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Author: Liu, N.
Title: Development of kinase inhibitors and activity-based probes
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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. 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/AKT 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 Kinomescan™ assay, which was performed by the company LeadHunter discovery services. 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 Kinomescan™ kinase assay applied to identify off targets of compounds 2 and 3.
Chapter 3

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

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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).
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.\textsuperscript{14} This sequence started with reduction of nitrile 14 using DiBAIH 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\textsubscript{4} and the crude isoquinolinesulfonamide 18 was protected with a Boc-group to yield pure E-isoquinolinesulfonamide 19. A Suzuki reaction (Pd(PPh\textsubscript{3})\textsubscript{4}, K\textsubscript{2}CO\textsubscript{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) DiBAIH, -78 °C, Et\textsubscript{2}O/DCM 1:1 v/v; c) i) SOCl\textsubscript{2}, reflux, DMF; ii) ethylenediamine, DCM, 0 °C, 69%; d) i) MeOH, -100 °C; ii) 17, MeOH, RT; iv) NaBH\textsubscript{4}, -10 °C – RT; e) Boc\textsubscript{2}O, TEA, DCM, 0 °C. 48%; f) 20, K\textsubscript{2}CO\textsubscript{3}, Pd(PPh\textsubscript{3})\textsubscript{4}, DMF, 90 °C; g) TFA, DCM, H\textsubscript{2}O, 13%.
Table 2. Yields (%) of the Suzuki cross coupling reaction.

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## Chapter 3

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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 LiAlH₄ 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 (NH₄)₆Mo₇O₂₄·4H₂O (25 g/L) and (NH₄)₄Ce(SO₄)₄·2H₂O (10 g/L) in 10% sulphuric acid, a solution of KMnO₄ (20 g/L) and K₂CO₃ (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. ¹H- and ¹³C-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 (¹H-NMR) or CDCl₃ (¹³C-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 [α]D²⁵ 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/H₂O. 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. NaHSO₃ (800 mL). The mixture was diluted with H₂O (800 mL) and Et₂O (800 mL) and the layers were separated. The aqueous phase was extracted with Et₂O (3 x 600 mL) and the combined organic phases were washed with sat. aq. NaHCO₃ and brine, dried over MgSO₄, 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%).

¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 16.4 Hz, 1H), 7.58 (dd, J₁ = 1.2 Hz, J₂ = 8.4 Hz, 1H), 7.50 (dd, J₁ = 1.6 Hz, J₂ = 8.0 Hz, 1H), 7.34 (t, J = 6.8 Hz, 1H), 7.26 (td, J₁ = 1.6 Hz, J₂ = 8.0 Hz, 1H), 5.84 (d, J = 16.4 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) 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%).

¹H NMR (400 MHz, CDCl₃) 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).

¹³C NMR (101 MHz, CDCl₃) 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%).

¹H NMR (400 MHz, CDCl₃) δ 7.51 (d, J = 8.8 Hz, 2H), 7.33 – 7.29 (m, 3H), 5.89 (d, J = 16.8 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) 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 H₂O (300 mL) at 0 °C. NaHCO₃ (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 MgSO₄. 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 MgSO₄, 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.

¹H NMR (400 MHz, CDCl₃, Me₄Si) δ 9.36 (1H, s, CH₆), 8.67 (1H, d, J = 8.4 Hz, CH₆), 8.47 – 8.43 (2H, m, 2 x CH₃), 8.21 (1H, d, J = 11.2 Hz, CH₆), 7.71 (1H, t, J = 10.0 Hz, CH₆), 3.45 (3H, bs, NH₂).
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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\(_3\)) \(\delta 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\(_2\)O (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 -10 °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\(_2\)O (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\(_2\)O (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\(_2\)O (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\(_3\)) \(\delta 9.30 (s, 1H), 8.59 (d, J = 6.0 \text{ Hz}, 1H), 8.44 (d, J = 6.0 \text{ Hz}, 1H), 8.40 (d, J = 7.2 \text{ Hz}, 1H), 8.11 (d, J = 8.0 \text{ Hz}, 1H), 7.60 (t, J = 8.0 \text{ Hz}, 1H), 7.50 (d, J = 7.6 \text{ Hz}, 1H), 7.38 (d, J = 7.6 \text{ Hz}, 1H), 7.23 (br s, 1H), 7.09 (t, J = 7.2 \text{ Hz}, 1H), 6.67 (d, J = 14.8 \text{ Hz}, 1H), 5.97 – 5.90 (m, 1H), 3.89 (d, J = 6.0 \text{ Hz}, 2H), 3.37 (s, 2H), 3.17 – 3.13 (m, 2H), 1.43 (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 153.26, 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\(_3\)) \(\delta 9.29 (s, 1H), 8.57 (d, J = 6.0 \text{ Hz}, 1H), 8.42 (d, J = 6.0 \text{ Hz}, 1H), 8.36 (d, J = 7.2 \text{ Hz}, 1H), 8.14 (d, J = 8.4 \text{ Hz}, 1H), 7.59 (t, J = 7.6 \text{ Hz}, 1H), 7.42 (s, 1H), 7.33 – 7.31 (m, 2H), 7.21 – 7.17 (m, 2H), 6.29 (d, J = 16.4 \text{ Hz}, 1H), 6.04 – 6.00 (m, 1H), 3.87 (d, J = 5.2 \text{ Hz}, 2H), 3.33 (s, 2H), 3.10 (s, 2H), 1.42 (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 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), 6.60 (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$_2$CO$_3$ (2M in H$_2$O) and Pd(PPh$_3$)$_4$ (0.017M in DCM) were thoroughly degassed in a sonication bath for 15 minutes. K$_2$CO$_3$ (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$_2$OD) 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$_2$OD) 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$_4$O$_3$ [M+H]$^+$: 508.20532; found: 508.20508.

