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Development of kinase inhibitors and activity-based probes

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Author: Liu, N.
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3 Synthesis of FLT3 kinase inhibitors: isoquinolinesulfonamide-based library

3.1 Introduction

Hematopoietic cells express specific receptors, which are activated by a variety of cytokines leading to cell proliferation, differentiation and survival. FMS (Feline McDonough Sarcoma)-like tyrosine kinase 3 (FLT3) ligand is one of the cytokines that regulates the hematopoietic system and the corresponding FLT3 receptor is expressed on both stem cells and progenitors.[1] FLT3 belongs to the receptor tyrosine kinase (RTK) family (subclass III) and is 993 amino acids in length. FLT3 is composed of five immunoglobulin-like extracellular domains, a transmembrane domain, a juxtamembrane domain and two intracellular tyrosine-kinase domains

(TKDs) linked by a kinase-insert domain. Non-stimulated FLT3 receptors are present as monomers in the plasma membrane. After stimulation with FLT3 ligand, membrane-bound FLT3 receptors quickly change conformation and form homodimers. Activated, homodimerized FLT3 receptors trigger the phosphatidylinositol 3-kinase (PI3K) and RAS/RAF pathways, thereby stimulate downstream proteins such as 3-phosphoinositide-dependent protein kinase 1 (PDK1) and protein kinase B (PKB/AKT), which ultimately leads to increased cell proliferation and inhibition of apoptosis.[2]

Despite the many checks and balances that are in place to regulate hematopoiesis, mutations of regulatory genes including FLT3 can disrupt hematopoiesis and promote leukemogenesis. FLT3 mutations occur in several hematopoietic malignancies, and may result in FLT3-ligand independent tyrosine kinase activation of the FLT3 receptor,[3] as first described Nakao *et al.*[4] The most common form of FLT3 mutation comprises internal tandem duplication (ITD) in exons 14 and 15, which occurs in 15-35% of patients suffering from acute myeloid leukemia (AML)[5,6,7] and 5-10% of patients with myelodysplasia (MDS).[8,9] The second most common type of FLT3 mutation concerns missense point mutations in exon 20 of the TKD. TKD mutations occur in patients suffering from AML (5-10%), MDS (2-5%) and acute lymphoblastic leukemia (ALL) (1-3%).[10,11] Thus, the wild-type and mutant FLT3 receptors are appealing drug targets for inhibition. Several small molecule inhibitors of tyrosine kinase such as the indolocarbazole derivatives lestaurtinib and midostaurin, which inhibit both the wild-type and mutant FLT3 next to a small spectrum of other tyrosine kinases, were studied in early phase clinical trials.[12]

At the basis of the work described in this chapter is the discovery of the isoquinolines **2** and **3** (Figure 1) as a new structural class of FLT3 kinase inhibitors. Compounds **2** and **3** are analogues of the known PKA inhibitor H-89 (**1**) and were identified from a focused library of H-89 analogues, which were assessed on their PKB/AKT1 inhibitory properties.

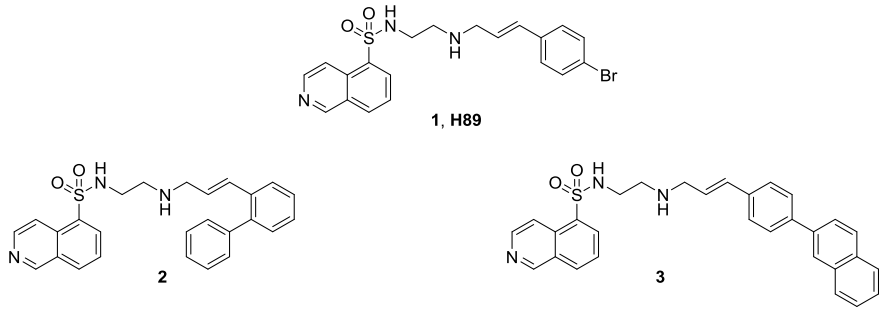


Figure 1. Lead compounds **1** (**H-89**), **2** and **3**.

In this screen, the *in vitro* activity of the compounds against PKB/AKT1 was determined together with the translocation activity of the AKT-regulated forkhead transcription factor, FOXO3a, into the nucleus. The latter is a way to measure the cellular activity of an inhibitor, since nuclear translocation of FOXO3a is correlated to inactivation of the AKT pathway. Apart from the identification of **2** as the most potent PKB/AKT1 inhibitor of the compounds tested (Figure 1), a set of compounds was discovered that showed hardly any PKB/AKT1 inhibition, but a high translocation activity of FOXO3a into the nucleus. In subsequent studies, it was found that these compounds, exemplified by **3**, inhibit FLT3, which is upstream of AKT1 in the same pathway. Therefore, a higher FOXO3a translocation into the nucleus has been observed without inhibition of PKB/AKT1. The most potent inhibitor of this set of compounds proved to be isoquinolinesulfonamide **3** (Figure 1), with an IC_{50} against FLT3 of 1.01 µM. To obtain insight in the specificity of this compound, the activities of compound **2** and **3** towards a panel of 111 human kinases were determined using the Kinome*scan*™ assay, which was performed by the company LeadHunter discovery services.[13] Briefly, the Kinomescan assay is conducted as follows. Purified recombinant kinases (111 in total) tagged with DNA for qPCR detection are incubated with 10 µM of test compound (here: **2** or **3**) for 1 hour. Subsequently the mixture of kinases and test compound is transferred to an immobilized ligand that binds to the panel of kinases. Compounds that bind the kinase active site will prevent kinase binding to the immobilized ligand. As a result, the amount of kinase captured on the solid support will be reduced (Figure 2A and C). Compounds that do not bind the kinase have no effect on the amount of kinase captured on the solid support (Figure 2B). Potential inhibitors are identified by measuring the amount of kinase captured in test versus control samples by quantitative qPCR.

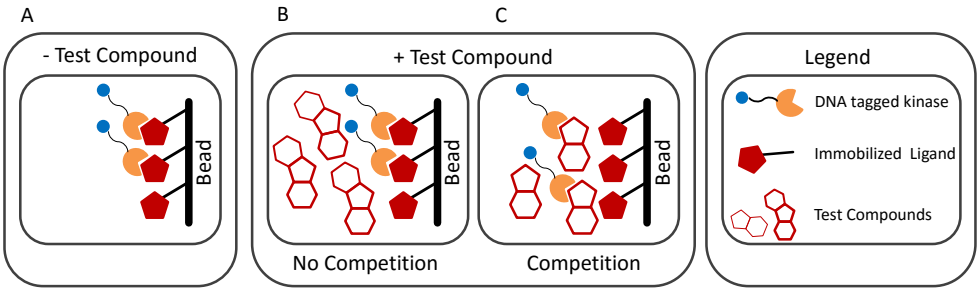


Figure 2. General outline of the Kinome*scan*™ kinase assay applied to identify off targets of compounds **2** and **3**.

Table 1. Kinase activity relative to control sample (%) after inhibition by compounds **2** and **3** (10 μM). [a]

Kinase	2	3	Kinase	2	3	Kinase	2	3
ABL1	87	79	FLT1	78	70	PDPK1	56	67
ACVR1B	*28*	83	FLT3	*28*	**1.6**	PIK3C2B	100	94
ADCK3	*15*	87	GSK3B	100	100	PIK3CA	96	76
AKT1	**1.3**	46	HIPK2	100	75	PIK3CG	100	100
AKT2	*24*	94	IGF1R	75	100	PIK4CB	100	100
AKT3	**4.3**	40	IKK-alpha	100	100	PIM1	84	74
ALK	78	36	IKK-beta	87	97	PIM2	100	72
AMPK-α2	60	60	INSR	95	97	PIM3	85	60
AURKA	100	96	JAK2	91	70	PIP5K1A	*17*	52
AURKB	*28*	77	JAK3	82	75	PKAC-alpha	**1.6**	*19*
AXL	64	54	JNK1	93	73	PLK1	100	100
BMPR2	100	100	JNK2	100	76	PLK3	100	97
BRAF	67	96	JNK3	80	100	PLK4	70	76
BTK	52	100	KIT	66	55	PRKCD	**5**	40
CDK11	**4.3**	64	LKB1	100	100	PRKCE	67	*26*
CDK2	93	78	MAP3K4	*11*	96	PRKCH	**2.8**	*16*
CDK3	97	58	MAPKAPK2	60	59	PRKCI	30	77
CDK7	**5.6**	54	MARK3	*15*	41	PRKCQ	*12*	100
CDK9	100	95	MEK1	60	93	RAF1	38	68
CHEK1	46	87	MEK2	54	88	RET	71	51
CLK2	45	92	MET	89	93	RIOK2	67	90
CSF1R	47	69	MKNK1	59	100	ROCK2	**0.6**	**5**
CSNK1D	**3.4**	**6.6**	MKNK2	*24*	85	RSK2	71	78
CSNK1G2	66	100	MLCK	73	32	SGK3	63	74
CSNK1G3	97	96	MLK1	93	90	SNARK	*10*	39
DCAMKL1	80	100	MST2	51	92	SRC	69	78
DYRK1A	70	75	MTOR	97	67	SRPK3	93	63
DYRK1B	54	74	MUSK	**0.2**	62	TAOK1	*10*	84
EGFR	*29*	91	MYO3A	87	100	TGFBR1	34	48
EPHA2	48	84	p38-alpha	95	86	TIE2	*18*	91
ERBB2	38	100	p38-beta	40	93	TRKA	85	83
ERBB4	87	97	PAK1	59	77	TSSK1B	88	61
ERK1	77	100	PAK2	63	69	TYK2	100	100
ERN1	80	77	PAK4	72	91	ULK2	42	81
FAK	83	75	PCTK1	**1.1**	74	VEGFR2	59	98
FGFR2	33	54	PDGFRA	84	96	YANK3	56	68
FGFR3	*25*	68	PDGFRB	*16*	**5.4**	ZAP70	100	100

The results for binding interactions are reported as relative activity percentage, where lower numbers indicate stronger hits in the matrix (Table 1). Compound **3** proved 18 times more activity towards FLT3 than compound **2** and near 30 times more specific for FLT3 over PKB/AKT1. Since compound **3** also has affinity for other kinases including ROCK2, PDGFRB and CSNK1D, more active and specific FLT3 inhibitors would be desirable. With the purpose to discover such entities, a set of isoquinolinesulfonamide compounds were designed based on compound **3**.

This chapter describes the synthesis of a focused FLT3 inhibitor library, the core structures of which are given in Figure 3. The naphthalene moiety in **3** is either modified or substituted for by thiophene or pyrrole moieties. Since the FLT3 inhibitor library consists of compound **3** and H-89 (**1**) analogues, more potent PKB/AKT1 inhibitors might arise from the focused library as well.

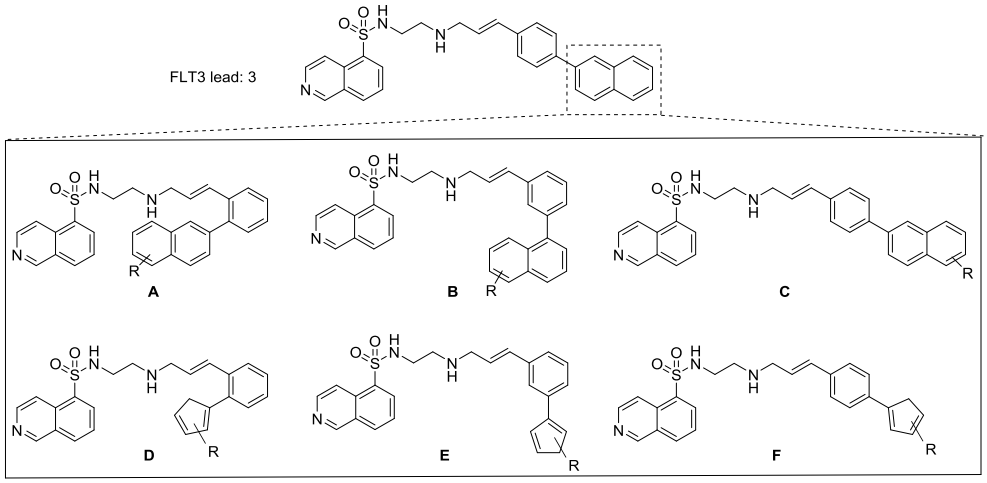
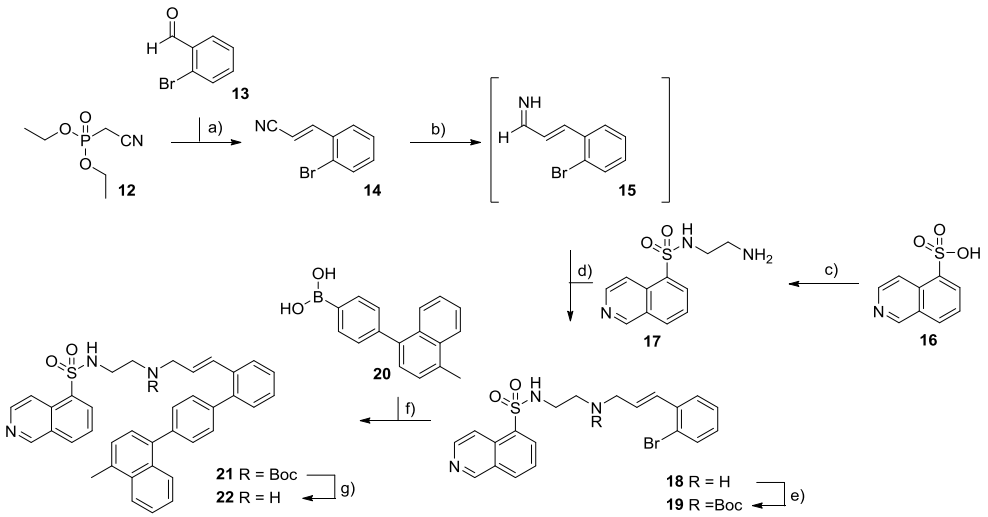


Figure 3. Target structures of the isoquinolinesulfonamide library described here and based on the scaffold of lead compound **3**. The naphthalene in **3** was modified (**A** – **C**) or substituted for thiophene or pyrrole containing moieties (**D** – **F**).

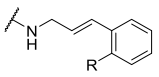
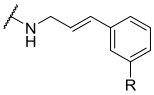
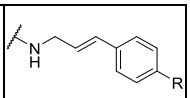
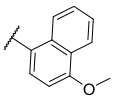
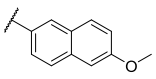
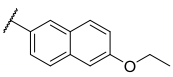
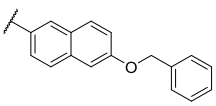
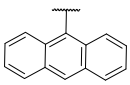
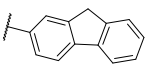
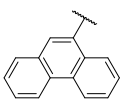
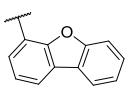
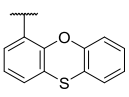
3.2 Results and discussion

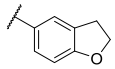
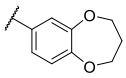
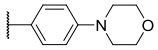
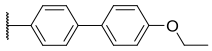
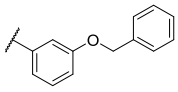
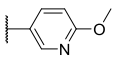
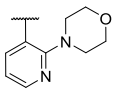
The focused isoquinoline library is synthesized in a similar way as compound **22**, the synthesis of which is depicted in scheme 1. The synthesis of compound **22** commenced with a Horner-Wadsworth-Emmons (HWE) reaction between commercially available diethyl cyanomethylphosphonate **12** and *o*-bromobenzaldehyde **13** to obtain the corresponding E-isomer cinnamonitrile **14** in 77% yield after column purification and recrystallization. Subsequently, E-isomer **14** was used in the four-step-one-pot trans-imination procedure according to Brussee *et al*.[14] This sequence started with reduction of nitrile **14** using DiBAlH to form imine **15**. The latter was reacted with amine **17**, which was obtained by conversion of isoquinoline sulfonic amine **16** into the corresponding isoquinoline sulfonic chloride, which was in turn reacted with ethylenediamine. Next, the resulting secondary imine was reduced by $NaBH_4$ and the crude isoquinolinesulfonamide **18** was protected with a Boc-group to yield pure E-isoquinolinesulfonamide **19**. A Suzuki reaction ($Pd(PPh_3)_4$, K_2CO_3) was used to couple aryl bromide **19** with aryl boronic acid **20** to form the Boc-protected isoquinolinesulfonamide **21**. Removal of the Boc protective group, and final HPLC purification, furnished isoquinolinesulfonamide **22** in 13% yield. The yields of the complete library are given in Table 2 and in the experimental section.

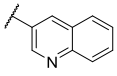
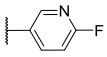
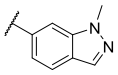
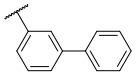
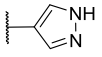
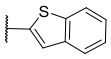
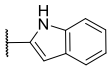
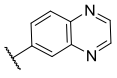
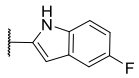
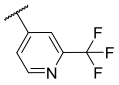
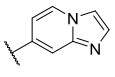


Scheme 1. Exemplified synthesis of bulky arylated isoquinolinesulfonamides. Reagents and conditions: a) NaH, **13**, 0 °C, THF, 77%; b) DiBAlH, -78 °C, Et_2O/DCM 1:1 v/v; c) i) $SOCl_2$, reflux, DMF; ii) ethylenediamine, DCM, 0 °C, 69%; d) i) MeOH, -100 °C; ii) **17**, MeOH, RT; iv) $NaBH_4$, -10 °C – RT; e) Boc_2O, TEA, DCM, 0 °C. 48%; f) **20**, K_2CO_3, $Pd(PPh_3)_4$, DMF, 90 °C; g) TFA, DCM, H_2O, 13%.

Table 2. Yields (%) of the Suzuki cross coupling reaction.

