S_NAr or Sulfonylation?

Chemoselective Amination of Halo(het)arene Sulfonyl Halides for Synthetic Applications and Ultralarge Compound Library Design

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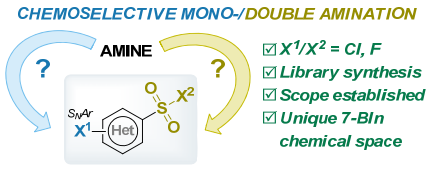


ABSTRACT. Chemoselectivity of halo(het)arene sulfonyl halide aminations is studied thoroughly under parallel synthesis conditions, and the scope and limitations of the method are established. It is shown that SNAr-reactive sulfonyl halides typically undergo sulfonamide synthesis at the first step; the second amination is also possible provided that the SNAr-active center has sufficient reactivity. On the contrary, sulfonyl fluorides bearing an arylating moiety undergo selective transformation at the latter reactive center under a proper control. Further sulfur-fluoride exchange (SuFEx) reaction is also possible, which can be especially valuable for some sulfonyl halide classes. The developed two-step parallel double amination protocol provides an access to a 6.67-Bln synthetically tractable REAL-type chemical space (76% expected synthesis success rate).

KEYWORDS: Organosulfur compounds; Sulfonamides; Arylation; Nucleophilic substitution; Chemoselectivity; REAL space.

INTRODUCTION

Sulfonyl halides are among the most widely used reagents (*building blocks*) in organic and medicinal chemistry.[1] While sulfonyl chlorides are mainly known for their classical application in the sulfonamide synthesis, sulfonyl fluorides have recently gained much attention as covalent warheads in chemical biology and drug discovery,[2] as well as building blocks[3] for the sulfur (VI) – fluoride exchange (SuFEx) click chemistry.[4]

Sulfonyl halides bearing additional functional groups are especially promising for organic synthesis and early drug discovery, especially in design of large compound libraries, provided that selective modification at both functionalities is possible.[5] Examples of such reagents include ethenesulfonyl fluoride (**1**)[6] and its derivatives (e.g., **2**[7]) sulfonyl fluorides bearing azide (e.g., 3),[8] boronic acid (e.g., **4**),[9] sulfonyl chloride (e.g., **5**),[10] or Suzuki reaction-compatible hetaryl bromide (e.g., **6**)[11] moieties (Figure 1). A possibility of selective modification for these bifunctional substrates is ensured either by the use of two mechanistically distinct transformations or dramatic difference in the reactivity of the two available centers.

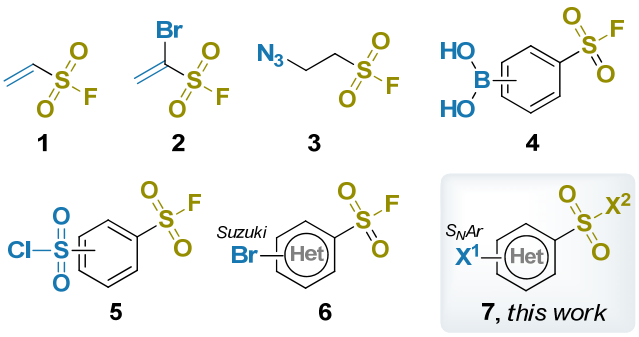


Figure 1. Examples of functionalized sulfonyl halides

In this work, we have turned our attention to sulfonyl halides bearing an S_NAr-active (het)aryl halide moiety (**7**) as bifunctional building blocks having a potential for orthogonal modification. We have aimed at the classification of these compounds according to the relative reactivity of both electrophilic centers towards amination and hence possibility of their application in one- and two-step parallel synthesis. Obviously, there are many literature precedents of chemoselective modification of compounds **7** in the reactions with amines,[12–20] but to the best of our knowledge, no systematic studies were made in this area. Furthermore, we demonstrate application of these building blocks for the generation of ultra-large readily accessible ("REAL"[21]) chemical space and illustrate its tractability by preparation of a nearly 700-member compound library.

Through the manuscript, compound numbering system common for the works on combinatorial chemistry was used: the building blocks used for the library synthesis were marked as **7**{*i*}, **8**{*j*}, **11**{*k*}, whereas the corresponding library members– **9**{*i,j*} (obtained from from **7**{*i*} and **8**{*j*}), **12**{*i,j,k*} (obtained from **7**{*i*}, **8**{*j*}, and **11**{*k*}), etc. The efficiency of parallel synthesis was assessed by synthesis success rate (SSR), i.e., percentage of experiments that allowed obtaining the target library member in pure form, along with average isolated yield.

RESULTS AND DISCUSSION

Sulfonyl chlorides. From our previous experience and general knowledge, sulfonyl chlorides can be expected to be more reactive towards nucleophilic substitution that most S_NAr-reactive (het)aryl halides. Therefore, we started our study with validation of 32 sulfonyl chlorides **7**{*1–32*} available from our stock (Figure 1) in the parallel sulfonamide synthesis

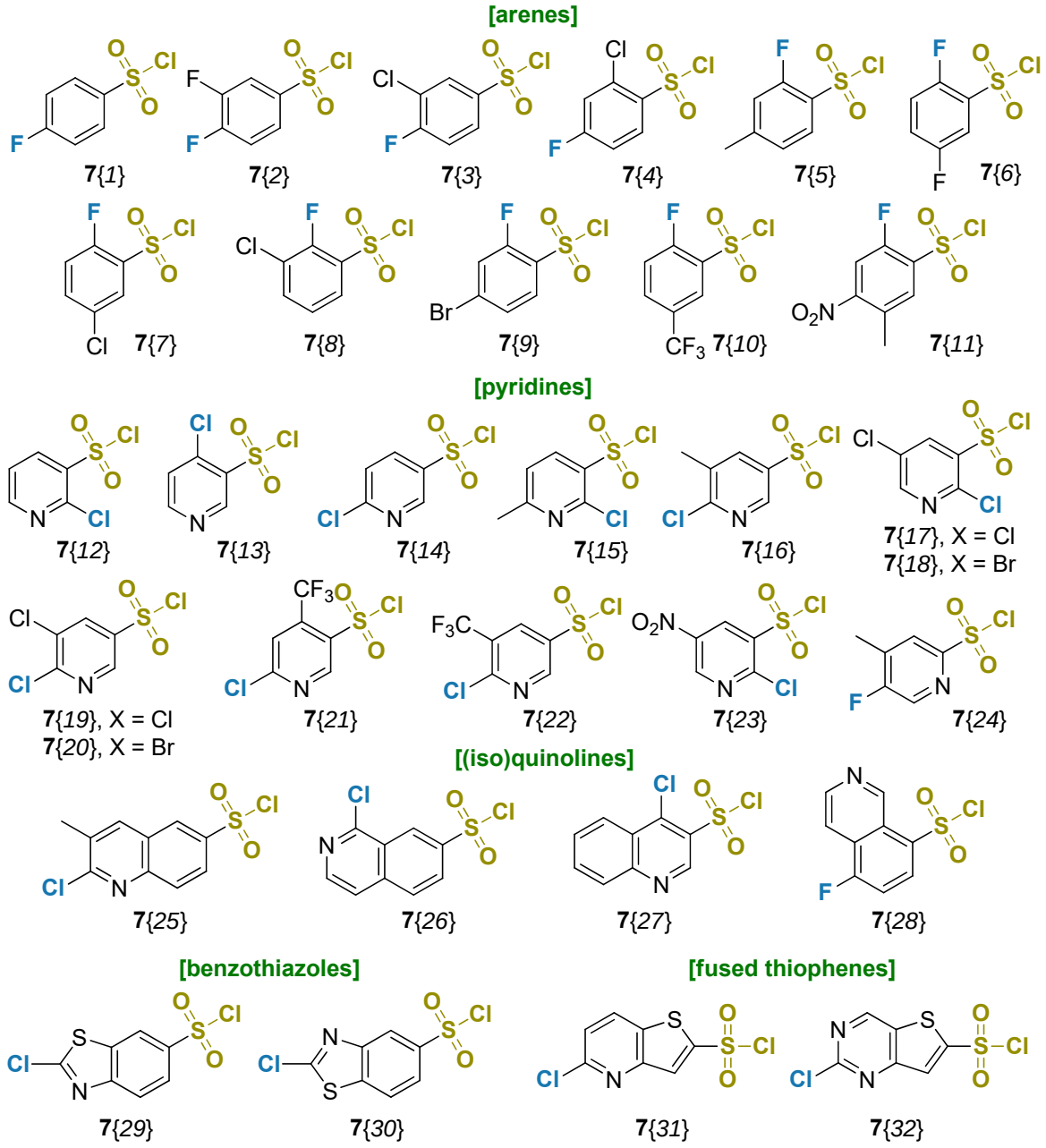
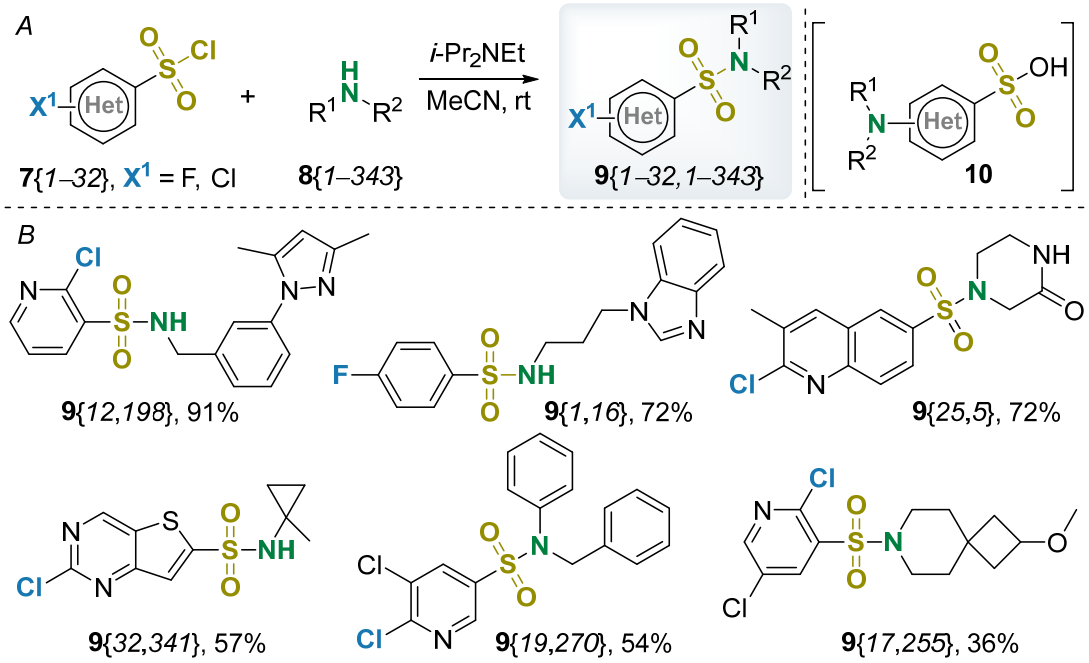


Figure 1. Halo(het)arene sulfonyl chlorides **7**{*1–32*} used in the parallel experiments on the selective monoamination.

under the typical reaction conditions (amine **8**{*1–343*}, *i*-Pr$_2$NEt, MeCN, rt; 5–20 experiments per each sulfonyl chloride). Aliphatic primary and secondary amines **8**{*1–343*} with previously

validated reactivity in the sulfonamide synthesis were selected deliberately from our stock. Of 410 planned sulfonamide library members **9**{*1–32*,*1–343*}, 259 products were isolated in pure form (63% synthesis success rate, 42% average yield) (Scheme 1). Poor performance was observed for the compounds **7**{*13*} and **7**{*27*} bearing a 4-chloropyridine-3-sulfonyl chloride fragment (only 2 out of 12 library members **9** were isolated), as well as for electron-deficient pyridine **7**{*23*} (2 out of 6 products were obtained). According to LC-MS analysis of the crude reaction mixtures, amination was not regiselective in these cases, so that apart from the target sulfonamides **9**, considerable amounts of sulfonic acids **10** could be also identified in the spectra. Similar effects were observed in the crude reaction mixtures obtained from compound **7**{*32*}, albeit in this case, corresponding sulfonamides **8** still could be obtained after the purification.



Scheme 1. (*A*) Synthesis of sulfonamide library **9** (*B*) Examples of the library members obtained.

Having in hands the above results on the synthesis of compound library **9**, we have aimed at selective two-step parallel double amination of sulfonyl chlorides **7**. For this purpose, the initial reagent set **7**{*1–32*} was extended with 35 additional sulfonyl chlorides **7**{*33–67*} (mostly heterocyclic ones) (Figure 2). Again, two aliphatic primary/secondary amine sets **8**{*1–1281*} and **11**{*1–934*} with previously validated reactivity in the sulfonamide synthesis and S_NAr reactions, respectively, were selected deliberately from our stock. The sulfonyl chloride amination step was performed under the conditions described above (i-Pr_2NEt, MeCN, rt); for the arylation step, the reagents were heated in *N*-methylpyrrolidone (NMP) in the presence of Hünig's base (*i*-Pr_2NEt) at 140 °C (Scheme 2). As a result, 689 out of 1000 library members **12**{*1–67*,*1–1281*,*1–943*} were isolated after HPLC purification (69% synthesis success rate, 44% average yield). The following sulfonyl chlorides were found to be problematic under the reaction conditions studied:

- compounds with comparable reactivities of the two electrophilic centers (i.e., 4-chloro-pyridine-3-sulfonyl chlorides **7**{*27*}, **7**{*40*}, **7**{*41*} (but not **7**{*13*}), electron-poor pyridine **7**{*23*}, thiazoles **7**{*64*} and **7**{*65*}, pyrimidines **7**{*32*}, **7**{*66*}, and **7**{*67*}. In this case, formation of sulfonic acid **10** was detected by LC-MS;
- compounds demonstrating poor reactivity in the S_NAr step, i.e., benzene sulfonyl chlorides **7**{*1*}, **7**{*5*}, **7**{*6*}, pyridine derivatives **7**{*24*} and **7**{*54*}. In this case, formation of monoamination products **9** was observed by LC-MS. Notably, even a single additional chlorine atom (like in **7**{*3*} or **7**{*4*}) was enough to activate corresponding intermediates **9** towards the nucleophilic substitution;
- methoxy-substituted derivatives **7**{*36*}, **7**{*49*}, **7**{*55*}, **7**{*59*}, and **7**{*60*}. The reasons behind this behavior are unclear, but in some cases, *O*-demethylation was probably observed by LC-MS.

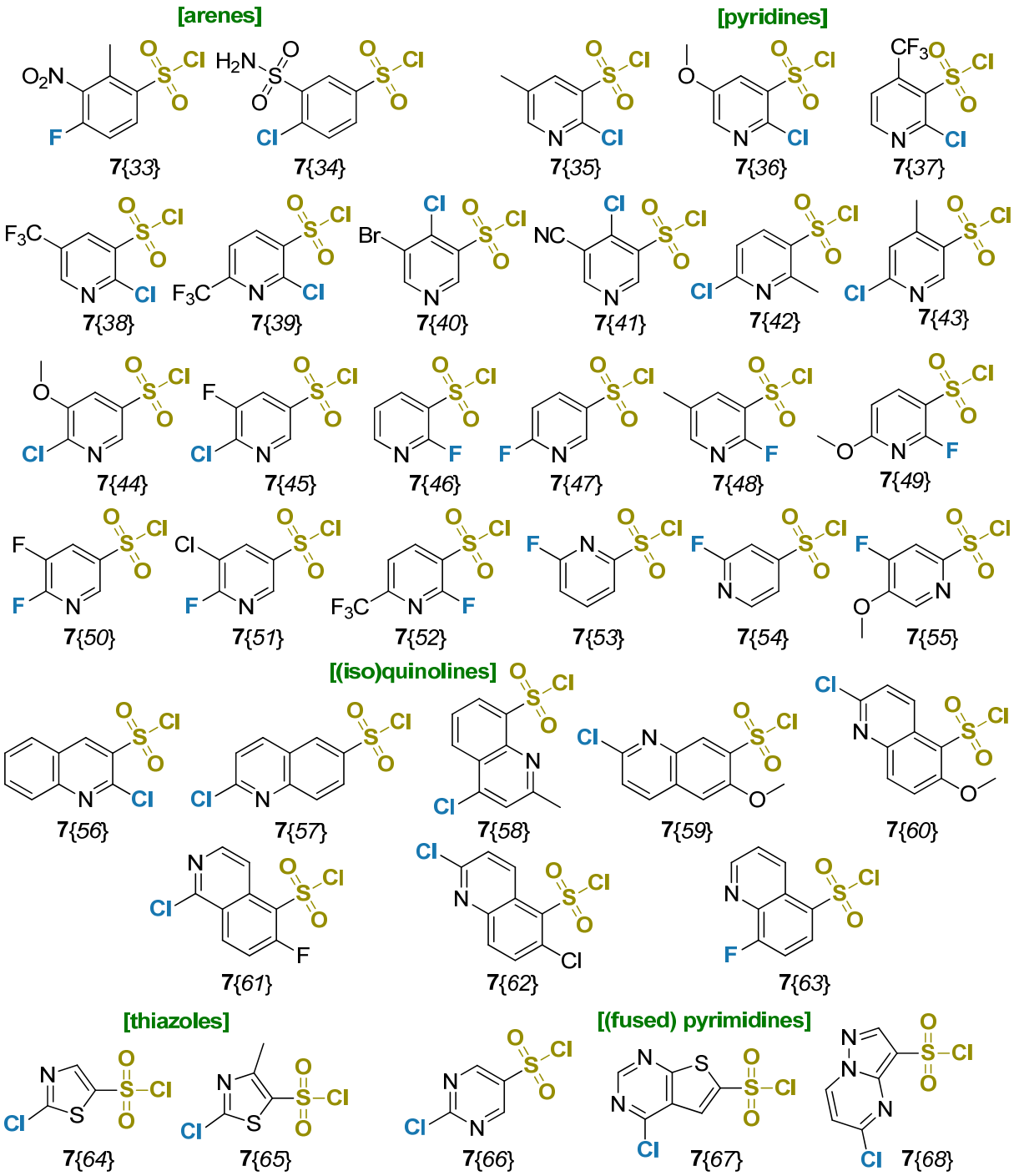
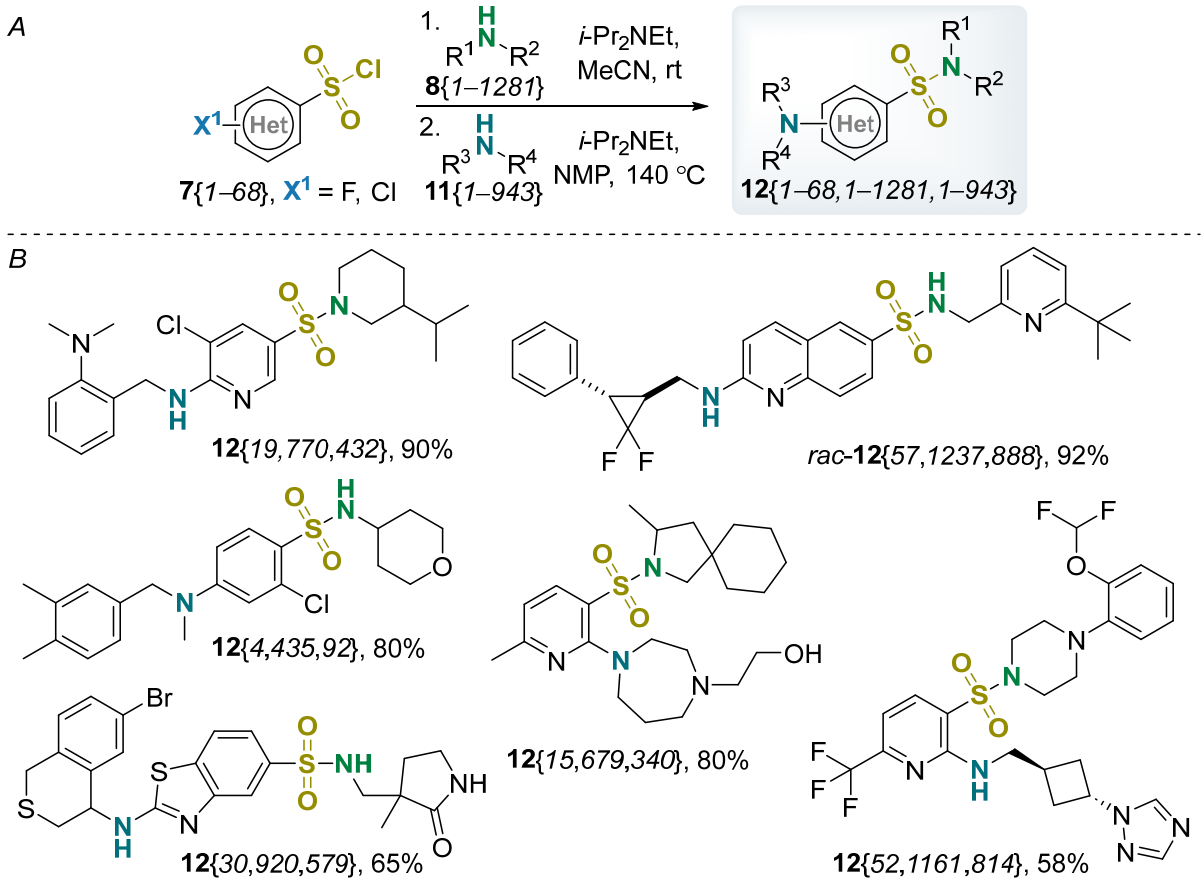


Figure 2. Additional halo(het)arene sulfonyl chlorides 7{*33–68*} used in the parallel experiments on the selective double amination.

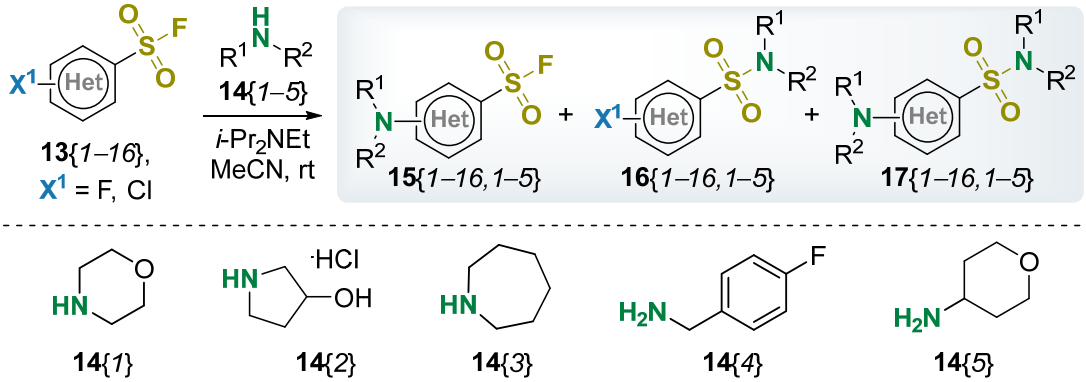


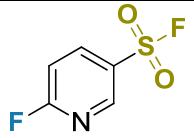
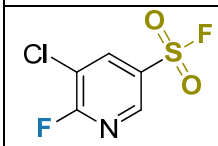
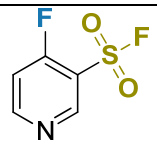
Scheme 2. (*A*) Synthesis of sulfonamide library **12**. (*B*) Examples of the library members obtained.

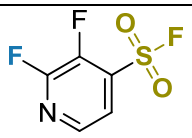
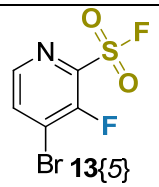
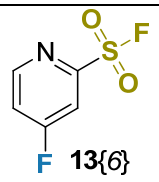
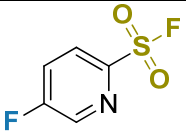
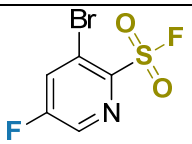
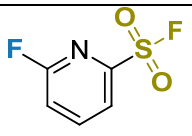
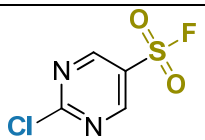
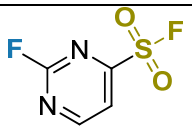
Sulfonyl fluorides. It has been recognized that commercial availability of sulfonyl fluorides remains relatively low;[1] nevertheless, the available diversity of SO_2F-substituted aryl halides was sufficient to evaluate the amination reaction chemoselectivity. Firstly, a possibility of chemoselective monoamination was checked. It was quickly revealed that in general, the reaction had poor selectivity at the common arylation conditions (*i.e.*, heating in DMF or NMP in the presence of an organic base, *i*-Pr$_2$NEt). Therefore, 16 available sulfonyl fluorides **13**{*1–16*} bearing a sufficiently S_NAr-reactive center and 5 model amines **14**{*1–5*} were selected to study

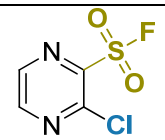
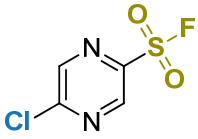
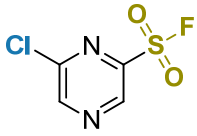
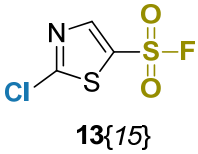
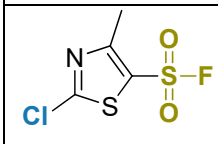
the process more thoroughly at lower temperature (Table 1). The reaction outcome was monitored by LC-MS. For the case of fluorohetarene sulfonyl flurides **13**{*1–9*}, this method alone was not sufficient to establish the reaction chemoselectivity, and the structure of corresponding products **15** and **16** was confirmed by ^{19}F NMR spectroscopy since the SO_2F and hetaryl fluoride signals are easily distinguishable by their chemical shifts.