**E-N-(2-((3-(2-(4-methoxy-naphthalen-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$_2$OD) 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$_2$OD) 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$_4$O$_3$ [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$_2$OD) 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), 7.46 – 7.38 (m, 2H), 7.31 – 7.20 (m, 4H), 6.99 (d, J = 7.6 Hz, 1H), 6.78 (d, J = 16.0 Hz, 1H), 6.50 (d, J = 8.0 Hz, 2H), 6.34 – 6.21 (m, 2H), 5.71 (d, J = 7.2 Hz, 2H).
7.68 – 7.66 (m, 1H), 7.63 (s, 1H), 7.41 – 7.33 (m, 4H), 7.22 (s, 1H), 7.09 (dd, J1 = 2.4 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C31H23N3O5S [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%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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 C32H33N3O5S [M+H]+: 538.21589; found: 538.21569.

(E)-N-(2-[(3-[(2-(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%. 1H NMR (400 MHz, CD3OD) 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), 6.89 (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). 13C NMR (101 MHz, CD3OD) δ 154.30, 153.37, 143.04, 142.81, 142.75, 139.45, 135.91, 135.85, 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 C38H33N3O5S [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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 5.2 Hz, J2 = 18.4 Hz, 4H). 13C NMR (101 MHz, CD3OD) 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 C34H33N3O5S [M+H]+: 544.20532; found: 544.20506.

(E)-N-(2-[(3-[(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%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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_{31}H_{29}N_{5}O_{5}S [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%. ^1H NMR (400 MHz, CD$_2$OD) 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). ^13C NMR (101 MHz, CD$_2$OD) δ 153.68, 143.60, 141.06, 138.59, 138.07, 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$_{48}$H$_{39}$N$_{5}$O$_{5}$S [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%. ^1H NMR (400 MHz, CD$_2$OD) 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 = 7.6 Hz, J = 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 = 4.4 Hz, J = 11.2 Hz, 4H). ^13C NMR (101 MHz, CD$_2$OD) 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, 124.25, 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$_{5}$O$_{5}$S [M+H]^+ 534.18459; found: 534.18422.

**(E)-N-[2-((3-([2-phenoxythien-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%. ^1H NMR (400 MHz, CD$_2$OD) 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). ^13C NMR (101 MHz, CD$_2$OD) 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$_{5}$O$_{5}$S [M+H]^+ 566.15656; found: 566.15650.

**(E)-N-[2-((3-([2-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%. ^1H NMR (400 MHz, CD$_2$OD) δ 9.66 (s, 1H), 8.83 (d, J = 6.4 Hz, 1H), 8.69 (d, J = 6.0 Hz, 1H), 8.58 (d, J = 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). ^13C NMR (101 MHz, CD$_2$OD) 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,
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109.70, 72.45, 50.52, 45.59, 40.01, 30.47. HRMS: calculated for $C_{29}H_{27}N_2O_3S$ [M+H]$^+$: 486.18459; found: 486.18411.

Prepared according to the general procedure. Yield: 58.8 mg, 114.0 µmol, 28.5%. $^1$H NMR (400 MHz, CD$_2$OD) $\delta$ 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$_2$OD) $\delta$ 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 $C_{29}H_{27}N_2O_3S$ [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$_2$OD) $\delta$ 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$_2$OD) $\delta$ 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 $C_{30}H_{28}N_4O_5S$ [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$_3$)$_2$SO) $\delta$ 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$_3$)$_2$SO) $\delta$ 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 $C_{30}H_{28}N_4O_5S$ [M+H]$^+$: 564.23154; found: 564.23131.

