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Article

Construction of Biaryl Sulfonamides via Pd(II)-Catalyzed Cross-Coupling of C(sp^2)-H Bonds with Iodobenzenesulfonamides

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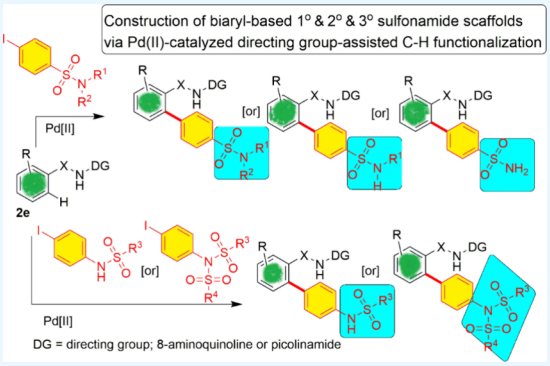
ABSTRACT: This study describes the utility of Pd(II)-catalyzed C−H arylation of benzamides for constructing biaryl sulfonamides. Sulfonamides are known for their promising applications in pharmaceuticals and agrochemicals. A literature review revealed that biaryl sulfonamides were generally constructed via the traditional cross-coupling reactions. We report a progressive method for obtaining biaryl sulfonamides via the Pd(II)-catalyzed bidentate directing group (8-aminoquinoline or picolinamide)-assisted cross-coupling of sp^2 C−H bonds of aromatic carboxamides with iodobenzenesulfonamides. After the C−H arylation reactions, we attempted the removal of the 8-aminoquinoline from the synthesized biaryl scaffolds possessing the carboxamide and sulfonamide moieties using triflic acid. In some cases, we observed the occurrence of decarboxylation and Friedel−Crafts acylation, affording interesting aromatic scaffolds possessing the sulfonamide moiety. The current work contributes toward developing alternative ways for assembling various biaryl sulfonamides.



INTRODUCTION

Since the discovery of medicinally active sulfonamides in the 1930s, sulfa- or sulfonamide-based drugs transformed the medicines.[1−3] Several bioactive sulfonamides gained colossal importance and are still present today in pharmaceuticals and agrochemicals, and sulfonamides were found to exhibit a wide range of bioactivities.[1−8]

Biaryls are highly regarded scaffolds and of particular interest, biaryl molecules possessing the sulfonamide unit have received significant attention in organic and medicinal chemistry (Figure 1).[4−6,9,10] For example, MK-996 and L-159,894 are angiotensin II antagonists.[4a] PF-4455242 was considered for the treatment of bipolar disorder.[4b] BPBTS is a sodium channel blocker,[4c] and BMS-207940 and BMS-187308 are identified as endothelin receptor antagonists.[5a,b] Valdecoxib and compound **1f** are COX inhibitors.[1f,4d] G2019SLRRK2 is a kinase inhibitor,[5c] and encorafenib (braftovi) is used for the treatment of melanoma cancer.[5d]

General routes toward synthesizing primary- or secondary- or tertiary-sulfonamide subunit-containing molecules are depicted in Scheme 1. Significant developments have occurred in the synthesis of a wide range of sulfonamides through C−N bond formation or N−S bond formation in the presence of metal catalysts or metal-free conditions (Scheme 1). Various research groups, including Mondal,[3d] Rivera,[3e] Hajra,[3h] Su,[3i] have compiled the available routes toward synthesizing sulfonamides. At times, primary sulfonamides are used as substrates for preparing secondary or tertiary sulfonamides.[3c] Of particular interest, it may be noted that the construction of biaryl sulfonamides (viz. the biaryl linkage) was generally accomplished using the traditional cross-coupling reaction (Scheme 1).[10]

In recent years, the transition metal-catalyzed C−H activation and functionalization have been considered a powerful variant of classical cross-coupling reactions for assembling biaryls and functionalized aliphatic molecules.[11−20] A limited number of reports revealed the synthesis of biaryl sulfonamides via the sulfonamide directing group-assisted *ortho* C−H bond functionalization (Figure 2).[18] You described[18d] the Rh-catalyzed sulfonamide-directed oxidative coupling of C−H bonds affording *ortho* aryl sulfonamides. Chen,[18b,c] Yu,[18e] and Singh[18a] independently reported the Pd-catalyzed sulfonamide-directed *ortho* C−H arylation affording *ortho* aryl sulfonamides (Figure 2). Some other *ortho* C−H functionalization reactions (e.g., acylation, amination, alkenylation, alkynylation, carbenoid insertion, etc.) of aryl sulfonamides were also reported.[19,20]

Given the notable bioactivities, there have been persistent efforts toward synthesizing sulfonamides. Thus, there is a scope for developing additional methods for obtaining new biaryl sulfonamides. In continuation of our lab's research program on expanding the application of C−H functionalization, we

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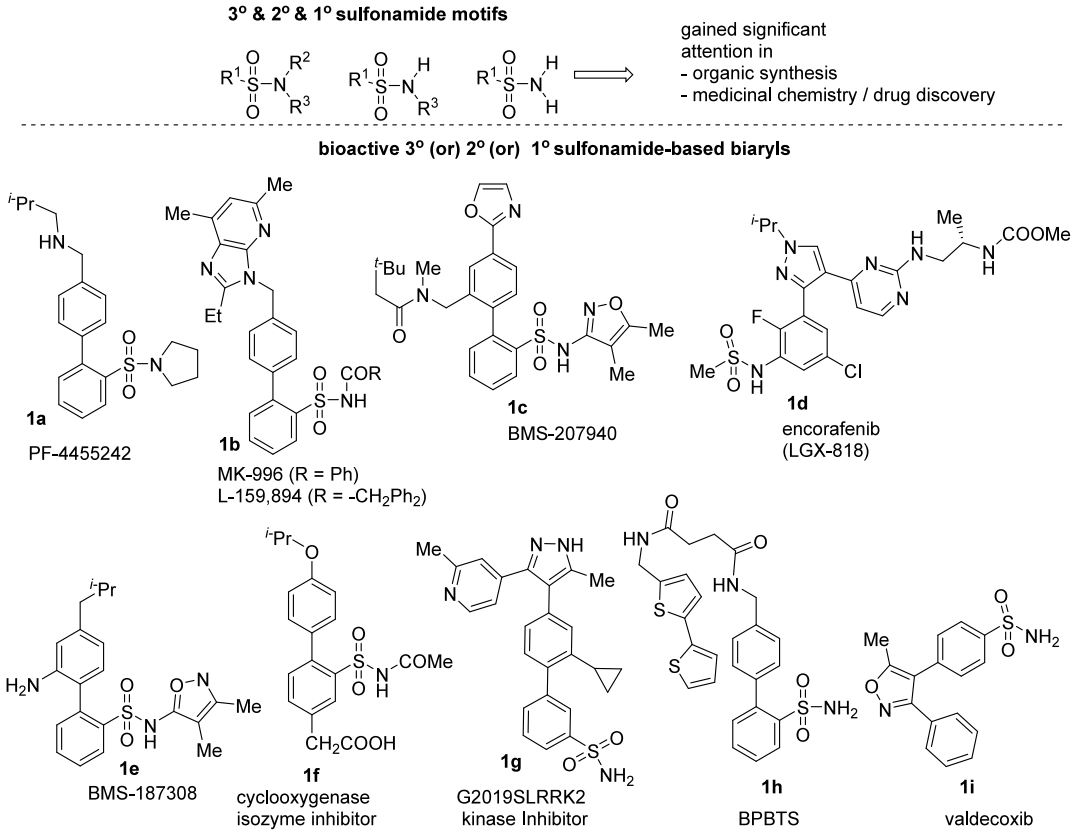

Figure 1. Representative examples of bioactive biaryl-based sulfonamides.

envisaged the assembling of biaryl sulfonamides via the bidentate directing group-assisted C−H functionalization as the key transformation.[13] Given that the biaryl sulfonamides (especially, the biaryl linkage in the biaryl sulfonamides) are generally constructed via classical cross-coupling reactions,[4d,5a,b,10] their synthesis through the direct C−H coupling method is expected to enable rapid assembly of biaryl sulfonamides (Figure 2). Accordingly, we herein describe Pd(II)-catalyzed, bidentate directing group 8-aminoquinoline- or picolinamide-assisted *ortho* C(sp^2)-H arylation of aromatic carboxamides using iodobenzenesulfonamides as the coupling partners for the construction of a library of biaryl sulfonamides.

RESULTS AND DISCUSSION

First, we attempted the synthesis of biaryl-based 3° sulfonamide derivative **5a** via the Pd(II)-catalyzed 8-aminoquinoline directing group-assisted coupling of *ortho* C(sp^2)-H bond of benzamide **3a** with iodobenzenesulfonamide (**4a**). Accordingly, *N*,*N*-dibenzyl-4-iodobenzenesulfonamide (**4a**) was synthesized from 4-iodobenzenesulfonyl chloride and *N*,*N*-dibenzylamine. On the other hand, 2-methoxybenzamide (**3a**), possessing the 8-aminoquinoline bidentate directing group (DG), was assembled from 2-methoxybenzoic acid and 8-aminoquinoline under a standard amide coupling procedure. It is documented that the Pd(II)-catalyzed, 8-aminoquinoline DG-aided *ortho* C(sp^2)−H functionalization of carboxamides using aryl iodides as arylating agents, follows a Pd(II)/Pd(IV) redox catalytic cycle[13−17] enabling the activation of the *ortho* C−H bond and subsequent arylation of the target molecule. The usage of an iodide ion scavenging additive (such as AgOAc, K_2CO_3, Ag_2CO_3, etc.) is essential, and this additive plays a role in restoring the Pd(II) catalyst in the proposed catalytic cycle.[13−17]

Optimization of the reaction conditions for the arylation of the *ortho*-C(sp^2)-H bond of **3a** with **4a** was conducted by employing a catalyst and an iodide ion scavenger (Table 1). The investigation commenced with heating a mixture of **3a**, **4a** (4 equiv), $Pd(OAc)_2$ (10 mol %) and AgOAc (2.2 equiv) in toluene (2 mL) at 110 °C for 6 h. This reaction did not yield the expected product **5a** (entry 1, Table 1). Extending the reaction time to 12 h afforded the expected biaryl-based 3° sulfonamide **5a** in 25% yield (entry 2, Table 1). Prolonging the reaction time to 18 and 24 h, **5a** was obtained in 60 and 82% yields, respectively (entries 3 and 4, Table 1). Next, we performed the same reaction by using 3 or 5 mol % of the $Pd(OAc)_2$ catalyst. These trials gave **5a** in a decreased yield (50 and 70% respectively, entries 5 and 6, Table 1). The reaction using $Ni(OTf)_2$ instead of $Pd(OAc)_2$ in the presence of $NaHCO_3$ as an additive did not afford **5a** (entry 7, Table 1). When we performed Pd(II)-catalyzed arylation of **3a** with **4a** by reducing the amounts of AgOAc (1 or 2 equiv), the product **5a** was obtained in 60 and 75% yields, respectively (entries 8 and 9, Table 1). Usage of K_2CO_3 instead of AgOAc gave the product **5a** in 35% yield (entry 10, Table 1). The usage of Ag_2CO_3 instead of AgOAc did not give **5a** (entry 11, Table 1). The Pd(II)-catalyzed reaction of **3a** with **4a** in the presence of AgOAc in toluene at 60 or 90 °C afforded **5a** in 0−30% yields (entries 12−13, Table 1). Next, the reaction using *p*-xylene solvent yielded the expected product **5a** in 76% yield (entry 14, Table 1). The Pd(II)-catalyzed reaction of **3a** with 1 or 3 equiv of **4a** gave the product **5a** in 48 and 72% yields, respectively (entries 15 and 16, Table 1).

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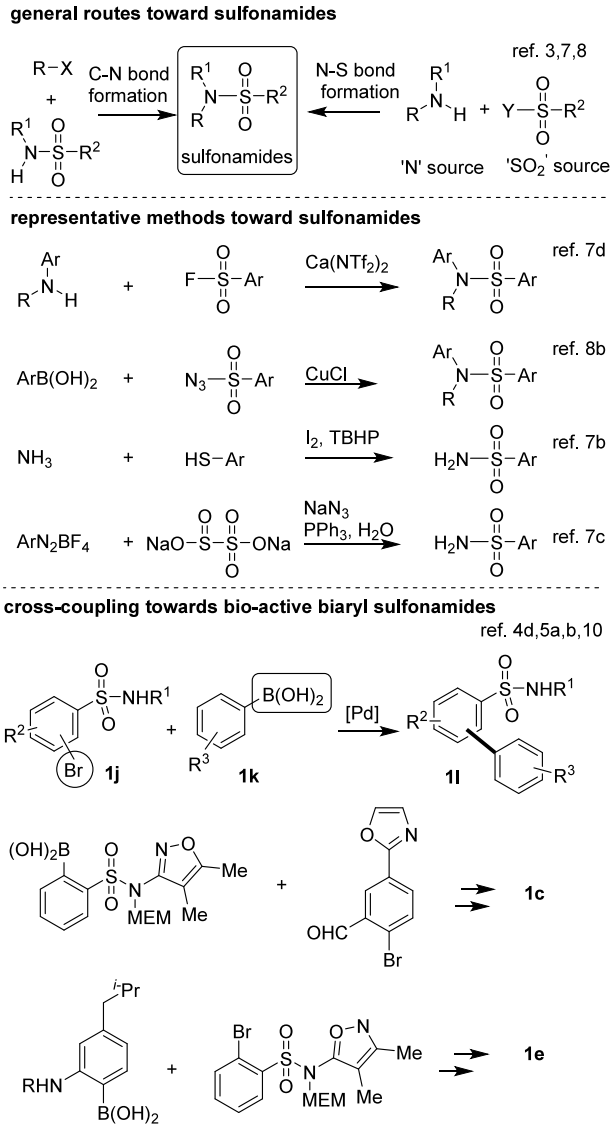
Scheme 1. Methods Enabling the Synthesis of Sulfonamides



Having explored the C−H arylation of benzamides with 8-AQ as the directing group, attention was paid to using other bidentate directing groups for the *ortho* C−H arylation of carboxamides (Scheme 2). Carboxamides **6a**−**d** were synthesized using 2-(methylthio)aniline (MTA) as the bidentate directing group. These compounds were subjected to the Pd(II)-catalyzed C−H arylation reactions with **4a** (4 equiv) in the presence of AgOAc in toluene at 110 °C to afford the biaryl-based 3° sulfonamides **7a**−**d** in 72−80% yields. Then, carboxamide **6e** possessing 4-amino-2,1,3-benzothiadiazole (ABTD) as a bidentate directing group was subjected to the Pd(II)-catalyzed C−H arylation reaction with **4a** to afford the product **7e** in 66% yield. We then explored the native carboxylic acid group-aided C−H arylation reaction of 2-methoxybenzoic acid. The β−C-H arylation of 2-methoxy benzoic acid (**6f**) with **4a** using $Pd(OAc)_2$ and AgOAc in AcOH at 130 °C for 48 h did not yield the expected product **8a**. Repeating the reaction in the presence of $Pd(OAc)_2$, NMe_4Cl, and KOAc in AcOH at 130 °C for 48 h did not yield the expected product **8a**. Next, benzamide **3a** was subjected to the Pd(II)-catalyzed C−H arylation reaction with primary sulfonamide moiety-based iodoaryl compound **9a** in the

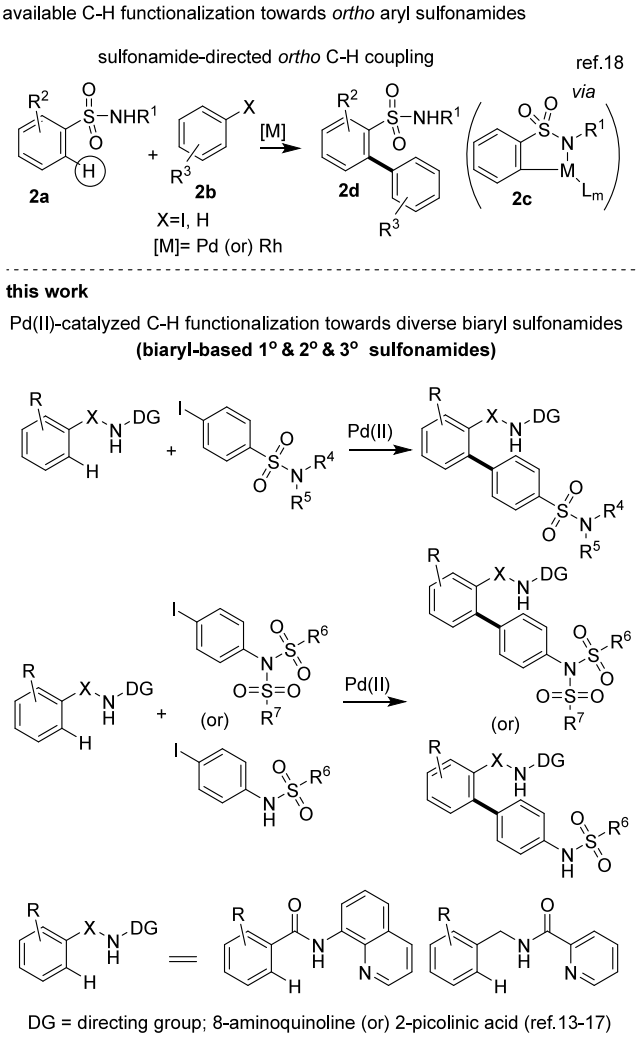


Figure 2. Biaryl-based sulfonamides via C−H functionalization.

presence of AgOAc in toluene at 110 °C. This reaction did not give the expected primary biaryl sulfonamide **8b** (Scheme 2).

We then embarked on the synthesis of various biaryl-based 3° sulfonamide scaffolds via Pd(II)-catalyzed 8-aminoquinoline directing group (DG)-assisted C−H arylation of different carboxamides (Schemes 3 and 4). Carboxamides **3a**−**i** having substituents at the *ortho*- or *meta*-positions (e.g., OMe, Me, OEt, OPh, F, Cl, and Br) were treated with **4a** in the presence of $Pd(OAc)_2$ (10 mol %) and AgOAc (2.2 equiv) in toluene at 110 °C. These reactions yielded the corresponding biaryl-based 3° sulfonamide scaffolds **5a**−**i** in 30−86% yields (Scheme 3). Then, biaryl carboxamide **3j**, naphthyl- and pyrene- carboxamides **3k,l**, and 2,3-dihydrobenzo[*b*][1,4]-dioxine-5-carboxamide **3m** were treated with **4a** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C. These reactions afforded the corresponding biaryl-based 3° sulfonamide scaffolds **5j**−**m** in 76−82% yields (Scheme 3).

Next, we intended to perform the Pd(II)-catalyzed DG-aided C−H arylation of heteroaryl carboxamides such as furan-2-carboxamide **3n**, thiophene-2-carboxamide **3o**, pyrrole-2-carboxamide **3p**, benzofuran-2-carboxamide **3q**, and benzothiophene-2-carboxamide **3r**. Accordingly, substrates **3n**−**r** were subjected to C−H arylation with **4a** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110−130 °C. These

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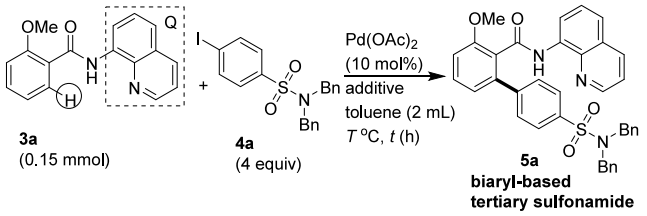
Table 1. Optimization of Reaction Conditions and Synthesis of Biaryl-Based Tertiary Sulfonamide 5a via the Coupling of the *Ortho* C−H Bond of 3a with Iodobenzenesulfonamide 4a



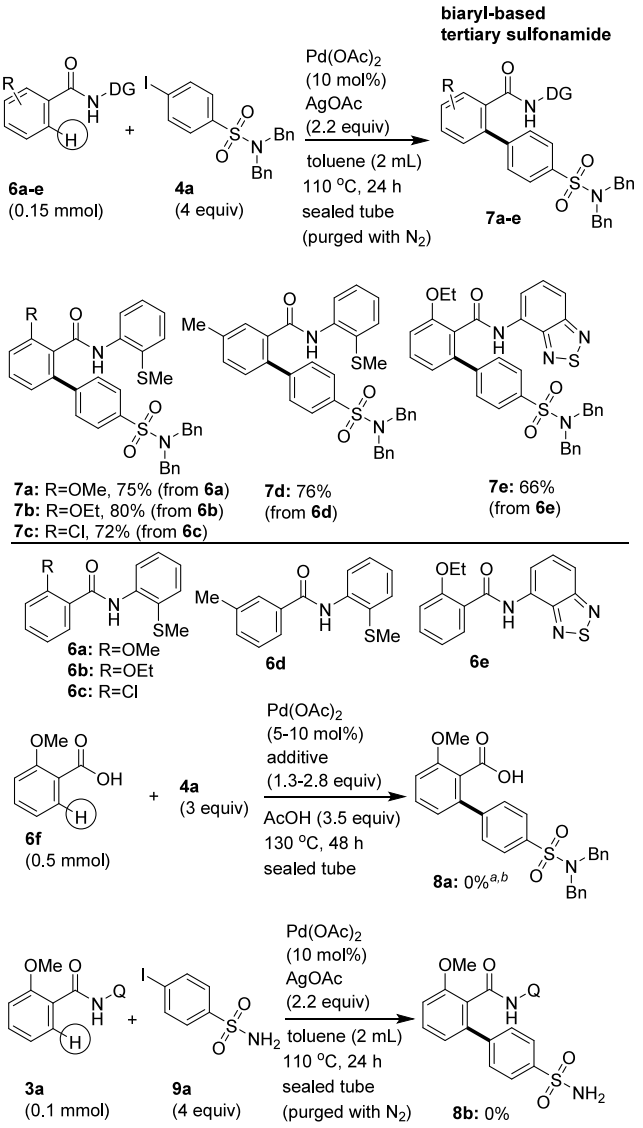
entry	additive (z equiv)	T (°C)	t (h)	**5a**: yield (%)[a]
1	AgOAc (2.2)	110	6	0
2	AgOAc (2.2)	110	12	25
3	AgOAc (2.2)	110	18	60
4	AgOAc (2.2)	110	24	82
5[b]	AgOAc (2.2)	110	24	50
6[c]	AgOAc (2.2)	110	24	70
7[d]	$NaHCO_3$ (2.0)	160	24	0
8[e]	AgOAc (1.0)	110	24	60
9	AgOAc (2.0)	110	24	75
10	K_2CO_3 (2.0)	110	24	35
11	Ag_2CO_3 (2.0)	110	24	0
12	AgOAc (2.2)	60	24	0
13	AgOAc (2.2)	90	24	30
14[f]	AgOAc (2.2)	130	24	76
15[g]	AgOAc (2.2)	110	24	48
16[h]	AgOAc (2.2)	110	24	72

[a]The reactions were carried out in a sealed tube purged with a nitrogen atm. [b]$Pd(OAc)_2$ (3 mol %). [c]$Pd(OAc)_2$ (5 mol %). [d]$Ni(OTf)_2$ (10 mol %). [e]1 Equiv of AgOAc. [f]*o*-Xylene solvent. [g]1 equiv of **4a**. [h]3 equiv of **4a**.

reactions afforded the corresponding biaryl-based 3° sulfonamide scaffolds (containing heteroaryl−aryl linkage) **5n−r** in 74−80% yields (Scheme 3). The Pd(II)-catalyzed, DG-aided β−C-H arylation of cinnamamide substrate **3s** with **4a** afforded the corresponding sulfonamide motif-based cinnamamide derivative **5s** in 72% yield. Similarly, acrylamide substrate **3t** containing the 8-aminoquinoline DG was treated with **4a** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. This reaction afforded sulfonamide motif-based cinnamamide **5t** with *Z* stereochemistry in 76% yield. The *Z*-selective arylation and stereochemistry of products **5s** and **5t** were proposed based on our earlier report[17d] dealing with the *Z*-selective β−C-H arylation of their parent substrates **3s** and **3t**, respectively (Scheme 3).