Table 1. Monoamination of halohetarene sulfonyl fluorides **13**{*1–16*} with amines **14**{*1–5*}



Sulfonyl fluoride	Product(s) of the amination[a] (yield by LC-MS[b] [/isolated yield], %)				
	14{*1*}	**14**{*2*}	**14**{*3*}	**14**{*4*}	**14**{*5*}
 **13**{*1*}	**15**{*1,1*} (69/53)	**15**{*1,2*} (61/34) **17**{*1,2*} (30)	**15**{*1,3*} (86/72)	**15**{*1,4*} (69/51) **17**{*1,4*} (17)	**15**{*1,5*} (67/55)
 **13**{*2*}	**15**{*2,1*} (69/57)	**15**{*2,2*} (68/56)	**15**{*2,3*} (79/60)	**15**{*2,4*} (64/56) **17**{*2,4*} (11)	**15**{*2,5*} (73/51)
 **13**{*3*}	**15**{*3,1*} (7) **17**{*1,2*} (20)[c]	**15**{*3,2*} (8)[c]	**15**{*3,3*} (32/16) **17**{*3,3*} (3)[c]	**15**{*3,4*} (8) **17**{*3,3*} (15)[c]	**15**{*3,5*} (9) **17**{*3,3*} (10)[c]

 **13**{*4*}	**15**{*4,1*} (33) **17**{*4,1*} (12)[c]	**15**{*4,2*} (20) **16**{*4,2*} (2) **17**{*4,2*} (11)[c]	**15**{*4,3*} (48) **17**{*4,1*} (1)	**17**{*4,4*} (70)	**15**{*4,5*} (44) **17**{*4,5*} (5)
 **13**{*5*}	**15**{*5,1*} (50/38) **16**{*5,1*} (<1)	**15**{*5,2*} (3)[c]	**15**{*5,3*} (32/19)[c]	**15**{*5,4*} (12/9) **17**{*5,4*} (24)[c]	**15**{*5,5*} (10) **17**{*5,5*} (16)[c]
 **13**{*6*}	**15**{*6,1*} (75/38)	**15**{*6,2*} (63/29)	**15**{*6,3*} (92/57)	**15**{*6,4*} (66/29) **16**{*6,4*} (22)	**15**{*6,5*} (73/40) **16**{*6,4*} (18)
 **13**{*7*}	**15**{*7,1*} (86/44) **16**{*7,1*} (*6*) **17**{*7,2*} (*7*)	**15**{*7,2*} (34/21) **16**{*7,2*} (26/15) **17**{*7,2*} (2)	**15**{*7,3*} (82/40) **16**{*7,3*} (3)	**15**{*7,3*} (60/27) **16**{*7,3*} (21)	**15**{*7,3*} (46/22) **16**{*7,3*} (40)
 **13**{*8*}	**15**{*8,1*} (70/49) **17**{*8,1*} (13)	**15**{*8,1*} (85/78)	**15**{*8,1*} (77/58)	**15**{*8,4*} (72/41) **16**{*8,4*} (11) **17**{*8,4*} (2)	**15**{*8,5*} (75/39) **17**{*8,5*} (9)
 **13**{*9*}	**15**{*9,1*} (45) **16**{*9,1*} (27) **17**{*9,2*} (19)	**15**{*9,2*} (38) **16**{*9,1*} (10) **17**{*9,2*} (18)	**15**{*9,1*} (60/31) **16**{*9,1*} (12) **17**{*9,2*} (12)	**15**{*9,1*} (34/19) **16**{*9,1*} (26) **17**{*9,2*} (23)	**15**{*9,1*} (42/22) **16**{*9,1*} (38) **17**{*9,2*} (14)
 **13**{*10*}	**15**{*10,1*} (90/62)	**15**{*10,2*} (90/51)	**15**{*10,3*} (75/47)	**15**{*10,4*} (82/42)	**15**{*10,5*} (70/55)
 **13**{*11*}	–[c]	**17**{*11,2*} (34)[c]	–[c]	N/A	N/A

 **13**{*12*}	**15**{*12*,*1*} (54/27) **17**{*12*,*1*} (16)	**15**{*12*,*2*} (53/26) **17**{*12*,*2*} (5)	**15**{*12*,*3*} (75/37) **17**{*12*,*3*} (4)	**17**{*12*,*4*} (23)[c]	**15**{*12*,*5*} (<1)[c]
 **13**{*13*}	**15**{*13*,*1*} (76/50)	**15**{*13*,*2*} (29/10) **17**{*13*,*2*} (5)	**15**{*13*,*3*} (81/50)	**15**{*13*,*4*} (73/47)	**15**{*13*,*5*} (66/49)
 **13**{*14*}	**15**{*14*,*1*} (21/7) **17**{*14*,*1*} (8)[c]	–[c]	**15**{*14*,*3*} (29/14) **17**{*14*,*3*} (3)[c]	**15**{*14*,*3*} (4) **17**{*14*,*3*} (4)[c]	**15**{*14*,*5*} (16) **17**{*14*,*5*} (3)[c]
 **13**{*15*}	**15**{*15*,*1*} (92/57)	**15**{*15*,*2*} (89/48)	**15**{*15*,*3*} (90/68)	**15**{*15*,*4*} (52/25) **17**{*15*,*4*} (3)	**15**{*15*,*5*} (79/57)
 **13**{*16*}	**15**{*16*,*1*} (92/71)	**15**{*16*,*2*} (99/56)	**15**{*16*,*3*} (90/50)	**15**{*16*,*4*} (82/47)	**15**{*16*,*5*} (97/67)

[a] Conditions: amine **14** (1 eq), *i*-Pr$_2$NEt (2.5 eq, 3.5 eq in the case of **14**{*2*}), MeCN, rt

[b] Yield by LC-MS, diode array detector at $\lambda = 215$ nm

[c] A complex mixture of products was formed containing the mentioned compounds (if any) according to LC-MS

It was found that when the reaction was performed in the presence of *i*-Pr$_2$NEt in CH$_3$CN at ambient temperature, arylation was either dominant or prevailing in most cases. In particular, fluoropyridines **13**{*1*}, **13**{*2*}, **13**{*6*}, and **13**{*8*}, α-chloropyrimidine **13**{*10*}, α-chloropyrazine **13**{*13*}, and α-chlorothiazoles **13**{*15*} and **13**{*16*} demonstrated excellent chemoselectivity, so that corresponding sulfonyl fluorides **15** could be obtained in 25–71% isolated yields. A common feature of these substrates seems to be sufficient activation the S$_N$Ar-reactive electrophilic center by azine atoms and additional electron-withdrawing substituents. With less activated pyridine

derivatives **13**{*7*} and **13**{*9*}, mixtures of target compounds **15**, sulfonamides **16**, and double amination products **17** were formed. Apparently, the chemoselectivity can be changed by a subtle difference in the substrate structures, e.g., steric effect of the bromine atom in the case of the **13**{*7*} and **13**{*8*} pair.

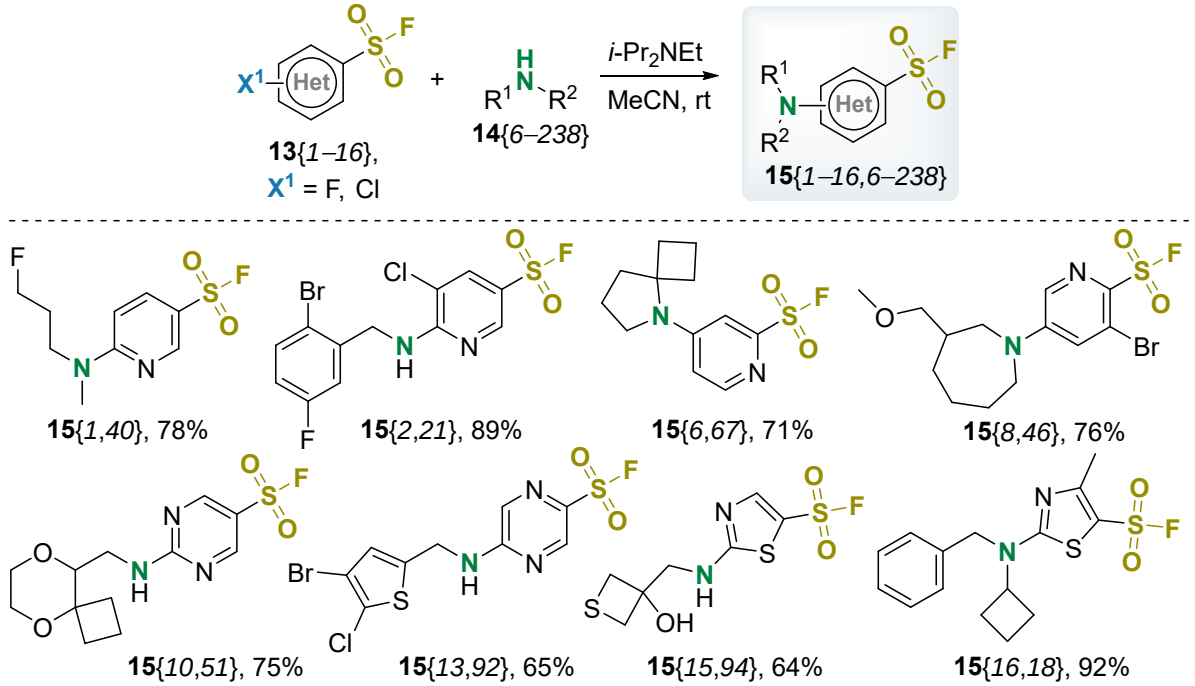
Pyridines **13**{*3–5*} having the hetaryl fluoride and SO_2F moieties at the neighboring positions, as well as pyrazine **13**{*14*} behaved poorly at the above conditions and gave complex mixtures of mostly unidentified products with low to modest content of the target arylation products **15**. Pyrazine derivative **13**{*12*} demonstrated good chemoselectivity in the case of secondary amines **14**{*1–3*}; with primary ones, complex mixtures were formed containing no products **15** at all.

Apparently, highly reactive α-fluoropyrimidine derivative **13**{*11*} had modest stability at the reaction conditions – complex mixtures were formed in this case too, with no products **15** or **16** detected by LC-MS.

In general, increasing the nucleophilicity of the aminating reagent improved the yield of arylation products **15**: the best results were obtained with azepane (**14**{*3*}), whereas primary amines **14**{*4*} and **14**{*5*} often demonstrated poor chemoselectivity (see, in particular, the example of sulfonyl fluoride **13**{*12*} mentioned above).

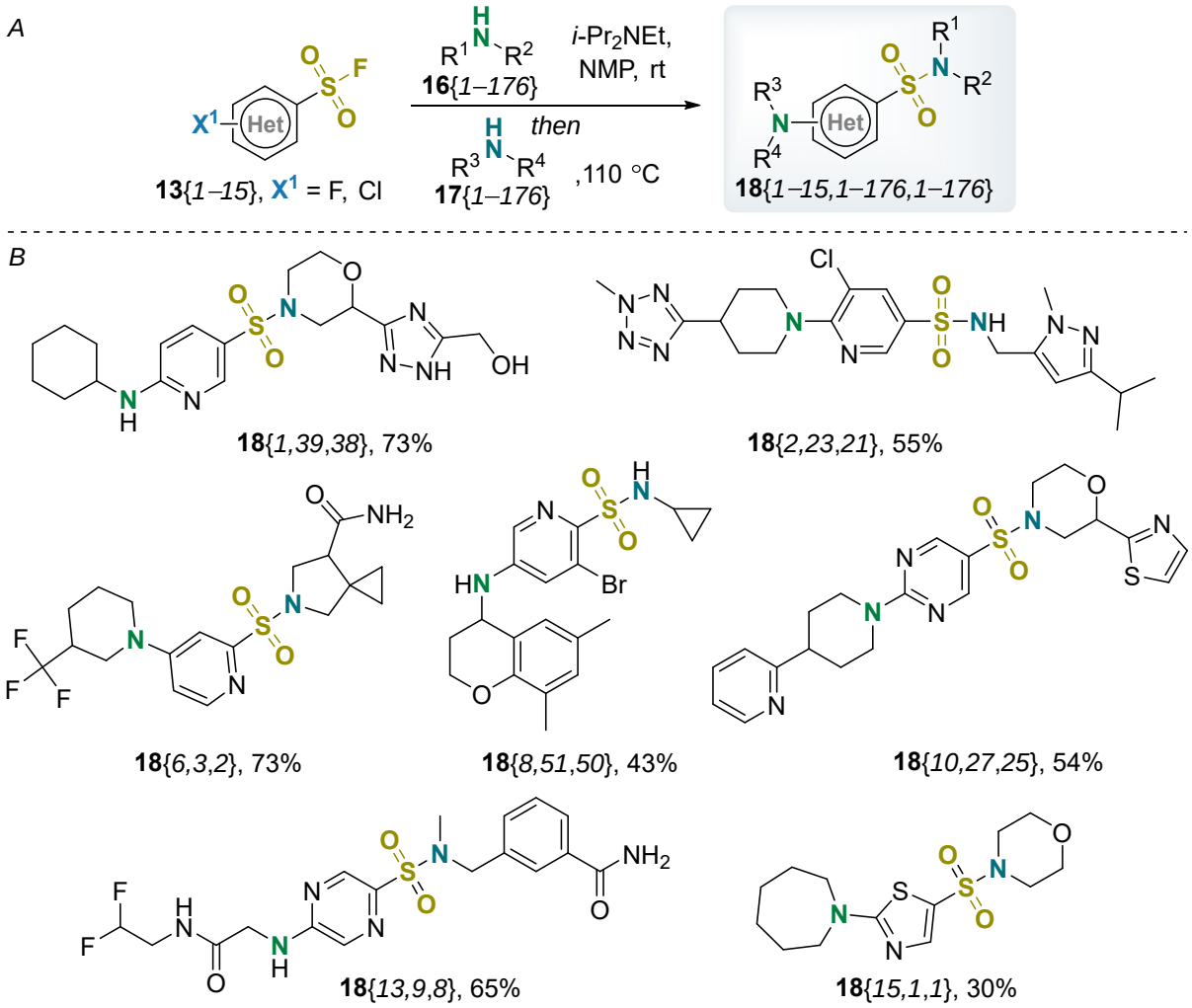
Based on the above results, we restricted the set of sulfonyl fluorides **13** by compounds **13**{*1*}, **13**{*2*}, **13**{*6*}, **13**{*8*}, **13**{*10*}, **13**{*13*}, **13**{*15*}, and **13**{*16*} and subjected them to parallel reaction with deliberately selected in-stock aliphatic primary/secondary amines **14**{*6–238*} with confirmed efficiency in the S_NAr aminations under the conditions described above. As a result, 223 out of 237 library members were obtained after HPLC (94% synthesis success rate),

211 of them (89% of the library) – with at least 10% yield; the average yield was 52% (Scheme 3).



Scheme 3. (*A*) Synthesis of sulfonamide library **15**. (*B*) Examples of the library members obtained.

Furthermore, compounds **13**{*1*}, **13**{*2*}, **13**{*6*}, **13**{*8*}, **13**{*10*}, **13**{*13*}, and **13**{*15*} were also used in the two-step parallel double amination with deliberately selected in-stock aliphatic primary/secondary amines **16**{*1–176*} and then – **17**{*1–176*}. Notably, *N*-methylpyrrolidone was used as the solvent for both steps, so that intermediate evaporation of the solvent was not necessary in this case. As a result, 143 out of 191 library members **18** were obtained (75% synthesis success rate), 131 of them (68% of the library) – with at least 10% yield; the average yield was 36% (Scheme 4).



Scheme 4. (*A*) Synthesis of sulfonamide library **18**. (*B*) Examples of the library members obtained.

It should be noted that since sulfonyl chlorides are typically more accessible and have considerably higher reactivity in the amination reactions than the corresponding sulfonyl fluorides, application of sulfonyl fluorides **13** for the double amination (according to Scheme 4) instead of sulfonyl chlorides **7** (according to Scheme 2) is reasonable when: (a) the SNAr-active and SO_2Cl moieties have comparable reactivities (e.g., the analogs of **13**{*10*} and **13**{*15*} –

7{*66*} and **7**{*64*}, respectively); (b) the corresponding sulfonyl chloride is unstable (e.g., analogs of **13**{*6*}, **13**{*8*}, and **13**{*13*}). Of course, reagents of type **13** are also valuable to obtain sulfonyl fluoride libraries (**15**).

Chemical space generation. Taking into account higher commercial accessibility of sulfonyl chlorides **7**, we have used the above results on the synthesis of compound library **12** for the generation of synthetically tractable chemical space. Thus, 27 sulfonyl chlorides **7** showing the highest synthesis success rate (**7**{*2–4*}, **7**{*9*}, **7**{*10*}, **7**{*13–15*}, **7**{*18*}, **7**{*19*}, **7**{*26*}, **7**{*28–30*}, **7**{*33*}, **7**{*34*}, **7**{*43*}, **7**{*44*}, **7**{*46–48*}, **7**{*53*}, **7**{*56–58*}, **7**{*62*}, and **7**{*68*}), as well as 20,354 amines **8** and 18,571 amines **11** complying with our in-house reactivity filters for the sulfonylation and arylation reactions, respectively, were used for the virtual coupling. After applying our exclusion filters and duplicate removals, a 6.67-Bln readily accessible (REAL) chemical space was generated. Since in the preliminary experiments according to Scheme 2, 542 out of 711 library members **12** derived from the 27 sulfonyl chlorides listed above were prepared, one might expect nearly 76% synthesis success rate for the generated ultra-large library.

Distribution of the obtained chemical space members according to main physicochemical descriptors is shown in Figure 3. It is apparent that the proposed space is rich in both drug-like (32%) and "beyond-Ro5" (68%) compounds.[22] Although it is obviously less suitable to get lead-like compounds, 110 Mln. of its members comply with "rule-of-four" (MW < 400, Log*P* < 4),[23] and 5.1 Mln. of them – with the strictest Churcher's rules (MW = 200…350, Log*P* = –1…3).[24]

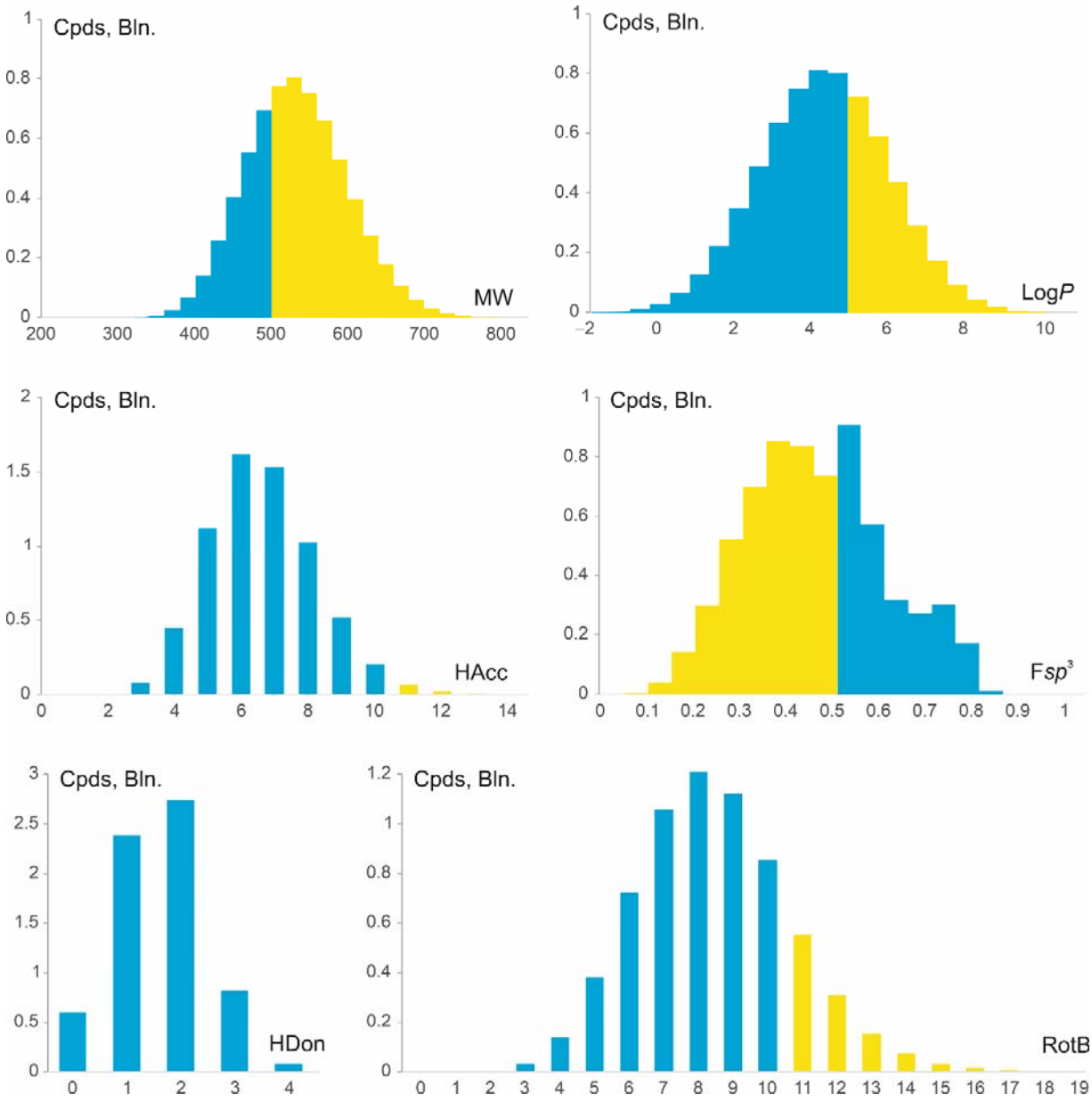


Figure 3. Physicochemical properties of the chemical space of 6.67 Bln. members obtained by virtual sulfonylation – arylation sequence (MW – molecular weight; HAcc/HDon – H-bond acceptor/donor count; Fsp3 – fraction of sp^3-hybrid carbon atoms; RotB – rotatable bond count); compounds complying with specific Lipinski/Veber rules, as well as compounds with Fsp^3 > 0.5 are highlighted in blue, the rest of the compounds are shown in yellow)

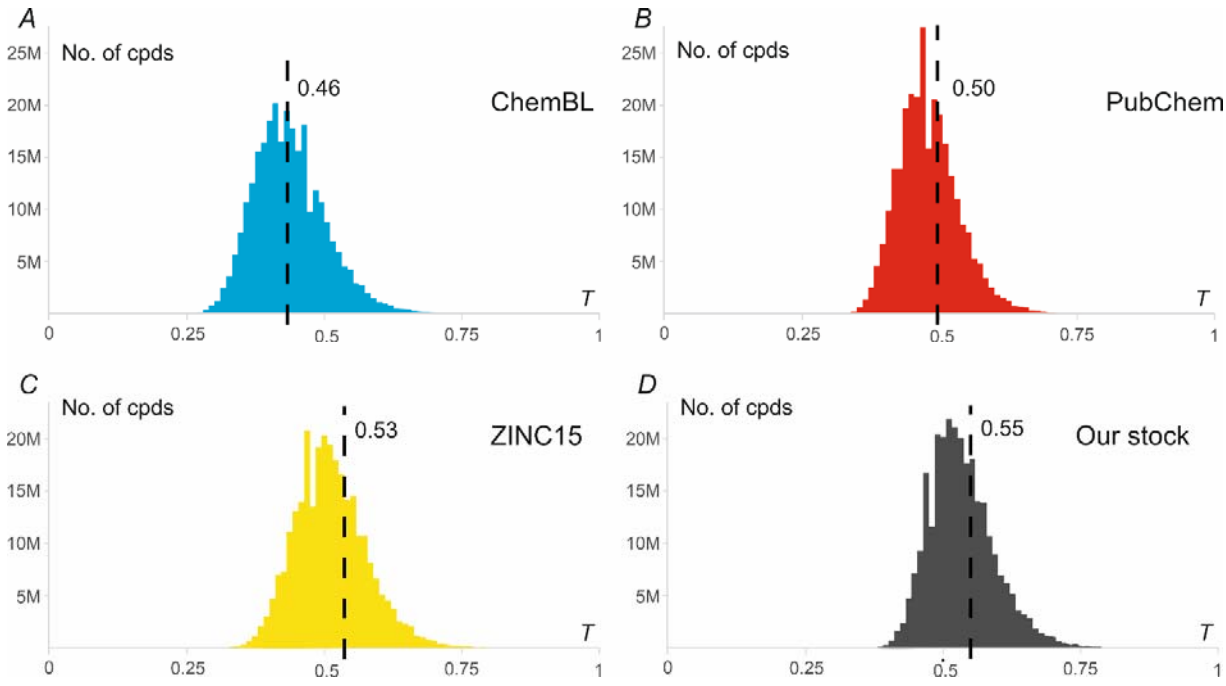


Figure 4. Distribution of maximal values among pairwise-calculated Tanimoto similarities (MFP2 fingerprints[29]) of Bemis-Murcko scaffolds for the generated chemical space members (280 Mln. scaffolds) to the Bemis-Murcko scaffolds of (*A*) ChEMBL compounds (v. 33); (*B*) PubChem compounds (due to the large size of the dataset, its preliminary clusterization was performed to achieve ca. 5-fold size reduction); (*C*) ZINC15 drug-like compounds; (*D*) Enamine's stock collection. Average Tanimoto coefficient values are shown by dotted lines

Since the generated chemical space was rather large, we used extended Bemis-Murcko scaffolds for its comparison with common chemical databases (ChemBL,[25] PubChem,[26] and ZINC15[27]), as well as our stock compound collection.[28] Pairwise Tanimoto similarity analysis using MFP2 fingerprints[29] gave average values of the similarity coefficient in a range of 0.46–0.55, which shows that the generated space is highly unprecedented in the available collections (Figure 4). This is even better illustrated by applying t-distributed stochastic neighbor embedding (t-SNE)[30] for the dimension reduction (Figure 5). In particular, only 115 space members were

also present in the ChemBL database;[25] among them, retinoic acid receptor-related orphan receptor γ (RORγ) inverse agonists,[31] antileishmanial[32] and antimalarial[33] agents can be found (Figure 6).

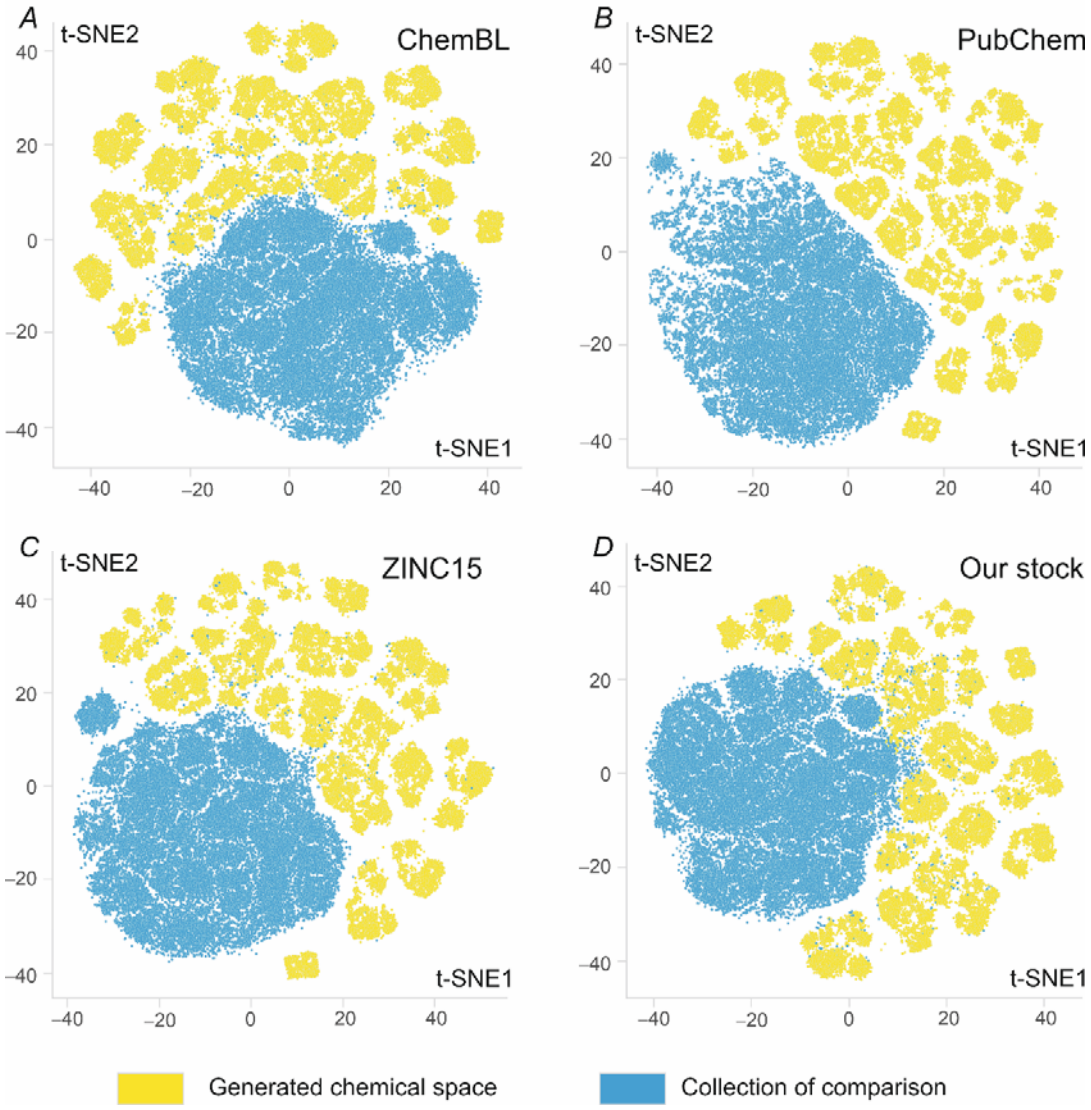


Figure 5. t-Distributed stochastic neighbor embedding (t-SNE) comparative analysis of 50 K randomly selected molecules picked from the generated chemical space and (*A*) ChemBL compounds; (*B*) PubChem compounds; (*C*) ZINC15 compounds; (*D*) Enamine's stock collection

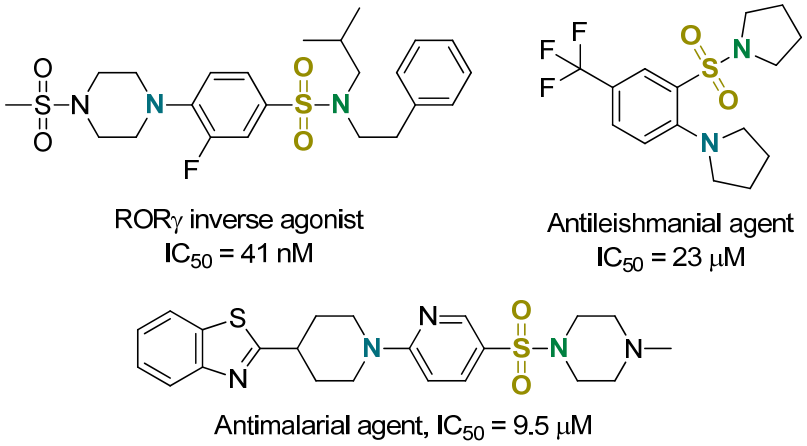


Figure 6. Selected biologically active members of the generated REAL space found in ChemBL database.