(E)-N-[2-[[3-[[3'-(benzyl oxygen)-[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$_2$OD) $\delta$ 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$_2$OD) $\delta$ 156.09, 153.36, 142.94, 142.76, 142.54, 140.97, 139.45, 136.02, 135.74, 135.61, 134.60, 133.27,

(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$_2$OD) 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$_2$OD) 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 $C_{33}H_{32}N_7O_5S [M+H]^+$: 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$_2$OD) 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$_2$OD) 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 $C_{33}H_{32}N_7O_5S [M+H]^+$: 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$_2$OD) 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$_2$OD) 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 $C_{38}H_{36}N_7O_5S [M+H]^+$: 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$_2$OD) 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$_2$OD) 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 $C_{38}H_{35}FNO_5S [M+H]^+$: 463.15985; found: 463.15949.
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(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%. ¹H NMR (400 MHz, CD₂OD) δ 9.59 (s, 1H), 9.16 (s, 1H), 8.78 – 8.74 (m, 3H), 8.69 – 8.67 (m, 1H), 8.55 (dd, J₁ = 7.2 Hz, J₂ = 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). ¹³C NMR (101 MHz, CD₂OD) δ 158.19, 158.03, 152.58, 141.14, 137.49, 136.70, 135.98, 135.75, 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 C₂₄H₂₃N₂O₂S [M+H⁺]: 446.16452; found: 446.16414.

(E)-N-(2-((3-(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%. ¹H NMR (400 MHz, CD₂OD) 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). ¹³C NMR (101 MHz, CD₂OD) δ 156.87, 160.56, 152.58, 141.14, 137.49, 136.70, 135.98, 135.75, 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 C₂₅H₂₄N₂O₃S [M+H⁺]: 476.17509; found: 476.17481.

(E)-N-(2-((3-(2-(morpholinpypyridin-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%. ¹H NMR (400 MHz, CD₂OD) δ 9.66 (s, 1H), 8.79 (d, J = 6.0 Hz, 1H), 8.72 (s, 1H), 8.59 (d, J₁ = 2.8 Hz, J₂ = 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). ¹³C NMR (101 MHz, CD₂OD) 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 C₂₅H₂₅N₂O₃S [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%. ¹H NMR (400 MHz, CD₂OD) 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, J₁ = 8.0 Hz, J₂ = 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). ¹³C NMR (101 MHz, CD₂OD) 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 C₂₅H₂₆N₂O₂S [M+H⁺]: 495.18429; 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%. ¹H NMR (400 MHz, CD₂OD) δ 9.67 (s, 1H), 8.84 (d, J = 6.8 Hz, 1H), 8.69 (d, J = 6.4 Hz, 1H), 8.60 (dd, J₁ = 7.2 Hz, J₂ = 28.0 Hz, 2H), 8.10 (s, 1H), 7.97 (t, J = 8.0 Hz, 1H), 7.71 (td, J₁ = 2.0 Hz, J₂ = 8.0 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.44 – 7.39 (m, 2H), 7.30 – 7.28
Synthesis of FLT3 kinase inhibitors: isoquinolinesulfonamide-based library

Prepared according to the general procedure. Yield: 62.2 mg, 138.4 µmol, 34.6%. \(^1\)H NMR (400 MHz, CD\(_2\)OD) 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\(_2\)OD) δ 152.89, 142.60, 141.67, 138.80, 136.31, 135.82, 135.73, 135.40, 134.97, 133.46, 131.72, 131.04, 50.41, 47.43, 39.84, 35.65. HRMS: calculated for C\(_{28}\)H\(_{27}\)N\(_2\)O\(_2\)S [M+H]^+: 434.16395; found: 434.16395.
(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%. \( ^1H \) NMR (400 MHz, CD\( _2 \)OD) \( \delta \) 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, 3H), 3.79 (d, \( J = 7.2 \) Hz, 2H), 3.16 (s, 4H). \( ^{13}C \) NMR (101 MHz, CD\( _2 \)OD) \( \delta \) 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\( _{23} \)H\( _{22} \)N\( _2 \)O\( _5 \)S \([M+H]^+\): 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%. \( ^1H \) NMR (400 MHz, CD\( _2 \)OD) \( \delta \) 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\( _2 \)OD) \( \delta \) 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\( _{23} \)H\( _{22} \)N\( _2 \)O\( _5 \)S \([M+H]^+\): 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%. \( ^1H \) NMR (400 MHz, CD\( _2 \)OD) \( \delta \) 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\( _2 \)OD) \( \delta \) 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\( _{23}H_{22}N_2O_5S \) \([M+H]^+\): 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%. \( ^1H \) NMR (400 MHz, CD\( _2 \)OD) \( \delta \) 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\( _2 \)OD) \( \delta \) 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, 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\( _{28}H_{25}FN_2O_5S \) \([M+H]^+\): 501.17550; found: 501.17528.
(E)-N-(2-((3-(2-(trifluoromethyl))pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide S4

Prepared according to the general procedure. Yield: 54.3 mg, 106.0 µmol, 26.5%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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, 126.15, 123.20 (q, J = 171.7 Hz), 122.55, 122.51, 119.99, 50.22, 47.65, 40.08. HRMS: calculated for C38H34F2N6O5S [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 S5

Prepared according to the general procedure. Yield: 120.7 mg, 249.6 µmol, 62.4%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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, 117.88, 50.04, 47.66, 40.00. HRMS: calculated for C27H25N6O5S [M+H]+: 484.18017; found: 484.17998.