Having explored the mono C−H arylation of various benzamides (**3a−m**) and heteroaryl carboxamides (**3n−r**), we shifted our focus to perform the 8-aminoquinoline-assisted double C−H arylation of *para*-substituted benzamides (**10a−c**). Accordingly, the *para*-substituted benzamides **10a,b** (having OMe and Me substituents), and simple benzamide **10c** were treated with **4a** (4 equiv) in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C. These reactions resulted in the formation of π-extended biaryl-based 3° sulfonamide scaffolds **12−14** in 75−82% yields (Scheme 4). Along this line, we performed the Pd(II)-catalyzed double C−H arylation of benzamide **11** possessing 4-amino-2,1,3-benzothiadiazole as the DG with **4a**. This reaction afforded the π-extended biaryl-based 3° sulfonamide **15** in 63% yield (Scheme 4).

Scheme 2. Optimization of Reaction Conditions and Screening of Directing Groups for the Coupling of the *ortho* C−H Bond of Benzamides with Iodobenzenesulfonamide



[a]$Pd(OAc)_2$ (5 mol %), AgOAc (1.3 equiv). [b]$Pd(OAc)_2$ (10 mol %), NMe_4Cl (2.2 equiv), KOAc (2.8 equiv).

Having successfully introduced sulfonamide motifs at the β-position of aromatic carboxamides, we then intended to assemble biaryl-based tertiary sulfonamide motifs by performing the (*ortho*) γ-C−H arylation of arylacetamides and benzylamine derivatives **16**/**18** (Scheme 4). Various mono- and bis-substituted arylacetamides **16a−h** possessing the 8-aminoquinoline directing group were assembled. Substrates **16a−h** were subjected to the Pd(II)-catalyzed *ortho* C(sp^2)−H arylation reactions with **4a**. These reactions gave the corresponding biaryl-based tertiary sulfonamide motifs **17a−h** in 50−72% yields. Next, we performed the picolinamide directing group-assisted Pd(II)-catalyzed (*ortho*) γ-C(sp^2)-H arylation of benzyl amine or 2-thiophenemethylamine derivatives **18a,b** with **4a** in the presence of AgOAc in toluene at 110 °C. These reactions afforded the corresponding biaryl-based tertiary sulfonamide motifs **19a,b** in 65−70% yields. Furthermore, the picolinamide DG-assisted double *ortho*

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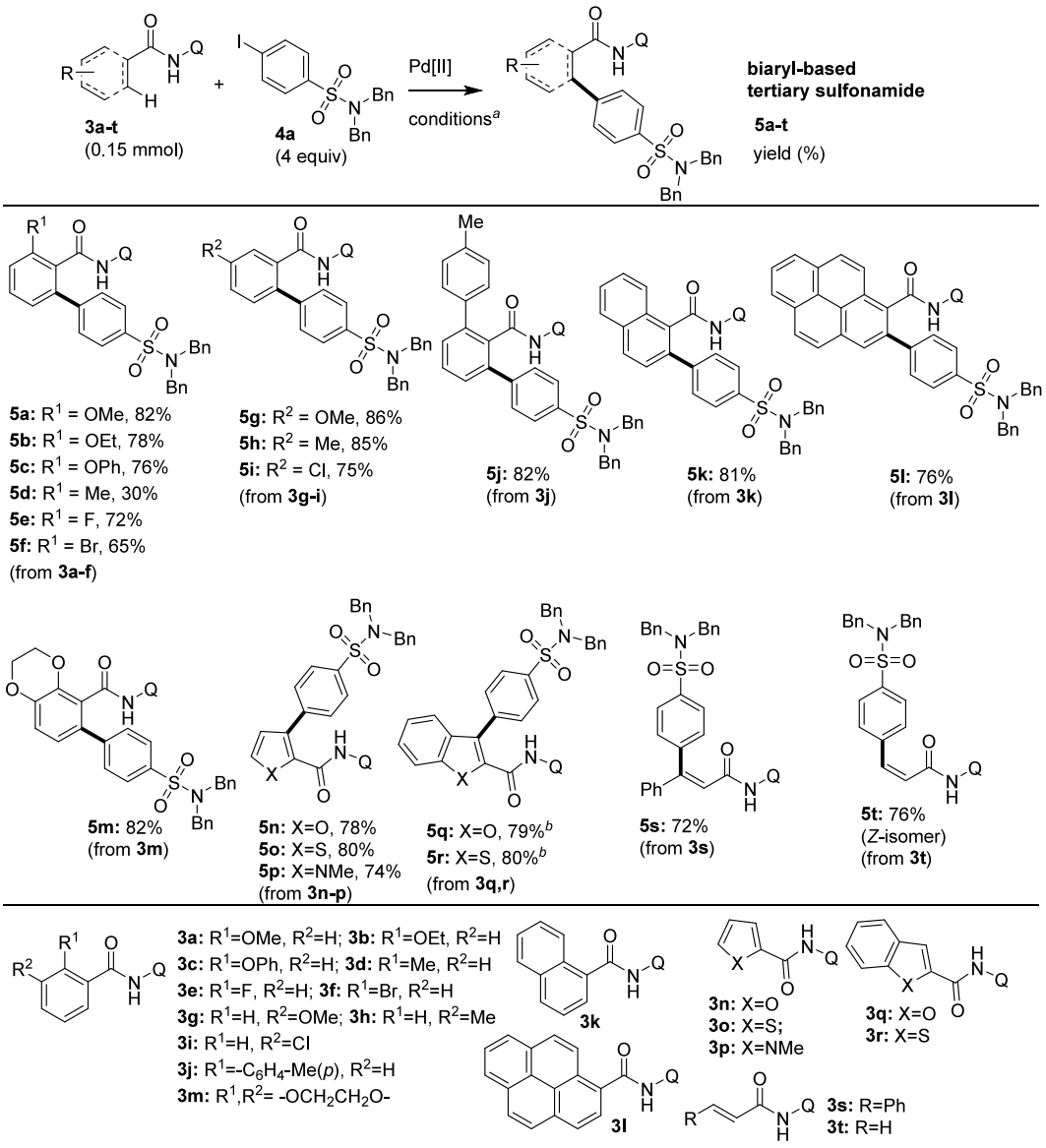
Scheme 3. Coupling of Carboxamides with Iodobenzenesulfonamide 4a and Synthesis of Biaryl-Based Tertiary Sulfonamide Motifs 5a−t



[a]Substrate (0.15 mmol), **4a** (4 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2.2 equiv), toluene (2 mL), 110 °C, 24 h, sealed tube purged with a nitrogen atm. [b]The reaction was conducted at 130 °C.

C(sp^2)−H arylation of benzylamine derivative **18c** with **4a** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C afforded the corresponding π-extended biaryl-based 3° sulfonamide **19c** in 70% yield (Scheme 4).

Having done the C−H arylation of various carboxamides with *N*,*N*-dibenzyl-4-iodobenzenesulfonamide (**4a**), we then desired to expand the generality and substrate scope of this protocol by using various tertiary and secondary sulfonamides **4b−e** as the coupling partners. We treated 2-methoxybenzamide (**3a**) with *N*-benzyl-*N*-methyl-4-iodobenzenesulfonamide **4b** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h to afford the corresponding biaryl-based tertiary sulfonamide **20a** in 78% yield (Scheme 5). The treatment of heteroaryl carboxamides **3n,o** with **4b** furnished the corresponding biaryl-based tertiary sulfonamide **20b,c** in 72−75% yields, respectively (Scheme 5). Additionally, biaryl-based tertiary sulfonamides **20d,e** were obtained in 79−82% yields from their corresponding substrates **3a,o** and 4-iodobenzenesulfonamide **4c** (Scheme 5).

Having obtained various biaryl-based tertiary sulfonamide motifs, we then focused on the synthesis of biaryl-based secondary sulfonamide motifs via Pd(II)-catalyzed DG-aided C−H arylation using 4-iodobenzenesulfonamides **4d,e** (Scheme 5). Benzamides **3h,i** and heteroaryl carboxamides **3n,o** were treated with *N*-benzyl-4-iodobenzenesulfonamide **4d** and *N*-butyl-4-iodobenzenesulfonamide **4e** to obtain the corresponding biaryl-based secondary sulfonamide motifs **21a−h** in 68−81% yields (Scheme 5).

We then shifted our attention to the synthesis of bis sulfonamide unit containing biaryl motifs via the Pd(II)-catalyzed, DG-aided coupling of the C−H bonds of carboxamides with bis sulfonamide unit-based iodoaryls (Table 2, Scheme 6). Toward this, we assembled bis sulfonamide-based 4-iodoaniline **4f** from 4-iodoaniline and

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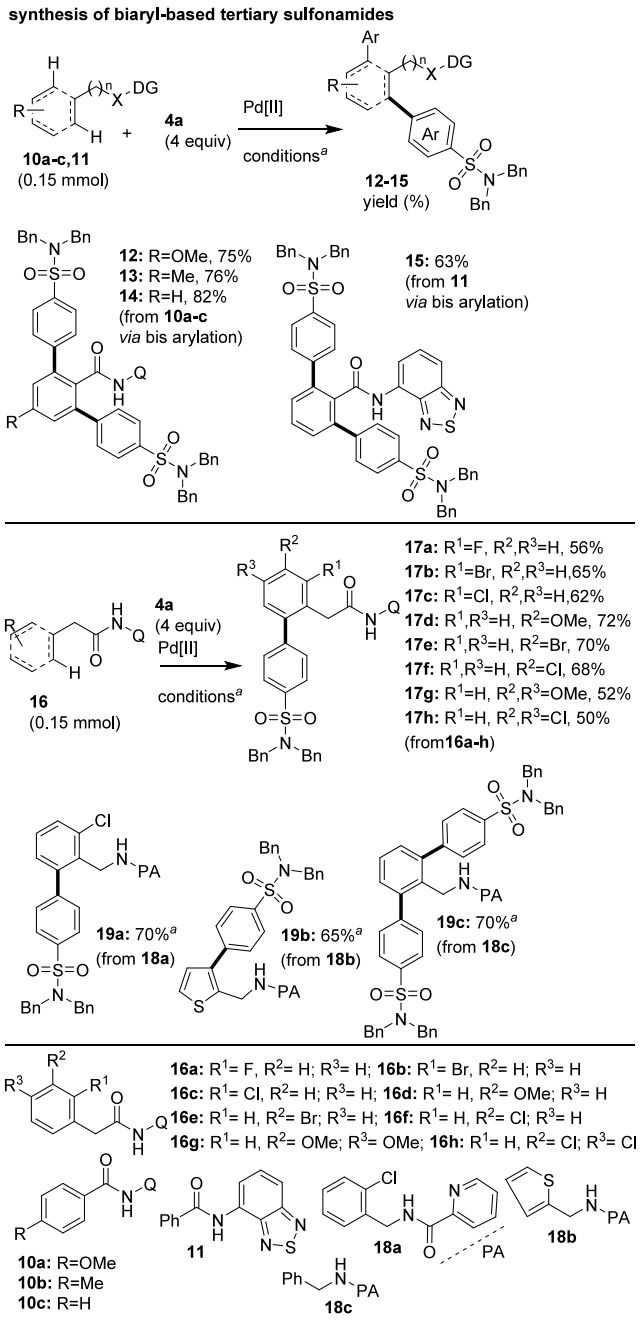
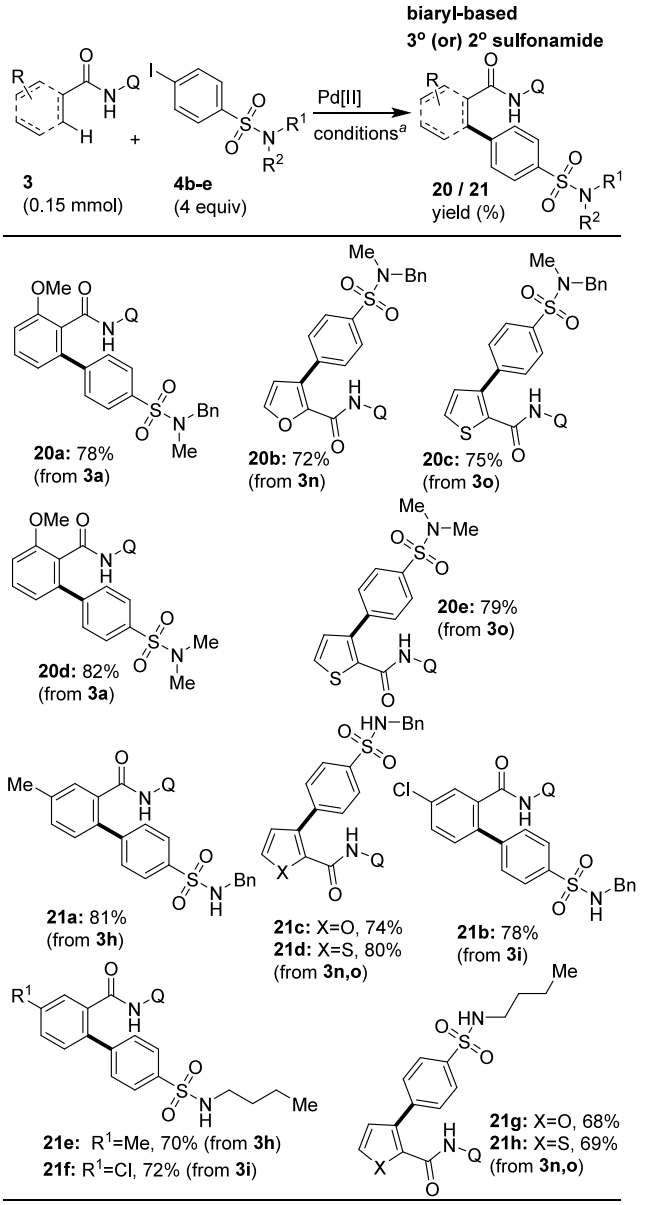
Scheme 4. Coupling of Carboxamides with Iodobenzenesulfonamide 4a and Synthesis of Biaryl-Based Tertiary Sulfonamide Motifs 12−15, 17, and 19



[a]Substrate (0.15 mmol), **4a** (4 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2.2 equiv), toluene (2 mL), 110 °C, 24 h, sealed tube (purged with a nitrogen atm).

Scheme 5. Coupling of Carboxamides with Iodobenzenesulfonamides and Synthesis of Biaryl-Based Tertiary Sulfonamide Motifs 20 and Secondary Sulfonamide Motifs 21



[a]Substrate (0.15 mmol), **4a** (4 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2.2 equiv), toluene (2 mL), 110 °C, 24 h, sealed tube (purged with a nitrogen atm).

benzenesulfonyl chloride. Table 2 describes a brief optimization of reaction conditions for the arylation of **3a** with **4f**. A mixture of benzamide **3a** and **4f** (1 equiv), $Pd(OAc)_2$ (10 mol %), and AgOAc (2.2 equiv) was heated in toluene (2 mL) at 110 °C for 24 h. This reaction afforded the desired bis sulfonamide unit containing biaryl **22a** in 52% yield (entry 1, Table 2). The treatment of **3a** with 3 equiv of **4f** furnished **22a** in 75% yield (entry 2, Table 2). The Pd(II)-catalyzed C−H arylation of **3a** with 4 equiv of **4f** provided **22a** with an improved yield of 88% (entry 3, Table 2). Heating a mixture of **3a** and **4f** with 3 or 5 mol % of the $Pd(OAc)_2$ catalyst resulted in the product **22a** in 65−72% yields (entries 4 and 5, Table 2). The Pd(II)-catalyzed C−H arylation of **3a** with **4f** with 1 or 2 equiv of AgOAc gave **22a** in 62−80% yield (entries 6 and 7, Table 2). The reaction using *p*-xylene solvent instead of toluene afforded **22a** in 82% yield (entry 8, Table 2). Treating **3a** with **4f** in the presence of Ag_2CO_3 additive in *t*-BuOH at 80 °C for 24 h gave **22a** in 75% yield (entry 9, Table 2).

Next, we ventured into expanding the substrate scope and synthesis of bis sulfonamide unit containing biaryls (Scheme 6). We treated various benzamides **3a,b,f,h,i,m** and thiophene-

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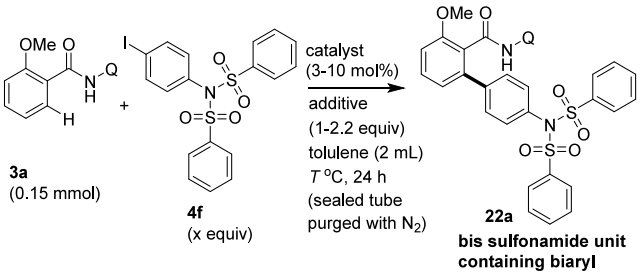
Table 2. Synthesis of Bis Sulfonamide Unit Containing Biaryl Motif 22a



entry	catalyst (mol %)	additive (equiv)	solvent (2 mL)	T (° C)	22a: yield (%)
1[a]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	toluene	110	52
2[b]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	toluene	110	75
3	$Pd(OAc)_2$ (10)	AgOAc (2.2)	toluene	110	88
4	$Pd(OAc)_2$ (3)	AgOAc (2.2)	toluene	110	65
5	$Pd(OAc)_2$ (5)	AgOAc (2.2)	toluene	110	72
6	$Pd(OAc)_2$ (10)	AgOAc (1.0)	toluene	110	62
7	$Pd(OAc)_2$ (10)	AgOAc (2.0)	toluene	110	80
8	$Pd(OAc)_2$ (10)	AgOAc (2.2)	*p*-xylene	130	82
9	$Pd(OAc)_2$ (10)	Ag_2CO_3 (2.0)	*t*-BuOH	80	75

[a]1 equiv of **4f**. [b]3 equiv of **4f**.

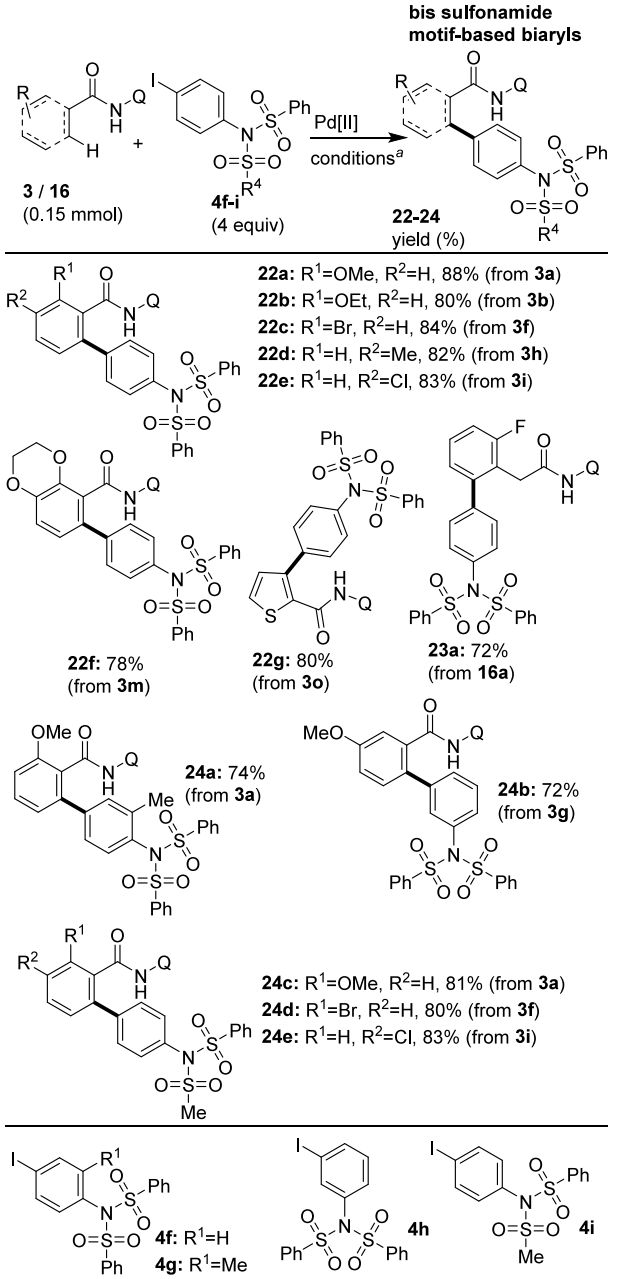
2-carbaxamide **3o** containing the 8-aminoquinoline DG with **4f** in the presence of $Pd(OAc)_2$ and AgOAc in toluene (2 mL) at 110 °C for 24 h. These reactions afforded the corresponding bis sulfonamide unit containing biaryls **22a−g** in 78−88% yields. The Pd(II)-catalyzed *ortho* C−H arylation reaction of arylacetamide **16a** with **4f** furnished bis sulfonamide unit containing biaryls **23a** in 72% yield.