CONCLUSIONS

Chemoselective transformations of functionalized sulfonyl halides can be a powerful approach to the synthesis of complex sulfonamides and other related derivatives, in particular, in the parallel synthesis format. While the SNAr-reactive and sulfonyl halide electrophilic centers are believed to have comparable reactivity towards nucleophiles, they can be subjected to controllable amination at one of the centers (and then – at another one). With sulfonyl chlorides, sulfonamide synthesis typically occurs first. The competing SNAr reaction becomes significant only with the most reactive arylating centers (e.g., pyrimidine, thiazole, or nitropyridine halides, Figure 7). For the two-step chemoselective double amination of SNAr-reactive sulfonyl chlorides, one more limitation of the method includes low reactivity of the arylating center. Notably, even small structural modifications (e.g., introducing a properly placed chlorine atom) can solve this

problem. In addition to that, methoxy group in the sulfonyl chloride molecule was not compatible with the arylation conditions.

While the SNAr-reactive sulfonyl fluorides undergo non-selective amination upon heating, it is possibly to achieve high preference for the arylation under the controlled temperature (rt) if the substrate has sufficient electrophilicity. In particular, this approach works for fluoropyridine, 2-chloropyrimidine, -pyrazine, or -thiazole bearing the SO_2F group. Using these reagents, synthesis of sulfonyl fluoride libraries can be achieved with very high efficiency. Limitations of the method include substrates with SO_2F and SNAr-reactive halogen at the neighboring positions, as well as too reactive arylating agents (e.g., 2-fluoropyrimidine derivatives). The method is especially valuable for the preparation of sulfonyl fluoride libraries – promising covalent ligands for early drug discovery and chemical biology.

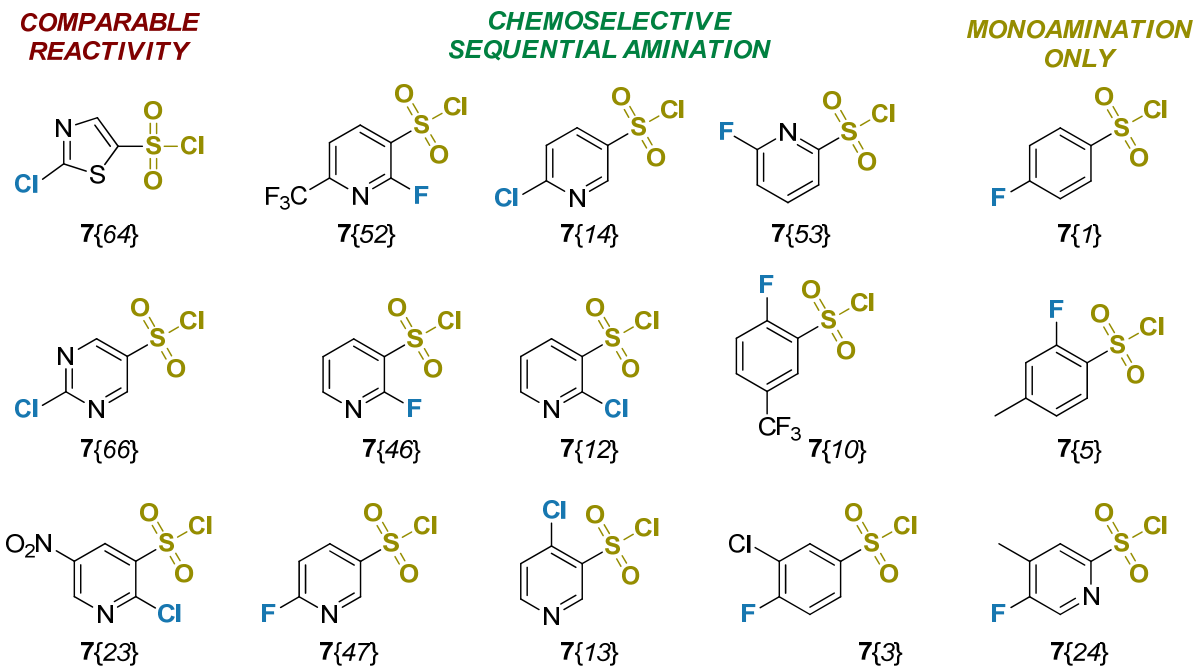


Figure 7. Summary on the chemoselective aminations of SNAr-reactive sulfonyl chlorides.

Furthermore, stepwise double amination (including the SuFEx click reaction as the second step) is also possible with the aforementioned substrate types. While the use of corresponding sulfonyl chloride counterparts is often preferable for this purpose due to higher reactivity and commercial availability, S_NAr-reactive sulfonyl fluorides can be also useful in some cases. These include comparable reactivity of the S_NAr-active and SO_2Cl moieties, as well as low stability of the corresponding sulfonyl chloride is unstable or otherwise inaccessible.

The two-step reaction sequences mentioned above work well under the parallel synthesis conditions and are valuable for generating ultra-large synthetically accessible chemical spaces (following the concept of REAL space). Thus, sulfonyl chloride amination – amine arylation sequence provides an access to a 6.67-billion virtual but tractable sulfonamide collection that can be synthesized with ca. 76% success rate. The generated chemical space is poorly covered by the current screening compound collections and contains both drug-like and "beyond-Ro5" compounds. Nevertheless, a few representatives of this space with annotated biological activity were found in the ChemBL database.

EXPERIMENTAL SECTION

General. The solvents were purified according to the standard procedures.[31] All the starting materials were received from commercial sources. Melting points were measured on MPA100 OptiMelt automated melting point system. ^1H, $^{13}C\{^1H\}$, and $^{19}F\{^1H\}$ NMR spectra were recorded on an Agilent ProPulse 600 spectrometer (at 600 MHz for ^1H NMR, 151 MHz for $^{13}C\{^1H\}$ NMR), a Bruker 170 Avance 500 spectrometer (at 500 MHz for ^1H NMR, 126 MHz for $^{13}C\{^1H\}$ NMR, 470 MHz for $^{19}F\{^1H\}$ NMR), or a Varian Unity Plus 400 spectrometer (at 400 MHz for ^1H NMR, 101 MHz for $^{13}C\{^1H\}$ NMR, 376 MHz for $^{19}F\{^1H\}$ NMR) using DMSO-d_6,

$CDCl_3$, CD_3OD, or D_2O as solvents. Chemical shifts are reported in ppm downfield from TMS as an internal standard. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (APCI)) and Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)). High-resolution mass spectra were obtained on an Agilent 1260 Infinity UHPLC instrument coupled with an Agilent 6224 Accurate Mass TOF mass spectrometer. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (APCI), electrospray ionization (ESI)) and Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)). HPLC purification was performed using Agilent 1260 Infinity systems equipped with DAD and mass-detector, Waters Sunfire C18 OBD Pre Column, 100 Å, 5 µm, 19 mm × 100 mm with SunFire C18 Prep Guard Cartridge, 100 Å, 10 µm, 19 mm × 10 mm, gradient deionized water – HPLC-grade acetonitrile or methanol (phase B) as eluent.

General procedure for the synthesis of compound library 9. Amine **8** (0.3 mmol) and *N*,*N*-diisopropylethylamine (0.75 mmol + 0.3 mmol per each hydrochloride) were mixed in dry acetonitrile (MeCN) (1 mL), and sulfonyl chloride **7** (0.36 mmol) was added to the mixture. The reaction mixture was stirred at rt for 16 h. The solvent was evaporated under reduced pressure, and the residue was dissolved in DMSO (1 mL). The resulting mixture was filtered, analyzed by LC-MS, and subjected to HPLC purification.

***N*-(Benzo[*d*]thiazol-2-ylmethyl)-6-chloropyridine-3-sulfonamide 9{*14,227*}, *Z*45505122.** Yield 125 mg (63%). Yellowish solid, mp = 164 – 165 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.14 (br s, 1H), 8.79 (d, J = 2.5 Hz, 1H), 8.21 (dd, J = 8.4, 2.5 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.44 – 7.40 (m, 1H), 4.59 (s, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 169.0, 153.7, 152.5, 147.8, 138.0, 136.4, 134.7, 126.2, 125.2, 124.9, 122.4, 122.3, 44.5. LC/MS (ES-API) *m/z* = 340/342 $[M+H]^+$. Anal. calcd.

for $C_{13}H_{10}ClN_3O_2S_2$: C 45.95; H 2.97; N 12.37; S 18.87; Cl 10.43. Found: C 45.74; H 2.95; N 12.47; S 18.88; Cl 10.22.

***N*-(3-(1*H*-Benzo[*d*]imidazol-1-yl)propyl)-4-fluorobenzenesulfonamide 9{*1*,*16*}, Z89389632.** Yield 290 mg (73%). Orangeish solid, mp 125 – 127 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.14 (s, 1H), 7.84 – 7.77 (m, 3H), 7.64 (d, J = 7.9 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 8.8 Hz, 2H), 7.24 (t, J = 7.3 Hz, 1H), 7.19 (t, J = 7.3 Hz, 1H), 4.25 (t, J = 7.0 Hz, 2H), 2.75 (q, J = 6.6 Hz, 2H), 1.89 (quint, J = 7.0 Hz, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 164.1 (d, J = 251 Hz), 143.9, 143.4, 136.5 (d, J = 3.2 Hz), 133.6, 129.4 (d, J = 9.5 Hz), 122.2, 121.4, 119.4, 116.4 (d, J = 22.6 Hz), 110.3, 41.4, 39.8, 29.3. LC/MS (ES-API) *m/z* = 334 $[M+H]^+$. Anal. calcd. for $C_{16}H_{16}FN_3O_2S$: C 57.64; H 4.84; N 12.60; S 9.62. Found: C 57.82; H 5.13; N 12.29; S 9.57.

***N*-(3-(1*H*-Benzo[*d*]imidazol-1-yl)propyl)-3-chloro-2-fluorobenzenesulfonamide 9{*8*,*16*}, Z408172920.** Yield 237 mg (99%). Orangeish solid, mp 199 – 202 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.28 (t, J = 5.7 Hz, 1H), 8.16 (s, 1H), 7.92 – 7.87 (m, 1H), 7.75 – 7.70 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 4.26 (t, J = 7.0 Hz, 2H), 2.89 (q, J = 6.5 Hz, 2H), 1.93 (p, J = 7.0 Hz, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 153.5 (d, J = 255 Hz), 143.9, 143.4, 135.2, 133.6, 129.8 (d, J = 14.0 Hz), 128.5, 125.8 (d, J = 4.9 Hz), 122.2, 121.5, 121.4 (d, J = 17.5 Hz), 119.5, 110.2, 41.4, 39.8, 29.5. LC/MS (ES-API) *m/z* = 368/370 $[M+H]^+$. Anal. calcd. for $C_{16}H_{15}ClFN_3O_2S$: C 52.25; H 4.11; N 11.42; S 8.72; Cl 9.64. Found: C 52.51; H 3.85; N 11.41; S 8.67; Cl 9.93.

3-Chloro-*N*-((2,3-dihydrobenzofuran-2-yl)methyl)-2-fluorobenzenesulfonamide 9{*8*,*142*}, Z408206896. Yield 140 mg (99%). Yellowish solid, mp 82 – 85 °C. ^{1}H NMR (600 MHz,

DMSO-d_6) δ 8.51 (t, J = 6.0 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.78 – 7.72 (m, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 7.5 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.78 (t, J = 7.5 Hz, 1H), 6.49 (d, J = 7.5 Hz, 1H), 4.81 – 4.70 (m, 1H), 3.30 – 3.23 (m, 1H), 3.23 – 3.13 (m, 2H), 2.94 (dd, J = 16.0, 7.2 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 158.5, 153.6 (d, J = 255 Hz), 134.9, 130.6 (d, J = 14.2 Hz), 128.2, 127.7, 126.3, 125.6 (d, J = 4.7 Hz), 124.0, 121.3 (d, J = 17.6 Hz), 120.3, 108.8, 80.8, 46.2, 31.8. LC/MS (ES-API) *m/z* = 340/342 $[M–H]^-$. Anal. calcd. for $C_{15}H_{13}ClFNO_3S$: C 52.71; H 3.83; N 4.10; S 9.38; Cl 10.37. Found: C 53.02; H 3.59; N 4.45; S 9.30; Cl 10.34.

6-Chloro-*N*-(2-(pyrrolidin-1-yl)benzyl)pyridine-3-sulfonamide 9{*14,226*}, Z752019268. Yield 144 mg (71%). Orangeish solid, mp 118 – 119 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 (d, J = 2.5 Hz, 1H), 8.25 (t, J = 5.9 Hz, 1H), 8.05 (dd, J = 8.4, 2.5 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.82 – 6.73 (m, 2H), 4.12 (d, J = 5.9 Hz, 2H), 3.05 – 2.88 (m, 4H), 1.88 – 1.76 (m, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 153.3, 148.2, 147.6, 137.7, 136.4, 130.1, 127.9, 126.5, 124.7, 119.9, 116.2, 51.1, 43.7, 24.5. LC/MS (ES-API) *m/z* = 352/354 $[M+H]^+$. Anal. calcd. for $C_{16}H_{18}ClN_3O_2S$: C 54.62; H 5.16; N 11.94; S 9.11; Cl 10.08. Found: C 54.55; H 5.27; N 12.25; S 8.97; Cl 9.72.

5-(1-((2,5-Difluorophenyl)sulfonyl)piperidin-4-yl)-3-methyl-1,2,4-oxadiazole 9{*6,119*}, Z805651228. Yield 124 mg (65%). Brownish solid, mp 109 – 110 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.69 – 7.64 (m, 1H), 7.63 – 7.57 (m, 2H), 3.76 – 3.64 (m, 2H), 3.22 – 3.12 (m, 1H), 2.87 – 2.76 (m, 2H), 2.30 (s, 3H), 2.17 – 2.08 (m, 2H), 1.78 – 1.64 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 180.5, 166.7, 157.4 (dd, J = 245, 2.0 Hz), 154.5 (dd, J = 250, 1.7 Hz), 125.8 (dd, J = 17.9, 6.1 Hz), 122.6 (dd, J = 24.1, 8.9 Hz), 119.7 (dd, J = 25.2, 8.2 Hz), 117.2 (d, J =

26.9 Hz), 44.6, 32.1, 28.3, 11.1. LC/MS (ES-API) *m/z* = 344 $[M+H]^+$. Anal. calcd. for $C_{14}H_{15}F_2N_3O_3S$: C 48.97; H 4.40; N 12.24; S 9.34. Found: C 49.29; H 4.14; N 12.32; S 9.29.

2-((6-Chloro-5-methylpyridine)-3-sulfonamido)-3-phenylpropanamide 9{*16,252*}, Z1223143626. Yield 202 mg (99%). Colorless solid, mp 193 – 195 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.44 (br s, 1H), 8.34 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 2.4 Hz, 1H), 7.48 (br s, 1H), 7.17 – 7.04 (m, 6H), 4.00 – 3.92 (m, 1H), 2.87 (dd, *J* = 13.8, 4.3 Hz, 1H), 2.63 (dd, *J* = 13.8, 10.4 Hz, 1H), 2.28 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 172.1, 153.4, 144.3, 137.2, 137.1, 136.7, 132.7, 129.1, 127.8, 126.1, 57.8, 38.3, 19.1. LC/MS (ES-API) *m/z* = 354/356 $[M+H]^+$. Anal. calcd. for $C_{15}H_{16}ClN_3O_3S$: C 50.92; H 4.56; N 11.88; S 9.06; Cl 10.02. Found: C 51.11; H 4.55; N 12.23; S 9.09; Cl 9.74.

5,6-Dichloro-*N*-(2-(3,4-difluorophenoxy)ethyl)pyridine-3-sulfonamide 9{*19,273*}, Z1241511849. Yield 252 mg (99%). Colorless solid, mp 136 – 137 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.73 (d, *J* = 2.2 Hz, 1H), 8.41 (d, *J* = 2.2 Hz, 1H), 8.38 (br s, 1H), 7.35 – 7.25 (m, 1H), 6.90 – 6.80 (m, 1H), 6.63 – 6.57 (m, 1H), 3.93 (t, *J* = 5.1 Hz, 2H), 3.32 – 3.31 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 154.4 (dd, *J* = 8.9, 1.4 Hz), 150.9, 149.5 (dd, *J* = 245, 13.8 Hz), 145.2, 144.1 (dd, *J* = 238, 12.5 Hz), 137.9, 137.1, 130.0, 117.5 (d, *J* = 18.4 Hz), 110.5 (dd, *J* = 6.1, 3.2 Hz), 103.9 (d, *J* = 20.3 Hz), 67.0, 42.0. LC/MS (ES-API) *m/z* = 381/383/385 $[M–H]^–$. Anal. calcd. for $C_{13}H_{10}Cl_2F_2N_2O_3S$: C 40.75; H 2.63; N 7.31; S 8.37; Cl 18.50. Found: C 40.35; H 2.66; N 7.01; S 8.21; Cl 18.74.

2-Fluoro-4-methyl-*N*-((2-oxo-1,2-dihydroquinolin-4-yl)methyl)benzenesulfonamide 9{*5,93*}, Z1262453912. Yield 176 mg (99%). Brownish solid, mp 208 – 211 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (s, 1H), 8.53 (t, *J* = 6.1 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.20 – 7.10 (m, 3H), 6.45 (s, 1H),

4.34 (d, J = 6.1 Hz, 2H), 2.35 (s, 3H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 161.3, 158.0 (d, J = 253 Hz), 146.4 (d, J = 8.6 Hz), 146.3, 138.8, 130.3, 129.3, 125.5 (d, J = 14.1 Hz), 125.1 (d, J = 2.9 Hz), 124.0, 121.6, 120.2, 117.3, 117.2, 115.5, 42.9, 20.8. LC/MS (ES-API) m/z = 347 $[M+H]^+$. Anal. calcd. for $C_{17}H_{15}FN_2O_3S$: C 58.95; H 4.37; N 8.09; S 9.26. Found: C 58.84; H 4.37; N 7.99; S 9.21.

5-(1-((3-Chloro-2-fluorophenyl)sulfonyl)piperidin-4-yl)-5-methylimidazolidine-2,4-dione 9{*8,138*}, Z1343514564. Yield 146 mg (87%). Colorless solid, mp 281 – 284 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 10.63 (s, 1H), 7.98 (s, 1H), 7.96 – 7.92 (m, 1H), 7.76 – 7.70 (m, 1H), 7.44 (t, J = 8.0 Hz, 1H), 3.80 – 3.65 (m, 2H), 2.60 – 2.52 (m, 2H), 1.84 – 1.75 (m, 1H), 1.67 – 1.58 (m, 1H), 1.48 – 1.40 (m, 1H), 1.33 – 1.17 (m, 5H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 178.0, 156.6, 153.6 (d, J = 255 Hz), 135.7, 129.5, 126.5 (d, J = 14.7 Hz), 125.9 (d, J = 4.5 Hz), 121.8 (d, J = 18.0 Hz), 63.9, 45.4, 45.0, 40.3, 25.4, 24.8, 21.0. LC/MS (ES-API) m/z = 388/390 $[M–H]^–$. Anal. calcd. for $C_{15}H_{17}ClFN_3O_4S$: C 46.22; H 4.40; N 10.78; S 8.22; Cl 9.09. Found: C 46.04; H 4.77; N 11.14; S 7.86; Cl 9.12.

***N*-([1,2,4]Triazolo[4,3-*a*]pyridin-3-ylmethyl)-3-chloro-2-fluorobenzenesulfonamide 9{*8,145*}, Z1396801940.** Yield 179 mg (95%). Colorless solid, mp 232 – 233 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 9.06 (t, J = 5.9 Hz, 1H), 8.38 (d, J = 6.8 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.62 (d, J = 9.2 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.34 (dd, J = 9.2, 6.5 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 7.01 (t, J = 6.8 Hz, 1H), 4.76 (d, J = 5.9 Hz, 2H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 153.1 (d, J = 255 Hz), 149.3, 142.5, 134.8, 129.2 (d, J = 13.7 Hz), 128.1, 127.7, 125.3 (d, J = 4.7 Hz), 123.5, 120.8 (d, J = 17.3 Hz), 115.1, 113.5, 36.6. LC/MS (ES-API) m/z = 341/343 $[M+H]^+$. Anal. calcd. for $C_{13}H_{10}ClFN_4O_2S$: C 45.82; H 2.96; N 16.44; S 9.41; Cl 10.40. Found: C 45.85; H 3.22; N 16.42; S 9.41; Cl 10.64.

2-Chloro-*N*-(4-methoxybenzyl)benzo[*d*]thiazole-6-sulfonamide 9{*29,331*}, Z1421346577. Yield 124 mg (61%). Colorless solid, mp 180 – 181 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.55 (d, J = 1.9 Hz, 1H), 8.23 (t, J = 6.2 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.89 (dd, J = 8.5, 1.9 Hz, 1H), 7.09 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 3.97 (d, J = 6.2 Hz, 2H), 3.66 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 158.3, 156.8, 152.3, 138.2, 136.0, 129.02, 128.97, 124.9, 122.9, 122.0, 113.5, 55.0, 45.8. LC/MS (ES-API) *m/z* = 369/371 $[M+H]^+$, 121 $[CH_3OC_7H_6]^+$ Anal. calcd. for $C_{15}H_{13}ClN_2O_3S_2$: C 48.85; H 3.55; N 7.59; S 17.38; Cl 9.61. Found: C 49.21; H 3.31; N 7.90; S 17.49; Cl 9.95.

6-Chloro-5-methyl-*N*-(2-((1-phenyl-1*H*-tetrazol-5-yl)amino)ethyl)pyridine-3-sulfonamide 9{*16,235*}, Z1505322496. Yield 358 mg (99%). Colorless solid, mp 198 – 201 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.16 (s, 1H), 8.54 (d, J = 2.4 Hz, 1H), 8.23 (s, 1H), 8.06 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 7.7 Hz, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.7 Hz, 1H), 4.42 (t, J = 5.9 Hz, 2H), 3.36 (t, J = 5.9 Hz, 2H), 2.36 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 154.0, 152.4, 144.6, 139.8, 137.5, 136.0, 133.5, 128.9, 121.8, 117.6, 45.2, 41.0, 19.0. LC/MS (ES-API) *m/z* = 394/396 $[M+H]^+$. Anal. calcd. for $C_{15}H_{16}ClN_7O_2S$: C 45.74; H 4.09; N 24.90; S 8.14; Cl 9.00. Found: C 45.60; H 3.92; N 25.10; S 8.49; Cl 8.82.

***N*-(1-(3-(1*H*-1,2,4-triazol-3-yl)-1,2,4-oxadiazol-5-yl)-3-methylbutyl)-3-chloro-4-fluorobenzenesulfonamide 9{*3,62*}, Z1547269259.** Yield 194 mg (98%). Colorless solid, mp 197 – 199 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 14.68 (br s, 1H), 9.14 – 8.94 (m, 1H), 8.78 (br s, 1H), 7.85 (dd, J = 6.8, 2.3 Hz, 1H), 7.75 – 7.66 (m, 1H), 7.50 (t, J = 8.8 Hz, 1H), 4.83 – 4.70 (m, 1H), 1.83 – 1.76 (m, 1H), 1.72 – 1.66 (m, 1H), 1.64 – 1.54 (m, 1H), 0.88 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.6 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 178.7, 162.2, 159.3 (d, J = 254 Hz), 151.1, 145.3, 137.9 (d, J = 3.6 Hz), 129.0, 127.7 (d, J = 9.0 Hz), 120.6 (d, J = 18.8 Hz),

117.8 (d, *J* = 22.5 Hz), 48.3, 41.4, 23.9, 22.3, 21.0. LC/MS (ES-API) *m/z* = 415/417 $[M+H]^+$. Anal. calcd. for $C_{15}H_{16}ClFN_6O_3S$: C 43.43; H 3.89; N 20.26; S 7.73; Cl 8.55. Found: C 43.21; H 3.82; N 20.48; S 8.08; Cl 8.54.

3-(1-((4-Fluorophenyl)sulfonyl)azepan-2-yl)-5-(methoxymethyl)-1,2,4-oxadiazole 9{*1*,*19*}, Z1626538070. Yield 262 mg (65%). Beige solid, mp 67 – 68 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.69 (dd, *J* = 8.9, 5.1 Hz, 2H), 7.30 (t, *J* = 8.9 Hz, 2H), 5.14 (dd, *J* = 11.2, 6.6 Hz, 1H), 4.59 (d, *J* = 14.8 Hz, 1H), 4.56 (d, *J* = 14.8 Hz, 1H), 3.84 – 3.72 (m, 1H), 3.38 – 3.32 (m, 1H), 3.27 (s, 3H), 2.30 – 2.20 (m, 1H), 1.88 – 1.69 (m, 4H), 1.58 – 1.47 (m, 1H), 1.45 – 1.35 (m, 1H), 1.35 – 1.24 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 176.4, 169.6, 164.2 (d, *J* = 252 Hz), 136.3 (d, *J* = 2.9 Hz), 129.6 (d, *J* = 9.6 Hz), 116.1 (d, *J* = 22.7 Hz), 64.1, 58.6, 52.1, 44.6, 33.3, 30.0, 28.6, 24.3. LC/MS (ES-API) *m/z* = 370 $[M+H]^+$. Anal. calcd. for $C_{16}H_{20}FN_3O_4S$: C 52.02; H 5.46; N 11.38; S 8.68. Found: C 52.10; H 5.10; N 11.03; S 8.66.

2-((4-Bromo-2-fluorophenyl)sulfonamido)pent-4-ynamide 9{*9*,*158*}, Z1725736044. Yield 210 mg (99%). Brownish solid, mp 196 – 198 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.34 (br s, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.71 (t, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.38 (s, 1H), 7.12 (s, 1H), 3.89 (dd, *J* = 8.4, 5.5 Hz, 1H), 2.78 (t, *J* = 2.6 Hz, 1H), 2.49 – 2.46 (m, 1H), 2.45 – 2.39 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 170.5, 158.2 (d, *J* = 259 Hz), 130.9, 128.3 (d, *J* = 14.2 Hz), 127.7 (d, *J* = 3.6 Hz), 127.1 (d, *J* = 9.2 Hz), 120.4 (d, *J* = 24.6 Hz), 80.0, 73.1, 55.2, 23.0. LC/MS (ES-API) *m/z* = 347/349 $[M-H]^-$. Anal. calcd. for $C_{11}H_{10}BrFN_2O_3S$: C 37.84; H 2.89; N 8.02; S 9.18; Br 22.88. Found: C 37.92; H 2.55; N 8.01; S 9.01; Br 22.99.

4-((3-Chloro-4-fluorophenyl)sulfonyl)-1-ethyl-2-(1*H*-imidazol-2-yl)piperazine 9{*3*,*61*}, Z1754551154. Yield 131 mg (66%). Colorless solid, mp 211 – 214 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 8.00 (dd, *J* = 6.8, 2.2 Hz, 1H), 7.86 – 7.77 (m, 1H), 7.72 (t, *J* = 8.8

Hz, 1H), 6.93 (s, 2H), 3.65 – 3.57 (m, 1H), 3.51 (dd, *J* = 10.2, 3.2 Hz, 1H), 3.45 – 3.40 (m, 1H), 3.08 – 3.01 (m, 1H), 2.57 – 2.53 (m, 1H), 2.49 – 2.45 (m, 1H), 2.35 – 2.18 (m, 2H), 2.04 – 1.94 (m, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 160.0 (d, *J* = 254 Hz), 145.0, 132.3 (d, *J* = 3.4 Hz), 130.1 (2C), 129.2 (d, *J* = 8.9 Hz, 2C), 121.2 (d, *J* = 18.7 Hz), 118.3 (d, *J* = 22.3 Hz), 58.9, 49.8, 49.1, 47.4, 45.9, 10.8. LC/MS (ES-API) *m/z* = 373/375 $[M+H]^+$. Anal. calcd. for $C_{15}H_{18}ClFN_4O_2S$: C 48.32; H 4.87; N 15.03; S 8.60; Cl 9.51. Found: C 48.19; H 5.12; N 14.99; S 8.64; Cl 9.52.

