$) 127.9 (t, J = 7.8 Hz, 3H, CH_3), 1.32-1.52 (m, 5H, CH_2), 1.68-1.93 (m, 5H, CH_2), 2.38-2.57 (m, 1H, CH), 2.73 (q, J = 7.8 Hz, 2H, CH_2), 3.86 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.93 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.53 (s, 1H, CH), 6.69 (d, J = 8.1 Hz, 1H, CH), 7.01 (d, J = 7.3 Hz, 2H, CH), 7.13 (d, J = 7.3 Hz, 2H, CH), 7.31-7.45 (m, 10H, CH), 7.69 (d, J = 7.5 Hz, 2H, CH), 7.85 (d, J = 8.1 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 15.2, 26.2, 27.0, 29.0, 34.6, 40.0, 44.4, 49.6, 53.0, 67.2, 70.9, 114.1, 120.3, 121.2, 127.1, 127.3, 127.8, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 133.3, 133.9, 135.8, 136.7, 147.9, 150.0, 159.0, 165.5, 166.7.



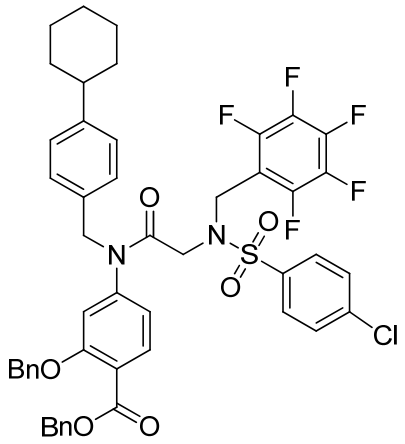
8j, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(2,4,6-trimethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8j** (19.3 mg, 66 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.48 (m, 5H, CH_2), 1.68-1.94 (m, 5H, CH_2), 2.29 (s, 3H, CH_3), 2.41-2.51 (m, 1H, CH), 2.53 (s, 6H, CH_3), 3.79 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.46 (s, 1H, CH), 6.57 (d, J = 8.0 Hz, 1H, CH), 6.90 (s, 2H, CH), 6.98 (d, J = 7.8 Hz, 2H, CH), 7.11 (d, J = 7.8 Hz, 2H, CH), 7.27-7.44 (m, 10H, CH), 7.81 (d, J = 8.1 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.0, 22.9, 26.2, 27.0, 34.6, 39.1, 44.4, 48.7, 53.0, 67.2, 70.8, 113.9, 120.2, 121.1, 127.1, 127.3, 128.2, 128.4, 128.5, 128.7, 128.7, 129.1, 131.9, 132.5, 133.2, 133.3, 134.0, 135.8, 135.8, 140.9, 143.1, 147.9, 159.0, 165.5, 166.5.



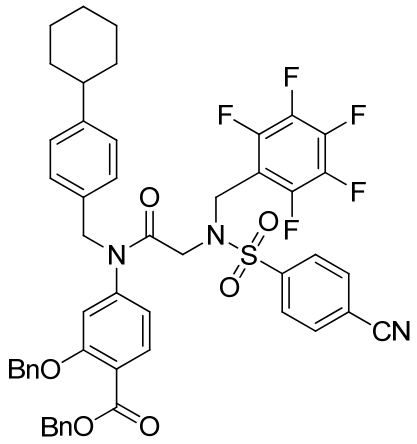
8k, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-2-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.04 mmol scale using General Procedure A to give **8k** (20.3 mg, 52 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.70-1.93(m, 5H, CH_2), 2.38-2.59 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.71(s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.46 (s, 1H, CH), 6.64 (d, J = 8.1 Hz, 1H, CH), 6.97 (d, J = 7.6 Hz, 2H, CH), 7.11 (d, J = 7.4 Hz, 2H, CH), 7.25-7.44 (m, 10H, CH), 7.65-7.76 (m, 2H, CH), 7.82 (d, J = 7.9 Hz, 1H, CH), 7.86-7.94 (m, 1H, CH), 8.23-8.36 (m, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.8, 34.5, 39.5, 44.3, 49.1, 53.0, 67.1, 70.8, 109.4, 113.9, 120.0, 121.2, 127.0, 127.1, 128.1, 128.2, 128.3, 128.6, 128.6, 129.0, 132.0, 132.1, 132.7, 133.2, 133.2, 133.7, 135.7, 135.8, 138.9, 144.5, 146.9, 147.8, 158.9, 165.4, 166.1.



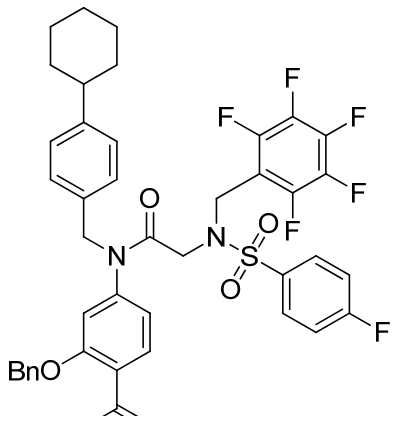
8l, benzyl 2-(benzyloxy)-4-(2-(4-chloro-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8l** (24.7 mg, 84 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.57 (m, 1H, CH), 3.85 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.48 (s, 1H, CH), 6.66 (d, J = 8.1 Hz, 1H, CH), 6.97 (d, J = 7.8 Hz, 1H, CH), 7.13 (d, J = 8.0 Hz, 2H, CH), 7.29-7.41 (m, 10H, CH), 7.45 (d, J = 8.4 Hz, 2H, CH), 7.74 (d, J = 8.5 Hz, 2H, CH), 7.84 (d, J = 8.1 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.9, 44.4, 49.4, 53.1, 67.3, 70.9, 114.0, 120.2, 121.4, 127.2, 127.2, 128.2, 128.4, 128.5, 128.7, 128.8, 129.1, 129.3, 129.3, 133.4, 133.8, 135.8, 135.8, 137.9, 139.6, 144.7, 148.1, 159.0, 165.5, 166.3.



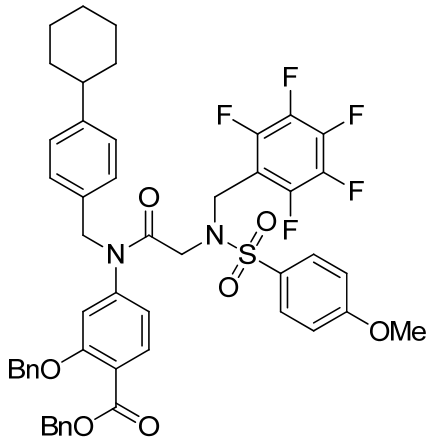
8m, benzyl 2-(benzyloxy)-4-(2-(4-cyano-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8m** (14.9 mg, 58 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.36-1.45 (m, 5H, CH_2), 1.70-1.91 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.47 (s, 1H, CH), 6.66 (d, J = 7.4 Hz, 1H, CH), 7.95 (d, J = 8.0 Hz, 1H, CH), 7.14 (d, J = 8.0 Hz, 2H, CH), 7.28-7.43 (m, 10H, CH), 7.76 (d, J = 8.2 Hz, 2H, CH), 7.84 (d, J = 7.4 Hz, 1H, CH), 7.92 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 25.6, 26.7, 34.5, 39.7, 44.2, 49.3, 50.8, 67.2, 70.8, 113.8, 116.6, 117.4, 120.0, 121.4, 127.0, 128.2, 128.3, 128.6, 128.7, 129.0, 132.6, 133.3, 133.5, 135.6, 135.6, 143.4, 144.3, 148.1, 158.9, 165.3, 165.8, 171.1.



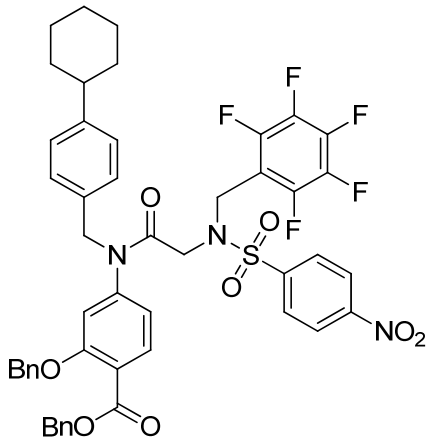
8n, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8n** (30.2 mg, 100 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.36-1.52 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.40-2.60 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.93 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.49 (s, 1H, CH), 6.67 (d, J = 7.8 Hz, 1H, CH), 6.97 (d, J = 7.92 Hz, 1H, CH), 7.09-7.21 (m, 4H, CH),7.30 – 7.48 (m, 9H, CH), 7.79-7.91 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 39.8, 44.4, 49.4, 53.1, 67.3, 70.9, 114.0, 116.1, 116.3, 120.2, 127.2, 127.2, 128.3, 128.4, 128.5, 128.7, 128.8, 129.1, 130.6, 130.7, 133.4, 133.8, 135.5, 135.8, 135.8, 148.1, 159.0, 165.5, 166.4.



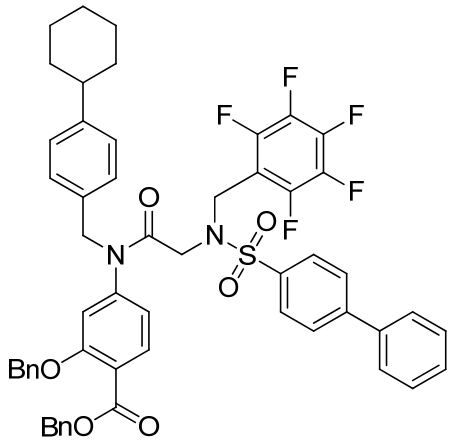
8o, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-methoxy-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8o** (27.8 mg, 97 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.35-1.49 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.40-2.57 (m, 1H, CH),3.85 (s, 2H, CH_2), 3.88 (s, 3H, CH_3), 4.62 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.51 (s, 1H, CH), 6.68 (d, J = 8.2 Hz, 1H, CH), 6.95 (d, J = 8.8 Hz, 2H, CH), 6.99 (d, J = 7.9 Hz, 2H, CH), 7.13 (d, J = 7.8 Hz, 2H, CH), 7.29-7.44 (m, 10H, CH), 7.74 (d, J = 8.8 Hz, 2H, CH), 7.84 (d, J = 8.2 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 29.8, 34.6, 39.9, 44.4, 49.5, 53.0, 55.7, 67.2, 70.6, 114.1, 120.3, 121.2, 127.1, 127.3, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 130.0, 130.9, 133.3, 133.9, 133.9, 135.8, 135.8, 144.9, 148.0, 159.0, 163.3, 165.5, 166.6.