Subsequently, the Pd(II)-catalyzed C−H arylation of benzamides **3a** and **3g** with bis sulfonamide-linked 4-iodo-2-methylaniline **4g** or bis sulfonamide-linked 3-iodoaniline **4h** afforded the corresponding tertiary sulfonamide unit containing biaryls **24a,b** in 72−74% yields. Then, the Pd(II)-catalyzed C−H arylation of benzamides **3a,f,i** with bis sulfonamide-linked 4-iodo-aniline **4i** afforded the corresponding tertiary sulfonamide unit containing biaryls **24c−e** in 80−83% yields (Scheme 6).

We then shifted our focus to employing different secondary sulfonamide-linked 4-iodoanilines in the Pd(II)-catalyzed C−H arylation reactions (Scheme 7). Accordingly, we performed the Pd(II)-catalyzed arylation of various benzamides **3a,d,f,h,i** and furan-2-carboxamide **3n** with secondary sulfonamide-based 4-iodoanilines **4j,k**. These reactions afforded the corresponding secondary sulfonamide unit containing biaryls **25a−k** in 68−75% yields (Scheme 7). Subsequently, we carried out the Pd(II)-catalyzed arylation of various benzamides **3d,e,f,g,h,i** and heteroaryl carboxamides **3n,o** with secondary sulfonamide-based 4-iodoanilines **4l,m** (prepared using the corresponding alkylsulfonyl chlorides). These reactions yielded the corresponding secondary sulfonamide unit containing biaryls **26a−l** in 70−80% yields (Scheme 7).

Having successfully synthesized a diverse range of tertiary as well as secondary sulfonamide-based biaryls, we then embarked

Scheme 6. Coupling of Carboxamides with Bis Sulfonamide-Based 4-iodoanilines and Synthesis of Bis Sulfonamide Unit Containing Biaryls 22−24



[a]Substrate (0.15 mmol), **4f−i** (4 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2.2 equiv), toluene (2 mL), 110 °C, 24 h, sealed tube (purged with a nitrogen atm).

on the removal of the 8-aminoquinoline (8-AQ) directing group (DG) (Table 3). At first, the tertiary sulfonamide-based biaryl carboxamide **5i** was subjected to the standard acid-mediated amide hydrolysis using CF_3SO_3H (0.2 mL) in a mixture of toluene/H_2O (1:1, 5:1, or 10:1 ratio, 3 mL) at 60−100 °C for 6−18 h. These reactions did not yield any carboxamide or sulfonamide hydrolysis products (entries 1−4, Table 3).

Then, substrate **5i** was treated with CF_3SO_3H (0.1−0.4 mL) in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 12−24 h. These reactions afforded the primary sulfonamide-

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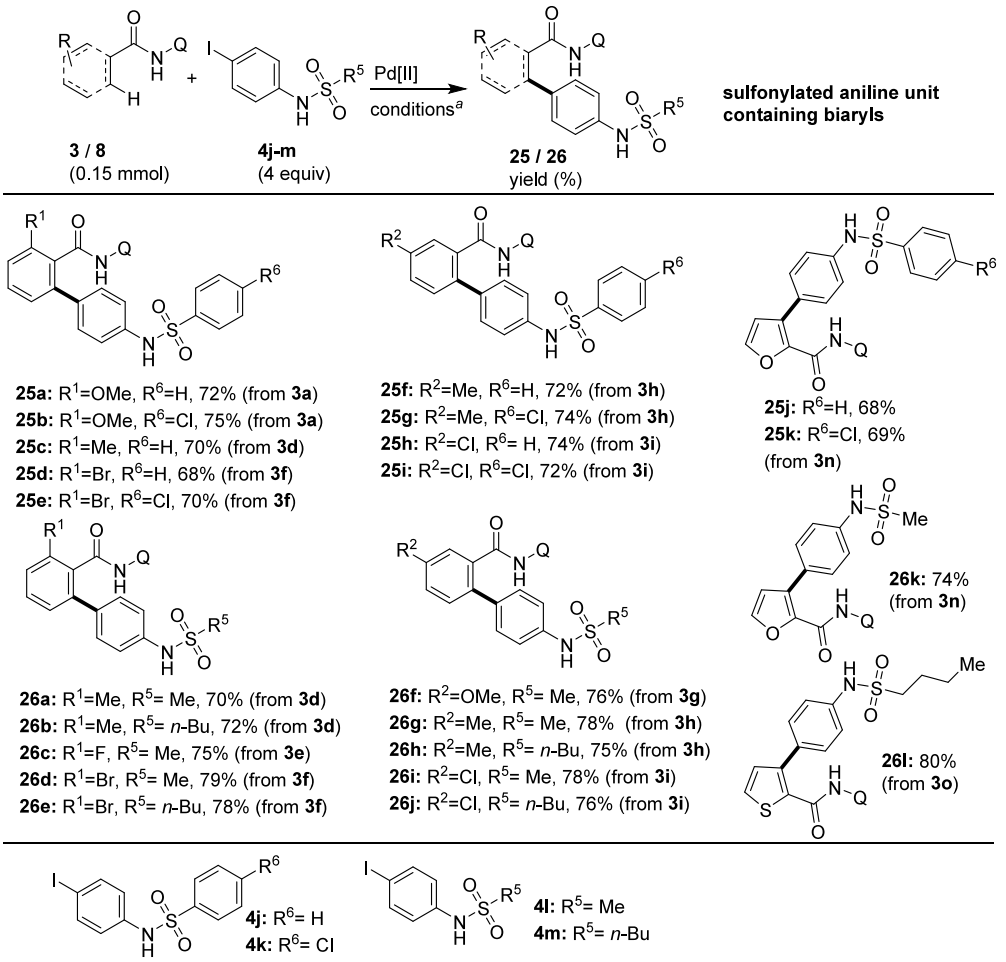
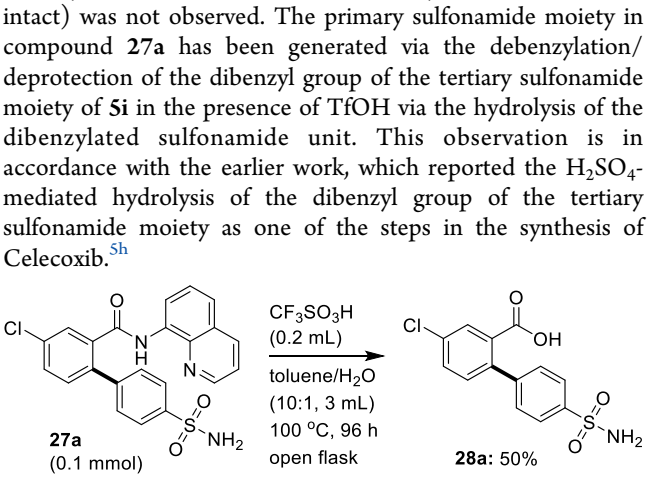
Scheme 7. Coupling of Carboxamides with Secondary Sulfonamide-Based 4-Iodoanilines and Synthesis of Secondary Sulfonamide-Based Biaryls 25 and 26



[a]Substrate (0.15 mmol), **4j−m** (4 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2.2 equiv), toluene (2 mL), 110 °C, 24 h, sealed tube (purged with a nitrogen atm).

based biaryl **27a** (20−73% yields) as the major product in which the 8-aminoquinoline (carboxamide unit) was intact (entries 5−9, Table 3). The anticipated 8-AQ DG-removed carboxylic acid **28a′** (in which the tertiary sulfonamide unit is intact) was not observed. The primary sulfonamide moiety in compound **27a** has been generated via the debenzylation/deprotection of the dibenzyl group of the tertiary sulfonamide moiety of **5i** in the presence of TfOH via the hydrolysis of the dibenzylated sulfonamide unit. This observation is in accordance with the earlier work, which reported the H_2SO_4-mediated hydrolysis of the dibenzyl group of the tertiary sulfonamide moiety as one of the steps in the synthesis of Celecoxib.[5h]



Next, substrate **5i** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for a prolonged reaction period of 48−96 h. These trials afforded the two products **27a** and **28a**. The product **27a** is a primary sulfonamide-based biaryl motif (obtained in 10−45% yields, in which the 8-aminoquinoline was intact). The product **28a** (obtained in 20−61% yields, entries 10−12, Table 3) is derived from the hydrolysis of the carboxamide- and sulfonamide groups from **5i**. Additionally, when **5i** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at a higher temperature (150 °C) for 18 h, the reaction gave both the products **27a** (40% yield) and **28a** (15% yield, entry 13, Table 3). These reactions indicated that the ratio of toluene/H_2O solvent mixture, the reaction period, and temperature have a role in the hydrolysis of the carboxamide and sulfonamide moieties of **5i**. At first, the sulfonamide moiety undergoes hydrolysis when **5i** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 18−24 h, affording **27a**. Prolonging the reaction period or increasing the temperature has enabled the hydrolysis of the carboxamide moiety in **5i** (through the 8-AQ removal), affording **28a** (along with **27a** due to low conversion of **27a**−**28a** through the hydrolysis reaction).

Noticeably, when **5i** was treated with CF_3SO_3H in neat condition or AcOH at 100 °C for 18 h selectively gave **28a** in 30−60% yields (entries 14 and 15, Table 3). These reactions indicated that in the presence of toluene/H_2O, the hydrolysis of the carboxamide and sulfonamide moieties of **5i** is slower

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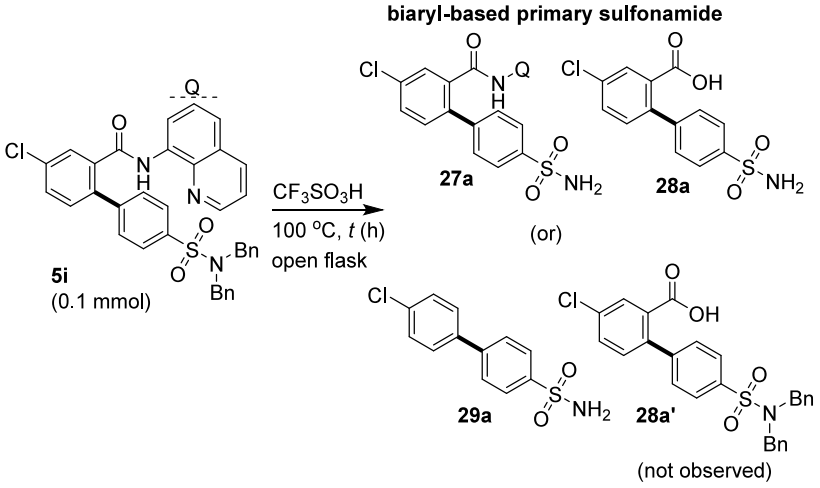
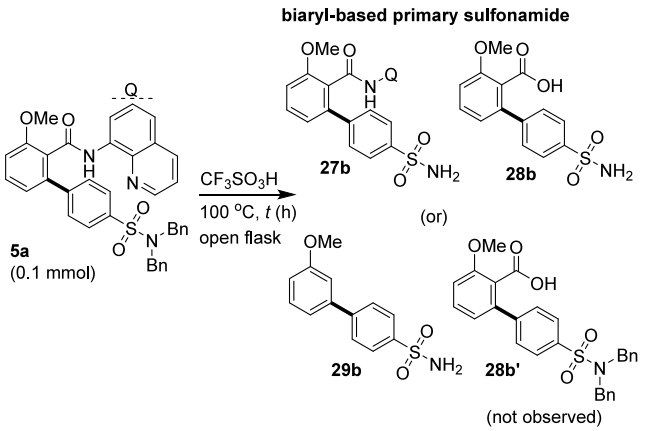
Table 3. Optimization of Reaction Conditions and Triflic Acid-Mediated Hydrolysis of the Carboxamide (8-AQ Removal) and Sulfonamide Moieties in 5i



entry	substrate	CF_3SO_3H (x mL)	solvent (y:z, 3 mL)	t (h)	**27a:** yield (%)	**28a:** yield (%)	**29a:** yield (%)
1	**5i**	0.2	toluene/H_2O (1:1)	18	0	0	0
2	**5i**	0.2	toluene/H_2O (5:1)	18	0	0	0
3	**5i**	0.2	toluene/H_2O (10:1)	6	0	0	0
4[a]	**5i**	0.2	toluene/H_2O (10:1)	18	0	0	0
5	**5i**	0.2	toluene/H_2O (10:1)	12	20	0	0
6	**5i**	0.2	toluene/H_2O (10:1)	18	73	0	0
7	**5i**	0.1	toluene/H_2O (10:1)	18	50	0	0
8	**5i**	0.4	toluene/H_2O (10:1)	18	70	0	0
9	**5i**	0.2	toluene/H_2O (10:1)	24	72	0	0
10	**5i**	0.2	toluene/H_2O (10:1)	48	40	24	0
11	**5i**	2.0	toluene/H_2O (10:1)	48	45	20	0
12	**5i**	0.2	toluene/H_2O (10:1)	96	10	61	0
13[b]	**5i**	0.2	toluene/H_2O (10:1)	18	40	15	0
14	**5i**	0.2	neat	18	0	60	0
15	**5i**	0.2	CH_3COOH	18	0	30	0

[a]60 °C. [b]150 °C.

Table 4. Optimization of Reaction Conditions and Triflic Acid-Mediated Hydrolysis of the Carboxamide (8-AQ Removal) and Sulfonamide Moieties in 5a



entry	substrate	CF_3SO_3H (x mL)	solvent (y:z, 3 mL)	t (h)	**27b:** yield (%)	**28b:** yield (%)	**29b:** yield (%)
1	**5a**	0.2	toluene/H_2O (5:1)	12	0	0	00
2	**5a**	0.2	toluene/H_2O (10:1)	6	0	0	20
3	**5a**	0.2	toluene/H_2O (10:1)	12	0	0	64
4	**5a**	0.2	toluene/H_2O (10:1)	24	0	0	63
5	**5a**	0.2	toluene/H_2O (10:1)	48	0	0	60
6	**5a**	0.2	toluene/H_2O (10:1)	96	0	0	56

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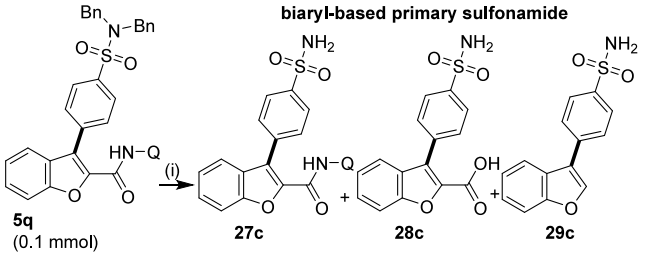
Table 5. Optimization of Reaction Conditions and Triflic Acid-Mediated Hydrolysis of the Carboxamide (8-AQ Removal) and Sulfonamide Moieties in 5q



(i) Conditions: CF_3SO_3H, 100 °C, *t* (h), open flask

entry	substrate	CF_3SO_3H (*x* mL)	solvent (*y*:*z*, 3 mL)	*t* (h)	**27c:** yield (%)	**28c:** yield (%)	**29c:** yield (%)
1	**5q**	0.2	toluene/H_2O (10:1)	6	25	0	10
2	**5q**	0.2	toluene/H_2O (10:1)	12	34	0	15
3	**5q**	0.2	toluene/H_2O (10:1)	18	25	0	35
4	**5q**	0.2	toluene/H_2O (10:1)	24	10	0	50
5	**5q**	0.2	toluene/H_2O (10:1)	48	0	0	58
6	**5q**	0.2	toluene/H_2O (10:1)	96	0	0	56

when compared to the reactions in neat conditions or without H_2O (entries 14 and 15, Table 3). To corroborate this, we also performed a control experiment using the primary sulfonamide-based biaryl compound **27a** in which the 8-aminoquinoline was intact. Substrate **27a** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 96 h, which afforded the 8-AQ removed, carboxylic acid product **28a** through the hydrolysis of the carboxamide moiety of **27a** in 50% yield (Table 3).

In contrast to the substrate **5i**, the tertiary sulfonamide-based biaryl carboxamide **5a**, having an OMe group next to the carboxamide moiety, behaved differently, affording the product **29b** when it was subjected to the CF_3SO_3H-mediated hydrolysis conditions. Accordingly, when **5a** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 6−96 h, the product **29b** was obtained selectively in 20−64% yields (entries 2−6, Table 4). These reactions indicated that **5a** has presumably undergone the sequential transformations including; (a) sulfonamide hydrolysis (affording **27b** as the initial product), (b) then the 8-AQ removal via the hydrolysis of carboxamide moiety in **27b** (affording **28b**) and (c) finally the decarboxylation of COOH moiety of **28b** affording **29b**. On the other hand, it may be noted that the decarboxylated product **29a** was not observed in characterizable amounts when the tertiary sulfonamide-based biaryl carboxamide **5i** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 18−96 h (entries 4−13, Table 3). It may be noted that the anticipated 8-AQ DG-removed carboxylic acid **28b′** (in which the tertiary sulfonamide unit is intact) was not observed in any of the trials involving substrate **5a**.

The formation of the decarboxylation product **29b** from **28b** may be ascribed via the ring-protonation mechanism proposed by Kluger[21] in substrate **28b** possessing an OMe group in proximity to the COOH group, enabling the decarboxylation to afford **29b** (Table 4). This observation is additionally supported by the results obtained using a similar substrate **5q** (Table 5). The substrate **5q** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 6−24 h. These trials afforded the primary sulfonamide-based biaryl **27c** (10−34% yields) in which the 8-aminoquinoline was intact and the decarboxylated product **29c** (10−50% yields, entries 1−4, Table 5). Subsequently, substrate **5q** was treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for a prolonged reaction time of 48−96 h. These trials afforded selectively the decarboxylated product **29c** (56−58% yields, entries 5 and 6, Table 5).

Accordingly, similar to the substrate **5a**, substrate **5q** underwent the sequential transformations including (a) sulfonamide hydrolysis (affording **27c** as the initial product), (b) then the 8-AQ removal via the hydrolysis of the carboxamide moiety in **27c** (affording **28c**) and (b) finally the decarboxylation of COOH moiety of **28c** to afford **29c**. It is believed that the reason for the formation of the decarboxylation product **29c** from **5q** may be attributed to the mechanism proposed by Kluger[21] in substate **28c**, enabling a facile decarboxylation to afford **29c**.

Having done the optimization trials involving triflic acid-mediated hydrolysis of biaryl-based sulfonamides obtained via C−H arylation reaction, our focus shifted toward synthesizing various biaryl-based primary sulfonamides using the best optimized conditions (of Tables 3, 4, and 5). Under the optimized reaction conditions (entry 6, Table 3), the tertiary sulfonamide-based biaryls **5e,f,h,i**, **13**, **14**, **17c** and heteroaryls **5q,n** were treated with CF_3SO_3H (0.2 mL) in toluene/H_2O (10:1, 3 mL) at 100 °C for 12−18 h. These substrates underwent the selective sulfonamide hydrolysis and yielded biaryl-based primary sulfonamides **27a**, **27c−j** in 34−73% yields (Scheme 8). In the products **27a**, **27c−j**, the carboxamide moiety (with 8-AQ DG) is intact, and only the tertiary sulfonamide moiety of their corresponding substrates had undergone hydrolysis.

Under the optimized reaction conditions (entries 10−13, Table 3) established for substrate **5i**, the substrates **5d,g,h**, having no OMe group in proximity to the carboxylic group, were treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 12−96 h. These trials afforded both the carboxamide and sulfonamide moieties hydrolyzed products **28d−f** in 41−65% yields (Scheme 9). Next, under the optimized reaction conditions (entries 2−6, Table 4) established for substrate **5a**, the substrates **5a,b,m** having the alkoxy group in proximity to the carboxylic group) were treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 12−24 h. These trials afforded the

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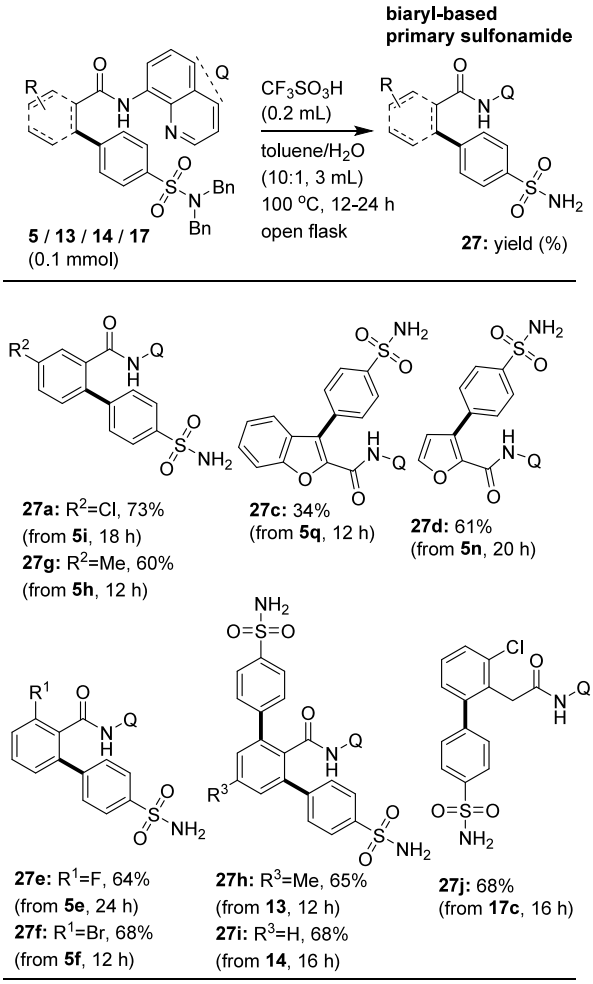
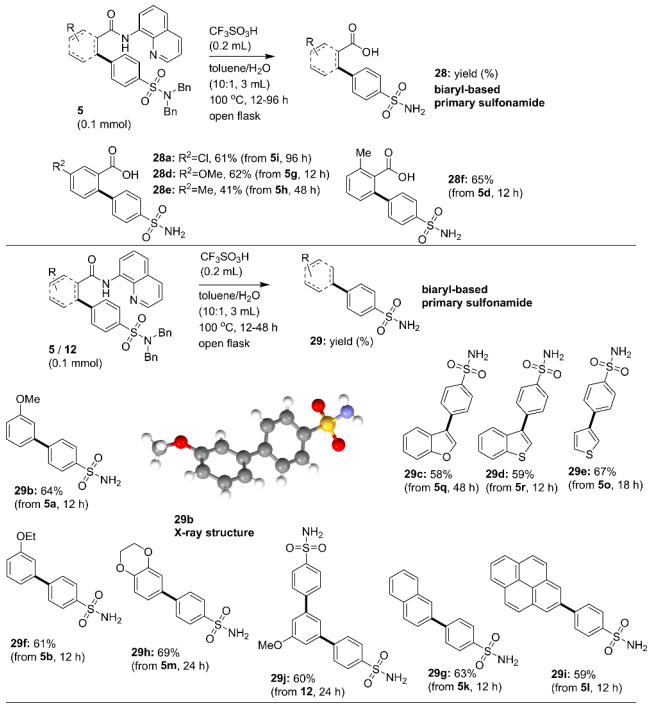
Scheme 8. Substrate Scope Investigation and Triflic Acid-Mediated Hydrolysis of the Tertiary Sulfonamide Moiety in 5e,f,h,i,q,n, 13, 14, and 17c toward Primary Sulfonamide-Based Biaryls 27



Scheme 9. Substrate Scope Investigation and Triflic Acid-Mediated Hydrolysis of the Sulfonamide and Carboxamide Moieties and Decarboxylation Reactions Affording Sulfonamides 28 or 29



corresponding decarboxylated, primary sulfonamide-based biaryls **29b,f,h** in 61−69% yields (Scheme 9). Similarly, under the optimized reaction conditions (entries 5 and 6, Table 5) established for substrate **5q**, the heteroaryl substrates **5o,q,r**, were treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 12−48 h. These trials afforded the corresponding decarboxylated, primary sulfonamide-based biaryls **29c−e** in 59−67% yields (Scheme 9). Additionally, under the optimized reaction conditions (entries 2−6, Table 4) established for substrate **5a**, other substrates **5k**, **5l**, and **12** were treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 12−24 h. These trials afforded the corresponding decarboxylated, primary sulfonamide-based biaryls **29g,i,j** in 59−63% yields (Scheme 9).