2-((5-Chloro-2-fluorophenyl)sulfonamido)-*N*-(pyridin-3-yl)acetamide 9{*7*,*133*}, Z2042641681. Yield 206 mg (99%). Brownish solid, mp 150 – 152 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.65 (d, *J* = 2.6 Hz, 1H), 8.62 (t, *J* = 6.1 Hz, 1H), 8.28 (d, *J* = 4.6 Hz, 1H), 7.97 – 7.90 (m, 1H), 7.77 (dd, *J* = 6.1, 2.6 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.48 (t, *J* = 9.3 Hz, 1H), 7.38 (dd, *J* = 8.4, 4.6 Hz, 1H), 3.92 (d, *J* = 6.1 Hz, 2H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 167.0, 157.1 (d, *J* = 254 Hz), 143.8, 140.0, 135.4, 134.7 (d, *J* = 8.9 Hz), 130.4 (d, *J* = 16.2 Hz), 128.6, 128.2 (d, *J* = 3.2 Hz), 126.8, 124.0, 119.3 (d, *J* = 23.4 Hz), 45.5. LC/MS (ES-API) *m/z* = 344/346 $[M+H]^+$. Anal. calcd. for $C_{13}H_{11}ClFN_3O_3S$: C 45.42; H 3.23; N 12.22; S 9.33; Cl 10.31. Found: C 45.34; H 3.27; N 12.02; S 9.05; Cl 10.23.

***N*-Benzyl-5-bromo-6-chloropyridine-3-sulfonamide 9{*20*,*276*}, Z2234039220.** Yield 192 mg (92%). Yellowish solid, mp 168 – 169 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 8.66 (d, *J* = 2.2 Hz, 1H), 8.59 (s, 1H), 8.29 (d, *J* = 2.2 Hz, 1H), 7.33 – 7.13 (m, 5H), 4.14 (s, 2H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 152.6, 145.8, 140.3, 137.6, 136.6, 128.2, 127.8, 127.3, 119.9, 46.2. LC/MS (ES-API) *m/z* = 361/363/365 $[M+H]^+$. Anal. calcd. for $C_{12}H_{10}BrClN_2O_2S$: C 39.86; H 2.79; N 7.75; S 8.87; Cl 9.80; Br 22.09. Found: C 39.55; H 2.87; N 7.54; S 8.97; Cl 9.57; Br 21.99.

General procedure for the synthesis of compound library 12. Amine **8** (0.3 mmol) and *N*,*N*-diisopropylethylamine (0.75 mmol + 0.3 mmol per each hydrochloride) were mixed in dry acetonitrile (MeCN) (1 mL), and sulfonyl chloride **7** (0.36 mmol) was added to the mixture. The reaction mixture was stirred at rt for 16 h. The solvent was evaporated under reduced pressure, and the residue was dissolved in *N*-methylpyrrolidone (1 mL). Amine **11** (0.6 mmol) and *N*,*N*-diisopropylethylamine (0.75 mmol + 0.3 mmol per each hydrochloride) were added to the solution, and the mixture was stirred at 140 °C for 16 h. The reaction mixture was cooled, the solvent was evaporated under reduced pressure, and the residue was dissolved in the DMSO (1 mL). The mixture was filtered, analyzed by LC-MS, and subjected to HPLC purification.

5-Bromo-*N*-(2-(4-fluorophenyl)propyl)-6-(1-(hydroxymethyl)-6-azaspiro[2.5]octan-6-yl)pyridine-3-sulfonamide 12{*20,784,446*}, Z5069786483. Yield 52.5 mg (79%). Colorless amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, J = 2.2 Hz, 1H), 8.01 (d, J = 2.2 Hz, 1H), 7.70 (t, J = 5.1 Hz, 1H), 7.24 – 7.14 (m, 2H), 7.08 – 6.96 (m, 2H), 4.45 (t, J = 5.1 Hz, 1H), 3.69 – 3.48 (m, 3H), 3.41 – 3.33 (m, 2H), 3.32 – 3.27 (m, 1H), 3.00 – 2.89 (m, 2H), 2.87 – 2.79 (m, 1H), 1.76 – 1.67 (m, 1H), 1.57 – 1.48 (m, 2H), 1.43 – 1.34 (m, 1H), 1.14 (d, J = 6.9 Hz, 3H), 0.94 – 0.83 (m, 1H), 0.49 (dd, J = 8.6, 4.3 Hz, 1H), 0.19 (t, J = 4.8 Hz, 1H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 160.8 (d, J = 242 Hz), 160.5, 144.5, 140.2, 140.1 (d, J = 2.3 Hz), 129.3, 129.0 (d, J = 8.0 Hz), 114.8 (d, J = 21.0 Hz), 109.1, 60.7, 49.1, 49.0, 48.8, 38.7, 36.1, 29.4, 25.5, 21.3, 19.3, 15.3. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –117.2. LC/MS (ES-API) *m/z* = 512/514 $[M+H]^+$. Anal. calcd. for $C_{22}H_{27}BrFN_3O_3S$: C 51.57; H 5.31; N 8.20; S 6.26; Br 15.59. Found: C 51.32; H 5.55; N 8.48; S 6.56; Br 15.20.

(1-(3-((2-Cyclopropylpyrrolidin-1-yl)sulfonyl)-5-(trifluoromethyl)pyridin-2-yl)piperidin-4-yl)dimethylphosphine oxide 12{*38,972,626*}, Z5069787900. Yield 52.4 mg (79%). Brownish

gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.77 (d, J = 2.2 Hz, 1H), 8.28 (d, J = 2.2 Hz, 1H), 4.26 – 4.15 (m, 1H), 4.07 – 3.99 (m, 1H), 3.51 – 3.44 (m, 1H), 3.38 – 3.32 (m, 1H), 3.21 – 3.11 (m, 1H), 3.04 (t, J = 11.7 Hz, 1H), 2.85 (t, J = 11.7 Hz, 1H), 1.98 – 1.78 (m, 4H), 1.79 – 1.49 (m, 5H), 1.36 (s, 3H), 1.34 (s, 3H), 0.87 – 0.75 (m, 1H), 0.40 – 0.31 (m, 1H), 0.29 – 0.18 (m, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.7, 147.8 (q, J = 3.4 Hz), 137.7 (q, J = 2.9 Hz), 124.1, 123.6 (q, J = 272 Hz), 117.0 (q, J = 33.2 Hz), 65.1, 51.8 (d, J = 13.6 Hz), 50.2 (d, J = 13.8 Hz), 48.6, 36.0 (d, J = 71.5 Hz), 31.4, 24.2 (d, J = 2.1 Hz), 24.0, 23.9 (d, J = 2.4 Hz), 16.2, 13.9 (d, J = 10.2 Hz), 13.4 (d, J = 10.2 Hz), 4.6, 2.5. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –60.5. LC/MS (ES-API) m/z = 480 $[M+H]^+$. Anal. calcd. for $C_{20}H_{29}F_3N_3O_3PS$: C 50.10; H 6.10; N 8.76; S 6.69. Found: C 50.16; H 5.88; N 8.69; S 6.68.

6-((3*R,4*S**)-3-(4-Chlorophenyl)-4-(hydroxymethyl)pyrrolidin-1-yl)-*N*-(chroman-4-yl)pyridine-3-sulfonamide 12{*14,668,328*}, Z6318330071.** Yield 56.5 mg (85%). Orangeish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (d, J = 2.6 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.87 (dd, J = 9.1, 2.6 Hz, 1H), 7.52 – 7.27 (m, 4H), 7.16 – 7.11 (m, 1H), 7.06 (d, J = 7.7 Hz, 1H), 6.87 – 6.81 (m, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.65 (d, J = 9.1 Hz, 1H), 4.84 – 4.72 (m, 1H), 4.44 – 4.31 (m, 1H), 4.18 – 4.09 (m, 2H), 4.06 – 3.78 (m, 2H), 3.55 – 3.39 (m, 3H), 2.62 – 2.50 (m, 3H), 1.91 – 1.72 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 157.7, 154.6, 147.5, 139.9, 135.3, 131.3, 129.6, 129.5, 128.8, 128.5, 124.4, 122.5, 120.2, 116.5, 106.1, 62.6, 60.4, 53.6, 50.1, 47.3, 46.6, 44.3, 29.2. LC/MS (ES-API) m/z = 500/502 $[M+H]^+$. Anal. calcd. for $C_{25}H_{26}ClN_3O_4S$: C 60.05; H 5.24; N 8.40; S 6.41; Cl 7.09. Found: C 59.85; H 4.90; N 8.70; S 6.17; Cl 7.32.

***N*-(3-((1-Benzylpiperidin-4-yl)oxy)propyl)-6-((2-(2-(*tert*-butyl)thiazol-4-yl)ethyl)amino)-pyridine-3-sulfonamide 12{*14,667,327*}, Z6318330090.** Yield 52.3 mg (78%). Yellowish

amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (d, J = 2.5 Hz, 1H), 7.62 (dd, J = 8.9, 2.5 Hz, 1H), 7.50 (t, J = 5.6 Hz, 1H), 7.32 – 7.19 (m, 6H), 7.15 (s, 1H), 6.54 (d, J = 8.9 Hz, 1H), 3.60 (q, J = 6.8 Hz, 2H), 3.40 (s, 2H), 3.35 – 3.28 (m, 4H), 3.20 – 3.10 (m, 1H), 2.93 (t, J = 7.2 Hz, 2H), 2.76 (q, J = 6.8 Hz, 2H), 2.65 – 2.54 (m, 2H), 2.02 (t, J = 10.6 Hz, 2H), 1.78 – 1.68 (m, 2H), 1.56 (quint, J = 6.8 Hz, 2H), 1.35 (s, 9H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 179.5, 160.2, 153.4, 147.6, 138.6, 134.8, 128.6, 128.1, 126.7, 123.0, 113.1, 74.3, 64.1, 62.1, 50.6, 40.2, 37.1, 31.0, 30.9, 30.6, 29.5. LC/MS (ES-API) m/z = 572 $[M+H]^+$. Anal. calcd. for $C_{29}H_{41}N_5O_3S_2$: C 60.92; H 7.23; N 12.25; S 11.21. Found: C 61.06; H 6.97; N 12.11; S 10.99.

2-Chloro-4-((10,10-difluoro-2-oxa-7-azaspiro[4.5]decan-7-yl)sulfonyl)-*N*-((6-(2,2,2-trifluoroethoxy)pyridin-2-yl)methyl)aniline 12{*3,418,75*}, Z6318398324. Yield 59.4 mg (89%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.77 (t, J = 7.8 Hz, 1H), 7.64 (d, J = 2.2 Hz, 1H), 7.46 (dd, J = 8.7, 2.2 Hz, 1H), 7.07 (t, J = 6.1 Hz, 1H), 7.03 (d, J = 7.8 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.78 (d, J = 8.7 Hz, 1H), 4.97 (q, J = 9.1 Hz, 2H), 4.53 (d, J = 6.1 Hz, 2H), 3.79 (q, J = 7.5 Hz, 1H), 3.72 (dd, J = 8.7, 6.3 Hz, 2H), 3.59 (d, J = 9.5 Hz, 1H), 3.16 – 2.88 (m, 3H), 2.87 – 2.75 (m, 1H), 2.24 – 1.95 (m, 3H), 1.75 – 1.64 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.7, 155.8, 147.8, 140.8, 128.2, 128.0, 124.0 (q, J = 278 Hz), 123.0 (t, J = 246 Hz), 121.6, 117.5, 115.5, 111.1, 108.9, 70.5, 67.3, 60.9 (q, J = 34.6 Hz), 51.7, 50.6 (t, J = 20.7 Hz), 47.0, 43.1 (t, J = 5.5 Hz), 31.5 (t, J = 23.8 Hz), 30.7. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –72.9, –107.6 (d, J = 243 Hz), –108.8 (d, J = 243 Hz). LC/MS (ES-API) m/z = 556/558 $[M+H]^+$. Anal. calcd. for $C_{22}H_{23}ClF_5N_3O_4S$: C 47.53; H 4.17; N 7.56; S 5.77; Cl 6.38. Found: C 47.77; H 4.04; N 7.18; S 5.99; Cl 6.52.

3-Chloro-4-((4-hydroxybut-2-en-1-yl)amino)-*N*-((4-(4-methylbenzyl)morpholin-2-yl)methyl)benzenesulfonamide 12{*3,409,67*}, Z6318398373. Yield 59.2 mg (89%). Yellowish

gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.59 (d, J = 2.2 Hz, 1H), 7.48 (dd, J = 8.6, 2.2 Hz, 1H), 7.43 (t, J = 6.3 Hz, 1H), 7.15 (d, J = 7.9 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 6.72 (d, J = 8.6 Hz, 1H), 6.39 (t, J = 5.8 Hz, 1H), 5.68 – 5.57 (m, 1H), 5.47 – 5.33 (m, 1H), 4.77 (t, J = 5.2 Hz, 1H), 4.11 (t, J = 5.2 Hz, 2H), 3.90 (t, J = 6.3 Hz, 2H), 3.73 – 3.66 (m, 1H), 3.43 – 3.35 (m, 3H), 2.75 – 2.63 (m, 3H), 2.56 – 2.51 (m, 2H), 2.27 (s, 3H), 2.04 – 1.93 (m, 1H), 1.74 – 1.62 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 146.9, 136.0, 134.5, 132.7, 128.8, 128.7, 127.5, 127.1, 127.0, 126.7, 117.0, 110.2, 73.9, 65.8, 62.0, 57.1, 55.6, 52.4, 45.1, 39.8, 20.7. LC/MS (ES-API) *m/z* = 480/482 $[M+H]^+$. Anal. calcd. for $C_{23}H_{30}ClN_3O_4S$: C 57.55; H 6.30; N 8.75; S 6.68; Cl 7.39. Found: C 57.17; H 6.01; N 8.69; S 6.43; Cl 7.13.

2-(((2-Chloro-4-((2-(3,4-dichlorophenyl)pyrrolidin-1-yl)sulfonyl)phenyl)amino)methyl)-3,3,3-trifluoropropan-1-ol 12{*3,393,51*}, Z6318398407. Yield 55.8 mg (84%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 – 7.49 (m, 4H), 7.35 (d, J = 8.4 Hz, 1H), 6.88 (dd, J = 8.4, 3.0 Hz, 1H), 6.52 – 6.36 (m, 1H), 5.18 (t, J = 5.3 Hz, 1H), 4.72 (dd, J = 8.2, 4.6 Hz, 1H), 3.78 – 3.61 (m, 2H), 3.59 – 3.47 (m, 3H), 3.32 – 3.24 (m, 1H), 2.80 – 2.69 (m, 1H), 2.05 – 1.94 (m, 1H), 1.83 – 1.63 (m, 2H), 1.59 – 1.47 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 147.1, 145.0, 130.7, 130.2, 128.32, 128.26, 128.20, 127.2 (q, J = 282 Hz), 126.7, 123.7, 123.6, 117.5, 110.1, 61.7, 56.8, 49.3, 43.6 (q, J = 22.8 Hz), 38.5, 35.3, 23.8. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –67.1. LC/MS (ES-API) *m/z* = 531/533/535/537 $[M+H]^+$. Anal. calcd. for $C_{20}H_{20}Cl_3F_3N_2O_3S$: C 45.17; H 3.79; N 5.27; S 6.03; Cl 20.00. Found: C 45.38; H 3.93; N 5.06; S 6.25; Cl 19.80.

(2*S*,6*R*)-4-((2-Chloro-4-(4-(3-methylpyridin-2-yl)piperidin-1-yl)phenyl)sulfonyl)-2,6-dimethyl-1-(2,2,2-trifluoroethyl)piperazine 12{*4,445,103*}, Z6318670996. Yield 57.3 mg (86%). Browhish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (dd, J = 4.7, 1.7 Hz, 1H), 7.69 (d,

J = 9.1 Hz, 1H), 7.53 (d, *J* = 7.3 Hz, 1H), 7.15 – 7.05 (m, 2H), 7.00 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.08 (d, *J* = 13.0 Hz, 2H), 3.42 (d, *J* = 11.4 Hz, 2H), 3.38 – 3.31 (m, 3H), 3.26 – 3.13 (m, 1H), 3.08 (td, *J* = 12.9, 2.7 Hz, 2H), 2.79 – 2.70 (m, 2H), 2.42 – 2.32 (m, 4H), 1.91 – 1.78 (m, 2H), 1.78 – 1.67 (m, 2H), 1.03 (d, *J* = 6.3 Hz, 6H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 161.6, 153.5, 146.4, 137.7, 133.2, 132.7, 130.1, 125.8 (q, *J* = 282 Hz), 121.3, 120.3, 115.4, 111.4, 55.3, 50.7, 47.0, 39.9, 39.0, 29.7, 18.0, 17.5. ^{19}F{H} NMR (376 MHz, DMSO-*d*$_6$) δ –67.6. LC/MS (ES-API) *m/z* = 545/547 $[M+H]^+$. Anal. calcd. for $C_{25}H_{32}ClF_3N_4O_2S$: C 55.09; H 5.92; N 10.28; S 5.88; Cl 6.50. Found: C 54.81; H 5.60; N 10.39; S 5.59; Cl 6.67.

2-(4-(6-Methyl-3-((3-methyl-2-azaspiro[4.5]decan-2-yl)sulfonyl)pyridin-2-yl)-1,4-diazepan-1-yl)ethan-1-ol 12{*15,679,340*}, Z6318910497. Yield 53.0 mg (79%). Orangeish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.95 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.35 – 4.26 (m, 1H), 3.97 – 3.89 (m, 1H), 3.69 – 3.51 (m, 4H), 3.48 – 3.41 (m, 2H), 3.32 (br s, 1H), 3.18 (d, *J* = 10.3 Hz, 1H), 2.89 (d, *J* = 10.3 Hz, 1H), 2.82 – 2.71 (m, 2H), 2.68 – 2.59 (m, 2H), 2.36 (s, 3H), 1.95 (dd, *J* = 12.6, 7.2 Hz, 1H), 1.90 – 1.76 (m, 2H), 1.48 – 1.11 (m, 13H), 1.11 – 1.04 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 159.3, 157.9, 140.7, 119.5, 113.8, 59.4, 59.1, 57.7, 55.2, 54.9, 54.6, 52.8, 51.7, 46.0, 40.9, 35.7, 33.5, 27.5, 25.5, 24.0, 23.2, 22.3, 21.8. LC/MS (ES-API) *m/z* = 451 $[M+H]^+$. Anal. calcd. for $C_{23}H_{38}N_4O_3S$: C 61.30; H 8.50; N 12.43; S 7.11. Found: C 61.46; H 8.32; N 12.24; S 6.93.

***N*-(1-Allylcyclobutyl)-5-fluoro-6-(4-(3-phenylpropanoyl)piperazin-1-yl)pyridine-3-sulfonamide 12{*45,858,695*}, Z6318918653.** Yield 54.8 mg (82%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 8.35 – 8.27 (m, 1H), 7.79 (s, 1H), 7.74 (dd, *J* = 13.3, 2.0 Hz, 1H), 7.31 – 7.22 (m, 4H), 7.20 – 7.14 (m, 1H), 5.75 – 5.66 (m, 1H), 5.08 – 4.95 (m, 2H), 3.64 – 3.50 (m, 8H), 2.87 – 2.77 (m, 2H), 2.69 – 2.64 (m, 2H), 2.42 (d, *J* = 6.9 Hz, 2H), 2.10 – 1.99 (m,

2H), 1.87 – 1.73 (m, 2H), 1.68 – 1.54 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 170.2, 150.0 (d, J = 6.0 Hz), 146.9 (d, J = 259 Hz), 141.34, 141.29 (d, J = 5.0 Hz), 134.0, 130.1, 128.4, 128.2, 125.9, 121.4 (d, J = 22.1 Hz), 118.1, 57.9, 46.6 (d, J = 6.8 Hz), 46.4 (d, J = 6.8 Hz), 44.4, 41.6, 40.7, 34.0, 32.1, 30.7, 14.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –128.0. LC/MS (ES-API) m/z = 487 $[M+H]^+$. Anal. calcd. for $C_{25}H_{31}FN_4O_3S$: C 61.71; H 6.42; N 11.51; S 6.59. Found: C 61.56; H 6.16; N 11.37; S 6.57.

***N*-Ethyl-1-(3-fluoro-5-((3-methoxypyrrolidin-1-yl)sulfonyl)pyridin-2-yl)-*N*-propylazetidin-3-amine 12{*45*,*884*,*687*}, Z6318918691.** Yield 50.2 mg (75%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.25 – 8.21 (m, 1H), 7.74 (dd, J = 11.8, 2.0 Hz, 1H), 4.30 – 4.20 (m, 2H), 4.03 – 3.96 (m, 2H), 3.87 – 3.79 (m, 1H), 3.75 – 3.68 (m, 1H), 3.28 – 3.18 (m, 3H), 3.14 – 3.00 (m, 4H), 2.55 – 2.51 (m, 2H), 2.41 – 2.32 (m, 2H), 1.86 – 1.75 (m, 2H), 1.43 – 1.32 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 151.2 (d, J = 10.4 Hz), 146.0 (d, J = 257 Hz), 143.2 (d, J = 4.8 Hz), 120.28 (d, J = 18.1 Hz), 120.25, 78.8, 56.3, 55.6, 52.8, 52.7, 52.4, 50.8, 46.1, 43.5, 30.5, 19.8, 11.8, 11.4. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –139.8. LC/MS (ES-API) m/z = 401 $[M+H]^+$. Anal. calcd. for $C_{18}H_{29}FN_4O_3S$: C 53.98; H 7.30; N 13.99; S 8.00. Found: C 54.37; H 7.24; N 14.04; S 7.87.

***N*-(2-(*tert*-Butoxy)propyl)-2-(5,8-dimethoxy-3,4-dihydroisoquinolin-2(1*H*)-yl)quinoline-6-sulfonamide 12{*57*,*1216*,*870*}, Z6319004801.** Yield 51.5 mg (77%). Orangeish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 (d, J = 9.3 Hz, 1H), 8.18 (d, J = 2.2 Hz, 1H), 7.82 (dd, J = 8.9, 2.2 Hz, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.55 (t, J = 6.3 Hz, 1H), 7.42 (d, J = 9.3 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.78 (d, J = 8.9 Hz, 1H), 4.79 (s, 2H), 3.97 (t, J = 5.9 Hz, 2H), 3.81 (s, 3H), 3.73 (s, 3H), 3.60 – 3.53 (m, 1H), 2.77 (t, J = 5.9 Hz, 2H), 2.72 – 2.66 (m, 1H), 2.59 – 2.54 (m, 1H), 1.04 (s, 9H), 0.97 (d, J = 6.1 Hz, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 157.9, 150.5, 149.7,

149.1, 138.3, 133.0, 127.2, 126.7, 126.3, 124.2, 123.3, 121.3, 111.3, 108.0, 107.7, 73.1, 65.9, 55.51, 55.49, 49.2, 42.4, 41.4, 28.0, 22.8, 20.7. LC/MS (ES-API) *m/z* = 514 $[M+H]^+$. Anal. calcd. for $C_{27}H_{35}N_3O_5S$: C 63.14; H 6.87; N 8.18; S 6.24. Found: C 62.82; H 7.01; N 8.08; S 6.16.

4-((2-(4-(2-Isopropoxyethyl)piperazin-1-yl)-5-(trifluoromethyl)phenyl)sulfonyl)-3-methylmorpholine 12{*10,604,260*}, Z6319012289. Yield 51.8 mg (78%). Browhish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.5 Hz, 1H), 8.00 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 3.87 – 3.81 (m, 1H), 3.78 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.62 – 3.42 (m, 5H), 3.31 – 3.24 (m, 2H), 3.22 – 3.12 (m, 3H), 2.98 – 2.86 (m, 2H), 2.67 – 2.51 (m, 6H), 1.08 (d, *J* = 6.1 Hz, 6H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 155.8, 136.0, 131.0 (q, *J* = 3.4 Hz), 127.8 (q, *J* = 3.2 Hz), 124.7, 124.4 (q, *J* = 32.9 Hz), 123.5 (d, *J* = 272.0 Hz), 70.7, 70.6, 66.4, 65.4, 57.5, 53.6, 53.0, 48.8, 41.4, 22.0, 14.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –61.4. LC/MS (ES-API) *m/z* = 480 $[M+H]^+$. Anal. calcd. for $C_{21}H_{32}F_3N_3O_4S$: C 52.60; H 6.73; N 8.76; S 6.69. Found: C 52.62; H 6.96; N 8.73; S 6.45.

6-(1-(Hydroxymethyl)-6-azaspiro[2.5]octan-6-yl)-*N*-((1-(2-methoxyethyl)cyclohexyl)-methyl)-4-(trifluoromethyl)pyridine-3-sulfonamide 12{*21,789,446*}, Z6319062744. Yield 57.0 mg (85%). Orangeish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 7.26 (br s, 1H), 7.15 (s, 1H), 4.46 (t, *J* = 5.1 Hz, 1H), 3.98 – 3.89 (m, 1H), 3.87 – 3.78 (m, 1H), 3.77 – 3.65 (m, 2H), 3.61 – 3.54 (m, 1H), 3.31 – 3.25 (m, 3H), 3.16 (s, 3H), 2.71 (s, 2H), 1.67 – 1.57 (m, 1H), 1.52 – 1.18 (m, 15H), 0.93 – 0.85 (m, 1H), 0.51 (dd, *J* = 8.6, 4.3 Hz, 1H), 0.22 (t, *J* = 4.8 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 159.2, 151.2, 135.4 (q, *J* = 33.1 Hz), 122.1 (q, *J* = 275 Hz), 119.5, 104.1 (q, *J* = 5.0 Hz), 67.9, 60.7, 57.9, 49.2, 44.8, 44.7, 35.8, 35.2, 34.5, 33.1, 29.2, 25.63, 25.57, 21.7, 20.9, 15.2. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –59.7. LC/MS (ES-

API) *m/z* = 520 $[M+H]^+$. Anal. calcd. for $C_{24}H_{36}F_3N_3O_4S$: C 55.48; H 6.98; N 8.09; S 6.17. Found: C 55.58; H 7.33; N 8.21; S 6.33.

6-((3-Bromo-4-chlorobenzyl)amino)-*N*-(3,3-difluorocycloheptyl)pyridine-3-sulfonamide 12{*14,643,302*}, Z7151782314. Yield 50.3 mg (75%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.32 (d, *J* = 2.5 Hz, 1H), 7.98 (t, *J* = 6.1 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.60 – 7.52 (m, 2H), 7.33 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.64 (d, *J* = 8.9 Hz, 1H), 4.54 (d, *J* = 6.1 Hz, 2H), 3.22 – 3.11 (m, 1H), 2.21 – 1.84 (m, 4H), 1.76 – 1.65 (m, 1H), 1.63 – 1.56 (m, 1H), 1.54 – 1.27 (m, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.0, 147.4, 141.1, 135.0, 132.3, 131.2, 130.3, 128.1, 125.0 (t, *J* = 239 Hz), 124.6, 121.3, 48.2 (dd, *J* = 11.9, 2.7 Hz), 44.1 (t, *J* = 26.4 Hz), 42.8, 36.8 (t, *J* = 25.6 Hz), 35.6, 24.4, 20.4 (t, *J* = 6.3 Hz). ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –80.0 (d, *J* = 243 Hz), –85.5 (d, *J* = 243 Hz). LC/MS (ES-API) *m/z* = 508/510/512 $[M+H]^+$. Anal. calcd. for $C_{19}H_{21}BrClF_2N_3O_2S$: C 44.85; H 4.16; N 8.26; S 6.30; Cl 6.97; Br 15.70. Found: C 44.96; H 4.44; N 7.95; S 6.19; Cl 6.59; Br 16.03.

1-(5-((4-(2-Methoxybenzyl)piperidin-1-yl)sulfonyl)pyridin-2-yl)-*N*,*N*,3-trimethylpiperidin-3-amine 12{*14,641,300*}, Z7151782946. Yield 55.1 mg (83%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.26 (d, *J* = 2.6 Hz, 1H), 7.60 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.15 (td, *J* = 7.5, 1.8 Hz, 1H), 7.04 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.94 – 6.86 (m, 2H), 6.82 (t, *J* = 7.5 Hz, 1H), 3.91 (d, *J* = 13.4 Hz, 1H), 3.72 (s, 3H), 3.69 – 3.63 (m, 1H), 3.57 – 3.42 (m, 3H), 3.37 – 3.33 (m, 2H), 2.44 (d, *J* = 7.0 Hz, 2H), 2.20 – 2.06 (m, 7H), 1.84 – 1.65 (m, 2H), 1.56 (d, *J* = 12.5 Hz, 2H), 1.53 – 1.36 (m, 3H), 1.27 – 1.12 (m, 2H), 0.80 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 159.7, 157.2, 148.0, 136.4, 130.5, 127.6, 127.3, 120.0, 117.5, 110.6, 105.3, 55.2, 55.0, 51.9, 45.9, 44.3, 37.8, 35.9, 34.8, 34.4, 30.8, 20.8, 13.7. LC/MS (ES-API) *m/z* = 487

$[M+H]^+$. Anal. calcd. for $C_{26}H_{38}N_4O_3S$: C 64.17; H 7.87; N 11.51; S 6.59. Found: C 64.46; H 8.18; N 11.83; S 6.58.