						
R =		**yield** (%)		**yield** (%)		**yield** (%)
	**22**	12.7	**56**	10.1	**90**	6.4
	**23**	14.3	**57**	11.6	**91**	9.6
	**24**	18.2	**58**	13.6	**92**	6.4
	**25**	16.1	**59**	12.9	**93**	6.5
	**26**	5.3	**60**	6.6	**94**	1.5
	**27**	5.5	**61**	9.3	**95**	2.6
	**28**	15.1	**62**	7.2	**96**	8.0
	**29**	17.9	**63**	17.0	**97**	9.9
	**30**	26.8	**64**	13.8	**98**	15.3
	**31**	24.6	**65**	15.3	**99**	13.7

	**32**	24.3	**66**	12.3	**100**	13.3
	**33**	28.5	**67**	17.1	**101**	14.6
	**34**	16.3	**68**	17.1	**102**	16.5
	**35**	15.6	**69**	10.2	**103**	7.3
	**36**	11.0	**70**	8.9	**104**	7.2
	**37**	18.2	**71**	15.6	**105**	7.2
	**38**	27.4	**72**	19.1	**106**	16.2
	**39**	22.1	**73**	16.0	**107**	15.1
	**40**	24.9	**74**	16.5	**108**	13.8
	**41**	24.8	**75**	14.9	**109**	21.1
	**42**	23.4	**76**	13.0	**110**	18.5
	**43**	12.9	**77**	16.5	**111**	12.6

	**44**	24.4	**78**	16.9	**112**	21.2
	**45**	38.9	**79**	12.8	**113**	20.9
	**46**	35.5	**80**	31.9	**114**	71.1
	**47**	50.2	**81**	34.2	**115**	43.9
	**48**	32.1	**82**	23.4	**116**	34.4
	**49**	34.6	**83**	30.2	**117**	6.6
	**50**	26.1	**84**	27.6	**118**	40.7
	**51**	12.0	**85**	13.9	**119**	26.6
	**52**	78.4	**86**	40.6	**120**	67.8
	**53**	15.8	**87**	10.4	**121**	22.3
	**54**	26.5	**88**	18.4	**122**	26.0
	**55**	62.4	**89**	20.6	**123**	22.7

3.3 Conclusion

In this chapter the synthesis of 102 new analogues of lead compound **3** is described. The library was assembled in a parallel synthesis fashion using 34 heterocyclic aromatic boronic acids and three isoquinolinesulfonamide-modified aryl bromides using Suzuki cross-coupling methodology. The biological evaluation of the 102 compounds as inhibitors of the four kinases, PKA, AKT1, AKT2 and FLT3 is described in Chapter 4.

Experimental

General: Tetrahydrofuran (THF) was distilled over $LiAlH_4$ before use. Acetonitrile (ACN), dichloromethane (DCM), N,N-dimethylformamide (DMF), methanol (MeOH) and trifluoroacetic acid (TFA) were of peptide synthesis grade, purchased at Biosolve, and used as received. All general chemicals (Fluka, Acros, Merck, Aldrich, Sigma) were used as received. Traces of water were removed from reagents used in reactions that require anhydrous conditions by coevaporation with toluene. Solvents that were used in reactions were stored over 4Å molecular sieves, except methanol and acetonitrile, which were stored over 3Å molecular sieves. Molecular sieves were flame dried before use. Unless noted otherwise all reactions were performed under an argon atmosphere. Column chromatography was performed on Silicycle Silia-P Flash Silica Gel, with a particle size of 40 – 63 µm. The eluents toluene and ethyl acetate were distilled prior to use. TLC analysis was conducted on Merck aluminium sheets (Silica gel 60 F254). Compounds were visualized by UV absorption (254 nm), by spraying with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ (10 g/L) in 10% sulphuric acid, a solution of $KMnO_4$ (20 g/L) and K_2CO_3 (10 g/L) in water, or ninhydrin (0.75 g/L) and acetic acid (12.5 mL/L) in ethanol, where appropriate, followed by charring at ca. 150°C. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker DMX-400 (400 MHz) or a Bruker DMX-600 (600 MHz) spectrometer. Chemical shifts are given in ppm (δ) relative to tetramethylsilane (^{1}H-NMR) or $CDCl_3$ (^{13}C-NMR) as internal standard. Mass spectra were recorded on a PE/Sciex API 165 instrument equipped with an Electrospray Interface (ESI) (Perkin-Elmer). High-resolution MS (HRMS) spectra were recorded with a Finnigan LTQ-FT (Thermo Electron). IR spectra were recorded on a Shimadzu FTIR-8300 and absorptions are given in cm^{-1}. Optical rotations $[\alpha]_D^{23}$ were recorded on a Propol automatic polarimeter at room temperature. LC-MS analysis was performed on a Jasco HPLC system with a Phenomenex Gemini 3 µm C18 50 x 4.6 mm column (detection simultaneously at 214 and 254 nm), coupled to a PE Sciex API 165 mass spectrometer with ESI. HPLC gradients were 10 → 90%, 0 → 50% or 10 → 50% ACN in 0.1% TFA/H_2O. Chiral HPLC analysis was performed on a Spectroflow 757 system (ABI Analytical Kratos Division, detection at 254 nm) equipped with a Chiralcel OD column (150 x 4.6 mm). The compounds were purified on a Gilson HPLC system coupled to a Phenomenex Gemini 5 µm 250 x 10 mm column and a GX281 fraction collector. The used gradients were either 0 → 30% or 10 → 40% ACN in 0.1% TFA/water, depending on the lipophilicity of the product. Appropriate fractions were pooled, and concentrated in a Christ rotary vacuum concentrator overnight at room temperature at 0.1 mbar.

(E)-3-(4-bromophenyl)acrylonitrile: ortho-14

Diethyl cyanomethylphosphonate (35.43 g, 200 mmol) was slowly added to an ice-cold solution of NaH (1.1 eq., 8.80 g, 220 mmol, 60% mineral oil) in DMF (900 mL) and the mixture was allowed to stir for 30 min. Hereafter, a solution of 2-bromobenzaldehyde **13** (1.1 eq., 40.70 g, 220 mmol) in DMF (100 mL) was dropwise added. The reaction was allowed to warm to RT and stirred overnight before being quenched with freshly prepared sat. aq. Na_2HSO_3 (800 mL). The mixture was diluted with H_2O (800 mL) and Et_2O (800 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 600 mL) and the combined organic phases were washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was purified by crystallization from EtOAc/PE (9/1, v/v) to provide ortho-**14** as a white solid (yield: 32.0 g, 154.0 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 16.4 Hz, 1H), 7.58 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 7.50 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H), 7.34 (t, J = 6.8 Hz, 1H), 7.26 (td, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H), 5.84 (d, J = 16.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.45, 133.19, 132.95, 131.87, 127.66, 126.70, 124.38, 117.35, 98.73.

(E)-3-(3-bromophenyl)acrylonitrile: meta-14

The same procedure as described for ortho-**14** was applied for the preparation of meta-**14**. The resulting residue was purified by crystallization from EtOAc/PE (9/1, v/v) to provide ortho-**14** as a white solid (yield: 33.8 g, 162.6 mmol, 81.3%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 2H), 7.37 (d, J = 8.0 Hz, 1H), 7.32 – 7.26 (m, 2H), 5.88 (d, J = 16.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.61, 135.22, 133.74, 130.43, 129.85, 125.85, 122.97, 117.45, 97.82.

(E)-3-(2-bromophenyl)acrylonitrile: para-14

The same procedure as described for ortho-**14** was applied for the preparation of para-**14**. The title compound was afforded by crystallization from EtOAc/PE (9/1, v/v) as a white solid (yield: 25.4 g, 122.0 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.8 Hz, 2H), 7.33 – 7.29 (m, 3H), 5.89 (d, J = 16.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.89, 132.12, 132.03, 128.52, 125.26, 117.67, 96.84.

***N*-(2-aminoethyl)isoquinoline-5-sulfonamide 17**

Isoquinoline-5-sulfonic acid **16** (20.92 g, 100 mmol) was treated with thionylchloride (13 eq., 91.5 mL, 1300 mmol) and a catalytic amount of DMF for 2 h at reflux. The reaction mixture was concentrated and the residue was thoroughly washed with DCM before being resuspended in H_2O (300 mL) at 0 °C. $NaHCO_3$ (1 eq., 8.42 g, 100.2 mmol) was added portion-wise. Next, the mixture was extracted with DCM (3x 500 mL) and dried over $MgSO_4$. The filtrate was dropwise added to a cooled solution of ethylenediamine (5 eq., 33.4 mL, 500 mL) in DCM (250 mL) and the reaction mixture was allowed to warm to RT and stirred for 1 h. The mixture was then evaporated partially before being washed with brine (50 mL). The aqueous layer was extracted with DCM (10 x 50 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated. The title compound was obtained as a thick yellowish oil (yield: 17.3 g, 69 mmol, 69%) and was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 9.36 (1H, s, CH_{ar}), 8.67 (1H, d, J = 8.4 Hz, CH_{ar}), 8.47 – 8.43 (2H, m, 2 x CH_{ar}), 8.21 (1H, d, J = 11.2 Hz, CH_{ar}), 7.71, (1H, t, J = 10.0 Hz, CH_{ar}), 3.45 (3H, bs, NH_2

and NH), 3.00 (2H, t, *J* = 5.2 Hz, CH_2), 2.76 (2H, t, *J* = 6.0 Hz, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.26, 145.06, 133.46, 133.19, 131.23, 129.01, 125.91, 117.22, 45.12, 40.76.

***Tert*-butyl (E)-(3-(4-bromophenyl)allyl)(2-(isoquinoline-5-sulfonamido)ethyl)carbamate: ortho-19**

A solution of nitrile ortho-**4** (11.18 g, 53.72 mmol) in anhydrous Et_2O (250 mL) was cooled to -78 °C before dropwise addition of DiBAL-H (2 eq., 100 mL, 100 mmol, 1M solution in hexanes) and the reaction mixture was allowed to warm to 0 °C and was stirred for 2 h, after which TLC analysis showed complete consumption of starting material. Next, the mixture was cooled to -100 °C followed by rapid addition of MeOH (100 mL). After 5 min a solution of isoquinoline amine **17** (2 eq., 25.18 g, 100 mmol) in MeOH (100 mL) was dropwise added and the reaction mixture was allowed to stir at RT overnight. Hereafter, the reaction was cooled to -10 °C and $NaBH_4$ (2 eq., 3.78 g, 100 mmol) was added and the mixture was allowed to stir at RT for 4 h. The reaction mixture was diluted with 0.5M aq. NaOH (250 mL) and the layers were separated. The aqueous layer was extracted with DCM (3 x 250 mL) and the combined organic phases were washed with H_2O (3 x 250 mL) and brine before being dried, filtered and evaporated. The crude product was subjected to the next step without further purification.

To the ice-cooled solution of crude product in THF (250 mL) Boc_2O (2.5 eq., 27.28 g, 125 mmol) was added and the reaction was allowed to warm to RT and was stirred overnight. The reaction mixture was diluted with H_2O (250 mL) and EtOAc (250 mL) were added before being separated. The aqueous phase was extracted with EtOAc (3x 250 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2x 250 mL) and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The title compound was obtained after purification by silica gel column chromatography (0.5 – 3% MeOH/DCM) as a white solid (yield: 14.0 g, 25.6 mmol, 47.6%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.59 (d, *J* = 6.0 Hz, 1H), 8.44 (d, *J* = 6.0 Hz, 1H), 8.40 (d, *J* = 7.2 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.23 (br s, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 14.8 Hz, 1H), 5.97 – 5.90 (m, 1H), 3.89 (d, *J* = 6.0 Hz, 2H), 3.37 (s, 2H), 3.17 – 3.13 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.98, 144.68, 136.09, 134.32, 133.22, 132.87, 132.64, 131.01, 130.58, 128.84, 128.81, 127.88, 127.37, 126.96, 125.71, 123.23, 117.21, 80.49, 50.17, 46.54, 42.42, 28.16.

***Tert*-butyl (E)-(3-(3-bromophenyl)allyl)(2-(isoquinoline-5-sulfonamido)ethyl)carbamate: meta-19**

An identical method was used as for the synthesis of ortho-**19** except that compound meta-**4** (12.48 g, 60 mmol) was used as starting material and the amounts of the other materials were adjusted accordingly. The title compound was obtained after purification by silica gel column chromatography (25 – 50% EtOAc/PE) as a white solid (yield: 13.4 g, 24.6 mmol, 41.0%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.57 (d, *J* = 6.0 Hz, 1H), 8.42 (d, *J* = 6.0 Hz, 1H), 8.36 (d, *J* = 7.2 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.42 (s, 1H), 7.33 – 7.31 (m, 2H), 7.21 – 7.17 (m, 2H), 6.29 (d, *J* = 16.4 Hz, 1H), 6.04 – 6.00 (m, 1H), 3.87 (d, *J* = 5.2 Hz, 2H), 3.33 (s, 2H), 3.10 (s, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.87, 144.53, 138.35, 134.25, 133.21, 132.78, 130.94, 130.28, 129.90, 128.89, 128.75, 126.46, 125.67, 124.86, 122.46, 117.18, 80.33, 50.09, 46.39, 42.16, 28.09.

***Tert*-butyl (E)-(3-(2-bromophenyl)allyl)(2-(isoquinoline-5-sulfonamido)ethyl)carbamate: para-19**

An identical method was used as for the synthesis of ortho-**19** except that compound para-**4** (10.40 g, 50 mmol) was used as starting material and the amounts of the other materials were adjusted accordingly. The title

compound was obtained after purification by silica gel column chromatography (0.1 – 2% MeOH/DCM) as a white solid (yield: 14.9 g, 27.4 mmol, 54.7%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.59 (d, *J* = 6.4 Hz, 1H), 8.44 (d, *J* = 6.0 Hz, 1H), 8.36 (d, *J* = 7.2 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.38 (s, 2H), 7.15 (d, *J* = 7.6 Hz, 2H), 6.77 (br s, 1H), 6.30 (d, *J* = 16.0 Hz, 1H), 6.06 – 5.99 (m, 1H), 3.87 (d, *J* = 5.2 Hz, 2H), 3.35 (s, 2H), 3.12 (s, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.93, 144.54, 135.13, 134.33, 133.23, 132.82, 131.43, 131.00, 128.80, 127.70, 125.72, 121.23, 117.25, 80.38, 50.16, 46.45, 42.11, 29.41, 28.12.

General procedure for the Suzuki coupling:

Stock solutions of ortho-**19** (1M in DCM), K_2CO_3 (2M in H_2O) and $Pd(PPh_3)_4$ (0.017M in DCM) were thoroughly degassed in a sonication bath for 15 minutes. K_2CO_3 (2.5 eq., 0.14 g, 1.0 mmol, 0.5 mL stock), ortho-**19** (0.22 g, 0.4 mmol, 0.4 mL stock) and $Pd(PPh_3)_4$ (0.05 eq., 0.02 g, 0.02 mmol, 1.2 mL stock) were added to arylbromide **20** (1.5 eq., 0.11 g, 0.6 mmol) and the resulting mixture was stirred at 90 °C overnight. The mixture was filtered over a short plug of silica and eluted with DCM/MeOH (4x column volume, 1:1, v/v). The eluent was evaporated and the residue was subjected to the next step without further purification.

The residue was dissolved in DCM (2.5 mL) and TFA (2.5 ML) and the reaction mixture was stirred for 1 hr. before being evaporated and coevaporated with toluene thrice. The resulting residue was purified by RP-HPLC gradient.

(E)-*N*-(2-((3-(2-(4-methylnaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 22

Prepared according to the general procedure. Yield: 25.8 mg, 50.8 µmol, 12.7%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.42 (s, 1H), 8.64 (d, *J* = 6.0 Hz, 1H), 8.51 (d, *J* = 6.4 Hz, 1H), 8.44 (dd, J_1 = 8.4 Hz, J_2 = 12.0 Hz, 2H), 8.00 (d, *J* = 16.0 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.40 – 7.34 (m, 3H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 6.39 (d, *J* = 15.6 Hz, 1H), 6.17 – 6.09 (m, 1H), 3.56 – 3.43 (m, 2H), 2.94 – 2.86 (m, 2H), 2.68 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.27, 144.73, 141.51, 138.86, 137.85, 136.04, 135.54, 135.44, 135.23, 135.15, 133.96, 133.60, 132.67, 132.69, 130.71, 129.76, 129.19, 128.17, 127.85, 127.66, 127.16, 126.94, 126.89, 126.74, 125.48, 119.76, 119.10, 50.08, 46.96, 39.69, 19.52. HRMS: calculated for $C_{31}H_{29}N_3O_2S$ $[M+H]^+$: 508.20532; found: 508.20508.

(E)-*N*-(2-((3-(2-(4-methoxynaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 23

Prepared according to the general procedure. Yield: 30.0 mg, 57.2 µmol, 14.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.47 (s, 1H), 8.64 (d, *J* = 6.0 Hz, 1H), 8.54 (d, *J* = 6.0 Hz, 1H), 8.45 (dd, J_1 = 8.4 Hz, J_2 = 16.4 Hz, 2H), 8.20 (d, *J* = 9.2 Hz, 1H), 7.86 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.39 – 7.32 (m, 2H), 7.29 – 7.22 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.16 – 6.08 (m, 1H), 4.02 (s, 3H), 3.57 – 3.44 (m, 2H), 2.88 – 2.77 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.59, 154.02, 144.18, 141.37, 139.07, 136.31, 135.53, 135.38, 135.29, 134.40, 132.83, 132.56, 131.59, 129.77, 129.08, 128.70, 128.02, 127.70, 126.85, 126.15, 123.23, 119.61, 104.49, 56.10, 50.07, 46.88, 39.66. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.20000.

(E)-*N*-(2-((3-(2-(6-methoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 24

Prepared according to the general procedure. Yield: 38.1 mg, 72.8 µmol, 18.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.39 (s, 1H), 8.60 – 8.55 (m, 2H), 8.38 (dd, J_1 = 7.2 Hz, J_2 = 23.6 Hz, 2H), 7.78 (t, *J* = 8.0 Hz, 2H), 7.73 – 7.71 (m, 1H),

7.68 – 7.66 (m, 1H), 7.63 (s, 1H), 7.41 – 7.33 (m, 4H), 7.22 (s, 1H), 7.09 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.79 (d, J = 16.0 Hz, 1H), 6.22 – 6.15 (m, 1H), 3.89 (s, 3H), 3.68 (d, J = 7.2 Hz, 2H), 3.08 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 159.43, 153.78, 143.85, 142.95, 139.24, 136.94, 135.44, 135.18, 134.88, 132.83, 131.54, 130.53, 130.03, 129.32, 128.70, 128.00, 127.87, 127.51, 120.27, 119.97, 119.47, 106.63, 55.80, 50.41, 47.33, 39.93. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.19987.