In concurrence with Kluger's mechanism,[21] the ring-protonation in substrate **28b** possessing the OMe group in proximity to the COOH group presumably generates the proposed initial species **28ba** and then the species **28bb**. Subsequently, the decarboxylation product **29b** is generated from the species **28ba**/**28bb** (Table 4 and Scheme 10). The positive charge in the ring protonated species **28ba**/**28bb** is presumably stabilized by the OMe group. The decarboxylation may be facile in substrates from which a favorable ring protonation species (e.g., **28ba**/**28bb**) is generated. Accordingly, substrates **5a,b,m** having the alkoxy group at the *ortho* position (and in proximity to the carboxylic group) afforded the corresponding decarboxylated, primary sulfonamide-based biaryls **29b,f,h**. On the other hand, it seems that the initial ring protonation step in substrate **28a** having a chloro substituent at the *meta* position (with respect to the carboxylic group) is not a facile process to generate the species **28aa** (as the positive charge in the ring protonated species **28aa** is presumably not stabilized by any substituent). Thus, the corresponding product **29a** was not observed. Accordingly, related products **28a,d,e** having substituents at the *meta* position (with respect to the carboxylic group) did not undergo decarboxylation. In addition, while the corresponding carboxylic acids of substrates **27e,f** did not form and the carboxylic acid group in substrates **27e,f** having the F or Br substituent at the *ortho* position (with respect to the carboxylic group) did not undergo decarboxylation under the experimental conditions. While the electronics due to F or Br substituents at the *ortho* position in **27e,f** (when compared to **28b**, which has the OMe group at the *ortho* position) could not be understood at this point. However, we noted that product **28f**, having a methyl substituent at the *ortho* position (with respect to the carboxylic group), also did not undergo decarboxylation. This suggests that substrates **5a,b,m** having only an alkoxy group at the *ortho* position (and in proximity to the carboxylic group) undergo a facile decarboxylation, affording the corresponding decarboxylated, primary sulfonamide-based biaryls **29b,f,h**. At this stage, the formation of the decarboxylation products **29g,i,j** may also be ascribed via a facile ring-protonation of the electronically rich aromatic rings in respective substrates as described using substrate **29b** in Scheme 10. Overall, the optimization reactions, substrate scope shown in Tables 3−5, Schemes 8 and 9 indicate that the ratio of toluene/H_2O solvent mixture,

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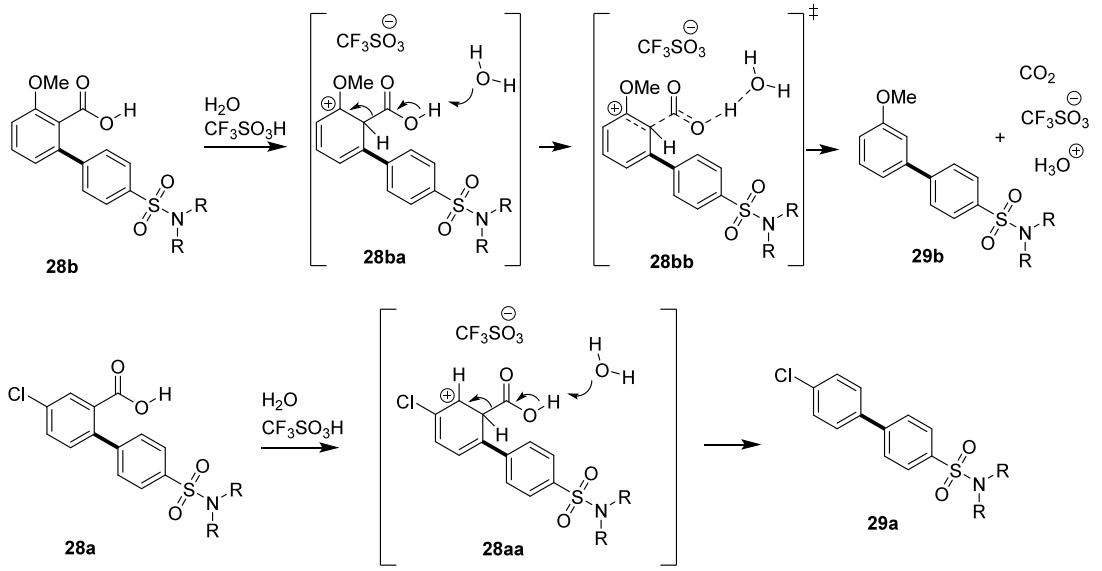
Scheme 10. Proposed Mechanism of Decarboxylation of 28b via the Ring-Protonation Process (Based on Kluger's Report[21]) under the Experimental Conditions



reaction period, and temperature have a role in the hydrolysis of the carboxamide and sulfonamide moieties and subsequent decarboxylation is influenced by the substituents in the substrate or nature of the substrate.

The structure of product **29b** has been confirmed by the X-ray structure analysis, which ascertained the occurrence of the hydrolysis of the carboxamide and sulfonamide moieties in **5a**. The occurrence of the Pd(II)-catalyzed 8-aminoquinoline-assisted *ortho* C−H arylation of **3a** with **4a** affording **5a** can be indirectly confirmed from the X-ray structure of the product **29b**. Accordingly, in concurrence with the literature reports it is proposed that Pd(II)-catalyzed, 8-aminoquinoline DG-aided *ortho* C(sp^2)−H arylation of carboxamide with aryl iodide undergoes via a Pd(II)/Pd(IV) redox catalytic cycle[13−17] enabling the activation of the *ortho* C−H bond of **3a** and subsequent arylation affording **5a**.

We also had some interesting observations when attempting the triflic acid-mediated hydrolysis of carboxamide (directing group-removal) and sulfonamide moiety in some specific substrates **5c**, **5j**, and **5i** (Scheme 11). When substrates **5c** and **5j** were treated with CF_3SO_3H in a mixture of toluene/H_2O (10:1 ratio, 3 mL) at 100 °C for 18−20 h, we obtained the corresponding products **31a** and **31b** in 60−63% yields. While the substrates **5c** and **5j** have undergone the hydrolysis of the carboxamide and sulfonamide moieties, as expected. But the presence of an aryl ring in the proximity of the carboxylic group has led to the intramolecular Friedel−Crafts acylation[22] affording the corresponding cyclized products **31a** and **31b** (via **31aa**/**31ab** and **31ba**/**31bb**, respectively).

Additionally, when substrate **5i** was treated with CF_3SO_3H in toluene or *o*-xylene in the absence of H_2O at 100 °C for 18 h, we obtained the corresponding products **30a** and **30b** in 44−52% yields. While the substrate **5i** has undergone the sulfonamide hydrolysis as expected and the carboxamide group has undergone the Friedel−Crafts acylation, affording the corresponding products **30a** and **30b** (via **30aa**−**ac**, respectively) under the experimental conditions. It may be noted that the TfOH-mediated hydrolysis of the sulfonamide and carboxamide moieties in **5i** in the presence of H_2O in toluene did not result in the Friedel−Crafts acylation products (Table 3). Accordingly, the formation of **30a,b** is an additional result when compared to the results discussed in Table 3 using the substrate **5i**.

Furthermore, having done the amide hydrolysis of substrates using an acidic condition, we also attempted the NaOH-mediated selective removal of the 8-aminoquinoline directing group from representative biaryl sulfonamide motifs obtained via C−H functionalization. The 8-AQ directing group-linked carboxamide and secondary sulfonamide moiety containing biaryl substrates **21b** and **26i** were treated with NaOH in EtOH at 130 °C for 24 h. These attempts successfully furnished the corresponding 8-aminoquinoline DG-removed, secondary sulfonamide motif-based biaryl carboxylic acids **32a,b** in 75−78% yields (Scheme 12).

CONCLUSIONS

In summary, we have shown the application of Pd(II)-catalyzed 8-aminoquinoline directing group-assisted C−H arylation method for the construction of new biaryl sulfonamides (biaryl-based primary-, secondary- and tertiary-sulfonamides). In general, the biaryl sulfonamides were synthesized using the traditional cross-coupling reactions. We have shown the Pd(II)-catalyzed *ortho* coupling of C−H bonds of aromatic carboxamides with iodobenzenesulfonamide as a progressive route toward diverse biaryl-based sulfonamides. After the C−H arylation reactions, we attempted the removal of the 8-aminoquinoline from the synthesized biaryl scaffolds possessing carboxamide and sulfonamide moieties. The attempts comprising triflic acid-mediated hydrolysis have enabled the 8-aminoquinoline removal from carboxamide and debenzylation/deprotection of the dibenzyl group of the tertiary sulfonamide moiety in specific substrates. In some cases, we noted the occurrence of decarboxylation and Friedel-Crafts acylation reactions under experimental conditions, affording interesting biaryl-based sulfonamides. All the compounds have been characterized by NMR and HRMS analysis. The structure of a representative product **29b** has been confirmed by the X-ray structure analysis, and the occurrence of the Pd(II)-catalyzed 8-aminoquinoline-assisted *ortho* C−H arylation of **3a** with **4a** affording **5a** was indirectly

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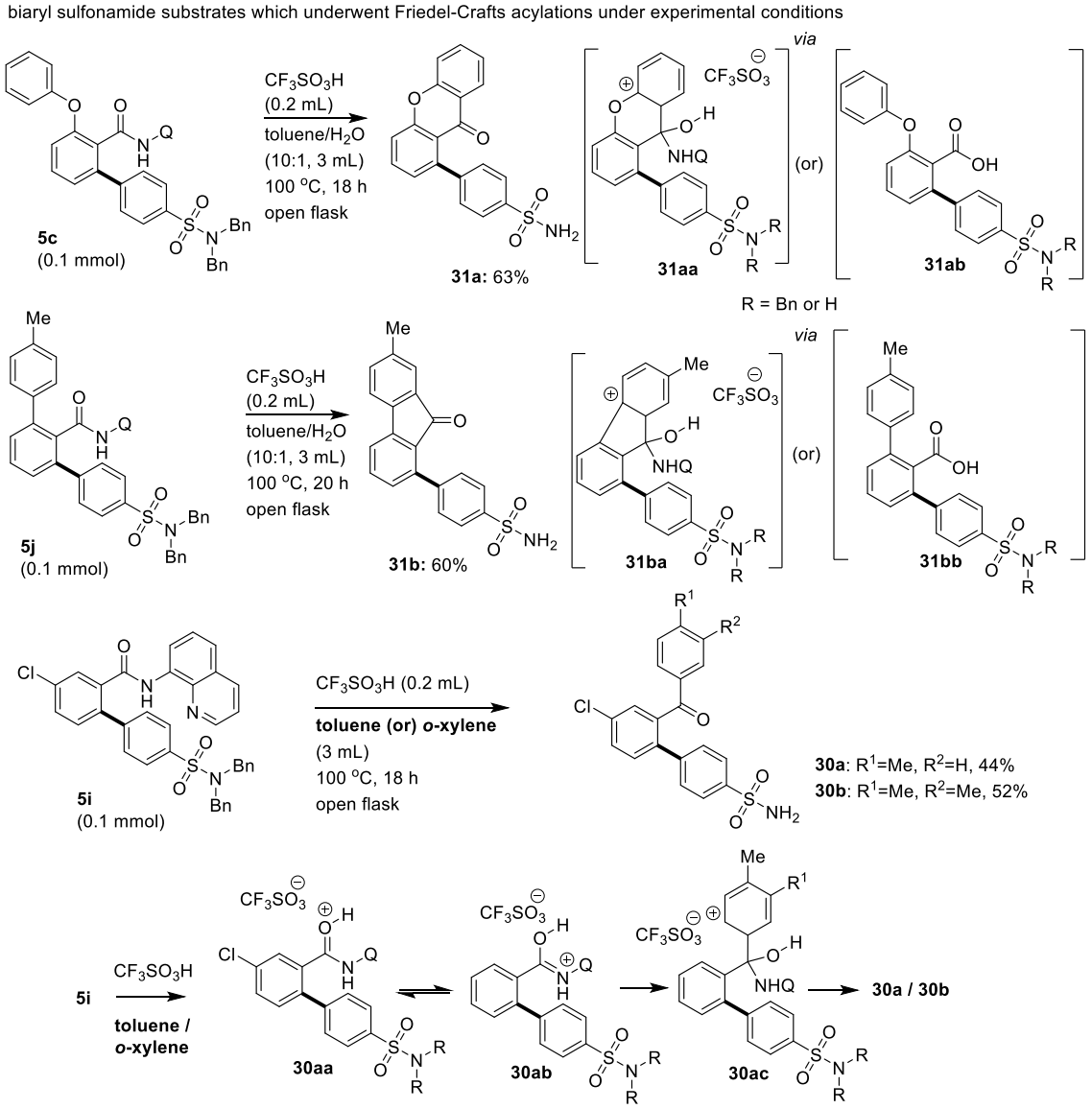
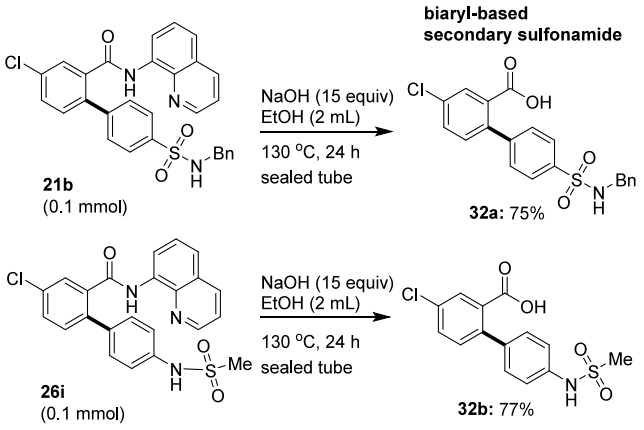
Scheme 11. Synthetic Elaboration and Triflic Acid-Mediated Transformation Involving Friedel-Crafts-Type Reactions on Sulfonamides 5c,j,i Affording the Corresponding Products 31a,b and 30a,b



Scheme 12. NaOH-Mediated Selective Removal of the 8-Aminoquinoline Directing Group from Representative Biaryl Sulfonamide Motifs 21b/26i Affording 32a/32b



confirmed from the X-ray structure of the product **29b**. Considering the applications of sulfonamides in drug discovery and medicinal chemistry research areas, the current method is a contribution toward the development of alternative and effective methods for assembling new biaryl sulfonamides (biaryl-based primary-, secondary-, and tertiary- sulfonamides). We are also in the process of exploring the antiviral properties (via a high-content screening against influenza A virus infection and cytotoxicity profile) of the synthesized compounds, and the results of the investigation will be reported in the future.

EXPERIMENTAL SECTION

General. The ^{1}H, ^{13}C, and ^{19}F NMR spectra of compounds were recorded (using TMS as an internal standard) in 400, ~101, and ~376 MHz NMR spectrometers, respectively. The HRMS analysis data of samples reported here were obtained from a QTOF mass analyzer using the electrospray ionization (ESI) method. IR spectra of samples reported here were recorded as neat or thin films. Column chromatography

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purification was carried out on silica gel (100−200 mesh). Reactions were conducted in anhydrous solvents in sealed tubes (filled with ambient air) or sealed tubes purged with a nitrogen atm. The organic layers obtained after the workup were dried using anhydrous Na_2SO_4. Thin layer chromatography (TLC) analyses were performed on silica gel or alumina plates, and components were visualized by observation under iodine vapor or using a UV lamp. Isolated yields of all the products are reported, and yields were not optimized. In all the cases, after the Pd(II)-catalyzed reactions, the respective crude reaction mixtures were subjected to the column chromatographic purification, and we were focused to isolate the corresponding main C−H coupled products shown in the respective Tables/Schemes and any other byproducts were not obtained in characterizable or demonstrable amounts of yields. Most of the aromatic and aliphatic carboxamides possessing the corresponding bidentate directing groups used in this work are known compounds (see the Supporting Information for the corresponding references), and they were assembled using standard amide coupling methods from their corresponding carboxylic acids/acid chlorides and amines. Iodobenzenesulfonamides used in this work were assembled via the standard amide coupling methods from their corresponding sulfonyl chloride and amine, and the crude iodobenzenesulfonamides were used as such after preparation.

Caution! Some of the reactions have been carried out in a sealed tube under heating conditions above the solvent's boiling point. The reaction may be performed in a fume hood, or use of a safety screen is recommended.

General Procedure for the Preparation of Biaryl-Based Tertiary and Secondary Sulfonamides 5a−t, 7a−e, 12−15, 17a−h, 19a−c, 20a−e, and 21a−h via the Pd(II)-Catalyzed C−H Arylation of Corresponding Carboxamides. A mixture of an appropriate carboxamide (0.15 mmol, 1 equiv), $Pd(OAc)_2$ (10 mol %), iodobenzenesulfonamide (4 equiv), and AgOAc (2.2 equiv) in anhydrous toluene (2 mL) was heated at 110 °C for 24 h under a nitrogen atm. After the reaction period, the reaction mixture was concentrated in vacuo, and the resulting crude residue was purified by column chromatography on silica or neutral alumina gel (eluent = EtOAc/hexane) to furnish the corresponding biaryls-based tertiary and secondary sulfonamide (see the corresponding Table/Scheme for the specific entry).

General Procedure for the Preparation of Bis and Mono Sulfonamide Unit Containing Biaryls 22a−g, 23a, 24a−e, 25a−k, and 26a−l via the Pd(II)-Catalyzed C−H Arylation of Corresponding Carboxamides. A mixture of an appropriate carboxamide (0.15 mmol, 1 equiv), $Pd(OAc)_2$ (10 mol %), sulfonamide-linked iodoanilines (4 equiv), and AgOAc (2.2 equiv) in anhydrous toluene (2 mL) was heated at 110 °C for 24 h under a nitrogen atm. After the reaction period, the reaction mixture was concentrated in vacuo, and the resulting crude residue was purified by column chromatography on silica or neutral alumina gel (eluent = EtOAc/hexane) to furnish the corresponding bis and mono sulfonamide unit containing biaryl (see the corresponding Table/Scheme for the specific entry).

Procedure for the Synthesis of Biaryl-Based Primary Sulfonamides 27a, 27c−j, 28a, 28d−f, 29b−j, 31a,b. A solution of biaryl-based tertiary and secondary sulfonamide (0.1 mmol) and CF_3SO_3H (0.3 mL) in toluene/H_2O (10:1, 3 mL) was heated at 100 °C for 12−96 h. After this period, the reaction mixture was diluted with water and extracted with EtOAc (2 × 10 mL). The organic layers were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to afford a crude mixture, which was then purified by column chromatography on silica gel to afford the corresponding biaryls-based primary sulfonamide (see the corresponding Table/Scheme for the specific entry). The compounds **30a** and **30b** were obtained using only toluene or *o*-xylene as solvent.

Procedure for the Removal of Directing Group 8-Aminoquinoline and the Synthesis of Biaryl-Based Secondary Sulfonamides 32a,b. A solution of biaryl-based secondary sulfonamide (0.1 mmol, 1 equiv) and NaOH (1.5 mmol, 15 equiv) in ethanol (2 mL) was heated in a sealed tube at 130 °C for 24 h. After this period, the reaction mixture was diluted with water and extracted with EtOAc (2 × 10 mL). Then, the aqueous layer was acidified with 1 N HCl and extracted with EtOAc (2 × 10 mL). The organic layers were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to afford a crude mixture, which was then purified by column chromatography on silica gel to afford the corresponding biaryls-based secondary sulfonamide (see the corresponding Table/Scheme for the specific entry).

*4′-(N,N-Dibenzylsulfamoyl)-3-methoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5a**).* Following the general procedure, **5a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (82%, 76 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 122−124 °C; IR (DCM): 3341, 2928, 1671, 1517, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.98 (1H, br. s), 8.78 (1H, dd, J_1 = 5.4 Hz, J_2 = 3.6 Hz), 8.69 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.09 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.72 (2H, d, J = 8.4 Hz), 7.67 (2H, d, J = 8.4 Hz), 7.53−7.48 (3H, m), 7.38 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.15−7.12 (6H, m), 7.09 (1H, d, J = 8.3 Hz), 7.05 (1H, d, J = 7.6 Hz), 6.95−6.93 (4H, m), 4.09 (4H, s), 3.92 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.2, 156.8, 148.1, 144.6, 139.8, 139.1, 138.3, 136.2, 135.4, 134.3, 130.7, 129.3, 128.4, 128.3, 127.8, 127.5, 127.3, 127.0, 126.3, 122.2, 121.8, 121.5, 116.6, 111.0, 56.1, 50.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{32}N_3O_4S$: 614.2114; found: 614.2117.