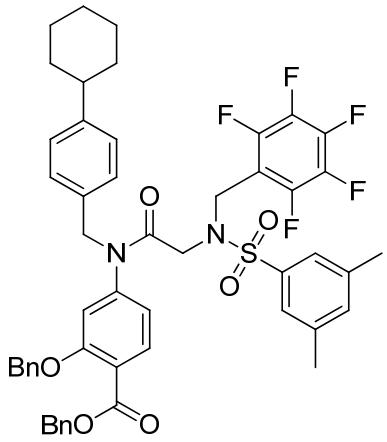
8p, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-nitro-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.04 mmol scale using General Procedure A to give **8p** (24.8 mg, 75 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.47 (m, 5H, CH_2), 1.71-1.92 (m, 5H, CH_2), 2.45-2.57 (m, 1H, CH),3.88 (s, 2H, CH_2), 4.63 (s, 2H, CH_3), 4.68 (s, 2H, CH_2), 4.93 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.47 (s, 1H, CH), 6.66 (d, J = 8.0 Hz, 1H, CH), 6.94 (d, J = 8.0 Hz, 2H, CH), 7.14 (d, J = 7.9 Hz, 2H, CH), 7.30-7.46 (m, 10H, CH), 7.85 (d, J = 8.2 Hz, 1H, CH), 8.00 (d, J = 8.7 Hz, 2H, CH), 8.34 (d, J = 8.8 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 39.9, 44.4, 49.4, 53.2, 67.3, 70.9, 113.9, 120.1, 121.7, 124.2, 127.2, 128.3, 128.5, 128.5, 128.7, 128.8, 129.1, 129.2, 133.5, 133.6, 133.9, 135.7, 135.8, 144.4, 145.1, 148.3, 150.3, 159.1, 165.4, 165.9.



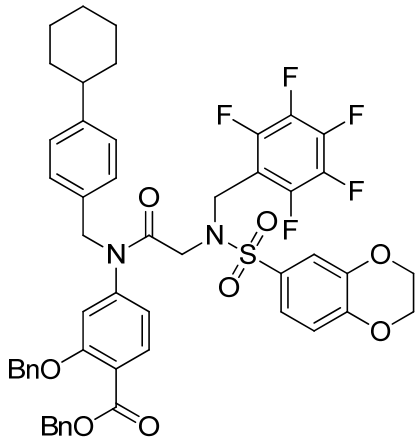
8q, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-[1,1'-biphenyl]-4-ylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8q** (24.8 mg, 85 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.71-1.89 (m, 5H, CH_2), 2.40-2.52 (m, 1H, CH), 3.89 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.69 (d, J = 8.2 Hz, 1H, CH), 7.98 (d, J = 8.0 Hz, 2H, CH), 7.07 (d, J = 8.0 Hz, 2H, CH), 7.27-7.43 (m, 12H, CH),7.45 (d, J = 7.2 Hz, 1H, CH), 7.51 (t, J = 7.6 Hz, 2H, CH), 7.63 (d, J = 7.2 Hz, 2H, CH), 7.69 (d, J = 8.4 Hz, 2H, CH), 7.84-7.89 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 40.0, 44.3, 49.4, 53.1, 67.2, 70.9, 110.3, 114.1, 120.3, 121.2, 127.1, 127.2, 127.5, 127.6, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.1, 129.2, 133.4, 133.9, 135.8, 135.8, 138.0, 139.5, 146.0, 148.0, 159.0, 165.5, 166.6.



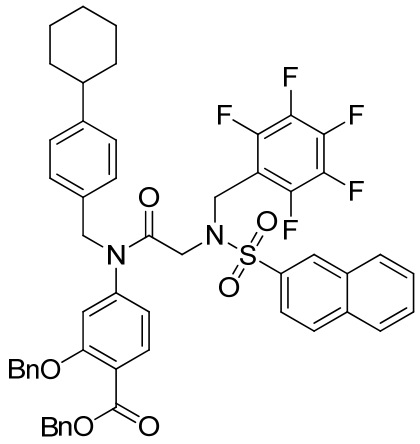
8r, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(3,5-dimethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8r** (24.5 mg, 87 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.44-1.57 (m, 5H, CH_2), 1.68-1.91 (m, 5H, CH_2), 2.34 (s, 6H, CH_3), 2.42-2.56 (m, 1H, CH), 3.82 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 4.93 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.56 (s, 1H, CH), 6.70 (d, J = 8.0 Hz, 1H, CH), 7.02 (d, J = 7.8 Hz, 2H, CH), 7.13 (d, J = 7.8 Hz, 2H, CH), 7.17 (s, 1H, CH), 7.24-7.46 (m, 12H, CH), 7.84 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.1, 26.1, 26.8, 34.6, 39.9, 44.2, 49.5, 52.8, 67.1, 70.8, 114.1, 120.2, 121.0, 124.9, 127.0, 127.2, 128.1, 128.3, 128.3, 128.6, 128.6, 128.9, 129.0, 133.2, 133.9, 134.5, 135.8, 135.8, 138.8, 139.1, 147.8, 158.9, 165.4, 166.7.



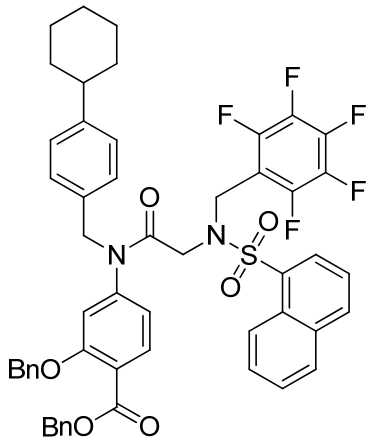
8s, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.04 mmol scale using General Procedure A to give **8s** (39.0 mg, 98 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.34-1.47 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.42-2.56 (m, 1H, CH), 3.82 (s, 2H, CH_2), , 4.72 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.60 (d, J = 8.1 Hz, 1H, CH), 7.02 (d, J = 7.4 Hz, 2H, CH), 7.10 (d, J = 7.4 Hz, 2H, CH), 7.15 (s, 2H, CH), 7.26-7.42 (m, 10H, CH), 7.80 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 11.0, 14.0, 23.5, 24.8, 26.1, 26.8, 29.7, 34.5, 44.2, 47.7, 52.9, 67.1, 68.2, 70.7, 113.9, 120.2, 120.8, 123.8, 126.9, 127.2, 128.0, 128.2, 128.3, 128.6, 128.8, 129.1, 129.4, 130.8, 133.2, 133.9, 135.7, 135.7, 147.7, 151.8, 153.6, 158.9, 165.4, 166.0.



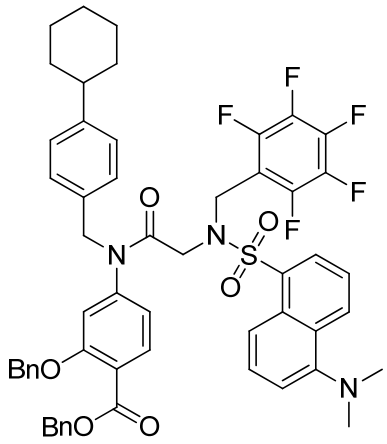
8t, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)naphthalene-2-sulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8t** (28.0 mg, 97 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.34-1.46 (m, 5H, CH_2), 1.72-1.89 (m, 5H, CH_2), 2.41-2.54 (m, 1H, CH), 3.89 (s, 2H, CH_2), 4.72 (s, 4H, 2 CH_2), 4.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.68 (d, J = 8.0 Hz, 1H, CH), 6.95 (d, J = 7.8 Hz, 2H, CH), 7.07 (d, J = 7.8 Hz, 2H, CH), 7.27-7.43 (m, 10H, CH), 7.57-7.76 (m, 4H, CH), 7.85 (d, J = 8.0 Hz, 1H, CH), 7.89-7.95 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.8, 34.5, 39.9, 44.2, 49.4, 52.8, 67.1, 70.7, 114.0, 120.1, 121.1, 122.7, 127.0, 127.2, 127.5, 127.9. 128.1, 128.3, 128.3, 128.6, 128.6, 128.9, 129.0, 129.2, 129.2, 129.7, 130.9, 131.9, 133.2, 133.7, 134.9, 135.6, 135.7, 136.2, 144.7, 158.9, 165.4, 166.5.



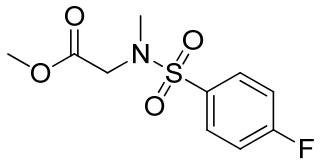
8u, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)naphthalene-1-sulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8u** (15.1 mg, 48 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.43 (m, 5H, CH_2), 1.67-1.86 (m, 5H, CH_2), 2.40-2.51 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.71 (s, 4H, 2 CH_2), 4.74 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.68 (d, J = 8.2 Hz, 1H, CH), 6.98 (d, J = 8.0 Hz, 2H, CH), 7.09 (d, J = 8.0 Hz, 2H, CH), 7.27-7.41 (m, 10H, CH), 7.44-7.56 (m, 3H, CH), 7.81-7.88 (m, 2H, CH), 7.99 (d, J = 8.2 Hz, 1H, CH), 8.25-8.35 (m, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.8, 34.5, 39.9, 44.2, 49.6, 52.9, 67.1, 70.7, 114.0, 120.2, 121.0, 123.9, 124.4, 126.8, 127.0, 127.1, 128.1, 128.2, 128.3, 128.4, 128.4, 128.6, 128.6, 128.7, 129.1, 130.6, 133.2, 133.8, 134.0, 134.2, 134.6, 135.6, 135.7, 144.8, 147.8, 158.9, 165.5, 166.6.



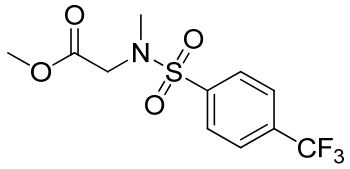
8v, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(5-(dimethylamino)-N-((perfluorophenyl)methyl)naphthalene-1-sulfonamido)acetamido)benzoate

Amine **7** was functionalized on a 0.03 mmol scale using General Procedure A to give **8v** (23.4 mg, 76 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.43 (m, 5H, CH_2), 1.67-1.86 (m, 5H, CH_2), 2.39-2.51 (m, 1H, CH), 2.83 (s, 6H, 2 CH_3), 4.03 (s, 2H, CH_2), 4.71 (s, 4H, 2 CH_2), 4.77 (s, 2H, CH_2), 4.89 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.56 (s, 1H, CH), 6.70 (d, J = 8.2 Hz, 1H, CH), 7.01 (d, J = 8.0 Hz, 2H, CH), 7.06-7.12 (m, 3H, CH), 7.22-7.47 (m, 12H, CH), 7.84 (d, J = 8.2 Hz, 1H, CH), 7.90 (d, J = 8.6 Hz, 1H, CH), 8.26 (d, J = 7.2 Hz, 1H, CH), 8.46 (d, J = 8.5 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.8, 34.5, 39.9, 44.2, 45.3, 49.8, 53.0, 67.1, 70.7, 114.0, 115.1, 118.8, 120.2, 120.9, 122.9, 127.0, 127.2, 128.0, 128.2, 128.3, 128.4, 128.6, 128.6, 129.1, 129.7, 129.8, 130.6, 130.9, 133.2, 133.9, 134.2, 135.7, 135.7, 144.9, 147.8, 151.7, 158.8, 165.5, 166.8.



