Supporting Information

Inhibiting Aberrant Signal Transducer and Activator of Transcription (STAT) Protein Activation with Tetrapodal, Small Molecule Src Homology 2 domain binders: Promising Agents Against Multiple Myeloma

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S.1 GOLD Docking Simulations

Inhibitors were docked using GOLD docking software to Stat3 crystal structure, pdb 1BG1. Compounds were first optimized into a low energy geometry. The compound binding site was set to an area with a 12Å radius surrounding Ser636. Top solutions were visualized using Pymol, which was utilized to create the images shown in Figures 2 and 3 and in supplementary Figure S.1. In these docking orientations, the N-alkyl group seemingly contributes to binding at the protein surface, which may help to explain the increased activity of these inhibitors relative to parent compounds **7** and **9**.

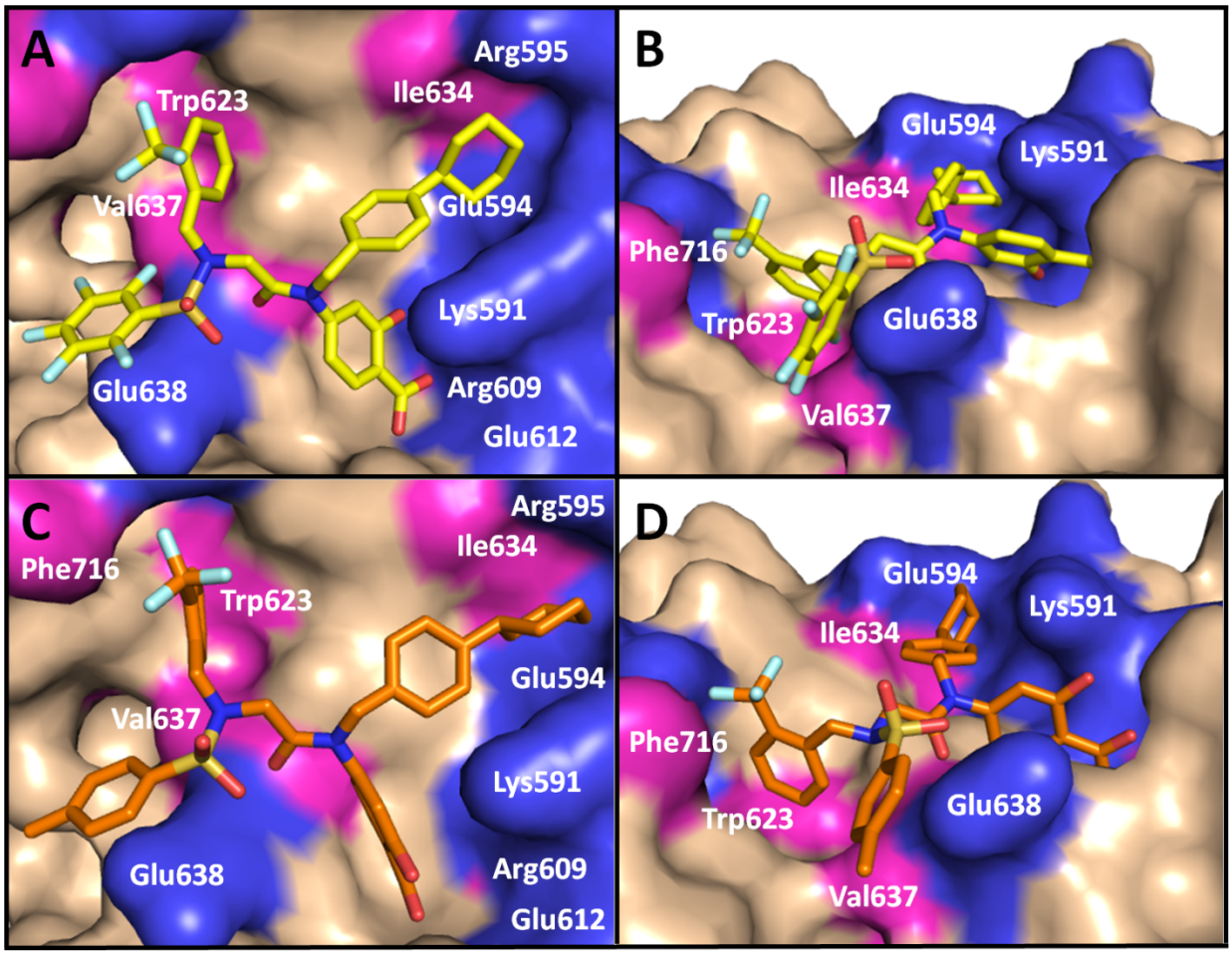


Figure S.1. GOLD docking images of lead compounds **21h** (A and B) **16i** (C and D). Compounds were found to optimally bind in a similar conformation to compound **8**. The N-alkyl group improves binding potency due to a more complete occupation of the Stat3 SH2 domain.

S.2 Fluorescence Polarization Assay

The fluorescence polarization assay was performed as previously reported. Briefly, fluorescently labelled peptide probe (5-FAM-GpYLPQTV-NH_2, CanPeptide, Pointe-Claire (Montreal), Quebec, Canada) was incubated with Stat3 protein (SignalChem, Richmond, British Columbia, Canada), and inhibitor for 30 minutes then analyzed on a Tecan M1000 fluorimeter (Tecan, Mannedorf, Switzerland). Polarized fluorescence was plotted against concentration of inhibitor

and IC_{50} values were determined by fitting to a dose response curve. Representative curves of the top compounds are shown below.

N-Alkyl-tolyl Derivatives Fluorescence Polarization Curves

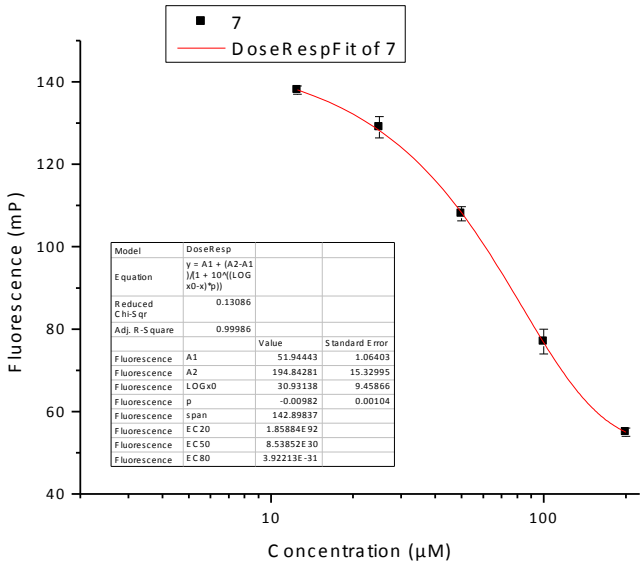


Figure S.2. Competitive binding of **7** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 30 ± 9 µM. Curve fitted using ORIGIN software

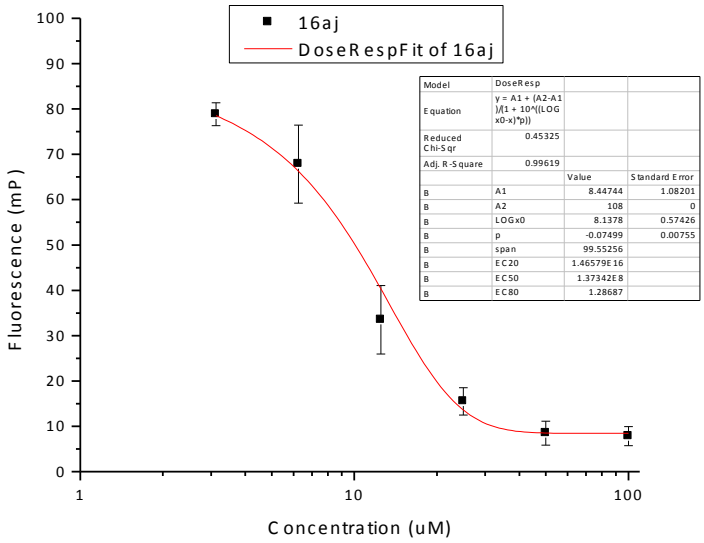


Figure S.3. Competitive binding of **16aj** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 8.1 ± 0.6 µM. Curve fitted using ORIGIN software

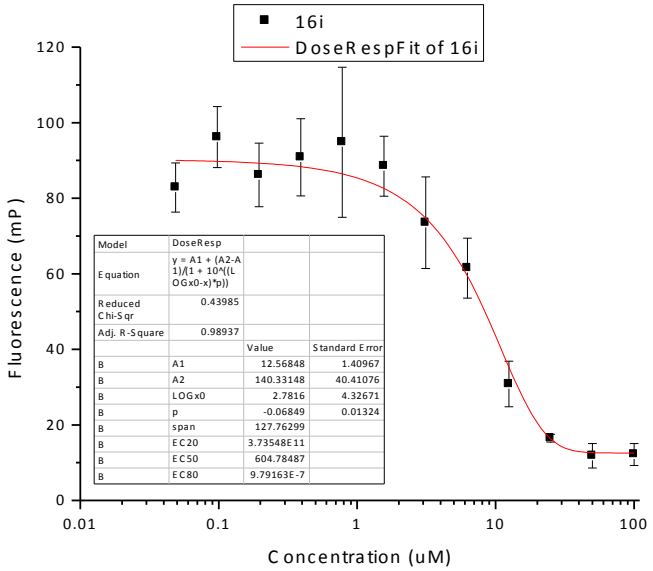


Figure S.4. Competitive binding of **16i** measured by fluorescence polarization assay, with a calculated IC_{50} = 2.8 ± 4.3 µM. Curve fitted using ORIGIN software

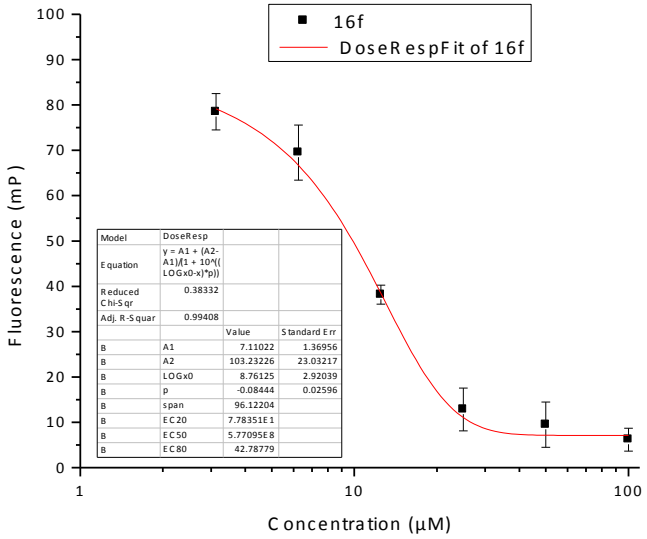


Figure S.5. Competitive binding of **16f** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 8.8 ± 2.9 µM. Curve fitted using ORIGIN software

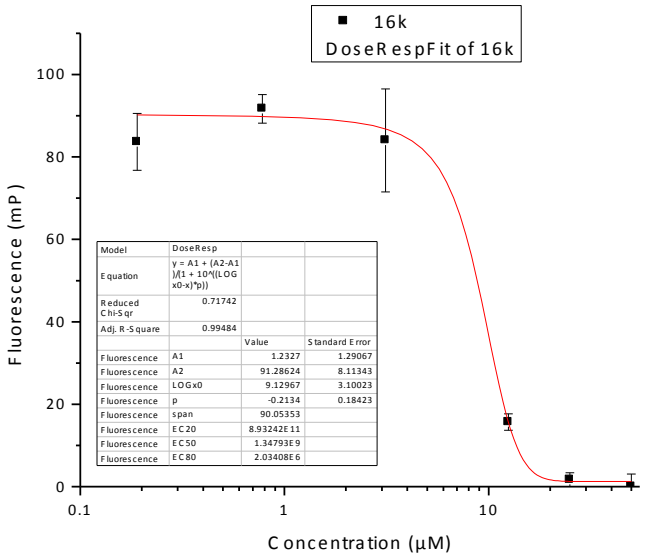


Figure S.6. Competitive binding of **16k** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 9.1 ± 8.1 µM. Curve fitted using ORIGIN software

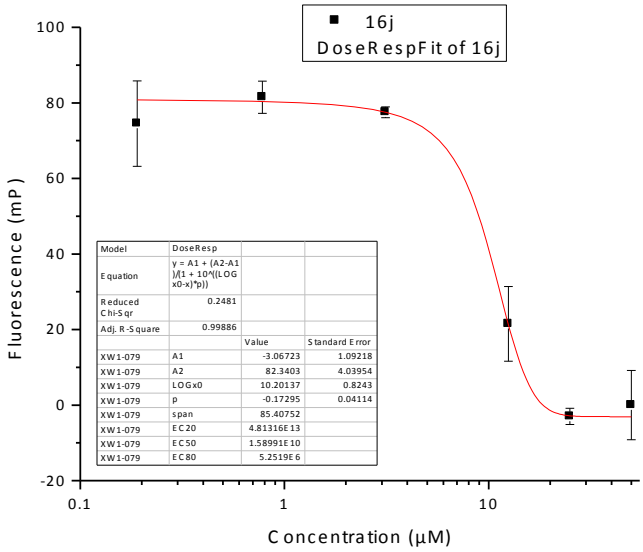


Figure S.7. Competitive binding of **16j** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 10.2 ± 0.8 µM. Curve fitted using ORIGIN software

N-Alkyl-perfluorobenzene Derivatives Fluorescence Polarization Curves

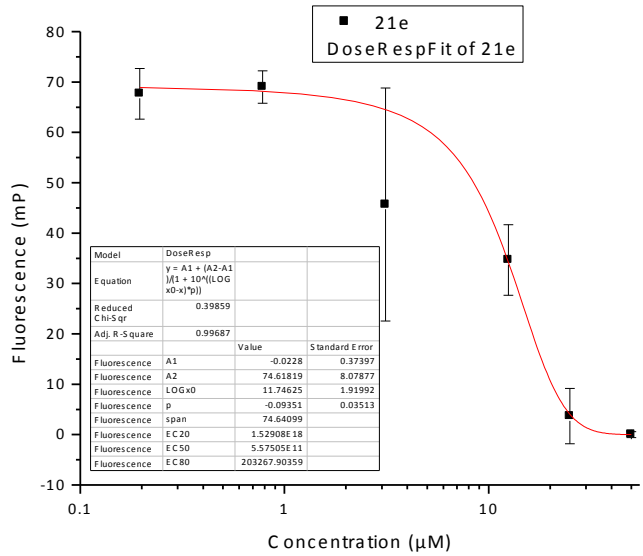


Figure S.8. Competitive binding of **21e** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 11.7 ± 1.9 µM. Curve fitted using ORIGIN software

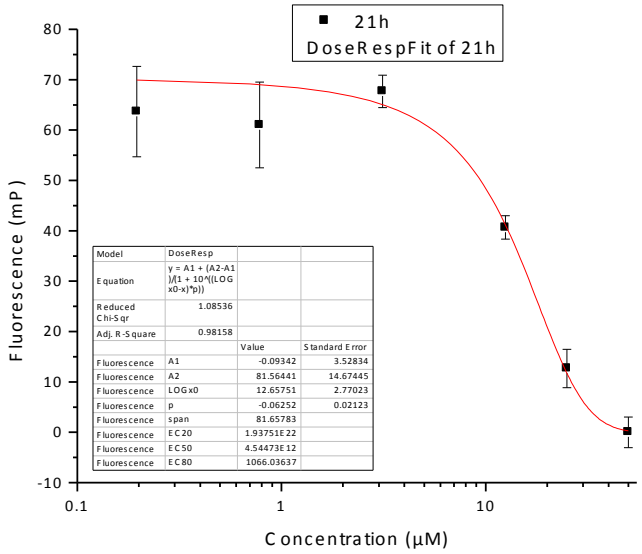


Figure S.9. Competitive binding of **21h** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 12.7 ± 2.8 µM. Curve fitted using ORIGIN software

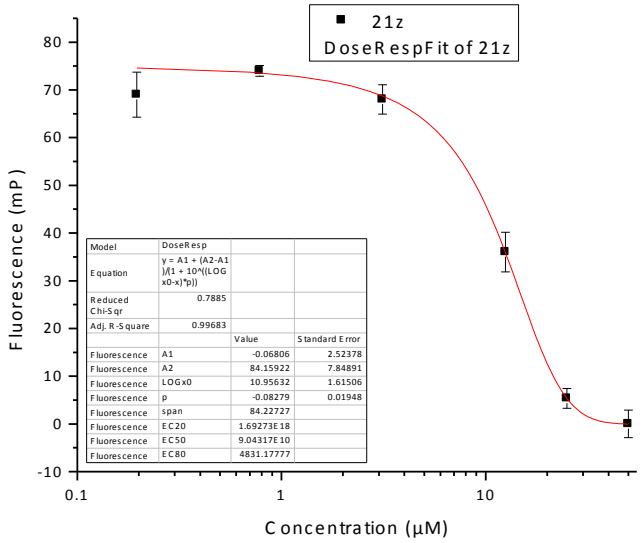


Figure S.10. Competitive binding of **21z** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 11.0 ± 1.6 µM. Curve fitted using ORIGIN software

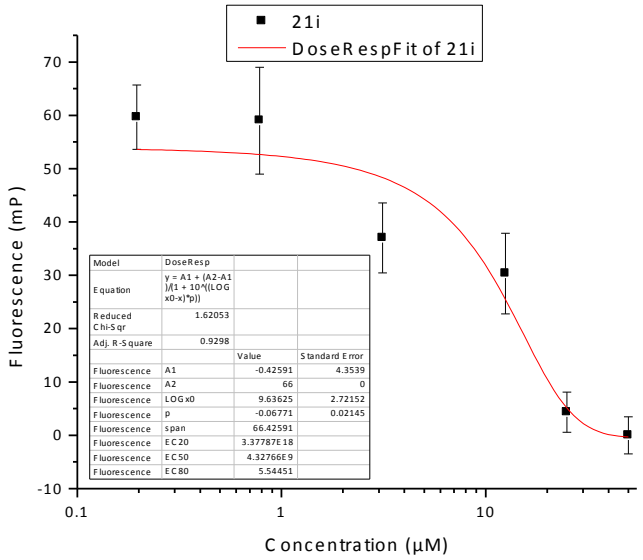


Figure S.11. Competitive binding of **21i** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 9.4 ± 2.7 µM. Curve fitted using ORIGIN software

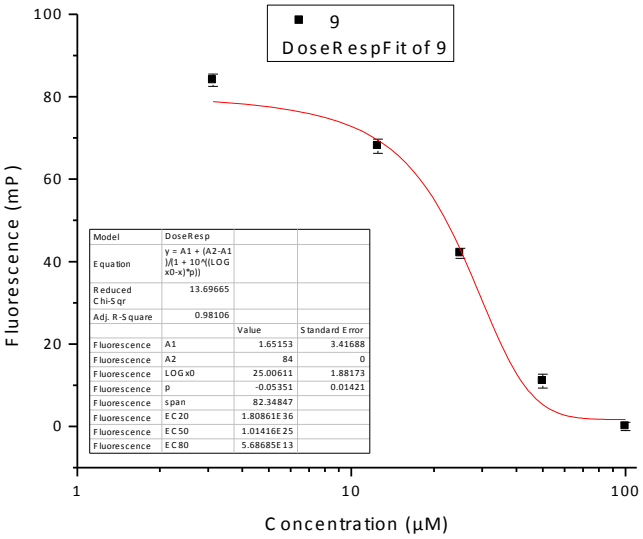


Figure S.12. Competitive binding of **9** measured by fluorescence polarization assay, with a calculated IC_{50} = 25 ± 2 µM. Curve fitted using ORIGIN software

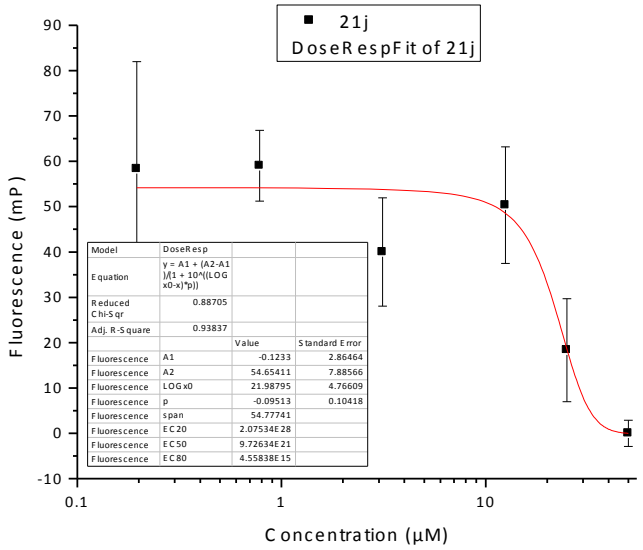


Figure S.13. Competitive binding of **21j** to Stat3 measured by fluorescence polarization assay, with a calculated IC_{50} = 22 ± 5 µM. Curve fitted using ORIGIN software

S.3 MTS Assay AML2, DU145 and MDA468 Representative Plots

MDA-468 (breast), DU145 (prostate) and OCI-AML2 (Leukemia) cells were loaded in 96 well plates at 10 000 cells per well and incubated with various concentration of inhibitor for 72 hours followed by 3 hour incubation with MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium).[15] Relative cell viability (to DMSO control) was determined colorometrically and IC_{50} values determined by fitting to a standard dose response curve.

AML2

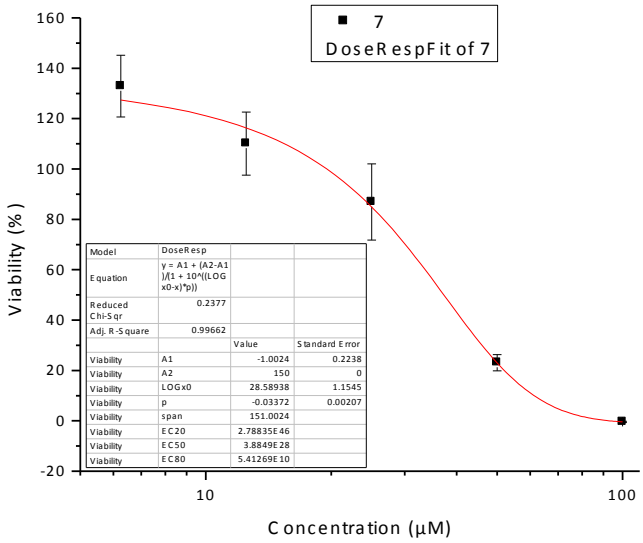


Figure S.14. AML2 cell viability after 72 hour incubation with **7** measured by MTS assay relative to DMSO control: calculated IC_{50} = 29 ± 1 µM, curve fitted using ORIGIN software

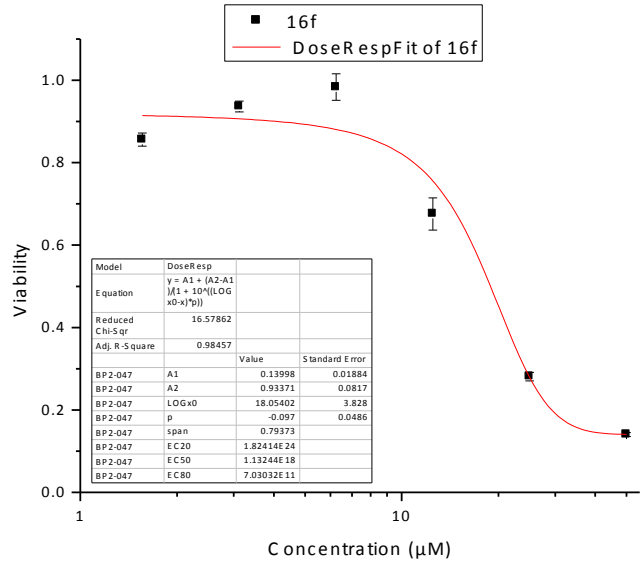


Figure S.15. AML2 cell viability after 72 hour incubation with **16f** measured by MTS assay relative to DMSO control: calculated IC_{50} = 18 ± 4 µM, curve fitted using ORIGIN software

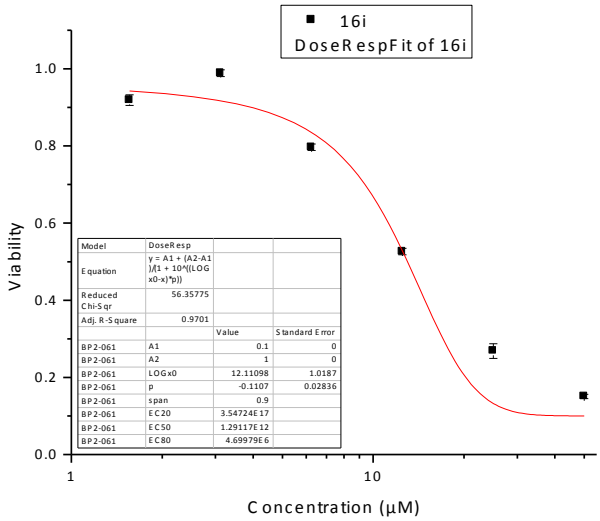


Figure S.16. AML2 cell viability after 72 hour incubation with **16i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 12 ± 1 µM, curve fitted using ORIGIN software

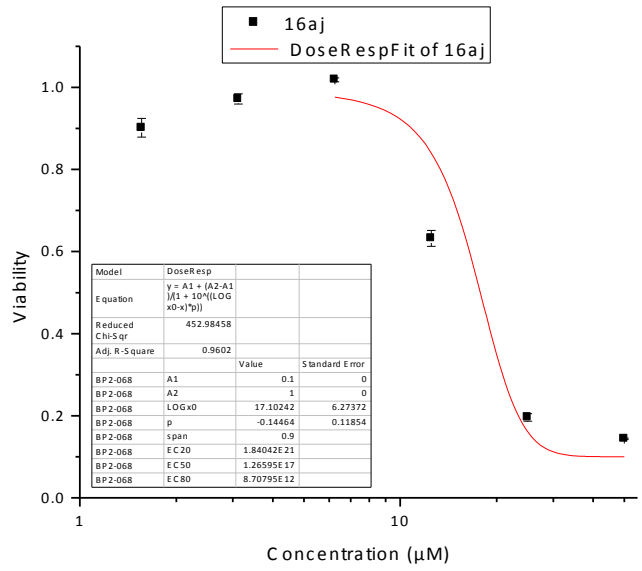


Figure S.17. AML2 cell viability after 72 hour incubation with **16aj** measured by MTS assay

relative to DMSO control: calculated IC_{50} = 17 ± 6 µM, curve fitted using ORIGIN software

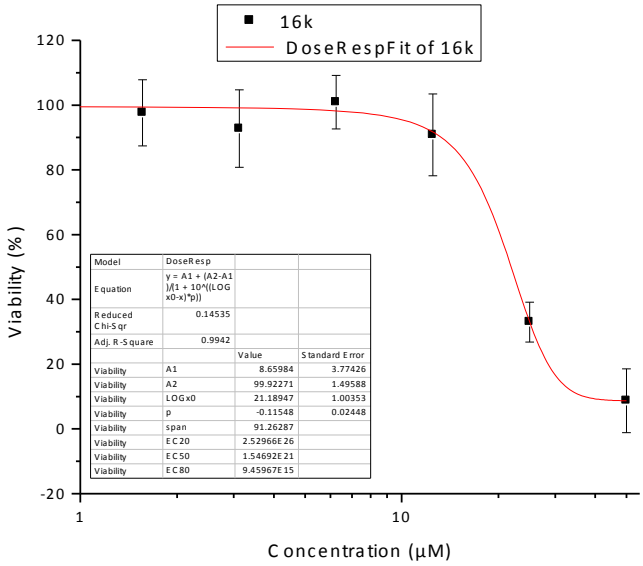


Figure S.18. AML2 cell viability after 72 hour incubation with **16k** measured by MTS assay relative to DMSO control: calculated IC_{50} = 21 ± 1 µM, curve fitted using ORIGIN software

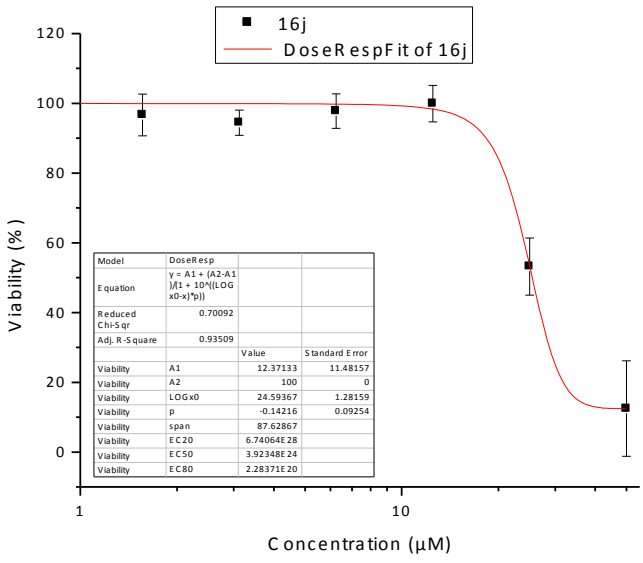


Figure S.19. AML2 cell viability after 72 hour incubation with **16j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 25 ± 1 µM, curve fitted using ORIGIN software

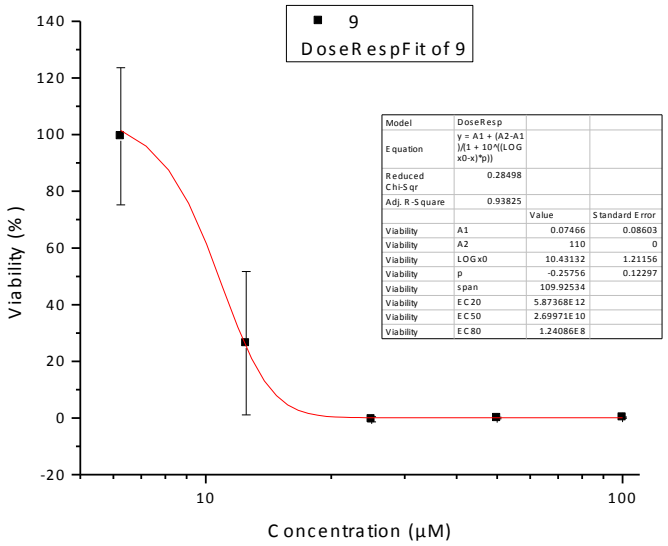


Figure S.20. AML2 cell viability after 72 hour incubation with **9** measured by MTS assay relative to DMSO control: calculated IC_{50} = 10 ± 1 µM, curve fitted using ORIGIN software

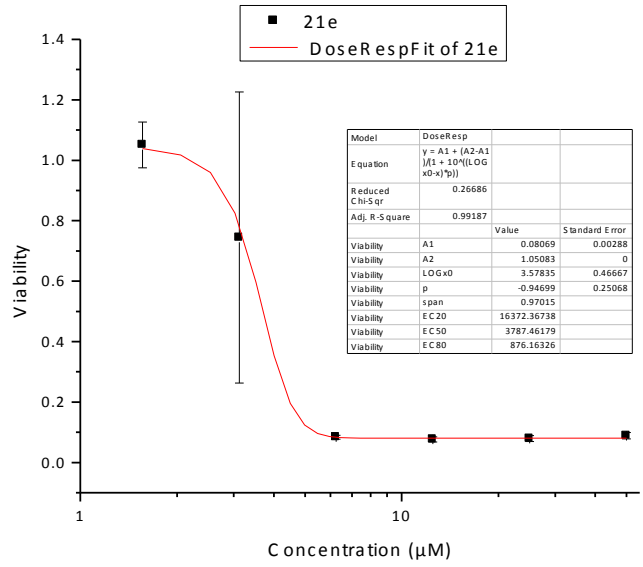


Figure S.21. AML2 cell viability after 72 hour incubation with **21e** measured by MTS assay relative to DMSO control: calculated IC_{50} = 3.6 ± 0.5 µM, curve fitted using ORIGIN software

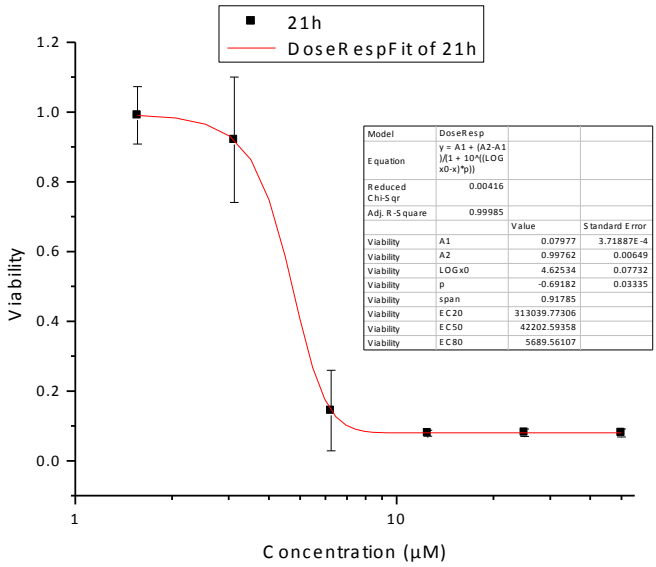


Figure S.22. AML2 cell viability after 72 hour incubation with **21h** measured by MTS assay relative to DMSO control: calculated IC_{50} = 4.6 ± 0.1 µM, curve fitted using ORIGIN software

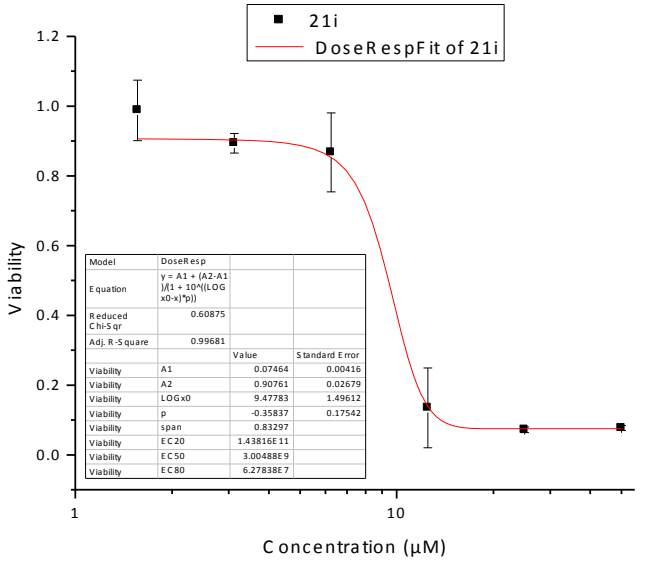


Figure S.23. AML2 cell viability after 72 hour incubation with **21i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 9.5 ± 1.5 µM, curve fitted using ORIGIN software

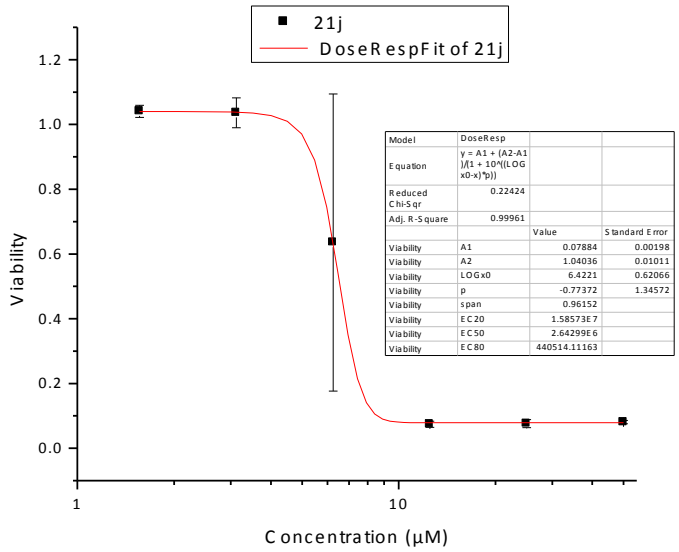


Figure S.24. AML2 cell viability after 72 hour incubation with **21j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 6.4 ± 0.6 µM, curve fitted using ORIGIN software

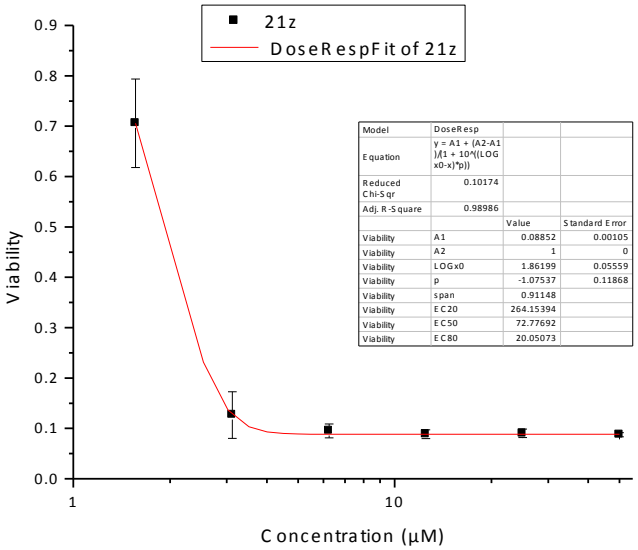


Figure S.25. AML2 cell viability after 72 hour incubation with **21z** measured by MTS assay relative to DMSO control: calculated IC_{50} = 1.9 ± 0.1 µM, curve fitted using ORIGIN software

MDA468 Breast Cancer Cells

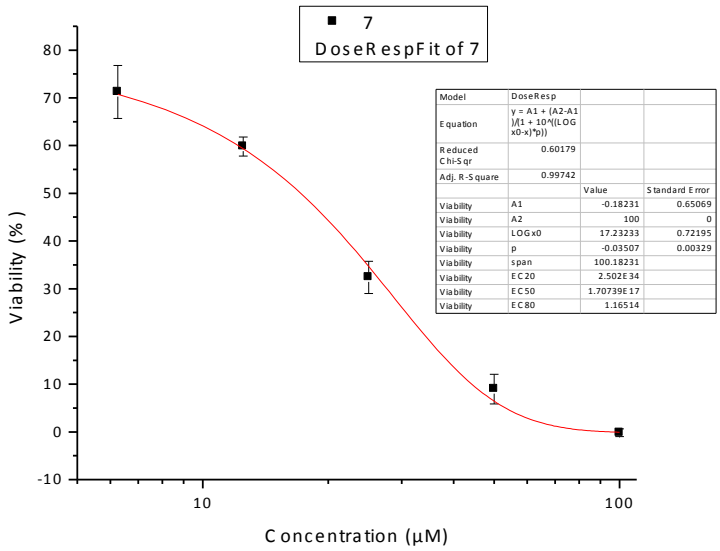


Figure S.26. MDA-468 cell viability after 72 hour incubation with **7** measured by MTS assay relative to DMSO control: calculated IC_{50} = 17 ± 1 µM, curve fitted using ORIGIN software