(E)-*N*-(2-((3-(2-(6-ethoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 25

Prepared according to the general procedure. Yield: 34.6 mg, 64.4 µmol, 16.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.33 (s, 1H), 8.58 (s, 1H), 8.50 (d, J = 6.0 Hz, 1H), 8.38 (d, J = 7.2 Hz, 1H), 8.32 – 8.30 (m, 1H), 7.77 – 7.67 (m, 4H), 7.62 (s, 1H), 7.38 – 7.28 (m, 4H), 7.19 (s, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 15.6 Hz, 1H), 6.22 – 6.14 (m, 1H), 4.11 (q, J = 6.8 Hz, 2H), 3.68 (d, J = 7.2 Hz, 2H), 3.08 (s, 4H), 1.43 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.66, 154.16, 144.70, 142.95, 139.23, 136.84, 135.28, 135.20, 135.00, 134.86, 132.55, 131.54, 130.51, 129.97, 129.78, 129.28, 128.69, 127.83, 127.72, 127.51, 120.55, 119.94, 119.08, 107.36, 64.55, 50.40, 47.33, 39.91, 15.12. HRMS: calculated for $C_{32}H_{31}N_3O_3S$ $[M+H]^+$: 538.21589; found: 538.21569.

(E)-*N*-(2-((3-(2-(6-(benzyloxy)naphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 26

Prepared according to the general procedure. Yield: 12.7 mg, 21.2 µmol, 5.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.64 (s, 2H), 8.45 (t, J = 8.0 Hz, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.69 – 7.64 (m, 3H), 7.39 – 7.35 (m, 3H), 7.29 (d, J = 8.8 Hz, 1H), 7.22 – 7.19 (m, 3H), 7.14 (t, J = 7.2 Hz, 2H), 7.04 (t, J = 6.8 Hz, 1H), 6.80 (d, J = 15.6 Hz, 1H), 6.21 – 6.13 (m, 1H), 4.41 (s, 2H), 3.66 (d, J = 7.2 Hz, 2H), 3.05 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.30, 153.37, 143.04, 142.81, 142.75, 139.45, 135.91, 135.80, 135.71, 135.55, 134.87, 134.21, 133.21, 131.63, 130.13, 130.06, 129.80, 129.39, 129.17, 129.05, 128.62, 128.41, 127.43, 126.57, 124.48, 119.77, 119.66, 119.53, 50.36, 47.32, 39.92, 31.42. HRMS: calculated for $C_{37}H_{33}N_3O_3S$ $[M+H]^+$: 600.23154; found: 600.23150.

(E)-*N*-(2-((3-(2-(anthracen-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 27

Prepared according to the general procedure. Yield: 12.0 mg, 22.0 µmol, 5.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.67 (s, 1H), 8.60 – 8.58 (m, 1H), 8.53 (d, J = 8.0 Hz, 1H), 8.49 (s, 1H), 8.42 (d, J = 7.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.93 – 7.89 (m, 2H), 7.60 – 7.55 (m, 2H), 7.43 – 7.27 (m, 7H), 3.35 – 3.34 (m, 2H), 3.67 (dd, J_1 = 5.2 Hz, J_2 = 18.4 Hz, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.33, 142.67, 139.21, 138.39, 137.03, 136.01, 135.80, 135.67, 135.49, 133.28, 132.99, 132.81, 131.60, 130.07, 129.71, 128.52, 128.17, 127.24, 127.11, 127.02, 126.39, 120.36, 49.75, 46.62, 39.47. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20506.

(E)-*N*-(2-((3-(2-(9H-fluoren-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 28

Prepared according to the general procedure. Yield: 32.1 mg, 60.4 µmol, 15.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.41 (s, 1H), 8.56 (s, 2H), 8.42 (d, J = 7.2 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.68 – 7.66 (m, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.43 (s, 1H), 7.38 – 7.33 (m, 4H), 7.27 (t, J = 7.2 Hz, 2H), 6.82 (d, J = 15.6 Hz, 1H), 6.22 – 6.15 (m, 1H), 3.87 (s, 2H), 3.71 (d, J = 7.2 Hz, 2H), 3.16 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.46, 144.71, 143.18, 143.14, 142.34, 142.16, 140.33, 139.24, 135.63, 135.54, 135.44, 134.78, 133.01, 131.39, 130.49, 129.77,

129.67, 128.70, 128.20, 128.02, 127.92, 127.49, 127.37, 126.09, 120.80, 120.57, 119.88, 119.76, 50.40, 47.37, 39.91, 37.65. HRMS: calculated for $C_{33}H_{29}N_3O_2S$ $[M+H]^+$: 532.20532; found: 532.20521.

(E)-*N*-(2-((3-(2-(phenanthren-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 29

Prepared according to the general procedure. Yield: 38.9 mg, 71.6 μmol, 17.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.44 (s, 1H), 8.68 (t, *J* = 12.4 Hz, 2H), 8.60 (d, *J* = 5.6 Hz, 1H), 8.51 (d, *J* = 6.0 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.35 (d, *J* = 7.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.78 (m, 2H), 7.62 – 7.40 (m, 7H), 7.35 – 7.30 (m, 2H), 6.42 (d, *J* = 16 Hz, 1H), 6.18 – 6.11 (m, 1H), 3.49 – 3.37 (m, 2H), 2.81 – 2.69 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.68, 143.60, 141.06, 138.59, 138.07, 136.12, 135.52, 135.26, 132.88, 132.69, 132.05, 131.66, 131.32, 130.53, 129.86, 129.72, 129.41, 129.07, 128.14, 128.11, 128.08, 127.94, 127.85, 126.86, 124.08, 123.59, 120.14, 119.54, 49.88, 46.76, 39.52. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20519.

(E)-*N*-(2-((3-(2-(dibenzo[b,d]furan-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 30

Prepared according to the general procedure. Yield: 57.2 mg, 107.2 μmol, 26.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.41 (s, 1H), 8.61 – 8.59 (m, 1H), 8.52 (d, *J* = 6.4 Hz, 1H), 8.39 – 8.37 (m, 2H), 7.97 (dd, J_1 = 7.6 Hz, J_2 = 18.4 Hz, 2H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 9.2 Hz, 1H), 7.47 – 7.38 (m, 5H), 7.34 – 7.30 (m, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.25 – 6.17 (m, 1H), 3.58 (d, *J* = 7.2 Hz, 2H), 2.88 (dd, J_1 = 4.4 Hz, J_2 = 11.2 Hz, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.34, 154.76, 153.71, 143.72, 138.65, 137.25, 135.60, 135.45, 135.24, 132.82, 131.99, 130.50, 129.86, 129.76, 129.53, 128.54, 128.06, 127.16, 126.05, 125.52, 125.28, 124.24, 124.12, 121.93, 121.36, 120.23, 119.48, 112.49, 50.14, 46.91, 39.72. HRMS: calculated for $C_{32}H_{27}N_3O_3S$ $[M+H]^+$: 534.18459; found: 534.18422.

(E)-*N*-(2-((3-(2-(phenoxathiin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 31

Prepared according to the general procedure. Yield: 55.7 mg, 98.4 μmol, 24.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.64 (s, 1H), 8.76 – 8.71 (m, 2H), 8.58 – 8.55 (m, 2H), 7.96 (t, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.20 – 7.05 (m, 5H), 7.01 – 6.97 (m, 1H), 6.65 (d, *J* = 15.6 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.25 – 6.18 (m, 1H), 3.63 – 3.57 (m, 2H), 3.01 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.36, 152.56, 150.62, 140.93, 138.91, 138.05, 136.82, 136.11, 135.82, 135.48, 133.85, 131.78, 131.57, 131.12, 129.72, 129.39, 129.09, 129.00, 127.81, 127.74, 126.70, 126.10, 125.72, 122.54, 121.90, 120.87, 120.17, 118.94, 50.26, 47.11, 39.90. HRMS: calculated for $C_{32}H_{27}N_3O_3S_2$ $[M+H]^+$: 566.15666; found: 566.15650.

(E)-*N*-(2-((3-(2-(2,3-dihydrobenzofuran-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 32

Prepared according to the general procedure. Yield: 47.2 mg, 97.2 μmol, 24.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.66 (s, 1H), 8.83 (d, *J* = 6.4 Hz, 1H), 8.69 (d, *J* = 6.0 Hz, 1H), 8.58 (dd, J_1 = 7.2 Hz, J_2 = 27.2 Hz, 2H), 7.95 (t, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.4, 1H), 7.35 – 7.29 (m, 2H), 7.24 – 7.22 (m, 1H), 7.10 (s, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 15.6 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.21 – 6.13 (m, 1H), 4.54 (t, *J* = 8.8 Hz, 2H), 3.74 (d, *J* = 7.2 Hz, 2H), 3.22 – 3.14 (m, 6H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.92, 151.89, 143.01, 139.61, 139.31, 137.33, 136.26, 136.03, 134.69, 134.17, 133.98, 131.39, 130.60, 130.34, 129.68, 129.43, 128.73, 128.29, 127.37, 127.32, 121.44, 119.55,

109.70, 72.45, 50.52, 45.59, 40.01, 30.47. HRMS: calculated for $C_{28}H_{27}N_3O_3S$ $[M+H]^+$: 486.18459; found: 486.18411.

(E)-*N*-(2-((3-(2-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 33

Prepared according to the general procedure. Yield: 58.8 mg, 114.0 μmol, 28.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.61 (s, 1H), 8.79 (d, *J* = 6.4 Hz, 1H), 8.68 (d, *J* = 6.0 Hz, 1H), 8.56 (dd, J_1 = 7.2 Hz, J_2 = 33.2 Hz, 2H), 7.92 (t, *J* = 7.6 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.32 (t, *J* = 4.4 Hz, 2H), 7.23 – 7.21 (m, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.83 (s, 1H), 6.81 – 6.75 (m, 2H), 6.21 – 6.13 (m, 1H), 4.16 – 4.12 (m, 4H), 3.75 (d, *J* = 7.2 Hz, 2H), 3.16 (dd, J_1 = 4.4 Hz, J_2 = 12.0 Hz, 4H), 2.15 – 2.10 (m, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.25, 152.14, 152.10, 141.85, 140.21, 139.15, 137.07, 137.03, 136.13, 135.90, 134.66, 133.94, 131.14, 130.34, 129.73, 129.22, 128.68, 127.50, 125.85, 123.94, 122.59, 121.14, 119.96, 71.98, 71.91, 50.42, 47.33, 40.01, 33.14. HRMS: calculated for $C_{29}H_{29}N_3O_4S$ $[M+H]^+$: 516.19515; found: 516.19480.

(E)-*N*-(2-((3-(4'-morpholino-[1,1'-biphenyl]-2-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 34

Prepared according to the general procedure. Yield: 34.5 mg, 65.2 μmol, 16.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.66 (s, 1H), 8.83 (d, *J* = 6.4 Hz, 1H), 8.70 (d, *J* = 5.6 Hz, 1H), 8.59 (dd, J_1 = 7.2 Hz, J_2 = 26.8 Hz, 2H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.29 – 7.28 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.23 – 6.15 (m, 1H), 3.87 (t, *J* = 4.4 Hz, 4H), 3.75 (d, *J* = 7.2 Hz, 2H), 3.26 (t, *J* = 4.4 Hz, 4H), 3.18 – 3.15 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.06, 150.36, 142.36, 139.89, 139.34, 137.24, 136.24, 136.04, 134.85, 134.71, 134.12, 131.78, 131.27, 130.40, 129.80, 129.37, 128.50, 127.57, 121.34, 119.83, 117.45, 67.48, 51.38, 47.49, 40.05. HRMS: calculated for $C_{30}H_{32}N_4O_3S$ $[M+H]^+$: 529.22679; found: 529.22658.

(E)-*N*-(2-((3-(4''-ethoxy-[1,1':4',1''-terphenyl]-2-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 35

Prepared according to the general procedure. Yield: 35.2 mg, 62.4 μmol, 15.6%. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.47 (s, 1H), 8.70 (d, *J* = 5.6 Hz, 1H), 8.44 – 8.42 (m, 2H), 8.36 (d, *J* = 7.2 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 3H), 7.44 – 7.42 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 3H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 15.6 Hz, 1H), 6.25 – 6.18 (m, 1H), 4.07 (q, *J* = 6.8 Hz, 2H), 3.71 (d, *J* = 6.4 Hz, 2H), 3.06 (d, *J* = 31.6 Hz, 4H), 1.35 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 158.34, 153.43, 144.70, 140.23, 138.76, 138.13, 135.78, 133.87, 133.77, 133.31, 132.75, 131.73, 130.31, 130.08, 128.74, 128.60, 127.69, 126.39, 126.01, 120.75, 117.08, 114.92, 63.12, 49.30, 45.29, 14.67. HRMS: calculated for $C_{34}H_{33}N_3O_3S$ $[M+H]^+$: 564.23154; found: 564.23131.

(E)-*N*-(2-((3-(3'-(benzyloxy)-[1,1'-biphenyl]-2-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 36

Prepared according to the general procedure. Yield: 24.2 mg, 44.0 μmol, 11.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.52 (s, 1H), 8.67 (s, 1H), 8.50 (dd, J_1 = 7.2 Hz, J_2 = 22.0 Hz, 2H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.65 – 7.63 (m, 1H), 7.37 – 7.32 (m, 2H), 7.29 – 7.17 (m, 6H), 7.13 – 7.10 (m, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 15.6 Hz, 1H), 6.74 (s, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.19 – 6.12 (m, 1H), 3.94 (s, 2H), 3.72 (d, *J* = 7.2 Hz, 2H), 3.10 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.09, 153.36, 142.94, 142.76, 142.54, 140.97, 139.45, 136.02, 135.74, 135.61, 134.60, 133.27,

131.28, 129.99, 129.69, 129.24, 128.58, 128.47, 127.28, 126.79, 122.10, 119.54, 117.28, 50.44, 47.37, 39.99, 36.42. HRMS: calculated for $C_{33}H_{31}N_3O_3S$ $[M+H]^+$: 550.21589; found: 550.21576.

(E)-*N*-(2-((3-(2-(pyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 37

Prepared according to the general procedure. Yield: 32.4 mg, 72.8 μmol, 18.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.62 (s, 1H), 8.84 – 8.76 (m, 3H), 8.68 (s, 1H), 8.61 – 8.52 (m, 2H), 8.48 – 8.46 (m, 1H), 8.06 – 8.04 (m, 1H), 7.96 – 7.91 (m, 1H), 7.74 – 7.73 (m, 1H), 7.54 – 7.41 (m, 3H), 6.77 – 6.73 (m, 1H), 6.33 – 6.26 (m, 1H), 3.86 – 3.75 (m, 2H), 3.21 – 3.14 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.33, 146.81, 144.38, 142.92, 140.88, 140.51, 137.01, 136.75, 136.13, 135.87, 135.57, 135.45, 133.91, 131.53, 131.12, 130.41, 129.16, 128.39, 127.84, 123.37, 121.04, 50.79, 47.67, 40.06. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16911.

(E)-*N*-(2-((3-(2-(pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 38

Prepared according to the general procedure. Yield: 48.7 mg, 109.6 μmol, 27.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.55 (s, 1H), 8.87 (d, J = 5.2 Hz, 2H), 8.69 (s, 2H), 8.54 (dd, J_1 = 7.2 Hz, J_2 = 21.6 Hz, 2H), 8.01 (d, J = 6.0 Hz, 2H), 7.91 (t, J = 7.6 Hz, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.64 – 7.50 (m, 3H), 6.82 (d, J = 15.6 Hz, 1H), 6.38 – 6.31 (m, 1H), 3.83 (d, J = 6.8 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.81, 153.15, 143.17, 142.34, 137.12, 136.65, 136.25, 135.84, 135.60, 135.37, 133.38, 131.90, 131.16, 130.47, 128.92, 128.69, 128.61, 123.71, 120.24, 50.01, 47.76, 40.03. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16914 .

(E)-*N*-(2-((3-(2-(6-methoxypyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 39

Prepared according to the general procedure. Yield: 42.0 mg, 88.4 μmol, 22.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.57 (s, 1H), 8.75 – 8.68 (m, 2H), 8.54 (dd, J_1 = 7.2 Hz, J_2 = 28.4 Hz, 2H), 8.04 (s, 1H), 7.91 (t, J = 8.0 Hz, 1H), 7.67 – 7.65 (m, 2H), 7.40 – 7.38 (m, 2H), 7.29 – 7.27 (m, 1H), 6.89 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 15.6 Hz, 1H), 6.27 – 6.20 (m, 1H), 3.93 (s, 3H), 3.78 (d, J = 7.2 Hz, 2H), 3.21 – 3.15 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 164.84, 152.64, 147.69, 145.61, 141.91, 141.27, 138.60, 138.33, 136.61, 135.95, 135.79, 135.17, 133.66, 131.37, 130.78, 130.44, 130.01, 129.29, 128.90, 127.79, 120.98, 111.25, 54.38, 50.470, 47.52, 40.04. HRMS: calculated for $C_{26}H_{26}N_4O_3S$ $[M+H]^+$: 475.17984; found: 475.17944.

(E)-*N*-(2-((3-(2-(2-fluoropyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 40

Prepared according to the general procedure. Yield: 46.1 mg, 99.6 μmol, 24.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.54 (s, 1H), 8.71 – 8.67 (m, 2H), 8.52 (dd, J_1 = 7.2 Hz, J_2 = 25.6 Hz, 2H), 8.24 (d, J = 4.8 Hz, 1H), 7.90 (t, J = 7.6 Hz, 1H), 7.71 (d, J = 7.2 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.35 – 7.33 (m, 1H), 7.27 (d, J = 4.8 Hz, 1H), 7.04 (s, 1H), 6.77 (d, J = 15.6 Hz, 1H), 6.32 – 6.25 (m, 1H), 3.80 (d, J = 7.2 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 166.27, 163.90, 156.07, 155.98, 152.90, 148.43, 148.28, 141.85, 138.54, 137.39, 136.34, 135.85, 135.69, 134.73, 133.48, 130.80, 130.56, 130.47, 130.15, 128.72, 128.01, 124.19, 122.11, 120.43, 111.93, 111.16, 50.25, 47.63, 40.05. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15949.