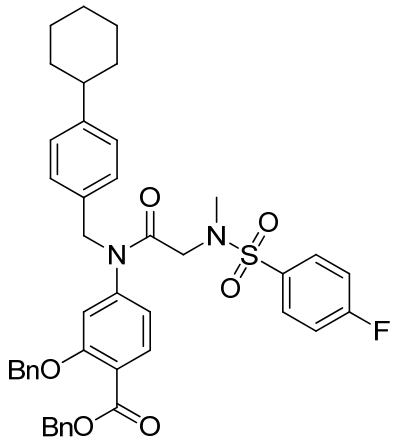
10a, methyl 2-(4-fluoro-N-methylphenylsulfonamido)acetate

Sarcosine methyl ester hydrochloride was functionalized on a 0.7 mmol scale using General Procedure A to give **10a** (136 mg, 73 %); δ_H (400 MHz, *d*-$CDCl_3$) 2.85 (s, 3H, CH_3), 3.60 (s, 3H, CH_3), 3.96 (s, 2H, CH_2), 7.16 (d, J = 8.4 Hz, 2H CH), 7.79 (d, J = 8.4 Hz, 2H, CH);); δ_C (100 MHz, *d*-$CDCl_3$) 35.4, 50.6, 52.0, 116.1 (d), 129.9 (d), 134.3 (d), 165.0 (d), 168.7.



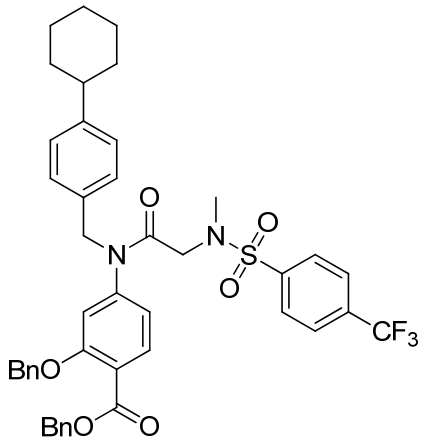
10b, methyl 2-(N-methyl-4-(trifluoromethyl)phenylsulfonamido)acetate

Sarcosine methyl ester hydrochloride was functionalized on a 0.7 mmol scale using General Procedure A to give **10b** (189 mg, 84 %); δ_H (400 MHz, *d*-$CDCl_3$) 2.89 (s, 3H, CH_3), 3.59 (s, 3H, CH_3), 4.01 (s, 2H, CH_2), 7.75 (d, J = 8.2 Hz, 2H CH), 7.92 (d, J = 8.2 Hz, 2H, CH);); δ_C (100 MHz, *d*-$CDCl_3$) 35.4, 50.6, 52.0, 123.1 (q), 125.9 (q), 127.7, 134.1 (q), 142.0, 168.5.



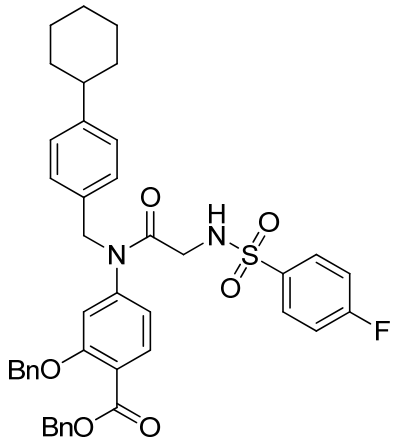
12a, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-methylphenylsulfonamido)acetamido)benzoate

Secondary aniline **4** and carboxylic acid **11a** were combined according to General Procedure E to give **12a** (164 mg, 43 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.42 (m, 5H, CH_2), 1.70-1.86 (m, 5H, CH_2), 2.42-2.52 (m, 1H, CH), 2.84 (s, 3H, CH_3), 3.71 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.95 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.49 (s, 1H, CH), 6.67 (dd, J = 8.4 and 1.6 Hz, 1H, CH), 7.00 (d, J = 8.0 Hz, 2H, CH), 7.10-7.15 (m, 4H, CH), 7.29-7.38 (m, 8H, CH), 7.39-7.41 (m, 2H, CH), 7.75-7.79 (m, 2H, CH), 7.84 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.4, 35.8, 44.1, 51.3, 52.8, 67.0, 70.6, 114.1, 115.5, 116.1, 120.0, 120.8, 126.9, 127.0, 128.0, 128.2, 128.2, 128.5, 128.5, 128.8, 130.1, 130.2, 133.1, 133.8, 134.7, 135.7, 135.7, 144.9, 147.7, 158.7, 163.7, 165.3, 166.6; LRMS (ESI+) Calcd for [$C_{43}H_{43}FN_2O_6S$ + Na] 757.27 found 757.35.



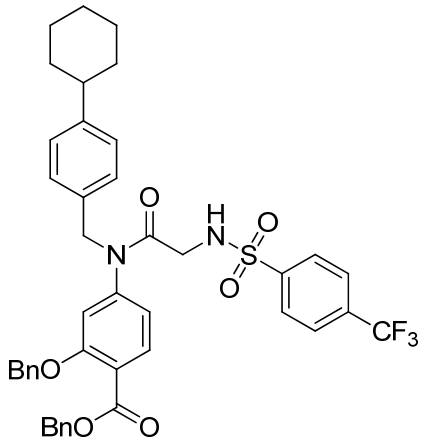
12b, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-methyl-4-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

Secondary aniline **4** and carboxylic acid **11b** were combined according to General Procedure E to give **12b** (211 mg, 42 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.48 (m, 5H, CH_2), 1.71-1.94 (m, 5H, CH_2), 2.45-2.57 (m, 1H, CH), 2.90 (s, 3H, CH_3), 3.78 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.99 (s, 2H, CH_2), 5.38 (s, 2H, CH_2), 6.55 (s, 1H, CH), 6.67 (d of d, J = 8.2 and 1.2 Hz, 1H, CH), 7.03 (d, J = 8.0 Hz, 2H, CH), 7.14 (d, J = 8.0 Hz, 2H, CH), 7.27-7.47 (m, 10, CH), 7.75 (d, J = 8.4 Hz, 2H, CH), 7.87 (d, J = 8.2 Hz, 1H, CH), 7.92 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.4, 35.8, 44.1, 51.3, 52.8, 67.0, 70.6, 114.1, 120.0, 123.3 (q), 128.5 (q), 126.9, 127.0, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.5, 128.5, 128.8, 133.1, 133.8, 135.6, 135.7, 142.4, 144.7, 147.7, 158.7, 165.2, 166.3.



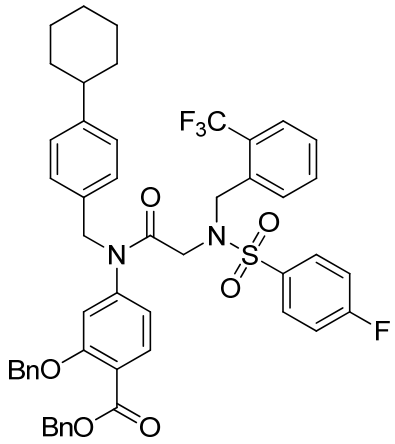
14a, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-fluorophenylsulfonamido)acetamido)benzoate

Primary amine **6** was functionalized on a 0.3 mmol scale using General Procedure B to give **14a** (97.4, 48 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.26-1.46 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.41-2.54 (m, 1H, CH), 3.43 (d, J = 3.8 Hz, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.89 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 5.91 (t, J = 4.6 Hz, 1H, NH), 6.40 (s, 1H, CH), 6.52 (d, J = 8.0 Hz, 1H, CH), 6.92 (d, J = 8.0 Hz, 2H, CH), 7.07-7.16 (m, 4H, CH), 7.31-7.44 (m, 10, CH), 7.76-7.85 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 25.9, 26.7, 34.3, 44.1, 44.2, 53.0, 67.0, 70.7, 113.8, 116.1 (d), 119.8, 121.2, 126.9, 128.0, 128.2, 128.2, 128.5, 128.8, 129.8, 129.9, 131.2, 131.2, 135.3, 135.4, 135.5, 143.7, 147.9, 158.7, 163.7, 165.0 (d), 165.2, 166.5.



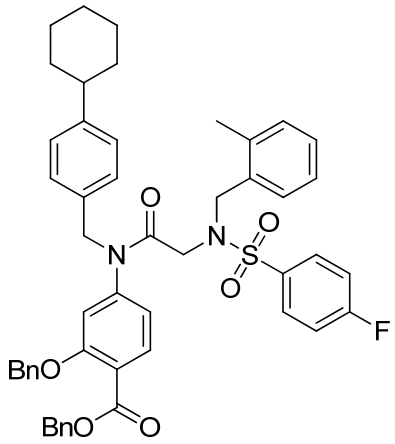
14b, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

Primary amine **6** was functionalized on a 0.28 mmol scale using General Procedure B to give **14b** (155.4 mg, 72 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.44 (m, 5H, CH_2), 1.71-1.89 (m, 5H, CH_2), 2.40-2.54 (m, 1H, CH), 3.49 (s (br), 2H, CH_2), 4.74 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 6.18 (s (br), 1H, NH), 6.44 (s, 1H, CH), 6.56 (d, J = 8.0 Hz, 1H, CH), 6.95 (d, J = 7.4 Hz, 2H, CH), 7.10 (d, J = 8.0 Hz, 2H, CH), 7.30-7.44 (m, 10, CH), 7.73 (d, J = 8.2 Hz, 2H, CH), 7.82 (d, J = 8.2 Hz, 1H, CH), 7.93 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 25.9, 26.7, 34.3, 44.1, 44.2, 53.0, 67.0, 70.7, 113.8, 119.8, 121.3, 123.2 (q), 126.0 (q), 126.9, 127.6, 128.0, 128.2, 128.2, 128.5, 128.5, 128.8, 133.2, 133.2, 134.0, 134.3, 135.4, 135.5, 143.1, 143.7, 147.9, 158.7, 165.2, 166.5.