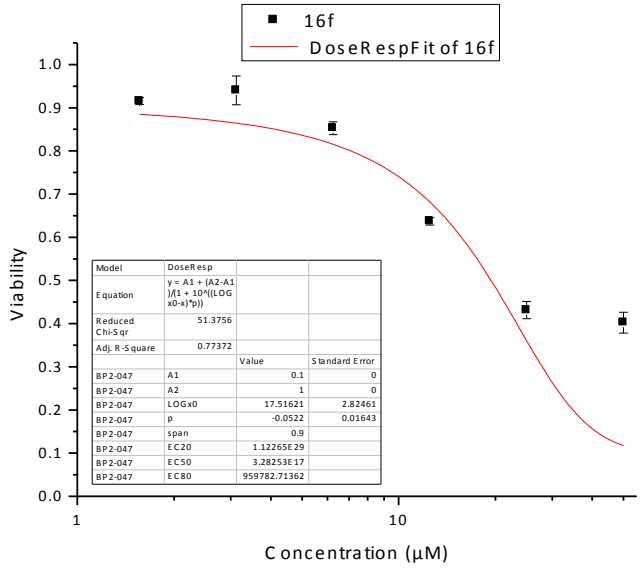
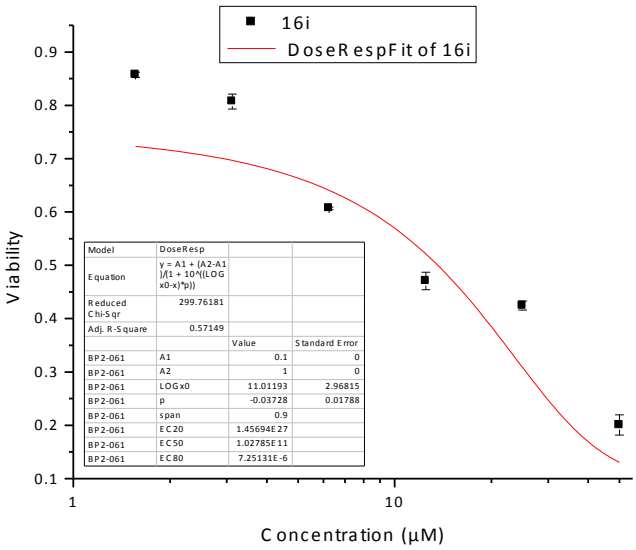
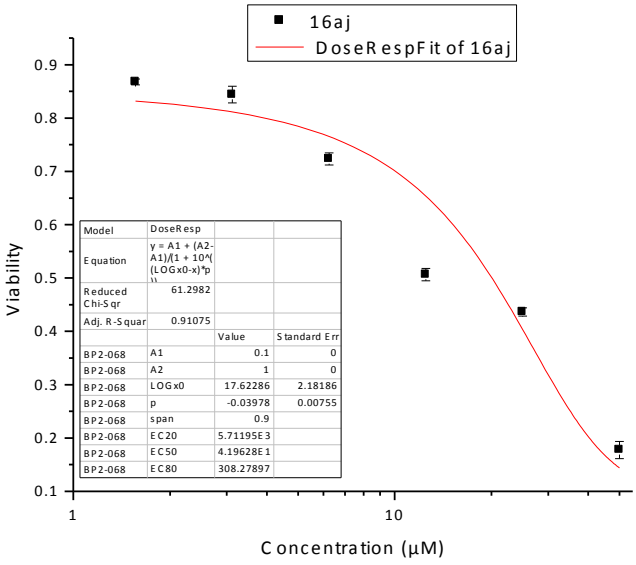


Figure S.27. MDA-468 cell viability after 72 hour incubation with **16f** measured by MTS assay relative to DMSO control: calculated IC_{50} = 17 ± 3 µM, curve fitted using ORIGIN software



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOGx0-x)*p))		
Reduced Chi-Sqr	299.76181		
Adj. R-Square	0.57149		
		Value	Standard Error
BP2-061	A1	0.1	0
BP2-061	A2	1	0
BP2-061	LOGx0	11.01193	2.96815
BP2-061	p	-0.03728	0.01788
BP2-061	span	0.9	
BP2-061	EC20	1.45694E27	
BP2-061	EC50	1.02785E11	
BP2-061	EC80	7.25131E-6	

Figure S.28. MDA-468 cell viability after 72 hour incubation with **16i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 11 ± 3 µM, curve fitted using ORIGIN software



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOGx0-x)*p))		
Reduced Chi-Sqr	61.2982		
Adj. R-Squar	0.91075		
		Value	Standard Err
BP2-068	A1	0.1	0
BP2-068	A2	1	0
BP2-068	LOGx0	17.62286	2.18186
BP2-068	p	-0.03978	0.00755
BP2-068	span	0.9	
BP2-068	EC20	5.71195E3	
BP2-068	EC50	4.19628E1	
BP2-068	EC80	308.27897	

Figure S.29. MDA-468 cell viability after 72 hour incubation with **16aj** measured by MTS assay relative to DMSO control: calculated IC_{50} = 17 ± 2 µM, curve fitted using ORIGIN software

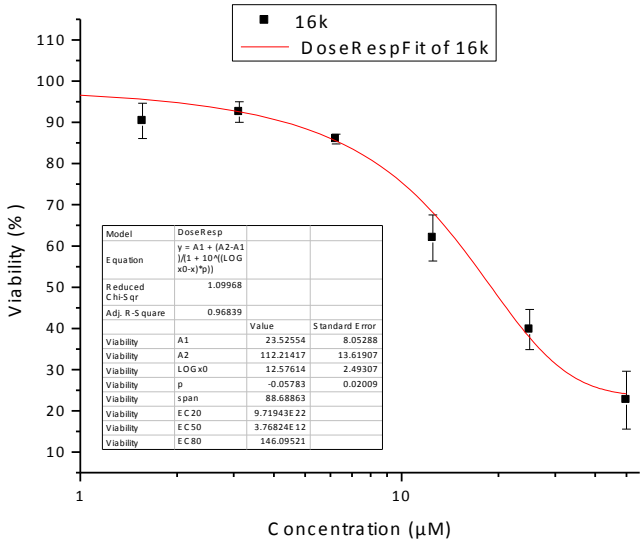


Figure S.30. MDA-468 cell viability after 72 hour incubation with **16k** measured by MTS assay relative to DMSO control: calculated IC_{50} = 13 ± 2 µM, curve fitted using ORIGIN software

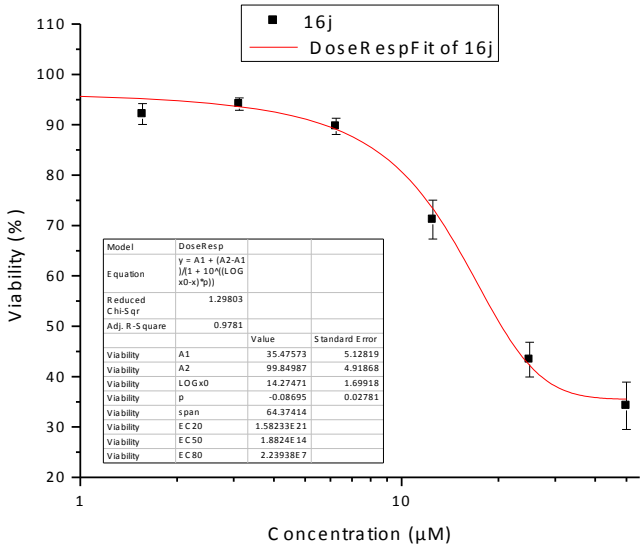


Figure S.31. MDA-468 cell viability after 72 hour incubation with **16j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 14 ± 2 µM, curve fitted using ORIGIN software

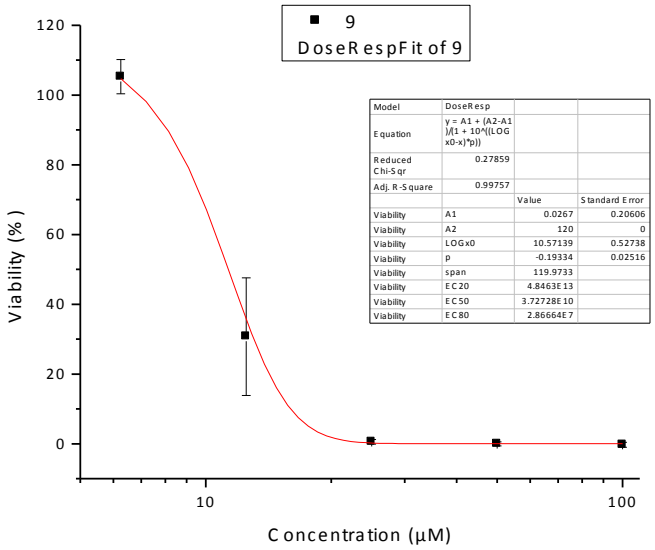


Figure S.32. MDA-468 cell viability after 72 hour incubation with **9** measured by MTS assay relative to DMSO control: calculated IC_{50} = 11 ± 1 µM, curve fitted using ORIGIN software

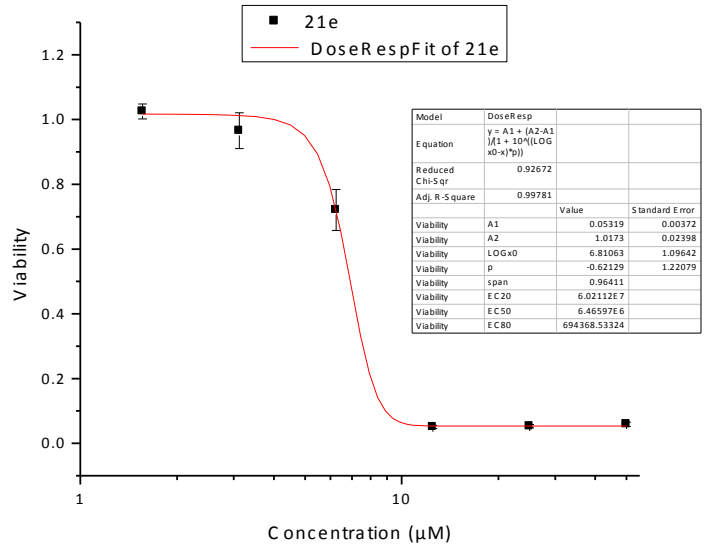


Figure S.33. MDA-468 cell viability after 72 hour incubation with **21e** measured by MTS assay relative to DMSO control: calculated IC_{50} = 6.8 ± 1.1 µM, curve fitted using ORIGIN software

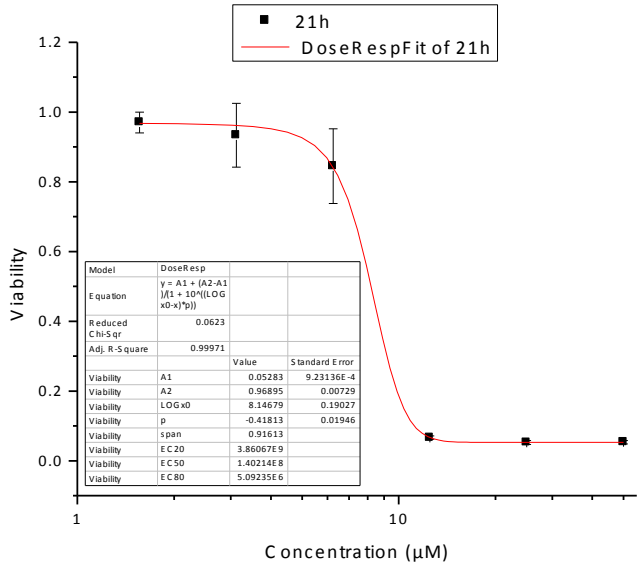


Figure S.34. MDA-468 cell viability after 72 hour incubation with **21h** measured by MTS assay relative to DMSO control: calculated IC_{50} = 8.1 ± 0.2 µM, curve fitted using ORIGIN software

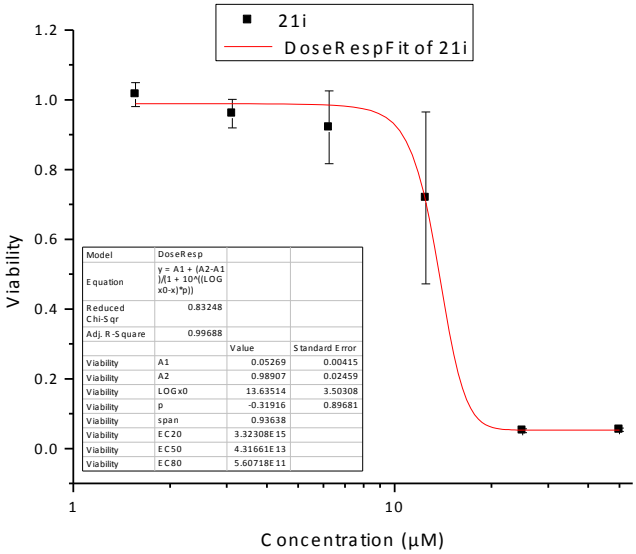
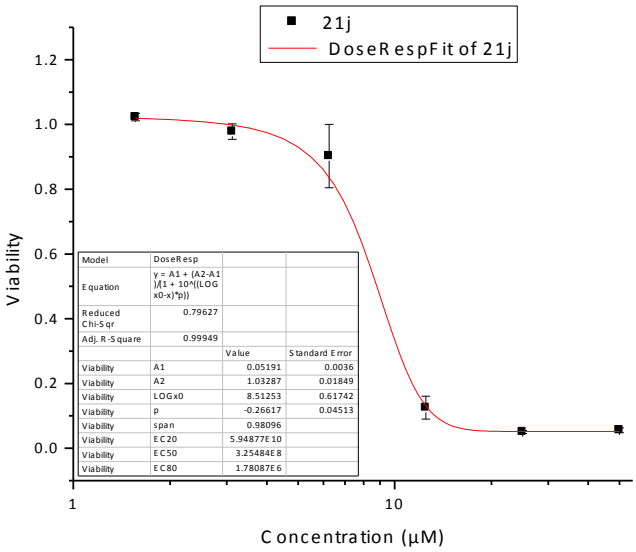
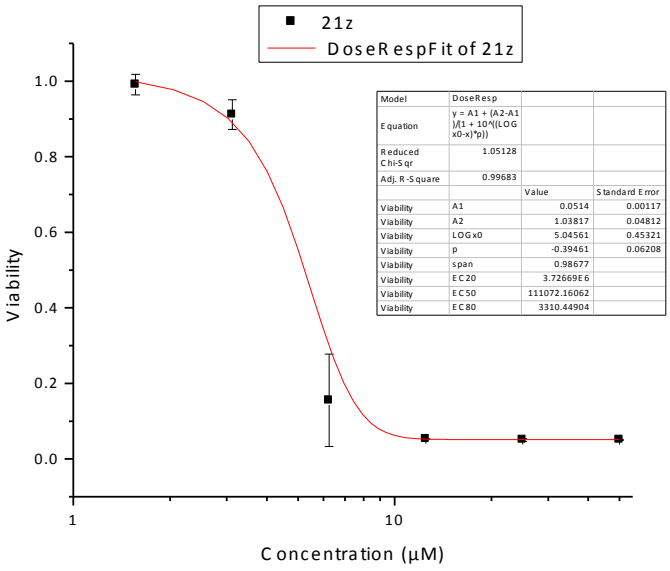


Figure S.35. MDA-468 cell viability after 72 hour incubation with **21i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 13.6 ± 3.5 µM, curve fitted using ORIGIN software



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOG x0-x)*p))		
Reduced Chi-Sqr	0.79627		
Adj. R-Square	0.99949		
		Value	Standard Error
Viability	A1	0.05191	0.0036
Viability	A2	1.03287	0.01849
Viability	LOGx0	8.51253	0.61742
Viability	p	-0.26617	0.04513
Viability	span	0.98096	
Viability	EC20	5.94877E10	
Viability	EC50	3.25484E8	
Viability	EC80	1.78087E6	

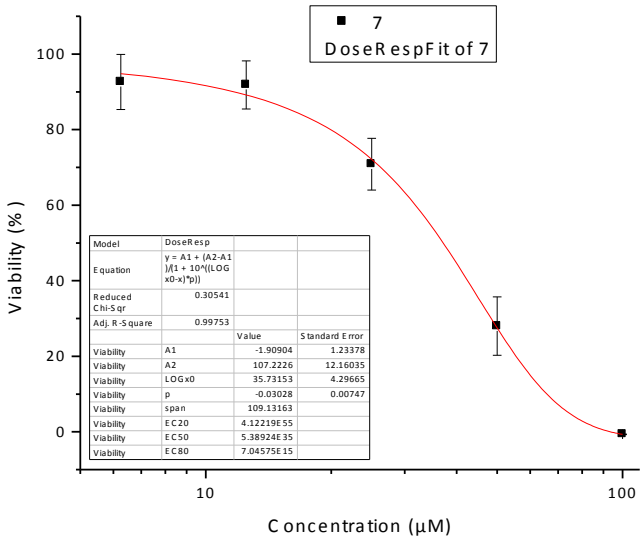
Figure S.36. MDA-468 cell viability after 72 hour incubation with **21j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 8.5 ± 0.6 µM, curve fitted using ORIGIN software



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOG x0-x)*p))		
Reduced Chi-Sqr	1.05128		
Adj. R-Square	0.99683		
		Value	Standard Error
Viability	A1	0.0514	0.00117
Viability	A2	1.03817	0.04812
Viability	LOGx0	5.04561	0.45321
Viability	p	-0.39461	0.06208
Viability	span	0.98677	
Viability	EC20	3.72669E6	
Viability	EC50	111072.16062	
Viability	EC80	3310.44904	

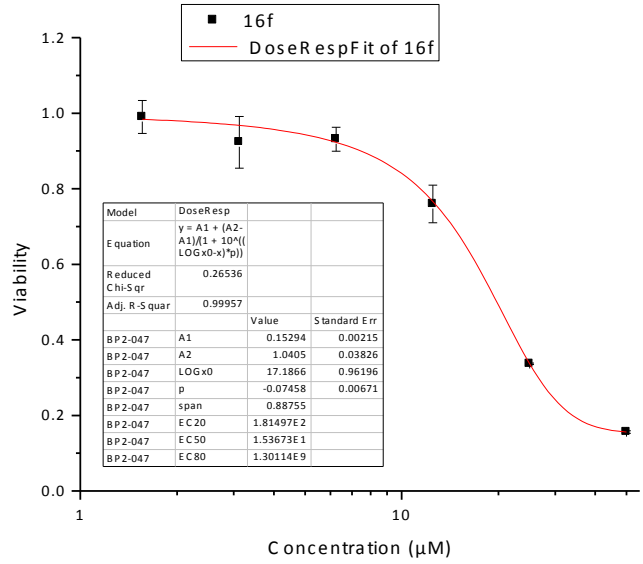
Figure S.37. MDA-468 cell viability after 72 hour incubation with **21z** measured by MTS assay relative to DMSO control: calculated IC_{50} = 5.0 ± 0.5 µM, curve fitted using ORIGIN software

DU145 Prostate Cancer Cells



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOG x0-x)*p))		
Reduced Chi-Sqr	0.30541		
Adj. R-Square	0.99753		
		Value	Standard Error
Viability	A1	-1.90904	1.23378
Viability	A2	107.2226	12.16035
Viability	LOGx0	35.73153	4.29665
Viability	p	-0.03028	0.00747
Viability	span	109.13163	
Viability	EC20	4.12219E55	
Viability	EC50	5.38924E35	
Viability	EC80	7.04575E15	

Figure S.38. DU145 cell viability after 72 hour incubation with **7** measured by MTS assay relative to DMSO control: calculated IC_{50} = 35 ± 4 µM, curve fitted using ORIGIN software



Model	DoseResp		
Equation	y = A1 + (A2-A1)/(1 + 10^((LOGx0-x)*p))		
Reduced Chi-Sqr	0.26536		
Adj. R-Squar	0.99957		
		Value	Standard Err
BP2-047	A1	0.15294	0.00215
BP2-047	A2	1.0405	0.03826
BP2-047	LOGx0	17.1866	0.96196
BP2-047	p	-0.07458	0.00671
BP2-047	span	0.88755	
BP2-047	EC20	1.81497E2	
BP2-047	EC50	1.53673E1	
BP2-047	EC80	1.30114E9	

Figure S.39. DU145 cell viability after 72 hour incubation with **16f** measured by MTS assay relative to DMSO control: calculated IC_{50} = 17 ± 1 µM, curve fitted using ORIGIN software

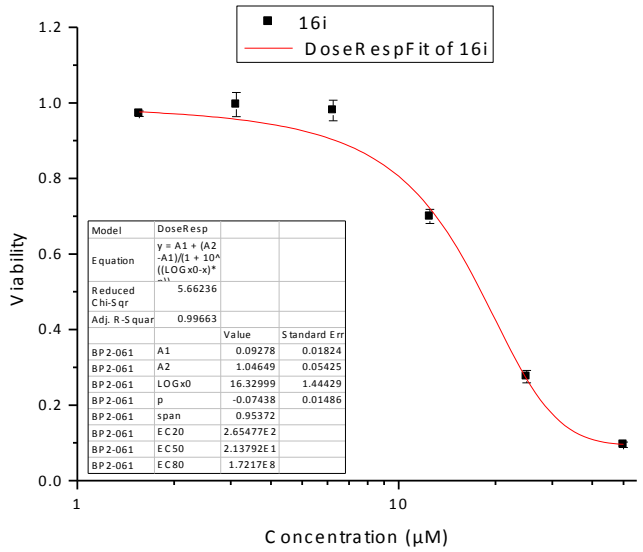


Figure S.40. DU145 cell viability after 72 hour incubation with **16i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 16 ± 1 µM, curve fitted using ORIGIN software

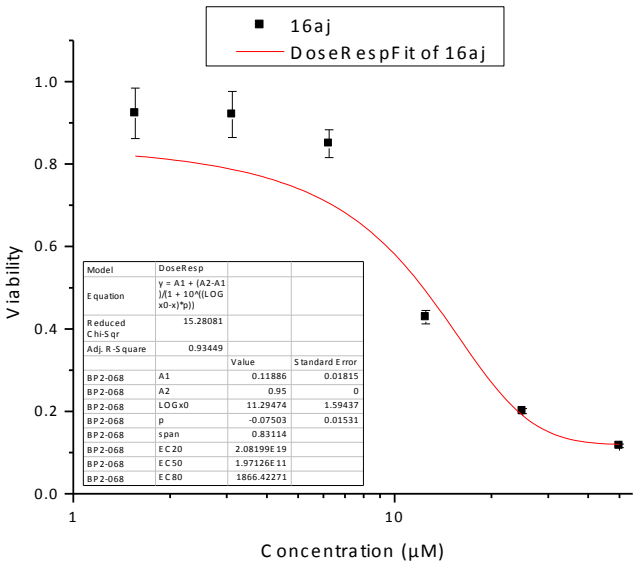


Figure S.41. DU145 cell viability after 72 hour incubation with **16aj** measured by MTS assay relative to DMSO control: calculated IC_{50} = 11 ± 2 µM, curve fitted using ORIGIN software

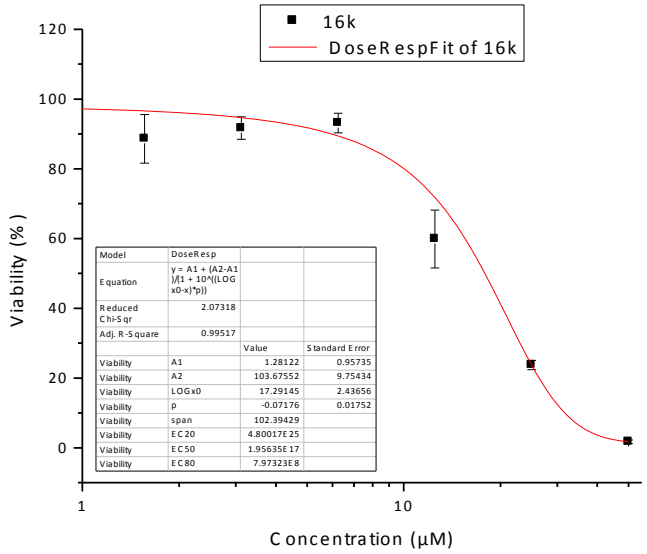


Figure S.42. DU145 cell viability after 72 hour incubation with **16k** measured by MTS assay relative to DMSO control: calculated IC_{50} = 17 ± 2 µM, curve fitted using ORIGIN software

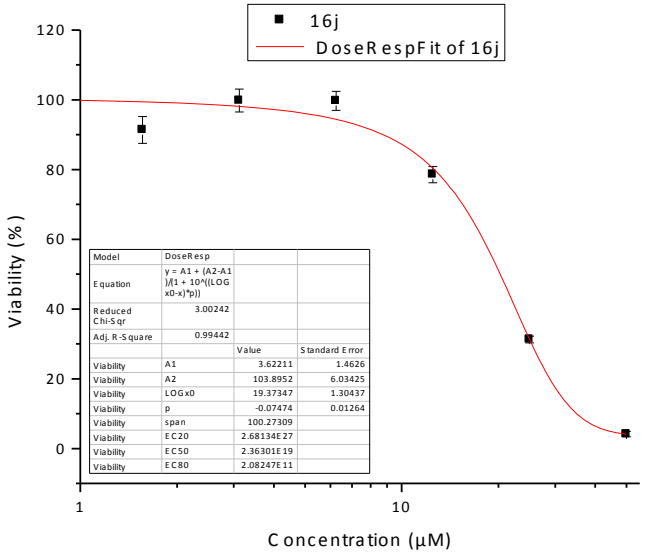


Figure S.43. DU145 cell viability after 72 hour incubation with **16j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 19 ± 1 µM, curve fitted using ORIGIN software

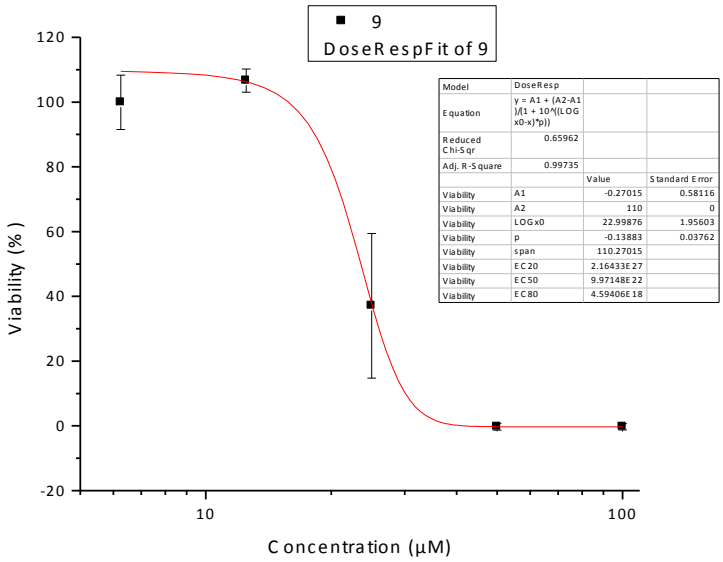


Figure S.44. DU145 cell viability after 72 hour incubation with **9** measured by MTS assay relative to DMSO control: calculated IC_{50} = 23 ± 2 µM, curve fitted using ORIGIN software

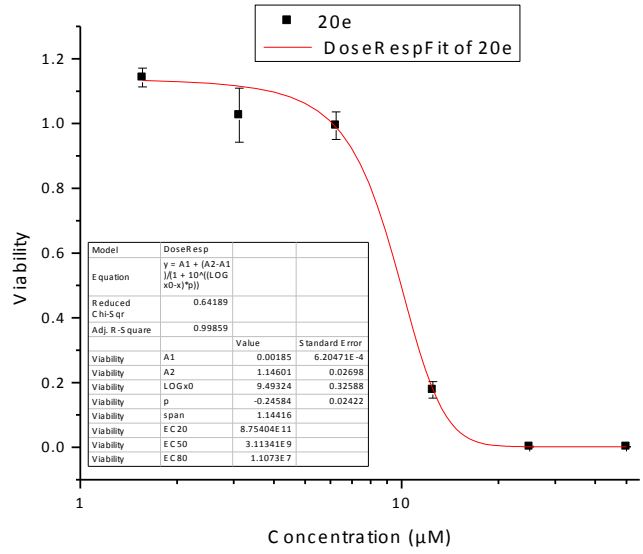


Figure S.45. DU145 cell viability after 72 hour incubation with **20e** measured by MTS assay relative to DMSO control: calculated IC_{50} = 9.5 ± 0.3 µM, curve fitted using ORIGIN software

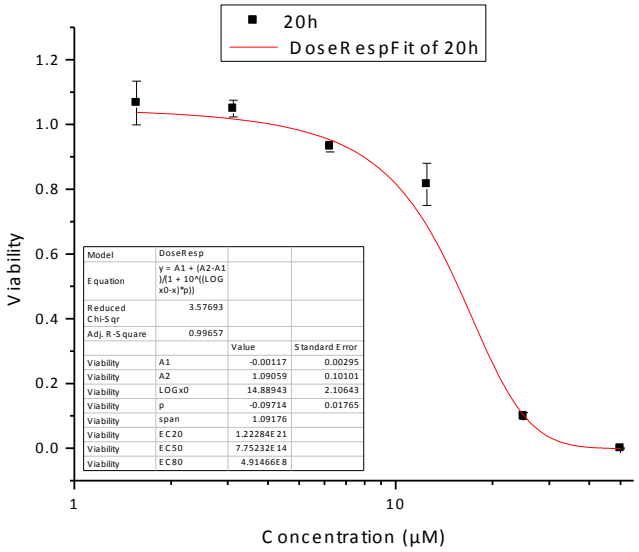


Figure S.46. DU145 cell viability after 72 hour incubation with **20h** measured by MTS assay relative to DMSO control: calculated IC_{50} = 14 ± 2 µM, curve fitted using ORIGIN software

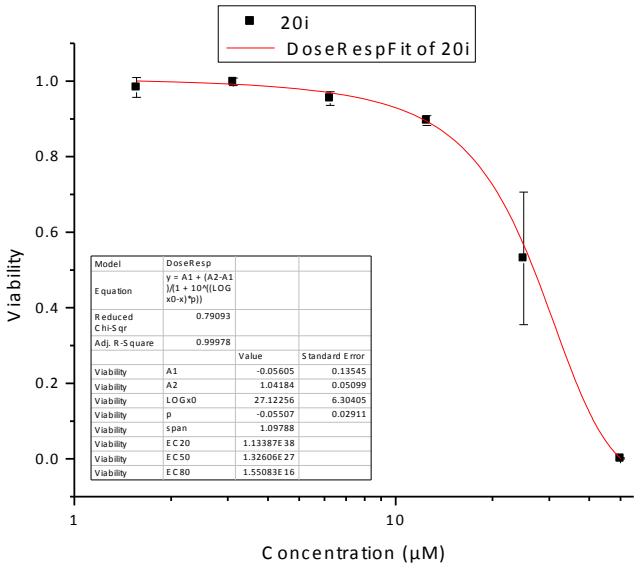


Figure S.47. DU145 cell viability after 72 hour incubation with **20i** measured by MTS assay relative to DMSO control: calculated IC_{50} = 27 ± 6 µM, curve fitted using ORIGIN software

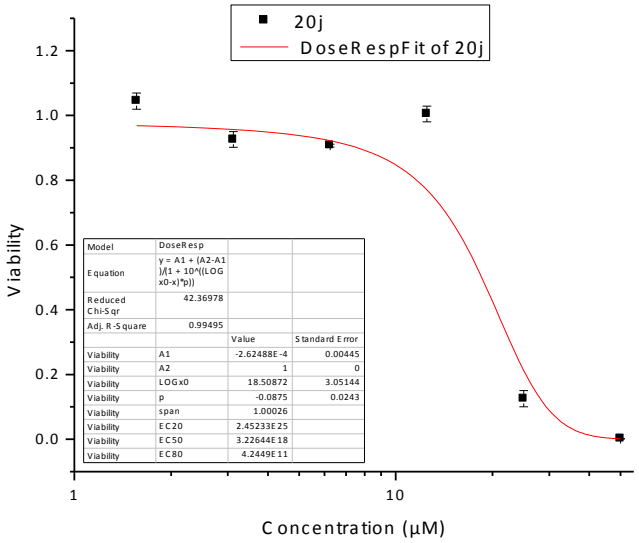


Figure S.48. DU145 cell viability after 72 hour incubation with **20j** measured by MTS assay relative to DMSO control: calculated IC_{50} = 19 ± 3 µM, curve fitted using ORIGIN software

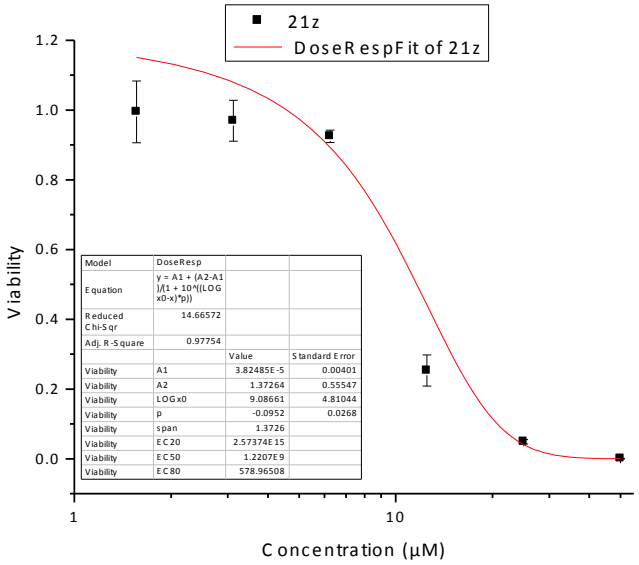


Figure S.49. DU145 cell viability after 72 hour incubation with **21z** measured by MTS assay relative to DMSO control: calculated IC_{50} = 9.1 ± 4.8 µM, curve fitted using ORIGIN software

S.4 Western Blot Protocol

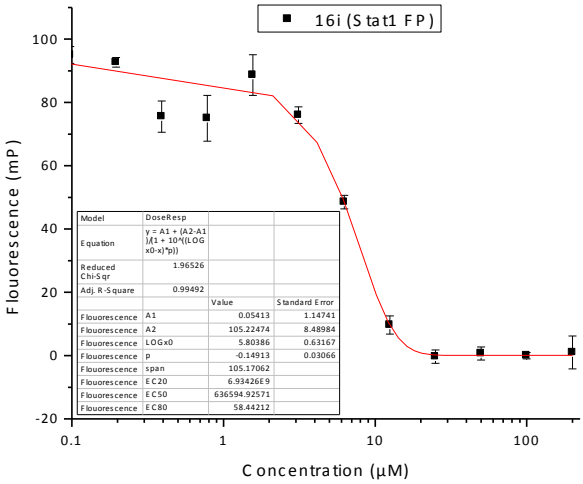
Cell pellets were lysed by incubation on ice for 30 minutes in lysis buffer (50mM Tris-HCl, 1mM EDTA, 1% NP-40, 150 mM NaCl, 1 mM Na_3VO_4, 1 mM phenylmethylsulfonyl fluoride and protease inhibitor cocktail from Roche) and exposure to one freeze/thaw cycle. Cell lysates were centrifuged at 14000 rpm for 15 minutes and supernatants were subsequently collected to quantify protein concentration. Equal amounts of protein were fractionated by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) and transferred to PVDF membranes. Membranes were probed with indicated primary antibodies, then HRP-conjugated secondary antibodies were used for detection of protein signals and membranes developed by Western Lightning^{TM} Plus-ECL (Perkin Elmer).

S.5 Luciferase Reporter Assay

Reporter constructs were introduced to HMCLs by lentivirus infection and selected with Puromycin/Hygromycin for two weeks to obtain stable clones. The indicated HMCLs were treated with various concentrations of **16i** and **21h** for 6 hours and lysed for subsequent use in a Dual-Luciferase^{R} Reporter Assay System (Promega).

S.6 STAT Isoform Selectivity

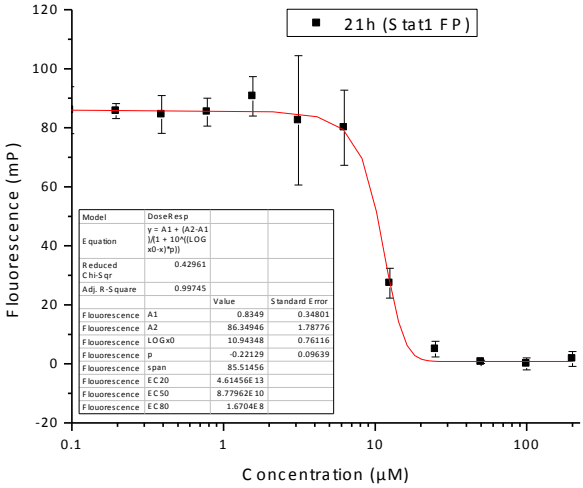
A fluorescence polarization assay with Stat1 was conducted with lead inhibitors **16i** and **21h** to investigate isoform selectivity (as previously reported).[2] Data plots and IC_{50} values are shown below.



Isoform Selectivity for **16i** (FP assay)

Stat1 IC_{50} = 5.8 ± 0.6 µM

Stat3 IC_{50} = 2.8 ± 4.3 µM



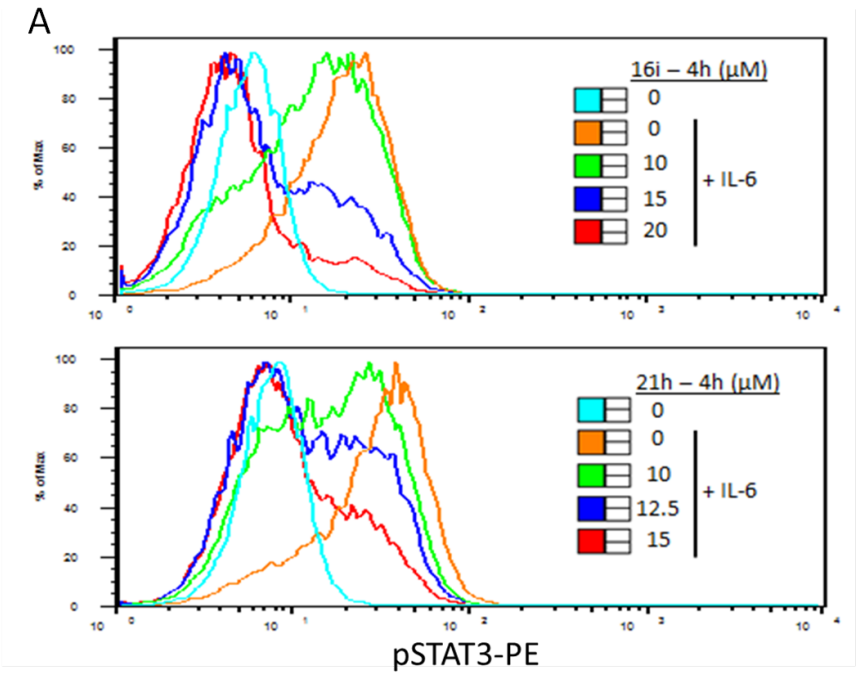
Isoform Selectivity for **21h** (FP assay)

Stat1 IC_{50} = 10.9 ± 0.8 µM

Stat3 IC_{50} = 12.8 ± 2.8 µM

Phosphoflow Cytometry

To determine cellular STAT isoform selectivity, U937 cells were starved overnight in serum free media, 0.3 mL cells / tube. Inhibitors were added at indicated concentrations and incubated for 4 hours at 37 °C. Cells were then split into 3 tubes, 0.1 mL cells / tube. Stimulated with 20 unit IFN gamma, 10 ng hIL6 or 1 ng hGM-CSF and incubated for 10-15 minutes before fixing the cells using 40 µL of 10 % formaldehyde solution. Cells were fixed for 10 minutes at room temperature then ice cold methanol was added dropwise to each tube while vortexing. After cooling for 30 minutes over ice, the methanol was removed and cells were washed with PBS+3% FCS (washing buffer) then stained with pStat5 PE for GM-CSF stimulated samples, pStat3 PE for IL6 stimulated samples, pStat1 Alexafluor® 488 for IFN gamma stimulated samples. (All antibodies are from BD Biosciences). Samples were run on FaCSCalibur and analysed by Flowjo.