*4′-(N,N-Dibenzylsulfamoyl)-3-ethoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5b**).* Following the general procedure, **5b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 45:65) as a colorless solid (78%, 74 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 128−130 °C; IR (DCM): 3342, 2927, 1673, 1515, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.15 (1H, br. s), 8.75−8.73 (2H, m), 8.13 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.75 (2H, d, J = 8.2 Hz), 7.66 (2H, d, J = 8.2 Hz), 7.50−7.45 (3H, m), 7.41 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.20−7.15 (6H, m), 7.08 (1H, d, J = 8.4 Hz), 7.03 (1H, d, J = 7.6 Hz), 6.98−6.96 (4H, m), 4.20 (2H, q, J = 7.0 Hz), 4.17 (4H, s), 1.37 (3H, t, J = 7.0 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.2, 156.2, 148.1, 145.1, 140.5, 139.2, 138.4, 136.2, 135.5, 134.5, 130.7, 129.3, 128.5, 128.4, 127.9, 127.5, 127.4, 127.0, 126.4, 122.3, 121.7, 121.6, 116.7, 112.0, 64.6, 50.5, 14.6; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{38}H_{34}N_3O_4S$: 628.2270; found: 628.2268.

*4′-(N,N-Dibenzylsulfamoyl)-3-phenoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5c**).* Following the general procedure, **5c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a

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yellow colored solid (76%, 77 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 130−132 °C; IR (DCM): 3349, 2930, 1678, 1514, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.19 (1H, br. s), 8.71 (1H, dd, J_1 = 6.4 Hz, J_2 = 2.6 Hz), 8.68 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.07 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.77 (2H, d, J = 8.4 Hz), 7.71 (2H, d, J = 8.4 Hz), 7.47−7.43 (3H, m), 7.37 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.34−7.30 (2H, m), 7.20−7.08 (10H, m), 7.01 (1H, d, J = 8.2 Hz), 6.97−6.95 (4H, m), 4.15 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 164.3, 156.3, 155.0, 148.1, 144.3, 140.5, 139.4, 138.2, 136.2, 135.4, 134.1, 130.7, 129.8, 129.3, 128.4, 128.3, 127.8, 127.5, 127.2, 127.0, 124.7, 124.0, 121.8, 121.6, 119.6, 117.9, 116.6, 50.4; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{42}H_{34}N_3O_4S$: 676.2270; found: 676.2274.

*4′-(N,N-Dibenzylsulfamoyl)-3-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5d**).* Following the general procedure, **5d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (30%, 27 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 83−85 °C; IR (DCM): 3339, 3029, 1674, 1520, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.75 (1H, br. s), 8.83 (1H, d, J = 7.0 Hz), 8.68 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.10 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.74 (4H, s), 7.57−7.48 (3H, m), 7.41−7.37 (2H, m), 7.35 (1H, d, J = 7.5 Hz), 7.19−7.15 (6H, m), 6.98−6.95 (4H, m), 4.03 (4H, s), 2.61 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.5, 148.1, 144.8, 138.7, 138.1, 137.7, 136.6, 136.1, 136.0, 135.3, 133.9, 130.4, 129.4, 129.3, 128.3, 128.1, 127.7, 127.4, 127.3, 127.1, 126.9, 122.0, 121.6, 116.5, 50.6, 19.6; HRMS (ESI): m/z $(M - H)^+$ calcd for $C_{37}H_{30}N_3O_3S$: 596.2008; found: 596.2007.

*4′-(N,N-Dibenzylsulfamoyl)-3-fluoro-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5e**).* Following the general procedure, **5e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (72%, 65 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 124−126 °C; IR (DCM): 3335, 2927, 1672, 1514, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.99 (1H, br. s), 8.77 (1H, dd, J_1 = 5.0 Hz, J_2 = 4.0 Hz), 8.68 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.10 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.74 (2H, d, J = 8.4 Hz), 7.66 (2H, d, J = 8.4 Hz), 7.57−7.50 (3H, m), 7.39 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.29−7.25 (2H, m), 7.16−7.13 (6H, m), 6.96−6.94 (4H, m), 4.12 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 162.4, 159.7 (d, J_{C-F} = 251.0 Hz), 148.3, 143.4 (d, J_{C-F} = 2.2 Hz), 140.6 (d, J_{C-F} = 3.2 Hz), 139.8, 138.2, 136.3, 135.3, 133.8, 131.3 (d, J_{C-F} = 9.0 Hz), 129.3, 128.4, 128.3, 127.8, 127.6, 127.2, 127.2, 125.9, 125.9, 125.0 (d, J_{C-F} = 17.7 Hz), 122.3, 121.7, 116.8, 115.9 (d, J_{C-F} = 22.3 Hz), 50.5; ^{19}F {^1H} NMR (∼376 MHz, $CDCl_3$): δ_F −114.30; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{36}H_{29}FN_3O_3S$: 602.1914; found: 602.1912.

*3-Bromo-4′-(N,N-dibenzylsulfamoyl)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5f**).* Following the general procedure, **5f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (65%, 65 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 108−110 °C; IR (DCM): 3330, 2927, 1678, 1528, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.85 (1H, br. s), 8.75 (1H, dd, J_1 = 6.1 Hz, J_2 = 2.9 Hz), 8.69 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.10 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.74−7.66 (5H, m), 7.52−7.49 (2H, m), 7.44−7.38 (3H, m), 7.13−7.12 (6H, m), 6.93−6.91 (4H, m), 4.07 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.3, 148.3, 143.5, 140.0, 139.7, 138.2, 138.0, 136.3, 135.3, 133.7, 132.8, 130.7, 129.3, 129.0, 128.4, 128.3, 127.8, 127.5, 127.2, 127.1, 122.3, 121.7, 120.8, 116.8, 50.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{36}H_{29}BrN_3O_3S$: 662.1113; found: 662.1110.

*4′-(N,N-Dibenzylsulfamoyl)-4-methoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5g**).* Following the general procedure, **5g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (86%, 79 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 136−138 °C; IR (DCM): 3335, 2928, 1672, 1513, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.81−8.79 (1H, m), 8.55 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.02 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.71 (2H, d, J = 8.3 Hz), 7.62 (2H, d, J = 8.3 Hz), 7.52 (1H, t, J = 8.1 Hz), 7.47−7.45 (2H, m), 7.40 (1H, d, J = 8.5 Hz), 7.32 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.15−7.11 (7H, m), 6.95−6.92 (4H, m), 4.05 (4H, s), 3.92 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.8, 159.7, 148.0, 144.3, 138.8, 138.2, 137.2, 136.1, 135.4, 134.1, 131.8, 130.7, 129.6, 128.4, 128.2, 127.7, 127.5, 127.2, 127.1, 121.9, 121.6, 117.0, 116.3, 114.0, 55.6, 50.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{32}N_3O_4S$: 614.2114; found: 614.2110.

*4′-(N,N-Dibenzylsulfamoyl)-4-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5h**).* Following the general procedure, **5h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (85%, 76 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 132−134 °C; IR (DCM): 3337, 2928, 1672, 1526, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.77 (1H, br. s), 8.81−8.79 (1H, m), 8.57 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.03 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.74 (1H, s), 7.73 (2H, d, J = 8.5 Hz), 7.63 (2H, d, J = 8.4 Hz), 7.52 (1H, t, J = 8.1 Hz), 7.46 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.3 Hz), 7.42 (1H, dd, J_1 = 7.9 Hz, J_2 = 1.2 Hz), 7.37 (1H, d, J = 7.8 Hz), 7.33 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.16−7.13 (6H, m), 6.95−6.93 (4H, m), 4.06 (4H, s), 2.50 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.3, 148.0, 144.6, 139.1, 138.7, 138.2, 136.1, 136.1, 135.6, 135.4, 134.2, 131.4, 130.4, 129.7, 129.6, 128.4, 128.3, 127.7, 127.5, 127.2, 121.8, 121.6, 116.3, 50.5, 21.1; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{32}N_3O_3S$: 598.2164; found: 598.2165.

*4-Chloro-4′-(N,N-dibenzylsulfamoyl)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**5i**).* Following the general procedure, **5i** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (75%, 70 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 136−138 °C; IR (DCM): 3330, 2929, 1677, 1532, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.79 (1H, br. s), 8.76 (1H, dd, J_1 = 7.3 Hz, J_2 = 1.5 Hz), 8.59 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.06 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.93 (1H, d, J = 2.2 Hz), 7.74 (2H, d, J = 8.4 Hz), 7.62 (2H, d, J = 8.4 Hz), 7.59 (1H, dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.55−7.47 (2H, m), 7.42 (1H, d, J = 8.2 Hz), 7.37 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.18−7.13 (6H, m), 6.96−6.93 (4H, m), 4.09 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.5, 148.1, 143.3, 139.8, 138.1, 137.5, 136.8, 136.2, 135.3, 134.8, 133.8, 131.8, 130.8, 129.5, 129.3, 128.4, 128.3, 127.7, 127.6, 127.3, 127.1, 122.2, 121.7, 116.5, 50.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{36}H_{29}ClN_3O_3S$: 618.1618; found: 618.1620.

*4-(N,N-Dibenzylsulfamoyl)-4″-methyl-N-(quinolin-8-yl)-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**5j**).* Following the general procedure, **5j** was obtained after purification by

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column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (82%, 83 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; mp: 174−176 °C; IR (DCM): 3337, 2929, 1677, 1512, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.65 (1H, br. s), 8.59 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.52 (1H, dd, J_1 = 6.4 Hz, J_2 = 2.5 Hz), 8.03 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.72−7.67 (4H, m), 7.60 (1H, t, J = 7.7 Hz), 7.53 (1H, dd, J_1 = 7.7 Hz, J_2 = 1.0 Hz), 7.45−7.39 (5H, m), 7.34 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.17−7.14 (6H, m), 7.08 (2H, d, J = 8.0 Hz), 6.95−6.93 (4H, m), 4.05 (4H, s), 2.21 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.0, 147.9, 145.0, 140.8, 139.1, 138.8, 138.2, 137.3, 137.0, 136.0, 135.5, 134.0, 130.3, 129.5, 129.5, 129.0, 128.9, 128.5, 128.3, 127.6, 127.5, 127.2, 127.0, 121.7, 121.5, 116.5, 50.6, 21.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{43}H_{36}N_3O_3S$: 674.2477; found: 674.2479.

*2-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-1-naphthamide (**5k**).* Following the general procedure, **5k** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (81%, 77 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 150−152 °C; IR (DCM): 3336, 2929, 1677, 1517, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (1H, br. s), 8.92 (1H, d, J = 7.5 Hz), 8.56 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.26−8.23 (1H, m), 8.06 (2H, d, J = 8.4 Hz), 7.97−7.95 (1H, m), 7.80 (2H, d, J = 8.4 Hz), 7.73 (2H, d, J = 8.4 Hz), 7.60−7.54 (4H, m), 7.50 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.33 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.14−7.11 (6H, m), 6.94−6.91 (4H, m), 4.00 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.2, 148.2, 144.8, 139.1, 138.2, 136.2, 135.4, 135.1, 134.2, 132.9, 130.3, 130.1, 129.7, 128.4, 128.3, 128.1, 127.8, 127.8, 127.5, 127.3, 127.2, 127.0, 125.7, 122.2, 121.7, 116.7, 50.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{40}H_{32}N_3O_3S$: 634.2164; found: 634.2166.

*5-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-pyrene-4-carboxamide (**5l**).* Following the general procedure, **5l** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 30:70) as a yellow colored solid (76%, 81 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 134−136 °C; IR (DCM): 3338, 2931, 1670, 1513, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.01 (1H, br. s), 8.98 (1H, dd, J_1 = 7.5 Hz, J_2 = 1.3 Hz), 8.56 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.49 (1H, d, J = 9.2 Hz), 8.30−8.15 (6H, m), 8.11−8.07 (2H, m), 7.94 (2H, d, J = 8.4 Hz), 7.79 (2H, d, J = 8.5 Hz), 7.59 (1H, t, J = 8.2 Hz), 7.53 (1H, dd, J_1 = 8.4 Hz, J_2 = 1.3 Hz), 7.35 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.17−7.15 (6H, m), 6.97−6.94 (4H, m), 4.02 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.6, 148.2, 145.3, 139.0, 138.3, 136.2, 135.5, 135.3, 134.3, 132.0, 131.3, 131.2, 130.7, 130.1, 129.4, 129.3, 128.9, 128.5, 128.3, 127.8, 127.5, 127.3, 127.2, 127.0, 126.6, 126.1, 126.0, 125.8, 124.5, 124.2, 122.2, 121.7, 116.7, 50.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{46}H_{34}N_3O_3S$: 708.2321; found: 708.2327.

*6-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-2,3-dihydrobenzo(b)(1,4)dioxine-5-carboxamide (**5m**).* Following the general procedure, **5m** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 30:70) as a colorless solid (82%, 79 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 162−164 °C; IR (DCM): 3341, 2928, 1678, 1529, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.92 (1H, br. s), 8.80 (1H, dd, J_1 = 6.5 Hz, J_2 = 2.4 Hz), 8.67 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.09 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.69 (2H, d, J = 8.4 Hz), 7.64 (2H, d, J = 8.4 Hz), 7.52−7.47 (2H, m), 7.38 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.14−7.12 (6H, m), 7.07 (1H, d, J = 8.4 Hz), 6.96 (1H, d, J = 8.4 Hz), 6.94−6.92 (4H, m), 4.36 (4H, s), 4.06 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 164.5, 148.1, 144.4, 143.9, 141.3, 138.7, 138.2, 136.2, 135.5, 134.1, 131.6, 129.2, 128.4, 128.3, 127.8, 127.5, 127.3, 127.0, 126.2, 122.8, 121.9, 121.6, 118.5, 116.7, 64.6, 64.2, 50.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{38}H_{32}N_3O_5S$: 642.2063; found: 642.2064.

*3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-furan-2-carboxamide (**5n**).* Following the general procedure, **5n** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a yellow colored solid (78%, 67 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 150−152 °C; IR (DCM): 3339, 2926, 1673, 1520, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.88 (1H, br. s), 8.87 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.84 (1H, dd, J_1 = 5.5 Hz, J_2 = 3.5 Hz), 8.17 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.95−7.90 (4H, m), 7.68 (1H, d, J = 1.8 Hz), 7.54−7.53 (2H, m), 7.47 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.26−7.20 (6H, m), 7.11−7.08 (4H, m), 6.73 (1H, d, J = 1.8 Hz), 4.37 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 156.4, 148.4, 143.6, 142.4, 139.8, 138.6, 136.3, 135.5, 134.1, 130.4, 130.2, 128.6, 128.4, 128.0, 127.6, 127.2, 126.9, 121.9, 121.7, 116.6, 114.6, 114.6, 50.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{28}N_3O_4S$: 574.1801; found: 574.1804.

*3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-thiophene-2-carboxamide (**5o**).* Following the general procedure, **5o** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 35:65) as a colorless solid (80%, 71 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 176−178 °C; IR (DCM): 3311, 2926, 1654, 1530, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.95 (1H, br. s), 8.79 (1H, dd, J_1 = 7.5 Hz, J_2 = 1.2 Hz), 8.44 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz), 8.01 (1H, d, J = 8.3 Hz), 7.87 (2H, d, J = 8.4 Hz), 7.68 (2H, d, J = 8.3 Hz), 7.59 (1H, d, J = 5.0 Hz), 7.49 (1H, t, J = 8.0 Hz), 7.44 (1H, d, J = 8.2 Hz), 7.31 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.21−7.16 (6H, m), 7.12 (1H, d, J = 5.0 Hz), 7.05−7.03 (4H, m), 4.31 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 159.9, 148.2, 140.9, 140.5, 139.5, 138.1, 136.5, 135.9, 135.3, 134.0, 130.7, 130.2, 129.7, 128.5, 128.4, 127.7, 127.7, 127.0, 121.8, 121.6, 116.3, 50.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{28}N_3O_3S_2$: 590.1572; found: 590.1570.

*3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-1-methyl-N-(quinolin-8-yl)-1H-pyrrole-2-carboxamide (**5p**).* Following the general procedure, **5p** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 30:70) as a colorless solid (74%, 65 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 182−184 °C; IR (DCM): 3322, 2928, 1659, 1516, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.81 (1H, dd, J_1 = 7.6 Hz, J_2 = 0.7 Hz), 8.32 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.00 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.70 (2H, d, J = 8.4 Hz), 7.60 (2H, d, J = 8.4 Hz), 7.51 (1H, t, J = 8.1 Hz), 7.43 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.0 Hz), 7.28 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.18−7.13 (6H, m), 7.01−6.99 (4H, m), 6.85 (1H, d, J = 2.6 Hz), 6.28 (1H, d, J = 2.6 Hz), 4.21 (4H, s), 4.04 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 159.9, 148.0, 140.3, 138.7, 138.1, 135.9, 135.5, 134.5, 130.1, 128.5, 128.3, 127.8, 127.6, 127.4, 127.2, 127.0, 124.1, 121.6, 121.4, 115.6, 109.2, 50.5, 37.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{31}N_4O_3S$: 587.2117; found: 587.2118.

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*3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-benzofuran-2-carboxamide (**5q**).* Following the general procedure, **5q** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 20:80) as a colorless solid (79%, 74 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.70; mp: 204−206 °C; IR (DCM): 3335, 2929, 1679, 1535, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.07 (1H, br. s), 8.93−8.92 (1H, m), 8.87 (1H, dd, J_1 = 5.4 Hz, J_2 = 3.5 Hz), 8.20 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 8.01 (2H, d, J = 8.1 Hz), 7.89 (2H, d, J = 8.2 Hz), 7.79 (1H, d, J = 8.2 Hz), 7.61−7.56 (4H, m), 7.51 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.40 (1H, t, J = 7.6 Hz), 7.29−7.21 (6H, m), 7.12−7.10 (4H, m), 4.43 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 156.9, 153.7, 148.6, 143.1, 140.4, 138.7, 136.4, 135.5, 135.4, 134.0, 131.0, 128.6, 128.5, 128.4, 128.0, 127.9, 127.7, 127.3, 127.1, 125.2, 124.2, 122.3, 121.8, 121.4, 117.0, 112.4, 50.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{38}H_{30}N_3O_4S$: 624.1957; found: 624.1960.

*3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-benzo(b)thiophene-2-carboxamide (**5r**).* Following the general procedure, **5r** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 35:65) as a yellow colored solid (80%, 77 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 220−222 °C; IR (DCM): 3302, 2911, 1655, 1532, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.05 (1H, br. s), 8.83 (1H, dd, J_1 = 7.5 Hz, J_2 = 1.4 Hz), 8.53 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.04 (2H, d, J = 8.4 Hz), 8.05−8.03 (1H, m), 7.99 (1H, d, J = 8.1 Hz), 7.74 (2H, d, J = 8.4 Hz), 7.55−7.50 (2H, m), 7.48−7.43 (3H, m), 7.36 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.25−7.21 (6H, m), 7.09−7.06 (4H, m), 4.40 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 160.1, 148.2, 141.5, 140.1, 140.0, 138.1, 138.0, 137.4, 135.9, 135.6, 135.2, 133.9, 131.2, 128.4, 127.9, 127.7, 127.6, 127.0, 126.8, 124.9, 124.0, 122.7, 122.0, 121.7, 116.4, 50.2; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{38}H_{30}N_3O_3S_2$: 640.1729; found: 640.1732.

*(Z)-3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-3-phenyl-N-(quinolin-8-yl)acrylamide (**5s**).* Following the general procedure, **5s** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 30:70) as a colorless solid (72%, 66 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 166−168 °C; IR (DCM): 3334, 2926, 1669, 1512, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.80 (1H, br. s), 8.75 (1H, dd, J_1 = 6.9 Hz, J_2 = 1.8 Hz), 8.68 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.08 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.85 (2H, d, J = 8.3 Hz), 7.52 (2H, d, J = 8.2 Hz), 7.49−7.45 (2H, m), 7.43−7.38 (4H, m), 7.33−7.31 (2H, m), 7.23−7.21 (6H, m), 7.03−7.00 (4H, m), 6.74 (1H, s), 4.27 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 163.6, 150.7, 148.1, 143.3, 140.5, 140.2, 138.2, 136.2, 135.4, 134.2, 130.4, 129.5, 128.6, 128.5, 128.4, 128.1, 127.8, 127.6, 127.2, 127.1, 123.3, 121.7, 121.6, 116.4, 50.2; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{38}H_{32}N_3O_3S$: 610.2164; found: 610.2169.

*(Z)-3-(4-(N,N-Dibenzylsulfamoyl)phenyl)-N-(quinolin-8-yl)acrylamide (**5t**).* Following the general procedure, **5t** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (76%, 61 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 142−144 °C; IR (DCM): 3336, 2925, 1675, 1513, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.91 (1H, br. s), 8.81 (1H, dd, J_1 = 6.9 Hz, J_2 = 2.0 Hz), 8.66 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.12 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.78−7.72 (4H, m), 7.56−7.50 (2H, m), 7.40 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.18−7.16 (6H, m), 7.03−7.00 (4H, m), 6.98 (1H, d, J = 12.6 Hz), 6.42 (1H, d, J = 12.5 Hz), 4.26 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 163.9, 148.2, 140.1, 139.2, 138.2, 137.1, 136.3, 135.4, 134.0, 130.0, 128.5, 128.3, 127.8, 127.6, 127.2, 127.0, 126.9, 122.0, 121.7, 116.6, 50.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{32}H_{28}N_3O_3S$: 534.1851; found: 534.1848.

*4′-(N,N-Dibenzylsulfamoyl)-3-methoxy-N-(2-(methylthio)-phenyl)-(1,1′-biphenyl)-2-carboxamide (**7a**).* Following the general procedure, **7a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (75%, 69 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; mp: 118−120 °C; IR (DCM): 3332, 2923, 1679, 1507, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.45 (1H, br. s), 8.20 (1H, dd, J_1 = 8.2 Hz, J_2 = 0.8 Hz), 7.75 (2H, d, J = 8.4 Hz), 7.58 (2H, d, J = 8.4 Hz), 7.43 (1H, t, J = 8.1 Hz), 7.36 (1H, dd, J_1 = 7.8 Hz, J_2 = 1.3 Hz), 7.18−7.10 (7H, m), 7.01−6.95 (7H, m), 4.20 (4H, s), 3.87 (3H, s), 2.13 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.1, 156.6, 144.5, 139.8, 139.6, 138.1, 135.5, 133.0, 130.8, 129.3, 128.9, 128.5, 128.4, 127.6, 127.2, 125.9, 125.3, 124.6, 122.4, 120.8, 111.0, 56.1, 50.6, 18.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{33}N_2O_4S_2$: 609.1882; found: 609.1889.