(E)-N-(2-((3-(3-(4-methylbenthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide S6

Prepared according to the general procedure. Yield: 20.5 mg, 40.4 µmol, 10.1%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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 C31H29N6O5S [M+H]+: 508.20532; found: 508.20510.

(E)-N-(2-((3-(3-(4-methoxybenthalen-1-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide S7

Prepared according to the general procedure. Yield: 24.3 mg, 46.4 µmol, 11.6%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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 C33H29N10O5S [M+H]+: 524.20024; found: 524.19998.

(E)-N-(2-((3-(6-methoxybenthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide S8

Prepared according to the general procedure. Yield: 28.5 mg, 54.4 µmol, 13.6%. 1H NMR (400 MHz, CD3OD) 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
Chapter 3

- 7.76 (m, 4H), 7.71 – 7.63 (m, 2H), 7.46 – 7.43 (m, 2H), 7.21 (s, 1H), 7.12 (dd, J1 = 2.4 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C13H23N2O5 [M+H]+: 524.20024; found: 524.19998.

(E)-N-(2-[(3-[(6-ethynaphthalen-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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 2.4 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) δ 158.71, 153.28, 141.34, 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, 126.58, 126.52, 120.53, 120.15, 119.34, 107.35, 64.59, 50.54, 47.56, 40.17, 15.14. HRMS: calculated for C12H13N2O5 [M+H]+: 538.21589; found: 538.21566.

(E)-N-(2-[(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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 2.4 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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, 126.50, 126.55, 120.53, 119.37, 108.14, 71.09, 50.51, 47.55, 40.14. HRMS: calculated for C12H13N2O5 [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%. 1H NMR (400 MHz, CD3OD) 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). 13C NMR (101 MHz, CD3OD) 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 C18H17N2O5 [M+H]+: 544.20532; found: 544.20504.

(E)-N-(2-[(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%. 1H NMR (400 MHz, CD3OD) 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).
Synthesis of FLT3 kinase inhibitors: isoquinolinesulfonamide-based library

\((E)-N^2-(2-((3-(3-(phenanthren-9-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 63\)
Prepared according to the general procedure. Yield: 37.0 mg, 68.0 µmol, 17.0%. \(^1\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 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, 128.50, 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\(_{33}\)H\(_{33}\)N\(_2\)S\(_2\) [M+H]^+: 544.20532; found: 544.20519.

\((E)-N^2-(2-((3-(3-(dibenz[b,d]furan-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 64\)
Prepared according to the general procedure. Yield: 29.5 mg, 55.2 µmol, 13.8%. \(^1\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 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, 128.27, 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\(_{35}\)H\(_{35}\)N\(_2\)S \([M+H]^+\): 534.18459; found: 534.18438.

\((E)-N^2-(2-((3-(3-(phenoxathiin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 65\)
Prepared according to the general procedure. Yield: 34.6 mg, 61.2 µmol, 15.3%. \(^1\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 154.29, 153.79, 150.41, 144.95, 139.96, 138.94, 136.78, 135.26, 135.23, 134.95, 132.51, 130.51, 130.15, 130.04, 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\(_{34}\)H\(_{34}\)N\(_2\)S\(_2\) [M+H]^+: 566.15666; found: 566.15641.

\((E)-N^2-(2-((3-(3,3-dihydrobenzofuran-5-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 66\)
Prepared according to the general procedure. Yield: 23.9 mg, 49.2 µmol, 12.3%. \(^1\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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, \(J = 1.6\) Hz, \(J = 8.4\) 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\(_2\)OD) \(\delta\) 161.35, 153.79, 143.77, 143.21, 140.47, 137.23, 135.53, 134.52, 134.71, 130.60, 130.22, 129.32, 128.17, 128.11, 127.87, 126.23, 125.92,
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124.66, 119.57, 119.18, 110.28, 72.52, 50.50, 47.50, 40.11, 30.51. HRMS: calculated for \( \text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_5\text{S} [\text{M+H}]^+ \): 586.18459; found: 586.18427.