B

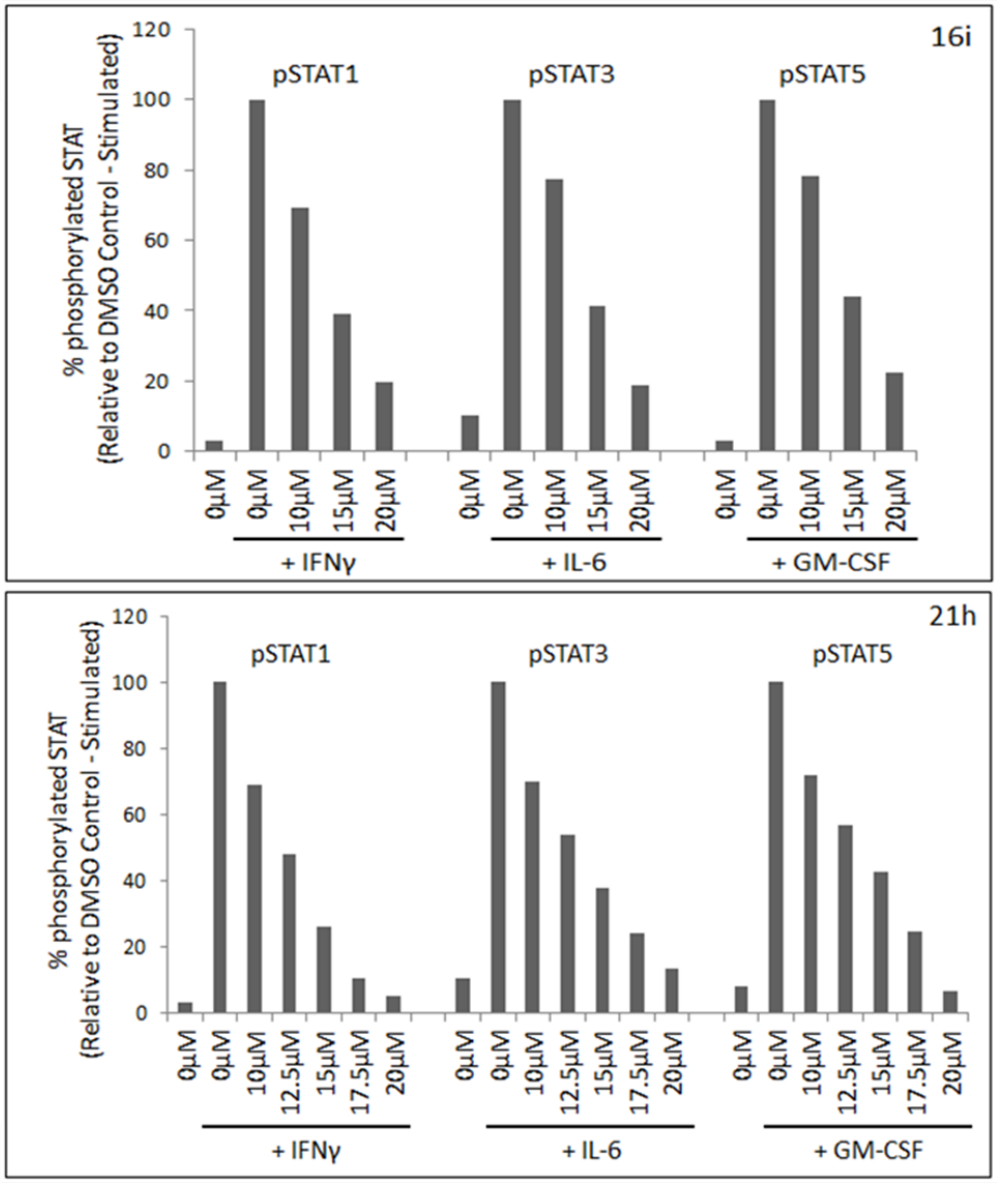


Figure S50. Analysis of **16i** and **21h** selectivity for cytokine-induced STAT phosphorylation. Serum-starved U937 cells were treated with **16i** or **21h** for 4 h prior to stimulation with indicated cytokine for 15 minutes. (A) Representative histograms from phospho-flow cytometric analysis of IL-6-induced Stat3 phosphorylation reveals that both **16i** (upper) and **21h** (lower) abrogate IL-6-stimulated pStat3. (B) Graphical comparison of **16i** and **21h** selectivity for inhibiting Stat1, 3, and 5 phosphorylation as assessed by phospho-flow cytometry.

S.7 Evaluation of 16i in KINOMEscan™

KINOMEscan™ was performed by discoverx Lead Hunter Discovery Services according to their established protocols. Compound **16i** was screened at 5 μM against 132 kinase targets including 37 with SH2 domains. The KINOMEscan™ is designed to indentify molecules that bind to kinases at the active site or allosterically to prevent kinase activity. A full list of kinases included in this screen and percentage activity upon treatment with **16i** at 5 μM can be found below.

KINOMEscan Gene Symbol	Entrez Gene Symbol	Percent Control
ABL1(E255K)-phosphorylated	ABL1	100
ABL1(F317I)-nonphosphorylated	ABL1	86
ABL1(F317I)-phosphorylated	ABL1	100
ABL1(F317L)-nonphosphorylated	ABL1	89
ABL1(F317L)-phosphorylated	ABL1	100
ABL1(H396P)-nonphosphorylated	ABL1	77
ABL1(H396P)-phosphorylated	ABL1	86
ABL1(M351T)-phosphorylated	ABL1	100
ABL1(Q252H)-nonphosphorylated	ABL1	80
ABL1(Q252H)-phosphorylated	ABL1	99
ABL1(T315I)-nonphosphorylated	ABL1	77
ABL1(T315I)-phosphorylated	ABL1	100
ABL1(Y253F)-phosphorylated	ABL1	98
ABL1-nonphosphorylated	ABL1	72
ABL1-phosphorylated	ABL1	79
ABL2	ABL2	66
ALK	ALK	100
ALK(C1156Y)	ALK	98
ALK(L1196M)	ALK	100
AXL	AXL	76
BLK	BLK	92
BMX	BMX	100
BRK	PTK6	96
BTK	BTK	77
CSF1R	CSF1R	82
CSF1R-autoinhibited	CSF1R	100

CSK	CSK	95
CTK	MATK	60
DDR1	DDR1	92
DDR2	DDR2	91
EGFR	EGFR	70
EGFR(E746-A750del)	EGFR	93
EGFR(G719C)	EGFR	72
EGFR(G719S)	EGFR	100
EGFR(L747-E749del, A750P)	EGFR	67
EGFR(L747-S752del, P753S)	EGFR	100
EGFR(L747-T751del,Sins)	EGFR	77
EGFR(L858R)	EGFR	70
EGFR(L858R,T790M)	EGFR	82
EGFR(L861Q)	EGFR	95
EGFR(S752-I759del)	EGFR	92
EGFR(T790M)	EGFR	100
EPHA1	EPHA1	97
EPHA2	EPHA2	86
EPHA3	EPHA3	98
EPHA4	EPHA4	93
EPHA5	EPHA5	82
EPHA6	EPHA6	95
EPHA7	EPHA7	81
EPHA8	EPHA8	93
EPHB1	EPHB1	100
EPHB2	EPHB2	100
EPHB3	EPHB3	91
EPHB4	EPHB4	88
EPHB6	EPHB6	85
ERBB2	ERBB2	90
ERBB3	ERBB3	61
ERBB4	ERBB4	93
FAK	PTK2	68
FER	FER	80
FES	FES	100
FGFR1	FGFR1	75
FGFR2	FGFR2	82
FGFR3	FGFR3	83
FGFR3(G697C)	FGFR3	96
FGFR4	FGFR4	91
FGR	FGR	97
FLT1	FLT1	75
FLT3	FLT3	100

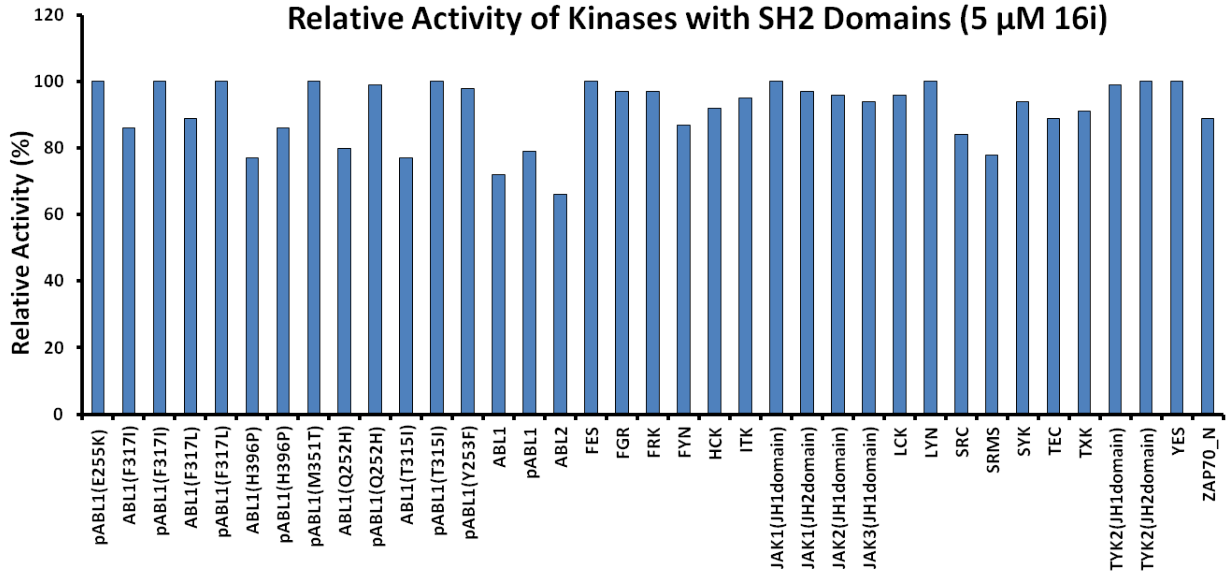
FLT3(D835H)	FLT3	78
FLT3(D835Y)	FLT3	72
FLT3(ITD)	FLT3	98
FLT3(K663Q)	FLT3	98
FLT3(N841I)	FLT3	46
FLT3(R834Q)	FLT3	90
FLT3-autoinhibited	FLT3	100
FLT4	FLT4	91
FRK	FRK	97
FYN	FYN	87
HCK	HCK	92
IGF1R	IGF1R	74
INSR	INSR	92
INSRR	INSRR	86
ITK	ITK	95
JAK1(JH1domain-catalytic)	JAK1	100
JAK1(JH2domain-pseudokinase)	JAK1	97
JAK2(JH1domain-catalytic)	JAK2	96
JAK3(JH1domain-catalytic)	JAK3	94
KIT	KIT	100
KIT(A829P)	KIT	91
KIT(D816H)	KIT	90
KIT(D816V)	KIT	88
KIT(L576P)	KIT	95
KIT(V559D)	KIT	100
KIT(V559D,T670I)	KIT	80
KIT(V559D,V654A)	KIT	93
KIT-autoinhibited	KIT	100
LCK	LCK	96
LTK	LTK	100
LYN	LYN	100
MERTK	MERTK	100
MET	MET	65
MET(M1250T)	MET	77
MET(Y1235D)	MET	100
MST1R	MST1R	96
MUSK	MUSK	92
PDGFRA	PDGFRA	100
PDGFRB	PDGFRB	100
PYK2	PTK2B	100
RET	RET	99
RET(M918T)	RET	90
RET(V804L)	RET	85

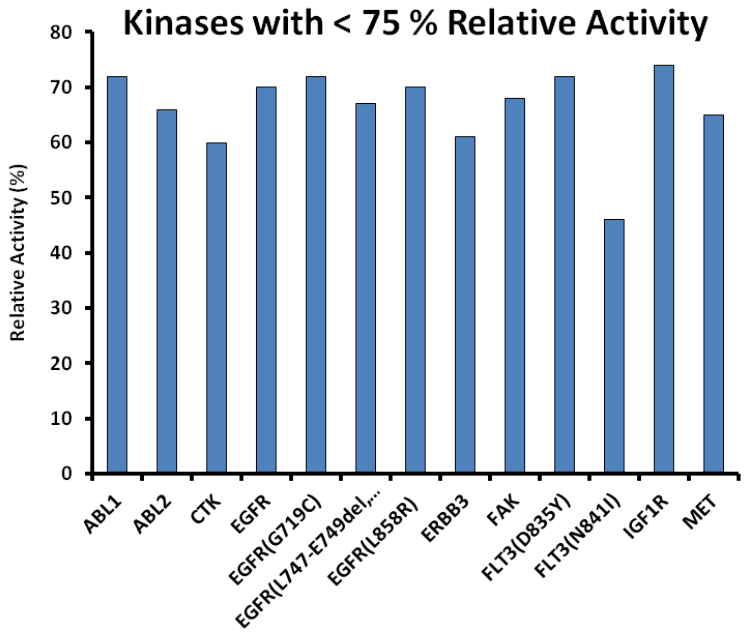
RET(V804M)	RET	100
ROS1	ROS1	93
SRC	SRC	84
SRMS	SRMS	78
SYK	SYK	94
TEC	TEC	89
TIE1	TIE1	89
TIE2	TEK	100
TNK1	TNK1	88
TNK2	TNK2	92
TRKA	NTRK1	100
TRKB	NTRK2	95
TRKC	NTRK3	95
TXK	TXK	91
TYK2(JH1domain-catalytic)	TYK2	99
TYK2(JH2domain-pseudokinase)	TYK2	100
TYRO3	TYRO3	98
VEGFR2	KDR	100
YES	YES1	100
ZAP70	ZAP70	89
ABL1(E255K)-phosphorylated	ABL1	70
ABL1(F317I)-nonphosphorylated	ABL1	79
ABL1(F317I)-phosphorylated	ABL1	85
ABL1(F317L)-nonphosphorylated	ABL1	82
ABL1(F317L)-phosphorylated	ABL1	100
ABL1(H396P)-nonphosphorylated	ABL1	80
ABL1(H396P)-phosphorylated	ABL1	67
ABL1(M351T)-phosphorylated	ABL1	90
ABL1(Q252H)-nonphosphorylated	ABL1	75
ABL1(Q252H)-phosphorylated	ABL1	81
ABL1(T315I)-nonphosphorylated	ABL1	77
ABL1(T315I)-phosphorylated	ABL1	95
ABL1(Y253F)-phosphorylated	ABL1	85
ABL1-nonphosphorylated	ABL1	75
ABL1-phosphorylated	ABL1	61
ABL2	ABL2	95
ALK	ALK	91
ALK(C1156Y)	ALK	100
ALK(L1196M)	ALK	100

AXL	AXL	74
BLK	BLK	76
BMX	BMX	78
BRK	PTK6	82
BTK	BTK	81
CSF1R	CSF1R	100
CSF1R-autoinhibited	CSF1R	85
CSK	CSK	94
CTK	MATK	76
DDR1	DDR1	75
DDR2	DDR2	86
EGFR	EGFR	81
EGFR(E746-A750del)	EGFR	91
EGFR(G719C)	EGFR	69
EGFR(G719S)	EGFR	100
EGFR(L747-E749del, A750P)	EGFR	72
EGFR(L747-S752del, P753S)	EGFR	97
EGFR(L747-T751del,Sins)	EGFR	85
EGFR(L858R)	EGFR	68
EGFR(L858R,T790M)	EGFR	74
EGFR(L861Q)	EGFR	97
EGFR(S752-I759del)	EGFR	95
EGFR(T790M)	EGFR	100
EPHA1	EPHA1	78
EPHA2	EPHA2	79
EPHA3	EPHA3	100
EPHA4	EPHA4	79
EPHA5	EPHA5	92
EPHA6	EPHA6	82
EPHA7	EPHA7	80
EPHA8	EPHA8	85
EPHB1	EPHB1	74
EPHB2	EPHB2	90
EPHB3	EPHB3	77
EPHB4	EPHB4	78
EPHB6	EPHB6	81
ERBB2	ERBB2	84
ERBB3	ERBB3	74
ERBB4	ERBB4	82
FAK	PTK2	90
FER	FER	50
FES	FES	88
FGFR1	FGFR1	90

FGFR2	FGFR2	76
FGFR3	FGFR3	73
FGFR3(G697C)	FGFR3	90
FGFR4	FGFR4	87
FGR	FGR	82
FLT1	FLT1	91
FLT3	FLT3	87
FLT3(D835H)	FLT3	61
FLT3(D835Y)	FLT3	67
FLT3(ITD)	FLT3	92
FLT3(K663Q)	FLT3	87
FLT3(N841I)	FLT3	42
FLT3(R834Q)	FLT3	89
FLT3-autoinhibited	FLT3	100
FLT4	FLT4	81
FRK	FRK	94
FYN	FYN	79
HCK	HCK	91
IGF1R	IGF1R	66
INSR	INSR	99
INSRR	INSRR	79
ITK	ITK	98
JAK1(JH1domain-catalytic)	JAK1	100
JAK1(JH2domain-pseudokinase)	JAK1	80
JAK2(JH1domain-catalytic)	JAK2	97
JAK3(JH1domain-catalytic)	JAK3	78
KIT	KIT	97
KIT(A829P)	KIT	57
KIT(D816H)	KIT	83
KIT(D816V)	KIT	80
KIT(L576P)	KIT	97
KIT(V559D)	KIT	92
KIT(V559D,T670I)	KIT	100
KIT(V559D,V654A)	KIT	82
KIT-autoinhibited	KIT	93
LCK	LCK	90
LTK	LTK	96
LYN	LYN	86
MERTK	MERTK	95
MET	MET	64
MET(M1250T)	MET	93
MET(Y1235D)	MET	99
MST1R	MST1R	63

MUSK	MUSK	80
PDGFRA	PDGFRA	100
PDGFRB	PDGFRB	92
PYK2	PTK2B	73
RET	RET	90
RET(M918T)	RET	85
RET(V804L)	RET	87
RET(V804M)	RET	91
ROS1	ROS1	96
SRC	SRC	85
SRMS	SRMS	70
SYK	SYK	100
TEC	TEC	94
TIE1	TIE1	82
TIE2	TEK	78
TNK1	TNK1	67
TNK2	TNK2	68
TRKA	NTRK1	93
TRKB	NTRK2	82
TRKC	NTRK3	81
TXK	TXK	88
TYK2(JH1domain-catalytic)	TYK2	100
TYK2(JH2domain-pseudokinase)	TYK2	91
TYRO3	TYRO3	75
VEGFR2	KDR	100
YES	YES1	74
ZAP70	ZAP70	91





S.8 Evaluation of compounds in MM patient samples

BM aspirates were obtained from MM patients with consent under a protocol approved by the Research Ethic Board of University Health Network, Toronto, Canada. Mononuclear cells (MNC) from MM patients were obtained by Ficoll-Paque separation of 6 patient derived bone marrow aspirates. Samples were cultured and treated with **16i** followed by staining with antibodies against CD138 (MM cell surface marker) or Annexin V (apoptosis). Alternatively, isolated MNCs were cultured in MethoCult (StemCell

Technologies), and treated with **16i** to evaluate the activity of this agent on healthy hematopoietic progenitor colony formation.

S.9 Chemical Methods and Characterization

Anhydrous solvents methanol, DMSO, CH_2Cl_2, THF and DMF were purchased from Sigma Aldrich and used directly from Sure-Seal bottles. All reactions were performed under an atmosphere of dry nitrogen in oven-dried glassware and were monitored for completeness by thin-layer chromatography (TLC) using silica gel (visualized by UV light, or developed by treatment with $KMnO_4$ stain or phosphomolybdic acid stain). ^1H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer in either $CDCl_3$, CD_3OD or d_6-DMSO. Chemical shifts (δ) are reported in parts per million after calibration to residual isotopic peak. Coupling constants (*J*) are reported in Hz. Before biological testing, inhibitor purity was evaluated by reversed-phase HPLC (rpHPLC). Analysis by rpHPLC was performed using a Microsorb-MV 300 Å C18 250 mm x 4.6 mm column run at 1 mL/min, and using gradient mixtures. The linear gradient consisted of a changing solvent composition of either (I) 100 % H_2O with 0.1 % TFA for two minutes to 100 % MeCN with 10 % H_2O and 0.1 % TFA (v/v) at 22 minutes and UV detection at 254nm or (I) 100 % H_2O with 0.1 % TFA for two minutes to 100 % MeCN with 10 % H_2O and 0.1 % TFA (v/v) at 22 minutes and UV detection at 254nm or (II) 100 % H_2O with 0.1 % TFA for two minutes to 100 % MeCN with 10 % H_2O and 0.1 % TFA (v/v) at 62 mins and UV detection at 254nm. For reporting HPLC data, percentage purity is given in parentheses after the retention time for each condition. All biologically evaluated compounds are > 95 % chemical purity as measured by HPLC.

General Procedure A (alkylation of sulfonamide). Activated alkyl halides (1.1 equiv.) were added to a stirred suspension of sulfonamide **14** or **19** (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 B (global deprotection of benzylated salicyclic acid). The dibenzyl protected salicylic 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 AcOH as the eluent (generally 92 % DCM, 7 % MeOH and 1 % AcOH in a 1:2 ratio with DCM was utilized).

General Procedure C (step-wise deprotection of benzylated salicylic acid). The dibenzyl protected salicylic acid (1 equiv.) was dissolved in THF and diluted with H_2O in a 1:3 ratio. $LiOH.H_2O$ (3 equiv.) was added and the reaction was then stirred at room temperature for 1-6 hours. THF was removed under reduced pressure then the mixture was acidified and the product was extracted into EtOAc. The combined organics were washed with 1M HCl, H_2O and brine then dried over Na_2SO_4, concentrated and used without further purification. The mono-benzyl protected salicylic acid (benzyl ether) was then dissolved in DMF and then treated with trifluoroacetic acid in a 9:1 ratio. The reaction mixture was stirred for 1 hour at room temperature then diluted with H_2O and organics were extracted into EtOAc. Organics were combined and washed with 1M HCl, H_2O and brine then dried over Na_2SO_4. Crude product was then purified using flash column chromatography using a mixture of DCM, MeOH and AcOH as the eluent (generally 92 % DCM, 7 % MeOH and 1 % AcOH in a 1:2 ratio with DCM was utilized).

General Procedure D (Acylation of sulfonamide nitrogen). Unfunctionalized sulfonamide (1 equiv.) was dissolved in DCM then treated with DMAP (0.1 equiv.) then anhydride and stirred for 30 minutes. The reaction mixture was diluted with DCM and washed with 1M HCl, saturated $NaHCO_3$, brine, then dried over Na_2SO_4 and concentrated. Crude product was purified using flash column chromatography in a mixture of hexanes and EtOAc.

Compounds **1-9** were prepared as previously reported[1, 2]

Compound 10

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, 2CH), 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 (ES+) Calcd for [$C_{21}H_{19}NO_3$ + H] 334.14 found 334.17.

Compound 11

Benzyl 2-(benzyloxy)-4-(4-cyclohexylbenzylamino)benzoate. To a solution of primary aniline (**10**) (2.65 g, 8.0 mmol) and acetic acid (0.26 g, 4.4 mmol) stirred in anhydrous MeOH (0.1 M) with activated 4Å mol. sieves was added 4-cyclohexylbenzaldehyde (**11**, 1.5 g, 8.0 mmol). The solution was then heated to 45 °C for 3 hours 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 **12** (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 (ES+) Calcd for [$C_{34}H_{35}NO_3$ + H] 506.27 found 506.22.

Compound 12

Methyl 2-(4-methylphenylsulfonamido)acetate. Glycine methyl ester hydrochloride (1.9 g, 15 mmol) and K_2CO_3 (4.6 g, 33 mmol) were dissolved in anhydrous acetonitrile (0.1 M) and cooled to 0 °C before tosyl chloride (2.9 g, 15 mmol) was added. The resultant solution was allowed to stir overnight at RT. The solvent was removed and the residue redissolved in CH_2Cl_2 and washed sequentially with 0.1 M HCl, saturated $NaHCO_3$ and brine then dried over Na_2SO_4 and concentrated *in vacuo* to furnish **12** (3.4g, 14 mmol, 93 %): δ_H (400 MHz, *d*-$CDCl_3$) 2.42 (s, 3H, CH_3), 3.66 (s, 3H, CH_3), 3.96 (s, 2H, CH_2), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.69 (d, *J* = 8.2 Hz, 2H, CH); LRMS (ES+) calcd for [$C_{10}H_{13}NO_4S$ + H] 244.06, found 244.28.

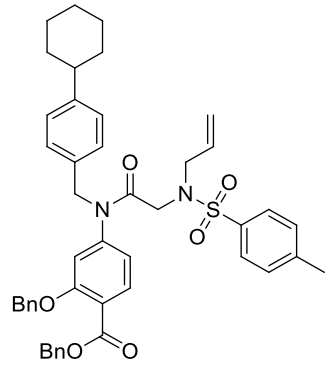
Compound 13

methyl 2-(N-(tert-butoxycarbonyl)-4-methylphenylsulfonamido)acetate. Compound **12** (3.40 g, 14 mmol) and DIPEA (2.40 g, 18 mmol) were dissolved in CH_2Cl_2 (0.1 M). Boc_2O (3.40 g, 15 mmol) and DMAP (0.17 g, 1.4 mmol) were added and the solution was stirred for 10 minutes. The mixture was then diluted with CH_2Cl_2, washed with saturated $NaHCO_3$, brine then dried over Na_2SO_4 then concentrated. The crude product was purified by silica gel chromatography using an eluent of 5:1 hexanes:ethyl acetate to give **13** (4.70 g, 13 mmol, 92 %).

Compound 14

benzyl 2-(benzyloxy)-4-(N-(4-cyclohexylbenzyl)-2-(4-methylphenylsulfonamido)acetamido)benzoate. Carboxylic acid **13** was stirred at room temperature with PPh_3Cl_2 in $CHCl_3$ for 15 minutes to form the activated acid. Aniline **11** 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.

Compound 15a

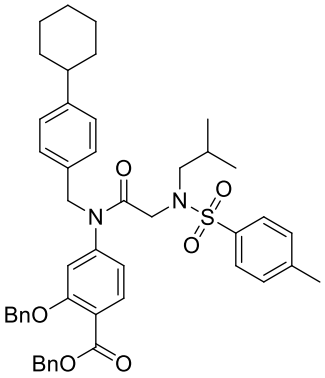


benzyl 4-(2-(*N*-allyl-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{46}H_{48}N_2O_6S$
Molecular Weight: 756.95

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15a** (53.7 mg, 100 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31-1.46 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.39-2.55 (m, 4H, CH and CH_3), 3.76 (s, 2H, CH_2), 3.90 (d, *J* = 6.8 Hz, 2H, CH_2), 3.91 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.06-5.15 (m, 2H, CH_2), 5.53-5.68 (m, 1H, CH), 6.52 (s, 1H, CH), 6.66 (d of d, *J* = 8.0 and 1.4 Hz, 1H, CH), 7.01 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.24-7.42 (m, 12H, CH), 7.70 (d, *J* = 8.0 Hz, 2H, CH), 7.82 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 47.2, 50.8, 52.9, 67.1, 70.8, 114.1, 119.5, 120.2, 127.0, 127.2, 127.6, 128.2, 128.3, 128.4, 128.7, 128.7, 129.0, 129.6, 133.0, 133.2, 134.1, 135.8, 137.1, 137.8, 143.3, 145.3, 147.8, 158.9, 165.5, 167.1; LRMS (ES+) Calcd for [$C_{46}H_{48}N_2O_6S$ + Na] 779.31 found 779.41.

Compound 15b

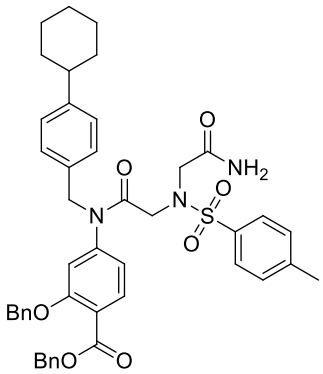


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-isobutyl-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{47}H_{52}N_2O_6S$
Molecular Weight: 772.99

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15b** (22.9 mg, 43 %)

δ_H (400MHz, *d*-$CDCl_3$) 0.81 (d, *J* = 6.8 Hz, 6H, CH_3), 1.30-1.44 (m, 5H, CH_2), 1.64-1.90 (m, 6H, CH_2 and CH), 2.37-2.52 (m, 4H, CH and CH_3), 3.07 (d, *J* = 7.2 Hz, 2H, CH_2), 3.73 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.52 (s, 1H, CH), 6.67 (d of d, *J* = 8.4 and 1.6 Hz, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.23 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.42 (m, 10H, CH), 7.65 (d, *J* = 8.4 Hz, 2H, CH), 7.83 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 20.1, 21.7, 26.2, 26.9, 26.9, 34.6, 44.3, 48.1, 52.8, 55.8, 67.1, 70.8, 114.2, 120.2, 120.9, 127.1, 127.2, 127.7, 128.2, 128.3, 128.4, 128.7, 128.7, 129.0, 129.4, 133.3, 134.2, 135.9, 137.1, 143.8, 145.4, 147.8, 158.9, 165.6, 167.1; LRMS (ES+) Calcd for [$C_{47}H_{52}N_2O_6S$ + Na] 795.34 found 795.56.

Compound 15c

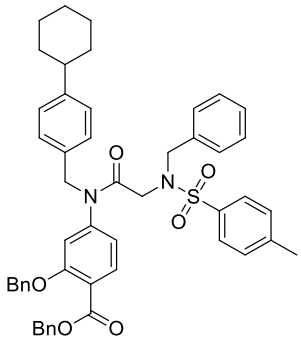


benzyl 4-(2-(*N*-(2-amino-2-oxoethyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{45}H_{47}N_3O_7S$
Molecular Weight: 773.94

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15c** (40.2 mg, 74 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.29-1.45 (m, 5H, CH_2), 1.68-1.92 (m, 5H, CH_2), 2.36 (s, 3H, CH_3), 2.42-2.54 (m, 1H, CH), 3.56 (s, 2H, CH_2), 3.64 (s, 2H, CH_2), 4.84 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 5.36 (s, 2H, CH_2), 5.59 (s, 1H, NH), 6.58 (s, 1H, CH), 6.76 (d, *J* = 8.0 Hz, 1H, CH), 7.08 (d, *J* = 8.0 Hz, 2H, CH), 7.13 (d, *J* = 8.0 Hz, 2H, CH), 7.22 (d, 2H, *J* = 8.0 Hz, 2H, CH), 7.25-7.36 (m, 8H, CH), 7.37-7.44 (m, 2H, CH), 7.55 (d, *J* = 8.4 Hz, 2H, CH) 7.83 (d, *J* = 8.0 Hz, 1H, CH), 8.73 (s, 1H, NH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 52.0, 53.0, 53.7, 67.3, 70.8, 114.3, 120.2, 121.4, 127.3, 127.3, 127.8, 128.3, 128.5, 128.7, 128.8, 129.0, 130.0, 133.3, 133.6, 134.4, 135.8, 135.8, 144.6, 144.7, 148.1, 158.7, 165.5, 168.3, 171.0; LRMS (ES+) Calcd for [$C_{45}H_{47}N_3O_7S$ + Na] 796.30 found 796.43.

Compound 15d

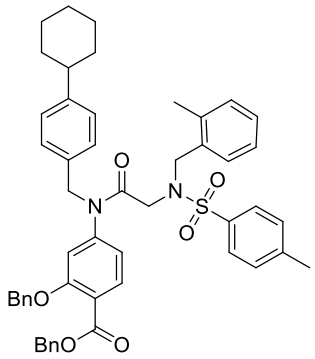


benzyl 4-(2-(*N*-benzyl-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{50}H_{50}N_2O_6S$
Molecular Weight: 807.01

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15d** (49.3 mg, 87 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.33-1.53 (m, 5H, CH_2), 1.68-1.98 (m, 5H, CH_2), 2.35-2.61 (m, 4H, CH and CH_3), 3.69 (s, 2H, CH_2), 4.57 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.28 (s, 1H, CH), 6.40 (s, 1H, CH), 6.89-7.49 (m, 21H, CH), 7.71 (d, *J* = 6.6 Hz, 1H, CH), 7.80 (d, *J* = 5.6 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 46.8, 51.1, 52.8, 67.1, 70.8, 113.9, 120.1, 120.8, 127.0, 127.3, 127.8, 128.1, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9, 129.1, 129.6, 133.1, 134.1, 135.4, 135.8, 137.2, 143.4, 145.1, 147.8, 158.8, 165.5, 166.8; LRMS (ES+) Calcd for [$C_{50}H_{50}N_2O_6S$ + Na] 829.33 found 829.46.

Compound 15e

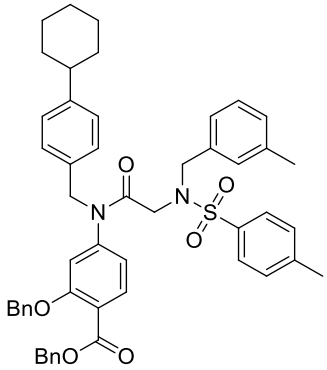


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{52}N_2O_6S$
Molecular Weight: 821.03

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15e** (45.7 mg, 80 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.71-1.92 (m, 5H, CH_2), 2.22 (s, 3H, CH_3), 2.42-2.54 (m, 4H, CH and CH_3), 3.61 (s, 2H, CH_2), 4.60 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.21 (s, 1H, CH), 6.34 (d, *J* = 5.6 Hz, 1H, CH), 6.94-7.20 (m, 8H, CH), 7.28-7.41 (m, 12H, CH), 7.69 (d, *J* = 8.0 Hz, 1H, CH), 7.77 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 19.1, 21.7, 26.2, 26.9, 34.6, 44.3, 46.9, 49.1, 52.7, 67.1, 70.8, 113.9, 120.2, 120.7, 126.0, 126.9, 127.2, 127.8, 128.2, 128.3, 128.3, 128.4, 128.6, 128.7, 129.2, 129.5, 130.1, 130.8, 133.0, 133.1, 134.0, 135.8, 137.0, 138.2, 143.3, 147.8, 158.8, 165.5, 166.7; LRMS (ES+) Calcd for [$C_{51}H_{52}N_2O_6S$ + Na] 843.34 found 843.52.

Compound 15f

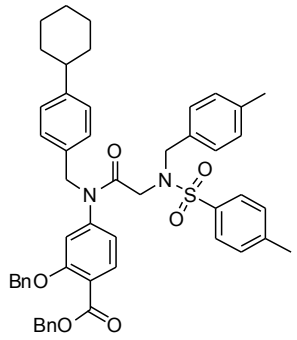


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{52}N_2O_6S$
Molecular Weight: 821.03

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15f** (54.4 mg, 95 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31-1.51 (m, 5H, CH_2), 1.69-1.97 (m, 5H, CH_2), 2.25 (s, 3H, CH_3), 2.37-2.57 (m, 4H, CH and CH_3), 3.70 (s, 2H, CH_2), 4.54 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.39 (d, *J* = 8.0 Hz, 1H, CH), 6.90 - 7.08 (m, 5H, CH), 7.08-7.22 (m, 4H, CH), 7.27 - 7.44 (m, 11H, CH) 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.80 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.4, 21.7, 26.2, 26.9, 34.6, 44.3, 47.6, 50.9, 52.7, 67.1, 70.8, 113.9, 120.1, 120.7, 126.0, 127.0, 127.3, 127.7, 128.2, 128.3, 128.4, 128.6, 128.6, 128.7, 128.8, 129.1, 129.5, 129.5, 133.1, 134.1, 135.3, 135.7, 137.4, 138.4, 143.3, 147.8, 158.8, 165.5, 166.8; LRMS (ES+) Calcd for [$C_{51}H_{52}N_2O_6S$ + Na] 843.34 found 843.65.

Compound 15g

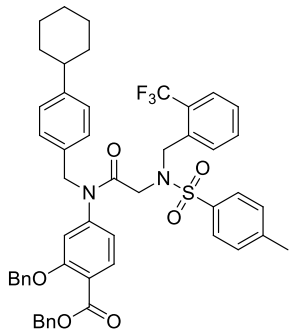


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{52}N_2O_6S$
Molecular Weight: 821.03

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15g** (49.0 mg, 85 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.71-1.91 (m, 5H, CH_2), 2.25 (s, 3H, CH_3), 2.42-2.53 (m, 4H, CH and CH_3), 3.68 (s, 2H, CH_2), 4.50 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.39 (d, *J* = 8.0 Hz, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.02-7.09 (m, 4H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.39 (m, 12H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH), 7.79 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.2, 21.7, 26.2, 26.9, 34.6, 44.3, 46.7, 50.8, 52.8, 67.1, 70.8, 113.9, 120.2, 120.7, 127.0, 127.3, 127.8, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8, 129.1, 129.4, 129.5, 132.3, 133.1, 134.1, 135.8, 137.3, 137.8, 143.3, 145.1, 147.8, 158.8, 165.5, 166.9; LRMS (ES+) Calcd for [$C_{51}H_{52}N_2O_6S$ + Na] 843.34 found 843.51.

Compound 15h

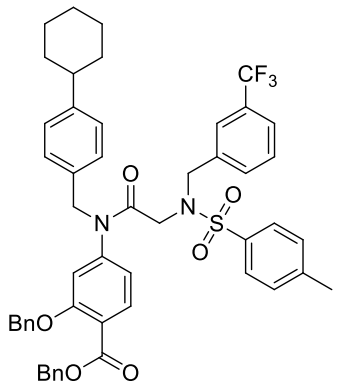


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_6S$
Molecular Weight: 875.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15h** (55.3 mg, 90 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.91 (m, 5H, CH_2), 2.42-2.52 (m, 4H, CH and CH_3), 3.72 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.36 (s, 1H, CH), 6.50 (d, *J* = 7.6 Hz, 1H, CH), 6.95 (d, *J* = 7.6 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.25-7.40 (m, 13H, CH), 7.49 (t, *J* = 7.6 Hz, 1H, CH), 7.60 (d, *J* = 7.6 Hz, 1H, CH) 7.70-7.76 (m, 2H, CH), 7.76-7.81 (m, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.8, 26.2, 26.9, 34.6, 44.3, 47.9 52.8, 67.1, 68.1, 70.8, 114.0, 120.1, 120.8, 125.7, 127.0, 127.2, 127.7, 127.9, 128.2, 128.3, 128.4, 128.7, 128.7, 129.1, 129.6, 130.1, 132.6, 133.2, 134.0, 135.1, 135.8, 135.8, 136.9, 143.6, 145.4, 147.8, 158.8, 165.5, 166.3; LRMS (ES+) Calcd for [$C_{51}H_{49}F_3N_2O_6S$ + Na] 897.32 found 897.26.

Compound 15i

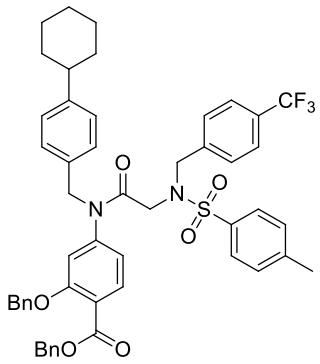


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_6S$
Molecular Weight: 875.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15i** (42.9 mg, 70 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.50 (m, 5H, CH_2), 1.69-1.95 (m, 5H, CH_2), 2.35-2.55 (m, 4H, CH and CH_3), 3.67 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.36 (s, 1H, CH), 6.44 (d, *J* = 8.4 Hz, 1H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.24 - 7.43 (m, 14H, CH), 7.46 (d, *J* = 8.0 Hz, 1H, CH), 7.51 (d, *J* = 8.0 Hz, 1H, CH), 7.69 - 7.79 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.4, 25.9, 26.7, 34.3, 44.1, 46.9, 50.7, 52.6, 66.9, 70.6, 113.7, 119.7, 120.7, 122.4, 124.6, 124.7, 125.1, 125.1, 126.8, 127.0, 127.9, 128.1, 128.1, 128.4, 128.4, 128.8, 129.1, 129.4, 131.9, 132.9, 133.7, 135.5, 135.6, 136.6, 136.8, 143.4, 144.6, 147.6, 158.6, 165.2, 166.4; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_6S$ + Na] 897.33, found 897.41.

Compound 15j

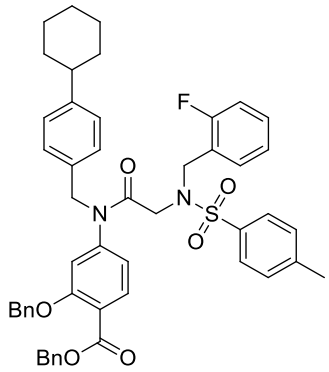


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_6S$
Molecular Weight: 875.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15j** (46.4 mg, 76 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.46 (m, 5H, CH_2), 1.66-1.93 (m, 5H, CH_2), 2.45-2.48 (m, 4H, CH and CH_3), 3.66 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.86 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.35 - 6.40 (m, 2H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.24-7.40 (m, 14H, CH), 7.52 (d, *J* = 8.0 Hz, 2H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH), 7.74 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 34.3, 44.1, 47.0, 50.8, 52.6, 66.9, 70.6, 113.7, 119.8, 120.9, 125.4, 125.4, 126.8, 127.0, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.7, 128.7, 128.8, 129.4, 130.2, 132.9, 133.7, 135.5, 135.6, 136.7, 139.6, 143.4, 147.7, 158.6, 165.2, 166.5; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_6S$ + H] 875.33, found 875.24.