*4′-(N,N-Dibenzylsulfamoyl)-3-ethoxy-N-(2-(methylthio)-phenyl)-(1,1′-biphenyl)-2-carboxamide (**7b**).* Following the general procedure, **7b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (80%, 75 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 163−165 °C; IR (DCM): 3340, 2929, 1730, 1469, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.45 (1H, br. s), 8.22 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.0 Hz), 7.82 (2H, d, J = 8.4 Hz), 7.66 (2H, d, J = 8.4 Hz), 7.47 (1H, t, J = 8.1 Hz), 7.42 (1H, dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz), 7.24−7.18 (7H, m), 7.07−7.01 (7H, m), 4.28 (4H, s), 4.19 (2H, q, J = 7.0 Hz), 2.23 (3H, s), 1.43 (3H, t, J = 7.0 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.2, 155.9, 144.6, 139.9, 139.5, 137.9, 135.5, 132.5, 130.7, 129.3, 128.6, 128.5, 128.4, 127.6, 127.1, 126.3, 125.6, 124.6, 122.2, 120.9, 112.0, 64.6, 50.5, 18.7, 14.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{36}H_{35}N_2O_4S_2$: 623.2038; found: 623.2037.

*3-Chloro-4′-(N,N-dibenzylsulfamoyl)-N-(2-(methylthio)-phenyl)-(1,1′-biphenyl)-2-carboxamide (**7c**).* Following the general procedure, **7c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a yellow colored semisolid (72%, 66 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; IR (DCM): 3319, 2926, 1677, 1508, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.28 (1H, br. s), 8.20 (1H, d, J = 8.1 Hz), 7.80 (2H, d, J = 8.2 Hz), 7.66 (2H, d, J = 8.2 Hz), 7.52−7.45 (2H, m), 7.39−7.33 (2H, m), 7.25−7.21 (1H, m), 7.17−7.15 (6H, m), 7.07 (1H, t, J = 7.6 Hz), 7.02−7.00 (4H, m), 4.24 (4H, s), 2.15 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 164.3, 143.1, 140.0, 139.6, 137.1, 135.7, 135.3, 132.4, 131.7, 130.6, 129.5, 129.3, 128.5, 128.4, 128.3, 127.6, 127.2, 126.2, 125.2, 121.0, 50.6, 18.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{30}ClN_2O_3S_2$: 613.1386; found: 613.1381.

*4′-(N,N-Dibenzylsulfamoyl)-4-methyl-N-(2-(methylthio)-phenyl)-(1,1′-biphenyl)-2-carboxamide (**7d**).* Following the general procedure, **7d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless semisolid (76%, 68 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; IR (DCM): 3338, 2930, 1681, 1514, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.39 (1H,

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d, J = 8.2 Hz), 8.26 (1H, br. s), 7.80 (2H, d, J = 8.2 Hz), 7.63−7.61 (3H, m), 7.41−7.34 (3H, m), 7.28 (1H, t, J = 7.6 Hz), 7.19−7.17 (6H, m), 7.06−7.03 (5H, m), 4.25 (4H, s), 2.48 (3H, s), 2.12 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.4, 144.3, 139.2, 138.8, 137.9, 136.0, 135.5, 135.0, 132.6, 131.5, 130.4, 129.4, 129.4, 128.7, 128.5, 128.3, 127.6, 127.4, 125.4, 124.6, 120.1, 50.8, 21.1, 18.9; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{33}N_2O_3S_2$: 593.1933; found: 593.1935.

*N-(Benzo(c)(1,2,5)thiadiazol-4-yl)-4′-(N,N-dibenzylsulfamoyl)-3-ethoxy-(1,1′-biphenyl)-2-carboxamide (**7e**).* Following the general procedure, **7e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 45:55) as a yellow colored solid (66%, 63 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; mp: 130−132 °C; IR (DCM): 3389, 2924, 1680, 1517, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.05 (1H, br. s), 8.35 (1H, d, J = 7.4 Hz), 7.73 (2H, d, J = 8.3 Hz), 7.60 (1H, d, J = 8.7 Hz), 7.54 (2H, d, J = 8.3 Hz), 7.47−7.42 (2H, m), 7.15−7.11 (6H, m), 7.01 (1H, d, J = 8.3 Hz), 6.97−6.93 (5H, m), 4.19 (4H, s), 4.15 (2H, q, J = 7.0 Hz), 1.34 (3H, t, J = 7.0 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.1, 156.1, 154.7, 147.7, 145.1, 141.1, 139.5, 135.4, 131.2, 131.1, 129.9, 129.2, 128.5, 128.4, 127.6, 127.0, 124.9, 122.7, 115.8, 115.0, 112.0, 64.8, 50.3, 14.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{31}N_4O_4S_2$: 635.1787; found: 635.1791.

*4,4″-Bis(N,N-dibenzylsulfamoyl)-5′-methoxy-N-(quinolin-8-yl)-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**12**).* Following the general procedure, **12** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a yellow colored solid (75%, 107 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 170−172 °C; IR (DCM): 3345, 2930, 1674, 1513, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.61 (1H, br. s), 8.59 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.49 (1H, dd, J_1 = 7.2 Hz, J_2 = 1.7 Hz), 8.00 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.73 (4H, d, J = 8.6 Hz), 7.69 (4H, d, J = 8.6 Hz), 7.42−7.37 (2H, m), 7.33 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.19−7.15 (12H, m), 7.02 (2H, s), 6.96−6.94 (8H, m), 4.07 (8H, s), 3.97 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.3, 159.9, 148.1, 144.5, 141.0, 139.5, 138.0, 136.2, 135.4, 133.8, 129.3, 129.1, 128.4, 128.3, 127.6, 127.6, 127.2, 127.1, 121.9, 121.7, 116.4, 115.3, 55.7, 50.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{57}H_{49}N_4O_6S_2$: 949.3094; found: 949.3127.

*4,4″-Bis(N,N-dibenzylsulfamoyl)-5′-methyl-N-(quinolin-8-yl)-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**13**).* Following the general procedure, **13** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a yellow colored solid (76%, 106 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 168−170 °C; IR (DCM): 3334, 2927, 1675, 1513, 719 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.65 (1H, br. s), 8.59 (1H, d, J = 4.0 Hz), 8.51 (1H, d, J = 7.2 Hz), 8.00 (1H, d, J = 8.2 Hz), 7.73 (4H, d, J = 8.3 Hz), 7.69 (4H, d, J = 8.3 Hz), 7.42−7.31 (5H, m), 7.19−7.15 (12H, m), 6.96−6.94 (8H, m), 4.06 (8H, s), 2.55 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.5, 148.1, 144.6, 140.0, 139.2, 139.0, 138.0, 136.1, 135.4, 133.7, 133.5, 130.6, 129.4, 128.4, 128.3, 127.6, 127.5, 127.1, 127.0, 122.0, 121.7, 116.4, 50.5, 21.3; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{57}H_{49}N_4O_5S_2$: 933.3144; found: 933.3177.

*4,4″-Bis(N,N-dibenzylsulfamoyl)-N-(quinolin-8-yl)-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**14**).* Following the general procedure, **14** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (82%, 113 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 192−194 °C; IR (DCM): 3334, 2925, 1677, 1511, 711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.68 (1H, br. s), 8.60 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.49 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.3 Hz), 8.02 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.75−7.66 (9H, m), 7.54 (2H, d, J = 7.7 Hz), 7.43 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.39 (1H, d, J = 7.6 Hz), 7.34 (1H, dd, J_1 = 8.4 Hz, J_2 = 4.4 Hz), 7.20−7.15 (12H, m), 6.96−6.94 (8H, m), 4.08 (8H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.3, 148.2, 144.4, 139.4, 139.0, 138.0, 136.2, 136.1, 135.4, 133.6, 130.0, 129.9, 129.4, 128.4, 128.3, 127.7, 127.6, 127.1, 127.1, 122.1, 121.7, 116.5, 50.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{56}H_{47}N_4O_5S_2$: 919.2988; found: 919.2986.

*N-(Benzo(c)(1,2,5)thiadiazol-4-yl)-4,4″-bis(N,N-dibenzylsulfamoyl)-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**15**).* Following the general procedure, **15** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a yellow colored solid (63%, 87 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; mp: 170−172 °C; IR (DCM): 3338, 2928, 1676, 1508, 745 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.31 (1H, br. s), 8.20 (1H, d, J = 7.2 Hz), 7.79 (4H, d, J = 8.4 Hz), 7.73−7.67 (5H, m), 7.62 (1H, dd, J_1 = 8.8 Hz, J_2 = 0.6 Hz), 7.54 (2H, d, J = 7.7 Hz), 7.45−7.41 (1H, m), 7.22−7.17 (12H, m), 7.01−6.97 (8H, m), 4.17 (8H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.4, 154.4, 147.2, 144.0, 139.9, 139.0, 135.3, 135.1, 130.7, 130.3, 130.1, 129.3, 128.9, 128.4, 128.4, 127.6, 127.3, 116.5, 115.2, 50.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{53}H_{44}N_5O_5S_3$: 926.2505; found: 926.2524.

*2-(4′-(N,N-Dibenzylsulfamoyl)-3-fluoro-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17a**).* Following the general procedure, **17a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless semisolid (56%, 52 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; IR (DCM): 3339, 2927, 1685, 1529, 724 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.75 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.72−8.69 (1H, m), 8.15 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.84 (2H, d, J = 8.4 Hz), 7.52−7.50 (4H, m), 7.44 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.32−7.27 (2H, m), 7.22−7.17 (6H, m), 7.13 (1H, td, J_1 = 8.3 Hz, J_2 = 2.6 Hz), 7.06−7.04 (4H, m), 4.34 (4H, s), 3.79 (2H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.3, 162.6 (d, J_{C-F} = 249.3 Hz), 148.3, 144.6, 139.8, 138.2, 136.9 (d, J_{C-F} = 3.3 Hz), 136.3, 135.4, 134.5 (d, J_{C-F} = 8.0 Hz), 134.0, 131.7 (d, J_{C-F} = 8.4 Hz), 130.1, 128.5, 128.4, 127.8, 127.7, 127.3, 121.9, 121.7, 117.7 (d, J_{C-F} = 21.7 Hz), 116.4, 114.7 (d, J_{C-F} = 21.3 Hz), 50.5, 42.3; ^{19}F {^{1}H} NMR (∼376 MHz, $CDCl_3$): δ_F −113.20; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{37}H_{31}FN_3O_3S$: 616.2070; found: 616.2076.

*2-(3-Bromo-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17b**).* Following the general procedure, **17b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless semisolid (65%, 66 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; IR (DCM): 3339, 2928, 1688, 1532, 717 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (1H, br. s), 8.75 (1H, dd, J_1 = 6.6 Hz, J_2 = 2.4 Hz), 8.72 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.15 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.81 (2H, d, J = 8.4 Hz), 7.71 (1H, dd, J_1 = 6.6 Hz, J_2 = 2.7 Hz), 7.56−7.50 (4H, m), 7.43 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.32−7.27 (2H, m), 7.20−7.15 (6H, m), 7.05−7.03 (4H, m), 4.34 (4H, s), 3.98 (2H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz,

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$CDCl_3$): δ_C 167.8, 148.2, 145.1, 143.6, 140.1, 138.3, 136.3, 135.4, 134.2, 133.0, 132.4, 129.8, 129.2, 128.7, 128.5, 128.4, 127.9, 127.7, 127.3, 127.1, 127.0, 121.7, 121.6, 116.4, 50.5, 42.9; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{31}BrN_3O_3S$: 676.1270; found: 676.1277.

*2-(3-Chloro-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17c**).* Following the general procedure, **17c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 35:65) as a colorless semisolid (62%, 59 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; IR (DCM): 2930, 1688, 1523, 1163, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (1H, br. s), 8.75 (1H, dd, J_1 = 6.5 Hz, J_2 = 2.2 Hz), 8.72−8.71(1H, m), 8.14−8.12 (1H, m), 7.82 (2H, d, J = 8.2 Hz), 7.56 (2H, d, J = 8.2 Hz), 7.53−7.48 (3H, m), 7.42 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.37 (1H, t, J = 7.8 Hz), 7.25−7.23 (1H, m), 7.20−7.12 (6H, m), 7.05−7.03 (4H, m), 4.34 (4H, s), 3.96 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.9, 148.2, 144.9, 143.4, 140.1, 138.2, 136.3, 136.2, 135.4, 134.2, 130.8, 129.8, 129.5, 128.5, 128.4, 128.3, 127.8, 127.6, 127.3, 127.1, 121.7, 121.6, 116.3, 50.5, 40.2; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{31}ClN_3O_3S$: 632.1775; found: 632.1783.

*2-(4′-(N,N-Dibenzylsulfamoyl)-4-methoxy-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17d**).* Following the general procedure, **17d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless semisolid (72%, 68 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; IR (DCM): 2923, 1682, 1526, 1159, 789 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.76 (1H, br. s), 8.73−8.70 (2H, m), 8.13 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.83 (2H, d, J = 8.3 Hz), 7.54 (2H, d, J = 8.4 Hz), 7.50−7.47 (3H, m), 7.42 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.21−7.17 (6H, m), 7.06−7.01 (5H, m), 6.86 (1H, d, J = 2.6 Hz), 4.34 (4H, s), 3.87 (3H, s), 3.75 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 169.5, 158.7, 148.2, 145.4, 142.0, 139.6, 138.3, 136.2, 135.4, 134.2, 132.2, 129.9, 128.5, 128.4, 127.8, 127.6, 127.2, 127.1, 124.2, 121.7, 121.6, 116.2, 115.6, 114.2, 55.4, 50.6, 41.6; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{38}H_{34}N_3O_4S$: 628.2270; found: 628.2273.

*2-(4-Bromo-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17e**).* Following the general procedure, **17e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 45:55) as a colorless semisolid (70%, 71 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.40; IR (DCM): 3335, 2927, 1684, 1527, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, br. s), 8.68 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.63−8.60 (1H, m), 8.07 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.77 (2H, d, J = 8.4 Hz), 7.52 (1H, dd, J_1 = 8.2 Hz, J_2 = 2.1 Hz), 7.45−7.43 (4H, m), 7.40−7.36 (3H, m), 7.14−7.10 (6H, m), 6.99−6.97 (4H, m), 4.26 (4H, s), 3.68 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.4, 148.3, 144.0, 142.7, 140.1, 138.2, 136.3, 135.4, 134.0, 132.7, 132.6, 131.6, 131.3, 129.9, 128.5, 128.4, 127.8, 127.7, 127.3, 127.2, 121.9, 121.7, 121.3, 116.3, 50.6, 41.8; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{31}BrN_3O_3S$: 676.1270; found: 676.1272.

*2-(4-Chloro-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17f**).* Following the general procedure, **17f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless semisolid (68%, 65 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.50; IR (DCM): 3337, 2928, 1684, 1526, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.79 (1H, br. s), 8.75 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.71−8.69 (1H, m), 8.12 (1H, dd, J_1 = 8.3 Hz, J_2 = 0.8 Hz), 7.84 (2H, d, J = 8.2 Hz), 7.57 (1H, d, J = 2.0 Hz), 7.51−7.49 (4H, m), 7.42 (1H, dd, J_1 = 8.4 Hz, J_2 = 4.4 Hz), 7.39 (1H, dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.25−7.23 (1H, m), 7.21−7.17 (6H, m), 7.06−7.04 (4H, m), 4.33 (4H, s), 3.77 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.2, 148.3, 144.2, 139.8, 139.3, 138.1, 136.2, 135.3, 134.4, 134.0, 133.9, 131.2, 130.8, 129.9, 128.4, 128.3, 127.8, 127.7, 127.6, 127.2, 127.1, 121.9, 121.7, 116.3, 50.5, 42.0; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{31}ClN_3O_3S$: 632.1775; found: 632.1777.

*2-(4′-(N,N-Dibenzylsulfamoyl)-4,5-dimethoxy-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17g**).* Following the general procedure, **17g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 35:65) as a colorless semisolid (52%, 51 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; IR (DCM): 3335, 2924, 1681, 1521, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.77 (1H, br. s), 8.67−8.65 (2H, m), 8.08 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.78 (2H, d, J = 8.4 Hz), 7.49−7.44 (4H, m), 7.37 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.15−7.10 (6H, m), 7.00−6.98 (5H, m), 6.75 (1H, s), 4.28 (4H, s), 3.90 (3H, s), 3.86 (3H, s), 3.69 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 169.4, 149.2, 148.3, 148.2, 145.4, 139.4, 138.3, 136.3, 135.5, 134.2, 133.3, 130.2, 128.5, 128.4, 127.9, 127.6, 127.3, 127.2, 124.3, 121.8, 121.7, 116.3, 113.4, 113.0, 56.1, 56.0, 50.6, 42.1; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{39}H_{36}N_3O_5S$: 658.2376; found: 658.2372.

*2-(4,5-Dichloro-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**17h**).* Following the general procedure, **17h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless semisolid (50%, 50 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; IR (DCM): 3353, 2930, 1690, 1533, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.77 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.69−8.67 (1H, m), 8.16 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.84 (2H, d, J = 8.2 Hz), 7.68 (1H, s), 7.53−7.49 (4H, m), 7.46 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.41 (1H, s), 7.21−7.18 (6H, m), 7.06−7.05 (4H, m), 4.33 (4H, s), 3.74 (2H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.9, 148.4, 143.1, 140.6, 140.4, 138.2, 136.4, 135.3, 133.8, 132.7, 132.6, 132.4, 131.5, 131.5, 129.8, 128.5, 128.4, 127.8, 127.7, 127.4, 127.2, 122.0, 121.8, 116.4, 50.6, 41.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{30}Cl_2N_3O_3S$: 666.1385; found: 666.1381.

*N-((3-Chloro-4′-(N,N-dibenzylsulfamoyl)-(1,1′-biphenyl)-2-yl)methyl)picolinamide (**19a**).* Following the general procedure, **19a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (70%, 61 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 149−151 °C; IR (DCM): 3387, 2927, 1676, 1514, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.53−8.51 (1H, m), 8.24−8.22 (1H, m), 8.16 (1H, d, J = 7.8 Hz), 7.86 (2H, d, J = 8.4 Hz), 7.82 (1H, td, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.51−7.46 (3H, m), 7.42−7.39 (1H, m), 7.35 (1H, t, J = 7.9 Hz), 7.25−7.17 (7H, m), 7.11−7.09 (4H, m), 4.68 (2H, d, J = 5.4 Hz), 4.38 (4H, s); ^{13}C $\{^1H\}$ NMR (∼101.0 MHz, $CDCl_3$): δ_C 163.4, 149.5, 148.0, 144.3, 143.2, 139.9, 137.3, 136.0, 135.4, 132.7, 129.7, 128.9, 128.7, 128.5, 128.3, 127.6, 127.1, 126.2, 122.1, 50.6, 39.3; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{33}H_{29}ClN_3O_3S$: 582.1618; found: 582.1622.

*N-((3-(4-(N,N-Dibenzylsulfamoyl)phenyl)thiophen-2-yl)-methyl)picolinamide (**19b**).* Following the general procedure,

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19b was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless semisolid (65%, 54 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; IR (DCM): 3376, 2929, 1674, 1514, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.53 (1H, d, J = 4.6 Hz), 8.44 (1H, br. s), 8.22 (1H, d, J = 7.8 Hz), 7.88 (2H, d, J = 8.2 Hz), 7.85−7.83 (1H, m), 7.55 (2H, d, J = 8.3 Hz), 7.45−7.42 (1H, m), 7.32 (1H, d, J = 5.2 Hz), 7.26−7.21 (6H, m), 7.09−7.07 (5H, m), 4.87 (2H, d, J = 5.8 Hz), 4.37 (4H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 164.0, 149.2, 148.1, 140.1, 139.2, 138.4, 137.4, 137.2, 135.4, 129.2, 128.8, 128.5, 128.3, 127.6, 127.4, 126.4, 124.7, 122.3, 50.5, 37.0; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{31}H_{28}N_3O_3S_2$: 554.1572; found: 554.1580.

*N-((4,4″-Bis(N,N-dibenzylsulfamoyl)-(1,1′:3′,1″-terphenyl)-2′-yl)methyl)picolinamide (**19c**).* Following the general procedure, **19c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 40:60) as a colorless solid (70%, 93 mg, 0.15 mmol); R_f (EtOAc/hexanes = 30:70) 0.60; mp: 154−156 °C; IR (DCM): 3381, 2928, 1677, 1513, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.45 (1H, d, J = 4.7 Hz), 7.97 (1H, d, J = 7.8 Hz), 7.83 (4H, d, J = 7.9 Hz), 7.80−7.78 (1H, m), 7.71 (1H, td, J_1 = 7.8 Hz, J_2 = 1.7 Hz), 7.54 (4H, d, J = 7.9 Hz), 7.49 (1H, t, J = 7.5 Hz), 7.37−7.32 (3H, m), 7.24−7.19 (12H, m), 7.10−7.08 (8H, m), 4.52 (2H, s), 4.34 (8H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 162.8, 149.0, 147.9, 145.2, 142.0, 139.5, 137.2, 135.4, 132.4, 130.2, 129.6, 128.4, 128.3, 127.8, 127.6, 127.1, 126.2, 121.8, 50.7, 38.9; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{53}H_{47}N_4O_5S_2$: 883.2988; found: 883.2953.

*4′-(N-Benzyl-N-methylsulfamoyl)-3-methoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**20a**).* Following the general procedure, **20a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (78%, 63 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 129−131 °C; IR (DCM): 3343, 2926, 1676, 1522, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.84 (1H, br. s), 8.79 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 8.66 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.08 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.73−7.67 (4H, m), 7.54−7.46 (3H, m), 7.37 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.32−7.26 (3H, m), 7.14−7.07 (4H, m), 3.93 (3H, s), 3.73 (2H, s), 2.16 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.2, 156.9, 148.0, 144.6, 139.7, 138.2, 136.2, 135.7, 135.4, 134.3, 130.8, 129.2, 128.5, 128.2, 127.8, 127.7, 127.4, 127.2, 126.3, 121.9, 121.7, 121.5, 116.5, 111.1, 56.1, 53.8, 33.9; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{31}H_{28}N_3O_4S$: 538.1801; found: 538.1799.