(E)-N-(2-((3-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)phenyl)allyl)amino)ethyl)isonicotinamide 67
Prepared according to the general procedure. Yield: 35.3 mg, 68.4 µmol, 17.1%. \(^{1}\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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, \(J = 15.6\) Hz, 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\(_2\)OD) \(\delta\) 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 \( \text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_5\text{S} [\text{M+H}]^+ \): 516.19515; found: 516.19490.

(E)-N-(2-((3-(4'-morpholino-1,1'-biphenyl)-3-yl)allyl)amino)ethyl)isonicotinamide 68
Prepared according to the general procedure. Yield: 36.2 mg, 68.4 µmol, 17.1%. \(^{1}\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 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 \( \text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_5\text{S} [\text{M+H}]^+ \): 529.22679; found: 529.22646.

(E)-N-(2-((3-(4''-ethoxy-[1,1'-4',1''-terphenyl]-3-yl)allyl)amino)ethyl)isonicotinamide 69
Prepared according to the general procedure. Yield: 23.0 mg, 40.8 µmol, 10.2%. \(^{1}\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 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 \( \text{C}_{34}\text{H}_{33}\text{N}_3\text{O}_5\text{S} [\text{M+H}]^+ \): 564.23154; found: 564.23135.

(E)-N-(2-((3-(3'-benzoxyl)-1,1'-biphenyl)-3-yl)allyl)amino)ethyl)isonicotinamide 70
Prepared according to the general procedure. Yield: 19.6 mg, 35.6 µmol, 8.9%. \(^{1}\)H NMR (400 MHz, CD\(_2\)OD) \(\delta\) 9.44 (s, 1H), 8.63 (q, \(J = 6.0\) Hz, 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\(_2\)OD) \(\delta\) 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,
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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_{2}O_{5}S [M+H]^+ 445.16927; found: 445.16911.

(E)-N-(2-((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%. ^1H NMR (400 MHz, CD_{2}OD) 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, J1 = 1.2 Hz, J2 = 7.6 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 7.95 (dd, J1 = 5.6 Hz, J2 = 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). C_{13} NMR (101 MHz, CD_{2}OD) δ 153.50, 144.05, 143.61, 142.39, 142.39, 130.05, 130.82, 135.85, 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_{23}H_{24}N_{2}O_{5}S [M+H]^+ 445.16927; found: 445.16911.

(E)-N-(2-((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%. ^1H NMR (400 MHz, CD_{2}OD) δ 9.46 (s, 1H), 8.84 (d, J = 6.8 Hz, 2H), 8.64 (q, J = 6.4 Hz, 2H), 8.53 (dd, J1 = 1.2 Hz, J2 = 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). C_{13} NMR (101 MHz, CD_{2}OD) 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_{23}H_{22}N_{2}O_{5}S [M+H]^+ 445.16927; found: 445.16904.

(E)-N-(2-((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%. ^1H NMR (400 MHz, CD_{2}OD) δ 9.62 (s, 1H), 8.80 (d, J = 6.4 Hz, 1H), 8.69 (d, J = 8.0 Hz, 1H), 8.62 (dd, J1 = 1.2 Hz, J2 = 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). C_{13} NMR (101 MHz, CD_{2}OD) 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_{23}H_{23}N_{2}O_{5}S [M+H]^+ 475.17984; found: 475.17964.

(E)-N-(2-((3-(6-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%. ^1H NMR (400 MHz, CD_{2}OD) δ 9.63 (s, 1H), 8.80 (d, J = 6.4, 1H), 8.70 (d, J = 6.0, 1H), 8.63 (dd, J1 = 1.2 Hz, J2 = 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). C_{13} NMR (101 MHz, CD_{2}OD) 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_{22}H_{24}F_{2}N_{2}O_{5}S [M+H]^+ 463.15985; found: 463.15946.
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(E)-N-(2-((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\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 158.08, 156.14, 152.48, 147.01, 140.86, 138.99, 138.92, 138.17, 136.87, 136.04, 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\(_{32}\)N\(_2\)O\(_5\)S [M+H]\(^+\): 446.16452; found: 446.16416.

(E)-N-(2-((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\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 166.19, 158.60, 152.90, 147.01, 140.86, 140.02, 138.99, 138.92, 138.17, 136.87, 136.04, 135.93, 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\(_{34}\)N\(_2\)O\(_5\)S [M+H]\(^+\): 476.17509; found: 476.17474.