Compound 15k

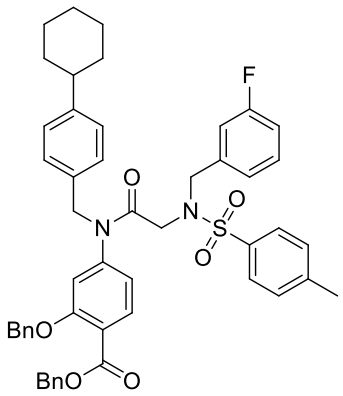


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(2-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}FN_2O_6S$
Molecular Weight: 825.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15k** (48.4 mg, 84 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.36-2.56 (m, 4H, CH and CH_3), 3.73 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.83 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.40 (s, 1H, CH), 6.52 (d, *J* = 8.0 Hz, 1H, CH), 6.94 (d, *J* = 9.2 Hz, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.05 (t, *J* = 7.6 Hz, 1H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.18-7.25 (m, 1H, CH), 7.26-7.39 (m, 13H, CH), 7.70-7.80 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 44.8, 47.8, 52.8, 67.1, 70.8, 114.0, 115.2, 115.5, 120.2, 120.8, 122.7, 122.9, 124.6, 124.6, 127.0, 127.3, 127.8, 128.2, 128.3, 128.4, 128.7, 128.7, 129.1, 129.5, 129.8, 129.9, 131.4, 131.4, 133.2, 134.1, 135.8, 137.2, 138.2, 138.3, 143.4, 147.8, 158.8, 160.0, 162.4, 165.5, 166.7; LRMS (ES+) Calcd for [$C_{50}H_{49}FN_2O_6S$ + Na] 847.32 found 847.41.

Compound 15l

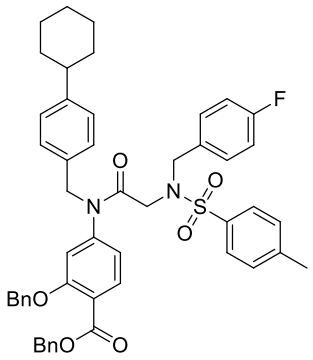


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(3-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}FN_2O_6S$
Molecular Weight: 825.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15l** (49.8 mg, 86 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.54 (m, 5H, CH_2), 1.70-1.99 (m, 5H, CH_2), 2.46 (s, 4H, CH and CH_3), 3.69 (s, 2H, CH_2), 4.55 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.46 (d, *J* = 8.0 Hz, 1H, CH), 6.84-7.05 (m, 5H, CH), 7.06 - 7.47 (m, 15H, CH), 7.67-7.86 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 46.9, 50.7, 52.8, 67.1, 70.8, 113.8, 114.9, 115.1, 115.5, 115.7, 120.1, 120.8, 124.3, 124.4, 127.1, 127.2, 127.7, 128.2, 128.3, 128.4, 128.7, 128.7, 129.1, 129.6, 130.3, 130.4, 133.2, 134.0, 135.8, 135.8, 137.1, 138.2, 138.3, 143.6, 144.9, 147.9, 158.8, 161.7, 164.2, 165.5, 166.7; LRMS (ES+) Calcd for [$C_{50}H_{49}FN_2O_6S$ + Na] 847.32 found 847.61.

Compound 15m

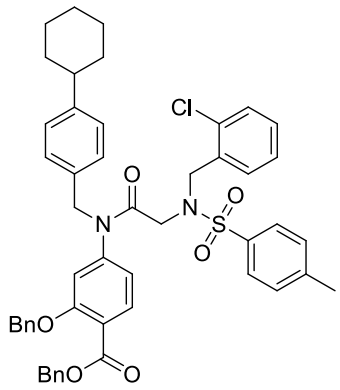


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}FN_2O_6S$
Molecular Weight: 825.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15m** (48.3 mg, 84 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.68-1.95 (m, 5H, CH_2), 2.35-2.57 (m, 4H, CH and CH_3), 3.65 (s, 2H, CH_2), 4.51 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.44 (d, *J* = 8.0 Hz, 1H, CH), 6.89 - 6.99 (m, 4H, CH), 7.04-7.21 (m, 4H, CH), 7.22 - 7.44 (m, 12H, CH), 7.69 - 7.80 (m, 3H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 46.8, 50.4, 52.8, 67.1, 70.8, 113.8, 115.5, 115.7, 120.1, 120.9, 127.0, 127.2, 127.7, 128.2, 128.3, 128.4, 128.7, 128.7, 129.1, 129.6, 130.6, 130.7, 131.2, 131.2, 133.2, 134.0, 135.8, 135.8, 137.1, 143.5, 145.0, 147.9, 158.8, 161.3, 163.8, 165.5, 166.7; LRMS (ES+) Calcd for [$C_{50}H_{49}FN_2O_6S$ + Na] 847.32 found 847.53.

Compound 15n

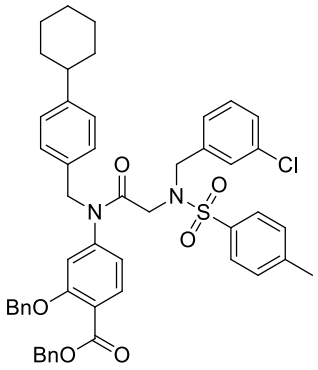


benzyl 2-(benzyloxy)-4-(2-(*N*-(2-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}ClN_2O_6S$
Molecular Weight: 841.45

Sulfonamide **14** was functionalized on a 0.1 mmol scale using General Procedure A to give **15n** (73.2 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31 - 1.48 (m, 5H, CH_2), 1.70 - 1.94 (m, 5H, CH_2), 2.40 - 2.55 (m, 4H, CH and CH_3), 3.74 (s, 2H, CH_2), 4.69 (s, 4H, $2CH_2$), 4.82 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.41 (s, 1H, CH), 6.54 (d, *J* = 7.8 Hz, 1H, CH), 6.99 (d, *J* = 6.6 Hz, 2H, CH), 7.10 (d, *J* = 6.6 Hz, 2H, CH), 7.14 - 7.21 (m, 2H, CH), 7.27 - 7.46 (m, 14H, CH), 7.71 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.6, 26.0, 26.8, 34.4, 44.2, 47.7, 48.5, 52.7, 67.0, 70.7, 113.8, 120.1, 120.7, 126.8, 127.1, 127.2, 127.7, 128.0, 128.2, 128.2, 128.5, 128.5, 129.0, 129.0, 129.1, 129.3, 129.3, 130.7, 133.0, 133.3, 133.7, 133.9, 135.6, 135.6, 137.0, 143.3, 144.9, 158.7, 165.3, 166.5; LRMS (ES+) Calcd for [$C_{50}H_{49}ClN_2O_6S$ + Na] 863.29 found 863.54.

Compound 15o

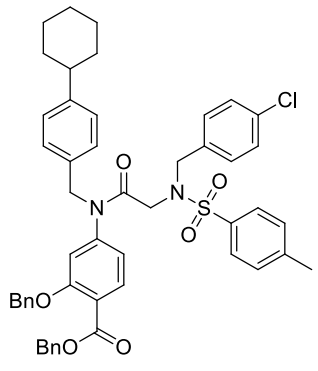


benzyl 2-(benzyloxy)-4-(2-(*N*-(3-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}ClN_2O_6S$
Molecular Weight: 841.45

Sulfonamide **14** was functionalized on a 0.1 mmol scale using General Procedure A to give **15o** (61.6 mg, 71 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33 - 1.47 (m, 5H, CH_2), 1.70-1.96 (m, 5H, CH_2), 2.42 - 2.52 (m, 4H, CH and CH_3), 3.67 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.47 (d, *J* = 7.6 Hz, 1H, CH), 6.97 (d, *J* = 7.8 Hz, 2H, CH), 7.10 (d, *J* = 7.8 Hz, 2H, CH), 7.12 - 7.24 (m, 5H, CH), 7.27 - 7.48 (m, 12H, CH), 7.71 - 7.84 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.6, 26.0, 26.8, 34.5, 44.2, 46.9, 50.5, 52.7, 67.0, 70.6, 113.8, 120.0, 120.7, 126.8, 126.9, 127.1, 127.6, 128.0, 128.1, 128.2, 128.2, 128.5, 128.5, 128.7, 128.9, 128.9, 130.0, 133.1, 133.8, 134.5, 135.7, 135.7, 137.0, 137.6, 143.4, 144.8, 147.7, 158.7, 165.3, 166.5; LRMS (ES+) Calcd for [$C_{50}H_{49}ClN_2O_6S$ + Na] 863.29 found 863.54.

Compound 15p

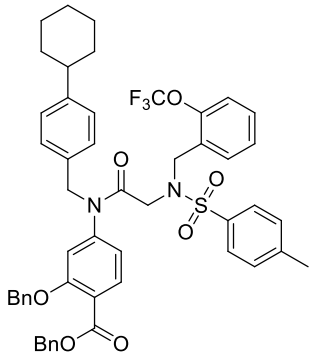


benzyl 2-(benzyloxy)-4-(2-(*N*-(4-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}ClN_2O_6S$
Molecular Weight: 841.45

Sulfonamide **14** was functionalized on a 0.1 mmol scale using General Procedure A to give **15p** (65.4 mg, 75.8 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32 - 1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.40 - 2.54 (m, 4H, CH and CH_3), 3.65 (s, 2H, CH_2), 4.52 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.83 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.43 (d, *J* = 8.0 Hz, 1H, CH), 6.96 (d, *J* = 7.8 Hz, 2H, CH), 7.07-7.17 (m, 4H, CH), 7.23 (d, *J* = 8.0 Hz, 2H, CH), 7.27 - 7.43 (m, 12H, CH), 7.70 - 7.83 (m, 3H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.4, 44.1, 46.7, 50.4, 52.6, 66.9, 70.6, 113.6, 119.8, 120.7, 126.8, 127.0, 127.5, 127.9, 128.1, 128.2, 128.4, 128.7, 128.9, 128.9, 129.4, 130.0, 131.9, 132.9, 133.7, 133.7, 133.8, 135.6, 135.6, 136.8, 143.3, 147.7, 158.6, 165.2, 166.5; LRMS (ES+) Calcd for [$C_{50}H_{49}ClN_2O_6S$ + Na] 863.29 found 863.48

Compound 15q

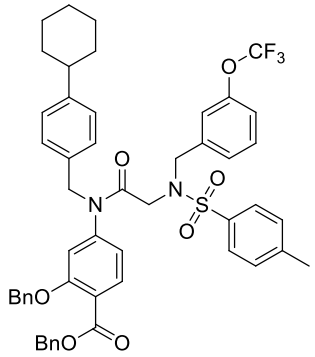


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_7S$
Molecular Weight: 891.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15q** (34.5, 56 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30 - 1.47 (m, 5H, CH_2), 1.67 - 1.92 (m, 5H, CH_2), 2.40 - 2.51 (m, 4H, CH and CH_3), 3.71 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.38 (s, 1H, CH), 6.52 (d, *J* = 8.0 Hz, 1H, CH), 6.95 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.13 - 7.40 (m, 15H, CH), 7.49 (d, *J* = 8 .0 Hz, 1H, CH), 7.74 (d, *J* = 8.0 Hz, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 29.5, 34.3, 44.1, 47.6, 52.6, 66.9, 70.5, 113.8, 118.7, 119.9, 120.3, 122.6, 126.7, 127.0, 127.2, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.5, 128.8, 129.1, 129.3, 130.7, 133.0, 133.8, 135.5, 135.6, 136.9, 143.3, 147.3, 147.5, 158.6, 165.2, 166.2; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_7S$ + Na] 913.32, found 913.40.

Compound 15r

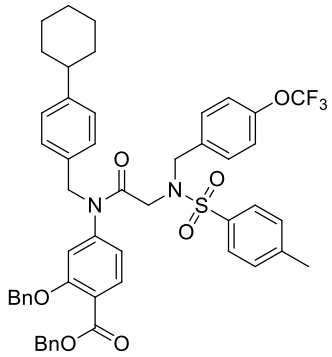


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_7S$
Molecular Weight: 891.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15r** (34.5 mg, 39 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33 - 1.44 (m, 5H, CH_2), 1.73 - 1.84 (m, 5H, CH_2), 2.42 - 2.52 (m, 4H, CH_3 and CH), 3.67 (s, 2H, CH_2), 4.58 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.82 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.35 (s, 1H, CH), 6.44 (d, *J* = 8.0 Hz, 1H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.01 (s, 1H, CH), 7.07 - 7.13 (m, 3H, CH), 7.17 (d, *J* = 8.0 Hz, 1H, CH), 7.26 - 7.38 (m, 13H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH), 7.75 (d, *J* = 8.0, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.7, 44.4, 47.1, 50.9, 52.9, 67.2, 70.9, 113.7, 119.8, 120.1, 120.7, 120.9, 126.8, 127.0, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.8, 129.4, 130.0, 132.9, 133.7, 135.5, 135.6, 136.8, 138.0, 143.4, 144.7, 147.6, 149.2, 158.6, 165.2, 166.5; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_7S$ + Na] 913.32, found 913.40.

Compound 15s

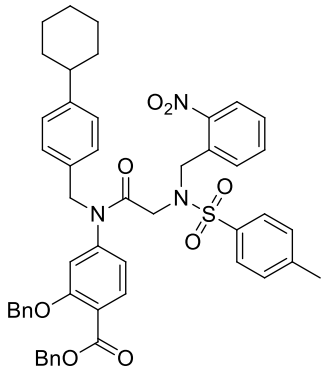


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_7S$
Molecular Weight: 891.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15s** (59.3 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30 - 1.48 (m, 5H, CH_2), 1.70 - 1.95 (m, 5H, CH_2), 2.35 - 2.55 (m, 4H, CH and CH_3), 3.65 (s, 2H, CH_2), 4.55 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.85 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.34 - 6.38 (m, 2H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.06 - 7.13 (m, 4H, CH), 7.22 (d, *J* = 7.6 Hz, 2H, CH), 7.28 - 7.40 (m, 12H, CH), 7.71 (d, *J* = 8.4 Hz, 1H, CH), 7.75 (d, *J* = 8.4 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 34.4, 44.1, 46.8, 50.4, 52.6, 66.9, 70.6, 113.7, 119.0, 119.7, 120.5, 120.7, 126.8, 127.0, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.8, 128.9, 129.4, 129.9, 132.9, 133.7, 134.1, 135.5, 135.6, 136.8, 143.3, 147.7, 148.7, 148.7, 158.6, 165.2, 166.5; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_7S$ + H] 913.32, found 913.34.

Compound 15t

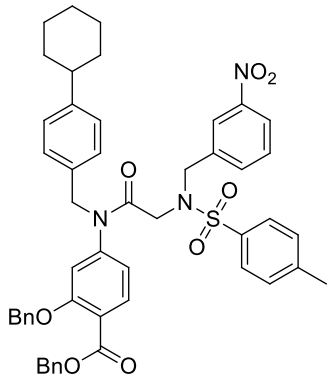


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-nitrobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}N_3O_8S$
Molecular Weight: 852.00

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15t** (194 mg, 81 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31 - 1.51 (m, 5H, CH_2), 1.70 - 1.96 (m, 5H, CH_2), 2.40 - 2.59 (m, 4H, CH and CH_3), 3.83 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.51 (s, 1H, CH), 6.63 (d, *J* = 8.0 Hz, 1H, CH), 6.90 (d, *J* = 8.0 Hz, 2H, CH), 7.13 (d, *J* = 8.0 Hz, 2H, CH), 7.25 - 7.44 (m, 14H, CH), 7.57 (t, *J* = 7.6 Hz, 1H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH), 7.81 (d, *J* = 8.0 Hz, 2H, CH), 7.91 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.8, 34.4, 44.1, 49.0, 52.7, 53.5, 66.9, 70.6, 113.9, 120.1, 120.7, 124.5, 126.9, 127.0, 127.5, 128.0, 128.2, 128.2, 128.4, 128.5, 128.8, 129.5, 130.6, 132.0, 133.0, 133.6, 133.8, 135.7, 136.4, 143.6, 144.8, 147.6, 148.5, 158.7, 165.3, 166.3.

Compound 15u

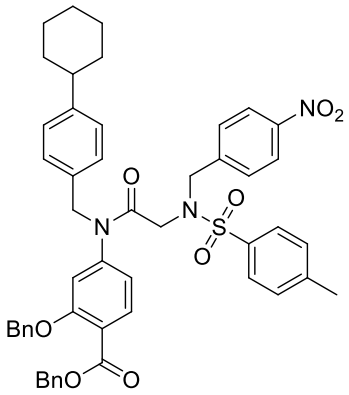


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-nitrobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}N_3O_8S$
Molecular Weight: 852.00

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15u** (200 mg, 84 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32 - 1.49 (m, 5H, CH_2), 1.70 - 1.96 (m, 5H, CH_2), 2.41 - 2.57 (m, 4H, CH and CH_3), 3.73 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.45 (s, 1H, CH), 6.56 (d, *J* = 8.0 Hz, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.25-7.41 (m, 12H, CH), 7.45 (t, *J* = 8.0 Hz, 1H, CH), 7.67 (d, *J* = 7.6 Hz, 1H, CH), 7.75 (d, *J* = 8.4 Hz, 2H, CH), 7.77 (d, *J* = 8.4 Hz, 1H, CH), 8.00 (s, 1H, CH), 8.05 - 8.14 (m, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.4, 44.1, 47.4, 52.7, 53.5, 67.0, 70.6, 113.8, 119.9, 120.8, 122.9, 123.1, 126.9, 127.0, 127.5, 127.9, 128.2, 128.2, 128.5, 128.8, 129.6, 129.7, 133.0, 133.7, 134.7, 135.6, 136.6, 138.1, 143.7, 144.7, 147.7, 148.2, 158.7, 165.2, 166.4.

Compound 15v

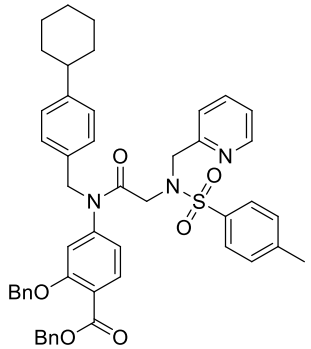


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-nitrobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{49}N_3O_8S$
Molecular Weight: 852.00

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15v** (185 mg, 78 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31 - 1.47 (m, 5H, CH_2), 1.69 - 1.93 (m, 5H, CH_2), 2.40 - 2.56 (m, 4H, CH and CH_3), 3.69 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.42 (s, 1H, CH), 6.50 (d, *J* = 8.0 Hz, 1H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.24 - 7.46 (m, 14H, CH), 7.67 - 7.80 (m, 3H, CH), 8.11 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.1, 26.8, 34.5, 44.2, 47.5, 51.1, 52.8, 67.1, 70.8, 113.9, 119.9, 121.0, 123.8, 127.0, 127.1, 127.6, 128.1, 128.3, 128.3, 128.6, 128.6, 129.0, 129.1, 129.6, 133.1, 133.8, 135.7, 135.7, 136.5, 143.5, 143.8, 144.7, 147.6, 147.9, 158.8, 165.3, 165.5.

Compound 15w

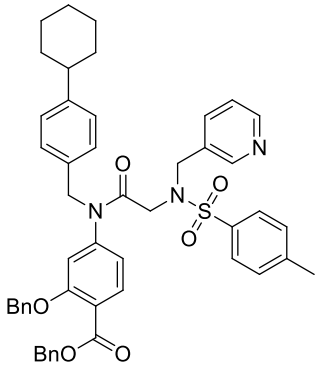


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-2-ylmethyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{49}N_3O_6S$
Molecular Weight: 807.99

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15w** (49.5 mg, 88 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.29 - 1.46 (m, 5H, CH_2), 1.69 - 1.90 (m, 5H, CH_2), 2.39 - 2.54 (m, 4H, CH and CH_3), 3.87 (s, 2H, CH_2), 4.61 (s, 2H, CH), 4.70 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.49 (s, 1H, CH), 6.72 (d of d, *J* = 8.0 and 1.8 Hz, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.11-7.16 (m, 1H, CH), 7.27 (d, *J* = 8.0 Hz, 2H, CH), 7.24 - 7.41 (m, 10H, CH), 7.43 (d, *J* = 8.0 Hz, 1H, CH), 7.61 (t of d, *J* = 7.6 and 1.8 Hz, 1H, CH), 7.72 - 7.79 (m, 3H, CH), 8.41 - 8.45 (m, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 48.8, 52.9, 53.6, 67.1, 70.8, 114.2, 120.3, 120.7, 122.7, 123.1, 127.0, 127.3, 127.8, 128.2, 128.3, 128.4, 128.7, 128.7, 129.0, 129.6, 133.1, 134.1, 135.9, 137.0, 137.1, 143.5, 145.2, 147.7, 149.0, 156.6, 158.8, 165.6, 166.8; LRMS (ES+) Calcd for [$C_{42}H_{43}N_3O_6S$ + H] 718.30 found 718.43.

Compound 15x

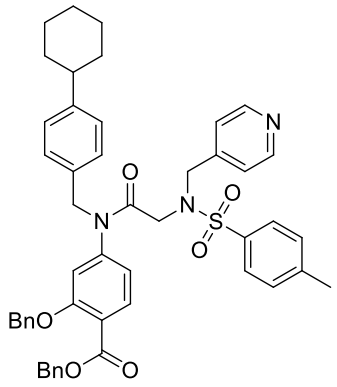


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-3-ylmethyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{49}N_3O_6S$
Molecular Weight: 807.99

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15x** (38.2 mg, 68 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.30 - 1.42 (m, 5H, CH_2), 1.67 - 1.89 (m, 5H, CH_2), 2.34 - 2.53 (m, 4H, CH and CH_3), 3.87 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.49 (s, 1H, CH), 6.58 (d, *J* = 8.0 Hz, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 7.6 Hz, 2H, CH), 7.11 - 7.18 (m, 1H, CH), 7.23 - 7.40 (m, 13H, CH), 7.41 - 7.49 (m, 1H, CH), 7.57 - 7.66 (m, 1H, CH), 7.69 - 7.80 (m, 3H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 29.8, 34.6, 44.3, 48.7, 52.9, 67.1, 70.8, 114.3, 120.3, 120.7, 122.8, 123.2, 127.0, 127.3, 127.8, 128.2, 128.3, 128.4, 128.7, 128.7, 129.0, 129.6, 133.1, 134.1, 135.9, 135.8, 136.9, 137.2 143.5, 145.3, 147.7, 149.0, 156.6, 158.8, 165.6, 166.8.

Compound 15y

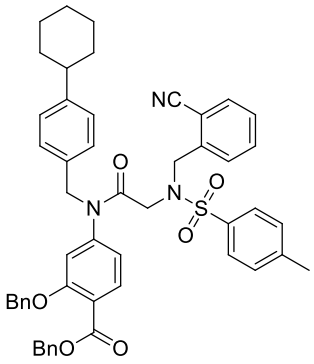


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-4-ylmethyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{49}N_3O_6S$
Molecular Weight: 807.99

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15y** (36.2 mg, 64 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31 - 1.50 (m, 5H, CH_2), 1.68 - 1.93 (m, 5H, CH_2), 2.37 - 2.57 (m, 4H, CH and CH_3), 3.68 (s, 2H, CH_2), 4.60 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.86 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.35 (s, 1H, CH), 6.42 - 6.54 (m, 1H, CH), 6.89 - 7.01 (m, 2H, CH), 7.04 - 7.21 (m, 4H, CH), 7.21 - 7.43 (m, 13H, CH) 7.68 - 7.80 (m, 3H, CH), 8.51 (s, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.1, 26.9, 34.6, 44.3, 47.5, 50.6, 52.8, 67.2, 70.8, 113.8, 120.0, 121.1, 123.2, 127.0, 127.2, 127.7, 128.2, 128.3, 128.4, 128.6, 128.7, 129.0, 129.7, 133.2, 133.8, 135.7, 136.6, 143.8, 145.4, 147.9, 150.0, 158.8, 165.4, 166.5.

Compound 15z

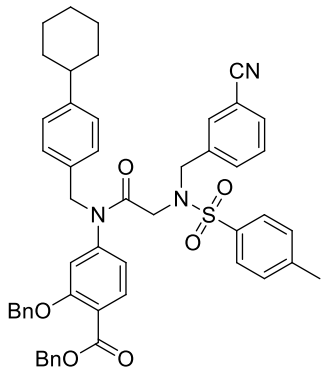


benzyl 2-(benzyloxy)-4-(2-(*N*-(2-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}N_3O_6S$
Molecular Weight: 832.02

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15z** (221 mg, 93 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.33 - 1.52 (m, 5H, CH_2), 1.70 - 1.97 (m, 5H, CH_2), 2.41 - 2.57 (m, 4H, CH and CH_3), 3.84 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.58 (s, 1H, CH), 6.65 (d, *J* = 8.0 Hz, 1H, CH), 7.01 (d, *J* = 8.0 Hz, 2H, CH), 7.13 (d, *J* = 8.0 Hz, 2H, CH), 7.27 - 7.44 (m, 14H, CH), 7.56 (d, *J* = 7.6 Hz, 2H, CH), 7.73 (d, *J* = 8.0 Hz, 2H, CH), 7.80 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.4, 44.1, 48.8, 49.9, 52.7, 66.9, 70.6, 111.8, 114.0, 117.3, 120.1, 120.6, 126.8, 127.1, 127.6, 128.0, 128.1, 128.2, 128.2, 128.5, 128.5, 128.9, 129.5, 129.5, 130.0, 132.5, 133.0, 133.2, 133.8, 135.7, 135.7, 136.5, 140.1, 143.5, 144.8, 147.5, 158.7, 165.3, 166.1; LRMS (ES+) Calcd for [$C_{51}H_{49}N_3O_6S$ + Na] 854.32 found 854.46.

Compound 15aa

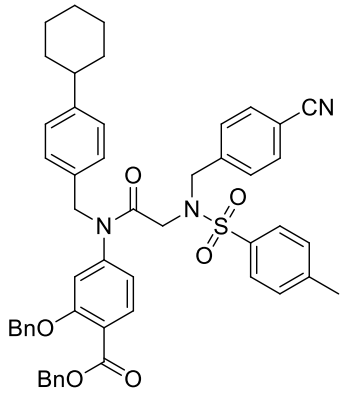


benzyl 2-(benzyloxy)-4-(2-(*N*-(3-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}N_3O_6S$
Molecular Weight: 832.02

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15aa** (184 mg, 79 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32-1.52 (m, 5H, CH_2), 1.70-1.98 (m, 5H, CH_2), 2.38-2.59 (m, 4H, CH and CH_3), 3.71 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.46 (s, 1H, CH), 6.55 (d, *J* = 8.0 Hz, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.14 (d, *J* = 7.6 Hz, 2H, CH), 7.23 - 7.47 (m, 14H, CH), 7.53 (t, *J* = 6.8 Hz, 2H, CH), 7.74 (d, *J* = 8.0 Hz, 2H, CH), 7.79 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.4, 44.1, 47.2, 50.7, 52.7, 66.9, 70.6, 112.5, 113.8, 118.3, 119.8, 120.8, 126.9, 127.0, 127.5, 127.9, 128.1, 128.2, 128.5, 128.5, 128.8, 129.5, 129.5, 131.5, 131.7, 132.8, 133.0, 133.7, 135.6, 136.6, 137.4, 143.6, 144.7, 147.7, 158.7, 165.2, 166.4; LRMS (ES+) Calcd for [$C_{51}H_{49}N_3O_6S$ + Na] 854.32 found 854.59.

Compound 15ab

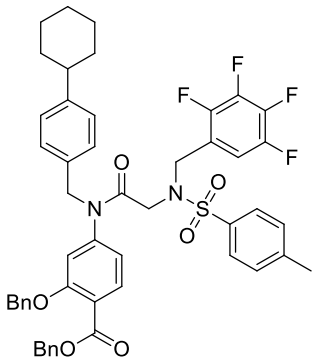


benzyl 2-(benzyloxy)-4-(2-(*N*-(4-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}N_3O_6S$
Molecular Weight: 832.02

Sulfonamide **14** was functionalized on a 0.3 mmol scale using General Procedure A to give **15ab** (205 mg, 88 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.32-1.52 (m, 5H, CH_2), 1.70-1.96 (m, 5H, CH_2), 2.41-2.57 (m, 4H, CH and CH_3), 3.70 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.46 (s, 1H, CH), 6.50 (d, *J* = 8.0 Hz, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.13 (d, *J* = 8.0 Hz, 2H, CH), 7.25-7.42 (m, 14H, CH), 7.55 (d, *J* = 8.0 Hz, 2H, CH), 7.74 (d, *J* = 8.0 Hz, 2H, CH), 7.77 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.4, 44.1, 47.3, 51.2, 52.7, 67.0, 70.7, 111.6, 113.8, 118.4, 119.8, 120.9, 126.9, 127.0, 127.5, 128.0, 128.2, 128.2, 128.5, 128.5, 128.9, 129.5, 132.3, 133.0, 133.7, 135.6, 136.5, 141.4, 143.6, 144.7, 147.7, 158.7, 165.2, 166.4; LRMS (ES+) Calcd for [$C_{51}H_{49}N_3O_6S$ + Na] 854.32 found 854.59.

Compound 15ac

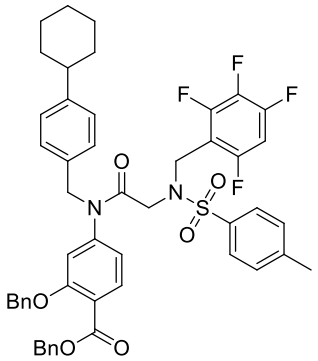


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,4,5-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{46}F_4N_2O_6S$
Molecular Weight: 878.97

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ac** (60.3 mg, 89 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31-1.45 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.39-2.54 (m, 4H, CH and CH_3), 3.81 (s, 2H, CH_2), 4.57 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.50 (s, 1H, CH), 6.62-6.73 (m, 2H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.24 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.41 (m, 10H, CH), 7.66 (d, *J* = 8.4 Hz, 2H, CH), 7.81 (d, *J* = 8.4 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 39.8, 44.4, 49.2, 52.9, 67.2, 70.8, 101.0, 110.1, 114.1, 120.3, 121.1 127.1, 127.3, 127.6, 127.8, 128.2, 128.4, 128.5, 128.7, 128.8, 129.1, 129.5, 129.7, 133.3, 134.0, 135.8, 135.9, 136.7, 143.7, 145.0, 144.8, 147.9, 159.0, 165.5, 166.7; LRMS (ES+) Calcd for [$C_{50}H_{46}F_4N_2O_6S$ + Na] 901.29 found 901.50.

Compound 15ad

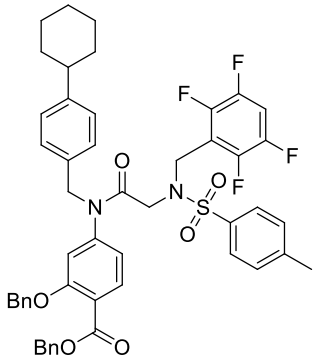


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,4,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{46}F_4N_2O_6S$
Molecular Weight: 878.97

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ad** (52.9 mg, 86 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.30-1.49 (m, 5H, CH_2), 1.67-1.92 (m, 5H, CH_2), 2.39-2.54 (m, 4H, CH and CH_3), 3.71 (s, 2H, CH_2), 4.55 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.89 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.45 (s, 1H, CH), 6.61 (d, *J* = 8.0 Hz, 1H, CH), 6.97 (d, *J* = 9.0 Hz, 2H, CH), 7.04-7.16 (m, 3H, CH), 7.27-7.43 (m, 12H, CH), 7.69 (d, *J* = 8.0 Hz, 2H, CH), 7.80 (d, *J* = 8.4 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.4, 44.6, 48.3, 52.9, 67.2, 70.8, 111.9, 112.2, 114.0, 119.9, 120.2, 121.2, 127.1, 127.2, 127.5, 127.7, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 129.7, 129.9, 133.3, 133.9, 135.8, 135.8, 136.6, 144.0, 144.8, 148.0, 158.9, 165.5, 166.4; LRMS (ES+) Calcd for [$C_{50}H_{49}F_4N_2O_6S$ + Na] 901.29 found 901.56.

Compound 15ae

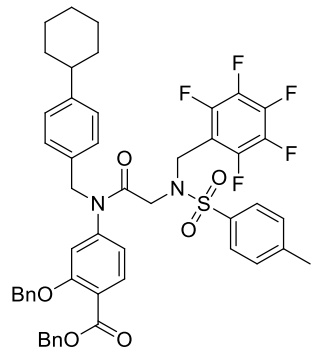


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,5,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{46}F_4N_2O_6S$
Molecular Weight: 878.97

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ae** (61.3 mg, 100 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.39-2.53 (m, 4H, CH and CH_3), 3.84 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.51 (s, 1H, CH), 6.67 (d of d, *J* = 8.0 and 1.6 Hz, 1H, CH), 6.92-7.04 (m, 3H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.25 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.42 (m, 10H, CH), 7.68 (d, *J* = 8.4 Hz, 2H, CH), 7.82 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 40.0, 44.4, 49.2, 52.9, 67.2, 70.8, 106.2, 106.4, 114.1, 115.9, 120.3, 121.1 127.1, 127.3, 127.6, 127.8, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 129.5, 129.7, 133.3, 134.0, 135.8, 136.6, 143.8, 144.0 145.0, 147.9, 159.0, 165.5, 166.6; LRMS (ES+) Calcd for [$C_{50}H_{49}F_4N_2O_6S$ + Na] 901.29 found 901.50.

Compound 15af

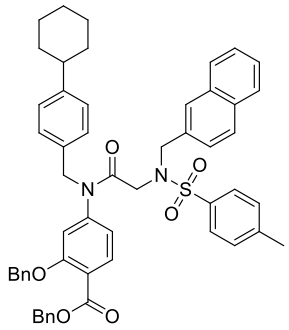


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{45}F_5N_2O_6S$
Molecular Weight: 896.96

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15af** (61.8 mg, 98 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.31-1.52 (m, 5H, CH_2), 1.65-1.97 (m, 5H, CH_2), 2.37-2.57 (m, 4H, CH and CH_3), 3.84 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.50 (s, 1H, CH), 6.67 (d of d, *J* = 8.0 and 1.2 Hz, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.21 - 7.45 (m, 12H, CH), 7.65 (d, *J* = 8.0 Hz, 2H, CH), 7.83 (d, 8.0 Hz, 1H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 39.9, 44.3, 49.5, 52.9, 67.2, 70.8, 110.3, 114.0, 120.2, 127.1, 127.2, 127.7, 128.2, 128.4, 128.4, 128.7, 128.7, 129.1, 129.5, 133.3, 133.9, 135.8, 135.8, 136.4, 143.9, 147.9, 158.9, 165.5, 166.6; LRMS (ES+) Calcd for [$C_{50}H_{45}F_5N_2O_6S$ + Na] 919.28 found 919.51.

Compound 15ag

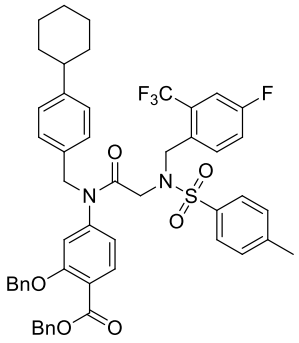


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(naphthalen-2-ylmethyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{54}H_{52}N_2O_6S$
Molecular Weight: 857.07

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ag** (60.3 mg, 100 %)

δ_H (400MHz, *d*-$CDCl_3$) 1.33-1.53 (m, 5H, CH_2), 1.69-1.98 (m, 5H, CH_2), 2.33-2.60 (m, 4H, CH and CH_3), 3.70 (s, 2H, CH_2), 4.44 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 5.28 (s, 2H, CH_2), 6.09 (s, 1H, CH), 6.29 (d, *J* = 8.0 Hz, 1H, CH), 6.97 (d, *J* = 7.5 Hz, 2H, CH), 7.10 (d, *J* = 7.4 Hz, 2H, CH), 7.12-7.46 (m, 15H, CH), 7.55 (d, *J* = 8.0 Hz, 1H, CH), 7.60 (s, 1H, CH), 7.68 (d, *J* = 8.0 Hz, 1H, CH), 7.73 (d, *J* = 8.4 Hz, 2H, CH), 7.85 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.6, 44.3, 46.9, 51.2, 52.7, 67.0, 70.4, 113.5, 120.0, 120.7, 126.4, 126.4, 126.5, 127.0, 127.4, 127.7, 127.8, 127.8, 128.0, 128.1, 128.3, 128.3, 128.5, 128.6, 128.8, 129.1, 129.6, 132.8, 133.0, 133.1, 133.1, 134.1, 135.7, 135.8, 137.3, 143.4, 147.8, 158.6, 165.4, 166.7; LRMS (ES+) Calcd for [$C_{46}H_{48}N_2O_6S$ + Na] 879.34 found 879.66.

Compound 15ah

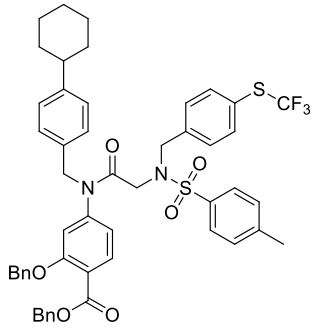


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-fluoro-2-(trifluoromethyl)benzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{48}F_4N_2O_6S$
Molecular Weight: 893.00

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ah** (56.5 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.50 (m, 5H, CH_2), 1.65-1.95 (m, 5H, CH_2), 2.35-2.50 (m, 4H, CH and CH_3), 3.68 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.84 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.39 (s, 1H, CH), 6.53 (d, *J* = 8.0 Hz, 1H, CH), 6.95 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.16-7.48 (m, 13H, CH), 7.75 (d, *J* = 7.6 Hz, 2H, CH), 7.76 (d, *J* = 7.6 Hz, 2H, CH), 7.79 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 34.3, 44.1, 47.0, 47.8, 52.6, 66.9, 70.6, 113.2, 113.8, 119.2, 119.4, 119.9, 120.8, 121.7, 126.8, 127.0, 127.6, 127.9, 128.1, 128.2, 128.4, 128.5, 128.8, 129.4, 130.7, 132.5, 132.6, 133.0, 133.7, 135.5, 135.6, 136.5, 143.5, 144.6, 147.6, 158.6, 165.2, 166.0; LRMS (ES+) calcd for [$C_{51}H_{48}F_4N_2O_6S$ + Na] 915.32, found 915.42.

Compound 15ai

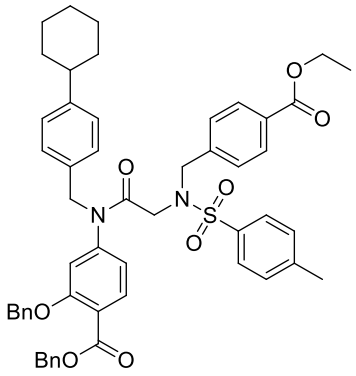


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-((trifluoromethyl)thio)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{49}F_3N_2O_6S_2$
Molecular Weight: 907.07

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ai** (37.5 mg, 60 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.47 (m, 5H, CH_2), 1.70-1.95 (m, 5H, CH_2), 2.40-2.55 (m, 4H, CH and CH_3), 3.68 (s, 2H, CH_2), 4.60 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.38 (d, *J* = 8.0 Hz, 1H, CH), 6.42 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.20-7.45 (m, 14H, CH), 7.55 (d, *J* = 8.0 Hz, 2H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.74 (d, *J* = 8.0 Hz, 2H, CH); 21.5, 25.9, 26.7, 34.3, 44.1, 47.0, 50.8, 52.6, 66.9, 70.6, 113.7, 113.7, 119.8, 125.2, 125.4, 125.4, 125.4, 125.5, 126.8, 127.0, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.7, 128.7, 128.8, 128.9, 129.4, 129.9, 130.2, 132.9, 133.7, 135.5, 135.6, 136.7, 139.6, 139.7, 143.4, 147.7, 158.6, 165.2, 166.5; LRMS (ES+) calcd for [$C_{51}H_{49}F_3N_2O_6S$ + Na] 929.30, found 929.34.