(E)-*N*-(2-((3-(2-(pyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 41

Prepared according to the general procedure. Yield: 44.2 mg, 99.2 µmol, 24.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.59 (s, 1H), 9.16 (s, 1H), 8.78 – 8.74 (m, 3H), 8.69 – 8.67 (m, 1H), 8.55 (dd, J_1 = 7.2 Hz, J_2 = 26.4 Hz, 2H), 7.93 (t, J = 7.6 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.51 – 7.46 (m, 2H), 7.38 – 7.36 (m, 1H), 7.76 (d, J = 15.6 Hz, 1H), 6.33 – 6.26 (m, 1H), 3.81 (d, J = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.19, 158.03, 152.57, 141.10, 137.16, 136.72, 135.99, 135.85, 125.51, 134.76, 133.72, 131.51, 130.61, 130.43, 130.33, 128.97, 128.16, 122.64, 120.78, 50.22, 47.59, 40.08. HRMS: calculated for $C_{24}H_{23}N_5O_2S$ $[M+H]^+$: 446.16452; found: 446.16414.

(E)-*N*-(2-((3-(2-(2-methoxypyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 42

Prepared according to the general procedure. Yield: 44.5 mg, 93.6 µmol, 23.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.59 (s, 1H), 8.74 (d, J = 6.0 Hz, 1H), 8.69 – 8.67 (m, 1H), 8.58 (d, J =7.2 Hz, 1H), 8.53 – 8.51 (m, 3H), 7.92 (t, J = 7.6 Hz, 1H), 7.71 – 7.69 (m, 1H), 7.46 – 7.43 (m, 2H), 7.33 – 7.31 (m, 1H), 6.78 (d, J = 15.6 Hz, 1H), 6.32 – 6.24 (m, 1H), 4.02 (s, 3H), 3.81 (d, J = 6.8 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.87, 160.56, 152.58, 141.14, 137.49, 136.70, 135.98, 135.78, 135.52, 134.92, 133.70, 131.43, 130.42, 130.24, 130.06, 129.13, 128.96, 128.01, 122.08, 120.77, 55.68, 50.26, 47.57, 40.07. HRMS: calculated for $C_{25}H_{25}N_5O_3S$ $[M+H]^+$: 476.17509; found: 476.17481.

(E)-*N*-(2-((3-(2-(2-morpholinopyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 43

Prepared according to the general procedure. Yield: 27.3 mg, 51.6 µmol, 12.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.66 (s, 1H), 8.79 (d, J = 6.0 Hz, 1H), 8.72 (s, 1H), 8.59 (dd, J_1 = 2.8 Hz, J_2 = 10.4 Hz, 2H), 8.22 – 8.20 (m, 1H), 7.97 (t, J = 8.0 Hz, 1H), 7.89 – 7.87 (m, 1H), 7.83 – 7.81 (m, 1H), 7.54 – 7.49 (m, 2H), 7.43 – 7.41 (m, 1H), 7.32 – 7.28 (m, 1H), 6.72 (d, J = 15.6 Hz, 1H), 6.39 – 6.31 (m, 1H), 3.87 – 3.77 (m, 2H), 3.54 (s, 4H), 3.23 – 3.21 (m, 4H), 3.17 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.11, 152.38, 148.33, 140.59, 140.31, 136.99, 136.16, 135.88, 134.79, 133.93, 131.07, 130.78, 130.73, 129.91, 129.18, 128.02, 122.39, 121.08, 117.80, 66.90, 49.98, 47.60, 40.03. HRMS: calculated for $C_{29}H_{31}N_5O_3S$ $[M+H]^+$: 530.22204; found: 530.22178.

(E)-*N*-(2-((3-(2-(quinolin-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 44

Prepared according to the general procedure. Yield: 48.3 mg, 97.6 µmol, 24.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.65 (s, 1H), 9.16 (s, 1H), 8.94 (s, 1H), 8.77 (d, J = 6.4 Hz, 1H), 8.68 – 8.66 (m, 1H), 8.57 – 8.54 (m, 2H), 8.27 (dd, J_1 = 8.0 Hz, J_2 = 16.0 Hz, 2H), 8.05 (t, J = 8.0 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.79 – 7.77 (m, 1H), 7.58 – 7.54 (m, 3H), 6.83 (d, J = 15.6 Hz, 1H), 6.39 – 6.32 (m, 1H), 3.80 (d, J = 7.2 Hz, 2H), 3.17 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 151.97, 148.09, 145.26, 140.82, 139.85, 137.26, 136.98, 136.22, 136.04, 135.90, 135.75, 135.59, 134.94, 134.07, 131.79, 130.86, 130.77, 130.41, 130.33, 130.05, 129.35, 128.31, 123.54, 123.17, 121.29, 50.48, 47.59, 40.00. HRMS: calculated for $C_{29}H_{26}N_4O_2S$ $[M+H]^+$: 495.18492; found: 495.18463.

(E)-*N*-(2-((3-(2-(6-fluoropyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 45

Prepared according to the general procedure. Yield: 72.0 mg, 155.6 µmol, 38.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.67 (s, 1H), 8.84 (d, J = 6.8 Hz, 1H), 8.69 (d, J = 6.4 Hz, 1H), 8.60 (dd, J_1 = 7.2 Hz, J_2 = 28.0 Hz, 2H), 8.10 (s, 1H), 7.97 (t, J = 8.0 Hz, 1H), 7.71 (td, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.44 – 7.39 (m, 2H), 7.30 – 7.28

(m, 1H), 7.13 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 6.73 (d, J = 16.0 Hz, 1H), 6.30 – 6.22 (m, 1H), 3.79 (d, J = 7.2 Hz, 2H), 3.22 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.41, 163.03, 151.81, 148.58, 148.44, 144.33, 144.25, 139.51, 137.70, 137.35, 136.24, 135.98, 135.69, 135.25, 134.16, 131.39, 130.28, 130.05, 129.84, 129.44, 127.88, 121.72, 121.44, 110.50, 110.14, 50.29, 47.53, 39.84. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15942.

(E)-*N*-(2-((3-(2-(1-methyl-1H-indazol-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 46

Prepared according to the general procedure. Yield: 70.6 mg, 142.0 μmol, 35.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.53 (s, 1H), 8.69 (d, J = 6.4 Hz, 1H), 8.65 – 8.63 (m, 1H), 8.48 (dd, J_1 = 7.6 Hz, J_2 = 18.0 Hz, 2H), 7.98 (s, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.41 – 7.33 (m, 4H), 7.05 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 6.78 (d, J = 16.0 Hz, 1H), 6.26 – 6.18 (m, 1H), 4.03 (s, 3H), 3.71 (d, J = 7.2 Hz, 2H), 3.16 – 3.10 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.69, 142.91, 141.50, 141.28, 140.64, 138.70, 136.43, 135.86, 135.69, 134.86, 133.66, 133.53, 131.55, 130.39, 129.00, 128.78, 127.38, 124.39, 124.22, 121.79, 120.54, 120.28, 110.99, 50.41, 47.43, 39.84, 35.65. HRMS: calculated for $C_{28}H_{27}N_5O_2S$ $[M+H]^+$: 498.19582; found: 498.19532.

(E)-*N*-(2-((3-([1,1':3',1''-terphenyl]-2-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 47

Prepared according to the general procedure. Yield: 104.3 mg, 200.8 μmol, 50.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.38 (s, 1H), 8.60 (d, J = 6.4 Hz, 1H), 8.52 (d, J = 6.4 Hz, 1H), 8.41 (d, J = 7.2 Hz, 1H), 8.52 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.60 – 7.53 (m, 3H), 7.49 – 7.45 (m, 2H), 7.41 – 7.36 (m, 2H), 7.34 – 7.30 (m, 3H), 7.26 – 7.23 (m, 1H), 7.21 – 7.18 (m, 1H), 6.79 (d, J = 16.0 Hz, 1H), 6.23 – 6.15 (m, 1H), 3.71 (d, J = 7.2 Hz, 2H), 3.03 – 2.96 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.08, 144.50, 142.70, 142.40, 141.92, 139.15, 135.34, 135.29, 135.14, 134.78, 132.65, 131.30, 130.57, 129.95, 129.91, 129.84, 129.70, 129.25, 128.50, 128.13, 127.99, 127.84, 127.53, 127.07, 120.17, 119.19, 50.33, 47.18, 39.86. HRMS: calculated for $C_{32}H_{29}N_3O_2S$ $[M+H]^+$: 520.20532; found: 520.20510.

(E)-*N*-(2-((3-(2-(1H-pyrazol-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 48

Prepared according to the general procedure. Yield: 55.7 mg, 128.4 μmol, 32.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.63 (s, 1H), 8.81 (d, J = 6.4 Hz, 1H), 8.71 (s, 1H), 8.64 (d, J = 7.2 Hz, 1H), 8.54 (d, J = 8.4 Hz, 1H), 7.95 (t, J = 8.0 Hz, 1H), 7.76 (s, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.46 – 7.29 (m, 3H), 7.04 (d, J = 16.0 Hz, 1H), 6.29 – 6.18 (m, 1H), 3.84 (d, J = 7.2 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.41, 140.71, 139.04, 139.92, 136.10, 135.96, 134.96, 133.92, 133.28, 131.032, 129.93, 129.13, 128.36, 127.80, 120.54, 50.60, 47.62, 40.12. HRMS: calculated for $C_{23}H_{23}N_5O_2S$ $[M+H]^+$: 434.16452; found: 434.16395.

(E)-*N*-(2-((3-(2-(thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 49

Prepared according to the general procedure. Yield: 62.2 mg, 138.4 μmol, 34.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.52 (s, 1H), 8.11 (d, J = 6.4 Hz, 1H), 8.67 (s, 1H), 8.55 (d, J = 7.2 Hz, 1H), 8.45 (d, J = 8.4 Hz, 1H), 7.87 (t, J = 8.0 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.44 (dd, J_1 = 1.2 Hz, J_2 = 5.2 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.37 – 7.32 (m, 2H), 7.11 – 7.09 (m, 1H), 7.04 – 7.00 (m, 2H), 3.80 (d, J = 7.2 Hz, 2H), 3.21 – 3.15 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.89, 142.60, 141.67, 138.80, 136.31, 135.82, 135.73, 135.40, 134.97, 133.46, 131.72, 130.45, 129.77, 129.28, 129.00,

128.68, 128.54, 128.02, 127.28, 120.82, 50.48, 47.53, 40.05. HRMS: calculated for $C_{24}H_{23}N_3O_2S_2$ $[M+H]^+$: 450.13044; found: 450.12986.

(E)-*N*-(2-((3-(2-(benzo[b]thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 50

Prepared according to the general procedure. Yield: 52.2 mg, 104.4 µmol, 26.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.55 (s, 1H), 8.73 (d, *J* = 6.4 Hz, 1H), 8.65 – 8.63 (m, 1H), 8.54 (d, *J* = 7.2 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 7.88 – 7.76 (m, 3H), 7.68 (dd, J_1 = 6.0 Hz, J_2 = 8.0 Hz, 1H), 7.50 – 7.48 (m, 1H), 7.42 – 7.38 (m, 2H), 7.37 – 7.28 (m, 2H), 7.25 (s, 1H), 7.07 (d, *J* = 15.6 Hz, 1H), 6.29 – 6.21 (m, 1H), 3.79 (d, *J* = 7.2 Hz, 2H), 3.16 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.53, 142.84, 141.56, 141.10, 138.51, 136.62, 135.93, 135.80, 134.88, 133.67, 131.92, 130.41, 129.91, 129.81, 128.89, 128.05, 125.70, 125.67, 125.61, 124.85, 122.94, 121.22, 120.73, 50.37, 47.51, 39.99. HRMS: calculated for $C_{28}H_{25}N_3O_2S_2$ $[M+H]^+$: 500.14610; found: 500.14576.

(E)-*N*-(2-((3-(2-(1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 51

Prepared according to the general procedure. Yield: 23.2 mg, 48.0 µmol, 12.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.65 (q, *J* = 7.6 Hz, 2H), 8.52 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.67 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.45 – 7.37 (m, 3H), 7.10 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 7.00 (td, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H), 6.26 – 6.18 (m, 1H), 3.81 (d, *J* = 6.8 Hz, 2H), 3.15 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.16, 142.36, 139.35, 138.43, 137.31, 136.15, 135.78, 135.65, 135.41, 134.10, 133.37, 130.63, 130.53, 130.01, 129.79, 129.04, 128.55, 128.08, 122.87, 121.19, 120.53, 120.33, 120.18, 112.13, 50.47, 47.43, 39.98. HRMS: calculated for $C_{28}H_{26}N_4O_2S$ $[M+H]^+$: 483.18492; found: 483.18449.

(E)-*N*-(2-((3-(2-(quinoxalin-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 52

Prepared according to the general procedure. Yield: 155.4 mg, 313.6 µmol, 78.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.46 (s, 1H), 8.83 (s, 2H), 8.61 (s, 2H), 8.47 (d, *J* = 7.2 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 7.92 (s, 1H), 7.84 – 7.76 (m, 2H), 7.71 – 7.69 (m, 1H), 7.47 – 7.39 (m, 3H), 6.77 (d, *J* = 15.6 Hz, 1H), 6.30 – 6.23 (m, 1H), 3.76 (d, *J* = 7.2 Hz, 2H), 3.17 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.99, 146.95, 146.61, 143.92, 143.32, 142.91, 142.20, 140.70, 138.40, 136.09, 135.69, 135.51, 135.03, 133.50, 133.23, 131.35, 130.42, 130.34, 130.02, 129.71, 128.51, 127.97, 121.37, 120.17, 50.29, 47.49, 39.98. HRMS: calculated for $C_{28}H_{25}N_5O_2S$ $[M+H]^+$: 496.18017; found: 496.17970.

(E)-*N*-(2-((3-(2-(5-fluoro-1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 53

Prepared according to the general procedure. Yield: 31.6 mg, 63.2 µmol, 15.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.52 (s, 1H), 8.66 (s, 2H), 8.61 (s, 2H), 8.52 (d, *J* = 7.2 Hz, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.35 (dd, J_1 = 4.4 Hz, J_2 = 8.8 Hz, 1H), 7.20 – 7.16 (m, 2H), 6.88 (td, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 1H), 6.47 (s, 1H), 6.28 – 6.21 (m, 1H), 3.84 (d, *J* = 6.8 Hz, 2H), 3.19 – 3.14 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.36, 158.04, 153.49, 143.02, 139.33, 139.19, 135.89, 135.73, 135.53, 135.45, 135.00, 133.78, 133.17, 130.62, 130.30, 130.26, 129.87, 129.32, 128.38, 128.12, 120.53, 112.97, 111.08, 110.81, 105.68, 105.44, 104.87, 104.82, 50.45, 47.49, 39.98. HRMS: calculated for $C_{28}H_{25}FN_4O_2S$ $[M+H]^+$: 501.17550; found: 501.17528.

(E)-*N*-(2-((3-(2-(2-(trifluoromethyl)pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 54

Prepared according to the general procedure. Yield: 54.3 mg, 106.0 μmol, 26.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.54 (s, 1H), 8.78 (d, *J* = 3.6 Hz, 1H), 8.68 – 8.66 (m, 2H), 8.54 (d, *J* = 4.4 Hz, 1H), 8.50 (d, *J* = 5.2 Hz, 1H), 7.90 (t, *J* = 5.2 Hz, 1H), 7.79 (s, 1H), 7.76 (d, *J* = 5.6 Hz, 1H), 7.64 (d, *J* = 3.6 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.41 (d, *J* = 4.8 Hz, 1H), 6.32 – 6.27 (m, 1H), 3.80 (d, *J* = 4.8 Hz, 2H), 3.32 – 3.31 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.45, 152,18, 151.19, 149.14 (q, *J* = 23.23 Hz), 142.94, 138.52, 137.43, 135.91, 135.75, 135.59, 134.89, 133,25, 131.07, 130.80, 130.38, 129.20, 128.42, 128.15, 123.20 (q, *J* = 171.7 Hz), 122.55, 122.51, 119.99, 50.22, 47,65, 40.08. HRMS: calculated for $C_{26}H_{23}F_3N_4O_2S$ $[M+H]^+$: 513.15666; found: 513.15631.

(E)-*N*-(2-((3-(2-(imidazo[1,2-a]pyridin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 55

Prepared according to the general procedure. Yield: 120.7 mg, 249.6 μmol, 62.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.54 (s, 1H), 8.82 (s, 1H), 8.68 – 8.65 (m, 2H), 8.50 (d, *J* = 5.2 Hz, 1H), 8.26 (s, 1H), 8.05 (s, 1H), 8.50 (d, *J* = 6.4 Hz, 1H), 7.94 (d, *J* = 6.0 Hz, 1H), 7.91 (t, *J* = 2.4 Hz, 1H), 7.78 (d, *J* = 5.2 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.45 (d, *J* = 0.8 Hz, 1H), 6.84 (d, *J* = 10.8 Hz, 1H), 6.35 – 6.30 (m, 1H), 3.80 (d, *J* = 4.4 Hz, 2H), 3.18 – 3.14 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.28, 142.55, 140.61, 137.31, 136.97, 136.11, 136.02, 135.82, 135.72, 135.54, 133.30, 132.01, 131.66, 130.72, 130.58, 130.28, 129.50, 128.52, 128.07, 124.14, 122.64, 120.11, 117.13, 112.88, 50.04, 47.66, 40.00. HRMS: calculated for $C_{27}H_{25}N_5O_2S$ $[M+H]^+$: 484.18017; found: 484.17998.

(E)-*N*-(2-((3-(3-(4-methylnaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 56

Prepared according to the general procedure. Yield: 20.5 mg, 40.4 μmol, 10.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.67 (s, 2H), 8.54 (d, *J* = 7.6 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.86 (t, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.46 (m, 4H), 7.42 – 7.36 (m, 3H), 7.26 (d, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.36 – 6.28 (m, 1H), 3.85 (d, *J* = 7.2, 2H), 3.18 (s, 4H), 2.71 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.23, 142.98, 140.04, 139.91, 139.32, 137.19, 136.90, 136.05, 135.72, 135.66, 135.25, 134.18, 133.31, 132.86, 131.67, 129.83, 129.49, 128.58, 127.55, 127.19, 127.04, 126.76, 125.48, 120.13, 119.48, 50.78, 47.52, 39.88, 19.59. HRMS: calculated for $C_{31}H_{29}N_3O_2S$ $[M+H]^+$: 508.20532; found: 508.20510.