6-(((1-Methyl-1*H*-pyrazol-3-yl)methyl)amino)-*N*-(1-((trifluoromethyl)sulfonyl)piperidin-4-yl)pyridine-3-sulfonamide 12{*47,1065,715*}, Z7151846832. Yield 54.7 mg (82%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.36 (d, J = 2.5 Hz, 1H), 7.74 (t, J = 5.6 Hz, 1H), 7.69 – 7.62 (m, 2H), 7.58 (d, J = 2.2 Hz, 1H), 6.62 (d, J = 8.9 Hz, 1H), 6.13 (d, J = 2.2 Hz, 1H), 4.44 (d, J = 5.6 Hz, 2H), 3.78 (s, 3H), 3.69 – 3.57 (m, 2H), 3.32 – 3.18 (m, 3H), 1.80 – 1.69 (m, 2H), 1.46 – 1.34 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 160.1, 149.2, 147.3, 134.6, 131.4, 124.3, 119.6 (q, J = 324 Hz), 108.3, 104.0, 48.0, 44.8, 38.34, 38.29, 32.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –76.2. LC/MS (ES-API) *m/z* = 483 $[M+H]^+$. Anal. calcd. for $C_{16}H_{21}F_3N_6O_4S_2$: C 39.83; H 4.39; N 17.42; S 13.29. Found: C 39.63; H 4.41; N 17.09; S 13.32.

(1-(6-((4-(*o*-Tolylsulfonyl)piperazin-1-yl)sulfonyl)pyridin-2-yl)-3-(trifluoromethyl)pyrolidin-3-yl)methanol 12{*53,1174,829*}, Z7151847595. Yield 56.3 mg (84%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.79 – 7.69 (m, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.06 (d, J = 7.2 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 5.42 (t, J = 5.7 Hz, 1H), 3.69 – 3.48 (m, 6H), 3.32 – 3.24 (m, 4H), 3.20 – 3.08 (m, 4H), 2.51 (s, 3H), 2.22 (t, J = 7.2 Hz, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 156.0, 153.5, 138.8, 137.3, 135.0, 133.3, 133.0, 129.6, 128.3 (q, J = 282 Hz), 126.5, 111.0, 110.1, 60.8, 52.1, 51.9, 48.7, 46.0, 45.7, 45.5, 44.8, 27.1, 20.1. LC/MS (ES-API) *m/z* = 549 $[M+H]^+$. Anal. calcd. for $C_{22}H_{27}F_3N_4O_5S_2$: C 48.17; H 4.96; N 10.21; S 11.69. Found: C 48.51; H 5.23; N 10.34; S 11.80.

***N*-(1-Allylcyclopent-3-en-1-yl)-4-(((2-(2-methoxyethoxy)pyridin-3-yl)methyl)amino)-pyridine-3-sulfonamide 12{*13,626,283*}, Z7151848999.** Yield 52.6 mg (79%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.48 (s, 1H), 8.15 (d, J = 6.0 Hz, 1H), 8.06

(dd, *J* = 5.0, 1.8 Hz, 1H), 7.83 (s, 1H), 7.56 (dd, *J* = 7.3, 1.8 Hz, 1H), 6.97 – 6.87 (m, 2H), 6.63 (d, *J* = 6.0 Hz, 1H), 5.74 – 5.60 (m, 1H), 5.48 (s, 2H), 5.01 – 4.93 (m, 2H), 4.52 – 4.41 (m, 4H), 3.78 – 3.65 (m, 2H), 3.33 (s, 3H), 2.47 (d, *J* = 15.2 Hz, 2H), 2.36 (d, *J* = 7.0 Hz, 2H), 2.26 (d, *J* = 15.2 Hz, 2H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 160.6, 152.5, 149.1, 148.9, 145.4, 136.7, 134.0, 128.2, 121.3, 119.9, 118.2, 117.0, 106.4, 70.2, 64.9, 64.8, 58.3, 43.9, 43.6, 40.0. LC/MS (ES-API) *m/z* = 445 $[M+H]^+$. Anal. calcd. for $C_{22}H_{28}N_4O_4S$: C 59.44; H 6.35; N 12.60; S 7.21. Found: C 59.54; H 5.99; N 12.78; S 7.17.

(1-((2-((2-(4-Methoxyphenyl)-2-(piperidin-1-yl)ethyl)amino)-6-methylpyridin-3-yl)sulfonyl)-4,4-dimethylpiperidin-3-yl)methanol 12{*15*,*689*,*352*}, Z7151877790. Yield 50.8 mg (76%). The compound was obtained as 1:1 mixture of diastereomers. Brownish gum. ^1H NMR (500 MHz, DMSO-d_6) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.25 – 7.15 (m, 3H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.54 (d, *J* = 7.9 Hz, 1H), 4.49 (q, *J* = 5.2 Hz, 1H), 3.78 – 3.56 (m, 8H), 3.40 – 3.36 (m, 0.5×1H), 3.32 – 3.28 (m, 0.5×1H), 3.07 – 2.98 (m, 1H), 2.56 (dd, *J* = 12.8, 9.7 Hz, 1H), 2.46 – 2.14 (m, 8H), 1.56 – 1.22 (m, 9H), 0.91 (s, 0.5×3H), 0.90 (s, 0.5×3H), 0.64 (s, 0.5×3H), 0.63 (s, 0.5×3H). $^{13}C\{H\}$ NMR (126 MHz, DMSO-d_6) δ 162.3, 158.4, 153.7, 139.3, 129.72, 129.66, 128.6, 128.5, 113.2, 110.4, 110.2, 110.1, 79.2, 66.6, 66.5, 58.9, 54.9, 49.8, 47.0, 47.0, 44.7, 44.6, 42.1, 41.9, 41.2, 30.0, 29.2, 25.8, 24.5, 24.4, 19.2. LC/MS (ES-API) *m/z* = 531 $[M+H]^+$. Anal. calcd. for $C_{28}H_{42}N_4O_4S$: C 63.37; H 7.98; N 10.56; S 6.04. Found: C 63.30; H 7.80; N 10.23; S 6.05.

***N*-(2-(1,1-Difluoroethyl)benzyl)-2-((3-ethoxy-4-methoxybenzyl)amino)-5-methylpyridine-3-sulfonamide 12{*48*,*1082*,732}, Z7151888822.** Yield 51.4 mg (77%). Brownish gum. ^1H NMR (500 MHz, DMSO-d_6) δ 8.43 (t, *J* = 6.1 Hz, 1H), 8.04 (d, *J* = 2.2 Hz, 1H), 7.65 (d, *J* = 2.2 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.40 – 7.29 (m, 2H), 6.96 (s, 1H), 6.90 – 6.81 (m, 2H), 6.68 (t, *J* = 5.6

Hz, 1H), 4.55 (d, *J* = 5.6 Hz, 2H), 4.18 (d, *J* = 5.9 Hz, 2H), 3.93 (q, *J* = 7.0 Hz, 2H), 3.71 (s, 3H), 2.10 (s, 3H), 1.93 (t, *J* = 19.1 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 152.1, 151.6, 147.84, 147.80, 138.3, 134.6, 134.3 (t, *J* = 25.3 Hz), 132.2, 130.0, 129.4, 127.3, 125.4 (t, *J* = 8.0 Hz), 123.2 (t, *J* = 239 Hz), 120.0, 119.3, 116.4, 112.5, 111.8, 63.5, 55.5, 44.0, 42.5, 25.3 (t, *J* = 28.5 Hz), 16.4, 14.7. ^{19}F{H} NMR (376 MHz, DMSO-*d*$_6$) δ –81.6. LC/MS (ES-API) *m/z* = 506 $[M+H]^+$. Anal. calcd. for $C_{25}H_{29}F_2N_3O_4S$: C 59.39; H 5.78; N 8.31; S 6.34. Found: C 59.38; H 5.94; N 8.01; S 6.03.

4-Methyl-*N*-(1-(4-methyl-1,2,3-thiadiazol-5-yl)ethyl)-6-((2,2,3-trimethylbutyl)amino)-pyridine-3-sulfonamide 12{*43*,*1032*,*682*}, Z7151894681. Yield 57.8 mg (87%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 8.33 (d, *J* = 7.0 Hz, 1H), 8.19 (s, 1H), 7.02 (t, *J* = 6.1 Hz, 1H), 6.36 (s, 1H), 4.71 (quint, *J* = 7.0 Hz, 1H), 3.32 – 3.25 (m, 1H), 3.14 (dd, *J* = 13.6, 5.8 Hz, 1H), 2.46 (s, 3H), 2.29 (s, 3H), 1.59 – 1.53 (m, 1H), 1.37 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 6H), 0.79 (s, 6H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 161.4, 155.5, 154.6, 149.3, 144.7, 121.5, 109.6, 48.7, 45.0, 36.7, 33.0, 23.6, 22.1, 19.4, 17.4, 11.9. LC/MS (ES-API) *m/z* = 412 $[M+H]^+$. Anal. calcd. for $C_{18}H_{29}N_5O_2S_2$: C 52.53; H 7.10; N 17.02; S 15.58. Found: C 52.43; H 7.29; N 16.83; S 15.42.

1-(1-((6-((1,8-Dioxaspiro[4.5]decan-3-yl)amino)-4-methylpyridin-3-yl)sulfonyl)piperidin-3-yl)imidazolidin-2-one 12{*43*,*1012*,*666*}, Z7151895125. Yield 50.8 mg (76%). Yellowish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 8.29 (s, 1H), 7.60 (d, *J* = 6.5 Hz, 1H), 6.42 (s, 1H), 6.33 (s, 1H), 4.62 – 4.39 (m, 1H), 4.02 (dd, *J* = 9.0, 6.2 Hz, 1H), 3.72 – 3.62 (m, 2H), 3.60 – 3.40 (m, 6H), 3.31 – 3.25 (m, 2H), 3.20 – 3.16 (m, 2H), 2.61 – 2.54 (m, 1H), 2.48 – 2.42 (m, 1H), 2.35 (s, 3H), 2.18 (dd, *J* = 12.9, 8.1 Hz, 1H), 1.78 – 1.43 (m, 9H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 161.3, 160.3, 150.7, 145.9, 119.5, 110.2, 78.9, 70.5, 64.5, 64.4, 51.3, 48.2, 46.9, 44.6, 42.9, 40.7,

37.7, 37.5, 36.9, 26.8, 24.0, 19.9. LC/MS (ES-API) *m/z* = 480 $[M+H]^+$. Anal. calcd. for $C_{22}H_{33}N_5O_5S$: C 55.10; H 6.94; N 14.60; S 6.68. Found: C 55.30; H 7.33; N 14.26; S 6.44.

6-(2-(2-Methoxyethyl)-2-methylmorpholino)-4-methyl-*N*-(2-((tetrahydrofuran-2-yl)-methoxy)ethyl)pyridine-3-sulfonamide 12{*43,995,286*}, Z7151895589. Yield 53.9 mg (81%). Yellowish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.50 (s, 1H), 6.79 (s, 1H), 3.85 – 3.78 (m, 1H), 3.71 – 3.64 (m, 3H), 3.61 – 3.33 (m, 9H), 3.22 (d, *J* = 5.2 Hz, 2H), 3.21 (s, 3H), 2.94 – 2.83 (m, 2H), 2.45 (s, 3H), 1.89 – 1.63 (m, 5H), 1.50 – 1.39 (m, 1H), 1.13 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.1, 148.6, 147.0, 123.1, 107.7, 77.1, 72.9, 72.2, 69.1, 67.5, 67.2, 59.5, 57.9, 52.3, 44.0, 41.9, 35.7, 27.7, 25.1, 21.8, 19.7. LC/MS (ES-API) *m/z* = 458 $[M+H]^+$. Anal. calcd. for $C_{21}H_{35}N_3O_6S$: C 55.12; H 7.71; N 9.18; S 7.01. Found: C 54.97; H 7.89; N 8.82; S 7.37.

4-(((5,7-Dimethyl-[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)methyl)amino)-3-fluoro-*N*-(4-hydroxybutan-2-yl)-*N*-methylbenzenesulfonamide 12{*2,358,15*}, Z7151910110. Yield 57.3 mg (70%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.38 (dd, *J* = 11.4, 2.3 Hz, 1H), 7.35 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.13 (s, 1H), 7.08 – 6.98 (m, 1H), 6.92 (t, *J* = 8.6 Hz, 1H), 4.63 (d, *J* = 6.0 Hz, 2H), 4.43 – 4.32 (m, 1H), 3.97 (h, *J* = 7.0 Hz, 1H), 3.32 – 3.25 (m, 2H), 2.68 (s, 3H), 2.58 – 2.52 (m, 6H), 1.56 – 1.33 (m, 2H), 0.79 (d, *J* = 7.0 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 165.1, 164.4, 155.0, 149.3 (d, *J* = 242 Hz), 146.8, 140.2 (d, *J* = 11.6 Hz), 125.2 (d, *J* = 5.4 Hz), 124.6 (d, *J* = 2.6 Hz), 113.1 (d, *J* = 20.8 Hz), 111.4 (d, *J* = 4.1 Hz), 110.7, 57.9, 49.5, 40.7, 36.6, 27.4, 24.4, 16.6, 16.5. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ – 133.7. LC/MS (ES-API) *m/z* = 437 $[M+H]^+$. Anal. calcd. for $C_{19}H_{25}FN_6O_3S$: C 52.28; H 5.77; N 19.25; S 7.34. Found: C 52.30; H 5.91; N 19.35; S 7.52.

3-Fluoro-*N*-(4-(hydroxymethyl)phenethyl)-4-(((1-isopropyl-1*H*-pyrazol-3-yl)methyl)-amino)benzenesulfonamide 12{*2,371,28*}, Z7151910112. Yield 54.3 mg (84%). Yellowish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.62 (d, J = 2.3 Hz, 1H), 7.39 – 7.31 (m, 3H), 7.19 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 6.85 (t, J = 8.5 Hz, 1H), 6.78 – 6.72 (m, 1H), 6.09 (d, J = 2.3 Hz, 1H), 5.10 (t, J = 5.7 Hz, 1H), 4.47 – 4.37 (m, 3H), 4.32 (d, J = 6.0 Hz, 2H), 2.90 – 2.84 (m, 2H), 2.62 (t, J = 7.5 Hz, 2H), 1.37 (d, J = 6.7 Hz, 6H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 149.3 (d, J = 242 Hz), 148.6, 140.4, 140.2 (d, J = 11.6 Hz), 137.1, 128.3, 128.2, 126.5, 125.4 (d, J = 5.2 Hz), 124.3 (d, J = 1.8 Hz), 112.7 (d, J = 21.0 Hz), 111.0 (d, J = 4.2 Hz), 103.2, 62.7, 52.6, 44.2, 40.1, 34.9, 22.7. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –134.0. LC/MS (ES-API) *m/z* = 447 $[M+H]^+$. Anal. calcd. for $C_{22}H_{27}FN_4O_3S$: C 59.18; H 6.09; N 12.55; S 7.18. Found: C 59.55; H 6.33; N 12.36; S 7.00.

***N*-(3-Bromo-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-6-yl)-3-fluoro-4-(2-(methoxy-methyl)morpholino)benzenesulfonamide 12{*2,370,27*}, Z7151910149.** Yield 51.1 mg (70%). The compound was obtained as 1:1 mixture of diastereomers. Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 (d, J = 7.5 Hz, 1H), 7.60 – 7.48 (m, 2H), 7.26 (dd, J = 8.0, 2.0 Hz, 1H), 7.20 (td, J = 8.6, 2.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 6.83 (t, J = 2.4 Hz, 1H), 3.92 (d, J = 11.4 Hz, 1H), 3.81 – 3.74 (m, 1H), 3.69 (td, J = 11.4, 2.5 Hz, 1H), 3.50 – 3.40 (m, 2H), 3.40 – 3.35 (m, 2H), 3.27 (s, 3H), 3.07 – 2.95 (m, 1H), 2.94 – 2.86 (m, 1H), 2.82 (dd, J = 13.6, 9.7 Hz, 1H), 2.75 – 2.66 (m, 1H), 2.66 – 2.59 (m, 2H), 2.55 (d, J = 13.6 Hz, 1H), 1.88 – 1.70 (m, 2H), 1.64 – 1.54 (m, 1H), 1.30 – 1.20 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 153.4 (d, J = 248 Hz), 142.72 (d, J = 1.5 Hz), 142.67 (d, J = 1.7 Hz), 142.4, 140.3, 133.9 (d, J = 6.6 Hz), 132.1, 130.9, 129.2, 123.9, 118.9, 118.6, 114.6 (d, J = 4.5 Hz), 114.4 (d, J = 4.5 Hz), 73.8, 72.8, 65.5, 58.6, 51.98, 51.78, 51.75, 51.74, 51.71, 49.4, 49.34, 49.31, 49.28, 42.0, 38.2, 33.8, 24.8. ^{19}F{H} NMR

(376 MHz, DMSO-d_6) δ –120.4, –120.5. LC/MS (ES-API) *m/z* = 527/529 $[M+H]^+$. Anal. calcd. for $C_{23}H_{28}BrFN_2O_4S$: C 52.38; H 5.35; N 5.31; S 6.08; Br 15.15. Found: C 52.70; H 5.27; N 5.24; S 5.76; Br 15.53.

***N*-(1-((3-Fluoro-4-(((2,2,5,5-tetramethyltetrahydrofuran-3-yl)methyl)amino)phenyl)-sulfonyl)piperidin-4-yl)pyrimidin-2-amine 12{*2,360,17*}, Z7151910186.** Yield 58.1 mg (78%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 (d, *J* = 4.8 Hz, 2H), 7.36 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.32 (dd, *J* = 11.4, 2.1 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 8.5 Hz, 1H), 6.53 (t, *J* = 4.8 Hz, 1H), 6.45 (t, *J* = 3.9 Hz, 1H), 3.71 – 3.61 (m, 1H), 3.53 – 3.40 (m, 2H), 3.26 – 3.17 (m, 1H), 3.12 – 3.02 (m, 1H), 2.47 – 2.37 (m, 3H), 2.03 (dd, *J* = 12.2, 6.7 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.65 (t, *J* = 12.2 Hz, 1H), 1.59 – 1.48 (m, 2H), 1.21 (s, 3H), 1.21 (s, 3H), 1.11 (s, 3H), 1.04 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 161.6, 157.9, 149.2 (d, *J* = 242 Hz), 140.9 (d, *J* = 11.7 Hz), 125.6, 119.9 (d, *J* = 5.5 Hz), 113.6 (d, *J* = 21.0 Hz), 110.5 (d, *J* = 4.2 Hz), 110.0, 81.0, 78.0, 46.9, 46.4, 45.0, 43.4, 42.9, 30.7, 30.4, 30.0, 29.6, 23.8. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –133.7. LC/MS (ES-API) *m/z* = 492 $[M+H]^+$. Anal. calcd. for $C_{24}H_{34}FN_5O_3S$: C 58.63; H 6.97; N 14.25; S 6.52. Found: C 58.79; H 7.09; N 14.22; S 6.31.

2-Chloro-4-((3,4-dimethylbenzyl)(methyl)amino)-*N*-(tetrahydro-2*H*-pyran-4-yl)benzene-sulfonamide 12{*4,435,92*}, Z7151910228. Yield 58.0 mg (80%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.69 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.95 (s, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 6.72 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.58 (s, 2H), 3.72 (dt, *J* = 11.6, 3.5 Hz, 2H), 3.18 (td, *J* = 11.6, 2.5 Hz, 2H), 3.14 – 3.05 (m, 4H), 2.21 – 2.12 (m, 6H), 1.52 – 1.38 (m, 4H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 152.2, 136.4, 134.8, 132.1, 131.7, 129.7, 127.7, 124.0, 123.9, 113.0, 109.4, 65.6, 54.6, 49.2, 38.7, 33.2,

19.5, 19.0. LC/MS (ES-API) *m/z* = 423/425 $[M+H]^+$. Anal. calcd. for $C_{21}H_{27}ClN_2O_3S$: C 59.63; H 6.43; N 6.62; S 7.58; Cl 8.38. Found: C 59.96; H 6.76; N 6.29; S 7.29; Cl 8.73.

2-Chloro-4-(3-cyclopropyl-1-oxa-2,8-diazaspiro[4.5]dec-3-en-8-yl)-*N*-(2-(4-(tetrahydro-furan-3-yl)-1*H*-pyrazol-1-yl)ethyl)benzenesulfonamide 12{*4,469,127*}, Z7151910281. Yield 60.3 mg (88%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.66 (d, *J* = 9.0 Hz, 1H), 7.60 (t, *J* = 5.7 Hz, 1H), 7.48 (s, 1H), 7.30 (s, 1H), 7.07 (d, *J* = 2.6 Hz, 1H), 6.95 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.07 (t, *J* = 6.5 Hz, 2H), 3.92 (t, *J* = 7.5 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.74 (q, *J* = 7.5 Hz, 1H), 3.49 – 3.37 (m, 5H), 3.23 – 3.16 (m, 1H), 3.13 (q, *J* = 6.3 Hz, 2H), 2.63 (s, 2H), 2.24 – 2.14 (m, 1H), 1.82 – 1.63 (m, 6H), 0.85 – 0.78 (m, 2H), 0.75 – 0.68 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 160.8, 153.0, 137.5, 132.2, 131.9, 127.9, 124.0, 121.6, 115.5, 111.5, 82.5, 73.6, 67.1, 50.5, 44.4, 43.5, 42.5, 34.6, 34.3, 33.7, 9.1, 5.2. LC/MS (ES-API) *m/z* = 534/536 $[M+H]^+$. Anal. calcd. for $C_{25}H_{32}ClN_5O_4S$: C 56.22; H 6.04; N 13.11; S 6.00; Cl 6.64. Found: C 56.22; H 6.40; N 13.28; S 6.06; Cl 6.79.

2-Chloro-4-((isochroman-4-ylmethyl)amino)-*N*-(3-(methoxymethyl)cyclobutyl)benzene-sulfonamide 12{*4,448,106*}, Z7151910316. Yield 55.4 mg (68%). The compound was obtained as 1:1 mixture of diastereomers. Yellowish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71 – 7.54 (m, 2H), 7.30 (dd, *J* = 5.6, 3.5 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.10 – 6.99 (m, 2H), 6.75 (d, *J* = 2.2 Hz, 1H), 6.66 (dd, *J* = 8.9, 2.2 Hz, 1H), 4.77 (d, *J* = 15.2 Hz, 1H), 4.67 (d, *J* = 15.2 Hz, 1H), 4.03 (dd, *J* = 11.6, 2.0 Hz, 1H), 3.74 (dd, *J* = 11.6, 3.3 Hz, 1H), 3.47 – 3.35 (m, 1H), 3.33 – 3.20 (m, 3H), 3.19 – 3.14 (m, 4H), 2.91 – 2.82 (m, 1H), 2.27 – 2.14 (m, 0.5H), 2.01 – 1.91 (m, 2.5H), 1.76 – 1.71 (m, 0.5H), 1.64 – 1.54 (m, 1.5H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 152.6, 134.9, 134.5, 132.21, 132.16, 132.0, 129.0, 126.43, 126.36, 124.2, 123.4, 123.3, 113.1, 109.2, 76.2, 75.0, 67.4, 65.6, 58.0, 57.9, 46.1, 45.8, 44.2, 36.1, 33.6, 31.9, 27.8, 27.7. LC/MS (ES-API) *m/z* =

451/453 $[M+H]^+$. Anal. calcd. for $C_{22}H_{27}ClN_2O_4S$: C 58.59; H 6.03; N 6.21; S 7.11; Cl 7.86. Found: C 58.91; H 6.13; N 6.07; S 7.27; Cl 7.59.

5-Chloro-2-((4-(2-hydroxyethoxy)benzyl)amino)-*N*-(3-methoxy-2,2-dimethylcyclobutyl)-benzenesulfonamide 12{*7,508,165*}, Z7151910348. Yield 65.2 mg (77%). The compound was obtained as 1:1 mixture of diastereomers. Beige gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.14 (d, J = 8.5 Hz, 0.5H), 8.06 (d, J = 8.5 Hz, 0.5H), 7.51 (dd, J = 5.6, 2.5 Hz, 1H), 7.34 (dt, J = 9.0, 2.5 Hz, 1H), 7.28 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.72 (d, J = 9.0 Hz, 1H), 6.48 – 6.40 (m, 1H), 4.83 (t, J = 5.6 Hz, 1H), 4.38 (d, J = 5.6 Hz, 2H), 3.95 (t, J = 5.1 Hz, 2H), 3.69 (q, J = 5.1 Hz, 2H), 3.32 – 3.23 (m, 1H), 3.19 – 3.03 (m, 3.5H), 2.89 (q, J = 8.6 Hz, 0.5H), 2.25 – 2.16 (m, 0.5H), 1.96 – 1.89 (m, 1H), 1.65 – 1.58 (m, 0.5H), 0.92 (s, 2H), 0.87 (s, 1H), 0.85 (s, 1H), 0.79 (s, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 157.8, 143.9, 143.8, 133.42, 133.40, 130.29, 130.28, 128.34, 128.31, 123.0, 122.95, 118.14, 118.11, 114.4, 114.21, 114.17, 79.0, 76.2, 69.5, 59.6, 56.2, 56.1, 52.9, 48.7, 46.5, 45.67, 45.65, 44.8, 32.6, 31.0, 27.1, 21.7, 21.0, 15.3. LC/MS (ES-API) *m/z* = 467/469 $[M–H]^–$. Anal. calcd. for $C_{22}H_{29}ClN_2O_5S$: C 56.34; H 6.23; N 5.97; S 6.84; Cl 7.56. Found: C 56.59; H 6.63; N 6.27; S 6.92; Cl 7.26.

4-(2-Benzylmorpholino)-3-chloro-*N*-(2-(3-methylpyrrolidin-1-yl)ethyl)benzene-sulfonamide trifluoroacetate 12{*3,400,58*}, Z7151910433. Yield 50.1 mg (70%). The compound was obtained as 1:1 mixture of diastereomers. Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.02 – 9.87 (m, 1H), 8.03 (t, J = 6.1 Hz, 1H), 7.71 (dd, J = 8.5, 2.2 Hz, 1H), 7.76 (d, J = 2.2 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.23 – 7.17 (m, 1H), 3.98 – 3.89 (m, 1H), 3.87 – 3.77 (m, 1H), 3.72 – 3.46 (m, 4H), 3.32 – 2.98 (m, 7H), 2.94 – 2.79 (m, 2H), 2.74 (dd, J = 13.8, 6.2 Hz, 1H), 2.67 – 2.57 (m, 1.5H), 2.54 – 2.51 (m, 0.5H), 2.48 – 2.42 (m, 0.5H), 2.31 – 2.25 (m, 0.5H), 2.18 – 2.03 (m, 1H), 1.62 – 1.55 (m, 0.5H), 1.50 – 1.41 (m, 0.5H), 1.13 – 0.92

(m, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 158.2 (q, J = 30.8 Hz), 152.1, 137.8, 133.7, 129.2, 128.7, 128.2, 127.1, 126.9, 126.2, 121.1, 117.17 (q, J = 298.7 Hz), 76.1, 66.0, 59.6, 59.2, 54.9, 54.3, 53.7, 53.6, 53.1, 50.1, 38.7, 38.6, 31.6, 31.5, 30.7, 30.3, 18.2, 17.1. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ -74.1. LC/MS (ES-API) *m/z* = 478/480 $[M–TFA+H]^+$. Anal. calcd. for $C_{26}H_{33}ClF_3N_3O_5S$: C 52.74; H 5.62; N 7.10; S 5.41; Cl 5.99. Found: C 53.09; H 5.73; N 6.80; S 5.23; Cl 5.65.

1-((3-Chloro-4-(((4-chloro-1-methyl-1*H*-pyrazol-3-yl)methyl)amino)phenyl)sulfonyl)-*N*,*N*-bis(2-methoxyethyl)azetidin-3-amine 12{*3,397,55*}, Z7151910450. Yield 57.1 mg (80%). Yellowish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.91 (s, 1H), 7.62 – 7.59 (m, 1H), 7.53 (dd, J = 8.8, 2.0 Hz, 1H), 6.95 (d, J = 8.8 Hz, 1H), 6.71 (t, J = 5.7 Hz, 1H), 4.41 (d, J = 5.7 Hz, 2H), 3.78 (s, 3H), 3.68 (t, J = 7.5 Hz, 2H), 3.52 – 3.46 (m, 1H), 3.41 (t, J = 7.5 Hz, 2H), 3.21 – 3.10 (m, 10H), 2.42 (t, J = 5.7 Hz, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 147.6, 144.2, 129.8, 128.8, 128.7, 120.0, 117.5, 110.7, 106.3, 70.2, 57.9, 55.3, 51.2, 49.3, 39.2, 38.2. LC/MS (ES-API) *m/z* = 506/508/510 $[M+H]^+$. Anal. calcd. for $C_{20}H_{29}Cl_2N_5O_4S$: C 47.43; H 5.77; N 13.83; S 6.33; Cl 14.00. Found: C 47.59; H 5.67; N 13.94; S 6.07; Cl 14.38.