(E)-N-(2-((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\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 158.46, 152.50, 147.01, 14086, 140.02, 138.99, 138.92, 138.13, 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\(_{25}\)H\(_{34}\)N\(_2\)O\(_5\)S [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\(_2\)OD) \(\delta\) 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\(_2\)OD) \(\delta\) 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\(_{32}\)H\(_{35}\)N\(_2\)O\(_5\)S [M+H]\(^+\): 495.18492; found: 495.18465.
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(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%. 1H NMR (400 MHz, CD3OD) δ 9.58 (s, 1H), 8.75 (d, J = 6.4 Hz, 1H), 8.69 (d, J = 6.0 Hz, 1H), 8.60 (dd, J1 = 1.2 Hz, J2 = 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, J1 = 2.8 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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, 126.64, 120.13, 110.91, 110.54, 50.44, 47.61, 40.16. HRMS: calculated for C23H23F4N4O5S+[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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 1.2 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) δ 152.30, 143.05, 141.81, 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 C33H37N5O4S+[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%. 1H NMR (400 MHz, CD3SO) 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). 13C NMR (101 MHz, CD3SO) 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 C19H22N4O4S+[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%. 1H NMR (400 MHz, CD3OD) δ 9.56 (s, 1H), 8.75 (d, J = 6.4 Hz, 1H), 8.67 (d, J = 6.4 Hz, 1H), 8.60 (dd, J1 = 1.2 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C25H23N5O5S+[M+H]+: 434.16452; found: 434.16425.
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(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$_2$OD) 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$_2$OD) 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$_{28}$H$_{25}$N$_2$O$_5$S [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$_2$OD) 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$_2$OD) 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$_2$O$_5$S [M+H]$^+$: 500.14610; found: 500.14564.

(E)-N-(2-((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$_2$OD) 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$_2$OD) 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$_{25}$N$_2$O$_5$S [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$_2$OD) 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$_2$OD) δ 153.27, 146.94, 146.34, 143.91, 143.74, 143.13, 142.76, 140.89, 139.59, 137.92, 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, 127.19, 127.03, 120.05, 119.95, 50.44, 47.58, 40.13. HRMS: calculated for C$_{28}$H$_{25}$N$_2$O$_5$S [M+H]$^+$: 496.18017; found: 496.17984.

(E)-N-(2-((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$_2$OD) 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
Synthesis of FLT3 kinase inhibitors: isoquinolinesulfonamide-based library

(E)-N-{2-{[3-{3-(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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 0.4 Hz, J2 = 4.8 Hz, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.10 (s, 1H), 7.96 (dd, J1 = 0.8 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C38H35F3N4O5S [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%. 1H NMR (400 MHz, CD3OD) 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, J1 = 0.8 Hz, J2 = 4.8 Hz, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.30 (dd, J1 = 1.2 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C27H23F3N4O5S [M+H]+: 484.18017; found: 484.17986.

(E)-N-{2-{[3-{4-(4-methynaphthalen-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%. 1H NMR (400 MHz, CD3OD) δ 9.46 (s, 1H), 8.66 (s, 1H), 8.62 (d, J = 6.0 Hz, 1H), 8.53 (dd, J1 = 1.2 Hz, J2 = 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). 13C NMR (101 MHz, CD3OD) 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 C32H27N4O5S [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%. 1H NMR (400 MHz, CD3OD) δ 9.49 (s, 1H), 8.67 (s, 1H), 8.56 (dd, J1 = 1.2 Hz, J2 = 7.2 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.28 (dd, J1 = 1.6 Hz, J2 = 8.4 Hz,
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1H), 7.87 (t, J = 7.6 Hz, 1H), 7.78 (dd, J1 = 1.6 Hz, J2 = 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). 13C NMR (101 MHz, CD2OD) 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 C31H28N2O5S [M+H]+: 524.20024; found: 524.20000.

(E)-N-(2-((3-(4-(6-methynaphthalen-2-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 92
Prepared according to the general procedure. Yield: 14.0 mg, 26.0 µmol, 6.5%. 1H NMR (400 MHz, CD2OD) δ 9.53 (s, 1H), 8.71 – 8.67 (m, 2H), 8.57 (dd, J1 = 1.2 Hz, J2 = 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, J1 = 2.4 Hz, J2 = 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). 13C NMR (101 MHz, CD2OD) 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, 128.54, 128.30, 128.04, 126.36, 126.32, 120.40, 102.24, 118.77, 107.33, 64.56, 50360, 47.55, 40.14. HRMS: calculated for C32H29N3O5S [M+H]+: 538.21589; found: 538.21568.

(E)-N-(2-((3-(4-(6-ethynaphthalen-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%. 1H NMR (400 MHz, CD2OD) δ 9.46 (s, 1H), 8.67 (br s, 1H), 8.60 (d, J = 6.4 Hz, 1H), 8.52 (dd, J1 = 1.2 Hz, J2 = 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, J1 = 2.0 Hz, J2 = 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). 13C NMR (101 MHz, CD2OD) 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 C32H28N2O5S [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%. 1H NMR (400 MHz, CD2OD) δ 9.55 (s, 1H), 8.73 (t, J = 6.0 Hz, 2H), 8.60 (dd, J1 = 1.2 Hz, J2 = 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), 5.93 (d, J = 7.2 Hz, 2H), 3.27 – 3.20 (m, 4H). 13C NMR (101 MHz, CD2OD) 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 C43H32N2O2S [M+H]+: 544.20532; found: 544.20500.