(E)-*N*-(2-((3-(3-(4-methoxynaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 57

Prepared according to the general procedure. Yield: 24.3 mg, 46.4 μmol, 11.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.54 (s, 1H), 8.73 (d, *J* = 6.0 Hz, 1H), 8.68 (s, 1H), 8.57 (d, *J* = 7.6 Hz, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.37 (m, 6H), 7.30 (d, *J* = 8.0 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.36 – 6.28 (m, 1H), 4.03 (s, 3H), 3.85 (d, *J* = 6.8 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.45, 152.85, 142.84, 141.67, 140.12, 136.90, 136.43, 135.88, 135.80, 133.63, 133.22, 131.78, 130.51, 129.84, 129.71, 128.77, 128.11, 127.57, 127.00, 126.54, 126.34, 126.09, 123.25, 120.53, 119.38, 104.51, 56.08, 50.49, 47.52, 40.13. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.19998.

(E)-*N*-(2-((3-(3-(6-methoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 58

Prepared according to the general procedure. Yield: 28.5 mg, 54.4 μmol, 13.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.48 (s, 1H), 8.69 (d, *J* = 6.0 Hz, 1H), 8.64 (s, 1H), 8.54 (d, *J* = 7.6 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 7.97 (s, 1H), 7.85

– 7.76 (m, 4H), 7.71 – 7.63 (m, 2H), 7.46 – 7.43 (m, 2H), 7.21 (s, 1H), 7.12 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.92 (d, J = 16.0 Hz, 1H), 6.39 – 6.32 (m, 1H), 3.89 (s, 3H), 3.86 (d, J = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 159.38, 152.98, 142.94, 142.08, 140.14, 137.40, 136.84, 136.21, 135.76, 135.67, 135.47, 133.39, 130.70, 130.54, 130.39, 128.56, 126.64, 126.50, 120.21, 119.38, 106.56, 55.77, 50.49, 47.50, 40.12. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.19998.

(E)-*N*-(2-((3-(3-(6-ethoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 59

Prepared according to the general procedure. Yield: 27.7 mg, 51.6 µmol, 12.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.53 (s, 1H), 8.71 – 8.67 (m, 2H), 8.58 (d, J = 7.6 Hz, 1H), 8.49 (d, J = 8.0 Hz, 1H), 8.02 (s, 1H), 7.90 (t, J = 7.6 Hz, 1H), 7.85 – 7.81 (m, 3H), 7.74 – 7.69 (m, 2H), 7.50 – 7.47 (m, 2H), 7.24 (s, 1H), 7.15 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.97 (d, J = 16.0 Hz, 1H), 6.42 – 6.35 (m, 1H), 4.17 (q, J = 6.8 Hz, 2H), 3.89 (d, J = 3.2 Hz, 2H), 3.14 (s, 4H), 1.46 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.71, 153.28, 143.14, 142.53, 140.29, 137.43, 136.87, 136.11, 135.80, 135.72, 135.59, 133.39, 130.69, 130.58, 130.44, 128.67, 128.54, 126.69, 126.58, 126.52, 120.53, 120.15, 119.34, 107.35, 64.59, 50.54, 47.56, 40.17, 15.14. HRMS: calculated for $C_{32}H_{31}N_3O_3S$ $[M+H]^+$: 538.21589; found: 538.21566.

(E)-*N*-(2-((3-(3-(6-(benzyloxy)naphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 60

Prepared according to the general procedure. Yield: 15.8 mg, 26.4 µmol, 6.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.47 (s, 1H), 8.65 (s, 2H), 8.53 (d, J = 7.2 Hz, 2H), 8.43 (d, J = 8.4 Hz, 1H), 8.01 (s, 1H), 7.86 – 7.80 (m, 4H), 7.72 – 7.67 (m, 2H), 7.50 – 7.47 (m, 4H), 7.39 (t, J = 6.8 Hz, 2H), 7.33 – 7.30 (m, 2H), 7.22 (dd, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 1H), 6.95 (d, J = 15.6 Hz, 1H), 6.41 – 6.33 (m, 1H), 5.19 (s, 2H), 3.87 (d, J = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.46, 153.55, 143.21, 143.03, 140.23, 138.54, 137.43, 137.05, 135.78, 135.64, 135.59, 135.45, 133.13, 130.82, 130.72, 130.43, 129.54, 128.95, 128.68, 128.65, 128.61, 128.29, 126.70, 126.55, 120.53, 119.37, 108.14, 71.09, 50.51, 47.55, 40.14. HRMS: calculated for $C_{37}H_{33}N_3O_3S$ $[M+H]^+$: 600.23154; found: 600.23139.

(E)-*N*-(2-((3-(3-(anthracen-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 61

Prepared according to the general procedure. Yield: 20.2 mg, 37.2 µmol, 9.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.40 (s, 1H), 8.63 (d, J = 6.0 Hz, 1H), 8.57 (d, J = 6.0 Hz, 1H), 8.52 (s, 1H), 8.48 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.79 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.48 (s, 1H), 7.43 (t, J = 7.2 Hz, 2H), 7.33 – 7.29 (m, 3H), 6.94 (d, J = 16.0 Hz, 1H), 6.36 – 6.28 (m, 1H), 3.83 (d, J = 7.2 Hz, 2H), 3.15 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.87, 143.98, 140.75, 139.85, 137.33, 137.19, 135.44, 132.85, 132.75, 131.34, 130.61, 130.10, 129.54, 128.10, 128.00, 127.29, 126.61, 126.20, 119.76, 119.44, 50.42, 47.52, 40.09. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20504.

(E)-*N*-(2-((3-(3-(9H-fluoren-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 62

Prepared according to the general procedure. Yield: 15.3 mg, 28.8 µmol, 7.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.37 (s, 1H), 8.62 (d, J = 6.0 Hz, 1H), 8.55 (d, J = 6.0 Hz, 1H), 8.48 (d, J = 7.2 Hz, 1H), 8.36 (d, J = 8.0 Hz, 1H), 7.84 – 7.77 (m, 4H), 7.72 (s, 1H), 7.61 – 7.59 (m, 2H), 7.53 (d, J = 7.6 Hz, 2H), 7.44 – 7.43 (m, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 6.92 (d, J = 15.6 Hz, 1H), 6.39 – 6.31 (m, 1H), 3.90 (s, 2H), 3.86 (d, J = 7.2 Hz, 2H), 3.18 (s, 4H).

^{13}C NMR (101 MHz, CD_3OD) δ 154.14, 145.33, 144.79, 144.57, 143.32, 142.47, 142.43, 140.49, 140.18, 137.35, 135.37, 135.32, 135.16, 132.67, 130.62, 130.36, 128.58, 127.95, 127.91, 127.83, 126.90, 126.65, 126.56, 126.07, 121.13, 120.93, 119.35, 119.17, 50.49, 47.51, 40.10, 37.68. HRMS: calculated for $C_{33}H_{29}N_3O_2S$ $[M+H]^+$: 532.20532; found: 532.20509.

(E)-*N*-(2-((3-(3-(phenanthren-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 63

Prepared according to the general procedure. Yield: 37.0 mg, 68.0 μmol, 17.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.30 (s, 1H), 8.78 – 8.76 (m, 1H), 8.73 – 8.70 (m, 1H), 8.59 (d, *J* = 6.0 Hz, 2H), 8.50 (d, *J* = 6.0 Hz, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.86 – 7.84 (m, 1H), 7.80 – 7.69 (m, 2H), 7.65 – 7.34 (m, 9H), 6.88 (d, *J* = 16 Hz, 1H), 6.34 – 6.27 (m, 1H), 3.80 (d, *J* = 6.8 Hz, 2H), 3.14 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.28, 145.00, 142.60, 139.83, 139.40, 137.02, 135.23, 135.18, 134.90, 132.78, 132.47, 132.06, 131.95, 131.49, 131.26, 130.57, 129.90, 129.73, 129.50, 128.48, 128.01, 127.90, 127.72, 127.63, 127.52, 127.00, 124.12, 123.59, 119.66, 118.98, 50.40, 47.47, 40.06, 31.11. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20519.

(E)-*N*-(2-((3-(3-(dibenzo[b,d]furan-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 64

Prepared according to the general procedure. Yield: 29.5 mg, 55.2 μmol, 13.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.32 (s, 1H), 8.59 (s, 1H), 8.53 (s, 1H), 8.45 (d, *J* = 7.2 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.02 – 7.96 (m, 2H), 7.82 – 7.80 (m, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.50 – 7.40 (m, 5H), 7.35 (t, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.39 – 6.32 (m, 1H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.36, 154.41, 154.16, 144.72, 140.01, 138.21, 137.79, 135.31, 135.26, 135.04, 132.56, 130.20, 130.15, 128.53, 128.34, 127.84, 127.74, 127.15, 126.37, 126.18, 125.23, 124.63, 124.14, 121.82, 121.11, 119.56, 112.58, 50.45, 47.49, 40.08. HRMS: calculated for $C_{32}H_{27}N_3O_3S$ $[M+H]^+$: 534.18459; found: 534.18438.

(E)-*N*-(2-((3-(3-(phenoxathiin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 65

Prepared according to the general procedure. Yield: 34.6 mg, 61.2 μmol, 15.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.32 (s, 1H), 8.59 (s, 1H), 8.52 – 8.51 (m, 1H), 8.44 (d, *J* = 7.2 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.55 (s, 1H), 7.48 – 7.43 (m, 3H), 7.18 – 7.09 (m, 5H), 7.07 – 7.02 (m, 1H), 6.96 (d, *J* = 30.4 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.35 – 6.28 (m, 1H), 3.85 (d, *J* = 6.8 Hz, 2H), 3.17 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.29, 153.79, 150.41, 144.95, 139.96, 138.94, 136.78, 135.26, 135.23, 134.95, 132.51, 132.40, 131.05, 130.84, 130.59, 130.35, 129.69, 129.13, 127.88, 127.68, 127.47, 127.00, 126.06, 125.78, 123.09, 122.34, 119.45, 119.02, 118.47, 50.43, 47.49, 40.07. HRMS: calculated for $C_{32}H_{27}N_3O_3S_2$ $[M+H]^+$: 566.15666; found: 566.15641.

(E)-*N*-(2-((3-(3-(2,3-dihydrobenzofuran-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 66

Prepared according to the general procedure. Yield: 23.9 mg, 49.2 μmol, 12.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.40 (s, 1H), 8.63 (d, *J* = 6.0 Hz, 1H), 8.58 (d, *J* = 5.6 Hz, 1H), 8.49 (d, *J* = 7.2 Hz, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 7.81 (t, *J* = 8.0 Hz, 1H), 7.61 (s, 1H), 7.50 – 7.49 (m, 1H), 7.45 (s, 1H), 7.38 (d, *J* = 4.8 Hz, 2H), 7.33 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 6.89 (d, *J* = 16.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.36 – 6.29 (m, 1H), 4.56 (t, *J* = 8.8 Hz, 2H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.23 (t, *J* = 8.8 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 161.35, 153.79, 143.77, 143.21, 140.47, 137.23, 135.53, 135.48, 134.52, 132.93, 130.60, 130.22, 129.32, 128.17, 128.11, 127.87, 126.23, 125.92,

124.66, 119.57, 119.18, 110.28, 72.52, 50.50, 47.50, 40.11, 30.51. HRMS: calculated for $C_{28}H_{27}N_3O_3S$ $[M+H]^+$: 486.18459; found: 486.18427.

(E)-*N*-(2-((3-(3-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 67

Prepared according to the general procedure. Yield: 35.3 mg, 68.4 µmol, 17.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.47 (s, 1H), 8.65 (s, 2H), 8.53 (d, *J* = 7.2 Hz, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.60 (s, 1H), 7.51 – 7.47 (m, 1H), 7.39 – 7.36 (m, 2H), 7.21 – 7.16 (m, 2H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 15.6 1H), 6.36 – 6.29 (m, 1H), 4.18 (q, *J* = 5.2 Hz, 4H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H), 2.19 – 2.13 (m, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.95, 152.68, 152.49, 142.02, 141.38, 140.06, 137.32, 136.56, 135.93, 135.80, 133.63, 130.31, 128.86, 128.16, 126.49, 126.24, 123.10, 122.89, 121.07, 120.68, 119.41, 71.97, 50.48, 47.50, 40.13, 33.22. HRMS: calculated for $C_{29}H_{29}N_3O_4S$ $[M+H]^+$: 516.19515; found: 516.19490.

(E)-*N*-(2-((3-(4'-morpholino-[1,1'-biphenyl]-3-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 68

Prepared according to the general procedure. Yield: 36.2 mg, 68.4 µmol, 17.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.68 (t, *J* = 6.0 Hz, 2H), 8.55 (d, *J* = 6.4 Hz, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 7.89 (t, *J* = 8.0 Hz, 1H), 7.63 (s, 1H), 7.55 – 7.50 (m, 3H), 7.39 – 7.38 (m, 2H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 16.0 Hz, 2H), 6.37 – 6.29 (m, 1H), 3.86 – 3.83 (m, 6H), 3.21 – 3.19 (m, 8H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.47, 150.86, 142.36, 140.89, 140.16, 137.33, 136.78, 136.02, 135.87, 134.58, 133.77, 130.32, 129.01, 128.75, 127.92, 126.14, 126.01, 120.87, 119.32, 117.82, 67.54, 51.18, 50.50, 47.50, 40.13. HRMS: calculated for $C_{30}H_{32}N_4O_3S$ $[M+H]^+$: 529.22679; found: 529.22646.

(E)-*N*-(2-((3-(4''-ethoxy-[1,1':4',1''-terphenyl]-3-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 69

Prepared according to the general procedure. Yield: 23.0 mg, 40.8 µmol, 10.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.66 (s, 2H), 8.55 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.74 (s, 1H), 7.69 – 7.59 (m, 5H), 7.59 – 7.56 (m, 2H), 7.48 – 7.43 (m, 2H), 7.00 – 6.92 (m, 3H), 6.40 – 6.33 (m, 1H), 4.06 (q, *J* = 6.8 Hz, 2H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H), 1.40 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.17, 153.10, 142.62, 142.20, 141.38, 140.18, 139.97, 137.42, 136.25, 135.84, 135.76, 134.01, 133.47, 130.56, 130.41, 128.86, 128.64, 128.32, 127.93, 126.68, 126.44, 120.31, 119.41, 115.91, 64.55, 50.52, 47.55, 40.15, 15.18. HRMS: calculated for $C_{34}H_{33}N_3O_3S$ $[M+H]^+$: 564.23154; found: 564.23135.

(E)-*N*-(2-((3-(3'-(benzyloxy)-[1,1'-biphenyl]-3-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 70

Prepared according to the general procedure. Yield: 19.6 mg, 35.6 µmol, 8.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.44 (s, 1H), 8.63 (q, *J* = 6.0, 2H), 8.52 (d, *J* = 7.2 Hz, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.67 (s, 1H), 7.56 – 7.54 (m, 1H), 7.45 – 7.43 (m, 4H), 7.36 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 3H), 7.31 – 7.28 (m, 1H), 7.23 – 7.19 (m, 2H), 7.00 (dd, J_1 = 2.0 Hz, J_2 = 7.6 Hz, 1H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.38 – 6.31 (m, 1H), 5.13 (s, 2H), 3.87 (d, *J* = 6.8 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.69, 153.79, 148.30, 143.74, 143.41, 142.92, 140.10, 138.86, 137.36, 135.55, 135.48, 132.97, 131.00, 130.61, 130.35, 129.92, 129.51, 128.90, 128.62, 128.21, 126.69,

126.65, 120.70, 119.58, 119.44, 114.96, 114.84, 71.07, 50.46, 47.50, 40.12. HRMS: calculated for $C_{33}H_{31}N_3O_3S$ $[M+H]^+$: 550.21589; found: 550.21565.

(E)-*N*-(2-((3-(3-(pyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 71

Prepared according to the general procedure. Yield: 27.7 mg, 62.4 µmol, 15.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.47 (s, 1H), 9.07 (s, 1H), 8.75 (d, *J* = 5.6 Hz, 1H), 8.66 – 8.62 (m, 3H), 8.54 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 7.95 (dd, J_1 = 5.6 Hz, J_2 = 8.0 Hz, 1H), 7.89 – 7.84 (m, 2H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.48 – 6.40 (m, 1H), 3.89 (d, *J* = 6.8 Hz, 2H), 3.24 – 3.21 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.50, 144.05, 143.61, 143.5, 142.39, 140.35, 139.09, 138.25, 136.85, 135.84, 135.63, 135.54, 133.12, 131.07, 130.55, 128.87, 128.65, 128.32, 127.60, 126.90, 120.77, 119.86, 50.35, 47.63, 40.13. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16911.

(E)-*N*-(2-((3-(3-(pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 72

Prepared according to the general procedure. Yield: 34.0 mg, 76.4 µmol, 19.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.46 (s, 1H), 8.84 (d, *J* = 6.8 Hz, 2H), 8.64 (q, *J* = 6.4 Hz, 2H), 8.53 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.30 (d, *J* = 6.8 Hz, 2H), 8.01 (s, 1H), 7.89 – 7.85 (m, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 15.6 Hz, 1H), 6.52 – 6.44 (m, 1H), 3.91 (d, *J* = 7.2 Hz, 2H), 3.25 – 3.20 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.53, 153.65, 144.21, 143.48, 138.75, 138.51, 136.98, 135.70, 135.58, 135.51, 133.04, 131.28, 130.76, 130.59, 129.14, 129.00, 128.23, 127.47, 125.32, 121.29, 119..72, 50.31, 47.67, 40.13. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16904 .