1-((2-Chloro-4-(((2*R,4*S**)-2-methyl-4-(trifluoromethyl)pyrrolidin-1-yl)sulfonyl)phenyl)amino)-3-(3,4-dihydroisoquinolin-2(1*H*)-yl)propan-2-ol trifluoroacetate 12{*3,413,71*}, Z7151910463.** Yield 55.1 mg (85%). The compound was obtained as 1:1 mixture of diastereomers. Orangeish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.04 (br s, 1H), 7.65 (t, J = 1.8 Hz, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.32 – 7.20 (m, 3H), 7.18 (d, J = 7.4 Hz, 1H), 6.98 (d, J = 8.8 Hz, 1H), 6.41 – 6.28 (m, 1H), 4.66 – 4.47 (m, 1H), 4.46 – 4.32 (m, 1H), 4.31 – 4.20 (m, 1H), 3.82 – 3.36 (m, 9H), 3.26 – 2.95 (m, 3H), 2.81 – 2.67 (m, 1H), 2.28 – 2.15 (m, 1H), 1.61 – 1.48 (m, 1H), 1.29 (d, J = 6.1 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 158.8 (q, J = 31.3 Hz),

148.5, 132.0, 131.8, 129.2, 129.1, 128.9, 128.8, 128.4, 127.4 (q, J = 277 Hz), 127.3, 123.1, 118.3, 117.8 (q, J = 298 Hz), 111.6, 64.5, 64.4, 59.1, 58.4, 56.4, 54.4, 52.3, 51.0, 48.9, 48.7, 47.5, 34.1, 25.3, 25.0, 22.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –69.9, –74.2. LC/MS (ES-API) *m/z* = 532/534 $[M–TFA+H]^+$. Anal. calcd. for $C_{26}H_{30}ClF_6N_3O_5S$: C 48.34; H 4.68; N 6.50; S 4.96; Cl 5.49. Found: C 48.19; H 4.42; N 6.58; S 4.74; Cl 5.45.

4-(((2-Chloro-4-((3-methyl-8-oxa-2-azaspiro[4.5]decan-2-yl)sulfonyl)phenyl)amino)methyl)-2-methylbenzenesulfonamide 12{*3,420,77*}, Z7151910516. Yield 57.4 mg (80%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.78 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 2.2 Hz, 1H), 7.48 (dd, J = 8.7, 2.2 Hz, 1H), 7.30 (s, 2H), 7.26 (d, J = 1.7 Hz, 1H), 7.22 (dd, J = 8.1, 1.7 Hz, 1H), 7.09 (t, J = 6.2 Hz, 1H), 6.59 (d, J = 8.7 Hz, 1H), 4.52 (d, J = 6.2 Hz, 2H), 3.52 – 3.46 (m, 1H), 3.42 – 3.37 (m, 1H), 3.33 – 3.30 (m, 2H), 3.24 – 3.18 (m, 2H), 3.05 (d, J = 11.3 Hz, 1H), 2.54 (s, 3H), 1.85 (dd, J = 12.6, 6.8 Hz, 1H), 1.47 – 1.25 (m, 6H), 0.85 – 0.77 (m, 1H), 0.40 – 0.33 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 147.2, 142.9, 140.8, 136.0, 130.1, 128.2, 127.8, 127.4, 123.9, 123.6, 117.4, 110.7, 64.4, 63.4, 57.3, 54.5, 45.9, 45.1, 38.4, 35.3, 33.4, 22.6, 19.9. LC/MS (ES-API) *m/z* = 528/530 $[M+H]^+$. Anal. calcd. for $C_{23}H_{30}ClN_3O_5S_2$: C 52.31; H 5.73; N 7.96; S 12.14; Cl 6.71. Found: C 52.64; H 6.10; N 7.99; S 12.46; Cl 6.89.

5-Chloro-6-((1-cyclopentylpiperidin-4-yl)amino)-*N*-methyl-*N*-(1-(*p*-tolyl)ethyl)pyridine-3-sulfonamide 12{19,*741,405*}, Z7151910574. Yield 54.6 mg (75%). Yellowish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (d, J = 2.2 Hz, 1H), 7.79 (d, J = 2.2 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 7.9 Hz, 1H), 5.10 (q, J = 7.1 Hz, 1H), 4.01 – 3.93 (m, 1H), 2.93 (d, J = 10.8 Hz, 2H), 2.52 (s, 3H), 2.47 – 2.42 (m, 1H), 2.27 (s, 3H), 1.96 (t, J = 11.1 Hz, 2H), 1.83 – 1.72 (m, 4H), 1.69 – 1.55 (m, 4H), 1.52 – 1.43 (m, 2H), 1.35 – 1.27 (m, 2H),

1.26 (d, *J* = 7.1 Hz, 3H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 155.0, 145.8, 136.9, 136.6, 134.0, 128.8, 127.0, 123.1, 113.7, 66.6, 54.5, 51.2, 48.7, 31.1, 30.1, 28.4, 23.7, 20.6, 15.9. LC/MS (ES-API) *m/z* = 491/493 $[M+H]^+$. Anal. calcd. for $C_{25}H_{35}ClN_4O_2S$: C 61.14; H 7.18; N 11.41; S 6.53; Cl 7.22. Found: C 61.23; H 7.35; N 11.52; S 6.65; Cl 7.04.

5-Chloro-*N*-(1-(furan-2-yl)-2-phenylethyl)-6-((3-methoxycyclobutyl)amino)pyridine-3-sulfonamide 12{*19,763,425*}, Z7151910596. Yield 56.8 mg (70%). The compound was obtained as 4:1 mixture of diastereomers. Brownish gum. ^1H NMR (500 MHz, DMSO-d_6) δ 8.24 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 2.2 Hz, 0.2H), 8.06 (d, *J* = 2.2 Hz, 0.8H), 7.43 – 7.36 (m, 2H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.18 – 7.03 (m, 5H), 6.20 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.09 (d, *J* = 3.2 Hz, 1H), 4.50 (q, *J* = 8.0 Hz, 1H), 4.14 – 4.03 (m, 1H), 3.67 – 3.56 (m, 1H), 3.15 (s, 3H), 3.00 (dd, *J* = 13.6, 6.9 Hz, 1H), 2.91 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.67 – 2.56 (m, 2H), 2.06 – 1.93 (m, 2H). $^{13}C\{H\}$ NMR (126 MHz, DMSO-d_6) δ 154.6, 153.3, 144.8, 141.9, 137.2, 133.3, 129.0, 127.9, 126.2, 125.3, 113.4, 110.0, 107.1, 68.0, 54.7, 52.6, 40.0, 38.0, 37.3, 37.3. LC/MS (ES-API) *m/z* = 462/464 $[M+H]^+$. Anal. calcd. for $C_{22}H_{24}ClN_3O_4S$: C 57.20; H 5.24; N 9.10; S 6.94; Cl 7.67. Found: C 56.92; H 5.02; N 9.27; S 6.58; Cl 7.78.

5-Bromo-2-(((2*R,4*R**)-4-methoxy-2-methylpiperidin-1-yl)sulfonyl)-*N*-(2-(2-methylmorpholino)ethyl)aniline 12{*9,585,241*}, Z7151910651.** Yield 54.4 mg (81%). The compound was obtained as 1:1 mixture of diastereomers. Brownish gum. ^1H NMR (500 MHz, DMSO-d_6) δ 7.50 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 1.8 Hz, 1H), 6.83 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.48 – 6.40 (m, 1H), 4.03 – 3.93 (m, 1H), 3.80 – 3.73 (m, 1H), 3.57 – 3.36 (m, 4H), 3.30 – 3.14 (m, 6H), 2.78 – 2.70 (m, 1H), 2.69 – 2.61 (m, 1H), 2.59 – 2.52 (m, 2H), 2.12 – 2.01 (m, 1H), 1.83 – 1.63 (m, 3H), 1.56 – 1.48 (m, 1H), 1.45 – 1.35 (m, 1H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.06 (d, *J* = 2.3 Hz, 1.5H), 1.05 (d, *J* = 2.3 Hz, 1.5H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 146.3, 131.5, 128.1,

120.3, 117.5, 114.6, 72.3, 71.2, 71.1, 65.83, 65.80, 59.3, 58.9, 55.5, 55.4, 52.3, 51.9, 47.6, 38.6, 35.5, 32.02, 31.99, 28.41, 28.38, 18.9, 18.7. LC/MS (ES-API) *m/z* = 490/492 $[M+H]^+$. Anal. calcd. for $C_{20}H_{32}BrN_3O_4S$: C 48.98; H 6.58; N 8.57; S 6.54; Br 16.29. Found: C 48.67; H 6.25; N 8.84; S 6.88; Br 16.48.

4-Bromo-2-(((6-chloropyridin-2-yl)methyl)amino)-*N*-((3*R,4*R**)-3,4-dimethoxy-cyclopentyl)benzenesulfonamide 12{*9,590,246*}, Z7151910693.** Yield 53.3 mg (68%). The compound was obtained as 1:1 mixture of diastereomers. Browhish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (d, *J* = 7.9 Hz, 1H), 7.84 (t, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 6.90 – 6.85 (m, 2H), 6.82 (t, *J* = 5.9 Hz, 1H), 4.58 (d, *J* = 5.9 Hz, 2H), 3.58 – 3.52 (m, 1H), 3.51 – 3.42 (m, 2H), 3.18 (s, 3H), 3.12 (s, 3H), 2.12 – 2.03 (m, 1H), 1.73 – 1.64 (m, 1H), 1.60 – 1.51 (m, 1H), 1.31 – 1.23 (m, 1H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 159.4, 149.7, 145.8, 140.5, 131.3, 127.8, 122.8, 121.3, 120.3, 118.2, 114.5, 83.5, 82.9, 56.3, 55.8, 50.5, 47.3, 37.0, 36.3. LC/MS (ES-API) *m/z* = 504/506/508 $[M+H]^+$. Anal. calcd. for $C_{19}H_{23}BrClN_3O_4S$: C 45.21; H 4.59; N 8.32; S 6.35; Cl 7.02; Br 15.83. Found: C 45.22; H 4.51; N 8.44; S 6.69; Cl 6.90; Br 16.16.

***N*-(Cyclopentylmethyl)-2-((1-(4-(2-oxoimidazolidin-1-yl)phenyl)ethyl)amino)benzo[*d*]-thiazole-6-sulfonamide 12{*29,888,549*}, Z7151911164.** Yield 51.4 mg (77%). Beige amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 2.0 Hz, 1H), 7.58 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.42 (t, *J* = 6.0 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 6.90 (s, 1H), 5.08 – 4.95 (m, 1H), 3.80 (dd, *J* = 9.2, 6.8 Hz, 2H), 3.38 (t, *J* = 8.0 Hz, 2H), 2.59 (t, *J* = 6.8 Hz, 2H), 1.93 – 1.84 (m, 1H), 1.64 – 1.53 (m, 2H), 1.52 – 1.35 (m, 7H), 1.13 – 1.02 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 168.1, 159.0, 155.3, 139.6, 136.8, 132.3, 130.6, 126.2, 124.3, 120.1, 117.6, 117.0, 53.2, 47.5, 44.5, 39.0, 36.6, 29.7,

24.7, 22.9. LC/MS (ES-API) *m/z* = 500 $[M+H]^+$. Anal. calcd. for $C_{24}H_{29}N_5O_3S_2$: C 57.69; H 5.85; N 14.02; S 12.83. Found: C 58.05; H 5.94; N 14.14; S 12.64.

2-((4-(Azepane-1-carbonyl)benzyl)amino)-*N*-(hexa-3,4-dien-1-yl)benzo[*d*]thiazole-5-sulfonamide 12{*30*,*924*,*582*}, Z7151919590. Yield 53.2 mg (80%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.85 (t, *J* = 5.9 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 1.8 Hz, 1H), 7.57 (t, *J* = 5.9 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.12 – 4.93 (m, 2H), 4.66 (d, *J* = 5.8 Hz, 2H), 3.53 (t, *J* = 5.8 Hz, 2H), 3.29 (t, *J* = 5.8 Hz, 2H), 2.77 (q, *J* = 6.9 Hz, 2H), 2.07 – 1.95 (m, 2H), 1.74 – 1.66 (m, 2H), 1.64 – 1.37 (m, 9H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 204.5, 170.0, 167.8, 152.5, 139.3, 138.0, 136.3, 135.0, 127.3, 126.5, 121.6, 118.7, 115.4, 87.1, 85.8, 49.1, 47.0, 45.4, 42.5, 28.9, 28.7, 27.2, 26.8, 25.8, 14.1. LC/MS (ES-API) *m/z* = 525 $[M+H]^+$. Anal. calcd. for $C_{27}H_{32}N_4O_3S_2$: C 61.81; H 6.15; N 10.68; S 12.22. Found: C 61.90; H 5.92; N 10.79; S 12.12.

***N*-(2-Hydroxyethyl)-*N*-(4-methoxybenzyl)-2-((3-((2-methoxyphenyl)thio)-2-methyl-propyl)amino)quinoline-3-sulfonamide 12{*56*,*1204*,*862*}, Z7151933517.** Yield 50.9 mg (76%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.71 – 7.63 (m, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.24 (m, 1H), 7.19 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.12 – 7.07 (m, 1H), 6.95 (t, *J* = 5.6 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.78 (dd, *J* = 7.6, 1.3 Hz, 1H), 4.79 (t, *J* = 5.0 Hz, 1H), 4.40 (s, 2H), 3.78 (s, 3H), 3.72 – 3.60 (m, 4H), 3.55 – 3.46 (m, 1H), 3.32 – 3.27 (m, 2H), 3.27 – 3.21 (m, 2H), 3.07 (dd, *J* = 12.9, 5.0 Hz, 1H), 2.72 (dd, *J* = 12.9, 8.3 Hz, 1H), 2.25 – 2.15 (m, 1H), 1.05 (d, *J* = 6.7 Hz, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 158.8, 156.2, 151.0, 148.9, 140.5, 132.5, 129.6, 129.4, 127.9, 126.9, 126.1, 125.6, 124.9, 122.7, 121.2, 120.9, 120.6, 113.8, 110.7, 58.9,

55.6, 55.0, 50.7, 48.4, 46.1, 35.4, 32.1, 17.5. LC/MS (ES-API) *m/z* = 582 $[M+H]^+$. Anal. calcd. for $C_{30}H_{35}N_3O_5S_2$: C 61.94; H 6.06; N 7.22; S 11.02. Found: C 61.97; H 5.91; N 7.23; S 10.78.

***N*-Methyl-6-((2-methyl-6,7-dihydrooxazolo[4,5-*c*]pyridin-5(4*H*)-yl)sulfonyl)-*N*-propylquinolin-2-amine 12{*57*,*1239*,*890*}, Z7151937556.** Yield 50.7 mg (76%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 (d, *J* = 2.2 Hz, 1H), 8.16 (d, *J* = 9.3 Hz, 1H), 7.76 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.58 (d, *J* = 8.9 Hz, 1H), 7.19 (d, *J* = 9.3 Hz, 1H), 4.05 (t, *J* = 2.1 Hz, 2H), 3.60 (t, *J* = 7.4 Hz, 2H), 3.44 (t, *J* = 5.7 Hz, 2H), 3.16 (s, 3H), 2.68 – 2.62 (m, 2H), 2.31 (s, 3H), 1.64 – 1.55 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 160.0, 158.0, 149.9, 143.5, 137.9, 129.6, 128.3, 128.2, 126.5, 126.4, 121.0, 111.1, 50.9, 43.6, 43.3, 36.0, 21.8, 20.2, 13.5, 11.1. LC/MS (ES-API) *m/z* = 401 $[M+H]^+$. Anal. calcd. for $C_{20}H_{24}N_4O_3S$: C 59.98; H 6.04; N 13.99; S 8.00. Found: C 59.97; H 6.19; N 14.37; S 7.95.

***N*-(1-(4-Fluorophenyl)-3-hydroxypropyl)-2-((3*R**,5*S**)-3-hydroxy-5-methylpiperidin-1-yl)quinoline-6-sulfonamide 12{*57*,*1226*,*139*}, Z7151937673.** Yield 52.5 mg (79%). The compound was obtained as 1:1 mixture of diastereomers. Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (d, *J* = 8.6 Hz, 1H), 8.00 (dd, *J* = 9.4, 1.7 Hz, 1H), 7.84 (t, *J* = 2.7 Hz, 1H), 7.59 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.28 (d, *J* = 9.4 Hz, 1H), 7.13 (dd, *J* = 8.6, 5.6 Hz, 2H), 6.85 (t, *J* = 8.8 Hz, 2H), 4.99 (d, *J* = 4.6 Hz, 1H), 4.79 – 4.66 (m, 1H), 4.51 – 4.32 (m, 3H), 3.50 – 3.41 (m, 1H), 3.26 – 3.18 (m, 1H), 3.15 – 3.06 (m, 1H), 2.55 – 2.51 (m, 1H), 2.42 (t, *J* = 12.3 Hz, 1H), 2.05 – 1.94 (m, 1H), 1.85 – 1.74 (m, 1H), 1.67 – 1.54 (m, 2H), 1.07 (q, *J* = 11.7 Hz, 1H), 0.95 (d, *J* = 6.5 Hz, 3H. ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.8 (d, *J* = 243 Hz), 157.5, 148.9, 138.2, 138.1, 133.6 (d, *J* = 2.8 Hz), 128.4 (d, *J* = 8.1 Hz), 127.0 (d, *J* = 2.6 Hz), 126.1, 120.8, 114.6, 114.4, 110.9, 65.3, 57.2, 54.0, 51.3, 51.2, 42.9, 40.2, 29.5, 18.7. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –116.68, –116.70. LC/MS (ES-API) *m/z* = 474

[M+H]$^+$. Anal. calcd. for $C_{24}H_{28}FN_3O_4S$: C 60.87; H 5.96; N 8.87; S 6.77. Found: C 60.77; H 6.23; N 9.11; S 6.59.

4-((1-((2-(3-(2,2-Difluoroethyl)-3-phenylazetidin-1-yl)quinolin-6-yl)sulfonyl)piperidin-3-yl)methyl)morpholine 12{*57,396,443*}, Z7151938251. Yield 54.7 mg (82%). Orangeish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 8.25 (d, *J* = 9.0 Hz, 1H), 8.18 (d, *J* = 2.1 Hz, 1H), 7.73 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.44 – 7.37 (m, 4H), 7.30 – 7.27 (m, 1H), 6.90 (d, *J* = 9.0 Hz, 1H), 5.72 (tt, *J* = 55.8, 4.9 Hz, 1H), 4.42 (s, 4H), 3.61 – 3.43 (m, 6H), 2.70 – 2.61 (m, 2H), 2.39 – 2.18 (m, 5H), 2.13 – 1.97 (m, 3H), 1.77 – 1.68 (m, 1H), 1.66 – 1.60 (m, 1H), 1.59 – 1.52 (m, 1H), 1.49 – 1.40 (m, 1H), 0.90 – 0.79 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 159.3, 149.5, 143.6, 138.0, 128.60, 128.57, 128.4, 127.0, 126.8, 126.4, 126.2, 121.9, 116.7 (t, *J* = 238 Hz), 110.7, 66.2, 61.5, 60.9, 53.7, 50.0, 46.6, 44.2 (t, *J* = 20.3 Hz), 40.1, 32.1, 27.7, 23.7. ^{19}F{H} NMR (376 MHz, DMSO-*d*$_6$) δ –114.3. LC/MS (ES-API) *m/z* = 571 [M+H]$^+$. Anal. calcd. for $C_{30}H_{36}F_2N_4O_3S$: C 63.14; H 6.36; N 9.82; S 5.62. Found: C 63.44; H 6.55; N 10.16; S 6.00.

(9-(5-((2-(Isopropoxymethyl)morpholino)sulfonyl)isoquinolin-8-yl)-1,4-dioxa-9-azaspiro[5.5]undecan-2-yl)methanol 12{*28,878,541*}, Z7151946532. Yield 56.0 mg (84%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 9.45 (s, 1H), 8.63 (d, *J* = 6.1 Hz, 1H), 8.36 (d, *J* = 6.1 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 4.67 (t, *J* = 5.6 Hz, 1H), 3.87 – 3.77 (m, 3H), 3.71 (d, *J* = 11.3 Hz, 1H), 3.61 – 3.39 (m, 6H), 3.33 – 3.10 (m, 10H), 2.47 – 2.39 (m, 1H), 2.34 – 2.27 (m, 1H), 1.95 – 1.79 (m, 2H), 1.65 – 1.55 (m, 1H), 0.99 (d, *J* = 6.0 Hz, 6H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 155.8, 149.4, 144.7, 135.8, 133.4, 122.2, 122.2, 117.2, 113.7, 79.2, 73.9, 73.2, 71.2, 68.85, 68.79, 68.5, 67.8, 65.1, 61.8, 48.8, 48.1, 47.0, 44.9, 33.7, 28.4, 21.85, 21.82. LC/MS (ES-API) *m/z* = 536 [M+H]$^+$. Anal. calcd. for $C_{26}H_{37}N_3O_7S$: C 58.30; H 6.96; N 7.84; S 5.99. Found: C 58.44; H 6.86; N 8.16; S 5.85.

General procedure for the synthesis of compound library 15. Amine **14** (0.3 mmol) and *N*,*N*-diisopropylethylamine (0.75 mmol + 0.3 mmol per each hydrochloride) were mixed in dry acetonitrile (MeCN) (1 mL), and sulfonyl fluoride **15** (0.3 mmol) was added to the mixture. The reaction mixture was stirred at rt for 16 h. The solvent was evaporated under reduced pressure, and the residue was dissolved in DMSO (1 mL). The resulting mixture was filtered, analyzed by LC-MS, and subjected to HPLC purification.

6-(Azepan-1-yl)pyridine-3-sulfonyl fluoride 15{*1*,*3*}, Z2967413501. Yield 90.3 mg (72%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, J = 1.7 Hz, 1H), 7.96 (dd, J = 9.4, 2.6 Hz, 1H), 6.86 (d, J = 9.4 Hz, 1H), 3.85 (s, 2H), 3.61 (s, 2H), 1.72 (s, 4H), 1.48 (s, 4H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 160.4, 150.2, 136.4, 112.6, 112.4, 105.9, 48.3, 47.3, 27.0, 26.2, 26.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.6. LC/MS (ES-API) *m/z* = 259 $[M+H]^+$. Anal. calcd. for $C_{11}H_{15}FN_2O_2S$: C 51.15; H 5.85; N 10.85; S 12.41. Found: C 51.16; H 5.86; N 10.83; S 12.43.

6-(((4-(3-Methylbenzyl)morpholin-2-yl)methyl)amino)pyridine-3-sulfonyl fluoride trifluoroacetate 15{*1*,*13*}, Z8759276329. Yield 80.6 mg (97%). Yellowish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (br s, 1H), 8.58 (s, 1H), 8.43 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.30 (dt, J = 31.9, 9.8 Hz, 4H), 6.74 (d, J = 9.2 Hz, 1H), 4.30 (s, 2H), 4.03 (d, J = 11.6 Hz, 1H), 3.87 (s, 1H), 3.70 (t, J = 12.1 Hz, 1H), 3.55 (s, 2H), 3.31 (dd, J = 25.0, 12.2 Hz, 2H), 3.05 (t, J = 10.4 Hz, 1H), 2.86 (t, J = 11.2 Hz, 1H), 2.32 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 158.3 (q, J = 34.5 Hz), 150.5, 138.2, 135.5, 131.9, 130.3, 129.0, 128.7, 128.5, 115.1, 114.0, 113.8, 109.8, 71.84, 63.1, 59.5, 52.6, 50.3, 42.3, 20.9. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.1, –74.9. LC/MS (ES-API) *m/z* = 380 $[M+H]^+$. Anal. calcd. for $C_{20}H_{23}F_4N_3O_5S$: C 48.68; H 4.70; N 8.52; S 6.50. Found: C 48.64; H 4.71; N 8.56; S 6.54.

6-(3-(4-(Morpholinomethyl)-1*H*-pyrazol-5-yl)piperidin-1-yl)pyridine-3-sulfonyl fluoride trifluoroacetate 15{*1,16*}, Z8759276463. Yield 77.5 mg (93%). Brownish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.98 (s, 1H), 8.66 (s, 1H), 8.00 (dd, *J* = 9.4, 2.5 Hz, 1H), 7.71 (s, 1H), 7.10 (d, *J* = 9.5 Hz, 1H), 4.59 (s, 2H), 4.22 (s, 2H), 3.98 (s, 2H), 3.62 (t, *J* = 11.9 Hz, 2H), 3.40 – 3.17 (m, 3H), 3.07 (s, 4H), 2.07 (s, 1H), 1.92 (d, *J* = 16.7 Hz, 1H), 1.85 (d, *J* = 11.8 Hz, 2H), 1.56 (d, *J* = 13.0 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.4, 158.3 (q, *J* = 35.4 Hz), 150.1, 118.1, 116.9, 116.3, 115.0, 113.0 (d, *J* = 23.7 Hz), 106.7, 105.1, 63.5, 50.2, 49.8, 49.0, 32.4, 31.1, 24.7, 1.2. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.4, –75.1. LC/MS (ES-API) *m/z* = 410 $[M+H]^+$. Anal. calcd. for $C_{20}H_{25}F_4N_5O_5S$: C 45.89; H 4.81; N 13.38; S 6.12. Found: C 45.84; H 4.96; N 13.16; S 5.95.

5-Chloro-6-(4-((3-fluorophenyl)sulfonyl)piperazin-1-yl)pyridine-3-sulfonyl fluoride 15{*2,9*}, Z8759353344. Yield 86.1 mg (99%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.73 (s, 1H), 8.39 (s, 1H), 7.73 (d, *J* = 5.6 Hz, 1H), 7.61 (t, *J* = 8.4 Hz, 3H), 3.76 (s, 4H), 3.12 (s, 4H).^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 161.90 (d, *J* = 249.2 Hz), 159.9, 146.5, 138.6, 137.1 (d, *J* = 6.7 Hz), 132.0 (d, *J* = 8.0 Hz), 123.8, 120.7 (d, *J* = 21.1 Hz), 119.1 (d, *J* = 24.6 Hz), 118.4, 114.6 (d, *J* = 24.4 Hz), 47.1, 45.6. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 68.8, –110.3. LC/MS (ES-API) *m/z* = 438 $[M+H]^+$. Anal. calcd. for $C_{15}H_{14}ClF_2N_3O_4S_2$: C 41.15; H 3.22; N 9.60; S 14.64. Found: C 41.16; H 3.26; N 9.61; S 14.65.

5-Chloro-6-((2-chloro-4-fluorobenzyl)amino)pyridine-3-sulfonyl fluoride 15{*2,11*}, Z8759353335. Yield 82.0 mg (98%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.61 (s, 2H), 8.32 (d, *J* = 2.1 Hz, 1H), 7.45 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.31 – 7.22 (m, 1H), 7.16 (td, *J* = 8.5, 2.5 Hz, 1H), 4.72 (d, *J* = 5.7 Hz, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 161.0 (d, *J* = 246.4 Hz), 157.5, 148.5, 134.9, 132.4 (d, *J* = 10.6 Hz), 131.8 (d, *J* = 2.8 Hz), 129.5

(d, J = 8.9 Hz), 116.5 (d, J = 25.1 Hz), 115.1 (d, J = 24.3 Hz), 114.9, 114.3 (d, J = 21.0 Hz), 42.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.2, –114.3. LC/MS (ES-API) m/z = 353 $[M+H]^+$. Anal. calcd. for $C_{12}H_8Cl_2F_2N_2O_2S$: C 40.81; H 2.28; N 7.93; S 9.08. Found: C 40.79; H 2.27; N 7.95; S 9.10.