(E)-N-[(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%. 1H NMR (400 MHz, CD2OD) 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). 13C NMR (101 MHz, CD2OD) 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, 127.71, 127.69, 124.46, 121.17, 120.94, 118.79, 50.60, 47.56, 40.14, 37.69. HRMS: calculated for C33H26N2O2S [M+H]+: 532.20532; found: 532.20511.

(E)-N-[(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%. 1H NMR (400 MHz, CD2OD) 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). 13C NMR (101 MHz, CD2OD) 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 C33H26N2O2S [M+H]+: 544.20532; found: 544.20505.

(E)-N-[(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%. 1H NMR (400 MHz, CD2OD) 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). 13C NMR (101 MHz, CD2OD) 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, 112.11, 119.46, 119.30, 112.56, 50.52, 47.54, 40.10. HRMS: calculated for C33H26N2O2S [M+H]+: 534.18459; found: 534.18432.

(E)-N-[(3-[4-(phenoxythiin-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%. 1H NMR (400 MHz, (CD3)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). 13C NMR (101
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**[(E)-N-2-[[3-(4-(2,3-dihydrobenzofuran-5-yl)phenyl)allyl]amino]ethylisoquinoline-5-sulfonamide 100](#)**

Prepared according to the general procedure. Yield: 25.8 mg, 53.2 µmol, 13.3%. $^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 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$_3$OD) $\delta$ 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$_{32}$H$_{27}$N$_3$O$_5$S [$M+H]^+$: 566.15666; found: 566.15645.


Prepared according to the general procedure. Yield: 30.1 mg, 58.4 µmol, 14.6%. $^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 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), 7.78 (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, $J = 15.6$ Hz, 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$_3$OD) $\delta$ 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, 132.11, 122.74, 120.84, 118.82, 71.98, 71.95, 50.54, 47.52, 40.11, 33.20. HRMS: calculated for C$_{50}$H$_{32}$N$_3$O$_3$S [$M+H]^+$: 516.19515; found: 516.19496.

**[(E)-N-2-[[3-(4′-morpholinoo-[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$_3$OD) $\delta$ 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$_3$OD) $\delta$ 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$_{28}$H$_{29}$N$_3$O$_5$S [$M+H]^+$: 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$_3$)$_2$OD) $\delta$ 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$_3$)$_2$OD) $\delta$ 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, 78
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114.91, 63.12, 48.40, 45.39, 38.67, 14.67. HRMS: calculated for C_{34}H_{23}N_{10}O_{3} [M+H]^+: 564.23154; found: 564.23129.

\((E)-N(2-((3-(3′-(benzoxyl)-[1,1′-biphenyl]-4-yl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 104\)

Prepared according to the general procedure. Yield: 15.8 mg, 28.8 µmol, 7.2%. \(^1\)H NMR (400 MHz, CD\_OD\_δ) \(δ\) 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, \(J_1 = 7.2\) 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\_OD\_δ) \(δ\) 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, 128.60, 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\_{34}H_{23}N_{10}O_{3} [M+H]^+: 550.21589; found: 550.21560.

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

Prepared according to the general procedure. Yield: 12.8 mg, 28.8 µmol, 7.2%. \(^1\)H NMR (400 MHz, CD\_OD\_δ) \(δ\) 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\_OD\_δ) \(δ\) 153.15, 143.40, 142.89, 142.48, 142.25, 138.86, 135.46, 136.25, 134.92, 135.75, 133.49, 129.11, 128.36, 128.10, 121.06, 120.34, 50.41, 47.73, 40.16. HRMS: calculated for C\_{25}H_{22}N_{10}O_{3} [M+H]^+: 445.16927; found: 445.16925.

\((E)-N(2-((3-(4-(pyridin-4-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 107\)

Prepared according to the general procedure. Yield: 28.7 mg, 64.8 µmol, 16.2%. \(^1\)H NMR (400 MHz, CD\_OD\_δ) \(δ\) 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\_OD\_δ) \(δ\) 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_{22}N_{10}O_{3} [M+H]^+: 445.16927; found: 445.16901.