(E)-*N*-(2-((3-(3-(6-methoxypyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 73

Prepared according to the general procedure. Yield: 30.4 mg, 64.0 µmol, 16.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.62 (s, 1H), 8.80 (d, *J* = 6.4 Hz, 1H), 8.69 (d, *J* = 8.0 Hz, 1H), 8.62 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.54 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 2.8 Hz, 1H), 7.99 – 7.92 (m, 2H), 7.65 (s, 1H), 7.54 – 7.52 (m, 1H), 7.48 – 7.42 (m, 2H), 6.94 – 6.90 (m, 2H), 6.41 – 6.33 (m, 1H), 3.96 (s, 3H), 3.88 (d, *J* = 7.2 Hz, 2H), 3.22 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.06, 152.34, 145.32, 140.53, 139.79, 139.53, 139.24, 137.66, 136.96, 136.10, 135.94, 133.93, 131.16, 130.59, 130.43, 129.16, 128.06, 126.95, 136.16, 121.03, 119.81, 111.70, 54.51, 50.46, 47.57, 40.15. HRMS: calculated for $C_{26}H_{26}N_4O_3S$ $[M+H]^+$: 475.17984; found: 475.17964.

(E)-*N*-(2-((3-(3-(2-fluoropyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 74

Prepared according to the general procedure. Yield: 30.5 mg, 66.0 µmol, 16.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.63 (s, 1H), 8.80 (d, *J* = 6.4, 1H), 8.70 (d, *J* = 6.0, 1H), 8.63 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 5.2, 1H), 7.95 (t, *J* = 8.0 Hz, 1H), 7.83 (s, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.61 – 7.60 (m, 2H), 7.52 (t, *J* = 7.6, 1H), 7.36 (s, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.46 – 6.38 (m, 1H), 3.90 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 167.07, 164.70, 155.57, 155.48, 152.43, 148.98, 1548.83, 140.71, 139.26, 138.59, 138.01, 136.91, 136.09, 135.94, 133.91, 130.87, 130.47, 129.18, 128.51, 126.72, 120.90, 120.86, 120.52, 108.24, 107.87, 50.40, 47.63, 40.17. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15946.

(E)-*N*-(2-((3-(3-(pyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 75

Prepared according to the general procedure. Yield: 26.6 mg, 59.6 µmol, 14.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.62 (s, 1H), 9.15 (s, 1H), 9.07 (s, 2H), 8.79 (d, *J* = 6.4 Hz, 1H), 8.70 (d, *J* = 6.0 Hz, 1H), 8.63 (d, *J* = 7.2 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 7.95 (t, *J* = 8.4 Hz, 1H), 7.80 (s, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 16.0 Hz, 1H), 6.47 – 6.39 (m, 1H), 3.90 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.08, 156.14, 152.48, 140.79, 139.27, 138.17, 136.87, 136.08, 135.93, 135.85, 135.62, 133.88, 131.03, 130.48, 129.10, 128.53, 128.47, 126.63, 120.93, 120.56, 50.40, 47.64, 40.18. HRMS: calculated for $C_{24}H_{23}N_5O_2S$ $[M+H]^+$: 446.16452; found: 446.16416.

(E)-*N*-(2-((3-(3-(2-methoxypyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 76

Prepared according to the general procedure. Yield: 24.7 mg, 52.0 µmol, 13.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.56 (s, 1H), 8.82 (s, 2H), 8.73 (d, *J* = 6.4 Hz, 1H), 8.68 (d, *J* = 6.4 Hz, 1H), 8.59 (d, *J* = 7.2 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.92 (t, *J* = 8.0 Hz, 1H), 7.70 (s, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.52 – 7.47 (m, 2H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.43 – 6.35 (m, 1H), 4.05 (s, 3H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.22 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 166.19, 158.60, 152.90, 141.79, 139.49, 137.97, 136.42, 136.04, 135.90, 135.79, 133.58, 130.86, 130.51, 129.32, 128.77, 127.97, 127.68, 126.09, 120.49, 120.24, 55.69, 50.42, 47.61, 40.16. HRMS: calculated for $C_{25}H_{25}N_5O_3S$ $[M+H]^+$: 476.17509; found: 476.17474.

(E)-*N*-(2-((3-(3-(2-morpholinopyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 77

Prepared according to the general procedure. Yield: 35.0 mg, 66.0 µmol, 16.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.63 (s, 1H), 8.79 (d, *J* = 6.4 Hz, 1H), 8.70 (d, *J* = 6.4 Hz, 1H), 8.62 (dd, J_1 = 0.8 Hz, J_2 = 7.2 Hz, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 8.18 (dd, J_1 = 2.0 Hz, J_2 = 6.0 Hz, 1H), 8.00 – 7.94 (m, 2H), 7.71 (s, 1H), 7.59 – 7.54 (m, 3H), 7.31 (dd, J_1 = 6.0 Hz, J_2 = 7.6 Hz, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.46 – 6.38 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.54 (t, *J* = 4.4 Hz, 4H), 3.25 – 3.23 (m, 8H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.46, 152.50, 147.01, 140.86, 140.02, 138.99, 138.92, 138.13, 136.87, 136.07, 135.90, 133.87, 131.22, 131.05, 130.48, 129.11, 129.08, 128.44, 127.42, 120.92, 120.76, 118.32, 66.85, 50.35, 50.25, 47.03, 40.15. HRMS: calculated for $C_{29}H_{31}N_5O_3S$ $[M+H]^+$: 530.22204; found: 530.22183.

(E)-*N*-(2-((3-(3-(quinolin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 78

Prepared according to the general procedure. Yield: 33.4 mg, 67.6 µmol, 16.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.55 (s, 1H), 9.41 (s, 1H), 9.11 (s, 1H), 8.73 (d, *J* = 6.4 Hz, 1H), 8.66 (d, *J* = 6.4 Hz, 1H), 8.58 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 8.25 – 8.19 (m, 2H), 8.02 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.95 – 7.78 (m, 4H), 7.61 – 7.55 (m, 2H), 6.97 (d, *J* = 15.6 Hz, 1H), 6.50 – 6.43 (m, 1H), 3.91 (d, *J* = 7.2 Hz, 2H), 3.24 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.73, 148.30, 146.84, 141.68, 141.45, 139.16, 138.26, 137.04, 136.54, 135.92, 135.77, 135.45, 134.38, 133.61, 131.08, 130.51, 130.44, 130.32, 130.18, 129.92, 128.84, 128.77, 127.02, 124.07, 120.73, 120.59, 5038, 47.63, 40.15. HRMS: calculated for $C_{29}H_{26}N_4O_2S$ $[M+H]^+$: 495.18492; found: 495.18465.

(E)-*N*-(2-((3-(3-(6-fluoropyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 79

Prepared according to the general procedure. Yield: 23.7 mg, 51.2 μmol, 12.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.58 (s, 1H), 8.75 (d, *J* = 6.4 Hz, 1H), 8.69 (d, *J* = 6.0 Hz, 1H), 8.60 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 2.4 Hz, 1H), 8.22 – 8.17 (m, 1H), 7.93 (t, *J* = 8.4 Hz, 1H), 7.71 (s, 1H), 7.60 – 7.47 (m, 3H), 7.16 (dd, J_1 = 2.8 Hz, J_2 = 8.8 Hz, 1H), 6.94 (d, *J* = 15.6 Hz, 1H), 6.43 – 6.38 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.21 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.77, 163.38, 152.77, 146.56, 146.42, 141.81, 141.72, 139.58, 138.39, 137.82, 136.57, 136.04, 136.00, 135.96, 133.68, 130.75, 130.51, 128.88, 128.49, 127.66, 126.62, 120.64, 120.13, 110.91, 110.54, 50.44, 47.61, 40.16. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15945.

(E)-*N*-(2-((3-(3-(1-methyl-1H-indazol-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 80

Prepared according to the general procedure. Yield: 63.4 mg, 127.6 μmol, 31.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.56 (s, 1H), 8.77 (d, *J* = 6.8 Hz, 1H), 8.65 (d, *J* = 6.4 Hz, 1H), 8.59 (d, *J* = 7.2 Hz, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.76 (s, 1H), 7.74 (s, 1H), 7.67 (s, 1H), 7.63 – 7.61 (m, 1H), 7.45 – 7.42 (m, 2H), 7.38 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.41 – 6.34 (m, 1H), 4.05 (s, 3H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.22 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.30, 143.05, 141.81, 140.77, 140.63, 139.93, 137.44, 136.89, 136.03, 135.88, 133.85, 133.58, 130.38, 130.34, 129.01, 127.12, 126.93, 124.47, 122.45, 121.80, 120.96, 119.63, 108.27, 50.49, 47.54, 40.14, 35.58. HRMS: calculated for $C_{28}H_{27}N_5O_2S$ $[M+H]^+$: 498.19582; found: 498.19539.

(E)-*N*-(2-((3-([1,1':3',1''-terphenyl]-3-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 81

Prepared according to the general procedure. Yield: 71.1 mg, 136.8 μmol, 34.2%. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.48 (s, 1H), 8.71 (d, *J* = 6.4 Hz, 1H), 8.45 – 8.43 (m, 2H), 8.39 (d, *J* = 7.2 Hz, 1H), 7.90 (s, 1H), 7.85 – 7.81 (m, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.40 – 7.36 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.42 – 6.35 (m, 1H), 3.78 (d, *J* = 6.4 Hz, 2H), 3.13 – 3.07 (m, 4H). ^{13}C NMR (101 MHz, $(CD_3)_2SO$) δ 153.49, 144.67, 141.13, 140.80, 140.66, 140.21, 136.94, 136.33, 133.97, 133.93, 133.87, 133.04, 130.50, 129.77, 129.08, 128.85, 127.76, 127.24, 127.05, 126.60, 126.23, 126.03, 125.85, 125.33, 125.30, 120.21, 117.27, 48.45, 45.48, 38.77, 38.69. HRMS: calculated for $C_{32}H_{29}N_3O_2S$ $[M+H]^+$: 520.20532; found: 520.20573.

(E)-*N*-(2-((3-(3-(1H-pyrazol-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 82

Prepared according to the general procedure. Yield: 40.6 mg, 93.6 μmol, 23.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.56 (s, 1H), 8.75 (d, *J* = 6.4 Hz, 1H), 8.67 (d, *J* = 6.4 Hz, 1H), 8.60 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 7.99 (s, 2H), 7.91 (t, *J* = 8.4 Hz, 1H), 7.65 (s, 1H), 7.52 (d, *J* = 7.2 Hz, 1H), 7.37 – 7.30 (m, 2H), 6.87 (d, *J* = 15.6 Hz, 1H), 6.37 – 6.29 (m, 1H), 3.86 (d, *J* = 6.8 Hz, 2H), 3.21 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.66, 141.26, 140.08, 137.41, 136.63, 135.97, 135.86, 134.51, 133.73, 132.18, 130.46, 130.37, 128.90, 127.05, 125.86, 125.03, 123.21, 120.70, 119.31, 50.51, 47.53, 40.15 HRMS: calculated for $C_{23}H_{23}N_5O_2S$ $[M+H]^+$: 434.16452; found: 434.16425.

(E)-*N*-(2-((3-(3-(thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 83

Prepared according to the general procedure. Yield: 54.3 mg, 120.8 µmol, 30.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 8.71 (d, *J* = 6.4 Hz, 1H), 8.65 (d, *J* = 6.4 Hz, 1H), 8.56 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.87 (t, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.57 – 7.54 (m, 1H), 7.40 – 7.33 (m, 4H), 7.08 (dd, J_1 = 3.6 Hz, J_2 = 5.2 Hz, 1H), 6.86 (d, *J* = 16.0 Hz, 1H), 6.36 – 6.28 (m, 1H), 3.86 (d, *J* = 7.2 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.90, 144.71, 141.88, 139.67, 137.53, 136.30, 136.27, 135.81, 135.73, 133.47, 130.48, 130.44, 129.20, 128.66, 127.11, 126.77, 126.21, 125.17, 124.64, 120.38, 119.78, 50.42, 47.53, 40.12. HRMS: calculated for $C_{24}H_{23}N_3O_2S_2$ $[M+H]^+$: 450.13044; found: 450.13002.

(E)-*N*-(2-((3-(3-(benzo[b]thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 84

Prepared according to the general procedure. Yield: 55.2 mg, 110.4 µmol, 27.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.33 (s, 1H), 8.59 (d, *J* = 6.4 Hz, 1H), 8.54 (d, *J* = 6.4 Hz, 1H), 7.46 (dd, J_1 = 0.8 Hz, J_2 = 7.2 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 7.81 – 7.73 (m, 4H), 7.65 – 7.61 (m, 2H), 7.42 – 7.36 (m, 2H), 7.34 – 7.26 (m, 2H), 6.86 (d, *J* = 16.0 Hz, 1H), 6.37 – 6.30 (m, 1H), 3.84 (d, *J* = 7.2 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.06, 144.49, 144.46, 142.07, 140.68, 139.48, 136.04, 135.31, 135.12, 134.99, 132.63, 130.57, 127.77, 127.65, 127.58, 127.40, 125.76, 125.70, 124.79, 123.16, 121.18, 120.01, 119.17, 50.38, 47.53, 40.08. HRMS: calculated for $C_{28}H_{25}N_3O_2S_2$ $[M+H]^+$: 500.14610; found: 500.14564.

(E)-*N*-(2-((3-(3-(1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 85

Prepared according to the general procedure. Yield: 26.8 mg, 55.6 µmol, 13.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.70 (d, *J* = 6.4 Hz, 2H), 8.65 (d, *J* = 6.0 Hz, 1H), 8.56 (d, *J* = 7.2 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.2 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 16.0 Hz, 1H), 6.40 – 6.33 (m, 1H), 3.86 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.00, 142.04, 140.02, 138.91, 138.58, 137.42, 136.26, 135.82, 135.73, 134.73, 133.46, 130.50, 130.39, 130.36, 128.64, 126.61, 126.48, 124.72, 122.97, 121.25, 120.63, 120.32, 119.53, 122.16, 50.49, 47.54, 40.13. HRMS: calculated for $C_{28}H_{26}N_4O_2S$ $[M+H]^+$: 483.18492; found: 483.18448.

(E)-*N*-(2-((3-(3-(quinoxalin-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 86

Prepared according to the general procedure. Yield: 80.5 mg, 162.4 µmol, 40.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.44 (s, 1H), 8.86 (d, *J* = 1.6 Hz, 1H), 8.82 (d, *J* = 1.6 Hz, 1H), 8.65 – 8.61 (m, 2H), 8.52 (dd, J_1 = 0.8 Hz, J_2 = 7.2 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 8.19 (s, 1H), 8.09 – 8.05 (m, 2H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.78 (s, 1H), 7.51 – 7.44 (m, 2H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.44 – 6.36 (m, 1H), 3.90 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.27, 146.94, 146.34, 143.91, 143.74, 143.13, 142.76, 140.89, 139.59, 137.72, 135.91, 135.63, 135.50, 133.13, 130.91, 130.67, 130.49, 130.43, 130.13, 128.86, 128.37, 128.20, 127.77, 127.198, 127.03, 120.05, 119.95, 50.44, 47.58, 40.13. HRMS: calculated for $C_{28}H_{25}N_5O_2S$ $[M+H]^+$: 496.18017; found: 496.17984.

(E)-*N*-(2-((3-(3-(5-fluoro-1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 87

Prepared according to the general procedure. Yield: 20.8 mg, 41.6 µmol, 10.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.41 (s, 1H), 8.65 (d, *J* = 4.4 Hz, 1H), 8.57 (d, *J* = 4.4 Hz, 1H), 8.51 (dd, J_1 = 0.8 Hz, J_2 = 4.8 Hz, 1H), 8.42 (d, *J* = 5.6

Hz, 1H), 7.89 (s, 1H), 7.84 (t, *J* = 5.2 Hz, 1H), 7.76 (dt, J_1 = 1.2 Hz, J_2 = 4.8 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.36 (dd, J_1 = 2.8 Hz, J_2 = 5.6 Hz, 1H), 7.20 (dd, J_1 = 2.0 Hz, J_2 = 6.8 Hz, 1H), 6.94 (d, *J* = 10.4 Hz, 1H), 6.88 (td, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 1H), 6.84 (s, 1H), 6.41 – 6.36 (m, 1H), 3.90 (d, *J* = 4.8 Hz, 2H), 3.22 – 3.16 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.12, 158.58, 154.24, 144.71, 140.59, 140.00, 137.49, 135.51, 135.44, 135.35, 135.17, 134.52, 132.70, 130.77, 130.70, 130.48, 127.86, 126.89, 126.77, 126.61, 124.91, 119.61, 119.14, 112.93, 111.10, 110.92, 105.66, 105.50, 100.33, 50.50, 47.59, 40.12. HRMS: calculated for $C_{28}H_{25}FN_4O_2S$ $[M+H]^+$: 501.17550; found: 501.17552.

(E)-*N*-(2-((3-(3-(2-(trifluoromethyl)pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 88

Prepared according to the general procedure. Yield: 37.7 mg, 73.6 μmol, 18.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.43 (s, 1H), 8.77 (d, *J* = 3.2 Hz, 1H), 8.66 (d, *J* = 4.0 Hz, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 8.51 (dd, J_1 = 0.4 Hz, J_2 = 4.8 Hz, 1H), 8.44 (d, *J* = 5.2 Hz, 1H), 8.10 (s, 1H), 7.96 (dd, J_1 = 0.8 Hz, J_2 = 3.6 Hz, 1H), 7.90 (s, 1H), 7.85 (t, *J* = 5.2 Hz, 1H), 7.79 (d, *J* = 5.2 Hz, 1H), 7.66 (d, *J* = 5.2 Hz, 1H), 7.58 (t, *J* = 5.2 Hz, 1H), 6.99 (d, *J* = 10.4 Hz, 1H), 6.46 – 6.41 (m, 1H), 3.91 (d, *J* = 4.4 Hz, 2H), 3.23 – 3.21 (m, 2H), 3.18 – 3.16 (m, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.29, 151.74, 151.64, 149.70 (q, *J* = 23.23 Hz), 144.80, 139.31, 138.61, 138.17, 135.43, 135.34, 135.14, 132.70, 131.07, 130.74, 129.28, 128.72, 128.66, 128.08, 127.83, 126.88, 125.87, 123.20 (q, *J* = 171.7 Hz), 120.58, 119.56, 119.52, 119.12, 50.39, 47.66, 40.14. HRMS: calculated for $C_{26}H_{23}F_3N_4O_2S$ $[M+H]^+$: 513.15666; found: 513.15630.