5-Chloro-6-(((2-(dimethylamino)thiazol-4-yl)methyl)amino)pyridine-3-sulfonyl fluoride 15{*2,17*}, Z8759353264. Yield 77.2 mg (93%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (d, J = 1.6 Hz, 1H), 8.45 (t, J = 5.7 Hz, 1H), 8.26 (d, J = 2.2 Hz, 1H), 6.34 (s, 1H), 4.56 (d, J = 5.8 Hz, 2H), 3.00 (s, 6H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 170.7, 157.5, 149.8, 148.5, 134.6, 114.6, 114.5 (d, J = 24.0 Hz), 101.7, 97.2, 41.9. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.3. LC/MS (ES-API) m/z = 351 $[M+H]^+$. Anal. calcd. for $C_{11}H_{12}ClFN_4O_2S_2$: C 37.66; H 3.45; N 15.97; S 18.28. Found: C 37.44; H 3.61; N 16.16; S 18.15.

6-((2-Bromo-5-fluorobenzyl)amino)-5-chloropyridine-3-sulfonyl fluoride 15{*2,21*}, Z8759353379. Yield 74,2 mg (89%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (d, J = 6.5 Hz, 2H), 8.33 (d, J = 2.2 Hz, 1H), 7.67 (dd, J = 8.7, 5.3 Hz, 1H), 7.11 (td, J = 8.5, 3.0 Hz, 1H), 7.02 (dd, J = 9.7, 2.9 Hz, 1H), 4.69 (d, J = 5.8 Hz, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 161.6 (d, J = 244.5 Hz), 157.5, 148.4, 139.8 (d, J = 7.1 Hz), 134.9, 134.1 (d, J = 8.1 Hz), 116.3 (d, J = 2.6 Hz), 115.9 (d, J = 22.6 Hz), 115.4 (d, J = 24.3 Hz), 115.1, 115.0 (d, J = 24.2 Hz), 45.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.2, –114.8. LC/MS (ES-API) m/z = 399 $[M+H]^+$. Anal. calcd. for $C_{12}H_8BrClF_2N_2O_2S$: C 36.25; H 2.03; N 7.05; S 8.06. Found: C 36.24; H 2.06; N 7.16; S 7.85.

5-Chloro-6-(methyl(2-(2-methyl-1*H*-imidazol-1-yl)ethyl)amino)pyridine-3-sulfonyl fluoride trifluoroacetate 15{*2,30*}, Z8759353220. Yield 68.2 mg (82%). Brownish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.37 (s, 1H), 14.33 (s, 1H), 8.56 (s, 1H), 8.29 (d, J = 2.1 Hz,

1H), 7.59 (d, *J* = 1.8 Hz, 1H), 7.48 (d, *J* = 1.7 Hz, 1H), 4.45 (t, *J* = 6.0 Hz, 2H), 4.06 (t, *J* = 6.0 Hz, 2H), 3.34 (s, 3H), 2.64 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 158.9, 158.3 (q, *J* = 35.4 Hz), 146.2, 144.7, 122.5, 117.9, 117.7, 116.9, 116.7, 115.3, 114.9, 51.0, 44.2, 10.3. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 69.0, –74.7. LC/MS (ES-API) *m/z* = 333 $[M+H]^+$. Anal. calcd. for $C_{14}H_{15}ClF_4N_4O_4S$: C 37.64; H 3.38; N 12.54; S 7.18. Found: C 37.44; H 3.66; N 12.16; S 6.85.

5-((Tetrahydro-2*H*-pyran-4-yl)amino)pyridine-2-sulfonyl fluoride 15{*7,5*}, Z8613307691. Yield 18.7 mg (22%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, *J* = 2.7 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.14 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.87 (dd, *J* = 8.3, 3.1 Hz, 2H), 3.73 – 3.60 (m, 1H), 3.43 (td, *J* = 11.4, 1.9 Hz, 2H), 1.88 (d, *J* = 10.9 Hz, 2H), 1.59 – 1.28 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 148.4, 136.6, 133.2 (d, *J* = 28.0 Hz), 126.9, 115.9, 65.6, 47.5, 31.9. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 59.4. LC/MS (ES-API) *m/z* = 261 $[M+H]^+$. Anal. calcd. for $C_{10}H_{13}FN_2O_3S$: C 46.15; H 5.03; N 10.76; S 12.32. Found: C 46.01; H 4.86; N 10.78; S 12.33.

3-Bromo-5-(3-hydroxypyrrolidin-1-yl)pyridine-2-sulfonyl fluoride 15{*8,2*}, Z8105517272. Yield 97.9 mg (78%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.05 (d, *J* = 2.2 Hz, 1H), 7.37 (d, *J* = 2.2 Hz, 1H), 5.13 (d, *J* = 3.7 Hz, 1H), 4.44 (s, 1H), 3.52 (br. s, 3H), 2.04 (dtd, *J* = 13.2, 9.0, 4.5 Hz, 1H), 1.94 (d, *J* = 12.1 Hz, 1H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 147.1, 132.2, 131.5 (d, *J* = 31.6 Hz), 121.9, 120.0, 68.9, 56.0, 46.0, 33.3. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 58.8. LC/MS (ES-API) *m/z* = 326 $[M+H]^+$. Anal. calcd. for $C_9H_{10}BrFN_2O_3S$: C 33.25; H 3.10; N 8.62; S 9.86. Found: C 33.27; H 3.12; N 8.60; S 9.85.

6-Fluoro-*N*-(4-fluorobenzyl)pyridine-2-sulfonamide 16{*9,4*}. Yield 23.8 mg (19%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.61 (s, 1H), 8.20 (q, *J* = 7.8 Hz,

1H), 7.81 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.45 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.25 (dd, *J* = 8.2, 5.8 Hz, 2H), 7.06 (t, *J* = 8.8 Hz, 2H), 4.14 (s, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 162.6 (d, *J* = 90.1 Hz), 160.7 (d, *J* = 89.3 Hz), 155.5 (d, *J* = 12.0 Hz), 144.6 (d, *J* = 7.9 Hz), 133.8 (d, *J* = 2.8 Hz), 129.6 (d, *J* = 8.2 Hz), 119.8 (d, *J* = 3.4 Hz), 114.9 (d, *J* = 21.4 Hz), 113.6 (d, *J* = 36.0 Hz), 45.6. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –66.8, –116.1. LC/MS (ES-API) *m/z* = 307 $[M+Na]^+$. Anal. calcd. for $C_{12}H_{10}F_2N_2O_2S$: C 50.70; H 3.55; N 9.85; S 11.28. Found: C 50.41; H 3.86; N 10.16; S 11.25.

6-Fluoro-*N*-(tetrahydro-2*H*-pyran-4-yl)pyridine-2-sulfonamide 16{*9,5*}. Yield 33.7 mg (22%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.27 (q, *J* = 7.8 Hz, 1H), 8.18 (d, *J* = 5.4 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.49 (dd, *J* = 8.1, 1.5 Hz, 1H), 3.74 (d, *J* = 11.5 Hz, 2H), 3.23 (t, *J* = 11.0 Hz, 2H), 1.56 (d, *J* = 11.1 Hz, 2H), 1.40 (ddd, *J* = 15.6, 12.0, 4.3 Hz, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 162.1 (d, *J* = 244 Hz), 156.4 (d, *J* = 11.5 Hz), 144.8 (d, *J* = 17.6 Hz), 119.6 (d, *J* = 3.8 Hz), 113.7 (d, *J* = 35.9 Hz), 65.6, 49.8, 33.5. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –66.7. LC/MS (ES-API) *m/z* = 261 $[M+H]^+$. Anal. calcd. for $C_{10}H_{13}FN_2O_3S$: C 46.15; H 5.03; N 10.76; S 12.32. Found: C 46.31; H 4.86; N 10.56; S 12.25.

5-(Methyl((4-methylthiazol-2-yl)methyl)amino)pyrazine-2-sulfonyl fluoride 15{*13,26*}, *Z*8759413138. Yield 70.3 mg (84%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.84 (s, 1H), 8.50 (s, 1H), 7.21 (s, 1H), 5.19 (s, 2H), 3.31 (s, 3H), 2.33 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 164.3, 155.2, 152.2, 144.6, 132.0, 131.4 (d, *J* = 27.7 Hz), 114.8, 50.5, 36.7, 16.7. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 60.4. LC/MS (ES-API) *m/z* = 303 $[M+H]^+$. Anal. calcd. for $C_{10}H_{11}FN_4O_2S_2$: C 39.73; H 3.67; N 18.53; S 21.21. Found: C 39.44; H 3.56; N 18.36; S 21.25.

2-(Cycloheptyl(methyl)amino)thiazole-5-sulfonyl fluoride 15{*15*,*10*}, Z8759455527. Yield 83.8 mg (99%). Brownish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (d, J = 1.2 Hz, 1H), 4.38 (br. s, 1H), 3.03 (s, 3H), 1.75 (ddd, J = 21.1, 12.7, 4.3 Hz, 6H), 1.63 – 1.38 (m, 6H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 175.8, 154.0, 107.1, 68.9, 40.1, 31.1, 26.9, 24.3. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 72.7. LC/MS (ES-API) m/z = 293 $[M+H]^+$. Anal. calcd. for $C_{11}H_{17}FN_2O_2S_2$: C 45.19; H 5.86; N 9.58; S 21.93. Found: C 45.18; H 5.86; N 9.58; S 21.91.

***tert*-Butyl (3a*R**,7a*R**)-6-(5-(fluorosulfonyl)thiazol-2-yl)octahydro-1*H*-pyrrolo[2,3-*c*]pyridine-1-carboxylate 15{*15*,*20*}, Z8759455564.** Yield 74.5 mg (89%). Brownish amorphous solid. The compound existed as ca 1:1 mixture of rotamers. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 (s, 1H), 4.00 (s, 1H), 3.84 (dd, J = 12.5, 7.2 Hz, 1H), 3.77 – 3.40 (m, 2H), 3.32 – 3.27 (m, 2H), 2.03 – 1.57 (m, 4H), 1.44 (s, 0.5×9H), 1.40 (s, 0.5×9H), 1.30 – 1.17 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 175.9 and 175.8, 154.1 and 153.3, 108.1 and 108.0, 54.5 and 54.0, 53.5, 45.5 and 45.3, 41.7, 35.3 and 34.4, 28.1, 27.7 and 26.5, 24.3, 18.0 and 16.7, 12.4. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 72.6. LC/MS (ES-API) m/z = 392 $[M+H]^+$. Anal. calcd. for $C_{15}H_{22}FN_3O_4S_2$: C 46.02; H 5.66; N 10.73; S 16.38. Found: C 46.04; H 5.86; N 10.86; S 16.55.

2-(2-(3,4-Difluoro-5-methoxyphenyl)pyrrolidin-1-yl)thiazole-5-sulfonyl fluoride 15{*15*,*22*}, Z8759455458. Yield 73.8 mg (89%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.22 (s, 1H), 6.99 (s, 1H), 6.94 (s, 1H), 5.00 (s, 2H), 3.97 (s, 1H), 3.88 (s, 3H), 3.74 (d, J = 14.4 Hz, 1H), 2.05 (dd, J = 13.0, 5.8 Hz, 2H), 1.92 (dd, J = 11.1, 5.6 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 172.9, 153.6, 151.0 (d, J = 11.1 Hz), 149.4 (d, J = 10.4 Hz), 148.8, 139.0 (d, J = 259.1 Hz), 109.3, 109.0 (d, J = 27.9 Hz), 106.9 (d, J = 185.2 Hz), 64.7, 56.7, 51.8, 35.6, 23.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 72.8, –137.6, –161.4. LC/MS (ES-

API) *m/z* = 379 $[M+H]^+$. Anal. calcd. for $C_{14}H_{13}F_3N_2O_3S_2$: C 44.44; H 3.46; N 7.40; S 16.95. Found: C 44.64; H 3.52; N 7.16; S 16.85.

2-(1,4-Dimethyl-2-azabicyclo[2.2.1]heptan-2-yl)thiazole-5-sulfonyl fluoride 15{*15*,*25*}, Z8759455556. Yield 71.9 mg (86%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.21 (d, *J* = 1.2 Hz, 1H), 3.48 (d, *J* = 11.4 Hz, 1H), 3.10 (s, 1H), 1.84 (m, 1H), 1.80 – 1.76 (m, 3H), 1.76 – 1.53 (m, 5H), 1.20 (s, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 172.4, 153.8, 107.5 (d, *J* = 27.5 Hz), 72.6, 66.3, 52.2, 43.3, 35.1, 32.8, 18.7, 17.5. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 72.7. LC/MS (ES-API) *m/z* = 291 $[M+H]^+$. Anal. calcd. for $C_{11}H_{15}FN_2O_2S_2$: C 45.50; H 5.21; N 9.65; S 22.08. Found: C 45.44; H 5.36; N 9.76; S 22.15.

2-(3-(Ethylsulfonamido)azetidin-1-yl)thiazole-5-sulfonyl fluoride 15{*15*,*28*}, Z8759455543. Yield 69.4 mg (83%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.25 (s, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 4.51 (t, *J* = 8.4 Hz, 2H), 4.44 (m, 1H), 4.09 (dd, *J* = 9.5, 4.8 Hz, 2H), 3.03 (q, *J* = 7.3 Hz, 2H), 1.20 (t, *J* = 7.3 Hz, 3H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 174.9, 154.0, 109.8 (d, *J* = 28.0 Hz), 61.3, 46.4, 43.6, 8.0. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 72.6. LC/MS (ES-API) *m/z* = 330 $[M+H]^+$. Anal. calcd. for $C_8H_{12}N_3O_4S_3$: C 29.17; H 3.67; N 12.76; S 29.20. Found: C 29.44; H 3.66; N 12.16; S 29.35.

2-(Benzyl(cyclobutyl)amino)-4-methylthiazole-5-sulfonyl fluoride 15{*16*,*18*}, Z8759445871. Yield 76.8 mg (92%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.36 (t, *J* = 7.4 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 2H), 4.91 (s, 2H), 4.51 (s, 1H), 2.45 (s, 3H), 2.21 (q, *J* = 7.6 Hz, 4H), 1.70 – 1.60 (m, 2H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 171.8, 163.2, 136.5, 128.7, 127.4, 126.4, 103.3 (d, *J* = 26.0 Hz), 55.1, 50.2, 27.8, 17.0, 14.2. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 74.2. LC/MS (ES-API) *m/z* = 326 $[M+H]^+$.

Anal. calcd. for $C_{15}H_{17}FN_2O_2S_2$: C 52.92; H 5.03; N 8.23; S 18.83. Found: C 53.04; H 5.16; N 8.16; S 18.85.

2-(4-(3,5-Dimethyl-1*H*-1,2,4-triazol-1-yl)piperidin-1-yl)-4-methylthiazole-5-sulfonyl fluoride 15{*16*,*19*}, Z8759445848. Yield 74,6 mg (90%%). Brownish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.60 – 4.45 (m, 1H), 4.09 (s, 2H), 3.52 – 3.36 (m, 2H), 2.46 (s, 3H), 2.38 (s, 3H), 2.15 (s, 3H), 1.98 (d, J = 8.9 Hz, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 172.1, 164.0, 158.0, 151.4, 103.1 (d, J = 25.9 Hz), 52.6, 47.4, 30.5, 17.0, 13.7, 11.2. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 74.1. LC/MS (ES-API) *m/z* = 360 $[M+H]^+$. Anal. calcd. for $C_{13}H_{18}FN_5O_2S_2$: C 43.44; H 5.05; N 19.48; S 17.84. Found: C 43.44; H 4.86; N 19.16; S 17.85.

2-((1-(4-Methoxyphenyl)ethyl)amino)-4-methylthiazole-5-sulfonyl fluoride 15{*16*,*32*}, Z8759445921. Yield 67.5 mg (81%). Brownish gum. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.66 (s, 1H), 7.29 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 4.73 (s, 1H), 3.73 (s, 3H), 2.40 (s, 3H), 1.46 (d, J = 6.7 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 163.4, 158.6, 134.1, 127.4, 114.0, 102.0, 101.8, 57.5, 55.1, 22.8, 16.8. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 74.0. LC/MS (ES-API) *m/z* = 331 $[M+H]^+$. Anal. calcd. for $C_{13}H_{15}FN_2O_3S_2$: C 47.26; H 4.58; N 8.48; S 19.41. Found: C 46.99; H 4.66; N 8.16; S 19.75.

2-((2*R,3*R**)-3-Hydroxy-2-(2-methoxyphenyl)pyrrolidin-1-yl)-4-methylthiazole-5-sulfonyl fluoride 15{*16*,*34*}, Z8759445938.** Yield 67.3 mg (81%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.29 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 6.6 Hz, 1H), 6.89 (t, J = 7.4 Hz, 1H), 5.01 (d, J = 4.5 Hz, 2H), 4.53 (quint, J = 5.2 Hz, 1H), 3.92 (s, 1H), 3.84 (s, 4H), 2.42 (s, 3H), 2.23 – 2.14 (m, 1H), 1.99 (dq, J = 12.0, 6.0 Hz, 1H). ^{13}C{H} NMR (126 MHz, DMSO-d_6) δ 169.6, 163.0, 157.8, 128.8 (d, J = 52.6 Hz), 121.3, 120.1, 111.0, 102.9, 102.7, 71.0, 64.0, 55.7, 49.0, 32.2, 16.9. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ 74.2.

LC/MS (ES-API) *m/z* = 373 $[M+H]^+$. Anal. calcd. for $C_{15}H_{17}FN_2O_4S_2$: C 48.38; H 4.60; N 7.52; S 17.22. Found: C 48.44; H 4.86; N 7.36; S 17.23.

General procedure for the synthesis of compound library 18. Amine **16** (0.3 mmol) and *N*,*N*-diisopropylethylamine (0.75 mmol + 0.3 mmol per each hydrochloride) were mixed in dry *N*-methylpyrrolidone (MeCN) (1 mL), and sulfonyl fluoride **13** (0.3 mmol) was added to the mixture. The reaction mixture was stirred at rt for 16 h. Amine **11** (0.6 mmol) was added to the solution, and the mixture was stirred at 110 °C for 16 h. The reaction mixture was cooled, the solvent was evaporated under reduced pressure, and the residue was dissolved in the DMSO (1 mL). The mixture was filtered, analyzed by LC-MS, and subjected to HPLC purification.

5-Chloro-*N*-((2,6-dimethoxypyridin-3-yl)methyl)-6-((3-(2,2,2-trifluoroethoxy)propyl)-amino)pyridine-3-sulfonamide 18{*2*,*10*,*9*}, Z8763848205. Yield 42.4 mg (64%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.15 (s, 1H), 7.80 (t, *J* = 5.8 Hz, 1H), 7.60 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.30 (t, *J* = 5.2 Hz, 1H), 6.23 (d, *J* = 7.9 Hz, 1H), 4.04 (q, *J* = 9.4 Hz, 2H), 3.90 (d, *J* = 5.8 Hz, 2H), 3.77 (d, *J* = 8.4 Hz, 6H), 3.65 (t, *J* = 5.9 Hz, 2H), 3.47 (dd, *J* = 12.4, 6.1 Hz, 2H), 1.87 – 1.77 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 161.8, 159.3, 155.3, 145.3, 141.4, 133.5, 124.6 (q, *J* = 279.5 Hz), 124.4, 113.5, 109.8, 100.3, 69.9, 67.0 (q, *J* = 32.6 Hz), 53.1, 52.9, 40.3, 38.1, 28.7. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ -73.3. LC/MS (ES-API) *m/z* = 499 $[M+H]^+$. Anal. calcd. for $C_{18}H_{22}ClF_3N_4O_5S$: C 43.33; H 4.44; N 11.23; S 6.43. Found: C 43.43; H 4.39; N 11.11; S 6.48.

5-Chloro-*N*-((3-isopropyl-1-methyl-1*H*-pyrazol-5-yl)methyl)-6-(4-(2-methyl-2*H*-tetrazol-5-yl)piperidin-1-yl)pyridine-3-sulfonamide 18{*2*,*23*,*21*}, Z8763848196. Yield 36.8 mg (55%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, *J* = 2.0 Hz, 1H), 8.21 (t, *J* = 5.1 Hz, 1H), 7.91 (d, *J* = 2.0 Hz, 1H), 5.79 (s, 1H), 4.32 (s, 3H), 4.10 (d, *J* = 5.2 Hz, 2H),

4.03 (d, *J* = 13.1 Hz, 2H), 3.62 (s, 3H), 3.29 – 3.21 (m, 1H), 3.15 (t, *J* = 12.1 Hz, 2H), 2.70 (dq, *J* = 13.7, 6.9 Hz, 1H), 2.11 (d, *J* = 11.1 Hz, 2H), 1.92 – 1.78 (m, 2H), 1.08 (d, *J* = 6.9 Hz, 6H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 168.7, 159.0, 155.8, 144.2, 137.8, 136.9, 129.3, 119.2, 102.6, 47.9, 37.1, 35.8, 32.2, 30.2, 27.0, 22.6. LC/MS (ES-API) *m/z* = 494 $[M+H]^+$. Anal. calcd. for $C_{20}H_{28}ClN_9O_2S$: C 48.63; H 5.71; N 25.52; S 6.49. Found: C 48.41; H 5.86; N 25.31; S 6.62.

3-((3-Chloro-5-((3-isobutylpiperidin-1-yl)sulfonyl)pyridin-2-yl)amino)-1-(pyrrolidin-1-yl)propan-1-one 18{*2,26,24*}, Z8763848204. Yield 36.2 mg (54%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.30 (d, *J* = 1.9 Hz, 1H), 7.82 (d, *J* = 2.0 Hz, 1H), 7.42 (t, *J* = 5.6 Hz, 1H), 3.66 (dd, *J* = 12.9, 6.8 Hz, 2H), 3.44 (dd, *J* = 17.2, 8.5 Hz, 2H), 3.37 (t, *J* = 6.8 Hz, 2H), 3.28 (dd, *J* = 14.2, 7.3 Hz, 2H), 2.57 (t, *J* = 7.0 Hz, 2H), 2.31 (t, *J* = 10.4 Hz, 1H), 1.99 (t, *J* = 10.7 Hz, 1H), 1.90 – 1.81 (m, 2H), 1.76 (p, *J* = 6.7 Hz, 2H), 1.70 – 1.52 (m, 4H), 1.46 (dd, *J* = 22.2, 9.8 Hz, 1H), 1.10 – 0.95 (m, 2H), 0.84 (dd, *J* = 6.3, 4.8 Hz, 6H), 0.82 – 0.81 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 169.0, 155.7, 146.4, 134.3, 119.4, 114.0, 51.2, 46.3, 45.9, 45.16, 42.3, 37.2, 33.2, 32.7, 29.5, 25.5, 24.1, 23.9, 22.6, 22.5. LC/MS (ES-API) *m/z* = 457 $[M+H]^+$. Anal. calcd. for $C_{21}H_{33}ClN_4O_3S$: C 55.19; H 7.28; N 12.26; S 7.01. Found: C 55.39; H 6.97; N 12.13; S 6.85.

5-Chloro-6-((2-(4-cyclopropyl-1*H*-pyrazol-1-yl)ethyl)amino)-*N*-((1-ethyl-1*H*-pyrazol-3-yl)methyl)pyridine-3-sulfonamide 18{*2,31,30*}, Z8763848194. Yield 34.2 mg (51%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.24 (d, *J* = 2.0 Hz, 1H), 7.89 (t, *J* = 6.1 Hz, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 2.0 Hz, 1H), 7.43 (s, 1H), 7.35 (t, *J* = 5.5 Hz, 1H), 7.23 (s, 1H), 6.02 (d, *J* = 2.1 Hz, 1H), 4.21 (t, *J* = 6.4 Hz, 2H), 4.01 – 3.90 (m, 4H), 3.75 (q, *J* = 6.1 Hz, 2H), 1.69 – 1.57 (m, 1H), 1.27 (t, *J* = 7.3 Hz, 3H), 0.81 – 0.72 (m, 2H), 0.47 – 0.36 (m, 2H).. ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 155.2, 147.2, 145.3, 136.9, 134.0, 129.8, 127.19, 125.0, 123.5,

113.7, 104.0, 49.8, 45.9, 41.4, 40.4, 15.4, 7.9, 5.4. LC/MS (ES-API) *m/z* = 450 $[M+H]^+$. Anal. calcd. for $C_{19}H_{24}ClN_7O_2S$: C 50.72; H 5.38; N 21.79; S 7.13. Found: C 50.63; H 5.41; N 21.66; S 6.87.

5-Chloro-6-(4-(hydroxymethyl)-2-azabicyclo[2.2.1]heptan-2-yl)-*N*-(3-(4-hydroxypiperidin-1-yl)propyl)pyridine-3-sulfonamide 18{*2,34,33*}, Z8763848210. Yield 33.6 mg (50%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (d, *J* = 2.1 Hz, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.47 (s, 1H), 4.75 (s, 2H), 4.51 (s, 1H), 3.84 (dd, *J* = 9.5, 2.4 Hz, 1H), 3.61 (s, 2H), 3.28 (d, *J* = 9.5 Hz, 1H), 3.17 (s, 1H), 2.76 (t, *J* = 6.9 Hz, 2H), 2.62 – 2.53 (m, 2H), 2.17 (t, *J* = 6.9 Hz, 2H), 1.87 (t, *J* = 10.1 Hz, 2H), 1.79 (d, *J* = 5.6 Hz, 2H), 1.61 (dd, *J* = 32.6, 9.4 Hz, 4H), 1.53 – 1.43 (m, 2H), 1.39 (t, *J* = 11.0 Hz, 2H), 1.35 – 1.21 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 154.7, 144.7, 136.7, 124.6, 113.5, 66.4, 62.5, 59.9, 59.3, 54.9, 50.9, 48.6, 40.9, 34.4, 29.6, 29.2, 26.3. LC/MS (ES-API) *m/z* = 459 $[M+H]^+$. Anal. calcd. for $C_{20}H_{31}ClN_4O_4S$: C 52.34; H 6.81; N 12.21; S 6.98. Found: C 52.21; H 6.86; N 12.26; S 6.85.

4-((4-(Azepan-1-yl)pyridin-2-yl)sulfonyl)morpholine 18{*6,1,1*}, Z8614187519. Yield 51.9 mg (78%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.19 (d, *J* = 5.9 Hz, 1H), 7.01 (d, *J* = 2.5 Hz, 1H), 6.84 (dd, *J* = 5.9, 2.5 Hz, 1H), 3.63 – 3.57 (m, 4H), 3.52 (t, *J* = 6.0 Hz, 4H), 3.17 – 3.09 (m, 4H), 1.71 (s, 4H), 1.46 (s, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 155.6, 153.7, 149.8, 108.5, 104.7, 65.6, 48.5, 46.5, 26.1, 26.1. LC/MS (ES-API) *m/z* = 326 $[M+H]^+$. Anal. calcd. for $C_{15}H_{23}N_3O_3S$: C 55.36; H 7.12; N 12.91; S 9.85. Found: C 55.42; H 6.99; N 13.01; S 10.02.

***N*-(4-Fluorobenzyl)-2-(morpholinosulfonyl)pyridin-4-amine 18{*6,2,1*}, Z8614187512.** Yield 51.6 mg (77%). Brownish gum. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.14 (d, *J* = 5.7 Hz, 1H), 7.75 (t, *J* = 5.5 Hz, 1H), 7.38 (dd, *J* = 8.1, 5.8 Hz, 2H), 7.18 (t, *J* = 8.8 Hz, 2H), 7.04 (s,

1H), 6.71 (s, 1H), 4.38 (d, *J* = 5.8 Hz, 2H), 3.61 – 3.54 (m, 4H), 3.06 (s, 4H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 161.3 (d, *J* = 242.6 Hz), 155.1, 154.8, 149.8, 134.3, 134.3, 129.2 (d, *J* = 8.1 Hz), 115.3 (d, *J* = 21.3 Hz), 109.0, 65.6, 46.4, 44.6. $^{19}F\{H\}$ NMR (376 MHz, DMSO-d_6) δ –116.2. LC/MS (ES-API) *m/z* = 352 $[M+H]^+$. Anal. calcd. for $C_{16}H_{18}FN_3O_3S$: C 54.69; H 5.16; N 11.96; S 9.12. Found: C 54.51; H 4.98; N 12.03; S 8.97.