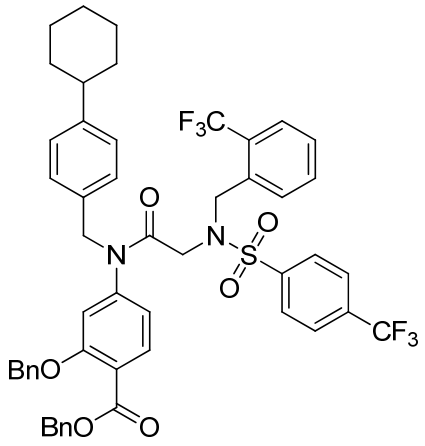
15a, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate

Sulfonamide **14b** was functionalized on a 0.06 mmol scale using General Procedure D to give **15c** (46.3 mg, 85 %); δ_H (400MHz, *d*-$CHCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.70-1.86 (m, 5H, CH_2), 2.40-2.55 (m, 1H, CH), 3.71 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.34 (s, 1H, CH), 6.48 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, J = 8.0 Hz, 2H, CH), 7.09 (d, J = 8.0 Hz, 2H, CH), 7.13-7.20 (m, 3H, CH), 7.27-7.39 (m, 12H, CH), 7.49 (t, J = 7.6 Hz, 1H, CH), 7.60 (d, J = 7.8 Hz, 1H, CH), 7.66-7.77 (m, 2H, CH), 7.85-7.92 (m, 2H, CH); δ_C (100MHz, *d*-$CHCl_3$) 25.9, 26.7, 34.3, 44.1, 47.4, 47.7, 52.7, 66.9, 70.5, 113.7, 115.9 (d), 119.8, 120.8, 122.6, 125.5 (d), 126.8, 126.9, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.4, 128.8, 129.8, 130.3, 130.4, 132.4, 133.0, 133.6, 134.5, 135.5, 135.5, 135.6, 135.7, 144.6, 147.7, 158.6, 165.0 (d), 165.2, 165.9.



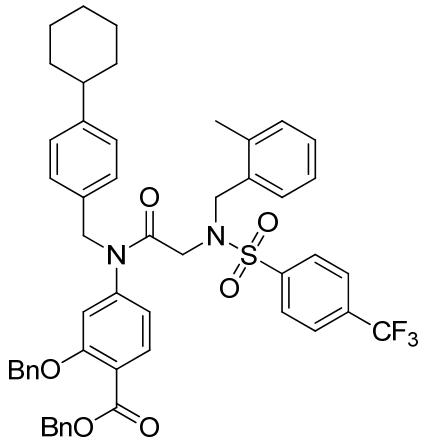
15b, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-(2-methylbenzyl)phenylsulfonamido)acetamido)benzoate

Sulfonamide **14b** was functionalized on a 0.08 mmol scale using General Procedure D to give **15d** (47.1 mg, 73 %); δ_H (400MHz, *d*-$CHCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.71-1.92 (m, 5H, CH_2), 2.23 (s, 3H, CH_3), 2.44-2.55 (m, 1H, CH), 3.61 (s, 2H, CH_2), 4.59 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.19 (s, 1H, CH), 6.32 (d, *J* = 7.8 Hz, 1H, CH), 6.96 (d, J = 8.0 Hz, 2H, CH), 7.05 (d, J = 7.2 Hz, 1H, CH), 7.09-7.21 (m, 7H CH), 7.30-7.39 (m, 10H, CH), 7.69 (d, J = 8.0 Hz, 1H, CH), 7.87-7.94 (m, 2H, CH); δ_C (100MHz, *d*-$CHCl_3$) 18.9, 25.9, 26.7, 34.4, 44.1, 46.7, 49.0, 52.6, 66.9, 70.6, 113.6, 115.9 (d), 119.9, 120.7, 125.9, 126.8, 127.0, 128.0, 128.1, 128.2, 128.2, 128.9, 129.9, 129.9, 130.2, 130.3, 130.7, 132.4, 132.9, 133.7, 135.5, 135.8, 135.8, 137.9, 144.7, 147.7, 158.5, 165.0 (d), 165.3, 166.3.



15c, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-(trifluoromethyl)-N-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate

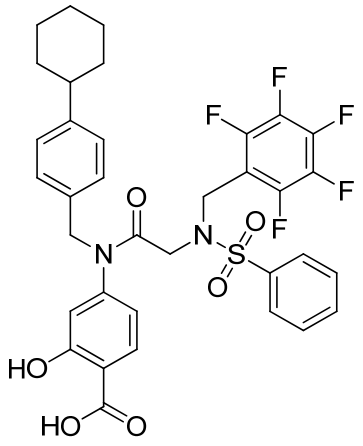
Sulfonamide **14d** was functionalized on a 0.09 mmol scale using General Procedure D to give **15g** (65.4 mg, 81 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.71-1.89 (m, 5H, CH_2), 2.42-2.53 (m, 1H, CH), 3.73 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.34 (s, 1H, CH), 6.48 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, J = 8.0 Hz, 2H, CH), 7.27-7.40 (m, 11H, CH), 7.50 (t, *J* = 7.6 Hz, 1H, CH), 7.60 (d, J = 7.8 Hz, 1H, CH), 7.69 (d, J = 7.8 Hz, 1H, CH), 7.72 (d, J = 8.0 Hz, 1H, CH), 7.78 (d, J = 8.2 Hz, 2H, CH), 8.00 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 25.9, 26.7, 34.3, 44.0, 47.4, 47.8, 52.7, 66.9, 70.6, 113.7, 119.8, 120.8, 125.5, 125.6, 125.8, 125.8, 126.8, 126.9, 127.8, 128.0, 128.1, 128.2, 128.4, 128.8, 129.9, 132.4, 133.0, 133.6, 134.0, 134.1, 134.3, 135.5, 135.5, 143.3, 144.5, 147.7, 158.6, 165.2, 165.7.



15d, benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(N-(2-methylbenzyl)-4-(trifluoromethyl)phenylsulfonamido)acetamido)benzoate

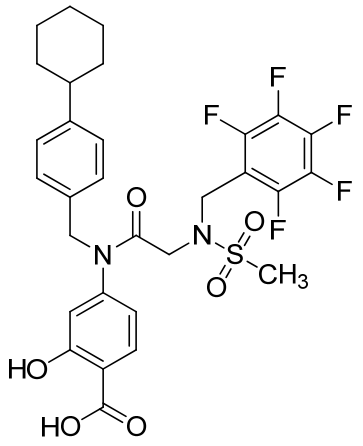
Sulfonamide **14d** was functionalized on a 0.10 mmol scale using General Procedure D to give **15h** (79.7 mg, 93 %); δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.70-1.90 (m, 5H, CH_2), 2.22 (s, 3H, CH_3), 2.42-2.54 (m, 1H, CH), 3.61 (s, 2H, CH_2), 4.46 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.17 (s, 1H, CH), 6.30 (d, J = 8.0 Hz, 1H, CH), 6.93 (d, J = 8.0 Hz, 2H, CH), 7.02-7.19 (m, 6H, CH), 7.29-7.37 (m, 10H, CH), 7.68 (d, J = 8.0 Hz, 1H, CH), 7.77 (d, J = 8.2 Hz, 2H, CH), 7.99 (d, J = 8.2 Hz, 2H CH); δ_C (100 MHz, *d*-$CDCl_3$) 18.8, 25.9, 26.7, 34.3, 44.1, 46.8, 49.0, 52.6, 66.9, 70.6, 113.6, 119.9, 120.8, 124.6, 125.7, 125.8, 125.9, 126.8, 127.0, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.9, 129.9, 130.7, 132.1, 132.9, 133.6, 135.5, 135.6, 137.9, 143.2, 144.5, 147.7, 158.8, 165.2, 166.1.

Final Molecules Characterization



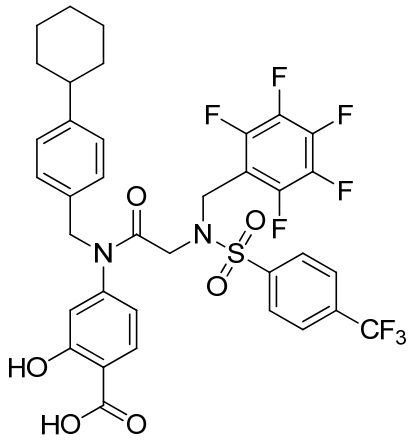
9a, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.34-1.50 (m, 5H, CH_2), 1.68-1.93 (m, 5H, CH_2), 2.39-2.57 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.50 (s (br), 1H, CH), 6.64 (s, 1H, CH), 6.99 (d, J = 7.8 Hz, 2H, CH), 7.09 (d, J = 7.8 Hz, 2H, CH), 7.47 (t, J = 7.2 Hz, 2H, CH), 7.58 (t, J = 7.1 Hz, 1H, CH), 7.82 (d, J = 6.8 Hz, 2H, CH), 7.88 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.2, 39.7, 44.1, 49.2, 52.9, 110.0, 116.6, 118.3, 125.4, 126.8, 127.4, 128.4, 128.7, 132.8, 133.4, 136.0, 139.0, 147.5, 155.9, 162.8, 166.4. HRMS (ESI) Calcd for [$C_{35}H_{31}F_5N_2O_6S$ + H] 703.1895 found 703.1927; HPLC (I) t_R = 25.06 min (91.2 %), (II) t_R = 59.77 min (90.5 %).



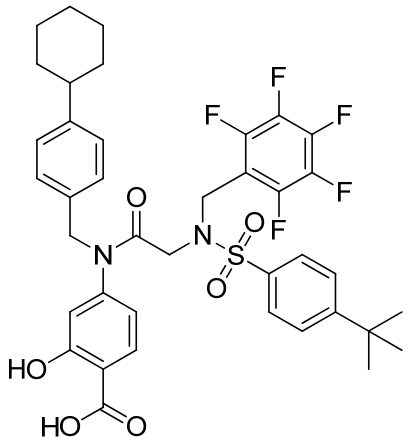
9b, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)methylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.53 (m, 5H, CH_2), 1.68-1.97 (m, 5H, CH_2), 2.35-2.57 (m, 1H, CH), 3.15 (s, 3H, C_3), 3.89 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.46(s (br), 1H, CH), 6.60 (s, 1H, CH),6.92-7.19 (m, 4H, CH), 7.83 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 39.4, 40.6, 44.3, 49.6, 53.3, 112.3, 118.6, 119.9, 125.6, 127.1, 127.2, 128.4, 128.5, 133.4, 136.4, 138.8, 148.0, 159.2, 167.2, 169.3. HRMS (ESI) Calcd for [$C_{30}H_{29}F_5N_2O_6S$ + H] 641.1739 found 641.1748; HPLC (I) t_R = 24.25 min (98.6 %), (II) t_R = 56.92 min (98.6 %).