Compound 15aj

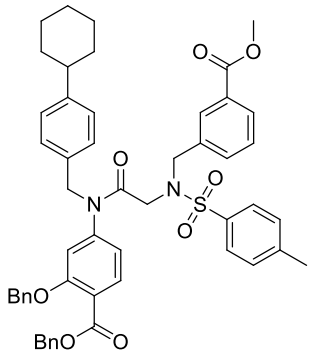


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-(ethoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{53}H_{54}N_2O_8S$
Molecular Weight: 879.07

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15aj** (40.1 mg, 65 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.43 (m, 8H, CH_2 and CH_3), 1.70-1.89 (m, 5H, CH_2), 2.42-2.53 (m, 4H, CH_3 and CH), 3.66 (s, 2H, CH_2), 4.29 (q, *J* = 7.2 Hz, 2H, CH), 4.62 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.44 (d, *J* = 8.0 Hz, 1H, CH), 6.95 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 1H, CH), 7.26-7.39 (m, 15H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.76 (d, *J* = 8.0 Hz, 2H, CH), 7.94 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 14.1 21.5, 25.9, 26.7, 34.3, 44.1, 46.9, 50.8, 51.9, 52.6, 66.9, 70.5, 113.6, 119.8, 120.7 126.3, 126.8, 127.1, 127.5, 127.9, 128.1, 128.7, 129.8, 130.7, 132.3, 132.9, 133.7, 135.5, 135.6, 136.8, 140.7, 143.3, 147.6, 158.6, 165.2, 166.4, 167.6; LRMS (ES+) calcd for [$C_{53}H_{54}N_2O_8S$ + Na] 901.36, found 901.44.

Compound 15ak

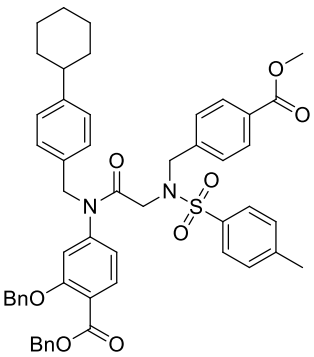


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(3-(methoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{52}H_{52}N_2O_8S$
Molecular Weight: 865.04

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15ak** (48.2 mg, 80 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.67-1.94 (m, 5H, CH_2), 2.35-2.55 (m, 4H, CH and CH_3), 3.67 (s, 2H, CH_2), 3.86 (s, 3H, CH_3), 4.60 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.34 (s, 1H, CH), 6.46 (d, *J* = 8.0 Hz, 1H, CH), 6.95 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.24-7.43 (m, 13H, CH), 7.47 (d, *J* = 7.6 Hz, 1H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.76 (d, *J* = 8.4 Hz, 2H, CH), 7.84 (s, 1H, CH), 7.93 (d, *J* = 8.4 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 34.3, 44.1, 46.8, 50.8, 52.0, 52.6, 66.9, 70.6, 113.6, 119.9, 120.6, 126.8, 127.0, 127.5, 127.9, 128.1, 128.1, 128.4, 128.4, 128.8, 129.1, 129.4, 129.5, 130.4, 132.9, 133.2, 133.7, 135.6, 135.9, 136.9, 143.3, 144.7, 147.6, 158.6, 165.2, 166.4, 166.5; LRMS (ES+) calcd for [$C_{52}H_{52}N_2O_8S$ + Na] 887.34, found 887.40.

Compound 15al

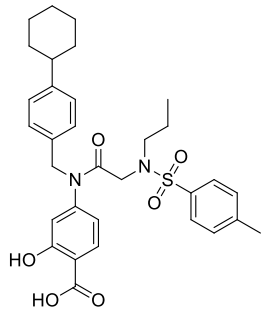


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-(methoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{52}H_{52}N_2O_8S$
Molecular Weight: 865.04

Sulfonamide **14** was functionalized on a 0.07 mmol scale using General Procedure A to give **15al** (51.1 mg, 84 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.48 (m, 5H, CH_2), 1.70-1.95 (m, 5H, CH_2), 2.38-2.60 (m, 4H, CH and CH_3), 3.67 (s, 2H, CH_2), 3.82 (s, 3H, CH_3), 4.62 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.29 (s, 1H, CH), 6.44 (d, *J* = 8.0 Hz, 1H, CH), 6.95 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.20-7.39 (m, 14H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.76 (d, *J* = 8.0 Hz, 2H, CH), 7.93 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 25.9, 26.7, 34.3, 44.1, 46.9, 50.8, 51.9, 52.6, 66.9, 70.5, 113.6, 119.8, 120.7, 126.3, 126.8, 127.1, 127.5, 127.9, 128.1, 128.1, 128.4, 128.7, 128.8, 129.4, 129.8, 130.7, 132.3, 132.9, 133.7, 135.5, 135.6, 136.8, 140.7, 143.3, 144.7, 129.7, 147.6, 158.6, 165.2, 166.4, 167.6; LRMS (ES+) calcd for [$C_{52}H_{52}N_2O_8S$ + H] 865.34, found 865.42.

Compound 16a

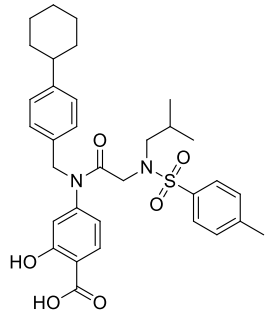


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-propylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{32}H_{38}N_2O_6S$
Molecular Weight: 578.72
Log P: 6.26

Compound **15a** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16a** (37.3 mg, 92 %)

δ_H (400 MHz, *d*-$CDCl_3$) 0.82 (t, *J* = 7.2 Hz, 3H, CH_3), 1.32-1.42 (m, 5H, CH_2), 1.42-1.54 (m, 2H, CH_2), 1.78-1.96 (m, 5H, CH_2), 2.38-2.52 (m, 4H, CH and CH_3), 3.25 (t, *J* = 7.6 Hz, 2H, CH_2), 3.93 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 6.60 (d, *J* = 8.0 Hz, 1H, CH), 6.70 (s, 1H, CH), 7.04 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.27 (d, *J* = 8.0 Hz, 2H, CH), 7.73 (d, *J* = 8.0 Hz, 2H, CH), 7.87 (d, *J* = 8.4 Hz, 1H, CH), 10.74 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 11.2, 21.3, 21.7, 26.2, 27.0, 34.5, 44.3, 48.2, 50.1, 53.1, 111.8, 117.2, 119.3, 127.1, 127.7, 128.6, 128.7, 129.6, 132.4, 133.7, 136.9, 143.4, 147.8, 163.1, 167.4, 172.5; HRMS (ES+) Calcd for [$C_{32}H_{38}N_2O_6S$ + H] 579.2523 found 579.2512; HPLC (I) t_R =15.83 min (97.2 %), (II) 40.90 min (96.5 %).

Compound 16b

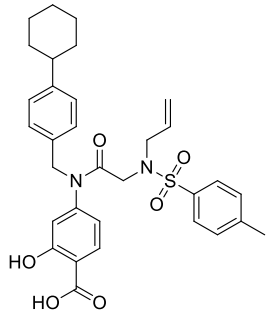


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-isobutyl-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{33}H_{40}N_2O_6S$
Molecular Weight: 592.75
Log P: 6.66

Compound **15b** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **16b** (16.8 mg, 94 %)

δ_H (400 MHz, *d*-$CDCl_3$) 0.8 (d, *J* = 6.4 Hz, 6H, 2 CH_3), 1.32-1.48 (m, 5H, CH_2), 1.66-1.92 (m, 6H, CH and CH_2), 2.32-2.53 (m, 4H, CH and CH_3), 3.14 (d, *J* = 7.2 Hz, 2H, CH_2), 3.92 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 6.59 (d, *J* = 8.0 Hz, 1H, CH), 6.70 (s, 1H, CH), 7.01 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.28 (d, *J* = 8.0 Hz, 2H, CH), 7.71 (d, *J* = 8.0 Hz, 2H, CH), 7.87 (d, *J* = 7.6 Hz, 1H, CH), 10.66 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 20.1, 21.7, 26.3, 27.0, 29.8, 34.6, 44.4, 48.6, 50.1, 53.1, 111.5, 117.2, 119.4, 127.1, 127.8, 128.6, 129.5, 132.5, 133.7, 137.0, 143.3, 146.0, 147.8, 163.2, 167.2, 172.6; HRMS (ES+) Calcd for [$C_{33}H_{40}N_2O_6S$ + H] 593.2679 found 593.2653; HPLC (I) t_R =23.42 min (100 %), (II) 53.02 min (100 %).

Compound 16c

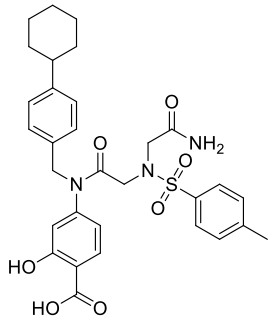


4-(2-(*N*-allyl-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{32}H_{36}N_2O_6S$
Molecular Weight: 576.70
Log P: 5.47

Compound **15a** was globally deprotected according to general procedure C on a 0.06 mmol scale to give compound **16c** (25.9 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.38-2.54 (m, 4H, CH and CH_3), 3.90 (s, 2H, CH_2), 3.94 (d, *J* = 6.4 Hz, 2H, CH_2) 4.79 (s, 2H, CH_2), 5.12-5.21 (m, 2H, CH_2), 5.59-5.71 (m, 1H, CH), 6.57 (d of d, *J* = 8.4 and 2.0 Hz, 1H, CH), 6.67 (d, *J* = 2.0 Hz, 1H, CH), 7.05 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.28 (d, *J* = 8.0 Hz, 2H, CH), 7.74 (d, *J* = 8.4 Hz, 2H, CH), 7.87 (d, *J* = 8.4 Hz, 1H, CH), 10.74 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.3, 27.0, 34.5, 44.3, 47.3, 50.9, 53.1, 111.9, 117.2, 119.3, 119.8, 127.1, 127.8, 128.6, 129.6, 132.4, 132.9, 133.7, 136.9, 143.5, 147.8, 148.0, 163.1, 167.4, 172.5; HRMS (ES+) Calcd for [$C_{32}H_{36}N_2O_6S$ + H] 577.2366 found 577.2388; HPLC (III) t_R =22.00 min (100 %), (IV) 50.92 min (100 %).

Compound 16d

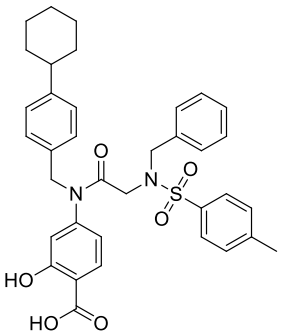


4-(2-(*N*-(2-amino-2-oxoethyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{31}H_{35}N_3O_7S$
Molecular Weight: 593.69
Log P: 3.29

Compound **15c** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **16d** (25.8 mg, 87 %)

δ_H (400 MHz, d_6-DMSO) 1.26-1.43 (m, 5H, CH_2), 1.63-1.83 (m, 5H, CH_2), 2.36 (s, 3H, CH_3), 2.40-2.49 (m, 1H, CH), 3.81 (s, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 6.72 (d of d, *J* = 8.4 and 2.0 Hz, 1H, CH), 6.79 (d, *J* = 2.0 Hz, 1H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.14 (d, *J* = 8.0 Hz, 2H, CH), 7.21 (s, 1H, NH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.57 (d, *J* = 8.4 Hz, 2H, CH), 7.78 (d, *J* = 8.4 Hz, 1H, CH), 8.01 (s, 1H, NH); δ_C (100 MHz, d_6-DMSO) 21.0, 25.6, 26.3, 33.9, 43.4, 50.1, 51.4, 54.9, 113.4, 116.2, 118.0, 126.6, 127.1, 127.6, 129.6, 131.4, 134.2, 135.6, 143.4, 146.5, 148.1, 162.0, 167.9, 170.0. 171.0; HRMS (ES+) Calcd for [$C_{31}H_{37}N_3O_7S$ + H] 627.2500 found 627.2523; HPLC (III) t_R =20.94 min (98.5 %), (IV) 47.57 min (98.5 %).

Compound 16e

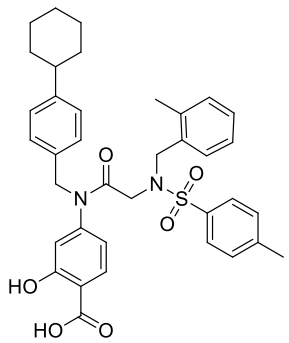


4-(2-(*N*-benzyl-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{38}N_2O_6S$
Molecular Weight: 626.76
Log P: 6.27

Compound **15d** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16e** (34.5 mg, 92 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.50 (m, 5H, CH_2), 1.69-1.96 (m, 5H, CH_2), 2.37-2.55 (m, 4H, CH and CH_3), 3.78 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 6.24 (d, *J* = 7.6 Hz, 1H, CH), 6.42 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.16-7.29 (m, 5H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH), 7.81 (d, *J* = 8.0 Hz, 2H, CH), 10.57 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.2, 27.0, 34.6, 44.4, 47.0, 51.2, 53.0, 111.6, 117.1, 119.2, 127.1, 127.8, 128.2, 128.6, 128.7, 128.7, 128.8, 128.9, 129.7, 132.2, 133.6, 137.1, 143.5, 147.8, 163.0, 167.0, 172.7; HRMS (ES+) Calcd for [$C_{36}H_{38}N_2O_6S$ + H] 627.2500 found 627.2523; HPLC (I) t_R =16.48 min (97.4 %), (II) 43.18 min (98.5 %).

Compound 16f

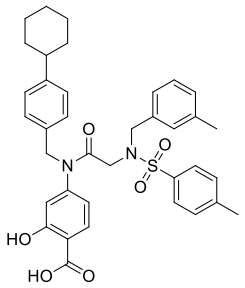


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{40}N_2O_6S$
Molecular Weight: 640.79
Log P: 6.69

Compound **15e** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16f** (32.5 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.49 (m, 5H, CH_2), 1.71-1.93 (m, 5H, CH_2), 2.24 (s, 3H, CH_3), 2.40-2.55 (m, 4H, CH and CH_3), 3.70 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 6.18 (d, *J* = 6.8 Hz, 1H, CH), 6.37 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.02-7.16 (m, 5H, CH), 7.17-7.24 (m, 1H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.80 (d, *J* = 8.0 Hz, 2H, CH), 10.51 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 19.2, 21.8, 26.3, 27.0, 34.6, 44.4, 46.9, 49.2, 52.9, 111.4, 117.2, 119.3, 126.2, 127.0, 127.9, 128.5, 128.7, 129.6, 130.1, 130.8, 132.2, 132.8, 133.6, 136.8, 138.0, 143.5, 147.8, 148.0, 163.0, 166.9, 172.7; HRMS (ES+) Calcd for [$C_{37}H_{40}N_2O_6S$ + H] 641.2679 found 641.2650; HPLC (I) t_R =23.94 min (100 %), (II) 54.87 min (100 %).

Compound 16g

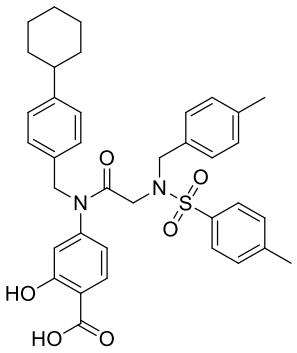


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{40}N_2O_6S$
Molecular Weight: 640.79
Log P: 6.69

Compound **15f** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16g** (38.2 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.52 (m, 5H, CH_2), 1.70-1.97 (m, 5H, CH_2), 2.26 (s, 3H, CH_3), 2.40-2.56 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.26 (d, *J* = 7.6 Hz, 1H, CH), 6.41 (s, 1H, CH), 6.95-7.04 (m, 4H, CH), 7.06-7.21 (m, 4H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.72 (d, *J* = 7.6 Hz, 1H, CH), 7.81 (d, *J* = 8.0 Hz, 2H, CH), 10.54 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.4, 21.7, 26.3, 27.0, 34.5, 44.4, 46.9, 51.1, 53.0, 111.5, 117.1, 119.2, 126.1, 127.1, 127.8, 128.1, 128.7, 129.0, 129.6, 129.6, 132.2, 133.6, 135.1, 137.2, 138.6, 143.5, 147.8, 148.0, 163.0, 167.0, 172.8; HRMS (ES+) Calcd for [$C_{37}H_{40}N_2O_6S$ + H] 641.2679 found 641.2648; HPLC (I) t_R =23.95 min (100 %), (II) 55.00 min (100 %).

Compound 16h

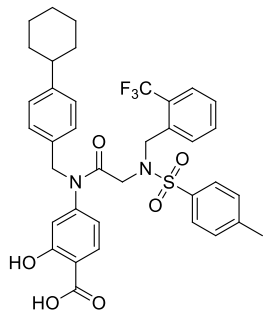


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{40}N_2O_6S$
Molecular Weight: 640.79
Log P: 6.69

Compound **15g** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16h** (33.2 mg, 87 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.50 (m, 5H, CH_2), 1.69-1.96 (m, 5H, CH_2), 2.33 (s, 3H, CH_3), 2.38-2.60 (m, 4H, CH and CH_3), 3.77 (s, 2H, CH_2), 4.52 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.24 (d, *J* = 7.8 Hz, 1H, CH), 6.36 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.04-7.09 (m, 4H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.72 (d, *J* = 8.4 Hz, 1H, CH), 7.81 (d, *J* = 8.0 Hz, 2H, CH), 10.56 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.3, 21.7, 26.2, 27.0, 34.6, 44.4, 46.8, 50.9, 53.0, 111.6, 117.1, 119.3, 127.1, 127.8, 128.7, 129.0, 129.5, 129.6, 132.0, 132.2, 133.6, 137.1, 138.1, 143.5, 147.8, 147.9, 163.0, 167.0, 172.7; HRMS (ES+) Calcd for [$C_{37}H_{40}N_2O_6S$ + H] 641.2679 found 641.2654; HPLC (I) t_R =16.65 min (97.8 %), (II) 44.47 min (98.8 %).

Compound 16i

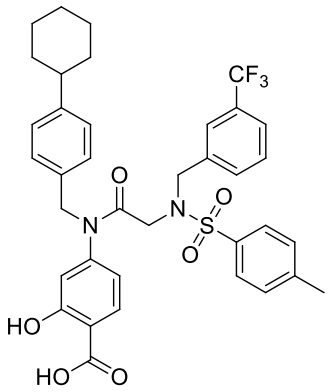


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_6S$
Molecular Weight: 694.76
Log P: 7.26

Compound **15h** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16i** (37.4 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.50 (m, 5H, CH_2), 1.67-1.91 (m, 5H, CH_2), 2.35-2.56 (m, 4H, CH and CH_3), 3.83 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 6.38 (d, *J* = 7.2 Hz, 1H, CH), 6.51 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.08 (d, *J* = 8.0 Hz, 2H, CH), 7.29-7.41 (m, 3H, CH), 7.44-7.53 (m, 1H, CH), 7.62 (d, *J* = 8.0 Hz, 1H, CH), 7.70-7.87 (m, 4H, CH), 10.63 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.2, 27.0, 34.5, 44.3, 47.7, 47.9, 53.0, 111.8, 117.2, 119.2, 125.6, 125.8, 125.9, 127.1, 127.8, 127.9, 128.3, 128.6, 129.7, 130.1, 132.3, 132.5, 133.5, 134.9, 136.8, 143.8, 147.8, 163.0, 166.5, 172.7; HRMS (ES+) Calcd for [$C_{37}H_{37}F_3N_2O_6S$ + H] 695.2397 found 695.2399; HPLC (I) t_R =23.90 min (100 %), (II) 54.98 min (100 %).

Compound 16j



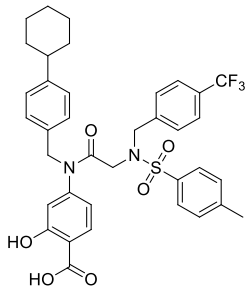
4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_6S$
Molecular Weight: 694.76
Log P: 7.26

Compound **15i** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **16j** (21.9 mg, 79 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.55 (m, 5H, CH_2), 1.65-1.95 (m, 5H, CH_2), 2.30-2.60 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.32 (d, *J* = 8.0 Hz, 1H, CH), 6.47 (s, 1H, CH), 6.99 (d, *J* = 8.4 Hz, 2H, CH), 7.10 (d, *J* = 8.4 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.36-7.44 (m, 2H, CH), 7.46 (d, *J* = 7.6 Hz, 1H, CH), 7.53 (d, *J* = 7.6 Hz, 1H, CH), 7.65-7.95 (m, 3H, CH), 10.60 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.3, 27.0, 34.5, 44.4, 47.3, 51.0, 53.0, 111.7, 117.1, 119.0, 119.1, 125.1, 125.4, 127.1, 127.8, 128.6, 129.4, 129.7, 132.2, 132.3, 133.5, 136.7, 136.9, 143.8, 147.4, 147.8, 147.9, 163.1, 166.9,

172.5; HRMS (ES+) calcd for [$C_{37}H_{37}N_2O_6F_3S$ + H] 695.2397, found 695.2406; HPLC (I) t_R = 23.87 min (100 %), (II) t_R = 54.89 min (100 %).

Compound 16k

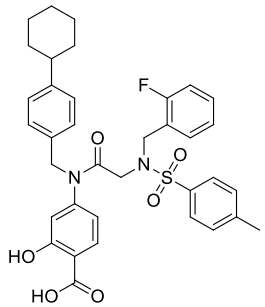


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_6S$
Molecular Weight: 694.76
Log P: 7.26

Compound **15j** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **16k** (28.9 mg, 83 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.48 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.38-2.54 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.27 (d, *J* = 8.0 Hz, 1H, CH), 6.46 (s, 1H, CH), 6.99 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.35 (d, *J* = 8.0 Hz, 2H, CH), 7.52 (d, *J* = 8.0 Hz, 2H, CH), 7.70-7.86 (m, 3H, CH), 10.60 (s, 1H, OH); δC (100 MHz, *d*-$CDCl_3$) 21.4, 26.0, 26.7, 34.3, 44.1, 47.0, 50.7, 52.8, 111.4, 116.8, 118.7, 125.2, 125.5, 125.5, 126.8, 127.5, 128.7, 129.4, 132.0, 132.0, 133.2, 136.6, 139.5, 143.5, 147.7, 162.8, 166.5, 166.6, 172.1; HRMS (ES+) calcd for [$C_{37}H_{37}N_2O_6F_3S$ + H] 695.2397, found 695.2414; HPLC (I) t_R = 23.98 min (98.6 %), (II) t_R = 55.45 min (96.6 %).

Compound 16l

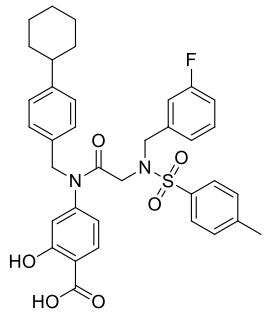


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(2-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}FN_2O_6S$
Molecular Weight: 644.75
Log P: 6.41

Compound **15k** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16l** (31.7 mg, 82 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.37-2.53 (m, 4H, CH and CH_3), 3.84 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 6.42 (d, *J* = 8.0 Hz, 1H, CH), 6.54 (s, 1H, CH), 6.96-7.04 (m, 3H CH), 7.06 (t, *J* = 7.6 Hz, 1H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.21-7.27 (m, 1H, CH), 7.29 (d, *J* = 8.0 Hz, 2H, CH), 7.33-7.41 (m, 1H, CH), 7.74-7.84 (m, 3H, CH) 10.56 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 44.8, 47.7, 53.0, 111.6, 115.3, 115.6, 117.2, 119.3, 122.5, 122.7, 124.6, 124.6, 127.1, 127.8, 128.6, 129.6, 130.0, 130.0, 131.4, 131.4, 132.3, 133.6, 137.0, 143.5, 147.8, 148.0, 160.1, 162.5, 163.0, 166.9, 172.8; HRMS (ES+) Calcd for [$C_{36}H_{37}FN_2O_6S$ + H] 645.2429 found 645.2396; HPLC (I) t_R =23.49 min (100 %), (II) 53.47 min (100 %).

Compound 16m

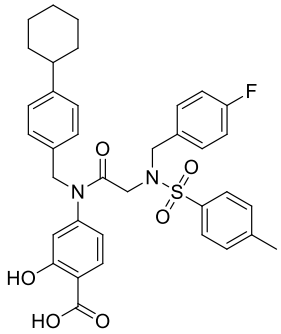


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(3-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}FN_2O_6S$
Molecular Weight: 644.75
Log P: 6.41

Compound **15l** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16m** (36.2 mg, 94 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.39-2.55 (m, 4H, CH and CH_3), 3.80 (s, 2H, CH_2), 4.58 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.33 (d, *J* = 8.0 Hz, 1H, CH), 6.47 (s, 1H, CH), 6.91-7.05 (m, 5H CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.20-7.27 (m, 1H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.79 (d, *J* = 8.0 Hz, 1H, CH), 10.56 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.2, 27.0, 34.5, 44.3, 47.1, 50.8, 53.0, 111.6, 115.1, 115.3, 115.5, 115.7, 117.0, 119.1, 124.3, 124.3, 127.1, 127.8, 128.6, 129.7, 130.3, 130.4, 132.3, 133.5, 136.9, 138.1, 138.1, 143.7, 147.8, 147.9, 161.9, 163.0, 164.3, 166.9, 172.7; HRMS (ES+) Calcd for [$C_{36}H_{37}FN_2O_6S$ + H] 645.2429 found 645.2406; HPLC (I) t_R =23.60 min (100 %), (II) 53.89 min (100 %).

Compound 16n

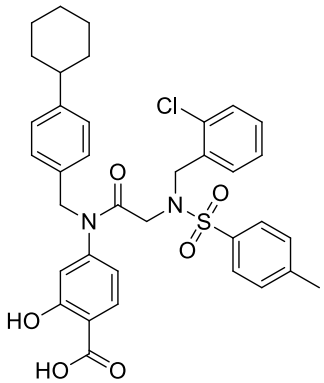


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-fluorobenzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}FN_2O_6S$
Molecular Weight: 644.75
Log P: 6.41

Compound **15m** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16n** (35.8 mg, 93 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.40-2.54 (m, 4H, CH and CH_3), 3.74 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.27 (d, *J* = 7.6 Hz, 1H, CH), 6.42 (s, 1H, CH), 6.90-7.03 (m, 4H CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.15-7.23 (m, 2H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.76 (d, *J* = 8.4 Hz, 1H, CH), 7.79 (d, *J* = 8.0 Hz, 2H, CH), 10.92 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.6, 44.4, 46.9, 50.5, 52.9, 110.8, 115.6, 115.8, 116.9, 118.9, 127.1, 127.8, 128.7, 129.7, 130.6, 130.7, 131.1 131.2, 132.2, 133.7, 137.1, 143.5, 147.8, 161.4, 163.0, 163.6, 166.8, 172.1; HRMS (ES+) Calcd for [$C_{36}H_{37}FN_2O_6S$ + H] 645.2429 found 645.2398; HPLC (I) t_R =23.63 min (100 %), (II) 53.98 min (100 %).

Compound 16o

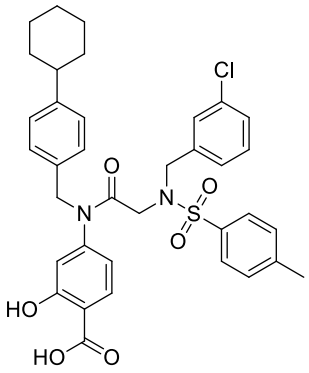


4-(2-(*N*-(2-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}ClN_2O_6S$
Molecular Weight: 661.21
Log P: 6.89

Compound **15n** was globally deprotected according to general procedure B on a 0.09 mmol scale to give compound **16o** (41.2 mg, 69 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.46 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.40-2.53 (m, 4H, CH and CH_3), 3.74 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.35 (d, *J* = 7.2 Hz, 1H, CH), 6.50 (s, 1H, CH), 7.00 (d, *J* = 7.8 Hz, 2H, CH), 7.09 (d, *J* = 7.8 Hz, 2H, CH), 7.13-7.23 (m, 2H, CH), 7.27-7.34 (m, 3H, CH), 7.40 (d, *J* = 6.5 Hz, 1H, CH), 7.73-7.81 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 26.0, 26.7, 34.3, 44.1, 47.6, 48.5, 52.8, 112.3, 116.7, 118.8, 126.7, 127.1, 127.6, 128.5, 128.7, 129.1, 129.3, 129.4, 130.5, 133.1, 133.5, 133.8, 136.8, 143.2, 147.4, 162.7, 163.5, 166.5, 171.8; HPLC (I) t_R =28.24 min (100 %). HRMS (ES+) Calcd for [$C_{36}H_{38}N_2O_6SCl$ + H] 661.2133 found 661.2151

Compound 16p

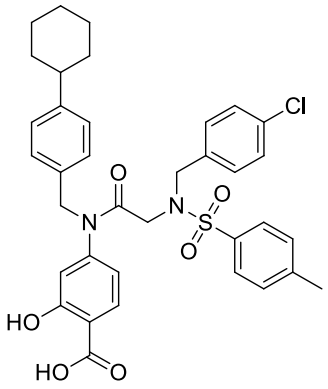


4-(2-(*N*-(3-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}ClN_2O_6S$
Molecular Weight: 661.21
Log P: 6.89

Compound **15o** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16p** (28.4 mg, 61 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.39-2.52 (m, 4H, CH and CH_3), 3.76 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.22 (d, *J* = 7.8 Hz, 1H, CH), 6.40 (s, 1H,CH), 6.99 (d. *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.16-7.23 (m, 2H, CH), 7.24-7.29 (m, 2H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.71 (d, *J* = 7.8 Hz, 1H, CH), 7.81 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.6, 26.1, 26.9, 34.4, 44.2, 46.7, 51.0, 52.8, 111.7, 116.9, 118.3, 126.9, 127.7, 128.1, 128.5, 128.5, 128.7, 128.8, 129.5, 132.0, 132.5, 133.6, 135.2, 137.1, 143.3, 147.6, 161.5, 162.8, 166.7, 170.8; HPLC (I) t_R =28.30 min (98.40 %), (II) 62.83 min (98.25 %); HRMS (ES+) Calcd for [$C_{36}H_{38}N_2O_6SCl$ + H] 661.2133 found 661.2137.

Compound 16q

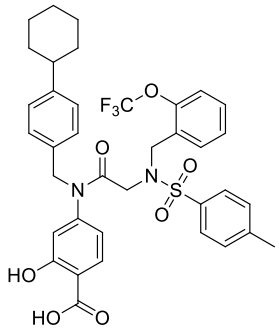


4-(2-(*N*-(4-chlorobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}ClN_2O_6S$
Molecular Weight: 661.21
Log P: 6.89

Compound **15p** was globally deprotected according to general procedure B on a 0.08 mmol scale to give compound **16q** (33.7 mg, 64 %).

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.54 (m, 4H, CH and CH_3), 3.76 (s, 2H, CH_2), 4.53 (s, 2H, CH_2), 4.70 (s, 4H, 2 CH_2), 6.30 (d, *J* = 7.2 Hz, 1H, CH), 6.46 (s, 1H, CH), 6.98 (d, *J* = 7.8 Hz, 2H, CH), 7.10 (d, *J* = 7.8 Hz, 2H, CH), 7.15 (d, *J* = 8.2 Hz, 2H, CH), 7.23 (d, *J* = 8.2 Hz, 2H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.73-7.81 (m, 3H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.6, 26.1, 26.8, 34.4, 44.2, 46.8, 50.5, 52.9, 110.7, 116.9, 118.9, 127.0, 127.7, 128.4, 128.8, 129.5, 130.1, 132.2, 133.4, 133.7, 134.0, 136.8, 143.5, 147.7, 162.9, 163.5, 166.8, 172.8; HPLC (I) t_R =28.10 min (100 %), (II) 62.98 min (100 %); HRMS (ES+) Calcd for [$C_{36}H_{38}N_2O_6SCl$ + H] 661.2133 found 661.2149.

Compound 16r

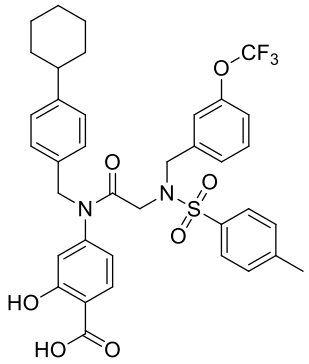


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_7S$
Molecular Weight: 710.76
Log P: 7.1

Compound **15q** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **16r** (29.6 mg, 83 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.40-2.53 (m, 4H, CH and CH_3), 3.81 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.40 (d, *J* = 8.0 Hz, 1H, CH), 6.53 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.18-7.24 (m, 2H, CH), 7.28-7.35 (m, 3H, CH), 7.51 (d, *J* = 8.0 Hz, 1H, CH), 7.77 (d, *J* = 8.0 Hz, 3H, CH), 10.67 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.3, 27.0, 34.5, 44.3, 45.7, 47.8, 53.0, 111.9, 117.1, 119.1, 119.3 120.7, 121.8, 127.0, 127.4, 127.8, 128.6, 129.4, 129.6, 131.1, 132.3, 133.6, 137.0, 143.6, 147.7, 147.8, 153.4, 163.0, 166.6, 172.5; HRMS (ES+) calcd for [$C_{37}H_{37}N_2O_7F_3S$ + H] 711.2346, Found 711.2348; HPLC (I) t_R = 23.97 min (98.3 %), (II) t_R = 55.46 min (96.0 %).

Compound 16s



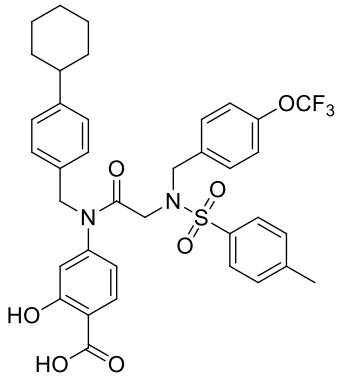
4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_7S$
Molecular Weight: 710.76
Log P: 7.1

Compound **15r** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **16s** (27.6 mg, 97 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.39-2.55 (m, 4H, CH and CH_3), 3.78 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.27 (d, *J* = 8.0 Hz, 1H, CH), 6.45 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.03 (s, 1H, CH), 7.06-7.17 (m,3H, CH), 7.20 (d, *J* = 7.6 Hz, 1H, CH), 7.29 (d, *J* = 8.0 Hz, 1H, CH), 7.33 (d, *J* = 8.4 Hz, 2H, CH), 7.73-7.85 (m, 3H, CH), 10.59 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.3, 27.0, 34.6, 44.4, 47.2, 50.9, 53.1, 111.8, 117.1, 119.0, 119.3, 120.5, 121.2, 127.1, 127.8, 128.6, 129.7, 130.3, 132.3, 133.6, 137.0, 138.1, 141.6, 143.8, 147.8, 147.9, 149.7, 163.1, 166.8, 172.3; HRMS

(ES+) calcd for [$C_{37}H_{38}N_2O_7F_3S$ + H] 711.2346, Found 711.2341; HPLC (I) t_R = 23.95 min (96.5 %), (II) t_R = 55.18 min (100 %).

Compound 16t

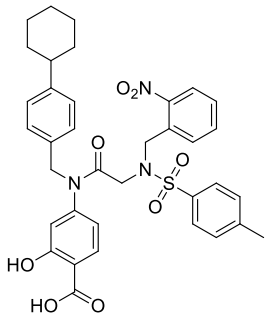


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_7S$
Molecular Weight: 710.76
Log P: 7.1

Compound **15s** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **16t** (25.1 mg, 88 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.50 (m, 5H, CH_2), 1.70-1.95 (m, 5H, CH_2), 2.30-2.55 (m, 4H, CH and CH_3), 3.77 (s, 2H, CH_2), 4.57 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 6.26 (d, *J* = 8.0 Hz, 1H, CH), 6.48 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 4H, CH), 7.25 (d, *J* = 8.0 Hz, 2H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.50-7.56 (m, 1H, CH), 7.68-7.82 (m, 3H, CH), 10.67 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.3, 26.7, 27.0, 34.6, 44.4, 47.2, 53.1, 110.9, 117.1, 119.1, 121.2, 127.1, 127.8, 129.0, 130.3, 131.0, 132.3, 132.7, 133.6, 134.3, 137.0, 143.7, 147.8, 148.0, 149.1, 163.1, 166.9, 172.3; HRMS (ES+) calcd for [$C_{37}H_{37}N_2O_7F_3S$ + H] 711.2346, Found 711.2333; HPLC (I) t_R = 24.03 min (90.9 %), (II) t_R = 55.80 min (96.4 %).

Compound 16u

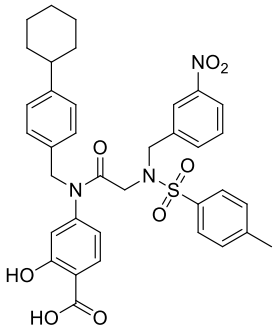


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2-nitrobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}N_3O_8S$
Molecular Weight: 671.76
Log P: 6.23

Compound **15t** was globally deprotected according to general procedure C on a 0.08 mmol scale to give compound **16u** (41.6 mg, 77 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.40-2.54 (m, 4H, CH and CH_3), 3.92 (s, 2H, CH_2), 4.74 (s, 2H, CH_2) 4.95 (s, 2H, CH_2), 6.49 (d, *J* = 8.0 Hz, 1H, CH), 6.60 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.29 (d, *J* = 8.0 Hz, 2H, CH), 7.41 (t, *J* = 8.0 Hz, 1H, CH), 7.58 (t, *J* = 7.2 Hz, 1H, CH), 7.71 (d, *J* = 8.0 Hz, 2H, CH), 7.76-7.84 (m, 2H, CH), 7.93 (d, *J* = 8.0 Hz, 1H, CH), 10.61 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 49.1, 49.2, 53.1, 111.7, 117.3, 119.3, 123.3, 124.9, 127.1, 127.8, 128.6, 128.7, 129.7, 130.7, 132.0, 132.4, 133.4, 133.7, 136.5, 143.9, 147.8, 148.8, 163.1, 166.7, 172.5; HRMS (ES+) Calcd for [$C_{36}H_{37}N_3O_8S$ + H] 672.2374 found 672.2369; HPLC (III) t_R =26.70 min (100 %), (IV) 59.40 min (100 %).

Compound 16v

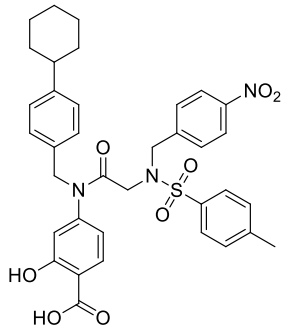


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(3-nitrobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}N_3O_8S$
Molecular Weight: 671.76
Log P: 6.23

Compound **15u** was globally deprotected according to general procedure C on a 0.10 mmol scale to give compound **16v** (60.5 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.48 (m, 5H, CH_2), 1.70-1.93 (m, 5H, CH_2), 2.40-2.54 (m, 4H, CH and CH_3), 3.82 (s, 2H, CH_2), 4.69 (s, 2H, CH_2) 4.73 (s, 2H, CH_2), 6.42 (d, *J* = 8.0 Hz, 1H, CH), 6.49 (s, 1H, CH), 6.69 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.47 (t, *J* = 8.0 Hz, 1H, CH), 7.74-7.85 (m, 3H, CH), 8.02 (s, 1H, CH), 8.12 (d, *J* = 8.0 Hz, 1H, CH), 10.56 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 47.6, 51.0, 53.1, 111.7, 117.0, 119.1, 123.2, 123.3, 127.2, 127.7, 128.6, 129.8, 129.9, 132.5, 133.4, 134.8, 136.6, 138.1, 144.0, 147.7, 148.0, 148.5, 163.0, 166.8, 172.5; HRMS (ES+) Calcd for [$C_{37}H_{37}N_3O_8S$ + H] 672.2374 found 672.2375; HPLC (III) t_R =26.74 min (100 %), (IV) 59.47 min (100 %).