(E)-*N*-(2-((3-(3-(imidazo[1,2-a]pyridin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 89

Prepared according to the general procedure. Yield: 39.8 mg, 82.4 μmol, 20.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.43 (s, 1H), 9.14 (s, 1H), 8.66 (d, *J* = 4.0 Hz, 1H), 8.58 (d, *J* = 4.0 Hz, 1H), 8.52 (dd, J_1 = 0.8 Hz, J_2 = 4.8 Hz, 1H), 8.44 (d, *J* = 5.2 Hz, 1H), 8.30 (dd, J_1 = 1.2 Hz, J_2 = 6.4 Hz, 1H), 8.26 (s, 1H), 8.08 (s, 1H), 8.03 (d, *J* = 6.4 Hz, 1H), 7.85 (t, *J* = 4.8 Hz, 1H), 7.72 (d, *J* = 5.2 Hz, 1H), 7.64 (d, *J* = 5.2 Hz, 1H), 7.58 (t, *J* = 5.2 Hz, 1H), 6.99 (d, *J* = 10.8 Hz, 1H), 6.48 – 6.43 (m, 1H), 3.91 (d, *J* = 4.8 Hz, 2H), 3.23 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.17, 144.54, 140.80, 139.24, 138.25, 136.95, 135.45, 135.39, 135.25, 134.92, 132.77, 132.39, 131.07, 130.71, 128.70, 128.47, 127.91, 127.59, 127.01, 124.41, 120.70, 119.24, 117.08, 113.32, 50.38, 47.68, 40.13. HRMS: calculated for $C_{27}H_{25}N_5O_2S$ $[M+H]^+$: 484.18017; found: 484.17986.

(E)-*N*-(2-((3-(4-(4-methylnaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 90

Prepared according to the general procedure. Yield: 13.0 mg, 25.6 μmol, 6.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.46 (s, 1H), 8.66 (s, 1H), 8.62 (d, *J* = 6.0 Hz, 1H), 8.53 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 16.0 Hz, 1H), 6.40 – 6.33 (m, 1H), 3.89 (d, *J* = 7.2, 2H), 3.22 – 3.18 (m, 4H), 2.72 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.92, 144.00, 143.09, 139.90, 139.20, 135.72, 135.52, 135.47, 135.28, 134.23, 132.92, 132.71, 131.61, 130.66, 128.07, 127.90, 127.4, 127.19, 127.16, 126.77, 125.49, 119.51, 119.10, 50.57, 47.58, 40.14. HRMS: calculated for $C_{31}H_{29}N_3O_2S$ $[M+H]^+$: 508.20532; found: 508.20508.

(E)-*N*-(2-((3-(4-(4-methoxynaphthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 91

Prepared according to the general procedure. Yield: 20.1 mg, 38.4 μmol, 9.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.67 (s, 1H), 8.56 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.28 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz,

1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.78 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.39 (m, 4H), 7.30 (d, *J* = 8.0 Hz, 1H), 6.95 – 6.92 (m, 2H), 6.39 – 6.31 (m, 1H), 4.02 (s, 3H), 3.88 (d, *J* = 7.2 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.46, 153.47, 143.05, 142.93, 139.92, 135.88, 135.66, 135.61, 135.47, 133.51, 133.18, 133.07, 131.64, 128.37, 128.12, 127.91, 127.56, 127.03, 126.32, 126.09, 123.25, 119.94, 118.94, 104.55, 56.06, 50.57, 47.55, 40.13. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.20000.

(E)-*N*-(2-((3-(4-(6-methoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 92

Prepared according to the general procedure. Yield: 13.4 mg, 25.6 µmol, 6.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.58 (s, 1H), 8.76 (d, *J* = 6.0 Hz, 1H), 8.70 (s, 1H), 8.60 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 1.6 Hz, 1H), 7.92 (t, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 9.2 Hz, 2H), 7.75 – 7.71 (m, 3H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.90 (d, *J* = 15.6 Hz, 1H), 6.36 – 6.29 (m, 1H), 3.91 (s, 3H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 159.46, 152.77, 142.85, 141.44, 139.85, 136.57, 136.55, 135.97, 135.86, 135.56, 133.68, 130.77, 130.62, 128.89, 128.56, 128.31, 126.41, .126.33, 120.66, 120.23, 118.79, 106.57, 55.78, 50.60, 47.56, 40.15. HRMS: calculated for $C_{31}H_{29}N_3O_3S$ $[M+H]^+$: 524.20024; found: 524.20015.

(E)-*N*-(2-((3-(4-(6-ethoxynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 93

Prepared according to the general procedure. Yield: 14.0 mg, 26.0 µmol, 6.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.53 (s, 1H), 8.71 – 8.67 (m, 2H), 8.57 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.01 (s, 1H), 7.89 (t, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.75 – 7.70 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.21 (s, 1H), 7.13 (dd, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 1H), 6.90 (d, *J* = 15.6 Hz, 1H), 6.36 – 6.28 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.86 (d, *J* = 6.8 Hz, 2H), 3.19 (s, 4H), 1.45 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.70, 153.18, 142.88, 142.46, 139.86, 136.47, 136.18, 135.80, 135.72, 135.59, 135.54, 133.40, 130.74, 130.57, 128.5,4 128.30, 128.04, 126.36, 126.32, 120.50, 120.24, 118.77, 107.33, 64.56, 50360, 47.55, 40.14. HRMS: calculated for $C_{32}H_{31}N_3O_3S$ $[M+H]^+$: 538.21589; found: 538.21568.

(E)-*N*-(2-((3-(4-(6-(benzyloxy)naphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 94

Prepared according to the general procedure. Yield: 3.6 mg, 6.0 µmol, 1.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.46 (s, 1H), 8.67 (br s, 1H), 8.60 (d, *J* = 6.4 Hz, 1H), 8.52 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 2.0 Hz, 1H), 7.92 – 7.80 (m, 2H), 7.76 – 7.72 (m, 3H), 7.66 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.23 – 7.12 (m, 5H), 7.08 (t, *J* = 6.8 Hz, 1H), 6.90 (d, *J* = 15.6 Hz, 1H), 6.35 – 6.27 (m, 1H), 4.44 (s, 2H), 3.87 (d, *J* = 6.8 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 154.30, 154.05, 144.25, 142.94, 142.78, 139.97, 135.51, 135.39, 135.36, 135.30, 134.61, 130.63, 129.54, 129.38, 129.16, 128.50, 128.23, 128.01, 127.10, 126.55, 126.06, 125.26, 119.62, 119.43, 118.60, 50.62, 47.56, 40.13, 31.40. HRMS: calculated for $C_{37}H_{33}N_3O_3S$ $[M+H]^+$: 600.23154; found: 600.23144.

(E)-*N*-(2-((3-(4-(anthracen-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 95

Prepared according to the general procedure. Yield: 5.7 mg, 10.4 µmol, 2.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.55 (s, 1H), 8.73 (t, *J* = 6.0 Hz, 2H), 8.60 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.51 – 8.49 (m, 2H), 8.05 (d, *J* = 8.4 Hz, 2H),

7.92 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.44 (t, *J* = 6.8 Hz, 2H), 7.38 – 7.31 (m, 4H), 7.03 (d, *J* = 16.0 Hz, 1H), 6.48 – 6.40 (m, 1H), 3.93 (d, *J* = 7.2 Hz, 2H), 3.27 – 3.20 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.13, 142.26, 140.83, 139.86, 137.28, 136.27, 136.23, 135.82, 135.74, 133.46, 132.83, 132.79, 131.30, 130.59, 129.55, 128.64, 128.08, 127.89, 127.27, 126.60, 126.20, 120.31, 119.53, 50.56, 47.62, 40.18. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20500.

(E)-*N*-(2-((3-(4-(9H-fluoren-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 96

Prepared according to the general procedure. Yield: 17.0 mg, 32.0 µmol, 8.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 8.68 (s, 2H), 8.56 (d, *J* = 7.2 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 7.91 – 7.80 (m, 4H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 3H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 15.6 Hz, 1H), 6.35 – 6.28 (m, 1H), 3.93 (s, 2H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.33, 145.38, 144.85, 143.19, 142.69, 142.55, 142.47, 140.18, 139.85, 136.03, 135.76, 135.66, 135.61, 133.31, 130.58, 128.50, 128.31, 127.98, 127.93, 126.77, 126.09, 124.46, 121.17, 120.94, 120.07, 118.79, 50.60, 47.56, 40.14, 37.69. HRMS: calculated for $C_{33}H_{29}N_3O_2S$ $[M+H]^+$: 532.20532; found: 532.20511.

(E)-*N*-(2-((3-(4-(phenanthren-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 97

Prepared according to the general procedure. Yield: 21.5 mg, 39.6 µmol, 9.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 8.79 (d, *J* = 8.4 Hz, 1H), 8.74 – 8.66 (m, 3H), 8.57 (d, *J* = 7.2 Hz, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.67 – 7.57 (m, 6H), 7.52 – 7.48 (m, 3H), 6.95 (d, *J* = 15.6 Hz, 1H), 6.41 – 6.33 (m, 1H), 3.88 (d, *J* = 7.2 Hz, 2H), 3.21 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.10, 142.69, 142.27, 139.79, 139.31, 136.18, 136.02, 135.77, 135.69, 133.39, 132.83, 132.00, 131.51, 131.29, 130.52, 129.76, 128.58, 128.46, 128.02, 127.99, 127.92, 127.74, 127.63, 127.50, 124.15, 123.60, 120.24, 119.30, 50.54, 47.58, 40.14. HRMS: calculated for $C_{34}H_{29}N_3O_2S$ $[M+H]^+$: 544.20532; found: 544.20505.

(E)-*N*-(2-((3-(4-(dibenzo[b,d]furan-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 98

Prepared according to the general procedure. Yield: 32.7 mg, 61.2 µmol, 15.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.40 (s, 1H), 8.63 (br s, 1H), 8.59 (d, *J* = 6.0 Hz, 1H), 8.49 (d, *J* = 7.2 Hz, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.62 – 7.57 (m, 4H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 16.0 Hz, 1H), 6.37 – 6.30 (m, 1H), 3.86 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.36, 154.42, 153.85, 143.96, 139.71, 138.08, 136.16, 135.44, 132.84, 130.57, 130.05, 128.54, 128.18, 128.00, 127.62, 126.23, 126.12, 125.58, 124.14, 121.81, 121.11, 119.46, 119.30, 112.56, 50.52, 47.54, 40.10. HRMS: calculated for $C_{32}H_{27}N_3O_3S$ $[M+H]^+$: 534.18459; found: 534.18432.

(E)-*N*-(2-((3-(4-(phenoxathiin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 99

Prepared according to the general procedure. Yield: 31.0 mg, 54.8 µmol, 13.7%. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.50 (s, 1H), 8.73 (d, *J* = 5.6 Hz, 1H), 8.47 – 8.42 (m, 2H), 8.38 (d, *J* = 7.2 Hz, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.60 – 7.56 (m, 4H), 7.35 – 7.31 (m, 3H), 7.27 – 7.21 (m, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 15.6 Hz, 1H), 6.35 – 6.28 (m, 1H), 3.79 (d, *J* = 6.4 Hz, 2H), 3.10 (t, *J* = 5.2 Hz, 2H), 3.04 (d, *J* = 4.4 Hz, 2H). ^{13}C NMR (101

MHz, $(CD_3)_2SO$) δ 153.47, 151.85, 148.52, 144.74, 136.52, 136.41, 134.78, 133.84, 133.79, 132.84, 130.50, 130.31, 129.74, 129.33, 128.74, 128.42, 127.13, 126.60, 126.46, 125.37, 125.13, 121.28, 120.43, 120.01, 117.49, 117.06, 48.34, 45.35, 38.66. HRMS: calculated for $C_{32}H_{27}N_3O_3S_2$ $[M+H]^+$: 566.15666; found: 566.15645.

(E)-*N*-(2-((3-(4-(2,3-dihydrobenzofuran-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 100

Prepared according to the general procedure. Yield: 25.8 mg, 53.2 μmol, 13.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.67 (s, 2H), 8.55 (d, *J* = 7.2 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 5.6 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 3H), 7.34 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 6.85 (d, *J* = 15.6 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.31 – 6.23 (m, 1H), 4.55 (t, *J* = 8.8 Hz, 2H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.22 (t, *J* = 8.4 Hz, 2H), 3.19 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 161.40, 153.30, 143.05, 142.69, 139.88, 136.00, 135.71, 135.64, 134.91, 134.28, 133.26, 129.35, 128.45, 128.38, 128.00, 127.78, 124.48, 120.06, 118.39, 110.30, 72.52, 50.59, 47.50, 40.11, 30.49 . HRMS: calculated for $C_{28}H_{27}N_3O_3S$ $[M+H]^+$: 486.18459; found: 486.18437.

(E)-*N*-(2-((3-(4-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 101

Prepared according to the general procedure. Yield: 30.1 mg, 58.4 μmol, 14.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 8.67 (t, *J* = 6.0 Hz, 2H), 8.56 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.21 – 7.17 (m, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 15.6 1H), 6.32 – 6.25 (m, 1H), 4.17 (q, *J* = 5.2 Hz, 4H), 3.85 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 4H), 2.19 – 2.13 (m, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.09, 152.96, 152.52, 142.23, 140.82, 139.71, 136.95, 136.20, 135.79, 135.69, 135.52, 133.39, 130.52, 128.60, 128.42, 127.89, 127.77, 123.11, 122.74, 120.88, 120.27, 118.82, 71.98, 71.95, 50.54, 47.52, 40.11, 33.20. HRMS: calculated for $C_{29}H_{29}N_3O_4S$ $[M+H]^+$: 516.19515; found: 516.19496.

(E)-*N*-(2-((3-(4'-morpholino-[1,1'-biphenyl]-4-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 102

Prepared according to the general procedure. Yield: 34.9 mg, 66.0 μmol, 16.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.65 (s, 1H), 8.82 (d, *J* = 6.4 Hz, 1H), 8.72 (br s, 1H), 8.64 (d, *J* = 7.6 Hz, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.61 (dd, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 4H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 15.6 Hz, 1H), 6.33 – 6.26 (m, 1H), 3.90 – 3.85 (m, 6H), 3.28 (t, *J* = 4.8 Hz, 4H), 3.21 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.33, 150.64, 142.25, 140.47, 139.87, 137.01, 136.16, 136.05, 135.26, 134.65, 134.01, 130.51, 129.23, 128.67, 128.48, 127.66, 121.13, 118.59, 118.00, 67.50, 51.39, 50.61, 47.55, 40.17. HRMS: calculated for $C_{30}H_{32}N_4O_3S$ $[M+H]^+$: 529.22679; found: 529.22648.

(E)-*N*-(2-((3-(4''-ethoxy-[1,1':4',1''-terphenyl]-4-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 103

Prepared according to the general procedure. Yield: 16.5 mg, 29.2 μmol, 7.3%. ^{1}H NMR (400 MHz, $(CD_3)_2OD$) δ 9.51 (s, 1H), 8.73 (d, *J* = 6.0 Hz, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.43 (d, *J* = 6.4 Hz, 1H), 8.38 (d, *J* = 7.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.78 – 7.69 (m, 6H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.32 – 6.24 (m, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.77 (br s, 2H), 3.08 (t, *J* = 5.6 Hz, 2H), 3.03 (s, 2H), 1.35 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2OD$) δ 158.33, 153.43, 144.64, 139.62, 139.09, 137.54, 136.49, 134.51, 133.88, 133.77, 132.88, 131.66, 130.33, 128.73, 127.65, 127.25, 126.97, 126.63, 126.50, 119.59, 117.07,

114.91, 63.12, 48.40, 45.39, 38.67, 14.67. HRMS: calculated for $C_{34}H_{33}N_3O_3S$ $[M+H]^+$: 564.23154; found: 564.23129.

(E)-*N*-(2-((3-(3'-(benzyloxy)-[1,1'-biphenyl]-4-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 104

Prepared according to the general procedure. Yield: 15.8 mg, 28.8 µmol, 7.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.44 (s, 1H), 8.65 (br s, 1H), 8.59 (d, *J* = 6.0 Hz, 1H), 8.51 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.39 – 7.32 (m, 4H), 7.23 – 7.20 (m, 2H), 6.99 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 6.89 (d, *J* = 16.0 Hz, 1H), 6.35 – 6.27 (m, 1H), 5.14 (s, 2H), 3.86 (d, *J* = 7.2 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.72, 154.10, 144.38, 143.06, 142.74, 139.78, 138.72, 135.94, 135.47, 135.29, 132.80, 131.00, 129.52, 128.90, 128.60, 128.44, 128.37, 127.95, 120.56, 119.32, 118.99, 115.09, 114.62, 71.09, 50.56, 47.57, 40.12. HRMS: calculated for $C_{33}H_{31}N_3O_3S$ $[M+H]^+$: 550.21589; found: 550.21560.

(E)-*N*-(2-((3-(4-(pyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 105

Prepared according to the general procedure. Yield: 12.8 mg, 28.8 µmol, 7.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.57 (s, 1H), 9.14 (s, 1H), 8.77 (d, *J* = 8.4 Hz, 2H), 8.73 – 8.68 (m, 2H), 8.60 (d, *J* = 7.2 Hz, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.05 (t, *J* = 6.4 Hz, 1H), 7.93 (t, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 15.6 Hz, 1H), 6.47 – 6.39 (m, 1H), 3.90 (d, *J* = 7.2 Hz, 2H), 3.21 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.15, 143.40, 142.89, 142.48, 142.25, 138.86, 135.46, 136.25, 135.92, 135.87, 135.78, 133.50, 129.11, 128.86, 128.67, 128.10, 121.06, 120.34, 50.41, 47.73, 40.16. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16925.

(E)-*N*-(2-((3-(4-(pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 106

Prepared according to the general procedure. Yield: 28.8 mg, 64.8 µmol, 16.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.46 (s, 1H), 8.81 (s, 2H), 8.66 (s, 1H), 8.61 (d, *J* = 6.0 Hz, 1H), 8.53 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 6.4 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 16.0 Hz, 1H), 6.52 – 6.44 (m, 1H), 3.91 (d, *J* = 7.2 Hz, 2H), 3.23 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.88, 153.92, 144.39, 144.00, 140.17, 138.54, 136.34, 135.53, 135.49, 132.91, 129.44, 127.14, 124.90, 122.05, 119.52, 50.32, 47.74, 40.12. HRMS: calculated for $C_{25}H_{24}N_4O_2S$ $[M+H]^+$: 445.16927; found: 445.16901.