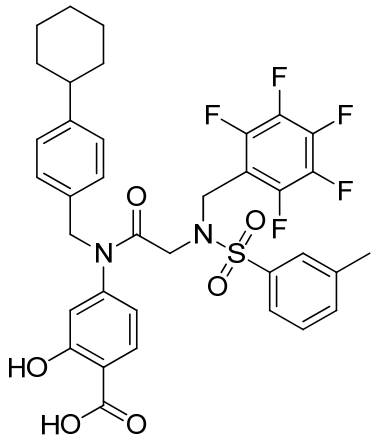
9c, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-4-(trifluoromethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.42 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.55 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.55 (s (br), 1H, CH), 6.69 (s, 1H, CH), 7.01 (d, J = 7.6 Hz, 2H, CH), 7.12 (d, J = 7.6 Hz, 2H, CH), 7.77 (d, J = 7.8 Hz, 2H, CH), 7.98 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 40.0, 44.4, 49.5, 53.3, 113.4, 117.6, 120.4, 122.1, 122.2, 125.7, 126.2, 127.2, 128.4, 128.7, 128.7, 133.5, 142.8, 148.0, 158.6, 163.0, 165.8. HRMS (ESI) Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.1769 found 771.1791; HPLC (I) t_R = 26.05 min (97.0 %), (II) t_R = 62.61 min (97.4 %).



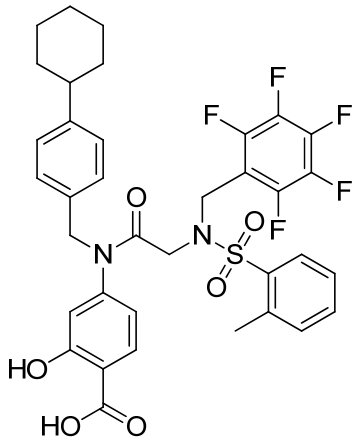
9d, 4-(2-(4-(tert-butyl)-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.36-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.39-2.55 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 6.58 (d, J = 6.9 Hz, 1H, CH), 6.70 (s, 1H, CH), 7.05 (d, J = 7.8 Hz, 2H, CH), 7.12 (d, J = 7.8 Hz, 2H, CH), 7.49 (d, J = 8.2 Hz, 2H, CH), 7.73 (d, J = 8.1 Hz, 2H, CH), 7.91 (s,1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.3, 27.0, 31.2, 34.5, 35.3, 40.1, 44.4, 49.9, 53.2, 110.2, 117.2, 119.0, 125.9, 127.2, 127.6, 128.6, 132.5, 133.6, 133.9, 136.3, 138.8, 147.9, 157.0, 163.1, 166.9. HRMS (ESI) Calcd for [$C_{39}H_{39}F_5N_2O_6S$ + H] 759.2521 found 759.2551; HPLC (I) t_R = 27.38 min (97.1 %), (II) t_R = 64.82 min (100 %).



9e, 4-(N-(4-cyclohexylbenzyl)-2-(3-methyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

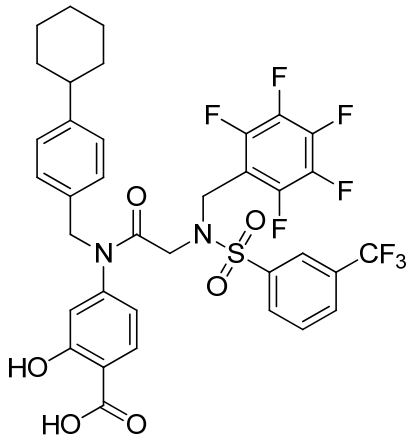
δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.43 (m, 5H, CH_2), 1.70-1.91 (m, 5H, CH_2), 2.39 (s, 3H, CH_3), 2.40-2.54 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.55 (s (br), 1H, CH), 6.68 (s, 1H, CH), 7.00 (d, J = 6.8 Hz, 2H, CH), 7.10 (d, J = 6.8 Hz, 2H, CH), 7.31-7.43 (m, 2H, CH), 7.56-7.68 (m, 2H, CH), 7.90 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.1, 26.0, 26.7, 34.2, 39.7, 44.1, 49.3, 53.0, 109.8, 116.2, 118.5, 123.0, 124.6, 125.4, 126.9, 127.8, 128.3, 128.6, 132.4, 133.3, 133.7, 146.8, 147.6, 159.1, 162.8, 166.7. HRMS (ESI) Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.2052 found 717.2087; HPLC (I) t_R = 25.56 min (97.3 %), (II) t_R = 61.08 min (98.2 %).



9f, 4-(N-(4-cyclohexylbenzyl)-2-(2-methyl-N-

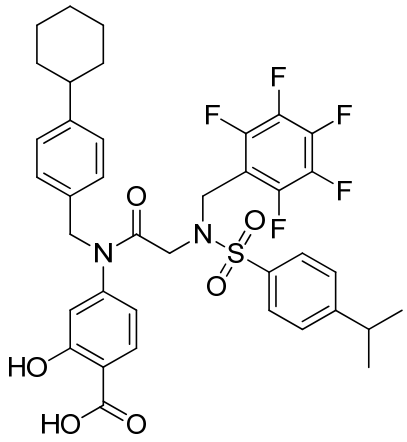
((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.42 (m, 5H, CH_2), 1.70-1.91 (m, 5H, CH_2), 2.40-2.52 (m, 1H, CH), 2.54 (s, 3H, CH_3), 3.93 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.48 (s (br), 1H, CH), 6.61 (s, 1H, CH), 7.00 (d, J = 7.2 Hz, 2H, CH), 7.09 (d, J = 7.2 Hz, 2H, CH), 7.27-7.32 (m, 2H, CH), 7.46 (t, J = 7.2 Hz, 1H, CH), 7.88 (s (br), 1H, CH), 7.99, d, (J = 7.4 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 20.1, 26.0, 26.7, 34.2, 39.2, 44.0, 48.6, 52.9, 112.2, 118.0, 118.6, 125.7, 126.8, 128.5, 130.2, 132.5, 133.1, 133.2, 136.8, 138.3, 140.2, 144.2, 147.6, 158.9, 162.9, 166.1. HRMS (ESI) Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.2052 found 717.2056; HPLC (I) t_R = 25.61 min (97.8 %), (II) t_R = 61.20 min (98.8 %).



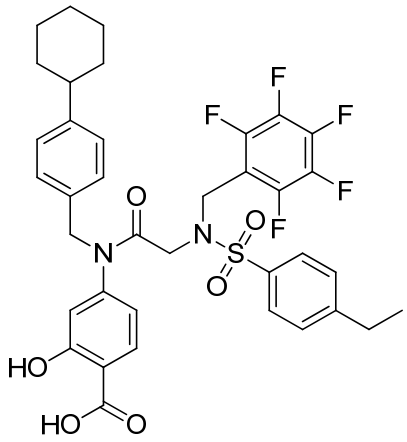
9g, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-3-(trifluoromethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.45 (m, 5H, CH_2), 1.65-1.93 (m, 5H, CH_2), 2.36-2.54 (m, 1H, CH), 3.98 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.53 (s (br), 1H, CH), 6.64 (s, 1H, CH), 7.99 (d, J = 7.2 Hz, 2H, CH), 7.06 (d, J = 7.2 Hz, 2H, CH), 7.62 (t, J = 7.0 Hz, 1H, CH), 7.82 (d, J = 7.0 Hz, 1H, CH), 7.90 (s (br), 1H, CH), 8.04 (d, J = 7.2 Hz, 1H, CH), 8.07, (s, 1H, CH); HRMS (ESI) Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.1769 found 771.1772; HPLC (I) t_R = 25.88 min (97.3 %), (II) t_R = 62.19 min (97.2 %).



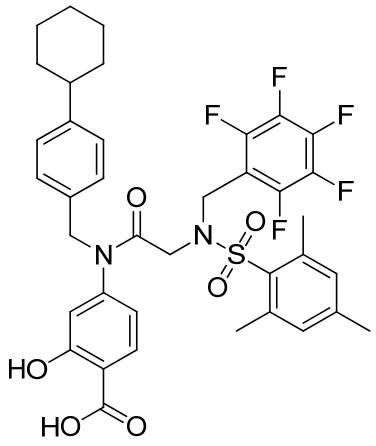
9h, 4-(N-(4-cyclohexylbenzyl)-2-(4-isopropyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.68-1.92 (m, 5H, CH_2), 2.35-2.55 (m, 1H, CH), 2.86-3.04 (m, 1H, CH), 3.98 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.56 (d, J = 5.5 Hz, 1H, CH), 6.68 (s, 1H, CH), 7.03 (d, J = 7.5 Hz, 1H, CH), 7.10 (d, J = 7.5 Hz, 2H, CH), 7.31 (d, J = 8.0 Hz, 2H, CH), 7.72 (d, J = 7.9 Hz, 2H, CH), 7.88 (d, J = 6.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 14.1, 23.6, 26.1, 26.9, 34.2, 34.4, 39.0, 44.2, 49.6, 53.1, 110.1, 117.0, 118.9, 125.5, 126.9, 127.0, 127.8, 128.5, 132.4, 133.4, 136.1, 136.4, 147.8, 154.6, 163.0, 166.8, 172.7. HRMS (ESI) Calcd for [$C_{38}H_{37}F_5N_2O_6S$ + H] 745.2365 found 745.2341; HPLC (I) t_R = 26.68 min (97.4 %), (II) t_R = 63.69 min (98.1 %).



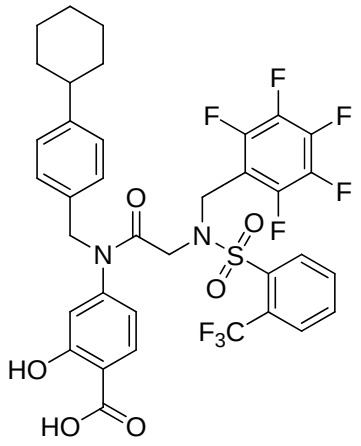
9i, 4-(N-(4-cyclohexylbenzyl)-2-(4-ethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.25 (t, J = 7.2 Hz, 3H, CH_3), 1.33-1.51 (m, 5H, CH_2), 1.67-1.96 (m, 5H, CH_2), 2.40-2.57 (m, 1H, CH), 2.72 (q, J = 7.2 Hz, 2H, CH_2), 3.97 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 6.56 (s (br), 1H, CH), 6.67 (s, 1H, CH), 7.02 (d, J = 7.5 Hz, 2H, CH), 7.10 (d, J = 7.5 Hz, 2H, CH), 7.29 (d, J = 7.8 Hz, 2H, CH), 7.71 (d, J = 7.7 Hz, 2H, CH), 7.86 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 15.2, 26.3, 27.0, 29.8, 34.5, 40.0, 44.4, 49.6, 53.2, 112.8, 117.2, 119.0, 125.7, 127.1, 127.9, 128.5, 128.6, 132.6, 133.6, 136.4, 147.9, 150.2, 163.1, 166.9. HRMS (ESI) Calcd for [$C_{37}H_{35}F_5N_2O_6S$ + H] 731.2208 found 731.2228; HPLC (I) t_R = 26.08 min (97.3 %), (II) t_R = 62.48 min (97.3 %).