\((E)-N(2-((3-(4-(6-methoxy pyridin-3-yl)phenyl)allyl)amino)ethyl)isoquinoline-5-sulfonamide 108\)

Prepared according to the general procedure. Yield: 28.7 mg, 64.0 µmol, 15.1%. \(^1\)H NMR (400 MHz, CD\_OD\_δ) \(δ\) 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\_OD\_δ) \(δ\) 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\_{25}H_{22}N_{10}O_{3} [M+H]^+: 475.17984; found: 475.17958.
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(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$_3$OD) 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$_3$OD) 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$_{24}$FNO$_5$S [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$_3$OD) 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$_3$OD) 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$_{25}$H$_{24}$N$_2$O$_5$S [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$_3$OD) 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$_3$OD) 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$_2$O$_5$S [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$_3$OD) 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$_3$OD) δ 157.16, 153.30, 146.03, 142.57, 142.57, 141.13, 139.11, 139.11, 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$_{28}$H$_{33}$N$_2$O$_5$S [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$_3$OD) 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 – 80
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6.40 (m, 1H), 3.91 (d, J = 7.2 Hz, 2H), 3.23 (s, 4H). $^{13}$C NMR (101 MHz, CD$_3$OD) 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$_{20}$H$_{15}$N$_2$O$_2$S [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$_3$OD) 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$_3$OD) 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$_{21}$N$_2$O$_2$S [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$_3$OD) 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$_3$OD) 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$_{23}$N$_2$O$_2$S [M+H]$^+$: 498.19582; found: 498.19516.

(E)-N-[(2-[(3,1'-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$_3$OD) 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$_3$OD) 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$_{26}$N$_2$O$_2$S [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$_3$OD) 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$_3$OD) δ 151.69, 139.79, 139.34,
(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_2OD) δ 9.49 (s, 1H), 8.68 (d, J = 6.0 Hz, 1H), 8.63 (d, J = 6.0 Hz, 1H), 8.54 (dd, J₁ = 1.2 Hz, J₂ = 7.2 Hz, 1H), 8.48 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 7.6 Hz, 1H), 7.66 (dd, J₁ = 2.0 Hz, J₂ = 6.4 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.44 – 7.37 (m, 2H), 7.11 (dd, J₁ = 4.0 Hz, J₂ = 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). ^1^C NMR (101 MHz, CD_2OD) 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_{29}H_{23}N_{13}O_{23}S [M+H]^+: 834.16452; found: 834.16436.

(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_2OD) 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_2OD) 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, 124.98, 124.93, 123.92, 122.53, 120.45, 120.28, 119.47, 48.44, 45.54, 38.76. HRMS: calculated for C_{29}H_{23}N_{13}O_{23}S [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_2OD) δ 9.43 (s, 1H), 8.66 (d, J = 6.0 Hz, 1H), 8.62 (d, J = 6.4 Hz, 1H), 8.51 (dd, J₁ = 1.2 Hz, J₂ = 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_2OD) 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_{29}H_{23}N_{13}O_{23}S [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_2OD) δ 9.63 (s, 1H), 8.83 – 8.77 (m, 3H), 8.70 (d, J = 6.4 Hz, 1H), 8.63 (dd, J₁ = 1.2 Hz, J₂ = 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_2OD) δ 151.90, 146.93, 146.34, 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, 121.37, 119.97, 50.49, 47.62, 40.16. HRMS: calculated for C_{29}H_{23}N_{13}O_{23}S [M+H]^+: 496.18017; found: 496.17969.
**Synthesis of FLT3 kinase inhibitors: isoquinolinesulfonamide-based library**

(E)-N-(2-[(3-[4-(5-fluoro-1H-indol-2-yl)phenyl]allylamino)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\(_2\)OD) 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\(_2\)OD) 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, 119.30, 118.89, 112.91, 112.84, 111.17, 111.00, 105.64, 105.48, 50.58, 47.58, 40.13. HRMS: calculated for C\(_{30}\)H\(_{33}\)FN\(_2\)O\(_2\)S [M+H]\(^+\): 501.17550; found: 501.17577.

(E)-N-(2-[3-(4-(2-(trifluoromethyl)pyridin-4-yl)phenyl]allylamino)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\(_2\)OD) 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\(_2\)OD) δ 153.77, 151.73, 151.22, 149.71 (q, J\(_2\) = 4.0 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). HRMS: calculated for C\(_{30}\)H\(_{33}\)FN\(_2\)O\(_2\)S [M+H]\(^+\): 513.15666; found: 513.15610.

(E)-N-(2-[(3-[(4-imidazo[1,2-a]pyridin-7-yl)phenyl]allylamino)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\(_2\)OD) 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), 3.22 – 3.18 (m, 4H). \(^13\)C NMR (101 MHz, CD\(_2\)OD) 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\(_{30}\)H\(_{33}\)FN\(_2\)O\(_2\)S [M+H]\(^+\): 484.18017; found: 484.17986.

References

Chapter 3


13. KINOMEScan®, A division of DiscoverX, San Diego, United States.