(E)-*N*-(2-((3-(4-(6-methoxypyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 107

Prepared according to the general procedure. Yield: 28.7 mg, 60.4 µmol, 15.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.56 (s, 1H), 8.73 – 8.68 (m, 2H), 8.59 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.52 (d, *J* = 8.0 Hz, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 7.99 (dd, J_1 = 2.8 Hz, J_2 = 8.8 Hz, 1H), 7.93 (t, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 6.93 (s, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 6.37 – 6.29 (m, 1H), 3.96 (s, 3H), 3.87 (d, *J* = 7.2 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.17, 153.08, 145.41, 142.09, 139.59, 139.19, 139.15, 136.33, 136.04, 135.88, 135.77, 133.51, 130.86, 130.64, 128.68, 127.76, 120.36, 119.25, 111.78, 54.40, 50.54, 47.59, 40.14. HRMS: calculated for $C_{26}H_{26}N_4O_3S$ $[M+H]^+$: 475.17984; found: 475.17958.

(E)-*N*-(2-((3-(4-(2-fluoropyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 108

Prepared according to the general procedure. Yield: 25.5 mg, 55.2 µmol, 13.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.67 (br s, 1H), 8.62 (d, *J* = 5.6, 1H), 8.54 (dd, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 5.2, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.65 – 7.62 (m, 3H), 7.39 (s, 1H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.44 – 6.37 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.22 – 3.16 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 167.15, 164.79, 155.21, 155.13, 153.86, 149.01, 148.87, 143.84, 139.06, 138.46, 135.15, 135.58, 135.49, 132.96, 128.84, 128.65, 128.15, 120.66, 120.62, 107.97, 107.59, 50.41, 47.68, 40.12. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15927.

(E)-*N*-(2-((3-(4-(pyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 109

Prepared according to the general procedure. Yield: 37.6 mg, 84.4 µmol, 21.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.54 (s, 1H), 9.14 (s, 1H), 9.09 (s, 2H), 8.69 (s, 2H), 8.58 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 7.92 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.44 – 6.36 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.24 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 158.02, 155.98, 153.31, 142.59, 139.12, 135.75, 136.11, 135.80, 135.68, 135.49, 135.34, 133.36, 129.00, 128.55, 128.51, 120.48, 120.13, 50.43, 47.68, 40.14. HRMS: calculated for $C_{24}H_{23}N_5O_2S$ $[M+H]^+$: 446.16452; found: 446.16479.

(E)-*N*-(2-((3-(4-(2-methoxypyrimidin-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 110

Prepared according to the general procedure. Yield: 35.2 mg, 74.0 µmol, 18.5%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.56 (s, 1H), 8.85 (s, 2H), 8.70 (s, 2H), 8.58 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 15.6 Hz, 1H), 6.40 – 6.33 (m, 1H), 4.06 (s, 3H), 3.88 (d, *J* = 7.6 Hz, 2H), 3.20 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 166.21, 158.53, 158.48, 153.31, 142.60, 139.35, 136.84, 136.10, 135.81, 135.71, 133.35, 129.09, 128.89, 128.56, 127.91, 119.86, 55.69, 50.48, 47.65, 40.15. HRMS: calculated for $C_{25}H_{25}N_5O_3S$ $[M+H]^+$: 476.17509; found: 476.17537.

(E)-*N*-(2-((3-(4-(2-morpholinopyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 111

Prepared according to the general procedure. Yield: 26.7 mg, 50.4 µmol, 12.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.58 (s, 1H), 8.71 (s, 2H), 8.59 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.16 (dd, J_1 = 1.6 Hz, J_2 = 5.6 Hz, 1H), 7.95 – 7.91 (m, 2H), 7.68 – 7.61 (m, 4H), 7.27 (dd, J_1 = 6.0 Hz, J_2 = 7.6 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.44 – 6.36 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.64 (t, *J* = 4.4 Hz, 4H), 3.23 – 3.18 (m, 8H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.16, 153.30, 146.03, 142.57, 141.13, 139.11, 137.39, 136.12, 135.82, 135.71, 130.74, 129.51, 128.88, 128.57, 120.44, 118.43, 66.95, 50.43, 50.33, 47.71, 40.15. HRMS: calculated for $C_{29}H_{31}N_5O_3S$ $[M+H]^+$: 530.22204; found: 530.22190.

(E)-*N*-(2-((3-(4-(isoquinolin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 112

Prepared according to the general procedure. Yield: 41.9 mg, 84.8 µmol, 21.2%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.66 (s, 1H), 9.56 (d, *J* = 2.4 Hz, 1H), 9.25 (d, *J* = 2.0 Hz, 1H), 8.82 (d, *J* = 6.0 Hz, 1H), 8.78 (br s, 1H), 8.65 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.57 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.08 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.98 (t, *J* = 7.6 Hz, 1H), 7.94 – 7.90 (m, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.48 –

6.40 (m, 1H), 3.91 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.28, 146.20, 142.24, 140.56, 140.36, 138.92, 138.06, 137.09, 136.27, 136.18, 136.01, 135.39, 134.93, 134.01, 130.89, 130.50, 130.40, 129.26, 129.12, 128.91, 128.79, 123.25, 121.23, 120.87, 50.43, 47.69, 40.16. HRMS: calculated for $C_{29}H_{26}N_4O_2S$ $[M+H]^+$: 495.18492; found: 495.18465.

(E)-*N*-(2-((3-(4-(6-fluoropyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 113

Prepared according to the general procedure. Yield: 38.7 mg, 83.6 µmol, 20.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.67 (s, 1H), 8.84 (d, *J* = 6.4 Hz, 1H), 8.72 (br s, 1H), 8.65 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.57 (d, *J* = 8.4 Hz, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 7.16 (td, J_1 = 2.4 Hz, J_2 = 7.6 Hz, 1H), 7.98 (t, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.14 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 6.90 (d, *J* = 16.0 Hz, 1H), 6.40 – 6.32 (m, 1H), 3.88 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 165.70, 163.33, 152.06, 146.39, 146.24, 141.58, 141.50, 139.88, 139.27, 137.99, 137.28, 136.81, 136.24, 136.06, 135.71, 135.67, 134.15, 130.43, 129.39, 128.76, 128.35, 121.37, 119.89, 110.92, 110.55, 50.48, 47.61, 40.15. HRMS: calculated for $C_{25}H_{23}FN_4O_2S$ $[M+H]^+$: 463.15985; found: 463.15904.

(E)-*N*-(2-((3-(4-(1-methyl-1H-indazol-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 114

Prepared according to the general procedure. Yield: 141.4 mg, 284.4 µmol, 71.1%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.74 (d, *J* = 6.8 Hz, 1H), 8.61 (d, *J* = 6.4 Hz, 1H), 8.55 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 7.89 (s, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.56 (s, 1H), 7.54 (s, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.29 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 6.80 (d, *J* = 16.0 Hz, 1H), 6.33 – 6.25 (m, 1H), 3.97 (s, 3H), 3.84 (d, *J* = 7.2 Hz, 2H), 3.23 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 152.10, 142.44, 141.65, 140.46, 140.13, 139.41, 136.79, 136.10, 135.92, 135.88, 135.72, 133.68, 133.48, 130.17, 128.96, 128.62, 128.37, 124.31, 122.36, 121.49, 120.89, 119.19, 107.91, 50.51, 47.52, 40.09, 15.54. HRMS: calculated for $C_{28}H_{27}N_5O_2S$ $[M+H]^+$: 498.19582; found: 498.19516.

(E)-*N*-(2-((3-([1,1':3',1''-terphenyl]-4-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 115

Prepared according to the general procedure. Yield: 91.3 mg, 175.6 µmol, 43.9%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.42 (s, 1H), 8.62 (s, 2H), 8.50 (dd, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.63 (t, *J* = 7.6 Hz, 4H), 7.57 – 7.53 (m, 3H), 7.51 – 7.47 (m, 2H), 7.45 – 7.41 (m, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 16.0, 1H), 6.34 – 6.26 (m, 1H), 3.84 (d, *J* = 6.8 Hz, 2H), 3.18 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.65, 143.54, 143.12, 142.69, 142.23, 142.12, 139.65, 135.92, 135.58, 135.52, 135.48, 132.97, 130.53, 130.45, 129.89, 128.50, 128.40, 128.29, 128.14, 128.09, 127.32, 126.83, 126.54, 126.46, 119.65, 119.06, 50.52, 47.53, 40.09. HRMS: calculated for $C_{32}H_{29}N_3O_2S$ $[M+H]^+$: 520.20532; found: 520.20502.

(E)-*N*-(2-((3-(4-(1H-pyrazol-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 116

Prepared according to the general procedure. Yield: 59.7 mg, 137.6 µmol, 34.4%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.66 (s, 1H), 8.87 (d, *J* = 6.8 Hz, 1H), 8.69 (d, *J* = 6.4 Hz, 1H), 8.65 (d, *J* = 7.2 Hz, 1H), 8.55 (d, *J* = 8.4 Hz, 1H), 8.00 (s, 2H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 15.6 Hz, 1H), 6.29 – 6.21 (m, 1H), 3.84 (d, *J* = 7.2 Hz, 2H), 3.23 – 3.21 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 151.69, 139.79, 139.34,

137.48, 136.30, 136.10, 134.85, 134.36, 132.18, 130.46, 130.30, 129.52, 128.50, 127.72, 126.73, 123.15, 121.59, 118.30, 50.59, 46.20, 40.14. HRMS: calculated for $C_{23}H_{23}N_5O_2S$ $[M+H]^+$: 434.16452; found: 434.16436.

(E)-*N*-(2-((3-(4-(thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 117

Prepared according to the general procedure. Yield: 11.9 mg, 26.4 µmol, 6.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.49 (s, 1H), 8.68 (d, *J* = 6.0 Hz, 1H), 8.63 (d, *J* = 6.0 Hz, 1H), 8.54 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.66 (dd, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.37 (m, 2H), 7.11 (dd, J_1 = 4.0 Hz, J_2 = 5.2 Hz, 1H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.34 – 6.26 (m, 1H), 3.86 (d, *J* = 7.2 Hz, 2H), 3.21 – 3.17 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.87, 143.85, 139.68, 136.36, 135.85, 135.61, 135.57, 133.01, 129.30, 128.60, 128.16, 126.99, 126.38, 124.69, 119.58, 118.89, 50.57, 47.60, 40.15. HRMS: calculated for $C_{24}H_{23}N_3O_2S_2$ $[M+H]^+$: 450.13044; found: 450.13040.

(E)-*N*-(2-((3-(4-(benzo[b]thiophen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 118

Prepared according to the general procedure. Yield: 81.3 mg, 162.8 µmol, 40.7%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 8.73 (d, *J* = 6.0 Hz, 1H), 8.48 (s, 1H), 8.46 (d, *J* = 3.2 Hz, 1H), 8.40 (d, *J* = 7.2 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.40 – 7.32 (m, 2H), 6.80 (d, *J* = 16.0 Hz, 1H), 6.35 – 6.27 (m, 1H), 3.74 (s, 2H), 3.12 (t, *J* = 5.6 Hz, 2H), 3.06 (d, *J* = 5.2 Hz, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.32, 144.30, 142.75, 140.56, 138.75, 136.30, 135.66, 134.05, 133.97, 133.90, 133.59, 133.15, 130.58, 128.83, 127.50, 126.68, 126.49, 124.98, 124.93, 123.92, 122.53, 120.45, 120.28, 117.41, 48.44, 45.54, 38.76. HRMS: calculated for $C_{28}H_{25}N_3O_2S_2$ $[M+H]^+$: 500.14610; found: 500.14564.

(E)-*N*-(2-((3-(4-(1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 119

Prepared according to the general procedure. Yield: 51.3 mg, 106.4 µmol, 26.6%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.43 (s, 1H), 8.66 (d, *J* = 6.0 Hz, 1H), 8.62 (d, *J* = 6.4 Hz, 1H), 8.51 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 6.4 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 16.0 Hz, 1H), 6.28 – 6.21 (m, 1H), 3.78 (d, *J* = 6.8 Hz, 2H), 3.15 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.05, 142.27, 139.63, 138.95, 138.44, 136.07, 135.70, 135.58, 134.44, 133.28, 130.42, 128.46, 126.26, 123.04, 121.27, 120.64, 120.14, 118.65, 112.16, 50.52, 47.48, 40.07. HRMS: calculated for $C_{28}H_{26}N_4O_2S$ $[M+H]^+$: 483.18492; found: 483.18492.

(E)-*N*-(2-((3-(4-(quinoxalin-6-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 120

Prepared according to the general procedure. Yield: 134.4 mg, 271.2 µmol, 67.8%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.63 (s, 1H), 8.83 – 8.77 (m, 3H), 8.70 (d, *J* = 6.4 Hz, 1H), 8.63 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.17 (s, 1H), 8.05 (s, 2H), 7.96 (t, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.40 – 6.32 (m, 1H), 3.89 (d, *J* = 7.2 Hz, 2H), 3.25 (s, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 151.90, 146.93, 146.27, 143.95, 143.34, 143.16, 140.45, 139.71, 139.24, 137.28, 136.93, 136.19, 136.00, 134.10, 130.67, 130.49, 130.30, 129.37, 127.73, 128.68, 127.06, 121.3,7, 119.97, 50.49, 47.62, 40.16. HRMS: calculated for $C_{28}H_{25}N_5O_2S$ $[M+H]^+$: 496.18017; found: 496.17969.

(E)-*N*-(2-((3-(4-(5-fluoro-1H-indol-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 121

Prepared according to the general procedure. Yield: 44.7 mg, 89.2 μmol, 22.3%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.44 (s, 1H), 8.66 (s, 1H), 8.59 (d, *J* = 4.0 Hz, 1H), 8.52 (d, *J* = 4.8 Hz, 1H), 8.43 (d, *J* = 5.2 Hz, 1H), 7.85 (t, *J* = 5.2 Hz, 1H), 7.80 (d, *J* = 5.6 Hz, 2H), 7.54 (d, *J* = 5.6 Hz, 2H), 7.34 (dd, J_1 = 3.2 Hz, J_2 = 6.0 Hz, 1H), 7.19 (dd, J_1 = 2.0 Hz, J_2 = 6.8 Hz, 1H), 6.90 – 6.83 (m, 2H), 6.34 – 6.29 (m, 1H), 3.87 (d, *J* = 4.8 Hz, 2H), 3.20 – 3.16 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.13, 158.59, 154.14, 144.45, 140.38, 139.74, 135.89, 135.62, 135.47, 135.43, 135.28, 134.35, 132.79, 130.73, 130.66, 128.54, 127.94, 126.48, 119.302, 118.89, 112.91, 112.84, 111.17, 111.00, 105.64, 105.48, 50.58, 47.58, 40.13. HRMS: calculated for $C_{28}H_{25}FN_4O_2S$ $[M+H]^+$: 501.17550; found: 501.17577.

(E)-*N*-(2-((3-(4-(2-(trifluoromethyl)pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 122

Prepared according to the general procedure. Yield: 53.3 mg, 104.0 μmol, 26.0%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.50 (s, 1H), 8.75 (d, *J* = 3.2 Hz, 1H), 8.68 (s, 1H), 8.64 (d, *J* = 4.0 Hz, 1H), 8.54 (d, *J* = 4.8 Hz, 1H), 8.48 (d, *J* = 5.6 Hz, 1H), 8.09 (s, 1H), 7.96 (d, *J* = 3.2 Hz, 1H), 7.89 (t, *J* = 5.2 Hz, 1H), 7.85 (d, *J* = 5.6 Hz, 2H), 7.67 (d, *J* = 5.6 Hz, 2H), 6.95 (d, *J* = 10.4 Hz, 1H), 6.44 – 6.39 (m, 1H), 3.89 (d, *J* = 4.8 Hz, 2H), 3.22 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.77, 151.73, 151.22, 149.71 (q, *J* = 23.23 Hz), 143.63, 139.03, 138.60, 138.00, 135.63, 135.55, 133.05, 130.71, 128.97, 128.74, 128.22, 125.53, 123.10 (q, *J* = 182.81 Hz), 120.86, 119.70, 119.28, 118.24, 50.42, 47.71, 40.14. HRMS: calculated for $C_{26}H_{23}F_3N_4O_2S$ $[M+H]^+$: 513.15666; found: 513.15610.

(E)-*N*-(2-((3-(4-(imidazo[1,2-a]pyridin-7-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 123

Prepared according to the general procedure. Yield: 43.9 mg, 90.8 μmol, 22.7%. ^{1}H NMR (400 MHz, CD_3OD) δ 9.51 (s, 1H), 9.14 (s, 1H), 8.68 (s, 1H), 8.65 (d, *J* = 4.0 Hz, 1H), 8.56 (dd, J_1 = 0.8 Hz, J_2 = 5.2 Hz, 1H), 8.48 (d, *J* = 5.6 Hz, 1H), 8.31 (dd, J_1 = 1.2 Hz, J_2 = 6.0 Hz, 1H), 8.08 (d, *J* = 1.2 Hz, 1H), 8.02 (d, *J* = 6.4 Hz, 1H), 7.90 (t, *J* = 4.8 Hz, 1H), 7.79 (d, *J* = 5.6 Hz, 2H), 7.68 (d, *J* = 5.6 Hz, 1H), 6.95 (d, *J* = 10.4 Hz, 1H), 6.44 – 6.39 (m, 1H), 3.89 (d, *J* = 4.8 Hz, 2H), 3.23 – 3.18 (m, 4H). ^{13}C NMR (101 MHz, CD_3OD) δ 153.62, 143.32, 140.69, 139.00, 137.81, 136.44, 135.79, 135.67, 135.60, 134.80, 133.15, 132.17, 130.67, 129.02, 128.73, 128.32, 127.41, 124.25, 120.63, 119.84, 117.12, 113.27, 50.43, 47.70, 40.14. HRMS: calculated for $C_{27}H_{25}N_5O_2S$ $[M+H]^+$: 484.18017; found: 484.17986.

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