Compound 16w

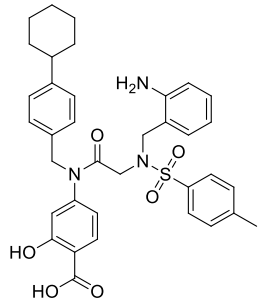


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-nitrobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{37}N_3O_8S$
Molecular Weight: 671.76
Log P: 6.23

Compound **15v** was globally deprotected according to general procedure C on a 0.06 mmol scale to give compound **16w** (32.5 mg, 81 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.48 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.40-2.53 (m, 4H, CH and CH_3), 3.80 (s, 2H, CH_2), 4.68 (s, 2H, CH_2) 4.70 (s, 2H, CH_2), 6.38 (d, *J* = 8.4 Hz, 1H, CH), 6.42 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.42 (d, *J* = 8.4 Hz, 2H, CH), 7.72-7.82 (m, 3H, CH), 8.11 (d, *J* = 8.4 Hz, 2H, CH), 10.66 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.5, 44.3, 47.5, 51.0, 53.1, 112.0, 117.0, 118.9, 124.0, 127.1, 127.8, 128.6, 128.9, 129.3, 129.8, 132.4, 133.4, 136.5, 143.4, 144.0, 147.8, 148.0, 163.0, 166.7, 172.4; HRMS (ES+) Calcd for [$C_{36}H_{37}N_3O_8S$ + H] 672.2374 found 672.2385; HPLC (III) t_R =26.88 min (88.8 %), (IV) 59.89 min (90.8 %).

Compound 16x

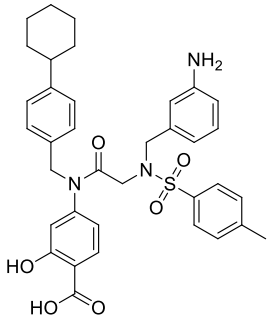


4-(2-(*N*-(2-aminobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{39}N_3O_6S$
Molecular Weight: 641.78
Log P: 5.46

Compound **15t** was globally deprotected according to general procedure B on a 0.14 mmol scale to give compound **16x** (67.2 mg, 75 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.38-2.54 (m, 4H, CH and CH_3), 3.74 (s, 2H, CH_2), 4.40 (s, 2H, CH_2) 4.68 (s, 2H, CH_2), 6.21 (d, *J* = 7.2 Hz, 1H, CH), 6.41 (s, 1H, CH), 6.70 (t, *J* = 7.2 Hz, 1H, CH), 6.77 (d, *J* = 8.0 Hz, 1H, CH), 6.89 (d, *J* = 7.2 Hz, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.16 (t, *J* = 7.6 Hz, 1H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.68 (d, *J* = 8.4 Hz, 1H, CH), 7.79 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 47.1, 49.5, 53.1, 112.9, 117.0, 117.7, 119.0, 119.2, 119.7, 127.0, 127.9, 128.7, 129.7, 130.2, 131.8, 132.1, 133.5, 135.9, 143.9, 144.6, 147.0, 147.8, 162.8, 167.2, 172.4; HRMS (ES+) Calcd for [$C_{36}H_{39}N_3O_6S$ + H] 642.2632 found 642.2647; HPLC (III) t_R =22.59 min (100 %), (IV) 48.06 min (100 %).

Compound 16y

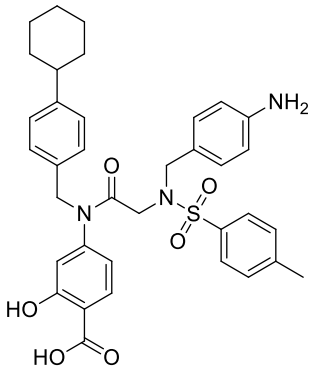


4-(2-(*N*-(3-aminobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{39}N_3O_6S$
Molecular Weight: 641.78
Log P: 5.46

Compound **15u** was globally deprotected according to general procedure B on a 0.10 mmol scale to give compound **16y** (60.8 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.36-2.52 (m, 4H, CH and CH_3), 3.78 (s, 2H, CH_2), 4.42 (s, 2H, CH_2) 4.66 (s, 2H, CH_2), 6.19 (d, *J* = 4.4 Hz, 1H, NH), 6.30 (s, 1H, NH), 6.65 (d, *J* = 6.8 Hz, 1H, CH), 6.69-6.84 (m, 2H, CH), 6.93-7.12 (m, 6H, CH), 7.22-7.33 (m, 3H, CH), 7.60 (d, *J* = 6.8 Hz, 1H, CH), 7.79 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 47.1, 51.0, 53.0, 113.3, 116.7, 117.3, 118.7, 121.6, 127.0, 127.8, 128.8, 129.7, 129.8, 132.2, 133.8, 136.6, 137.0, 143.5, 146.9, 147.7, 150.6, 157.8, 162.7, 167.0, 172.4; HRMS (ES+) Calcd for [$C_{36}H_{39}N_3O_6S$ + H] 642.2632 found 642.2641; HPLC (III) t_R =22.38 min (90.0 %), (IV) 47.4 min (90.2 %).

Compound 16z

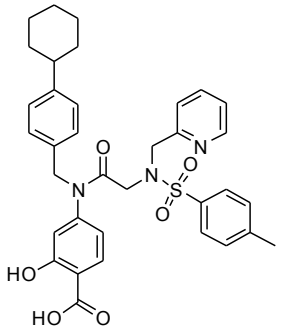


4-(2-(*N*-(4-aminobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{39}N_3O_6S$
Molecular Weight: 641.78
Log P: 5.46

Compound **15v** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **16z** (21.0 mg, 82 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.45 (m, 5H, CH_2), 1.62-1.85 (m, 5H, CH_2), 2.35-2.57 (m, 4H, CH and CH_3), 3.66 (s, 2H, CH_2), 4.39 (s, 2H, CH_2) 4.65 (s, 2H, CH_2), 6.16-6.40 (m, 2H, CH), 6.81-7.15 (m, 9H, CH), 7.27 (d, *J* = 8.0 Hz, 2H, CH), 7.50-7.73 (m, 2H, CH),7.79 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.6, 44.3, 46.9, 50.4, 53.0, 110.9, 113.3, 116.7, 118.7, 127.0, 127.8, 128.7, 128.8, 129.7, 130.3, 131.0, 133.8, 137.1, 143.5, 146.9, 147.7, 158.1, 162.6, 166.9, 172.4; HRMS (ES+) Calcd for [$C_{36}H_{39}N_3O_6S$ + H] 642.2632 found 642.2644; HPLC (III) t_R =22.38 min (70.7 %), (IV) 47.38 min (74.7 %).

Compound 16aa

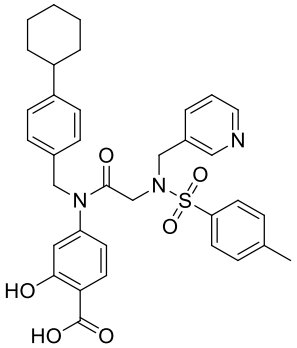


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-2-ylmethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{37}N_3O_6S$
Molecular Weight: 627.75
Log P: 5.4

Compound **15w** was globally deprotected according to general procedure C on a 0.07 mmol scale to give compound **16aa** (28.6 mg, 65 %)

δ_H (400 MHz, d_6-DMSO) 1.26-1.43 (m, 5H, CH_2), 1.63-1.83 (m, 5H, CH_2), 2.38 (s, 3H, CH_3), 2.40-2.49 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.47 (d, J = 7.6 Hz, 1H, CH), 6.57 (s, 1H, CH), 7.01 (d, J = 8.0 Hz, 2H, CH), 7.12 (d, J = 8.0 Hz, 2H, CH), 7.24-7.29 (m, 1H, CH), 7.52-7.68 (m, 6H, CH), 7.72 (t of d, J = 7.6 and 2.0 Hz, 1H, CH), 8.42-8.47 (m, 1H, CH); δ_C (100 MHz, d-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 49.9, 53.3, 56.2, 110.6, 116.4, 118.5, 120.6, 123.7, 125.0, 127.0, 127.6, 128.6, 128.7, 129.7, 132.2, 132.3, 139.6, 143.7, 147.3, 147.6, 157.3, 162.8, 167.3, 173.0; HRMS (ES+) Calcd for [$C_{35}H_{37}N_3O_6S$ + H] 628.2475 found 628.2467; HPLC (III) t_R =21.93 min (91.4 %), (IV) 50.10 min (91.6 %).

Compound 16ab

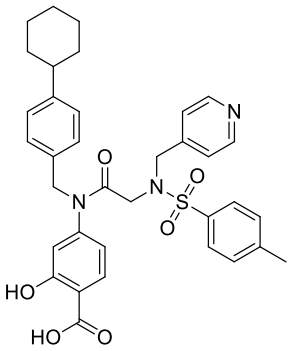


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-3-ylmethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{37}N_3O_6S$
Molecular Weight: 627.75
Log P: 5.16

Compound **15x** was globally deprotected according to general procedure C on a 0.04 mmol scale to give compound **16ab** (19.4 mg, 77 %)

δ_H (400 MHz, *d*$_6$-DMSO) 1.26-1.43 (m, 5H, CH_2), 1.63-1.83 (m, 5H, CH_2), 2.38 (s, 3H, CH_3), 2.40-2.49 (m, 1H, CH), 3.98 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.55 (d, *J* = 7.6 Hz, 1H, CH), 6.65 (s, 1H, CH), 7.01 (d, *J* = 8.0 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.24-7.29 (m, 1H, CH), 7.31-7.38 (m, 3H, CH), 7.65 (d, *J* = 8.4 Hz, 2H, CH), 7.68 (d, *J* = 8.4 Hz, 1H, CH), 7.73 (t of d, *J* = 7.6 and 2.0 Hz, 1H, CH), 8.43-8.47 (m, 1H, CH); δ_C (100 MHz, *d*$_6$-DMSO) 21.0, 25.6, 26.3, 33.9, 43.4, 51.7, 52.9, 54.9, 111.1, 116.5, 117.5, 122.2, 122.6, 126.5, 127.2, 129.5, 131.1, 134.3, 136.7, 136.8, 143.1, 146.4, 148.9, 150.4, 151.2, 156.4, 162.3, 167.1, 171.0; HRMS (ES+) Calcd for [$C_{35}H_{37}N_3O_6S$ + H] 628.2475 found 628.2482; HPLC (III) t_R =20.58 min (100 %), (IV) 54.54 min (100 %).

Compound 16ac

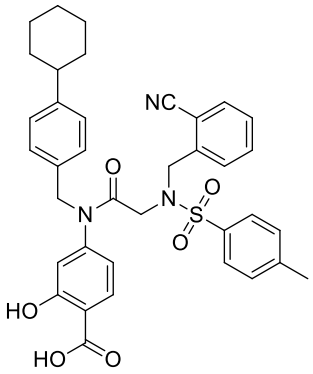


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(pyridin-4-ylmethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{37}N_3O_6S$
Molecular Weight: 627.75
Log P: 5.16

Compound **15y** was globally deprotected according to general procedure C on a 0.05 mmol scale to give compound **16ac** (23.1 mg, 74 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.41-2.52 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.27 (d, *J* = 8.4 Hz, 1H, CH), 6.45 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.34 (d, *J* = 8.4 Hz, 2H, CH), 7.42 (d, *J* = 5.6 Hz, 2H, CH), 7.77-7.86 (m, 3H, CH), 8.60 (d, *J* = 5.6 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.6, 44.3, 47.7, 50.5, 53.0, 111.2, 116.5, 118.3, 124.3, 125.7, 126.0, 127.1, 127.9, 128.8, 129.8, 132.4, 133.8, 139.9, 144.0, 145.8, 146.7, 147.8, 166.2, 173.0; HRMS (ES+) Calcd for [$C_{35}H_{37}N_3O_6S$ + H] 628.2475 found 628.2489; HPLC (I) t_R =22.56 min (100 %), (II) 51.04 min (100 %).

Compound 16ad

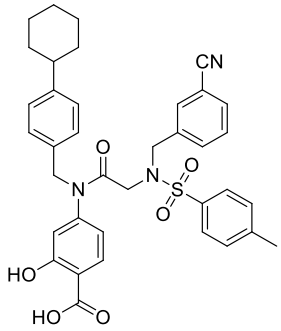


4-(2-(*N*-(2-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}N_3O_6S$
Molecular Weight: 651.77
Log P: 5.78

Compound **15z** was globally deprotected according to general procedure B on a 0.16 mmol scale to give compound **16ad** (80.5 mg, 77 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.37-2.52 (m, 4H, CH and CH_3), 3.91 (s, 2H, CH_2), 4.77 (s, 2H, CH_2) 4.79 (s, 2H, CH_2), 6.51 (d, *J* = 8.0 Hz, 1H, CH), 6.61 (s, 1H, CH), 7.01 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.29 (d, *J* = 8.0 Hz, 2H, CH), 7.36 (t, *J* = 7.6 Hz, 1H, CH), 7.58 (t, *J* = 4.6 Hz, 1H, CH), 7.59 (d, *J* = 7.6 Hz, 1H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH), 7.74 (d, *J* = 8.0 Hz, 2H, CH), 7.80 (d, *J* = 8.4 Hz, 1H, CH), 10.67 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.5, 44.3, 48.9, 50.1, 53.1, 111.7, 112.0, 117.0, 117.3, 119.2, 127.0, 127.7, 128.5, 128.6, 128.6, 129.7, 130.1, 132.3, 132.8, 133.4, 136.4, 140.0, 143.8, 147.6, 147.7, 163.0, 166.6, 172.4; HRMS (ES+) Calcd for [$C_{37}H_{37}N_3O_6S$ + H] 652.2475 found 652.2491; HPLC (III) t_R =26.44 min (100 %), (IV) 58.47 min (100 %).

Compound 16ae

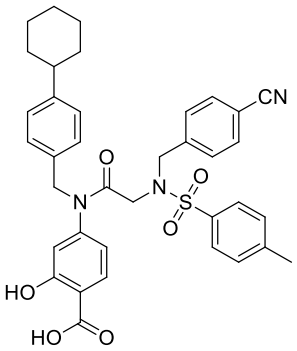


4-(2-(*N*-(3-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}N_3O_6S$
Molecular Weight: 651.77
Log P: 5.78

Compound **15aa** was globally deprotected according to general procedure B on a 0.13 mmol scale to give compound **16ae** (65.4 mg, 77 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.46 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.41-2.55 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.63 (s, 2H, CH_2) 4.72 (s, 2H, CH_2), 6.41 (d, *J* = 8.0 Hz, 1H, CH), 6.50 (s, 1H, CH), 7.00 (d, *J* = 8.0 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.39 (t, *J* = 7.6 Hz, 1H, CH), 7.47 (s, 1H, CH), 7.50-7.59 (m, 2H, CH), 7.75 (d, *J* = 8.0 Hz, 2H, CH), 7.81 (d, *J* = 8.4 Hz, 1H, CH), 10.67 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.5, 44.3, 47.4, 50.9, 53.1, 111.9, 112.8, 117.0, 118.4, 119.0, 127.1, 127.7, 128.6, 129.7, 129.8, 131.8, 131.9, 132.4, 133.1, 133.3, 136.6, 137.5, 144.0, 147.5, 147.9, 163.0, 166.8, 172.4; HRMS (ES+) Calcd for [$C_{37}H_{37}N_3O_6S$ + H] 652.2475 found 652.2487; HPLC (III) t_R =26.44 min (97.0 %), (IV) 58.49 min (96.5 %).

Compound 16af

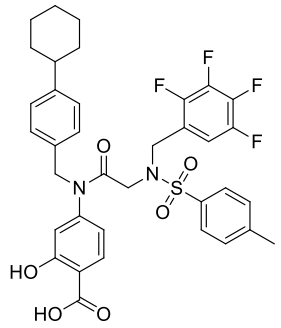


4-(2-(*N*-(4-cyanobenzyl)-4-methylphenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}N_3O_6S$
Molecular Weight: 651.77
Log P: 5.78

Compound **15ab** was globally deprotected according to general procedure B on a 0.10 mmol scale to give compound **16af** (58.0 mg, 89 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.70-1.95 (m, 5H, CH_2), 2.44-2.56 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.64 (s, 2H, CH_2) 4.70 (s, 2H, CH_2), 6.37 (d, *J* = 8.0 Hz, 1H, CH), 6.45 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.32 (d, *J* = 8.0 Hz, 2H, CH), 7.37 (d, *J* = 8.0 Hz, 2H, CH), 7.57 (d, *J* = 8.0 Hz, 2H, CH), 7.73-7.84 (m, 3H, CH), 10.62 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 26.9, 34.5, 44.3, 47.5, 51.2, 53.1, 111.8, 112.0, 117.0, 118.6, 119.0, 127.1, 127.8, 128.6, 129.2, 129.8, 132.4, 132.6, 133.4, 136.6, 141.4, 143.9, 147.6, 148.0, 163.0, 166.8, 172.5; HRMS (ES+) Calcd for [$C_{37}H_{37}N_3O_6S$ + H] 652.2475 found 652.2481; HPLC (III) t_R =26.46 min (96.5 %), (IV) 58.58 min (96.5 %).

Compound 16ag

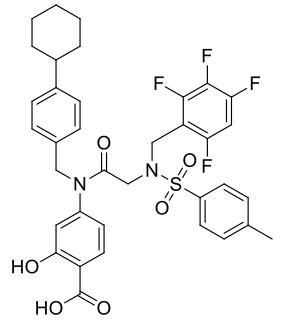


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,4,5-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{34}F_4N_2O_6S$
Molecular Weight: 698.72
Log P: 6.82

Compound **15ac** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16ag** (42.2 mg, 86 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.38-2.55 (m, 4H, CH and CH_3), 3.93 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.56 (d, *J* = 8.0 Hz, 1H, CH), 6.66 (s, 1H, CH), 6.68-6.77 (m, 1H, CH), 7.02 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.28 (d, *J* = 8.0 Hz, 2H, CH), 7.72 (d, *J* = 8.4 Hz, 2H, CH), 7.86 (d, *J* = 8.4 Hz, 1H, CH), 10.62 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 39.8, 44.3, 49.1, 53.1, 101.0, 110.2, 111.8, 117.3, 119.3, 127.1, 127.8, 128.6, 129.6, 132.5, 133.5, 136.4, 143.8, 145.1, 147.9, 163.1, 166.9, 172.8; HRMS (ES+) Calcd for [$C_{36}H_{34}F_4N_2O_6S$ + H] 699.2146 found 699.2117; HPLC (III) t_R =23.17 min (100 %), (IV) 54.08 min (98.7 %).

Compound 16ah

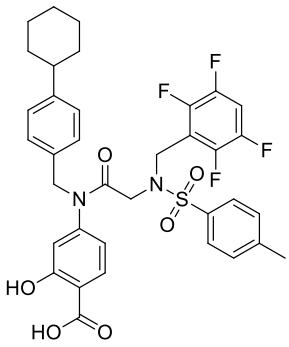


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,4,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{34}F_4N_2O_6S$
Molecular Weight: 698.72
Log P: 6.82

Compound **15ad** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **16ah** (35.6 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.40-2.53 (m, 4H, CH and CH_3), 3.86 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 6.51 (d, *J* = 8.4 Hz, 1H, CH), 6.61 (s, 1H, CH), 7.00 (d, *J* = 8.0 Hz, 2H, CH), 7.07-7.17 (m, 3H, CH), 7.31 (d, *J* = 8.0 Hz, 2H, CH), 7.73 (d, *J* = 8.4 Hz, 2H, CH), 7.85 (d, *J* = 8.4 Hz, 1H, CH), 10.61 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 44.6, 48.2, 53.1, 111.7, 111.9, 117.2, 119.1, 119.9, 127.2, 127.8, 128.6, 129.8, 132.5, 133.3, 136.4, 143.9, 144.1, 148.0, 163.1, 166.6, 172.7; HRMS (ES+) Calcd for [$C_{36}H_{34}F_4N_2O_6S$ + H] 699.2146 found 699.2134; HPLC (I) t_R =23.45 min (97.0 %), (II) 62.91 min (100 %).

Compound 16ai

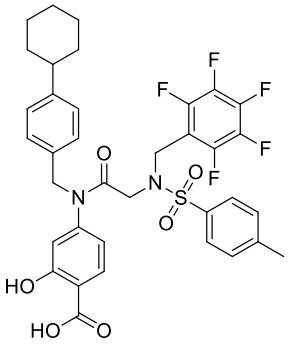


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(2,3,5,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{34}F_4N_2O_6S$
Molecular Weight: 698.72
Log P: 6.82

Compound **15ae** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16ai** (46.5 mg, 95 %)

δ_H (400 MHz, *d*$_6$-DMSO) 1.26-1.43 (m, 5H, CH_2), 1.63-1.83 (m, 5H, CH_2), 2.37 (s, 3H, CH_3), 2.40-2.49 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 6.75 (d of d, *J* = 8.4 and 2.0 Hz, 1H, CH), 6.82 (d, *J* = 2.0 Hz, 1H, CH), 7.03 (d, *J* = 8.0 Hz, 2H, CH), 7.13 (d, *J* = 8.0 Hz, 2H, CH), 7.33 (d, *J* = 8.0 Hz, 2H, CH), 7.55 (d, *J* = 8.4 Hz, 2H, CH), 7.75-7.86 (m, 2H, CH); δ_C (100 MHz, *d*$_6$-DMSO) 21.0, 25.6, 26.3, 33.9, 40.5, 43.4, 49.5, 51.6, 106.6, 112.7, 115.8, 116.6, 118.6, 126.6, 126.9, 127.6, 129.4, 131.3, 131.4, 134.1, 136.4, 143.3, 146.5, 161.6, 166.6, 171.2; HRMS (ES+) Calcd for [$C_{36}H_{34}F_4N_2O_6S$ + H] 699.2146 found 699.2176; HPLC (III) t_R =22.82 min (100 %), (IV) 53.57 min (100 %).

Compound 16aj

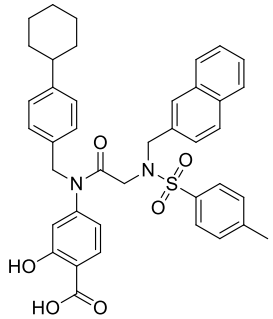


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{33}F_5N_2O_6S$
Molecular Weight: 716.71
Log P: 6.95

Compound **15af** was globally deprotected according to general procedure B on a 0.07 mmol scale to give compound **16aj** 0.08 (47.3 mg, 82 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.46 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.38-2.55 (m, 4H, CH and CH_3), 3.97 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.58 (d, *J* = 8.4 Hz, 1H, CH), 6.68 (s, 1H, CH), 7.01 (d, *J* = 8.0 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.29 (d, *J* = 8.0 Hz, 2H, CH), 7.71 (d, *J* = 8.0 Hz, 2H, CH), 7.89 (d, *J* = 8.4 Hz, 1H, CH), 10.62 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 40.0, 44.3, 49.5, 53.1, 110.3, 111.9, 117.4, 119.2, 127.2, 127.8, 128.6, 129.6, 132.6, 133.4, 136.2, 138.9, 140.1, 144.0, 144.4, 147.8, 147.9, 163.2, 166.8, 172.9; HRMS (ES+) Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.2052 found 717.2086; HPLC (I) t_R =23.77 min (100 %), (II) 54.55 min (100 %).

Compound 16ak

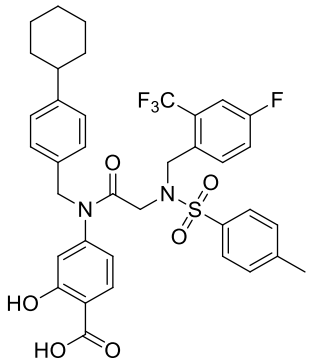


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(naphthalen-2-ylmethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{40}H_{40}N_2O_6S$
Molecular Weight: 676.82
Log P: 7.39

Compound **15ag** was globally deprotected according to general procedure B on a 0.08 mmol scale to give compound **16ak** (40.3 mg, 74 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.67-1.93 (m, 5H, CH_2), 2.34-2.56 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.08 (s, 1H, CH), 6.37 (s, 1H, CH), 6.96 (d, *J* = 6.8 Hz, 2H, CH), 7.06 (d, *J* = 6.8 Hz, 2H, CH), 7.29-7.42 (m, 3H, CH), 7.43-7.57 (m, 3H, CH), 7.61 (s, 1H, CH), 7.66-7.77 (m, 2H, CH), 7.79-7.90 (m, 3H, CH), 10.65 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.5, 44.3, 47.0, 51.4, 52.9, 111.9, 116.9, 119.0, 126.4, 126.4, 126.5, 127.1, 127.4, 127.8, 128.1, 128.4, 128.6, 128.6, 128.8, 129.7, 132.0, 132.7, 133.2, 133.3, 133.6, 137.1, 143.5, 147.7, 162.9, 167.0, 172.3; HRMS (ES+) Calcd for [$C_{40}H_{40}N_2O_6S$ + H] 677.2679 found 677.2647; HPLC (I) t_R =24.12 min (100 %), (II) 55.59 min (100 %).

Compound 16al

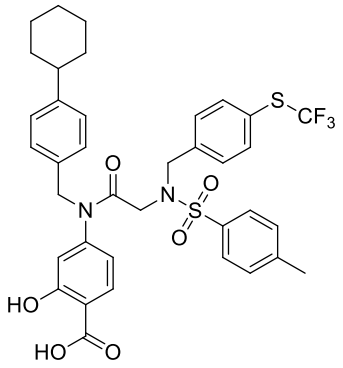


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-fluoro-2-(trifluoromethyl)benzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{36}F_4N_2O_6S$
Molecular Weight: 712.75
Log P: 7.39

Compound **15ah** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **16al** (34.5 mg, 97 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.93 (m, 5H, CH_2), 2.40-2.52 (m, 4H, CH and CH_3), 3.80 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.41 (d, *J* = 8.0 Hz, 1H, CH), 6.52 (s, 1H, CH), 6.96 (d, *J* = 8.0 Hz, 2H, CH), 7.08 (d, *J* = 8.0 Hz, 2H, CH), 7.19 (t of d, *J* = 8.0 and 2.0 Hz, 1H, CH), 7.32 (d, *J* = 8.4 Hz, 3H, CH), 7.72-7.83 (m, 4H, CH), 10.64 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.5, 44.4, 47.3, 48.0, 53.0, 111.8, 113.3, 113.6, 117.2, 119.2, 119.3, 119.5, 122.1, 127.1, 127.9, 128.6, 129.7, 130.8, 132.4, 132.7, 132.7, 133.5, 136.7, 143.9, 147.6, 147.8, 160.4, 162.9, 163.1, ; HRMS (ES+) calcd for [$C_{37}H_{36}N_2O_6F_4S$ + H] 713.2302, found 713.2308; HPLC (I) t_R = 24.22 min (100 %), (II) t_R = 55.87 min (100 %).

Compound 16am

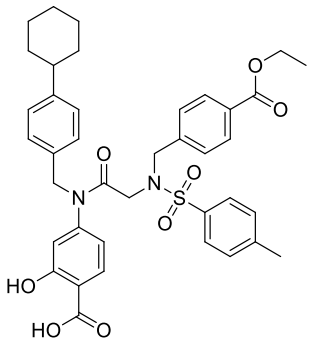


4-(*N*-(4-cyclohexylbenzyl)-2-(4-methyl-*N*-(4-((trifluoromethyl)thio)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{37}F_3N_2O_6S_2$
Molecular Weight: 726.82
Log P: 8.4

Compound **15ai** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **16am** (24.2 mg, 83 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.53 (m, 4H, CH and CH_3), 3.77 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.27 (d, *J* = 8.4 Hz, 1H, CH), 6.45 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.27-7.37 (m, 4H, CH), 7.55 (d, *J* = 8.0 Hz, 2H, CH), 7.73-7.82 (m, 3H, CH), 10.59 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.8, 26.3, 27.0, 34.6, 44.4, 47.3, 50.9, 53.0, 111.7, 117.2, 119.1, 127.1, 127.8, 129.7, 129.8, 132.3, 132.6, 133.4, 133.6, 136.7, 136.9, 138.9, 143.8, 144.1, 147.8, 148.0, 163.1, 167.4, 172.2; HRMS (ES+) calcd for [$C_{37}H_{37}N_2O_6F_3S_2$ + H] 727.2117, found 727.2096; HPLC (I) t_R = 24.24 min (91.4 %), (II) t_R = 56.23 min (90.8 %).

Compound 16an

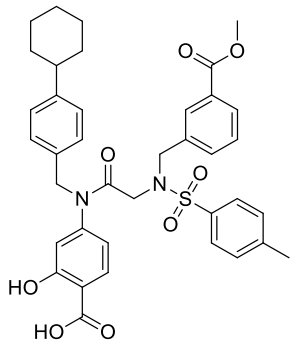


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-(ethoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{39}H_{42}N_2O_8S$
Molecular Weight: 698.82
Log P: 6.39

Compound **15aj** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **16an** (32.9 mg, 94 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.39-2.55 (m, 4H, CH and CH_3), 3.78 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 6.27 (d, *J* = 8.0 Hz, 1H, CH), 6.45 (s, 1H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.22-7.37 (m, 4H, CH), 7.55 (d, *J* = 8.0 Hz, 2H, CH), 7.69-7.86 (m, 3H, CH), 10.59 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 14.4, 21.8 26.3, 27.0, 34.5, 44.4, 47.2, 51.1, 53.0, 61.2, 112.0, 116.9, 119.0, 127.1, 127.8, 128.6, 129.7, 130.1, 130.3, 132.3, 133.6, 136.9, 140.7, 143.7, 146.2, 147.5, 147.9, 163.0, 165.0, 166.5, 172.3; HRMS (ES+) calcd for [$C_{39}H_{42}N_2O_8S$ + H] 699.2734, found 699.2731; HPLC (I) t_R = 23.86 min (98.4 %), (II) t_R = 54.73 min (96.8 %).

Compound 16ao

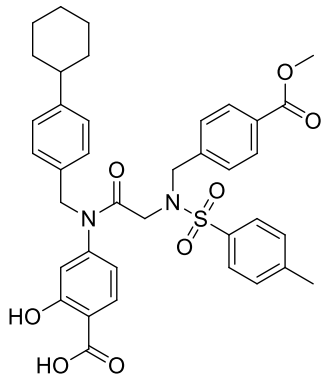


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(3-(methoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{38}H_{40}N_2O_8S$
Molecular Weight: 684.80
Log P: 6.1

Compound **15ak** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **16ao** (15.8 mg, 77 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.60 (m, 5H, CH_2), 1.65-2.10 (m, 5H, CH_2), 2.30-2.63 (m, 4H, CH and CH_3), 3.78 (s, 2H, CH_2), 3.90 (s, 3H, CH_3), 4.61 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.34 (d, *J* = 8.0 Hz, 1H, CH), 6.47 (s, 1H, CH), 6.98 (d, *J* = 7.6 Hz, 2H, CH), 7.09 (d, *J* = 7.6 Hz, 2H, CH), 7.28-7.42 (m, 3H, CH), 7.49 (d, *J* = 7.6 Hz, 1H, CH), 7.73 (d, *J* = 8.4 Hz, 1H, CH), 7.80 (d, *J* = 8.0 Hz, 2H, CH), 7.86 (s, 1H, CH), 7.96 (d, *J* = 7.6 Hz, 1H, CH), 10.60 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$ 21.7, 26.3, 27.0, 34.5, 44.4, 47.2, 51.1, 52.4, 53.0, 110.8, 117.0, 119.1, 127.1, 127.8, 128.6, 129.1, 129.5, 129.7, 129.8, 130.6, 132.3, 132.4, 133.5, 136.0, 137.0, 143.7, 147.7, 147.8, 163.0, 166.8, 167.0, 172.3; HRMS (ES+) calcd for [$C_{38}H_{40}N_2O_8S$ + H] 685.2578, found 685.2577; HPLC (I) t_R = 23.52 min (98.2 %), (II) t_R = 53.58 min (98.6 %).

Compound 16ap

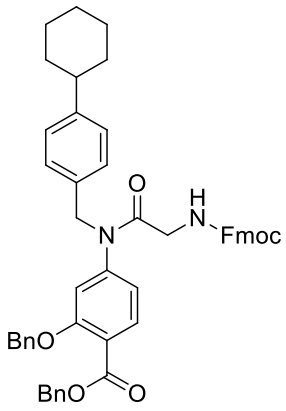


4-(*N*-(4-cyclohexylbenzyl)-2-(*N*-(4-(methoxycarbonyl)benzyl)-4-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{38}H_{40}N_2O_8S$
Molecular Weight: 684.80
Log P: 6.1

Compound **15al** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **16ap** (19.0 mg, 70 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.51 (m, 5H, CH_2), 1.70-2.12 (m, 5H, CH_2), 2.36-2.90 (m, 4H, CH and CH_3), 3.79 (s, 2H, CH_2), 3.92 (s, 3H, CH_3), 4.64 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 6.32 (d, *J* = 8.0 Hz, 1H, CH), 6.42 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.21-7.44 (m, 4H, CH), 7.68-7.84 (m, 3H, CH), 7.95 (d, *J* = 8.0 Hz, 2H, CH), 10.61 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.7, 26.2, 27.0, 34.5, 44.3, 47.2, 51.1, 52.3, 53.4, 111.7, 117.1, 119.0, 127.1, 127.8, 128.7, 129.7, 130.0, 130.1, 132.2, 132.3, 133.5, 136.9, 140.9, 143.7, 147.8, 147.9, 163.0, 166.8, 167.0, 172.3; HRMS (ES+) calcd for [$C_{38}H_{40}N_2O_8S$ + H] 685.2578, Found 685.2586; HPLC (I) t_R = 23.55 min (100 %), (II) t_R = 53.68 min (100 %).

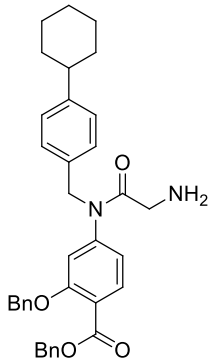
Compound 17



benzyl 4-(2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{51}H_{48}N_2O_6$
Molecular Weight: 784.94

Fmoc-glycine-OH was stirred at room temperature with PPh_3Cl_2 in $CDCl_3$ for 15 minutes to form the activated acid. Aniline **11** was added and the solution was heated to 110 °C for 30 minutes using a Biotage Initiator microwave reactor. Upon completion, $CDCl_3$ was removed under reduced pressure and the crude product was purified using flash column chromatography using a mixture of hexanes and EtOAc as eluent. 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).

Compound 18

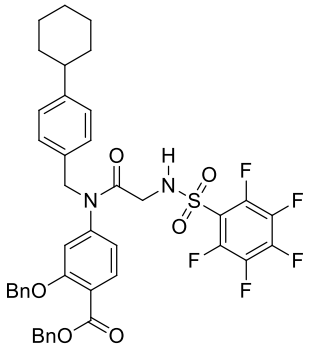


benzyl 4-(2-amino-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{36}H_{38}N_2O_4$
Molecular Weight: 562.70

Compound **17** was dissolved in a 5 % solution of piperidine in DMF and stirred for 10 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, 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.

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.

Compound 19



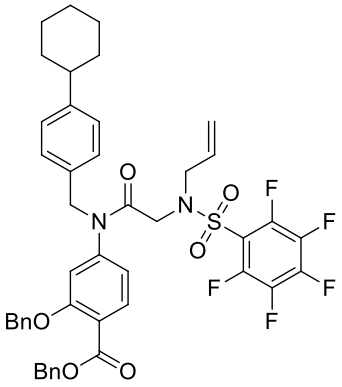
benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(perfluorophenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{42}H_{37}F_5N_2O_6S$
Molecular Weight: 792.81

Compound **18** (0.5 g, 0.89 mmol) was dissolved in anhydrous MeCN with K_2CO_3 (0.98mmol) and 4 Å molecular sieves and cooled to 0 °C. 2,3,4,5,6-pentafluorobenzenesulfonyl chloride (0.89 mmol) 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 $NaHCO_3$, H2O 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 to give compound **19** (0.45 g, 64 %).

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.40-2.53 (m, 1H, CH), 3.66 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.91 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.29 (s, 1H, NH), 6.43 (s, 1H, CH), 6.61 (d, *J* =

8.0 Hz, 1H, CH), 6.93 (d, *J* = 7.8 Hz, 2H, CH), 7.09 (d, *J* = 7.8 Hz, 1H, CH), 7.23-7.45 (m, 11H, CH), 7.83 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.3, 45.0, 53.4, 67.2, 70.8, 114,0, 120.1, 121.7, 127.2. 127.2, 128.3, 128.4, 128.5, 128.7, 128.8, 129.0, 133.3, 133.7, 135.8, 137.1, 143.8, 148.3, 159.0, 165.4, 166.3; LRMS (ES+) Calcd for [$C_{42}H_{37}F_5N_2O_6S$ + Na] 815.22 found 815.39.

Compound 20a

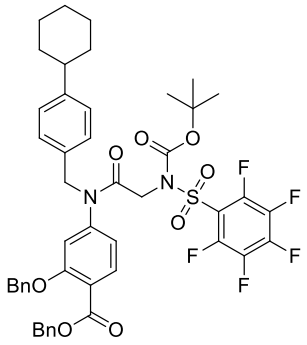


benzyl 4-(2-(*N*-allyl-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{45}H_{41}F_5N_2O_6S$
Molecular Weight: 832.87

Sulfonamide **19** was functionalized on a 0.11 mmol scale using General Procedure A to give **20a** (92.5 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.66-1.90 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.90 (s, 2H, CH_2), 4.09 (d, *J* = 4.4 Hz, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.90 (s, 2H, CH_2), 5.17-5.22 (m, 2H, CH), 5.33 (s, 2H, CH_2), 5.61-5.75 (m, 1H, CH), 6.44 (s, 1H, CH), 6.63 (d, *J* = 8.0 Hz, 1H, CH), 6.93 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.24-7.42 (m, 10H, CH), 7.82 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.1, 26.9, 34.5, 44.3, 48.0, 50.8, 52.9, 67.2, 70.8, 113.8, 120.0, 120.1, 121.3, 127.1, 127.2, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8, 132.1, 133.3, 133.6, 135.6, 135.7, 144.4, 148.0, 158.9, 162.6, 165.4, 166.0; LRMS (ES+) Calcd for [$C_{45}H_{43}F_5N_2O_6S$ + Na] 855.25 found 855.42.

Compound 20b

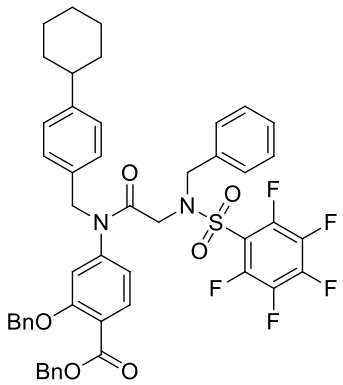


benzyl 2-(benzyloxy)-4-(2-(*N*-(*tert*-butoxycarbonyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{47}H_{45}F_5N_2O_8S$
Molecular Weight: 892.93

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure D to give **20b** (35.2 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.49 (m, 14H, CH_2 and 3 CH_3), 1.65-1.90 (m, 5H, CH_2), 2.36-2.54 (m, 1H, CH), 4.28 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.57 (s, 1H, CH), 6.73 (d, *J* = 8.0 Hz, 1H, CH), 7.00-7.15 (m,4H, CH), 7.28-7.45 (m, 10H, CH), 7.85 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 27.8, 34.6, 44.5, 53.5, 67.2, 70.9, 77.4, 114,1, 120.3, 121.3, 127.1, 127.3, 128.3, 128.4, 128.4, 128.7, 128.8, 129.1, 133.3, 133.4, 135.7, 135.9, 144.8, 148.0, 155.7, 159.0, 165.4, 164.7; LRMS (ES+) Calcd for [$C_{47}H_{45}F_5N_2O_8S$ + Na] 915.27 found 915.53.

Compound 20c

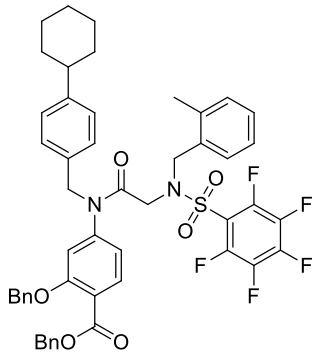


benzyl 4-(2-(*N*-benzyl-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-(benzyloxy)benzoate
Chemical Formula: $C_{49}H_{43}F_5N_2O_6S$
Molecular Weight: 882.93

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20c** (25.4 mg, 94 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.24 (s, 1H, CH), 6.36 (d, *J* = 7.6 Hz, 1H, CH), 6.94 (d, *J* = 7.6 Hz, 2H, CH), 7.13 (d, *J* = 7.6 Hz, 2H, CH), 7.20-7.43 (m, 15H, CH), 7.69 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.7, 51.4, 52.9, 67.2, 70.9, 113.7, 119.4, 121.3, 127.1, 127.3, 128.3, 128.4, 128.4, 128.6, 128.7, 128.7, 128.9, 129.0, 129.0, 129.1, 133.3, 133.6, 134.4, 135.6, 135.8, 144.3, 148.1, 158.9, 165.4, 165.9; LRMS (ES+) Calcd for [$C_{49}H_{43}F_5N_2O_6S$ + Na] 905.27 found 905.51.