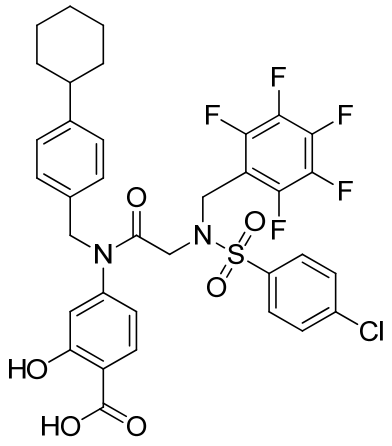
9j, 4-(N-(4-cyclohexylbenzyl)-2-(2,4,6-trimethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.41 (m, 5H, CH_2), 1.67-1.91 (m, 5H, CH_2), 2.28 (s, 3H, CH_3), 2.38-2.48 (m, 1H, CH), 2.52 (s, 6H, CH_3), 3.82 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 6.41 (s, 1H, CH), 6.51 (s, 1H, CH), 6.91 (s, 2H, CH), 6.97 (d, J = 6.2 Hz, 2H, CH), 7.07 (d, J = 7.4 Hz, 2H, CH), 7.76-7.92 (m, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 20.9, 22.7, 26.1, 26.9, 34.4, 38.9, 44.2, 48.3, 53.0, 107.2, 109.7, 117.1, 125.7, 127.1, 128.6, 128.6, 132.1, 132.1, 133.6, 141.0, 143.3, 147.3, 147.8, 163.1, 166.8. HRMS (ESI) Calcd for [$C_{38}H_{37}F_5N_2O_6S$ + H] 745.2365 found 745.2394; HPLC (I) t_R = 27.11 min (97.0 %), (II) t_R = 64.19 min (96.9 %).



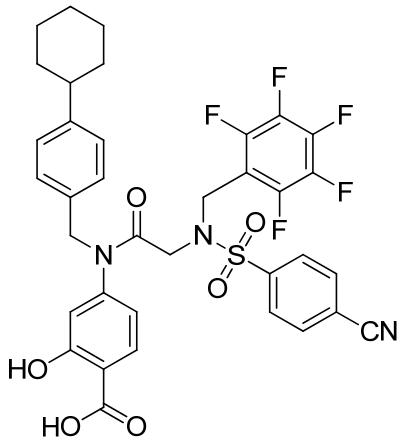
9k, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-2-(trifluoromethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.52 (m, 5H, CH_2), 1.67-1.93 (m, 5H, CH_2), 2.48-2.57 (m, 1H, CH), 3.91 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.86 (s, 2H, CH_2), 6.48 (s, 1H, CH), 6.59 (s, 1H, CH), 6.98 (d, J = 7.9 Hz, 2H, CH), 7.12 (d, J = 7.7 Hz, 2H, CH), 7.26 (s, 1H, OH), 7.29-7.40 (m, 1H, CH), 7.62-7.77 (m, 2H, CH), 7.83-7.96 (m, 2H, CH) 8.22-8.39 (m, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 40.0, 44.4, 49.2, 53.1, 109.5, 117.1, 118.9, 121.3, 124.0, 125.7, 126.5, 127.1, 127.2, 128.7, 128.8, 132.2, 132.3, 133.0, 133.5, 138.7, 147.9, 163.0, 166.2. HRMS (ESI) Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.1769 found 771.1802; HPLC (I) t_R = 25.42 min (85.3 %), (II) t_R = 61.01 min (85.7 %).



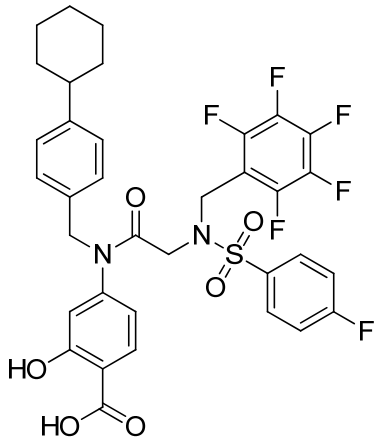
9l, 4-(2-(4-chloro-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.49 (m, 5H, CH_2), 1.67-1.92 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.95 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 6.53 (d, J = 6.8 Hz, 1H, CH), 6.65 (s, 1H, CH), 6.99 (d, J = 7.4 Hz, 1H, CH), 7.12 (d, J = 7.4 Hz, 2H, CH), 7.46 (d, J = 8.0 Hz, 2H, CH), 7.78 (d, J = 8.0 Hz, 2H, CH), 7.89 (d, J = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 40.0, 44.4, 49.4, 53.3, 112.3, 117.2, 119.0, 126.5, 127.2, 127.7, 128.7, 129.0, 129.3, 132.6, 133.1, 133.4, 137.8, 139.7, 148.0, 163.2, 166.4, 172.1. HRMS (ESI) Calcd for [$C_{35}H_{30}ClF_5N_2O_6S$ + H] 737.1506, found 737.1491; HPLC (I) t_R = 27.78 min (80.2 %), (II) t_R = 62.82 min (80.5%).



9m, 4-(2-(4-cyano-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid

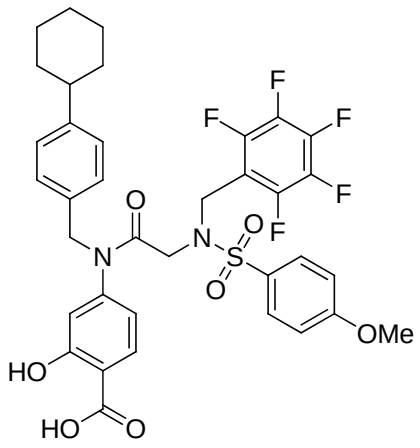
δ_H (400 MHz, *d*-$CDCl_3$) 1.35-1.46 (m, 5H, CH_2), 1.71-1.94 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.48 (s (br), 1H, CH), 6.62 (s, 1H, CH), 6.98 (d, J = 7.8 Hz, 2H, CH), 7.11 (d, J = 7.8 Hz, 2H, CH), 7.71 (d, J = 8.0 Hz, 2H, CH), 7.89-7.98 (m, 3H, CH), 8.11 (s,1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 39.9, 44.2, 49.4, 53.0, 110.2, 118.9, 122.3, 122.9, 127.0, 127.7, 128.5, 129.5, 132.7, 133.4, 136.1, 143.9, 147.8, 156.4, 163.1, 166.6; HRMS (ESI) Calcd for [$C_{36}H_{30}F_5N_3O_6S$ + H] 728.1848 found 728.1845. HPLC (I) t_R = 24.72 min (91.3 %), (II) t_R = 59.03 min (90.8 %).



9n, 4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-

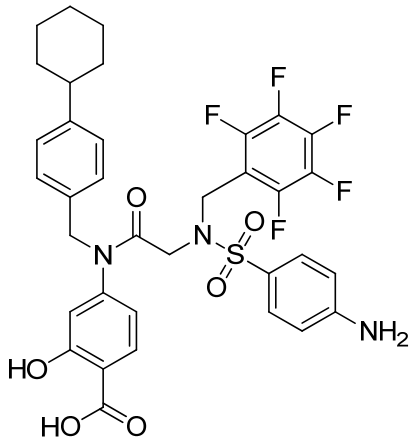
((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.46 (m, 5H, CH_2), 1.68-1.90 (m, 5H, CH_2), 2.38-2.52 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.51 (s (br), 1H, CH), 6.65 (s (br), 1H, CH), 6.99 (d, J = 7.2 Hz, 2H, CH), 7.06-7.21 (m, 4H, CH), 7.78-7.95 (m, 3H, CH); HRMS (ESI) Calcd for [$C_{35}H_{30}F_6N_2O_6S$ + H] 721.1801 found 721.1820; HPLC (I) t_R = 25.26 min (92.9 %), (II) t_R = 90.41 min (94.0 %).



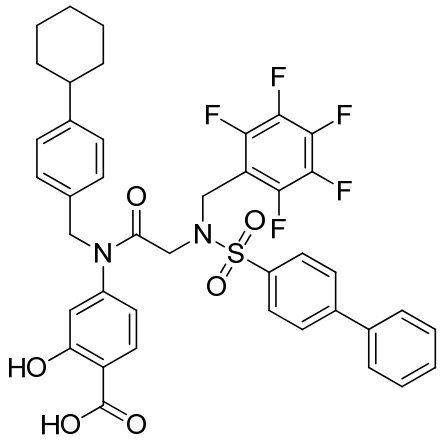
9o, 4-(N-(4-cyclohexylbenzyl)-2-(4-methoxy-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.35-1.49 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.40-2.57 (m, 1H, CH),3.64 (s, 3H, CH_3), 3.73 (s, 2H, CH_2), 4.40 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 6.32 (s (br), 1H, CH), 6.44 (s, 1H, CH), 6.71 (d, J = 7.6 Hz, 2H, CH), 6.79 (d, J = 8.0 Hz, 2H, CH), 6.89 (d, J = 8.0 Hz, 2H, CH), 7.54 (d, J = 7.6 Hz, 2H, CH), 7.64 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 39.8, 44.2, 49.4, 53.0, 55.6, 110.25, 114.1, 117.0, 118.9, 125.5, 127.0, 128.4, 128.8, 130.0, 130.5, 132.4, 133.4, 147.8, 163.2, 166.8, 172.5. HRMS (ESI) Calcd for [$C_{36}H_{33}F_5N_2O_7S$ + H] 733.2001 found 733.1986; HPLC (I) t_R = 24.97 min (96.3 %), (II) t_R = 59.58 min (96.7 %).