*3-(4-(N-Benzyl-N-methylsulfamoyl)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**20b**).* Following the general procedure, **20b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (72%, 54 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 164−166 °C; IR (DCM): 3338, 2924, 1671, 1527, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.91 (1H, br. s), 8.89 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.83 (1H, t, J = 4.5 Hz), 8.19 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 8.00 (2H, d, J = 8.5 Hz), 7.92 (2H, d, J = 8.4 Hz), 7.71 (1H, d, J = 1.7 Hz), 7.56 (2H, d, J = 4.6 Hz), 7.50 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.35−7.29 (5H, m), 6.76 (1H, d, J = 1.7 Hz), 4.22 (2H, s), 2.66 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 156.5, 148.4, 143.7, 142.3, 138.6, 136.6, 136.4, 136.3, 135.5, 134.0, 130.4, 130.2, 128.6, 128.3, 127.9, 127.8, 127.2, 122.0, 121.7, 116.6, 114.6, 54.0, 34.3; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{28}H_{24}N_3O_4S$: 498.1488; found: 498.1490.

*3-(4-(N-Benzyl-N-methylsulfamoyl)phenyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**20c**).* Following the general procedure, **20c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (75%, 58 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 199−201 °C; IR (DCM): 3305, 2921, 1642, 1527, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (1H, br. s), 8.73−8.71 (1H, m), 8.39 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz), 7.99 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.83 (2H, d, J = 8.3 Hz), 7.69 (2H, d, J = 8.3 Hz), 7.54 (1H, d, J = 5.1 Hz), 7.47−7.39 (2H, m), 7.30−7.19 (6H, m), 7.09 (1H, d, J = 5.0 Hz), 4.07 (2H, s), 2.52 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 160.0, 148.2, 140.9, 139.8, 138.2, 137.5, 136.6, 136.0, 135.4, 134.1, 130.6, 130.3, 129.7, 128.7, 128.3, 128.0, 128.0, 127.8, 127.2, 121.9, 121.7, 116.4, 54.1, 34.3; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{28}H_{24}N_3O_3S_2$: 514.1259; found: 514.1257.

*4′-(N,N-Dimethylsulfamoyl)-3-methoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**20d**).* Following the general procedure, **20d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (82%, 57 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 207−209 °C; IR (DCM): 3352, 2922, 1670, 1518, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.76 (1H, br. s), 8.77 (1H, dd, J_1 = 7.3 Hz, J_2 = 1.6 Hz), 8.64 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.10 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.69−7.67 (2H, m), 7.60−7.58 (2H, m), 7.54−7.44 (3H, m), 7.38 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.10−7.07 (2H, m), 3.94 (3H, s), 2.16 (6H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.3, 156.9, 148.0, 144.6, 139.7, 138.1, 136.1, 134.3, 133.7, 130.8, 129.1, 127.8, 127.5, 127.4, 126.4, 121.8, 121.6, 121.5, 116.5, 111.1, 56.1, 37.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{25}H_{24}N_3O_4S$: 462.1488; found: 462.1497.

*3-(4-(N,N-Dimethylsulfamoyl)phenyl)-N-(quinolin-8-yl)-thiophene-2-carboxamide (**20e**).* Following the general procedure, **20e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (79%, 52 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 198−200 °C; IR (DCM): 3302, 2922, 1640, 1525, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.91 (1H, br. s), 8.77 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 8.41 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.04 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.84−7.82 (2H, m), 7.74−7.72 (2H, m), 7.60 (1H, d, J = 5.0 Hz), 7.52−7.44 (2H, m), 7.34 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.14 (1H, d, J = 5.1 Hz), 2.69 (6H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 159.9, 148.1, 140.8, 139.6, 138.1, 136.5, 135.9, 135.4, 133.9, 130.6, 130.1, 129.6, 128.3, 127.7, 127.0, 121.8, 121.6, 116.2, 37.8, 37.8; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{22}H_{20}N_3O_3S_2$: 438.0946; found: 438.0938.

*4′-(N-Benzylsulfamoyl)-4-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**21a**).* Following the general procedure, **21a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (81%, 62 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 142−144 °C; IR (DCM): 3319, 2924, 1662, 1524, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.63 (1H, br. s), 8.65 (1H, dd, J_1 = 7.6 Hz, J_2 = 1.0 Hz), 8.41 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 7.84 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.63 (2H, d, J = 8.3 Hz), 7.64−7.62 (1H, m), 7.48 (2H, d, J = 8.4 Hz), 7.37 (1H, t, J = 8.0 Hz), 7.31−7.29 (2H, m), 7.23 (1H, d, J = 7.8 Hz), 7.16 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.07−7.06 (3H, m), 6.88−6.86 (2H, m), 5.08 (1H, t, J = 6.2 Hz), 3.57 (2H, d, J = 6.2 Hz), 2.37 (3H, s); ^{13}C {^1H}

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NMR (~101.0 MHz, $CDCl_3$): δ_C 167.3, 147.9, 144.5, 138.7, 138.5, 138.1, 136.0, 136.0, 135.8, 135.4, 134.0, 131.5, 130.3, 129.8, 129.6, 128.4, 127.6, 127.5, 127.1, 127.0, 121.8, 121.5, 116.2, 46.7, 21.0; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{30}H_{26}N_3O_3S$: 508.1695; found: 508.1685.

*4′-(N-Benzylsulfamoyl)-4-chloro-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**21b**).* Following the general procedure, **21b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (78%, 62 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 177−179 °C; IR (DCM): 3288, 2923, 1676, 1525, 752 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.14 (1H, br. s), 8.76 (1H, d, J = 4.0 Hz), 8.54 (1H, d, J = 7.4 Hz), 8.32 (1H, d, J = 8.3 Hz), 8.10 (1H, t, J = 6.2 Hz), 7.90 (1H, d, J = 1.6 Hz), 7.77−7.75 (3H, m), 7.69−7.66 (3H, m), 7.59−7.53 (3H, m), 7.26−7.19 (3H, m), 7.07 (2H, d, J = 7.1 Hz), 3.64 (2H, d, J = 6.2 Hz); ^{13}C {^1H} NMR (~101.0 MHz, DMSO-d_6): δ_C 165.3, 149.0, 142.6, 140.0, 138.2, 137.7, 137.4, 137.1, 136.5, 133.8, 133.2, 132.4, 130.6, 129.4, 128.4, 128.2, 127.7, 127.5, 127.2, 126.9, 126.7, 122.7, 122.2, 117.0, 45.9; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{29}H_{23}ClN_3O_3S$: 528.1149; found: 528.1141.

*3-(4-(N-Benzylsulfamoyl)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**21c**).* Following the general procedure, **21c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 65:35) as a colorless solid (74%, 54 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 171−173 °C; IR (DCM): 3329, 2924, 1669, 1520, 748 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.78 (1H, br. s), 8.97−8.96 (1H, m), 8.71 (1H, d, J = 7.6 Hz), 8.45 (1H, d, J = 8.3 Hz), 8.26 (1H, t, J = 6.3 Hz), 8.17 (1H, s), 8.00 (2H, d, J = 8.2 Hz), 7.88 (2H, d, J = 8.0 Hz), 7.72 (1H, d, J = 8.2 Hz), 7.67 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.61 (1H, t, J = 8.1 Hz), 7.32−7.23 (5H, m), 7.09 (1H, s), 4.04 (2H, d, J = 6.2 Hz); ^{13}C {^1H} NMR (~101.0 MHz, $CDCl_3$): δ_C 156.5, 148.4, 143.7, 142.4, 139.2, 138.7, 136.6, 136.4, 136.2, 134.1, 130.5, 130.3, 128.7, 128.0, 127.9, 127.3, 126.9, 122.0, 121.7, 116.7, 114.6, 47.3; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{27}H_{22}N_3O_4S$: 484.1331; found: 484.1340.

*3-(4-(N-Benzylsulfamoyl)phenyl)-N-(quinolin-8-yl)-thiophene-2-carboxamide (**21d**).* Following the general procedure, **21d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (80%, 60 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 178−180 °C; IR (DCM): 3302, 2924, 1643, 1529, 733 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 9.92 (1H, br. s), 8.65 (1H, d, J = 7.5 Hz), 8.47 (1H, d, J = 3.2 Hz), 8.31 (1H, d, J = 8.0 Hz), 8.26 (1H, t, J = 6.3 Hz), 8.00 (1H, d, J = 5.0 Hz), 7.89 (2H, d, J = 8.2 Hz), 7.78 (2H, d, J = 8.2 Hz), 7.64 (1H, d, J = 8.1 Hz), 7.58 (1H, t, J = 8.1 Hz), 7.48 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.30−7.20 (4H, m), 7.19−7.17 (2H, m), 3.91 (2H, d, J = 6.2 Hz); ^{13}C {^1H} NMR (~101.0 MHz, $CDCl_3$): δ_C 160.0, 148.1, 140.9, 139.9, 139.8, 138.2, 138.2, 136.6, 136.0, 136.0, 134.1, 130.7, 130.3, 129.7, 128.7, 128.0, 127.8, 127.7, 127.7, 127.2, 121.9, 121.7, 116.4, 47.3; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{27}H_{22}N_3O_3S_2$: 500.1103; found: 500.1104.

*4′-(N-Butylsulfamoyl)-4-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**21e**).* Following the general procedure, **21e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (70%, 50 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 147−149 °C; IR (DCM): 3319, 2927, 1664, 1524, 724 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 9.86 (1H, br. s), 8.68 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.58 (1H, d, J = 7.4 Hz), 8.34 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.3 Hz), 7.71 (2H, d, J = 8.3 Hz), 7.66−7.63 (4H, m), 7.57−7.53 (2H, m), 7.49−7.43 (3H, m), 2.44 (3H, s), 2.30−2.25 (2H, m), 1.14−1.00 (4H, m), 0.69 (3H, t, J = 7.2 Hz); ^{13}C {^1H} NMR (~101.0 MHz, DMSO-d_6): δ_C 166.7, 148.8, 143.6, 139.4, 138.3, 137.8, 136.4, 135.8, 135.4, 133.9, 131.5, 130.5, 129.4, 129.2, 127.6, 126.9, 126.6, 122.2, 116.0, 41.8, 30.9, 20.6, 19.1, 13.4; HRMS (ESI): m/z $(M+Na)^+$ calcd for $C_{27}H_{27}N_3NaO_3S$: 496.1671; found: 496.1650.

*4′-(N-Butylsulfamoyl)-4-chloro-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**21f**).* Following the general procedure, **21f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (72%, 53 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 162−164 °C; IR (DCM): 3306, 2930, 1664, 1525, 792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.66 (1H, br. s), 8.64 (1H, dd, J_1 = 6.7 Hz, J_2 = 2.2 Hz), 8.47 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.00 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.83 (1H, d, J = 2.2 Hz), 7.69 (2H, d, J = 8.3 Hz), 7.54 (2H, d, J = 8.3 Hz), 7.48 (1H, dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.44−7.38 (2H, m), 7.32 (1H, d, J = 8.3 Hz), 7.29 (1H, dd, J_1 = 8.4 Hz, J_2 = 4.4 Hz), 4.51−4.50 (1H, m), 2.50−2.45 (2H, m), 1.19−1.11 (2H, m), 1.07−0.98 (2H, m), 0.68 (3H, t, J = 7.3 Hz); ^{13}C {^1H} NMR (~101.0 MHz, $CDCl_3$): δ_C 165.5, 148.1, 143.3, 139.3, 138.1, 137.5, 136.7, 136.1, 134.8, 133.8, 131.8, 130.8, 129.5, 129.3, 127.6, 127.1, 122.1, 121.7, 116.4, 42.6, 31.4, 19.4, 13.4; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{25}ClN_3O_3S$: 494.1305; found: 494.1287.

*3-(4-(N-Butylsulfamoyl)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**21g**).* Following the general procedure, **21g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (68%, 46 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 188−190 °C; IR (DCM): 3301, 2958, 1645, 1526, 732 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.75 (1H, br. s), 8.94−8.93 (1H, m), 8.68 (1H, d, J = 7.5 Hz), 8.42 (1H, d, J = 8.2 Hz), 8.15 (1H, d, J = 1.4 Hz), 7.99 (2H, d, J = 8.3 Hz), 7.85 (2H, d, J = 8.3 Hz), 7.70−7.65 (3H, m), 7.58 (1H, t, J = 8.0 Hz), 7.08 (1H, d, J = 1.4 Hz), 2.79−2.74 (2H, m), 1.39−1.36 (2H, m), 1.28−1.22 (2H, m), 0.80 (3H, t, J = 7.3 Hz); ^{13}C {^1H} NMR (~101.0 MHz, DMSO-d_6): δ_C 155.8, 149.2, 145.4, 141.5, 140.1, 137.7, 136.8, 135.2, 133.6, 130.4, 130.2, 127.8, 127.1, 126.2, 122.4, 122.3, 116.0, 114.9, 42.3, 31.2, 19.3, 13.5; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{24}H_{24}N_3O_4S$: 450.1488; found: 450.1485.

*3-(4-(N-Butylsulfamoyl)phenyl)-N-(quinolin-8-yl)-thiophene-2-carboxamide (**21h**).* Following the general procedure, **21h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (69%, 48 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 144−146 °C; IR (DCM): 3329, 2927, 1670, 1530, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.95 (1H, br. s), 8.76 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 8.42 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.02 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.92 (2H, d, J = 8.4 Hz), 7.68 (2H, d, J = 8.3 Hz), 7.58 (1H, d, J = 5.0 Hz), 7.50−7.42 (2H, m), 7.32 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.10 (1H, d, J = 5.0 Hz), 4.95−4.92 (1H, m), 2.91−2.86 (2H, m), 1.43−1.37 (2H, m), 1.27−1.21 (2H, m), 0.81 (3H, t, J = 7.4 Hz); ^{13}C {^1H} NMR (~101.0 MHz, $CDCl_3$): δ_C 160.0, 148.1, 140.9, 139.9, 139.5, 138.1, 136.4, 135.9, 133.9, 130.7, 130.2, 129.7, 127.6, 127.5, 127.0, 121.8,

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121.6, 116.3, 42.9, 31.5, 19.6, 13.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{24}H_{24}N_3O_3S_2$: 466.1259; found: 466.1254.

*3-Methoxy-4′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**22a**).* Following the general procedure, **22a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (88%, 86 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 226−228 °C; IR (DCM): 3342, 2924, 1677, 1523, 727 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.68 (1H, br. s), 8.77 (1H, d, J = 7.6 Hz), 8.57 (1H, d, J = 3.9 Hz), 7.96 (1H, d, J = 8.1 Hz), 7.52−7.39 (11H, m), 7.27 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.24−7.18 (4H, m), 7.01−6.96 (2H, m), 6.75 (2H, d, J = 8.2 Hz), 3.83 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.4, 156.9, 148.3, 142.0, 139.8, 139.1, 138.1, 136.1, 134.4, 133.7, 133.2, 131.3, 130.6, 129.4, 128.8, 128.2, 127.8, 127.1, 126.4, 122.0, 121.7, 121.7, 116.4, 110.8, 56.1; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{28}N_3O_6S_2$: 650.1420; found: 650.1426.

*3-Ethoxy-4′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**22b**).* Following the general procedure, **22b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (80%, 80 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 150−152 °C; IR (DCM): 3331, 2924, 1678, 1522, 725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.80 (1H, br. s), 8.75 (1H, dd, J_1 = 7.6 Hz, J_2 = 0.9 Hz), 8.61 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.03−8.01 (1H, m), 7.54−7.47 (7H, m), 7.44−7.41 (3H, m), 7.39 (1H, t, J = 8.1 Hz), 7.32 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.29−7.25 (4H, m), 6.99−6.96 (2H, m), 6.77 (2H, d, J = 8.4 Hz), 4.11 (2H, d, J = 7.0 Hz), 1.31 (3H, t, J = 7.0 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.3, 156.2, 148.2, 142.4, 140.2, 139.2, 138.3, 136.1, 134.7, 133.7, 133.1, 131.3, 130.5, 129.4, 128.8, 128.3, 127.9, 127.2, 126.7, 122.0, 121.7, 121.6, 116.4, 111.9, 64.6, 14.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{36}H_{30}N_3O_6S_2$: 664.1576; found: 664.1577.

*3-Bromo-4′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**22c**).* Following the general procedure, **22c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (84%, 88 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 204−206 °C; IR (DCM): 3331, 2924, 1678, 1522, 725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (1H, br. s), 8.81 (1H, d, J = 7.6 Hz), 8.67 (1H, d, J = 4.0 Hz), 8.07 (1H, d, J = 8.2 Hz), 7.71 (1H, d, J = 7.6 Hz), 7.61−7.48 (10H, m), 7.45−7.36 (3H, m), 7.32−7.26 (4H, m), 6.84 (2H, d, J = 8.2 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.4, 148.4, 141.2, 140.3, 139.0, 138.1, 138.0, 136.2, 133.9, 133.8, 133.7, 132.6, 131.4, 130.7, 129.4, 128.8, 128.2, 127.8, 127.1, 122.2, 121.8, 120.9, 116.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{25}BrN_3O_5S_2$: 698.0419; found: 698.0437.

*4-Methyl-4′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**22d**).* Following the general procedure, **22d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (82%, 78 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 174−176 °C; IR (DCM): 3329, 2923, 1668, 1523, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, br. s), 8.79 (1H, d, J = 7.4 Hz), 8.51 (1H, d, J = 3.1 Hz), 7.92 (1H, d, J = 8.1 Hz), 7.62 (1H, s), 7.52 (1H, t, J = 7.9 Hz), 7.45−7.39 (5H, m), 7.31−7.29 (6H, m), 7.23 (1H, dd, J_1 = 8.0 Hz, J_2 = 3.8 Hz), 7.17−7.12 (4H, m), 6.76 (2H, d, J = 8.0 Hz), 2.38 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.7, 148.7, 142.1, 139.0, 138.4, 137.9, 136.2, 136.0, 135.5, 134.3, 133.7, 133.2, 131.5, 131.4, 130.3, 129.9, 129.7, 128.7, 128.1, 127.6, 127.1, 121.9, 121.6, 115.8, 21.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{28}N_3O_5S_2$: 634.1470; found: 634.1466.

*4-Chloro-4′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**22e**).* Following the general procedure, **22e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (83%, 82 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 201−203 °C; IR (DCM): 3323, 2924, 1670, 1525, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.76 (1H, br. s), 8.83 (1H, d, J = 7.6 Hz), 8.61 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.01 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.88 (1H, d, J = 2.1 Hz), 7.59 (1H, t, J = 8.0 Hz), 7.56−7.49 (6H, m), 7.43 (1H, d, J = 8.3 Hz), 7.39−7.37 (4H, m), 7.33 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.25−7.20 (4H, m), 6.87 (2H, d, J = 8.3 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.9, 148.8, 140.9, 139.0, 137.9, 137.7, 136.7, 135.9, 134.6, 134.0, 133.8, 133.7, 131.7, 130.6, 129.6, 129.4, 128.7, 128.1, 127.6, 127.0, 122.0, 121.9, 115.9; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{25}ClN_3O_5S_2$: 654.0924; found: 654.0939.

*6-(4-(N-(Phenylsulfonyl)phenylsulfonamido)phenyl)-N-(quinolin-8-yl)-2,3-dihydrobenzo(b)(1,4)dioxine-5-carboxamide (**22f**).* Following the general procedure, **22f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (78%, 79 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 210−212 °C; IR (DCM): 3338, 2924, 1675, 1521, 726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, br. s), 8.78 (1H, d, J = 7.3 Hz), 8.56 (1H, br. s), 7.96 (1H, d, J = 8.0 Hz), 7.51−7.38 (10H, m), 7.27 (1H, dd, J_1 = 7.9 Hz, J_2 = 3.4 Hz), 7.22−7.18 (4H, m), 6.97 (1H, d, J = 8.3 Hz), 6.90 (1H, d, J = 8.4 Hz), 6.72 (2H, d, J = 8.0 Hz), 4.27 (4H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 164.7, 148.3, 143.6, 141.9, 141.4, 139.1, 138.0, 136.1, 134.2, 133.7, 132.9, 131.7, 131.3, 129.3, 128.7, 128.4, 128.2, 127.8, 127.1, 126.2, 122.5, 121.8, 121.7, 118.5, 116.4, 64.6, 64.2; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{36}H_{28}N_3O_7S_2$: 678.1369; found: 678.1387.

*3-(4-(N-(Phenylsulfonyl)phenylsulfonamido)phenyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**22g**).* Following the general procedure, **22g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (80%, 75 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 200−202 °C; IR (DCM): 3317, 2924, 1656, 1526, 725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.08 (1H, br. s), 8.81 (1H, d, J = 7.5 Hz), 8.62 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.2 Hz), 8.04 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.1 Hz), 7.61−7.50 (11H, m), 7.30 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.27−7.23 (4H, m), 7.15 (1H, d, J = 5.0 Hz), 6.99 (2H, d, J = 8.3 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 160.6, 149.1, 141.3, 139.0, 138.0, 137.2, 135.9, 135.7, 134.1, 134.0, 133.8, 131.8, 130.6, 130.2, 129.0, 128.7, 128.2, 127.6, 127.2, 121.8, 121.7, 116.3; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{32}H_{24}N_3O_5S_3$: 626.0878; found: 626.0895.

*2-(4-Fluoro-4′-(N-(phenylsulfonyl)phenylsulfonamido)-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**23a**).* Following the general procedure, **23a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (72%, 70 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 182−184

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°C; IR (DCM): 3339, 2924, 1685, 1526, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.73 (1H, br. s), 8.64−8.61 (2H, m), 8.06 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.84−7.82 (4H, m), 7.54−7.51 (2H, m), 7.47−7.37 (6H, m), 7.33 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.30 (2H, d, J = 8.4 Hz), 7.26−7.18 (2H, m), 7.02 (1H, td, J_1 = 8.3 Hz, J_2 = 2.6 Hz), 6.97 (2H, d, J = 8.3 Hz), 3.74 (2H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.6, 162.4 (d, J_{C-F} = 248.7 Hz), 148.3, 142.2, 139.3, 138.3, 137.2 (d, J_{C-F} = 3.0 Hz), 136.3, 134.4 (d, J_{C-F} = 7.9 Hz), 134.1, 133.9, 133.4, 131.8 (d, J_{C-F} = 8.3 Hz), 131.5, 130.3, 129.0, 128.5, 127.8, 127.3, 121.8, 121.7, 117.5 (d, J_{C-F} = 21.8 Hz), 116.4, 114.5 (d, J_{C-F} = 21.2 Hz), 42.4; ^{19}F {^1H} NMR (∼376 MHz, $CDCl_3$): δ_F −113.75; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{27}FN_3O_5S_2$: 652.1376; found: 652.1373.