Compound 20d

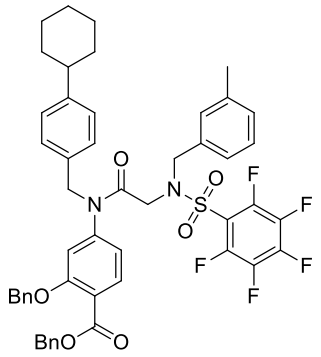


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{45}F_5N_2O_6S$
Molecular Weight: 896.96

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20d** (18.3, 68 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.31 (s, 3H, CH_3), 2.42-2.54 (m, 1H, CH), 3.66 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.15 (s, 1H, CH), 6.29 (d, *J* = 7.6 Hz, 1H, CH), 6.95 (d, *J* = 7.6 Hz, 2H, CH), 7.04-7.24 (m, 6H, CH), 7.28-7.42 (m, 10H, CH), 7.67 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 19.2, 26.2, 26.9, 34.6, 44.4, 47.6, 49.4, 52.9, 67.2, 70.9, 113.7, 120.0, 121.2, 126.2, 127.1, 127.3, 128.3, 128.4, 128.4, 128.7, 128.8, 128.9, 129.1, 130.4, 131.2, 131.9, 133.3, 133.7, 135.8, 138.4, 144.3, 148.2, 158.9, 165.5, 165.9; LRMS (ES+) Calcd for [$C_{50}H_{45}F_5N_2O_6S$ + Na] 919.28 found 919.48.

Compound 20e

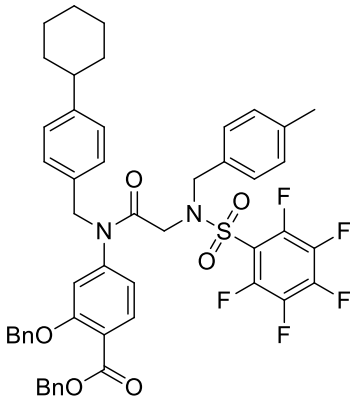


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{45}F_5N_2O_6S$
Molecular Weight: 896.96

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20e** (21.3 mg, 79 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.47 (s, 3H, CH_3), 2.42-2.54 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.64 (s, 4H, CH_2), 4.75 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.25 (s, 1H, CH), 6.36 (d, *J* = 8.0 Hz, 1H, CH), 6.94 (d, *J* = 8.0 Hz, 2H, CH), 7.01 (d, *J* = 7.6 Hz, 1H, CH), 7.08 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.18 (t, *J* = 7.6 Hz, 1H, CH), 7.27-7.39 (m, 10H, CH), 7.69 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.5, 26.2, 27.0, 34.6, 44.4, 47.8, 51.3, 52.9, 67.2, 70.9, 113.7, 120.0, 121.3, 126.0, 127.2, 127.4, 128.3, 128.4, 128.4, 129.0, 129.3, 129.6, 133.3, 133.7, 134.3, 135.7, 135.8, 138.9, 144.4, 148.1, 158.9, 165.5, 166.0; LRMS (ES+) Calcd for [$C_{50}H_{45}F_5N_3O_6S$ + Na] 919.28 found 919.41.

Compound 20f

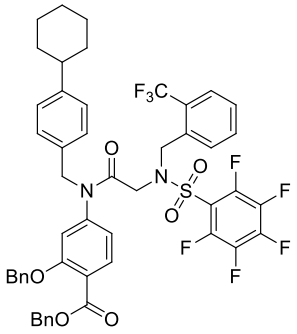


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-methylbenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{45}F_5N_2O_6S$
Molecular Weight: 896.96

Sulfonamide **19** was functionalized on a 0.05 mmol scale using General Procedure A to give **20f** (42.5 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.27 (s, 3H, CH_3) 2.41-2.57 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.64 (s, 4H, 2 CH_2), 4.77 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.28 (s, 1H, CH), 6.37 (d, *J* = 7.6 Hz, 1H, CH), 6.94 (d, *J* = 7.6 Hz, 2H, CH), 7.08-7.19 (m, 6H, CH), 7.28-7.42 (m, 10H, CH), 7.69 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 21.2, 26.2, 26.9, 34.6, 44.4, 47.7, 51.2, 52.9, 67.2, 70.8, 113.7, 120.0, 121.2, 127.1, 127.4, 128.3, 128.3, 128.4, 128.7, 128.7, 128.9, 129.1, 129.6, 131.3, 133.3, 133.6, 135.6, 135.8, 138.4, 148.1, 159.0, 164.4, 166.0; LRMS (ES+) Calcd for [$C_{50}H_{45}F_5N_2O_6S$ + Na] 919.28 found 919.54.

Compound 20g

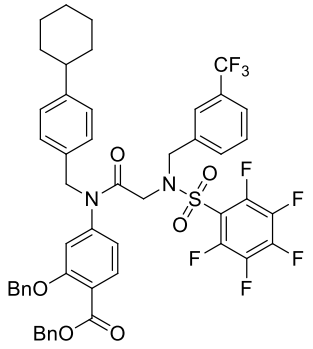


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_6S$
Molecular Weight: 950.93

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20g** (18.4 mg, 64 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.41-2.53 (m, 1H, CH), 3.77 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.48 (d, *J* = 7.6 Hz, 1H, CH), 6.91 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 7.6 Hz, 1H, CH), 7.27-7.42 (m, 11H, CH), 7.54 (t, *J* = 7.6 Hz, 1H, CH), 7.62 (d, *J* = 8.0 Hz, 1H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.5, 48.5, 53.0, 67.2, 70.8, 113.8, 116.6, 120.0, 121.2, 125.8, 127.1, 127.3, 128.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 130.6, 132.9, 133.4, 133.5, 134.0, 135.6, 135.8, 144.2, 148.1, 158.9, 165.5, 166.0; LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_6S$ + Na] 973.25 found 973.46.

Compound 20h

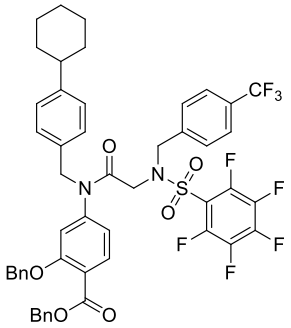


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_6S$
Molecular Weight: 950.93

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20h** (24.2 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.67-1.92 (m, 5H, CH_2), 2.38-2.54 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.79 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.43 (d, *J* = 7.6 Hz, 1H, CH), 6.92 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.24-7.40 (m, 10H, CH), 7.43 -7.62 (m, 4H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.4, 47.7, 51.1, 53.0, 67.2, 70.8, 111.7, 113.6, 116.2, 119.9, 121.4, 125.5, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 129.8, 133.2, 133.4, 135.6, 135.7, 135.8, 144.0, 148.2, 158.9, 165.4, 165.7; LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_6S$ + Na] 973.25 found 973.39.

Compound 20i

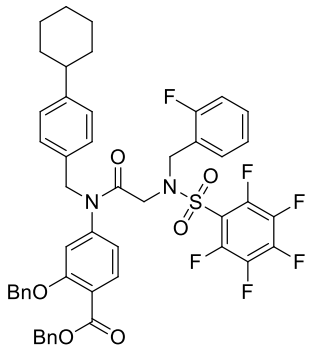


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_6S$
Molecular Weight: 950.93

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20i** (28.3 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.70-1.90 (m, 5H, CH_2), 2.41-2.54 (m, 1H, CH), 3.74 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.83 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.32 (s, 1H, CH), 6.36 (d, *J* = 7.6 Hz, 1H, CH), 6.90 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.36 (m, 10H, CH), 7.38 (d, *J* = 8.0 Hz, 2H, CH), 7.57 (d, *J* = 8.0 Hz, 2H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 48.0, 51.2, 53.0, 67.3, 70.9, 113.7, 119.9, 121.6, 125.9, 126.0, 126.0, 126.1, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 129.0, 129.0, 133.3, 133.4, 135.6, 135.7, 138.8, 148.3, 158.9, 165.4, 165.7; LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_6S$ + Na] 973.25 found 973.52

Compound 20j

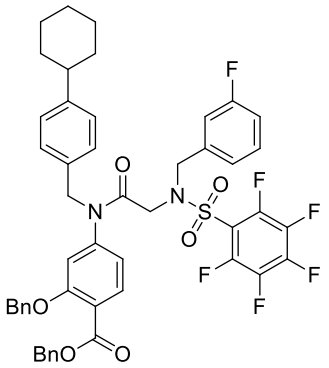


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-fluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}F_6N_2O_6S$
Molecular Weight: 900.92

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20j** (27.0 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.45 (m, 5H, CH_2), 1.70-1.89 (m, 5H, CH_2), 2.40-2.54 (m, 1H, CH), 3.83 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.82 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.37 (s, 1H, CH), 6.52 (d, *J* = 8.0 Hz, 1H, CH), 6.92-7.02 (m, 3H, CH), 7.08-7.16 (m, 3H, CH), 7.30-7.43 (m, 12H, CH), 7.74 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 48.5, 53.0, 60.5, 67.2, 70.9, 113.9, 115.4, 115.6, 120.1, 121.8, 121.9, 125.0, 125.0, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 130.5, 130.6, 131.7, 131.7, 133.4, 133.6, 135.7, 135.8, 148.1, 159.0, 164.4, 165.9; LRMS (ES+) Calcd for [$C_{49}H_{42}F_6N_2O_6S$ + Na] 923.26 found 923.43.

Compound 20k

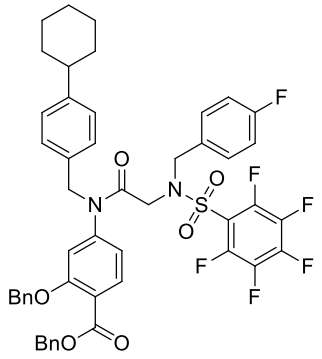


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-fluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}F_6N_2O_6S$
Molecular Weight: 900.92

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20k** (26.2 mg, 97 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.68-1.90 (m, 5H, CH_2), 2.39-2.54 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.28 (s, 1H, CH), 6.43 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 8.0 Hz, 2H, CH), 6.95-7.05 (m, 2H, CH), 7.05 (d, *J* = 7.6 Hz, 1H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.43 (m, 11H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.8, 51.0, 53.0, 67.2, 70.9, 113.7, 115.4, 115.7, 115.9, 119.9, 121.4, 124.4, 124.4, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 130.7, 130.7, 133.4, 133.5, 135.6, 135.8, 137.2, 137.2, 144.2, 145.1, 148.2, 158.9, 164.4, 165.8; LRMS (ES+) Calcd for [$C_{49}H_{42}F_6N_2O_6S$ + Na] 923.26 found 923.51.

Compound 20l

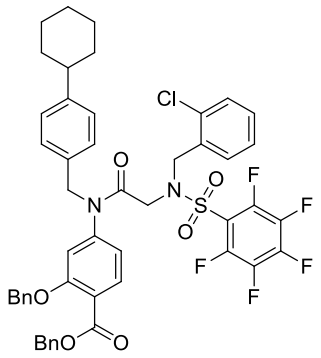


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-fluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}F_6N_2O_6S$
Molecular Weight: 900.92

Sulfonamide **19** was functionalized on a 0.03 mmol scale using General Procedure A to give **20l** (26.8 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.41-2.56 (m, 1H, CH), 3.73 (s, 2H, CH_2), 4.63 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.26 (s, 1H, CH), 6.41 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 8.0 Hz, 2H, CH), 6.95-7.03 (m, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.19-7.25 (m, 2H, CH), 7.28-7.42 (m, 10H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.7, 50.7, 53.0, 67.3, 70.9, 113.7, 115.9, 116.1, 119.9, 121.2, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.8, 129.0, 130.7, 130.8, 133.4, 133.5, 135.6, 135.8, 144.3, 148.2, 158.9, 165.4, 165.6; LRMS (ES+) Calcd for [$C_{49}H_{42}F_6N_2O_6S$ + Na] 923.26 found 923.51.

Compound 20m

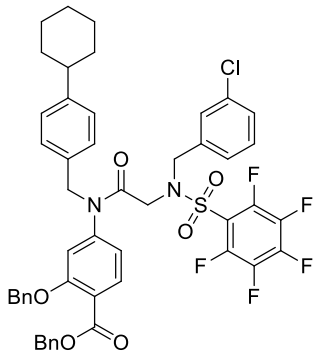


benzyl 2-(benzyloxy)-4-(2-(*N*-(2-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}ClF_5N_2O_6S$
Molecular Weight: 917.38

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20m** (35.0 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.43 (m, 5H, CH_2), 1.64-1.88 (m, 5H, CH_2), 2.36-2.52 (m, 1H, CH), 3.78 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.79 (s, 4H, 2 CH_2), 5.28 (s, 2H, CH_2), 6.35 (s, 1H, CH), 6.50 (d, *J* = 8.0 Hz, 1H, CH), 6.93 (d, *J* = 7.6 Hz, 2H, CH), 7.08 (d, *J* = 7.6 Hz, 2H, CH), 7.15-7.38 (m, 13H, CH), 7.43 (d, *J* = 8.0 Hz, 1H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.6, 44.4, 48.6, 48.7, 53.1, 67.2, 70.9, 113.9, 120.1, 121.3, 127.1, 127.3, 127.7, 128.3, 128.4, 128.4, 128.7, 128.8, 129.0, 129.6, 129.9, 131.4, 132.5, 133.4, 133.6, 134.2, 135.7, 135.8, 144.3, 148.1, 148.9, 165.4, 165.9; LRMS (ES+) Calcd for [$C_{49}H_{42}ClF_5N_2O_6S$ + Na] 939.23 found 939.42.

Compound 20n

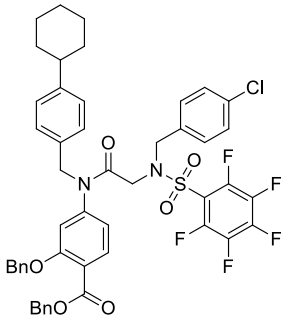


benzyl 2-(benzyloxy)-4-(2-(*N*-(3-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}ClF_5N_2O_6S$
Molecular Weight: 917.38

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20n** (34.5 mg, 94 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.45 (m, 5H, CH_2), 1.66-1.90 (m, 5H, CH_2), 2.39-2.53 (m, 1H, CH), 3.74 (s, 2H, CH_2), 4.63 (s, 4H, 2 CH_2), 4.78 (s, 4H, 2 CH_2), 5.29 (s, 2H, CH_2), 6.26 (s, 1H, CH), 6.43 (d, *J* = 7.8 Hz, 1H, CH), 6.91 (d, *J* = 8.0 Hz, 2H, CH), 7.10 (d, *J* = 8.0 Hz, 2H, CH), 7.19-7.27 (m, 4H, CH), 7.28-7.39 (m, 10H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.6, 44.4, 47.9, 50.9, 53.0, 67.2, 70.9, 113.6, 119.9, 121.4, 127.0, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.8, 128.9, 130.2, 130.5, 133.4, 133.5, 134.8, 135.6, 135.8, 136.7, 144.2, 148.2, 158.9, 165.4, 165.7; LRMS (ES+) Calcd for [$C_{49}H_{42}ClF_5N_2O_6S$ + Na] 939.23 found 939.36

Compound 20o

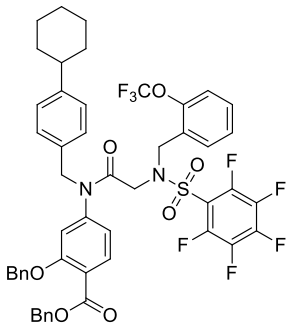


benzyl 2-(benzyloxy)-4-(2-(*N*-(4-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{49}H_{42}ClF_5N_2O_6S$
Molecular Weight: 917.38

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20o** (34.8 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.28-1.43 (m, 5H, CH_2), 1.64-1.87 (m, 5H, CH_2), 2.38-2.52 (m, 1H, CH), 3.72 (s, 2H, CH_2), 4.54-4.71 (m, 4H, 2 CH_2), 4.78 (s, 4H, 2 CH_2), 5.28 (s, 2H, CH_2), 6.24 (s, 1H, CH), 6.37 (d, *J* = 8.0 Hz, 1H, CH), 6.89 (d, *J* = 8.0 Hz, 2H, CH), 7.09 (d, *J* = 8.0 Hz, 2H, CH), 7.16 (d, *J* = 8.0 Hz, 2H, CH), 7.20-7.41 (m, 11H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.6, 47.8, 50.8, 53.0, 67.3, 70.9, 113.6, 119.9, 121.4, 127.2, 127.3, 127.4, 128.3, 128.4, 128.7, 128.7, 129.0, 129.2, 130.2, 133.0, 133.4, 133.5, 134.5, 135.6, 135.7, 144.2, 148.2, 158.9, 165.4, 165.8; LRMS (ES+) Calcd for [$C_{49}H_{42}ClF_5N_2O_6S$ + Na] 939.23 found 939.49.

Compound 20p

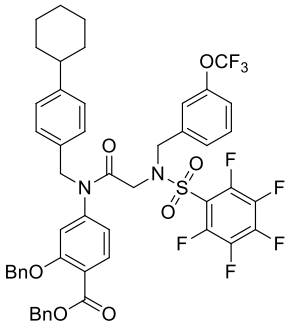


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_7S$
Molecular Weight: 966.93

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20p** (40.2 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.68-1.89 (m, 5H, CH_2), 2.38-2.54 (m, 1H, CH), 3.81 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.37 (s, 1H, CH), 6.52 (d, *J* = 7.6 Hz, 1H, CH), 6.93 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.21 (d, *J* = 8.0 Hz, 1H CH), 7.27-7.42 (m, 12H, CH), 7.52 (d, *J* = 7.2 Hz, 1H, CH) 7.75 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.3, 45.6, 48.4, 53.0, 67.2, 70.8, 113.8, 120.0, 120.7, 121.3, 121.9, 127.1, 127.3. 127.6, 127.8, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 130.0, 131.4, 133.4, 133.5, 135.6, 135.7, 144.2, 147.7, 148.1, 158.9, 165.4, 165.7; LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_7S$ + Na] 989.25 found 989.45

Compound 20q

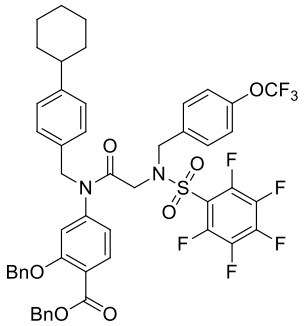


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_7S$
Molecular Weight: 966.93

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20q** (38.6 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.71-1.88 (m, 5H, CH_2), 2.40-2.52 (m, 1H, CH), 3.77 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.80 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.41 (d, *J* = 7.6 Hz, 1H, CH), 6.92 (d, *J* = 8.0 Hz, 2H, CH), 7.08-7.19 (m, 4H, CH), 7.21-7.26 (m, 1H, CH), 7.27-7.39 (m, 11H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.4, 47.9, 51.0, 53.0, 67.2, 70.8, 113.7, 119.8, 120.9, 121.3, 121.8, 127.1, 127.2. 127.3, 128.3, 128.4, 128.4, 128.7, 128.7, 128.9, 130.6, 133.4, 133.5, 135.6, 135.7, 137.1, 144.1, 148.2, 149.6, 158.9, 165.4, 165.8; LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_7S$ + Na] 989.25 found 989.45.

Compound 20r

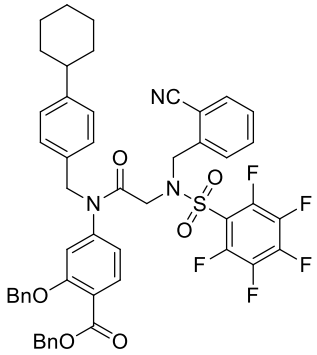


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_8N_2O_7S$
Molecular Weight: 966.93

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20r** (39.6 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.25-1.38 (m, 5H, CH_2), 1.60-1.78 (m, 5H, CH_2), 2.31-2.45 (m, 1H, CH), 4.00 (s, 2H, CH_2), 4.60 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 5.00 (s, 2H, CH_2), 5.24 (s, 2H, CH_2), 6.62 (d, *J* = 7.2 Hz, 1H, CH), 6.92-7.12 (m, 5H, CH), 7.22-7.42 (m, 14H, CH), 7.60 (d, *J* = 8.0 Hz, 1H, CH); LRMS (ES+) Calcd for [$C_{50}H_{42}F_8N_2O_7S$ + Na] 989.25 found 989.59.

Compound 20s

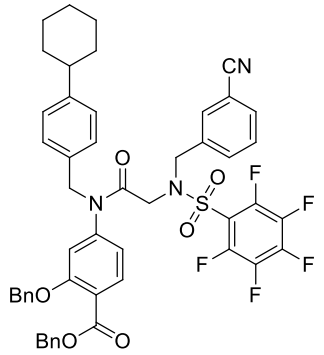


benzyl 2-(benzyloxy)-4-(2-(*N*-(2-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_5N_3O_6S$
Molecular Weight: 907.94

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20s** (36.7 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.68-1.90 (m, 5H, CH_2), 2.39-2.55 (m, 1H, CH), 3.90 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.86 (s, 2H, CH), 4.90 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.56 (s, 1H, CH), 6.61 (d, *J* = 8.0 Hz, 1H, CH), 6.93 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.27-7.45 (m, 10H, CH), 7.54-7.64 (m, 2H, CH), 7.71 (d, *J* = 8.0 Hz, 1H, CH), 7.75 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 27.0, 34.6, 44.4, 49.1, 49.6, 53.2, 67.2, 70.9, 112.5, 114.0, 117.4, 120.2, 121.3, 127.1, 127.3, 128.2, 128.4, 128.4, 128.7, 128.7, 128.9, 129.1, 130.8, 132.8, 133.3, 133.4, 133.9, 135.7, 135.8, 139.0, 144.2, 148.0, 159.0, 165.4, 165.5; LRMS (ES+) Calcd for [$C_{50}H_{42}F_5N_3O_6S$ + Na] 930.26 found 930.44.

Compound 20t

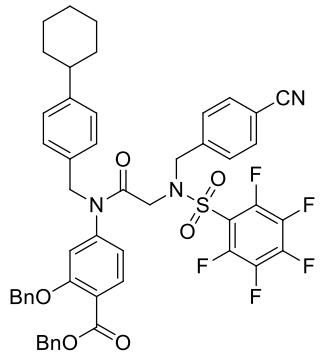


benzyl 2-(benzyloxy)-4-(2-(*N*-(3-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_5N_3O_6S$
Molecular Weight: 907.94

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20t** (33.4 mg, 92 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.68-1.91 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.58-4.78 (m, 4H, 2 CH_2), 4.84 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.34 (s, 1H, CH), 6.49 (d, *J* = 8.0 Hz, 1H, CH), 6.86-6.97 (m, 2H, CH), 7.12 (d, *J* = 7.8 Hz, 2H, CH), 7.23-7.40 (m, 10H, CH), 7.41-7.49 (m, 1H, CH), 7.52-7.63 (m, 3H, CH) 7.75 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.3, 48.0, 50.9, 53.1, 67.3, 70.9, 113.1, 113.7, 118.3, 119.8, 121.5, 127.3, 127.3, 128.3, 128.4, 128.5, 128.7, 128.7, 128.9, 130.0, 131.9, 132.2, 133.0 133.3, 133.4, 135.6, 135.7, 136.6, 144.0, 148.3, 159.0, 165.3, 165.6.

Compound 20u

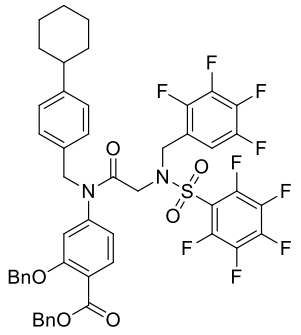


benzyl 2-(benzyloxy)-4-(2-(*N*-(4-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)benzoate
Chemical Formula: $C_{50}H_{42}F_5N_3O_6S$
Molecular Weight: 907.94

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20u** (31.5 mg, 87 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.66-1.90 (m, 5H, CH_2), 2.39-2.56 (m, 1H, CH), 3.77 (s, 2H, CH_2), 4.59-4.69 (m, 2H, CH_2), 4.72-80 (m, 2H, CH_2), 4.85 (s, 2H, CH_2), 5.31 (s, 2H, CH_2), 6.35 (s, 1H, CH), 6.44 (d, *J* = 8.2 Hz, 1H, CH), 6.93 (d, *J* = 7.6 Hz, 2H, CH), 6.99 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.24-7.44 (m, 12H, CH), 7.57-7.67 (m, 2H, CH), 7.73 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 48.2, 51.4, 53.1, 67.3, 70.9, 112.5, 113.8, 118.4, 119.8, 121.6, 127.2, 127.3, 128.3, 128.5, 128.5, 128.7, 128.8, 129.0, 129.1, 132.8, 133.3, 133.4, 135.5, 135.7, 140.4, 144.0, 148.3, 159.0, 165.4, 165.6; LRMS (ES+) Calcd for [$C_{50}H_{42}F_5N_3O_6S$ + Na] 930.26 found 930.46.

Compound 20v

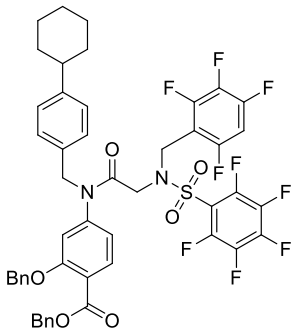


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,4,5-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{39}F_9N_2O_6S$
Molecular Weight: 954.89

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20v** (34.2 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.67-1.91 (m, 5H, CH_2), 2.39-2.54 (m, 1H, CH), 3.82 (s, 2H, CH_2), 4.67 (s, 4H, 2 CH_2), 4.87 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.41 (s, 1H, CH), 6.59 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 8.0 Hz, 2H, CH), 7.08-7.19 (m, 3H, CH), 7.27-7.42 (m, 10H, CH), 7.80 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 44.5, 48.7, 53.1, 67.3, 70.9, 112.2, 112.3, 113.7, 113.7, 120.0, 121.6, 127.2, 127.3, 128.3, 128.4, 128.5, 128.7, 128.8, 128.9, 133.4, 133.5, 135.6, 135.7, 144.0, 148.3, 159.0, 165.4, 165.5; LRMS (ES+) Calcd for [$C_{49}H_{39}F_9N_2O_6S$ + Na] 977.23 found 977.43.

Compound 20w

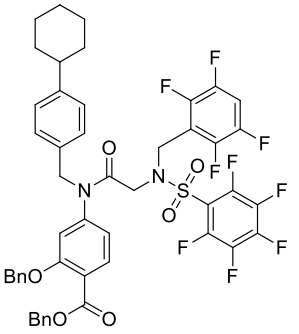


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,4,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{39}F_9N_2O_6S$
Molecular Weight: 954.89

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20w** (35.5 mg, 93 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.45 (m, 5H, CH_2), 1.68-1.91 (m, 5H, CH_2), 2.36-2.52 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.78 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.42 (s, 1H, CH), 6.60 (d, *J* = 8.0 Hz, 1H, CH), 6.94 (d, *J* = 8.0 Hz, 2H, CH), 6.70-6.82 (m, 1H, CH), 7.93 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.20-7.42 (m, 10H, CH), 7.80 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.6, 44.4, 48.8, 53.1, 67.3, 70.9, 108.7, 113.8, 114.6, 120.0, 120.2, 121.5, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.8, 128.9, 133.5, 133.5, 135.6, 135.7, 144.2, 148.2, 159.0 165.4, 165.6; LRMS (ES+) Calcd for [$C_{49}H_{39}F_9N_2O_6S$ + Na] 977.23 found 977.42.

Compound 20x

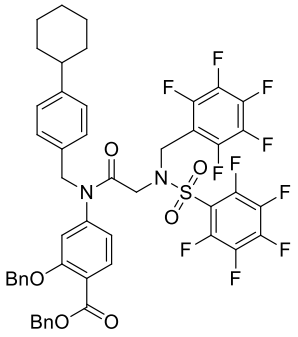


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,5,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{39}F_9N_2O_6S$
Molecular Weight: 954.89

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20x** (32.8 mg, 86 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.45 (m, 5H, CH_2), 1.68-1.90 (m, 5H, CH_2), 2.41-2.54 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.87 (s, 4H, 2 CH_2), 5.32 (s, 2H, CH_2), 6.43 (s, 1H, CH), 6.61 (d, *J* = 8.0 Hz, 1H, CH), 6.94 (d, *J* = 8.0 Hz, 2H, CH), 6.99-7.09 (m, 1H, CH), 7.12 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.42 (m, 10H, CH), 7.80 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.7, 44.4, 48.9, 53.1, 67.3, 70.8, 107.0, 113.7, 114.6, 120.0, 121.5, 127.2, 127.3, 128.3, 128.4, 128.4, 128.7, 128.8, 128.9, 133.5, 133.5, 135.6, 135.8, 144.1, 148.2, 159.1 165.4, 165.5; LRMS (ES+) Calcd for [$C_{49}H_{39}F_9N_2O_6S$ + Na] 977.23 found 977.42.

Compound 20y

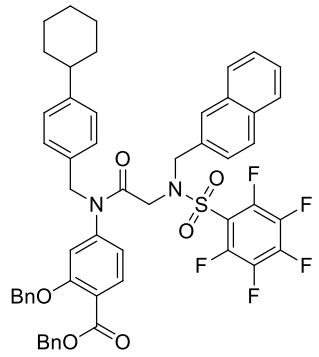


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{49}H_{38}F_{10}N_2O_6S$
Molecular Weight: 972.88

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20y** (38.4 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.66-1.90 (m, 5H, CH_2), 2.38-2.54 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.42 (s, 1H, CH), 6.61 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.27-7.42 (m, 10H, CH), 7.80 (d, *J* = 8.0 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 39.6, 44.4, 49.0, 53.1, 67.3, 70.9, 113.7, 120.0, 121.6, 127.2, 127.3, 127.4, 128.4, 128.5, 128.7, 128.8, 128.9, 133.4, 133.5, 135.6, 135.7, 144.0, 148.2, 159.1, 165.4, 165.5. LRMS (ES+) Calcd for [$C_{49}H_{38}F_{10}N_2O_6S$ + Na] 995.22 found 995.49.

Compound 20z

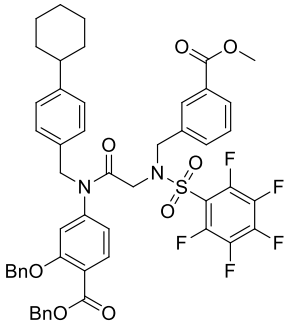


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(naphthalen-2-ylmethyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{53}H_{45}F_5N_2O_6S$
Molecular Weight: 932.99

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20z** (37.3, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.33-1.50 (m, 5H, CH_2), 1.68-1.94 (m, 5H, CH_2), 2.40-2.58 (m, 1H, CH), 3.77 (s, 2H, CH_2), 4.42 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 5.25 (s, 2H, CH_2), 6.06 (s, 1H, CH), 6.26 (d, *J* = 7.2 Hz, 1H, CH), 6.96 (d, *J* = 7.6 Hz, 2H, CH), 7.14 (d, *J* = 7.6 Hz, 2H, CH), 7.17-7.24 (m, 2H, CH), 7.27-7.36 (m, 8H, CH), 7.38-7.57 (m, 4H, CH),7.65 (s, 1H, CH), 7.72 (d, *J* = 8.0 Hz, 1H, CH), 7.74-7.89 (m, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.8, 51.5, 52.9, 67.2, 70.5, 113.3, 119.9, 121.1, 126.3, 126.7, 126.9, 127.2, 127.5, 127.7, 127.9, 128.1, 128.3, 128.3, 128.4, 128.6, 128.6, 129.1, 129.2, 131.7, 133.2, 133.2, 133.7, 135.5, 135.7, 158.8, 165.4, 165.9; LRMS (ES+) Calcd for [$C_{53}H_{45}F_5N_2O_6S$ + Na] 955.28 found 955.54.

Compound 20aa

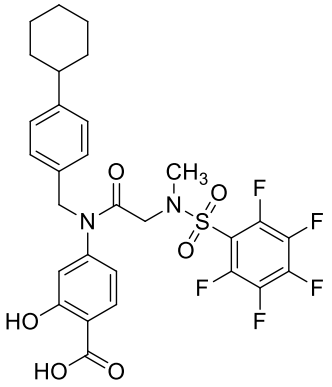


benzyl 2-(benzyloxy)-4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(methoxycarbonyl)benzyl)phenylsulfonamido)acetamido)benzoate
Chemical Formula: $C_{51}H_{45}F_5N_2O_8S$
Molecular Weight: 940.97

Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20aa** (36.1 mg, 96 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.40-2.53 (m, 1H, CH), 3.76 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 5.29 (s, 2H, CH_2), 6.30 (s, 1H, CH), 6.44 (d, *J* = 8.0 Hz, 1H, CH), 6.91 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.28-7.37 (m, 10H, CH), 7.41 (t, *J* = 7.6 Hz, 1H, CH), 7.52 (d, *J* = 7.6 Hz, 1H, CH), 7.69 (d, *J* = 8.0 Hz, 1H, CH), 7.90 (s, 1H, CH), 7.97 (d, *J* = 7.6 Hz, 1H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 32.6, 34.6, 44.4, 47.9, 51.2, 52.4, 67.2, 70.9, 113.7, 120.0, 121.4, 127.2, 127.4, 128.3, 128.4, 128.4, 128.7, 128.7, 129.3, 129.7, 129.8, 129.8, 130.2, 130.9, 133.4, 133.4, 133.6, 135.2, 135.6, 135.8, 148.1, 158.9, 165.4, 165.8, 166.6; LRMS (ES+) Calcd for [$C_{51}H_{45}F_5N_2O_8S$ + Na] 963.27 found 963.41.

Compound 20ab



4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-methylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{29}H_{27}F_5N_2O_6S$
Molecular Weight: 626.59
Log P: 5.74

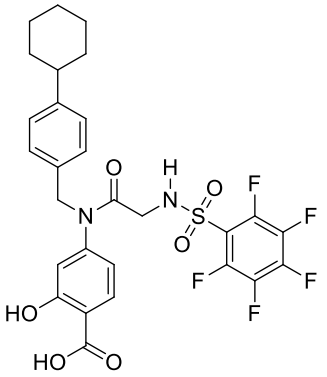
Sulfonamide **19** was functionalized on a 0.04 mmol scale using General Procedure A to give **20ab** (35.7 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.48 (m, 5H, CH_2), 1.66-1.90 (m, 5H, CH_2), 2.37-2.55 (m, 1H, CH), 3.63-3.88 (m, 5H, CH_2 and CH_3), 4.63 (s, 2H, CH_2), 4.75 (s, 4H, 2 CH_2), 5.29 (s, 2H, CH_2), 6.25 (s, 1H, CH), 6.41 (d, *J* = 8.0 Hz, 1H, CH), 6.92 (d, *J* = 7.4 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H, CH), 7.23-7.38 (m, 11H, CH), 7.46 (d, *J* = 8.0 Hz, 1H, CH), 7.70 (d, *J* = 8.0 Hz, 1H, CH), 7.99 (d, *J* = 8.0 Hz, 2H, CH); δ_C (100 MHz, *d*-$CDCl_3$) 26.2, 26.9, 34.6, 44.4, 47.9, 51.2, 52.3, 53.0, 67.2, 70.8, 113.6, 119.8, 120.3, 127.2. 127.4, 128.3, 128.4, 128.4,

128.7, 128.7, 128.7, 129.0, 129.1, 130.2, 130.3, 130.5, 133.3, 133.4, 133.5, 135.7, 139.7, 142.7, 148.2, 158.9, 165.4, 165.7, 166.5; LRMS (ES+) Calcd for [$C_{51}H_{45}F_5N_2O_8S$ + Na] 963.27 found 963.40.

Compound **9** was prepared as published previously.

Compound 21a

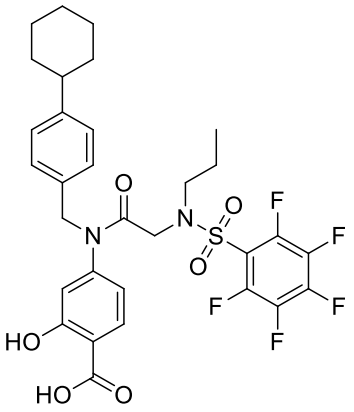


4-(*N*-(4-cyclohexylbenzyl)-2-(perfluorophenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{28}H_{25}F_5N_2O_6S$
Molecular Weight: 612.56
Log P: 5.44

Compound **19** was globally deprotected according to general procedure B on a 0.06 mmol scale to give compound **21a** (26.8 mg, 73 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.82 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 5.29 (s, 1H, NH), 6.50 (s (br), 1H, CH), 6.64 (s, 1H, CH), 6.99 (d, *J* = 7.2 Hz, 2H, CH), 7.10 (d, *J* = 7.2 Hz, 2H, CH), 7.90 (s, 1H, CH), 10.91 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 45.1, 53.6, 113.4, 117.1, 118.9, 127.2, 128.7, 132.8, 133.0, 143.4, 148.2, 163.2, 166.7, 172.5; HRMS (ES+) Calcd for [$C_{28}H_{25}F_5N_2O_6S$ + H] 613.1430 found 613.1426; HPLC (III) t_R = 25.52 min (88.3 %), (IV) t_R = 55.78 min (93.5 %).

Compound 21b

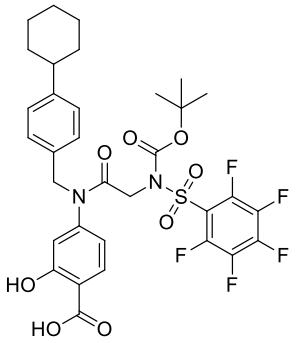


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-propylphenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{31}H_{31}F_5N_2O_6S$
Molecular Weight: 654.64
Log P: 6.57

Compound **20b** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21b** (29.6 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 0.89 (t, *J* = 7.2 Hz, 3H, CH_3), 1.30-1.46 (m, 5H, CH_2), 1.53 (m, 2H, CH_2) 1.69-1.92 (m, 5H, CH_2), 2.40-2.55 (m, 1H, CH), 3.41 (t, *J* = 7.2 Hz, 2H, CH_2), 4.06 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.56 (d, *J* = 6.4 Hz, 1H, CH), 6.71 (s, 1H, CH), 6.98 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.90 (d, *J* = 6.4 Hz, 1H, CH), 10.84 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 11.1, 21.3, 26.3, 27.0, 34.5, 44.4, 48.7, 49.8, 53.3, 110.6, 116.9, 119.2, 127.2, 128.5, 129.1, 133.2, 148.1, 146.3, 163.3, 166.2, 171.6; HRMS (ES+) Calcd for [$C_{31}H_{31}F_5N_2O_6S$ + H] 655.1881 found 655.1895; HPLC (III) t_R = 26.85 min (100 %), (IV) t_R = 63.45 min (98.6 %).

Compound 21c

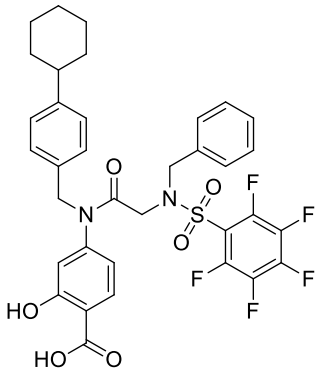


4-(2-(*N*-(*tert*-butoxycarbonyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{33}H_{33}F_5N_2O_8S$
Molecular Weight: 712.68
Log P: 6.61

Compound **20c** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21c** (25.5 mg, 72 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.52 (m, 14H, CH_2 and 3 CH_3), 1.70-1.92 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 4.41 (s, 2H, CH_2), 4.70 (s, 4H, 2 CH_2), 6.25 (s (br), 1H, CH), 6.49 (s, 1H, CH), 6.99 (d, *J* = 7.2 Hz, 2H, CH), 7.14 (d, *J* = 7.2 Hz, 2H, CH), 7.27-7.44 (m, 4H, CH), 7.78 (s (br), 1H, CH), 10.84 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 27.9, 34.5, 44.4, 49.6, 53.5, 86.3, 110.6, 117.2, 119.1, 127.1, 128.7, 132.6, 133.7, 147.9, 150.3, 163.9, 165.9, 169.6, 172.4; LRMS (ESI) Calcd for [$C_{33}H_{33}F_5N_2O_8S$ + H, BOC lost] 613.14 found 613.10; HPLC (III) t_R = 27.50 min (89.0 %), (IV) t_R = 61.66 min (90.2 %).