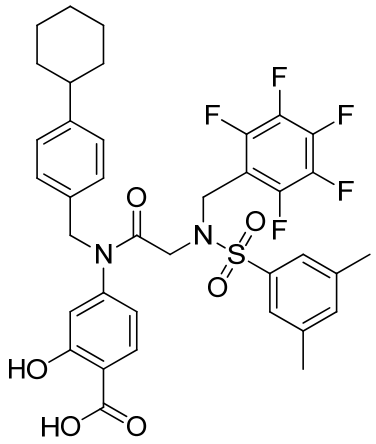
9p, 4-(2-(4-amino-N-((perfluorophenyl)methyl)phenylsulfonamido)-N-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.42 (m, 5H, CH_2), 1.65-1.90 (m, 5H, CH_2), 2.22-2.41 (m, 1H, CH),3.91 (s, 2H, CH_2), 4.63 (s, 2H, CH_3), 4.66 (s, 2H, CH_2), 6.46 (s (br), 1H, CH), 6.59 (s, 1H, CH), 6.86-7.00 (m, 4H, CH), 7.53 (d, J = 7.2 Hz, 2H, CH), 7.62 (d, J = 7.4 Hz, 2H, CH), 7.80 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.7, 26.8, 34.4, 39.9, 44.2, 49.4, 53.1, 110.2, 117.0, 118.8, 126.9, 127.4, 127.5, 128.2, 128.5, 129.0, 129.7, 133.4, 137.6, 139.3, 146.0, 147.7, 162.9, 167.9. HRMS (ESI) Calcd for [$C_{35}H_{32}F_5N_3O_6S$ + H] 718.2004 found 718.2011; HPLC (III) t_R = 25.22 min (85.6 %), (II) t_R = 55.14 min (93.0 %).



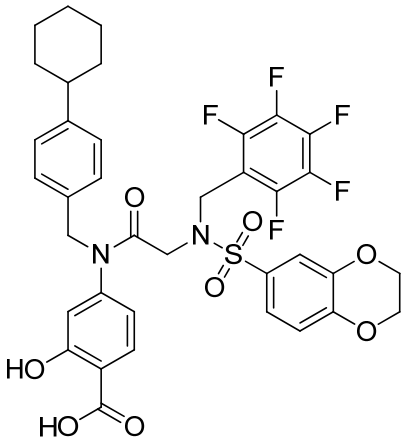
9q, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-[1,1'-biphenyl]-4-ylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.37-1.45 (m, 5H, CH_2), 1.68-1.80 (m, 5H, CH_2), 2.36-2.45 (m, 1H, CH), 3.91 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 6.46 (s (br), 1H, CH), 6.59 (s, 1H, CH), 6.85-6.99 (m, 4H, CH),7.30-7.48 (m, 3H, CH), 7.53 (d, J = 7.2 Hz, 2H, CH), 7.61 (d, J = 8.0 Hz, 2H, CH), 7.81 (m, 3H, CH); HRMS (ESI) Calcd for [$C_{41}H_{35}F_5N_2O_6S$ + H] 779.2208 found 779.2190; HPLC (I) t_R = 26.77 min (93.8 %), (II) t_R = 63.90 min (95.9 %).



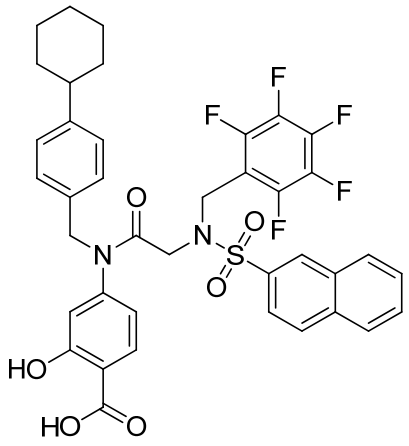
9r, 4-(N-(4-cyclohexylbenzyl)-2-(3,5-dimethyl-N-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.42-1.60 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.24 (s, 6H, CH_3), 2.39-2.52 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.46 (s (br), 1H, CH), 6.59 (s, 1H, CH), 6.91-7.05 (m, 4H, CH), 7.08 (s, 1H, CH), 7.29 (s, 2H, CH), 7.81 (s (br), 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.1, 26.1, 26.8, 34.4, 39.9, 44.2, 49.5, 53.1, 110.1, 116.9, 118.7, 125.1, 127.0, 128.4, 128.4, 133.5, 134.7, 138.6, 138.9, 146.9, 147.7, 162.9, 165.3, 167.0. HRMS (ESI) Calcd for [$C_{37}H_{35}F_5N_2O_6S$ + H] 731.2208 found 731.2242; HPLC (III) t_R = 27.74 min (90.3 %), (II) t_R = 62.10 min (91.0 %).



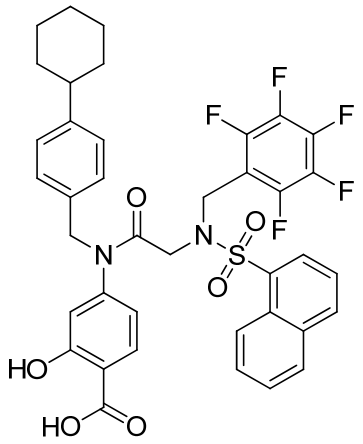
9s, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.52 (m, 1H, CH), 3.94 (s, 2H, CH_2),4.25-4.36 (m, 4H, 2 CH_2), 4.66 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 6.58 (d, J = 8.2 Hz, 1H, CH), 6.68 (s, 1H, CH), 6.92 (d, J = 8.4 Hz, 1H, CH), 7.03 (d, J = 8.0 Hz, 2H, CH), 7.11 (d, J = 8.0 Hz, 2H, CH), 7.27-7.35 (m, 2H, CH), 7.88 (d, J = 8.4 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 40.0, 44.2, 49.4, 53.0, 64.2, 64.6, 110.4, 117.2, 117.3, 117.6, 119.1, 121.4, 127.1, 128.5, 131.4, 132.5, 133.3, 143.4, 147.7, 147.8, 163.0, 166.7, 172.7, 177.3; HRMS (ESI) Calcd for [$C_{37}H_{33}F_5N_2O_8S$ + H] 761.1950 found 761.1942; HPLC (III) t_R = 26.42 min (96.1 %), (II) t_R = 58.72 min (96.3 %).



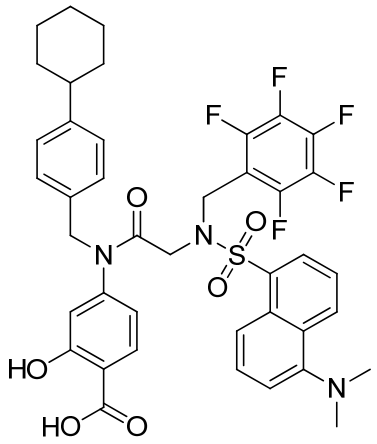
9t, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)naphthalene-2-sulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.27-1.45 (m, 5H, CH_2), 1.67-1.89 (m, 5H, CH_2), 2.37-2.50 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.52 (d, J = 7.0 Hz, 1H, CH), 6.66 (s, 1H, CH), 6.83 (d, J = 7.4 Hz, 2H, CH), 7.02 (d, J = 7.4 Hz, 2H, CH), 7.55-7.67 (m, 2H, CH), 7.74 (d, J = 8.5 Hz, 1H, CH), 7.84-7.98 (m, 4H, CH), 8.38 (s, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 40.0, 44.2, 49.4, 53.0, 110.1, 116.9, 118.8, 122.7, 127.0, 127.5, 127.9, 128.4, 129.0, 129.1, 129.2, 131.9, 132.6, 133.4, 134.9, 135.9, 144.3, 147.7, 162.9, 166.7, 173.3, 177.1; HRMS (ESI) Calcd for [$C_{39}H_{33}F_5N_2O_6S$ + H] 753.2052 found 753.2076; HPLC (III) t_R = 27.66 min (94.5 %), (II) t_R = 62.02 min (94.1 %).



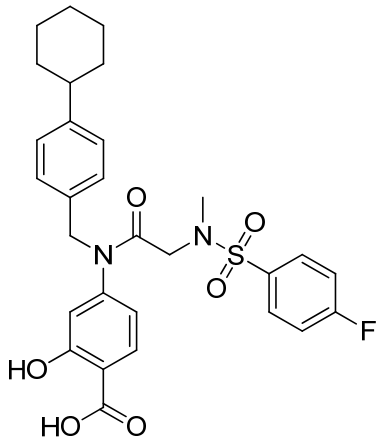
9u, 4-(N-(4-cyclohexylbenzyl)-2-(N-((perfluorophenyl)methyl)naphthalene-1-sulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.46 (m, 5H, CH_2), 1.69-1.89 (m, 5H, CH_2), 2.39-2.51 (m, 1H, CH), 4.12 (s, 2H, CH_2), 4.74 (s, 4H, 2 CH_2), 6.56 (d, J = 8.0 Hz, 1H, CH), 6.67 (s, 1H, CH), 6.98 (d, J = 7.8 Hz, 2H, CH), 7.09 (d, J = 7.8 Hz, 2H, CH), 7.46-7.61 (m, 3H, CH), 7.83-7.94 (m, 2H, CH), 8.02 (d, J = 8.2 Hz, 1H, CH), 8.32 (d, J = 7.3 Hz, 1H, CH), 8.41 (d, J = 8.2 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 39.9, 44.2, 49.6, 53.1, 109.9, 117.1, 119.1, 124.0, 124.4, 126.8, 127.0, 128.2, 128.5, 128.8, 130.7, 132.5, 133.3, 134.0, 134.1, 134.7, 147.5, 147.7, 163.0, 166.6, 173.1, 177.3; HRMS (ESI) Calcd for [$C_{39}H_{33}F_5N_2O_6S$ + H] 753.2052 found 753.2054; HPLC (III) t_R = 27.40 min (90.6 %), (II) t_R = 61.30 min (90.6 %).



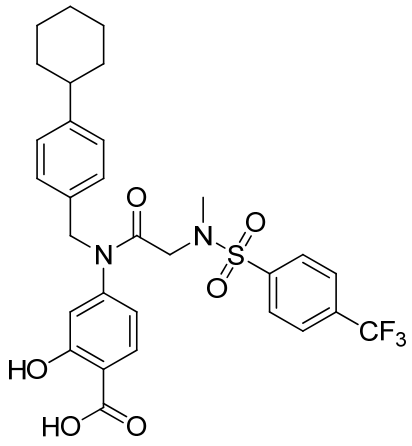
9v, 4-(N-(4-cyclohexylbenzyl)-2-(5-(dimethylamino)-N-((perfluorophenyl)methyl)naphthalene-1-sulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.45 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.40-2.53 (m, 1H, CH),2.86 (s, 6H, 2 CH_3), 4.13 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.57 (d, J = 8.2 Hz, 1H, CH), 6.67 (s, 1H, CH), 7.00 (d, J = 8.0 Hz, 2H, CH), 7.10 (d, J = 8.0 Hz, 2H, CH), 7.14 (d, J = 7.6 Hz, 1H, CH), 7.42-7.52 (m, 2H, CH), 7.89 (d, J = 8.3 Hz, 1H, CH), 8.04 (d, J = 8.6 Hz, 1H, CH), 8.31 (d, J = 7.3 Hz, 1H, CH), 8.50 (d, J = 8.5 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 40.0, 44.2, 49.4, 53.0, 110.1, 116.9, 118.8, 122.7, 127.0, 127.5, 127.9, 128.4, 129.0, 129.1, 129.2, 131.9, 132.6, 133.4, 134.9, 135.9, 138.7, 144.3, 146.8, 147.7, 162.9, 166.7; HRMS (ESI) Calcd for [$C_{41}H_{38}F_5N_3O_6S$ + H] 796.2474 found 796.2488; HPLC (III) t_R = 26.43 min (95.6 %), (II) t_R = 58.54 min (96.2 %).