***N*-((5-Chloropyridin-3-yl)methyl)-2-((3-(2-ethylphenyl)pyrrolidin-1-yl)sulfonyl)pyridin-4-amine 18{*6,5,4*}, Z8763849798.** Yield 47.5 mg (71%). Brownish amorphous solid. ^1H NMR (500 MHz, DMSO-d_6) δ δ 8.56 (d, *J* = 1.3 Hz, 1H), 8.53 (d, *J* = 2.2 Hz, 1H), 8.22 (d, *J* = 5.7 Hz, 1H), 7.90 (s, 1H), 7.77 (t, *J* = 5.9 Hz, 1H), 7.19 – 7.08 (m, 5H), 6.79 (d, *J* = 3.7 Hz, 1H), 4.50 (d, *J* = 5.9 Hz, 2H), 3.78 (dd, *J* = 9.9, 7.6 Hz, 1H), 3.55 (t, *J* = 8.0 Hz, 1H), 3.46 – 3.37 (m, 1H), 3.31 (d, *J* = 7.5 Hz, 1H), 3.18 (t, *J* = 9.9 Hz, 1H), 2.54 (d, *J* = 7.6 Hz, 1H), 2.09 – 2.01 (m, 1H), 1.96 – 1.85 (m, 1H), 1.04 (t, *J* = 7.5 Hz, 3H). $^{13}C\{H\}$ NMR (151 MHz, DMSO-d_6) δ 156.1, 154.5, 150.1, 147.2, 146.9, 142.0, 137.7, 135.9, 134.8, 131.0, 128.7, 126.6, 126.2, 125.6, 55.0, 48.4, 42.3, 38.7, 32.7, 25.3, 15.9. LC/MS (ES-API) *m/z* = 457 $[M+H]^+$. Anal. calcd. for $C_{23}H_{25}ClN_4O_2S$: C 60.45; H 5.51; N 12.26; S 7.02. Found: C 60.44; H 5.56; N 12.21; S 6.91.

***N*-(2-(*N*-Cyclohexylsulfamoyl)ethyl)-4-((3*R**,5*S**)-3-fluoro-5-methoxypiperidin-1-yl)pyridine-2-sulfonamide 18{*6,6,5*}, Z8763849800.** Yield 47.4 mg (71%). Brownish gum. ^1H NMR (600 MHz, DMSO-d_6) δ 8.22 (d, *J* = 5.9 Hz, 1H), 7.80 (s, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.09 (dd, *J* = 5.9, 2.5 Hz, 1H), 4.88 – 4.59 (m, 1H), 3.83 – 3.76 (m, 1H), 3.71 (dd, *J* = 15.9, 5.9 Hz, 1H), 3.63 – 3.55 (m, 1H), 3.46 – 3.39 (m, 2H), 3.29 (s, 3H), 3.25 (dd, *J* = 9.4, 6.0 Hz, 2H), 3.13 (dd, *J* = 9.6, 5.9 Hz, 2H), 3.00 (qd, *J* = 10.7, 5.7 Hz, 1H), 2.33 – 2.23 (m, 1H), 1.86 (dq, *J* = 19.5, 6.5 Hz, 1H), 1.76 (d, *J* = 11.9 Hz, 2H), 1.64 (d, *J* = 13.0 Hz, 2H), 1.50 (d, *J* = 12.9 Hz, 1H), 1.28 – 1.11 (m, 4H), 1.05 (dd, *J* = 24.1, 12.1 Hz, 1H). $^{13}C\{H\}$ NMR

(151 MHz, DMSO-d_6) δ 158.3, 155.4, 149.9, 109.9, 105.0, 85.6 (d, J = 175.5 Hz), 72.4 (d, J = 5.7 Hz), 56.0, 52.0 (d, J = 37.1 Hz), 49.0 (d, J = 24.9 Hz), 48.3, 38.1, 34.3, 34.2 , 33.8, 24.9, 24.6. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ –180.6. LC/MS (ES-API) m/z = 479 $[M+H]^+$. Anal. calcd. for $C_{19}H_{31}FN_4O_5S_2$: C 47.68; H 6.53; N 11.71; S 13.40. Found: C 47.52; H 6.81; N 11.76; S 13.26.

4-(((1*R*,5*S*,6*r*)-3-Oxabicyclo[3.1.0]hexan-6-yl)amino)-*N*-(4-ethoxy-3-methylbenzyl)pyridine-2-sulfonamide 18{*6*,*8*,*7*}, Z8763849817. Yield 44.8 mg (67%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 5.1 Hz, 1H), 8.02 (t, J = 5.9 Hz, 1H), 7.37 (s, 1H), 7.03 (d, J = 2.1 Hz, 1H), 6.98 (d, J = 8.3 Hz, 1H), 6.95 (s, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.69 (d, J = 3.8 Hz, 1H), 4.03 – 3.89 (m, 6H), 3.66 (d, J = 8.2 Hz, 2H), 2.19 (d, J = 1.7 Hz, 1H), 2.07 (s, 3H). 1.79 (s, 2H), 1.31 (t, J = 6.9 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 158.5, 155.6, 155.1, 149.7, 129.9, 129.4, 126.2, 125.2, 110.8, 68.4, 63.1, 46.1, 32.0, 25.3, 16.0, 14.8. LC/MS (ES-API) m/z = 404 $[M+H]^+$. Anal. calcd. for $C_{20}H_{25}N_3O_4S$: C 59.53; H 6.25; N 10.41; S 7.95. Found: C 59.41; H 6.27; N 10.17; S 7.89.

***N*-((8,8-Difluorodispiro[2.0.3^4.1^3]octan-6-yl)methyl)-4-((2-(*N*-methylmethylsulfonamido)-ethyl)amino)pyridine-2-sulfonamide 18{*6*,*15*,*14*}, Z8763849777.** Yield 40.7 mg (61%). Brownish gum. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.14 (d, J = 5.2 Hz, 1H), 7.68 (dt, J = 34.6, 5.7 Hz, 1H), 7.19 (t, J = 5.6 Hz, 1H), 7.10 (d, J = 9.9 Hz, 1H), 6.70 (d, J = 5.2 Hz, 1H), 3.36 (dd, J = 12.3, 6.1 Hz, 2H), 3.20 (t, J = 6.3 Hz, 2H), 2.88 (s, 3H), 2.85 (t, J = 6.3 Hz, 2H), 2.82 (s, 3H), 2.36 (dd, J = 14.5, 7.5 Hz, 1H), 2.31 – 2.17 (m, 2H), 1.99 – 1.83 (m, 1H), 1.65 (d, J = 7.7 Hz, 1H), 1.05 (s, 2H), 1.01 (s, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 158.2, 154.7, 149.8, 114.7(d, J = 293.2 Hz) , 48.0, 47.6, 47.5, 40.38, 40.1, 34.9 (d, J = 29.3 Hz), 28.6, 27.9 (d, J = 169.8 Hz), 26.0, 25.9, 21.4 (d, J = 9.7 Hz), 5.6, 5.6. ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ

–139.0. LC/MS (ES-API) *m/z* = 465 $[M+H]^+$. Anal. calcd. for $C_{18}H_{26}F_2N_4O_4S_2$: C 46.54; H 5.64; N 12.06; S 13.80. Found: C 46.44; H 5.86; N 12.16; S 13.85.

***N*,*N*-Dimethyl-1-((4-(2-((4-methylpiperazin-1-yl)methyl)morpholino)pyridin-2-yl)sulfonyl)piperidin-3-amine 18{*6*,*17*,*16*}, Z8763849821.** Yield 39.2 mg (59%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.28 (d, *J* = 5.9 Hz, 1H), 7.22 (d, *J* = 2.4 Hz, 1H), 7.01 (dd, *J* = 5.9, 2.5 Hz, 1H), 3.93 (dd, *J* = 11.6, 2.3 Hz, 1H), 3.81 (t, *J* = 14.3 Hz, 2H), 3.66 (t, *J* = 10.0 Hz, 2H), 3.59 – 3.48 (m, 2H), 2.92 (td, *J* = 12.2, 3.5 Hz, 1H), 2.71 – 2.65 (m, 1H), 2.59 (ddd, *J* = 28.3, 17.3, 10.2 Hz, 3H), 2.47 – 2.38 (m, 5H), 2.16 (s, 7H), 2.14 (s, 3H), 1.73 (dd, *J* = 16.1, 6.4 Hz, 2H), 1.47 – 1.34 (m, 1H), 1.23 (td, *J* = 14.2, 4.1 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 156.7, 155.6, 150.1, 110.0, 106.0, 72.9, 65.1, 60.12, 60.06, 54.7, 53.4, 48.5, 48.5, 46.5, 45.8, 45.1, 41.6, 26.2, 23.6. LC/MS (ES-API) *m/z* = 467 $[M+H]^+$. Anal. calcd. for $C_{22}H_{38}N_6O_3S$: C 56.63; H 8.21; N 18.01; S 6.87. Found: C 56.52; H 7.95; N 18.13; S 6.85.

6-(4-((4-((1-(4-Methylpyrimidin-2-yl)ethyl)amino)pyridin-2-yl)sulfonyl)piperazin-1-yl)picolinonitrile 18{*6*,*28*,*27*}, Z8763849804. Yield 35.5 mg (53%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (d, *J* = 5.1 Hz, 1H), 8.05 (d, *J* = 5.7 Hz, 1H), 7.75 (d, *J* = 7.3 Hz, 1H), 7.70 (dd, *J* = 8.8, 7.3 Hz, 1H), 7.27 (d, *J* = 5.1 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8.9 Hz, 1H), 7.08 (s, 1H), 6.61 (s, 1H), 4.71 (quint, *J* = 6.8 Hz, 1H), 3.58 (s, 4H), 3.20 – 3.06 (m, 4H), 2.44 (s, 3H), 1.51 (d, *J* = 6.8 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 170.0, 167.3, 158.3, 157.1, 155.1, 154.3, 149.6, 138.8, 130.1, 119.4, 118.3, 117.8, 112.3, 54.0, 48.6, 45.9, 43.8, 23.7, 20.5. LC/MS (ES-API) *m/z* = 465 $[M+H]^+$. Anal. calcd. for $C_{22}H_{24}N_8O_2S$: C 56.88; H 5.21; N 24.12; S 6.90. Found: C 56.63; H 4.91; N 23.99; S 7.01.

4-((5-(Azepan-1-yl)-3-bromopyridin-2-yl)sulfonyl)morpholine 18{*8*,*1*,*1*}, Z8614187525. Yield 37.4 mg (56%). Yellowish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.08 (d, *J* =

2.5 Hz, 1H), 7.39 (d, *J* = 2.5 Hz, 1H), 3.68 – 3.62 (m, 4H), 3.54 (t, *J* = 5.9 Hz, 4H), 3.44 – 3.37 (m, 4H), 1.71 (s, 4H), 1.47 (s, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 146.6, 140.1, 130.1, 122.0, 118.1, 66.0, 48.7, 46.8, 26.1, 26.1. LC/MS (ES-API) *m/z* = 406 $[M+H]^+$. Anal. calcd. for $C_{15}H_{22}BrN_3O_3S$: C 44.56; H 5.48; N 10.39; S 7.93. Found: C 44.42; H 5.62; N 10.37; S 8.02.

5-Bromo-6-((3,4-dihydroisoquinolin-2(1*H*)-yl)sulfonyl)-*N*-(1-(1-methyl-1*H*-1,2,3-triazol-4-yl)ethyl)pyridin-3-amine 18{*8,35,34*}, Z8763851017. Yield 33.4 mg (50%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.93 (s, 1H), 7.89 (d, *J* = 2.2 Hz, 1H), 7.35 (d, *J* = 7.1 Hz, 2H), 7.17 (t, *J* = 5.8 Hz, 4H), 4.90 – 4.80 (m, 1H), 4.56 (s, 2H), 3.99 (s, 3H), 3.65 (t, *J* = 5.8 Hz, 2H), 2.88 (t, *J* = 5.7 Hz, 2H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 149.2, 146.7, 141.1, 133.5, 132.3, 131.9, 128.8, 126.5, 126.2, 126.1, 122.7, 122.5, 117.9, 47.9, 44.4, 44.1, 36.2, 28.7, 21.2. LC/MS (ES-API) *m/z* = 477 $[M+H]^+$. Anal. calcd. for $C_{19}H_{21}BrN_6O_2S$: C 47.80; H 4.43; N 17.60; S 6.72. Found: C 47.76; H 4.56; N 17.37; S 6.85.

2-(Azepan-1-yl)-*N*-cyclopentylpyrimidine-5-sulfonamide 18{*10,1,26*}, Z8614187520. Yield 36.1 mg (54%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.59 (s, 2H), 7.55 (d, *J* = 6.9 Hz, 1H), 3.77 (t, *J* = 6.0 Hz, 4H), 3.42 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.71 (s, 4H), 1.68 – 1.61 (m, 2H), 1.54 (dt, *J* = 13.9, 8.7 Hz, 2H), 1.53 – 1.44 (m, 4H), 1.41 (dd, *J* = 6.8, 4.4 Hz, 2H), 1.36 – 1.25 (m, 2H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 161.1, 156.7, 122.9, 54.3, 47.0, 32.6, 26.8, 26.4, 22.9. LC/MS (ES-API) *m/z* = 325 $[M+H]^+$. Anal. calcd. for $C_{15}H_{24}N_4O_2S$: C 55.53; H 7.46; N 17.27; S 9.88. Found: C 55.44; H 7.53; N 16.98; S 10.03.

***tert*-Butyl (1-((5-((4-(methoxymethyl)-4-methylpiperidin-1-yl)sulfonyl)pyrimidin-2-yl)-amino)propan-2-yl)carbamate 18{*10,24,22*}, Z8763847913.** Yield 36.8 mg (55%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (d, *J* = 3.0 Hz, 1H), 8.49 (d, *J* = 2.4 Hz, 1H), 8.18 (t, *J* = 4.9 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 3.74 (dt, *J* = 13.6, 6.7 Hz, 1H), 3.38 –

3.28 (m, 7H), 3.19 – 3.11 (m, 2H), 3.02 (s, 2H), 2.72 (t, *J* = 9.5 Hz, 2H), 1.53 (t, *J* = 9.8 Hz, 2H), 1.33 (d, *J* = 17.8 Hz, 9H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.81 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 163.0, 157.6, 157.5, 155.0, 118.3, 80.3, 77.5, 58.7, 46.0, 45.3, 41.7, 32.6, 32.2, 28.2, 21.3, 18.2. LC/MS (ES-API) *m/z* = 458 $[M+H]^+$. Anal. calcd. for $C_{20}H_{35}FN_5O_5S$: C 52.50; H 7.71; N 15.31; S 7.01. Found: C 52.44; H 7.81; N 15.16; S 6.85.

5-((2-Oxa-8-azaspiro[4.5]decan-8-yl)sulfonyl)-*N*-(1-(phenylthio)propan-2-yl)pyrimidin-2-amine 18{*10*,*30*,*29*}, Z8763847917. Yield 34.4 mg (52%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (d, *J* = 11.0 Hz, 2H), 8.33 (d, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 4.21 (dt, *J* = 13.5, 6.8 Hz, 1H), 3.68 (t, *J* = 7.1 Hz, 2H), 3.37 (s, 2H), 3.23 (dd, *J* = 13.3, 6.7 Hz, 1H), 3.11 – 2.96 (m, 3H), 2.87 (dd, *J* = 11.5, 5.7 Hz, 2H), 1.59 (dt, *J* = 10.4, 6.0 Hz, 6H), 1.27 (d, *J* = 6.6 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 162.2, 157.7, 136.1, 129.0, 128.0, 125.6, 118.3, 76.6, 66.3, 46.3, 43.6, 40.7, 37.7, 36.1, 33.5, 19.3. LC/MS (ES-API) *m/z* = 449 $[M+H]^+$. Anal. calcd. for $C_{21}H_{28}N_4O_3S_2$: C 56.23; H 6.29; N 12.49; S 14.29. Found: C 58.44; H 6.86; N 8.16; S 5.85.

2-((2-(4,5-Dimethyl-1*H*-imidazol-1-yl)ethyl)amino)-*N*-(4-(2-methylcyclopropyl)butyl)-pyrimidine-5-sulfonamide 18{*10*,*32*,*31*}, Z8763847904. Yield 34.0 mg (51%). Brownish amorphous solid. The compound was obtained as ca. 1:1 mixture of diastereomers. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (d, *J* = 9.7 Hz, 2H), 8.21 (t, *J* = 5.8 Hz, 1H), 7.49 (dt, *J* = 8.4, 4.2 Hz, 1H), 7.38 (s, 1H), 4.01 (t, *J* = 6.1 Hz, 2H), 3.56 (q, *J* = 6.0 Hz, 2H), 2.80 – 2.68 (m, 2H), 2.05 (s, 3H), 1.98 (s, 3H), 1.47 – 1.25 (m, 4H), 1.25 – 1.05 (m, 2H), 0.96 (d, *J* = 6.1 Hz, 3H), 0.76 – 0.48 (m, 2H), 0.41 – 0.25 (m, 1H), 0.10 (ddt, *J* = 12.4, 8.5, 4.3 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 162.6, 157.0 and 156.8, 135.2, 132.1, 123.3, 121.8, 42.9 and 42.4, 41.4, 33.0, 28.8 and 28.7, 27.4, 26.7 and 26.2, 19.2 and 18.8, 15.1, 13.0 and 12.6, 12.6 and 12.1, 11.7,

8.9 and 7.9. LC/MS (ES-API) *m/z* = 407 $[M+H]^+$. Anal. calcd. for $C_{19}H_{30}N_6O_2S$: C 56.13; H 7.44; N 20.67; S 7.89. Found: C 56.31; H 7.56; N 20.87; S 7.81.

***N*-((2,2-Dimethylchroman-4-yl)methyl)-2-(((1*r*,3*r*)-3-hydroxycyclobutyl)amino)-pyrimidine-5-sulfonamide 18{*10*,*33*,*32*}, Z8763847918.** Yield 33.6 mg (50%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (d, *J* = 19.0 Hz, 2H), 8.48 (d, *J* = 6.4 Hz, 1H), 7.61 (d, *J* = 5.7 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.79 (t, *J* = 7.1 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 5.3 Hz, 1H), 4.37 (d, *J* = 6.3 Hz, 1H), 4.30 (dd, *J* = 11.3, 5.8 Hz, 1H), 3.40 – 3.34 (m, 1H), 2.92 (d, *J* = 4.9 Hz, 2H), 2.27 – 2.07 (m, 4H), 1.93 (dd, *J* = 13.6, 5.1 Hz, 1H), 1.54 – 1.44 (m, 1H), 1.34 (s, 3H), 1.12 (s, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 162.0, 156.9, 156.9, 153.5, 127.6, 127.3, 122.9, 121.9, 119.7, 117.0, 74.0, 63.0, 46.3, 42.2, 37.2, 31.2, 29.6, 24.0. LC/MS (ES-API) *m/z* = 419 $[M+H]^+$. Anal. calcd. for $C_{20}H_{26}N_4O_4S$: C 57.40; H 6.26; N 13.39; S 7.66. Found: C 57.37; H 6.51; N 13.13; S 7.85.

5-((3-Cyclopentylpiperidin-1-yl)sulfonyl)-*N*-(3,3-difluoropentyl)pyrazin-2-amine 18{*13*,*4*,*3*}, Z8763848227. Yield 47.9 mg (72%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.15 (s, 1H), 7.98 (s, 1H), 3.57 – 3.46 (m, 4H), 2.55 (t, *J* = 11.8 Hz, 1H), 2.33 (t, *J* = 10.9 Hz, 1H), 2.24 – 2.11 (m, 2H), 1.99 – 1.83 (m, 2H), 1.75 – 1.62 (m, 4H), 1.56 (d, *J* = 5.6 Hz, 2H), 1.51 – 1.37 (m, 4H), 1.23 (d, *J* = 9.6 Hz, 1H), 1.11 – 0.99 (m, 2H), 0.95 (dd, *J* = 15.6, 8.2 Hz, 4H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 155.3, 142.5, 136.8, 133.5, 125.4 (t, *J* = 240.0 Hz), 50.9, 46.5, 42.7, 41.0, 34.2 (t, *J* = 24.4 Hz), 30.0, 29.9, 29.0 (t, *J* = 25.3 Hz), 28.5, 24.7 and 24.5, 24.2, 6.4 (t, *J* = 5.4 Hz). ^{19}F{H} NMR (376 MHz, DMSO-d_6) δ -98.5. LC/MS (ES-API) *m/z* = 417 $[M+H]^+$. Anal. calcd. for $C_{19}H_{30}F_2N_4O_2S$: C 54.79; H 7.26; N 13.45; S 7.70. Found: C 54.68; H 7.31; N 13.29; S 7.73.

***N*-(4-(((5-((3-(Hydroxymethyl)-3-propylpyrrolidin-1-yl)sulfonyl)pyrazin-2-yl)amino)methyl)phenyl)cyclopropanecarboxamide 18{*13*,*12*,*11*}, Z8763848239.** Yield 42.0 mg (63%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.47 (t, J = 5.6 Hz, 1H), 8.37 (s, 1H), 8.03 (s, 1H), 7.55 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 4.67 (t, J = 5.2 Hz, 1H), 4.50 (d, J = 5.4 Hz, 2H), 3.33 – 3.28 (m, 2H), 3.12 (d, J = 5.8 Hz, 3H), 2.92 (d, J = 10.1 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.67 (dd, J = 12.7, 6.4 Hz, 1H), 1.50 – 1.39 (m, 1H), 1.22 – 1.01 (m, 4H), 0.81 – 0.72 (m, 7H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 171.5, 155.4, 142.4, 138.4, 136.9, 132.8, 127.9, 119.0, 63.4, 54.8, 48.6, 47.2, 47.0, 43.4, 36.7, 32.2, 17.0, 14.7, 14.5, 7.1. LC/MS (ES-API) *m/z* = 474 $[M+H]^+$. Anal. calcd. for $C_{23}H_{31}N_5O_4S$: C 58.33; H 6.60; N 14.79; S 6.77. Found: C 58.44; H 6.86; N 14.76; S 6.85.

5-((2-Isopropyl-2-methylmorpholino)sulfonyl)-*N*-((6-phenylpyridin-2-yl)methyl)pyrazin-2-amine 18{*13*,*13*,*12*}, Z8763848226. Yield 40.9 mg (61%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (s, 1H), 8.38 (s, 1H), 8.18 (d, J = 1.0 Hz, 1H), 8.07 (d, J = 7.4 Hz, 2H), 7.85 (dd, J = 7.6, 5.6 Hz, 2H), 7.48 (t, J = 7.4 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.33 (dd, J = 5.1, 3.3 Hz, 1H), 4.76 (d, J = 5.9 Hz, 2H), 3.64 (t, J = 4.8 Hz, 2H), 3.07 (dd, J = 10.5, 5.6 Hz, 1H), 2.96 (dd, J = 15.3, 8.6 Hz, 2H), 2.84 (d, J = 11.8 Hz, 1H), 2.00 (dt, J = 13.6, 6.8 Hz, 1H), 0.99 (s, 3H), 0.81 (dd, J = 11.9, 6.9 Hz, 6H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 157.6, 155.8, 155.5, 142.8, 138.4, 137.9, 136.5, 129.1, 128.7, 126.5, 120.0, 118.6, 74.7, 59.0, 52.5, 45.9, 45.8, 31.2, 16.9, 16.2, 15.7. LC/MS (ES-API) *m/z* = 468 $[M+H]^+$. Anal. calcd. for $C_{24}H_{29}N_5O_3S$: C 61.65; H 6.25; N 14.98; S 6.86. Found: C 61.59; H 6.37; N 15.19; S 7.02.

***N*-(1-(4-Fluoro-3-methylphenyl)ethyl)-5-((3-(methoxymethyl)piperidin-1-yl)sulfonyl)-pyrazin-2-amine 18{*13*,*14*,*13*}, Z8763848248.** Yield 40.8 mg (61%). Brownish amorphous solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (d, J = 7.3 Hz, 1H), 8.30 (s, 1H), 8.02 (s, 1H), 7.29

(d, *J* = 7.0 Hz, 1H), 7.21 (s, 1H), 7.08 (t, *J* = 9.0 Hz, 1H), 5.08 (s, 1H), 3.61 (d, *J* = 11.1 Hz, 1H), 3.51 (d, *J* = 11.1 Hz, 1H), 3.19 (d, *J* = 2.5 Hz, 4H), 3.10 (t, *J* = 8.6 Hz, 1H), 2.31 (t, *J* = 11.0 Hz, 1H), 2.21 (s, 3H), 1.75 (s, 1H), 1.61 (dd, *J* = 33.4, 12.2 Hz, 2H), 1.45 (d, *J* = 6.7 Hz, 4H), 0.97 (q, *J* = 11.0 Hz, 1H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 159.6 (d, *J* = 241.8 Hz). 154.6, 142.5, 139.8, 136.8, 129.3 (d, *J* = 4.9 Hz), 125.2 (d, *J* = 9.3 Hz), 124.0 (d, *J* = 17.2 Hz), 114.7 (d, *J* = 22.1 Hz), 74.2 (d, *J* = 3.9 Hz), 58.1, 49.3 (d, *J* = 3.5 Hz), 49.0, 46.6, 35.6, 25.9, 23.9, 22.7, 14.3, 14.2. ^{19}F{H} NMR (376 MHz, DMSO-*d*$_6$) δ -120.9. LC/MS (ES-API) *m/z* = 423 $[M+H]^+$. Anal. calcd. for $C_{20}H_{27}FN_4O_3S$: C 56.85; H 6.44; N 13.26; S 7.59. Found: C 56.74; H 6.81; N 13.32; S 7.52.

5-((3-(1*H*-Indol-3-yl)pyrrolidin-1-yl)sulfonyl)-*N*-(2-((2-methoxyethyl)sulfinyl)ethyl)pyrazin-2-amine 18{*13*,*18*,*17*}, Z8763848238. Yield 38.6 mg (58%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 10.87 (s, 1H), 8.43 (s, 1H), 8.37 (s, 1H), 8.02 (d, *J* = 7.1 Hz, 1H), 7.40 (dd, *J* = 7.6, 5.2 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.13 (s, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 3.85 (td, *J* = 9.6, 7.4 Hz, 1H), 3.81 – 3.70 (m, 2H), 3.70 – 3.66 (m, 2H), 3.58 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.48 – 3.37 (m, 2H), 3.28 (d, *J* = 4.1 Hz, 1H), 3.26 (d, *J* = 5.7 Hz, 3H), 3.14 – 3.04 (m, 2H), 2.98 – 2.87 (m, 2H), 2.26 – 2.17 (m, 1H), 1.99 – 1.90 (m, 1H). ^{13}C{H} NMR (151 MHz, DMSO-*d*$_6$) δ 155.4, 142.4, 137.4, 136.4, 126.3, 121.6, 121.1, 118.4, 113.7, 113.7, 111.6, 64.6, 58.1, 53.7, 51.4, 50.7, 50.7, 48.1, 35.6, 34.4, 31.7, 31.6. LC/MS (ES-API) *m/z* = 478 $[M+H]^+$. Anal. calcd. for $C_{21}H_{27}N_5O_4S_2$: C 52.81; H 5.70; N 14.66; S 13.43. Found: C 52.73; H 5.81; N 14.59; S 13.71.

***N*-(2-(7-Ethyl-1*H*-indol-3-yl)ethyl)-5-((2-(5-methyloxazol-2-yl)ethyl)amino)pyrazine-2-sulfonamide 18{*13*,*29*,*28*}, Z8763848244.** Yield 35.1 mg (53%). Brownish gum. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 10.78 (s, 1H), 8.39 (d, *J* = 0.9 Hz, 1H), 8.09 (s, 1H), 7.94 (d, *J* = 0.9 Hz, 1H),

7.69 (t, J = 5.8 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.10 (d, J = 2.0 Hz, 1H), 6.97 – 6.83 (m, 2H), 6.67 (d, J = 0.9 Hz, 1H), 3.68 (dd, J = 12.8, 6.7 Hz, 2H), 3.13 – 3.03 (m, 2H), 2.95 (t, J = 6.9 Hz, 2H), 2.86 – 2.73 (m, 4H), 2.20 (s, 3H), 1.23 (t, J = 7.5 Hz, 3H). ^{13}C{H} NMR (151 MHz, DMSO-d_6) δ 160.6, 155.3, 148.3, 141.2, 139.5, 134.8, 126.8, 122.5, 122.5, 119.6, 118.6, 115.6, 111.4, 43.5, 37.9, 27.2, 25.8, 23.6, 14.4, 10.4. LC/MS (ES-API) m/z = 455 $[M+H]^+$. Anal. calcd. for $C_{22}H_{26}N_6O_3S$: C 58.30; H 6.96; N 7.84; S 5.99. Found: C 58.44; H 6.86; N 8.16; S 5.85.

ASSOCIATED CONTENT

Data Availability Statement. The data underlying this study are available in the published article and its Supporting Information.

Supporting Information. The following files are available from the authors free of charge:

structures of the starting amines, Figures S1–S5 (PDF);

library synthesis details, Tables S1–S4 (XSLX);

copies of NMR spectra (PDF).

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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