Compound 21d

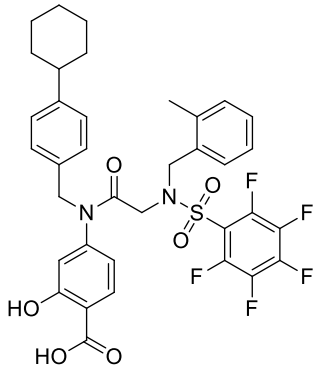


4-(2-(*N*-benzyl-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{31}F_5N_2O_6S$
Molecular Weight: 702.69
Log P: 6.54

Compound **20d** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21d** (18.0 mg, 85 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.48 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.42-2.56 (m, 1H, CH), 3.85 (s, 2H, CH_2), 4.69 (s, 4H, 2 CH_2), 6.26 (s (br), 1H, CH), 6.42 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.13 (d, *J* = 7.6 Hz, 2H, CH), 7.20-7.37 (m, 4H, CH), 7.75 (d, *J* = 8.4 Hz, 1H, CH), 10.48 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 47.9, 51.1, 53.1, 111.7, 117.2, 119.2, 127.2, 128.6, 128.7, 129.0, 129.1, 131.9 132.5, 133.2, 134.3, 148.1, 163.1, 166.1, 172.9; HRMS (DART) Calcd for [$C_{35}H_{31}F_5N_2O_6S$ + H] 703.1901 found 703.1903; HPLC (III) t_R = 25.97 min (97.6 %), (IV) t_R = 64.35 min (98.6 %).

Compound 21e

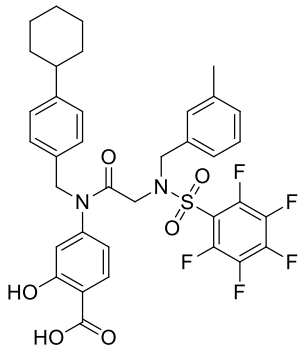


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{33}F_5N_2O_6S$
Molecular Weight: 716.71
Log P: 6.95

Compound **20e** was globally deprotected according to general procedure B on a 0.02 mmol scale to give compound **21e** (11.9 mg, 83 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.28 (s, 3H, CH_3) 2.40-2.55 (m, 1H, CH), 3.72 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.11 (s (br), 1H, CH), 6.31 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.03-7.19 (m, 5H, CH), 7.22 (t, *J* = 7.6 Hz, 1H, CH), 7.70 (d, *J* = 7.6 Hz, 1H, CH), 10.95 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 19.1, 25.7, 26.3, 27.0, 34.5, 44.4, 47.7, 49.4, 53.1, 110.7, 116.9, 118.7, 126.4, 127.1, 128.6, 128.8, 129.0, 130.3, 131.1, 131.7, 132.3, 133.4, 138.1, 148.0, 162.4, 166.1, 171.7; LRMS Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.21 found 717.18; HPLC (III) t_R = 30.30 min (100 %), (IV) t_R = 66.23 min (100 %).

Compound 21f

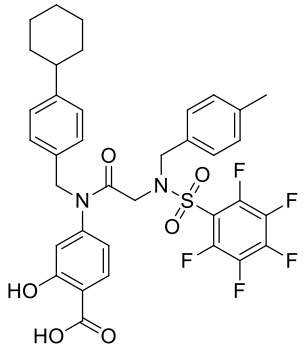


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{33}F_5N_2O_6S$
Molecular Weight: 716.71
Log P: 6.95

Compound **20f** was globally deprotected according to general procedure B on a 0.02 mmol scale to give compound **21f** (12.6 mg, 88 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.28 (s, 3H, CH_3) 2.40-2.54 (m, 1H, CH), 3.50 (s, 2H, CH_2), 4.61 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 6.20 (s (br), 1H, CH), 6.38 (s, 1H, CH), 6.97 (d, J = 7.6 Hz, 2H, CH), 7.03 (d, J = 7.6 Hz, 2H, CH), 7.06-7.21 (m, 3H, CH), 7.72 (s, 1H, CH), 11.08 (s, 1H, OH); δ_C (100 MHz, *d*-$CDCl_3$) 21.4, 25.7, 26.3, 27.0, 34.5, 44.4, 47.9, 51.3, 53.1, 113.4, 116.7, 118.6, 126.1, 127.1, 128.6, 128.9, 129.4, 129.7, 132.3, 133.5, 134.1, 138.8, 139.2, 147.9, 163.0, 166.0, 172.1; HRMS (DART) Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.2058 found 717.2047; HPLC (III) t_R = 30.00 min (100 %), (IV) t_R = 65.94 min (100 %).

Compound 21g

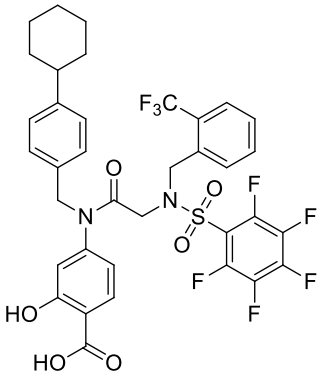


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-methylbenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{33}F_5N_2O_6S$
Molecular Weight: 716.71
Log P: 6.95

Compound **20g** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21g** (25.6 mg, 89 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.81 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.68 (s, 2H, CH_2) 6.27 (s (br), 1H, CH), 6.36 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.06-7.18 (m, 6H, CH), 7.25 (s, 1H, CH), 10.63 (s, 1H, CH); δ_C (100 Hz, *d*-$CDCl_3$) 21.3, 26.3, 27.0, 34.5, 44.4, 47.8, 51.1, 53.2, 110.8, 117.1, 119.1, 127.2, 128.6, 129.1, 129.8, 131.0. 132.5, 133.3, 138.6, 143.7, 148.1, 163.1, 166.1, 172.7; HRMS (DART) Calcd for [$C_{36}H_{33}F_5N_2O_6S$ + H] 717.2058 found 717.2045; HPLC (III) t_R = 29.25 min (100 %), (IV) t_R = 66.91 min (100 %).

Compound 21h

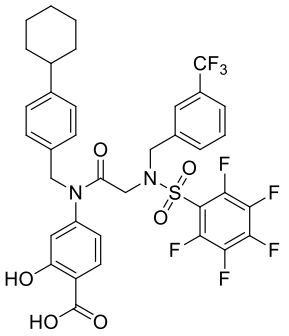


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_6S$
Molecular Weight: 770.69
Log P: 7.52

Compound **20h** was globally deprotected according to general procedure B on a 0.02 mmol scale to give compound **21h** (11.5 mg, 75 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.69-1.94 (m, 5H, CH_2), 2.38-2.54 (m, 1H, CH), 3.85 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 6.33 (s (br), 1H, CH), 6.47 (s, 1H, CH), 6.95 (d, *J* = 7.6 Hz, 2H, CH), 7.08 (d, *J* = 7.6 Hz, 2H, CH), 7.39 (t, *J* = 7.6 Hz, 1H, CH), 7.51 (t, *J* = 7.6 Hz, 1H, CH), 7.64 (d, *J* = 8.0 Hz, 1H, CH), 7.67-7.86 (m, 2H, CH), 11.16 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 25.7, 26.3, 27.0, 34.5, 44.4, 47.5, 48.5, 53.2, 111.8, 116.9, 118.7, 125.6, 126.0, 127.1, 128.4, 128.6, 130.6, 132.7, 133.3, 133.9, 134.8, 139.3, 147.9, 163.0, 165.6, 172.3; LRMS Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.18 found 771.23; HPLC (III) t_R = 30.27 min (100 %), (IV) t_R = 66.37 min (100 %).

Compound 21i

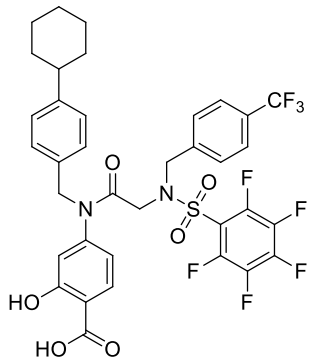


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_6S$
Molecular Weight: 770.69
Log P: 7.52

Compound **20i** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21i** (18.8 mg, 81 %)

δ_H (400 MHz, d_6-DMSO) 1.27-1.42 (m, 5H, CH_2), 1.64-1.85 (m, 5H, CH_2), 2.39-2.50 (m, 1H, CH), 4.13 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 6.61 (s (br), 1H, CH), 6.71 (s, 1H, CH), 7.00 (d, J = 8.0 Hz, 2H, CH), 7.11 (d, J = 8.0 Hz, 2H, CH), 7.52-7.68 (m, 4H, CH), 7.71 (d, J = 8.4 Hz, 1H, CH), 11.76 (s, 1H, OH); HRMS (DART) Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.1775 found 771.1787; HPLC (III) t_R = 29.43 min (100 %), (IV) t_R = 65.38 min (97.8 %).

Compound 21j

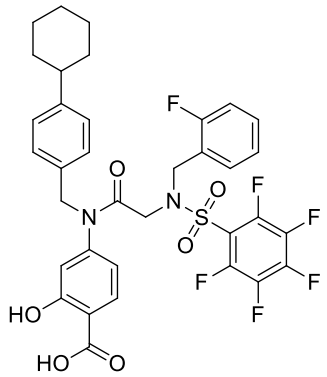


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-(trifluoromethyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_6S$
Molecular Weight: 770.69
Log P: 7.52

Compound **20j** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21j** (26.4 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.54 (m, 1H, CH), 3.85 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.23 (s (br), 1H, CH), 6.44 (s, 1H, CH), 6.96 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.38 (d, *J* = 7.6 Hz, 2H, CH), 7.56 (d, *J* = 7.6 Hz, 2H, CH), 7.75 (s, 1H, CH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 48.1, 51.1, 53.1, 111.8, 117.0, 118.7, 125.9, 126.0, 127.2, 128.6, 129.1, 131.4, 132.5, 135.8, 138.8, 148.1, 148.2, 163.2, 165.8, 172.6; HRMS (DART) Calcd for [$C_{36}H_{30}F_8N_2O_6S$ + H] 771.1775 found 771.1767; HPLC (III) t_R = 29.48 min (96.6 %), (IV) t_R = 65.57 min (100 %).

Compound 21k

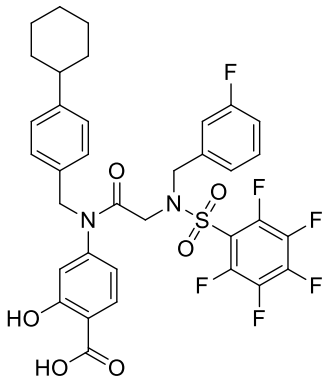


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-fluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}F_6N_2O_6S$
Molecular Weight: 720.68
Log P: 6.68

Compound **20k** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21k** (29.1 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.91 (s, 2H, CH_2), 4.71 (s, 4H, 2 CH_2), 6.37 (s (br), 1H, CH), 6.53 (s, 1H, CH), 6.95-7.16 (m, 6H, CH), 7.27-7.43 (m, 2H, CH), 7.79 (s, 1H, CH); HRMS (DART) Calcd for [$C_{35}H_{30}F_6N_2O_6S$ + H] 721.1807 found 721.1816; HPLC (III) t_R = 28.77 min (100 %), (IV) t_R = 64.18 min (100 %).

Compound 21l

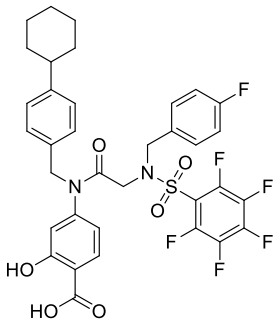


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-fluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}F_6N_2O_6S$
Molecular Weight: 720.68
Log P: 6.68

Compound **20l** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21l** (21.4 mg, 99 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.41-2.55 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.68 (s, 4H, 2 CH_2), 6.29 (s (br), 1H, CH), 6.45 (s, 1H, CH), 6.92-7.06 (m, 5H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.25-7.31 (t, *J* = 7.6 Hz, 1H, CH), 7.78 (s, 1H, CH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 48.0, 51.0, 53.2, 111.6, 115.6, 115.6, 115.8, 115.8, 116.9, 118.7, 124.4, 124.4, 127.2, 128.5, 130.6, 130.7, 132.6, 133.3, 135.0, 137.1, 137.1, 148.1, 161.9, 163.1, 164.4, 172.6; HRMS (DART) Calcd for [$C_{35}H_{30}F_6N_2O_6S$ + H] 721.1807 found 721.1827; HPLC (III) t_R = 28.78 min (94.4 %), (IV) t_R = 64.27 min (97.1 %).

Compound 21m

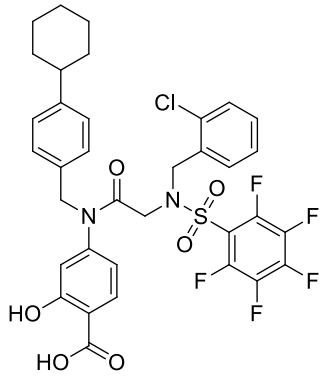


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-fluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}F_6N_2O_6S$
Molecular Weight: 720.68
Log P: 6.68

Compound **20m** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21m** (20.6 mg, 95 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.47 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.81 (s, 2H, CH_2), 4.62 (s, 2H, CH_2), 4.66 (s, 2H, CH_2) 6.23 (s (br), 1H, CH), 6.41 (s, 1H, CH), 6.87-7.04 (m, 4H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.21 (d, *J* = 7.6 Hz, 2H, CH), 7.74 (s, 1H, CH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 47.7, 50.8, 53.2, 111.6, 115.8, 116.6, 116.1, 118.4, 127.1, 127.6, 130.2, 132.4, 133.4, 136.6, 148.0, 163.0, 165.9, 172.2; HRMS (DART) Calcd for [$C_{35}H_{30}F_6N_2O_6S$ + H] 721.1807 found 721.1798; HPLC (III) t_R = 28.78 min (98.5 %), (IV) t_R = 64.27 min (93.6 %).

Compound 21n

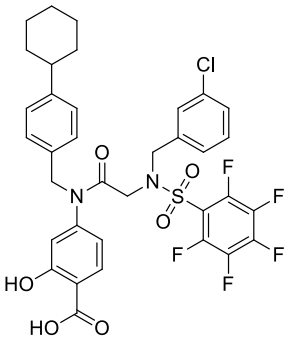


4-(2-(*N*-(2-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}ClF_5N_2O_6S$
Molecular Weight: 737.13
Log P: 7.16

Compound **20n** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21n** (21.1 mg, 72 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.91 (m, 5H, CH_2), 2.40-2.55 (m, 1H, CH), 3.90 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 6.39 (s (br), 1H, CH), 6.52 (s, 1H, CH), 6.99 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H ,CH), 7.18-7.29 (m, 2H, CH), 7.34 (d, *J* = 6.8 Hz, 1H, CH), 7.44 (d, *J* = 6.8 Hz, 1H, CH), 7.79 (d, *J* = 8.4 Hz, 1H, CH), 10.70 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 39.8, 44.4, 48.7, 53.3, 112.4, 117.2, 119.1, 127.2, 127.6, 128.6, 129.8, 130.0, 131.4, 132.3, 132.5, 133.2, 134.3, 134.4, 148.0, 163.1, 166.0, 172.5; HRMS (DART) Calcd for [$C_{37}H_{34}F_5N_2O_8S$ + H] 737.1503 found 737.1502; HPLC (III) t_R = 29.83 min (82.2 %), (IV) t_R = 65.71 min (80.5 %).

Compound 21o

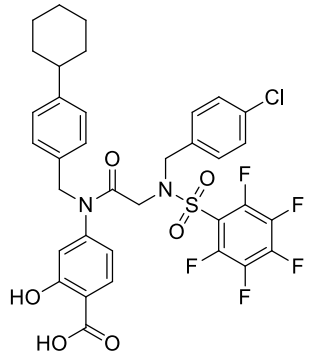


4-(2-(*N*-(3-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}ClF_5N_2O_6S$
Molecular Weight: 737.13
Log P: 7.16

Compound **20o** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21o** (21.2 mg, 72 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.41-2.56 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 4.71 (s, 2H, CH_2), 6.34 (s (br), 1H, CH), 6.49 (s, 1H, CH), 6.98 (d, *J* = 7.2 Hz, 2H, CH), 7.13 (d, *J* = 7.2 Hz, 2H, CH), 7.22-7.36 (m, 4H, CH), 7.79 (d, *J* = 8.0 Hz, 1H, CH), 10.69 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 48.0, 50.9, 53.2, 112.2, 117.1, 118.9, 127.0, 127.3, 128.6, 128.9, 130.4, 132.5, 132.6, 133.1, 133.2, 135.0, 136.5, 148.2, 163.1, 166.9, 172.4; HRMS (DART) Calcd for [$C_{35}H_{30}ClF_5N_2O_6S$ + H] 737.1512 found 737.1512; HPLC (III) t_R = 29.72 min (97.9 %), (IV) t_R = 65.61 min (100 %).

Compound 21p

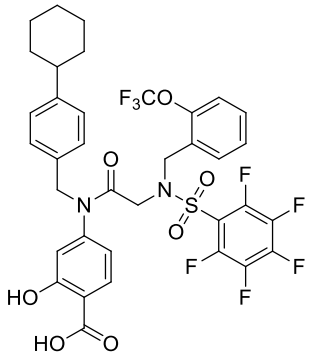


4-(2-(*N*-(4-chlorobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{30}ClF_5N_2O_6S$
Molecular Weight: 737.13
Log P: 7.16

Compound **20p** was globally deprotected according to general procedure B on a 0.05 mmol scale to give compound **21p** (27.8 mg, 75 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.41-2.58 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 6.31 (s (br), 1H, CH), 6.47 (s, 1H, CH), 6.98 (d, *J* = 7.2 Hz, 2H, CH), 7.14 (d, *J* = 7.2 Hz, 2H, CH), 7.20 (d, *J* = 7.2 Hz, 2H, CH), 7.30 (d, *J* = 7.2 Hz, 1H, CH), 7.79 (s (br), 1H, CH), 10.79 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 47.9, 50.8, 53.2, 112.4, 117.0, 118.8, 127.2, 128.6, 129.1, 129.2, 130.2, 132.5, 132.9, 133.1, 134.6, 148.2, 163.1, 165.9, 172.3; HRMS (DART) Calcd for [$C_{35}H_{30}ClF_5N_2O_6S$ + H] 737.1512 found 737.1512; HPLC (III) t_R = 29.03 min (71.8 %), (IV) t_R = 66.71 min (72.4 %).

Compound 21q

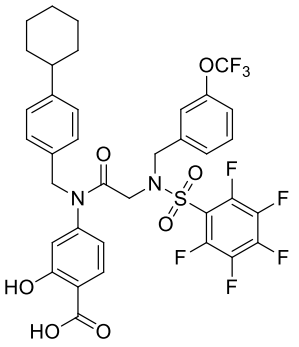


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_7S$
Molecular Weight: 786.68
Log P: 7.36

Compound **20q** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21q** (24.1 mg, 100 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.29-1.46 (m, 5H, CH_2), 1.68-1.90 (m, 5H, CH_2), 2.38-2.54 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 6.38 (s (br), 1H, CH), 6.51 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.09 (d, *J* = 7.6 Hz, 2H, CH), 7.17-7.29 (m, 2H, CH), 7.32 (d, *J* = 7.2 Hz, 1H, CH), 7.49 (d, *J* = 7.2 Hz, 1H, CH), 7.78 (d, *J* = 7.2 Hz, 1H, CH), 10.90 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 45.7, 48.5, 53.2, 111.2, 117.0, 118.9, 119.3, 120.8, 121.9, 127.2, 127.5, 127.7, 128.5, 130.1, 131.5, 132.5, 133.3, 147.8, 148.0, 163.1, 165.8, 172.4; HRMS (DART) Calcd for [$C_{36}H_{30}F_8N_2O_7S$ + H] 787.1724 found 787.1712; HPLC (III) t_R = 29.90 min (93.6 %), (IV) t_R = 66.34 min (93.1 %).

Compound 21r

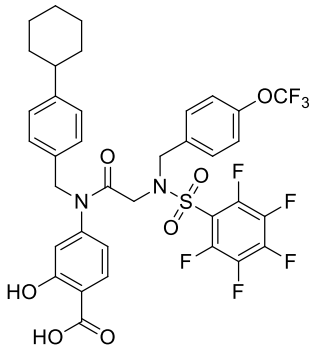


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_7S$
Molecular Weight: 786.68
Log P: 7.36

Compound **20r** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21r** (20.5 mg, 87 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.48 (m, 5H, CH_2), 1.69-1.93 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.87 (s, 2H, CH_2), 4.69 (s, 4H, 2 CH_2), 6.29 (s (br), 1H, CH), 6.46 (s, 1H, CH), 6.96 (d, *J* = 7.6 Hz, 2H, CH), 7.07-7.25 (m, 5H, CH), 7.35 (t, *J* = 7.2 Hz, 1H, CH), 7.75 (s, 1H, CH),10.88 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 45.7, 48.0, 51.0, 53.2, 109.9, 113.5, 116.9, 118.8, 121.0, 121.3, 127.1, 127.2, 128.6, 129.0, 130.6, 132.6, 137.0, 148.2, 149.8, 156.2, 163.1, 166.0, 172.6; HRMS (DART) Calcd for [$C_{39}H_{33}F_5N_2O_6S$ + H] 787.1724 found 787.1712; HPLC (III) t_R = 29.04 min (91.5 %), (IV) t_R = 66.91 min (91.3 %).

Compound 21s

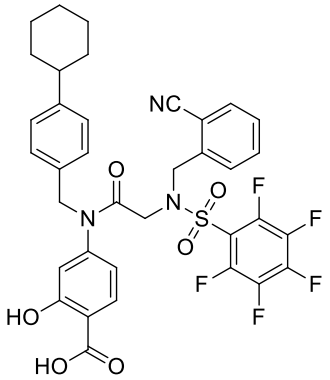


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-(trifluoromethoxy)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_8N_2O_7S$
Molecular Weight: 786.68
Log P: 7.36

Compound **20s** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21s** (21.2 mg, 90 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.32-1.49 (m, 5H, CH_2), 1.70-1.96 (m, 5H, CH_2), 2.42-2.58 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.84 (s, 2H, CH_2), 6.60 (s (br), 1H, CH), 6.73 (s, 1H, CH), 7.04-7.19 (m, 4H, CH), 7.90 (d, *J* = 7.6 Hz, 1H, CH), 10.92 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.4, 48.0, 50.7, 53.2, 112.0, 116.9, 118.6, 121.5, 127.2, 127.3, 128.5, 128.7, 128.8, 129.0, 130.3, 133.2, 148.1, 149.4, 163.0, 165.9, 171.6; HRMS (DART) Calcd for [$C_{36}H_{30}F_8N_2O_7S$ + H] 787.1724 found 787.1722; HPLC (III) t_R = 29.90 min (90.4 %), (IV) t_R = 66.04 min (75.0 %).

Compound 21t

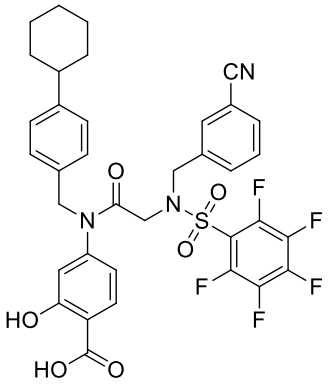


4-(2-(*N*-(2-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_5N_3O_6S$
Molecular Weight: 727.70
Log P: 6.05

Compound **20t** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21t** (24.9 mg, 86 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.92 (m, 5H, CH_2), 2.41-2.53 (m, 1H, CH), 3.95 (s, 2H, CH_2), 4.75 (s, 2H, CH_2), 4.87 (s, 2H, CH_2), 6.50 (d, *J* = 7.2 Hz, 1H, CH), 6.62 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 8.0 Hz, 2H ,CH), 7.42 (t, *J* = 7.6 Hz, 1H, CH), 7.59 (t, *J* = 7.6 Hz, 1H, CH), 7.62-7.70 (m, 2H, CH), 7.80 (d, *J* = 8.4 Hz, 1H, CH), 10.73 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 49.1, 49.6, 53.4, 112.1, 112.6, 116.4, 117.2, 119.1, 127.2, 128.5, 129.2, 130.6, 132.6, 132.6, 133.0, 133.1, 133.8, 138.7, 147.9, 163.1, 165.5, 172.2; HRMS (DART) Calcd for [$C_{37}H_{34}F_5N_2O_8S$ + H] 728.1854 found 728.1861; HPLC (III) t_R = 26.47 min (84.6 %), (IV) t_R = 62.94 min (88.1 %).

Compound 21u

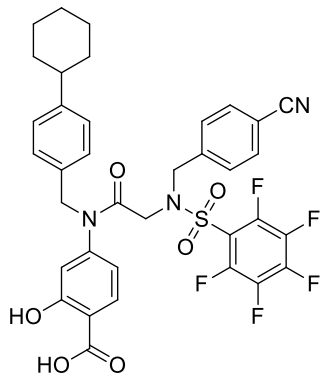


4-(2-(*N*-(3-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_5N_3O_6S$
Molecular Weight: 727.70
Log P: 6.05

Compound **20u** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21u** (22.6 mg, 78 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.68-1.93 (m, 5H, CH_2), 2.40-2.55 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.69 (s, 4H, 2 CH_2), 6.37 (s (br), 1H, CH), 6.47 (s, 1H, CH), 6.96 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H ,CH), 7.44 (t, *J* = 7.2 Hz, 1H, CH), 7.50-7.66 (m, 3H, CH), 7.81 (s (br), 1H, CH), 10.82 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 48.2, 50.9, 53.2, 111.5, 113.2, 116.9, 118.3, 118.7, 127.3, 128.6, 129.2, 130.0, 131.9, 132.3, 132.7, 133.0, 133.1, 136.5, 148.2, 163.1, 165.6, 172.3; HRMS (DART) Calcd for [$C_{36}H_{30}F_5N_3O_6S$ + H] 728.1854 found 728.1861; HPLC (III) t_R = 27.70 min (78.4 %), (IV) t_R = 62.18 min (82.7 %).

Compound 21v

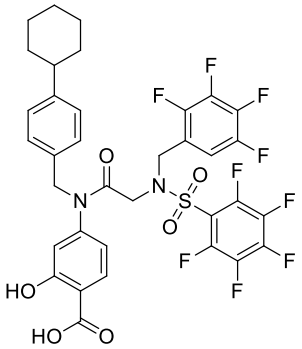


4-(2-(*N*-(4-cyanobenzyl)-2,3,4,5,6-pentafluorophenylsulfonamido)-*N*-(4-cyclohexylbenzyl)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{36}H_{30}F_5N_3O_6S$
Molecular Weight: 727.70
Log P: 6.05

Compound **20v** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21v** (25.8 mg, 89 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.68-1.91 (m, 5H, CH_2), 2.36-2.54 (m, 1H, CH), 3.86 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.33 (s (br), 1H, CH), 6.43 (s, 1H, CH), 6.96 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H ,CH), 7.39 (d, *J* = 7.2 Hz, 2H, CH), 7.60 (d, *J* = 7.2 Hz, 2H, CH), 7.79 (s (br), 1H, CH), (m, 3H, CH), 7.81 (s (br), 1H, CH), 10.86 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 48.2, 51.2, 53.2, 112.5, 112.9, 116.9, 118.4, 118.7, 127.2, 128.6, 129.2, 132.5, 132.7, 132.8, 133.1, 140.3, 148.2, 163.1, 166.1, 172.2; HRMS (DART) Calcd for [$C_{36}H_{30}F_5N_3O_6S$ + H] 728.1854 found 728.1851; HPLC (III) t_R = 27.71 min (70.5 %), (IV) t_R = 62.25 min (76.1 %).

Compound 21w

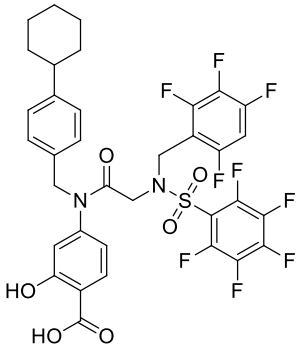


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,4,5-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{27}F_9N_2O_6S$
Molecular Weight: 774.65
Log P: 7.08

Compound **20w** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21w** (18.3 mg, 79 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.69-1.90 (m, 5H, CH_2), 2.39-2.56 (m, 1H, CH), 3.93 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 6.48 (s (br), 1H, CH), 6.59 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.03-7.23 (m, 3H, CH), 7.85 (s (br), 1H, CH), 10.89 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 44.5, 48.8, 53.3, 111.9, 112.1, 117.1, 118.8, 127.2, 128.5, 132.7, 133.1, 148.2, 163.2, 165.5, 172.5; HRMS (DART) Calcd for [$C_{35}H_{27}F_9N_2O_6S$ + H] 775.1524 found 775.1529; HPLC (III) t_R = 29.48 min (90.6 %), (IV) t_R = 65.49 min (91.3 %).

Compound 21x

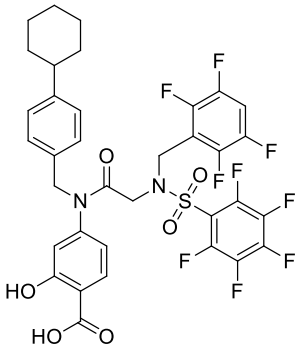


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,4,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{27}F_9N_2O_6S$
Molecular Weight: 774.65
Log P: 7.08

Compound **20x** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21x** (25.4 mg, 82 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.44 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.40-2.58 (m, 1H, CH), 3.93 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.77 (s, 2H, CH_2), 6.47 (s (br, 1H, CH), 6.60 (s, 1H, CH), 6.92-7.15 (m, 5H, CH), 7.84 (d, *J* = 8.0 Hz, 1H, CH), 10.90 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 39.5, 44.4, 48.8, 53.2, 112.0, 112.8, 117.1, 118.9, 127.2, 128.5, 132.7, 133.2, 148.1, 163.2, 165.6, 172.3; HRMS (DART) Calcd for [$C_{35}H_{27}F_9N_2O_6S$ + H] 775.1524 found 775.1536; HPLC (III) t_R = 29.02 min (98.2 %), (IV) t_R = 64.7 min (100 %).

Compound 21y

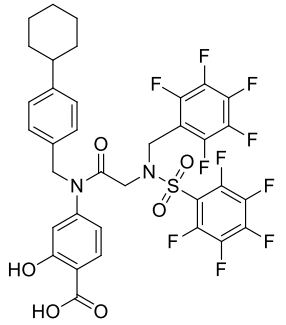


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(2,3,5,6-tetrafluorobenzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{27}F_9N_2O_6S$
Molecular Weight: 774.65
Log P: 7.08

Compound **20y** was globally deprotected according to general procedure B on a 0.04 mmol scale to give compound **21y** (24.6 mg, 79 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.46 (m, 5H, CH_2), 1.68-1.91 (m, 5H, CH_2), 2.38-2.55 (m, 1H, CH), 3.96 (s, 2H, CH_2), 4.72 (s, 2H, CH_2), 4.84 (s, 2H, CH_2), 6.48 (s (br, 1H, CH), 6.60 (s, 1H, CH), 6.89-7.21 (m, 5H, CH), 7.83 (s (br), 1H, CH), 10.89 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 39.8, 44.4, 49.2, 53.2, 113.0, 114.4, 117.1, 118.9, 127.2, 128.5, 132.7, 133.2, 148.1, 163.2, 165.6, 172.4; HRMS (DART) Calcd for [$C_{35}H_{27}F_9N_2O_6S$ + H] 775.1524 found 775.1522; HPLC (III) t_R = 28.74 min (92.2 %), (IV) t_R = 64.29 min (96.3 %).

Compound 21z

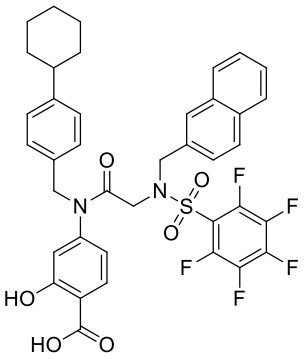


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-((perfluorophenyl)methyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{35}H_{26}F_{10}N_2O_6S$
Molecular Weight: 792.64
Log P: 7.22

Compound **20z** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21z** (19.2 mg, 81 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.91 (m, 5H, CH_2), 2.41-2.55 (m, 1H, CH), 3.98 (s, 2H, CH_2), 4.74 (s, 2H, CH_2), 4.81 (s, 2H, CH_2) 6.51 (d, *J* = 8.0 Hz, 1H, CH), 6.63 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.88 (d, *J* = 8.0 Hz, 1H, CH), 10.68 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 39.6, 44.4, 49.2, 53.3, 109.2, 117.3, 119.0, 127.3, 128.5, 133.0, 147.2, 130.6, 148.2, 163.4, 166.6, 172.1; HRMS (DART) Calcd for [$C_{35}H_{26}F_{10}N_2O_6S$ + H] 793.1430 found 793.1419; HPLC (III) t_R = 28.54 min (90.6 %), (IV) t_R = 66.34 min (99.2 %).

Compound 21aa

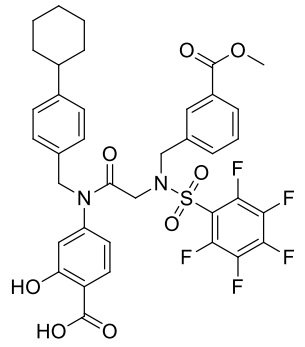


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(naphthalen-2-ylmethyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{39}H_{33}F_5N_2O_6S$
Molecular Weight: 752.75
Log P: 7.66

Compound **20aa** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21aa** (18.7 mg, 83 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.93 (m, 5H, CH_2), 2.40-2.56 (m, 1H, CH), 3.84 (s, 2H, CH_2), 4.67 (s, 2H, CH_2), 4.83 (s, 2H, CH_2) 6.06 (s (br), 1H, CH), 6.35 (s, 1H, CH), 6.97 (d, *J* = 7.6 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.39 (d, *J* = 7.6 Hz, 1H, CH), 7.45-7.57 (m, 3H, CH), 7.64 (s, 1H, CH), 7.72 (d, *J* = 7.2 Hz, 1H, CH), 7.76-7.86 (m, 2H, CH), 10.70 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.3, 27.0, 34.5, 44.4, 47.9, 51.7, 53.1, 112.3, 116.9, 118.8, 126.2, 126.7, 126.7, 127.2, 127.9, 127.9, 128.3, 128.7, 128.9, 129.2, 131.7, 132.3, 133.3, 133.3, 146.9, 148.1, 163.0, 166.1, 172.2; HRMS (DART) Calcd for [$C_{39}H_{33}F_5N_2O_6S$ + H] 753.2058 found 753.2047; HPLC (III) t_R = 29.97 min (98.5 %), (IV) t_R = 67.73 min (98.4 %).

Compound 21ad

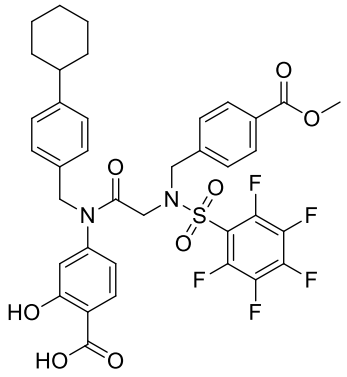


4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(3-(methoxycarbonyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{33}F_5N_2O_8S$
Molecular Weight: 760.72
Log P: 6.37

Compound **20ab** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21ab** (18.4 mg, 80 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.30-1.47 (m, 5H, CH_2), 1.70-1.94 (m, 5H, CH_2), 2.42-2.56 (m, 1H, CH), 3.84 (s, 2H, CH_2), 3.92 (s, 3H, CH_3), 4.70 (s, 4H, 2 CH_2), 6.32 (s (br), 1H, CH), 6.47 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, CH), 7.11 (d, *J* = 7.6 Hz, 2H, CH), 7.41 (t, *J* = 7.6 Hz, 1H, CH), 7.51 (d, *J* = 7.6 Hz, 1H, CH), 7.74 (d, *J* = 8.0 Hz, 1H, CH), 7.90 (s, 1H, CH), 7.99 (d, *J* = 7.6 Hz, 1H, CH), 10.81 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 26.9, 34.5, 44.3, 48.0, 51.1, 52.5, 53.2, 112.5, 116.9, 118.8, 126.8, 127.2, 128.5, 129.3, 129.9, 129.9, 130.2, 132.4, 133.4, 133.8, 135.0, 148.0, 163.0, 165.8, 166.7, 171.9; HRMS (DART) Calcd for [$C_{37}H_{34}F_5N_2O_8S$ + H] 761.1956 found 761.1960; HPLC (III) t_R = 28.47 min (84.1 %), (IV) t_R = 63.50 min (89.0 %).

Compound 21ac



4-(*N*-(4-cyclohexylbenzyl)-2-(2,3,4,5,6-pentafluoro-*N*-(4-(methoxycarbonyl)benzyl)phenylsulfonamido)acetamido)-2-hydroxybenzoic acid
Chemical Formula: $C_{37}H_{33}F_5N_2O_8S$
Molecular Weight: 760.72
Log P: 6.37

Compound **20ac** was globally deprotected according to general procedure B on a 0.03 mmol scale to give compound **21ac** (18.7 mg, 82 %)

δ_H (400 MHz, *d*-$CDCl_3$) 1.31-1.47 (m, 5H, CH_2), 1.70-1.92 (m, 5H, CH_2), 2.42-2.56 (m, 1H, CH), 3.85 (s, 2H, CH_2), 3.92 (s. 3H, CH_3), 4.68 (s, 2H, CH_2), 4.73 (s, 2H, CH_2), 6.29 (s (br), 1H, CH), 6.41 (s, 1H, CH), 6.95 (d, *J* = 7.6 Hz, 2H, CH), 7.12 (d, *J* = 7.6 Hz, 2H, CH), 7.33 (d, *J* = 8.0 Hz, 2H, CH), 7.75 (d, *J* = 8.0 Hz, 1H, CH), 7.98 (d, *J* = 8.0 Hz, 2H, CH), 10.70 (s, 1H, OH); δ_C (100 Hz, *d*-$CDCl_3$) 26.2, 27.0, 34.5, 44.3, 48.0, 51.2, 52.5, 53.2, 112.3, 117.2, 118.9, 127.2, 128.5, 128.7, 129.2, 129.7, 130.3, 130.4, 132.5, 139.7, 148.1, 163.1, 165.8, 166.8, 172.1; HRMS (DART) Calcd for [$C_{37}H_{33}F_5N_2O_8S$ + H] 761.1956 found 761.1945; HPLC (III) t_R = 28.54 min (88.0 %), (IV) t_R = 63.72 min (87.7 %).

References

1. Fletcher, S.; Singh, J.; Zhang, X.; Yue, P.; Page, B. D. G.; Sharmeen, S.; Shahani, V. M.; Zhao, W.; Schimmer, A. D.; Turkson, J.; Gunning, P. T. Disruption of transcriptionally active stat3 dimers with non-phosphorylated, salicylic acid-based small molecules: Potent in vitro and tumor cell activities. *ChemBioChem* **2009**, *10,* 1959-1964.

2. Page, B. D. G.; Fletcher, S.; Yue, P.; Li, Z.; Zhang, X.; Sharmeen, S.; Datti, A.; Wrana, J. L.; Trudel, S.; Schimmer, A. D.; Turkson, J.; Gunning, P. T. Identification of a non-phosphorylated, cell permeable, small molecule ligand for the Stat3 SH2 domain. *Bioorg. Med. Chem. Lett.* **2011**, *21,* 5605-5609.