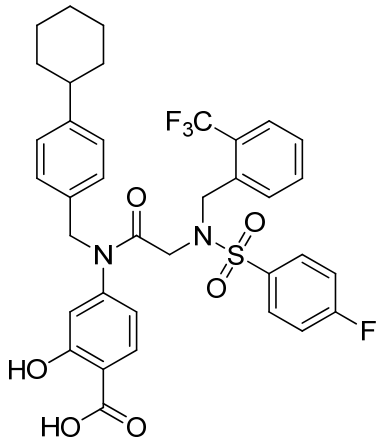
13a, 4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, d_6-DMSO) 1.28-1.39 (m, 5H, CH_2), 1.62 - 1.79 (m, 5H, CH_2), 2.37-2.46 (m, 1H, CH), 2.88 (s, 3H, CH_3), 3.95 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 6.80 (d of d, J = 8.4 and 2.4 Hz, 1H, CH), 6.88 (d, J = 2.0 Hz, 1H, CH), 7.02 (d, J = 8.0 Hz, 2H, CH), 7.08 (d, J = 8.0 Hz, 2H, CH), 7.62 - 7.73 (m, 3H, CH), 7.79 (d, J = 8.4 Hz, 1H, CH), 8.04 (d, J = 8.4 Hz, 1H, CH), 8.09 (d, J = 8.8 Hz, 1H, CH), 8.12 (d, J = 8.0 Hz, 1H, CH), 8.35 (d, J = 1.6 Hz, 1H, CH); δ_C (100 MHz, d_6-DMSO) 25.4, 26.2, 33.8, 35.9, 43.2, 50.8, 51.5, 112.5, 116.0, 118.5, 119.9, 122.5, 126.5, 127.4, 127.7, 127.8, 128.7, 129.1, 131.3, 131.6, 134.1, 134.2, 135.1, 146.3, 146.8, 161.5, 166.5, 171.1; HRMS (ESI+) calcd for [$C_{29}H_{31}FN_2O_6S$ + H] 555.1959, Found 555.1954; HPLC (III) t_R = 24.80 min (100 %), (II) t_R = 53.34 min (98.8 %).



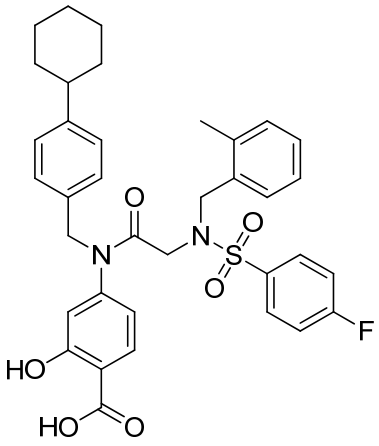
13b, 4-(N-(4-cyclohexylbenzyl)-2-(N-methyl-4-(trifluoromethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.67-1.91 (m, 5H, CH_2), 2.40-2.53 (m, 1H, CH), 2.91 (s, 3H, CH_3), 3.94 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 6.58 (d, J = 8.0 Hz, 1H, CH), 6.70 (s, 1H, CH), 7.04 (d, J = 7.8 Hz, 2H, CH), 7.11 (d, J = 7.8 Hz, 2H, CH), 7.72 (d, J = 8.0 Hz, 2H, CH), 7.86-7.97 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.4, 35.8, 44.0, 51.5, 53.1, 112.8, 116.7, 118.7, 121.8, 124.5, 125.9, 125.9, 126.9, 127.9, 128.3, 132.4, 133.2, 133.9, 134.2, 142.0, 146.9, 147.7, 162.7, 166.8, 172.8, 177.4; HRMS (ESI+) calcd for [$C_{30}H_{31}F_3N_2O_6S$ + H] 605.1927, Found 605.1924; HPLC (III) t_R = 25.75 min (100 %), (II) t_R = 56.40 min (100 %).



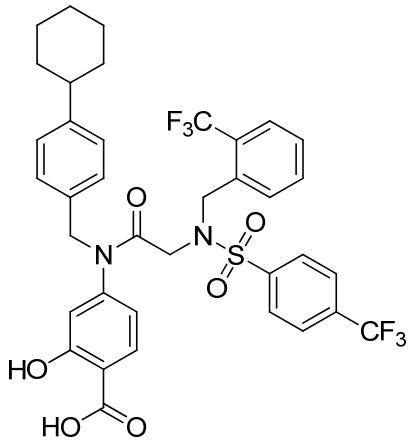
16a, 4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.39-2.52 (m, 1H, CH), 3.82 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 6.37 (s (br), 1H, CH), 6.50 (s, 1H, CH), 6.96 (d, J = 7.8 Hz, 2H, CH), 7.09 (d, J = 7.8 Hz, 2H, CH), 7.14-7.21 (m, 2H, CH), 7.36 (t, J = 7.5 Hz, 1H, CH), 7.48 (t, J = 7.7 Hz, 1H, CH), 7.63 (d, J = 7.8 Hz, 1H, CH), 7.69 (d, J = 7.8 Hz, 1H, CH), 7.77 (d, J = 8.2 Hz, 1H, CH), 7.87-7.98 (m, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.2, 44.1, 47.4, 47.7, 52.9, 111.7, 116.0 (d), 116.9, 118.8, 122.6, 125.3 (q), 125.7 (q), 126.8, 127.7, 128.4, 129.8, 130.3, 130.4, 132.1, 132.3, 133.1, 134.3, 135.6 (d), 147.6, 162.8, 163.8, 166.2, 172.3; HRMS (ESI+) Calcd for [$C_{36}H_{34}F_4N_2O_6S$ + H] 699.2146 found 699.2160; HPLC (III) t_R = 27.17 min (99.1 %), (II) t_R = 60.77 min (98.9 %).



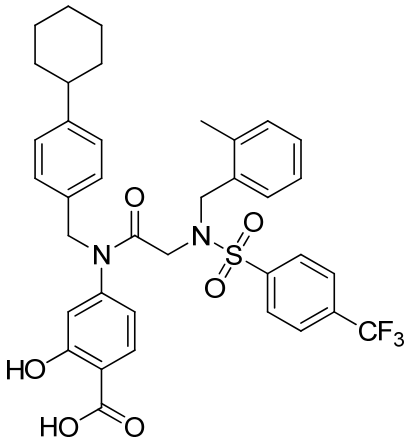
16b, 4-(N-(4-cyclohexylbenzyl)-2-(4-fluoro-N-(2-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.45 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.19 (s, 3H, CH_3), 2.40-2.56 (m, 1H, CH), 3.69 (s, 2H, CH_2), 4.57 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.11 (s (br), 1H, CH), 6.35 (s, 1H, CH), 6.98 (d, J = 7.6 Hz, 2H, CH), 7.00-7.23 (m, 8H, CH), 7.71 (s (br), 1H, CH), 7.86-7.97 (m, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.3, 44.1, 46.8, 49.0, 52.8, 110.4, 115.9 (d), 116.7, 118.6, 126.0, 126.8, 128.4, 128.5, 129.9, 130.3, 130.4, 130.7, 132.2, 133.3, 135.5 (d), 137.6, 147.6, 162.7, 163.7, 166.2, 166.6, 172.4; HRMS (ESI+) Calcd for [$C_{36}H_{37}FN_2O_6S$ + H] 645.2429 found 645.2411; HPLC (III) t_R = 27.08 min (99.7 %), (II) t_R = 60.22 min (98.4 %).



16c, 4-(N-(4-cyclohexylbenzyl)-2-(4-(trifluoromethyl)-N-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.43 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.40-2.52 (m, 1H, CH), 3.85 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 6.35 (d, J = 7.4 Hz, 1H, CH), 6.50 (s, 1H, CH), 6.96 (d, J = 8.0 Hz, 2H, CH), 7.09 (d, J = 8.0 Hz, 2H, CH), 7.38 (t, J = 7.6 Hz, 1H, CH), 7.49 (t, J = 7.5 Hz, 1H, CH), 7.65 (d, J = 7.8 Hz, 1H, CH), 7.70 (d, J = 7.8 Hz, 1H, CH), 7.74-7.83 (m, 3H, CH), 8.04 (d, J = 8.2 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.0, 26.7, 34.2, 44.1, 47.5, 47.7, 52.9, 112.0, 116.8, 118.7, 121.9, 122.6, 124.6, 125.3, 125.8 (m), 126.8, 127.9, 128.1, 128.4, 129.9, 132.2, 132.3, 133.1, 133.9, 134.0, 134.3, 143.2, 147.7, 162.8, 165.9, 172.1; HRMS (ESI+) Calcd for [$C_{37}H_{34}F_6N_2O_6S$ + H] 749.2114 found 749.2120; HPLC (III) t_R = 28.12 min (100 %), (II) t_R = 63.17 min (100 %).



16d (BP-5-087), 4-(N-(4-cyclohexylbenzyl)-2-(N-(2-methylbenzyl)-4-(trifluoromethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.49 (m, 5H, CH_2), 1.71-1.94 (m, 5H, CH_2), 2.23 (s,3H, CH_3), 2.42-2.55 (m, 1H, CH), 3.73 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 6.15 (s (br), 1H, CH), 6.37 (s, 1H, CH), 6.98 (d, J = 7.8 Hz, 2H, CH), 7.02-7.19 (m, 5H, CH), 7.23 (t, J = 7.8 Hz, 1H, CH), 7.72 (d, J = 8.2 Hz, 1H, CH), 7.79 (d, J = 8.2 Hz, 2H, CH), 8.04 (d, J = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 18.8, 26.0, 26.7, 34.3, 44.1, 46.9, 49.1, 52.9, 111.6, 116.8, 118.8, 121.9, 124.6, 125.8, 125.8, 126.1, 126.8, 128.1, 128.5, 130.0, 130.8, 131.8, 132.1, 133.1, 133.8, 134.2, 137.7, 143.1, 147.1, 147.7, 162.7, 166.4, 172.4; HRMS (ESI+) Calcd for [$C_{37}H_{37}F_3N_2O_6S$ + H] 695.2397 found 695.2417; HPLC (III) t_R = 28.07 min (100 %), (II) t_R = 62.81 min (100 %).