*3-Methoxy-3′-methyl-4′-(N-(phenylsulfonyl)-phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**24a**).* Following the general procedure, **24a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (74%, 74 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 242−244 °C; IR (DCM): 3338, 2923, 1679, 1522, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.74 (1H, br. s), 8.86−8.84 (1H, m), 8.65 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.04 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.59−7.46 (9H, m), 7.41 (1H, d, J = 1.7 Hz), 7.35 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.30−7.26 (5H, m), 7.08 (1H, d, J = 7.6 Hz), 7.04 (1H, d, J = 8.3 Hz), 6.63 (1H, d, J = 8.2 Hz), 3.91 (3H, s), 1.76 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.4, 156.9, 148.3, 141.9, 140.5, 140.0, 139.1, 138.1, 136.1, 134.5, 133.7, 132.3, 131.8, 131.7, 130.5, 128.7, 128.5, 127.8, 127.1, 126.5, 126.4, 121.9, 121.7, 116.3, 110.6, 56.1, 17.9; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{36}H_{30}N_3O_6S_2$: 664.1576; found: 664.1552.

*4-Methoxy-3′-(N-(phenylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**24b**).* Following the general procedure, **24b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (72%, 70 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 161−163 °C; IR (DCM): 3329, 2925, 1667, 1522, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.73 (1H, br. s), 8.79 (1H, d, J = 7.3 Hz), 8.49 (1H, d, J = 3.4 Hz), 7.97 (1H, d, J = 8.0 Hz), 7.59 (4H, d, J = 7.7 Hz), 7.56 (1H, d, J = 7.7 Hz), 7.47 (2H, t, J = 7.4 Hz), 7.40 (1H, t, J = 7.8 Hz), 7.36−7.34 (2H, m), 7.31−7.27 (4H, m), 7.23 (1H, dd, J_1 = 8.1 Hz, J_2 = 4.0 Hz), 7.19−7.16 (3H, m), 6.99 (1H, dd, J_1 = 8.5 Hz, J_2 = 2.4 Hz), 6.63−6.61 (1H, m), 3.81 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.0, 159.3, 148.0, 141.1, 139.2, 138.2, 137.0, 136.0, 134.2, 134.2, 133.7, 132.0, 131.9, 130.9, 130.5, 130.3, 128.8, 128.8, 128.3, 127.6, 127.1, 121.7, 121.4, 116.9, 116.5, 113.8, 55.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{35}H_{28}N_3O_6S_2$: 650.1420; found: 650.1422.

*3-Methoxy-4′-(N-(methylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**24c**).* Following the general procedure, **24c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (81%, 71 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 205−207 °C; IR (DCM): 3343, 2924, 1675, 1522, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.82 (1H, dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz), 8.67 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.08 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.59−7.48 (6H, m), 7.38 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.30−7.27 (2H, m), 7.18−7.14 (2H, m), 7.06 (2H, d, J = 8.1 Hz), 6.95 (2H, d, J = 8.4 Hz), 3.92 (3H, s), 3.35 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.4, 156.9, 148.2, 142.1, 139.8, 138.2, 137.7, 136.1, 134.4, 133.9, 132.7, 130.9, 130.6, 129.5, 128.6, 128.4, 127.8, 127.2, 126.4, 122.0, 121.7, 121.6, 116.5, 110.8, 56.1, 43.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{30}H_{26}N_3O_6S_2$: 588.1263; found: 588.1268.

*3-Bromo-4′-(N-(methylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**24d**).* Following the general procedure, **24d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 75:25) as a colorless solid (80%, 76 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 248−250 °C; IR (DCM): 3331, 2924, 1677, 1522, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.78 (1H, dd, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 8.69 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.10 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.72 (1H, dd, J_1 = 6.7 Hz, J_2 = 2.5 Hz), 7.58 (1H, t, J = 8.2 Hz), 7.54−7.51 (3H, m), 7.50−7.46 (1H, m), 7.43−7.38 (3H, m), 7.27−7.25 (2H, m), 7.17−7.13 (2H, m), 6.96 (2H, d, J = 8.2 Hz), 3.34 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.4, 148.4, 141.3, 140.2, 138.2, 138.0, 137.6, 136.2, 133.9, 133.9, 133.2, 132.6, 131.0, 130.7, 129.6, 128.8, 128.7, 128.4, 127.8, 127.1, 122.2, 121.8, 120.8, 116.7, 43.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{23}BrN_3O_5S_2$: 636.0262; found: 636.0272.

*4-Chloro-4′-(N-(methylsulfonyl)phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**24e**).* Following the general procedure, **24e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (83%, 74 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 186−188 °C; IR (DCM): 3323, 2927, 1669, 1524, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (1H, br. s), 8.73 (1H, d, J = 7.5 Hz), 8.55 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz), 7.96 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.79 (1H, d, J = 2.1 Hz), 7.51−7.41 (5H, m), 7.37−7.34 (1H, m), 7.32 (1H, d, J = 8.3 Hz), 7.28 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 6.97−6.88 (6H, m), 3.27 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.8, 148.7, 141.0, 137.9, 137.6, 137.4, 136.7, 136.0, 134.5, 133.9, 133.9, 133.2, 131.7, 131.3, 130.6, 129.7, 129.3, 128.5, 128.2, 127.6, 127.0, 121.9, 121.9, 116.0, 43.9; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{23}ClN_3O_5S_2$: 592.0768; found: 592.0769.

*3-Methoxy-4′-(phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25a**).* Following the general procedure, **25a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (72%, 55 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 184−186 °C; IR (DCM): 3334, 2923, 1672, 1522, 759 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.28 (1H, br. s), 9.90 (1H, br. s), 8.80 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.49 (1H, d, J = 7.6 Hz), 8.41 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.71−7.69 (1H, m), 7.63−7.56 (4H, m), 7.51−7.43 (2H, m), 7.34−7.29 (4H, m), 7.17 (1H, d, J = 8.4 Hz), 6.99−6.96 (3H, m), 3.81 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.0, 156.1, 149.0, 139.7, 139.4, 137.7, 137.0, 136.7, 135.3, 134.0, 132.8, 130.6, 129.1, 129.1, 127.8, 127.0, 126.5, 125.8, 122.3, 122.1, 122.0, 119.5, 116.1, 110.7, 56.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{24}N_3O_4S$: 510.1488; found: 510.1480.

*4′-((4-Chlorophenyl)sulfonamido)-3-methoxy-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25b**).* Following the general procedure, **25b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 65:35) as a colorless solid (75%, 61 mg, 0.15 mmol); R_f

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(EtOAc/hexanes = 50:50) 0.50; mp: 187−189 °C; IR (DCM): 3336, 2923, 1671, 1523, 757 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.38 (1H, br. s), 9.93 (1H, br. s), 8.80 (1H, d, J = 3.3 Hz), 8.51 (1H, d, J = 7.6 Hz), 8.40 (1H, d, J = 8.3 Hz), 7.69 (1H, d, J = 8.2 Hz), 7.62−7.56 (4H, m), 7.49 (1H, t, J = 8.1 Hz), 7.38−7.35 (4H, m), 7.17 (1H, d, J = 8.4 Hz), 7.01−6.96 (3H, m), 3.81 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.0, 156.1, 149.0, 139.7, 138.2, 137.8, 137.7, 136.7, 135.7, 134.1, 130.6, 129.3, 129.2, 128.4, 127.8, 127.0, 125.8, 122.3, 122.2, 122.0, 119.9, 116.1, 110.7, 56.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{23}ClN_3O_4S$: 544.1098; found: 544.1095.

*3-Methyl-4′-(phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25c**).* Following the general procedure, **25c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (70%, 52 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 178−180 °C; IR (DCM): 3336, 2924, 1671, 1522, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.24 (1H, br. s), 9.81 (1H, br. s), 8.74 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.44 (1H, d, J = 7.6 Hz), 8.40−8.38 (1H, m), 7.71 (1H, d, J = 8.2 Hz), 7.60−7.55 (4H, m), 7.44−7.40 (2H, m), 7.36 (2H, d, J = 8.5 Hz), 7.32 (1H, d, J = 7.6 Hz), 7.27−7.20 (3H, m), 6.98 (2H, d, J = 8.5 Hz), 2.38 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 167.4, 149.0, 139.4, 138.2, 138.0, 136.9, 136.6, 135.7, 134.9, 133.8, 132.7, 129.2, 129.2, 129.0, 127.8, 127.3, 126.9, 126.4, 122.6, 122.2, 119.7, 116.9, 19.2; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{24}N_3O_3S$: 494.1538; found: 494.1547.

*3-Bromo-4′-(phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25d**).* Following the general procedure, **25d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (68%, 57 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 120−122 °C; IR (DCM): 3332, 2924, 1675, 1522, 792 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.32 (1H, br. s), 10.21 (1H, br. s), 8.82 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.43−8.41 (2H, m), 7.75−7.71 (2H, m), 7.63−7.57 (4H, m), 7.47−7.38 (5H, m), 7.33−7.29 (2H, m), 7.00 (2H, d, J = 8.6 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.4, 149.1, 140.5, 139.3, 138.3, 137.8, 137.4, 136.6, 134.5, 133.7, 132.8, 131.3, 130.8, 129.3, 129.1, 129.0, 127.8, 126.8, 126.4, 122.8, 122.2, 119.7, 119.4, 117.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{28}H_{21}BrN_3O_3S$: 558.0487; found: 558.0488.

*3-Bromo-4′-((4-chlorophenyl)sulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25e**).* Following the general procedure, **25e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (70%, 62 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 141−143 °C; IR (DCM): 3332, 2924, 1676, 1521, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.68 (1H, br. s), 8.68−8.65 (1H, m), 8.63 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.09 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.5 Hz), 7.60 (1H, dd, J_1 = 6.7 Hz, J_2 = 2.4 Hz), 7.49−7.48 (2H, m), 7.38−7.35 (3H, m), 7.32−7.19 (4H, m), 6.95 (2H, d, J = 8.6 Hz), 6.89 (2H, d, J = 8.5 Hz), 6.37 (1H, br. s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.7, 148.4, 140.6, 139.4, 138.3, 138.0, 137.2, 136.9, 136.3, 135.7, 133.9, 132.1, 130.5, 129.8, 129.1, 129.0, 128.3, 127.9, 127.4, 122.3, 122.0, 121.8, 120.6, 116.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{28}H_{20}BrClN_3O_3S$: 592.0097; found: 592.0095.

*4-Methyl-4′-(phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25f**).* Following the general procedure, **25f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 75:25) as a colorless solid (72%, 53 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 222−224 °C; IR (DCM): 3318, 2923, 1664, 1522, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.74 (1H, br. s), 8.74 (1H, dd, J_1 = 7.3 Hz, J_2 = 1.6 Hz), 8.54 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.05 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.66 (1H, br. s), 7.52−7.44 (4H, m), 7.35−7.30 (5H, m), 7.27 (1H, d, J = 8.7 Hz), 7.09−7.05 (3H, m), 6.95 (2H, d, J = 8.5 Hz), 2.43 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.1, 148.7, 139.5, 137.7, 137.2, 137.1, 136.5, 135.9, 135.5, 135.2, 134.0, 132.8, 131.3, 130.3, 129.4, 129.1, 129.0, 127.6, 126.9, 126.5, 122.2, 122.1, 119.8, 115.9, 20.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{24}N_3O_3S$: 494.1538; found: 494.1537.

*4′-((4-Chlorophenyl)sulfonamido)-4-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25g**).* Following the general procedure, **25g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (74%, 59 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 195−197 °C; IR (DCM): 3317, 2923, 1652, 1523, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.79 (1H, br. s), 8.74 (1H, dd, J_1 = 7.0 Hz, J_2 = 1.9 Hz), 8.57 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.07 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.65 (1H, s), 7.53−7.47 (2H, m), 7.36−7.26 (7H, m), 7.17 (1H, br. s), 6.98−6.93 (4H, m), 2.44 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.1, 148.1, 139.1, 138.2, 137.8, 137.5, 137.4, 136.2, 136.1, 135.8, 135.5, 134.3, 131.3, 130.4, 129.8, 129.5, 128.9, 128.3, 127.7, 127.3, 122.2, 121.8, 121.7, 116.3, 21.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{29}H_{23}ClN_3O_3S$: 528.1149; found: 528.1141.

*4-Chloro-4′-(phenylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25h**).* Following the general procedure, **25h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (74%, 57 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; mp: 201−203 °C; IR (DCM): 3303, 2924, 1664, 1526, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.36 (1H, br. s), 9.99 (1H, br. s), 8.68 (1H, d, J = 4.0 Hz), 8.53 (1H, d, J = 7.5 Hz), 8.40 (1H, d, J_1 = 8.2 Hz), 7.81 (1H, d, J = 1.8 Hz), 7.72 (1H, d, J = 8.2 Hz), 7.66−7.59 (5H, m), 7.52 (1H, t, J = 7.4 Hz), 7.46 (1H, d, J = 8.2 Hz), 7.40−7.36 (4H, m), 7.06 (2H, d, J = 8.3 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.6, 148.8, 139.5, 138.0, 137.6, 137.3, 136.5, 133.9, 133.8, 132.8, 132.2, 130.3, 129.4, 129.1, 128.2, 127.7, 126.8, 126.4, 122.5, 122.2, 119.6, 116.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{28}H_{21}ClN_3O_3S$: 514.0992; found: 514.0991.

*4-Chloro-4′-((4-chlorophenyl)sulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**25i**).* Following the general procedure, **25i** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (72%, 59 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 210−212 °C; IR (DCM): 3317, 2923, 1668, 1524, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.44 (1H, br. s), 9.96 (1H, br. s), 8.64 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.3 Hz), 8.54 (1H, d, J = 7.4 Hz), 8.35−8.33 (1H, m), 7.79 (1H, d, J = 2.0 Hz), 7.66 (1H, d, J = 7.9 Hz), 7.62−7.52 (5H, m), 7.42−7.36 (5H, m), 7.07 (2H, d, J = 8.5 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.5, 148.7, 138.3, 138.0, 137.8, 137.6, 137.3, 137.3, 136.4, 134.3,

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133.9, 132.4, 132.2, 130.3, 129.6, 129.3, 128.4, 128.3, 127.6, 126.9, 122.5, 122.2, 119.9, 116.6; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{28}H_{20}Cl_2N_3O_3S$: 548.0602; found: 548.0605.

*3-(4-(Phenylsulfonamido)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**25j**).* Following the general procedure, **25j** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (68%, 48 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 162−164 °C; IR (DCM): 3331, 2924, 1674, 1529, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.71 (1H, br. s), 10.55 (1H, br. s), 8.91 (1H, d, J = 4.0 Hz), 8.69 (1H, d, J = 7.6 Hz), 8.44 (1H, d, J_1 = 8.2 Hz), 8.07 (1H, s), 7.85 (2H, d, J = 7.2 Hz), 7.73−7.70 (3H, m), 7.67 (1H, dd, J_1 = 8.4 Hz, J_2 = 4.2 Hz), 7.64−7.57 (4H, m), 7.17 (2H, d, J = 8.5 Hz), 6.96 (1H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 156.1, 149.1, 145.1, 140.6, 139.7, 137.8, 137.7, 136.8, 133.7, 133.1, 131.3, 130.4, 129.4, 127.8, 127.1, 126.7, 126.6, 122.4, 122.1, 118.9, 115.8, 114.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{20}N_3O_4S$: 470.1175; found: 470.1169.

*3-(4-((4-Chlorophenyl)sulfonamido)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**25k**).* Following the general procedure, **25k** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (69%, 52 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 120−122 °C; IR (DCM): 3330, 2924, 1675, 1526, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.70 (1H, br. s), 10.64 (1H, br. s), 8.90 (1H, d, J = 3.8 Hz), 8.68 (1H, d, J = 7.6 Hz), 8.41 (1H, d, J = 8.0 Hz), 8.06 (1H, s), 7.84 (2H, d, J = 8.5 Hz), 7.74 (2H, d, J = 8.5 Hz), 7.69−7.62 (4H, m), 7.58 (1H, t, J = 7.8 Hz), 7.18 (2H, d, J = 8.5 Hz), 6.95 (1H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 156.0, 149.1, 145.0, 140.6, 138.5, 138.0, 137.7, 137.4, 136.8, 133.7, 131.2, 130.5, 129.6, 128.6, 127.8, 127.1, 127.0, 122.4, 122.1, 119.2, 115.8, 114.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{19}ClN_3O_4S$: 504.0785; found: 504.0786.

*3-Methyl-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26a**).* Following the general procedure, **26a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (70%, 47 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 178−180 °C; IR (DCM): 3347, 2923, 1662, 1465, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.54 (1H, br. s), 8.65 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.2 Hz), 8.52 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 7.95 (1H, d, J = 8.3 Hz), 7.40−7.30 (5H, m), 7.25 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.20−7.16 (2H, m), 7.06−6.94 (1H, m), 6.95 (2H, d, J = 8.5 Hz), 2.42 (3H, s), 2.34 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.2, 148.1, 138.6, 138.1, 137.3, 136.6, 136.0, 136.0, 134.0, 129.8, 129.7, 129.3, 127.7, 127.3, 127.2, 121.8, 121.6, 120.2, 116.5, 38.3, 19.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{24}H_{22}N_3O_3S$: 432.1382; found: 432.1383.

*4′-(Butylsulfonamido)-3-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26b**).* Following the general procedure, **26b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (72%, 51 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 224−226 °C; IR (DCM): 3356, 2924, 1671, 1517, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.62 (1H, br. s), 8.76 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.63 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.08 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.52−7.47 (4H, m), 7.45−7.37 (2H, m), 7.31−7.26 (2H, m), 7.05 (2H, d, J = 8.6 Hz), 6.54 (1H, s), 2.69−2.65 (2H, m), 2.52 (3H, s), 1.58−1.50 (2H, m), 1.16−1.07 (2H, m), 0.74 (3H, t, J = 7.4 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.2, 148.1, 138.5, 138.2, 137.3, 136.7, 136.1, 136.0, 135.9, 134.2, 129.9, 129.7, 129.3, 127.7, 127.4, 127.2, 121.8, 121.6, 120.1, 116.4, 50.6, 25.2, 21.1, 19.7, 13.4; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{27}H_{28}N_3O_3S$: 474.1851; found: 474.1854.

*3-Fluoro-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26c**).* Following the general procedure, **26c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (75%, 49 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 176−178 °C; IR (DCM): 3321, 2924, 1662, 1526, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.84 (1H, br. s), 8.70−8.68 (1H, m), 8.60 (1H, d, J = 3.8 Hz), 8.05 (1H, d, J = 8.2 Hz), 7.47−7.40 (5H, m), 7.34 (1H, dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.19−7.11 (2H, m), 7.02 (2H, d, J = 8.3 Hz), 6.70 (1H, br. s), 2.58 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 163.2, 159.8 (d, J_{C-F} = 250.8 Hz), 148.1, 141.2 (d, J_{C-F} = 3.0 Hz), 138.0, 136.6, 136.4, 135.9 (d, J_{C-F} = 1.9 Hz), 133.9, 131.2 (d, J_{C-F} = 9.0 Hz), 129.9, 127.8, 127.4, 125.7 (d, J_{C-F} = 2.9 Hz), 124.8 (d, J_{C-F} = 17.3 Hz), 122.1, 121.7, 120.2, 116.9, 115.1 (d, J_{C-F} = 22.0 Hz), 38.9; ^{19}F {^1H} NMR (∼376 MHz, $CDCl_3$): δ_F −114.85; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{23}H_{19}FN_3O_3S$: 436.1131; found: 436.1141.

*3-Bromo-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26d**).* Following the general procedure, **26d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (79%, 59 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 224−226 °C; IR (DCM): 3327, 2925, 1675, 1520, 762 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.25 (1H, br. s), 9.78 (1H, br. s), 8.83−8.82 (1H, m), 8.48 (1H, d, J = 7.6 Hz), 8.38 (1H, d, J = 8.3 Hz), 7.74 (1H, d, J = 7.4 Hz), 7.70 (1H, d, J = 8.2 Hz), 7.61−7.56 (2H, m), 7.51−7.45 (4H, m), 7.12 (2H, d, J = 8.5 Hz), 2.79 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.9, 148.1, 140.8, 137.9, 136.5, 136.1, 133.8, 132.1, 130.6, 129.9, 128.9, 127.8, 127.4, 122.2, 121.7, 120.7, 120.1, 117.0, 38.9; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{23}H_{19}BrN_3O_3S$ 496.0330; found: 496.0331.

*3-Bromo-4′-(butylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26e**).* Following the general procedure, **26e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (78%, 63 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 198−200 °C; IR (DCM): 3327, 2923, 1664, 1523, 761 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 10.19 (1H, br. s), 9.79 (1H, br. s), 8.82 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.47 (1H, d, J = 7.6 Hz), 8.39 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.74 (1H, dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz), 7.70 (1H, d, J = 7.6 Hz), 7.61−7.55 (2H, m), 7.52−7.45 (4H, m), 7.11 (2H, d, J = 8.5 Hz), 2.84−2.80 (2H, m), 1.47−1.40 (2H, m), 1.11−1.06 (2H, m), 0.65 (3H, t, J = 7.4 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 165.9, 148.3, 140.8, 138.3, 137.9, 136.6, 136.2, 135.8, 133.9, 132.0, 130.6, 129.9, 129.0, 127.8, 127.2, 122.1, 121.7, 120.7, 119.8, 116.8, 51.0, 25.2, 21.2, 13.4; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{25}BrN_3O_3S$: 538.0800; found: 538.0792.

*4-Methoxy-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26f**).* Following the general procedure, **26f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (76%, 51 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 185−187 °C; IR (DCM): 3315, 2926, 1662, 1524, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.75

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(1H, br. s), 8.78 (1H, d, J = 7.4 Hz), 8.55 (1H, d, J = 3.2 Hz), 8.04 (1H, d, J = 8.2 Hz), 7.50 (1H, t, J = 8.2 Hz), 7.44−7.42 (4H, m), 7.37−7.32 (2H, m), 7.12−7.02 (4H, m), 3.90 (3H, s), 2.50 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.6, 159.2, 148.1, 138.2, 137.0, 136.8, 136.2, 136.0, 134.3, 131.7, 131.6, 130.3, 127.7, 127.3, 121.7, 121.6, 120.6, 117.2, 116.3, 113.9, 55.6, 38.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{24}H_{22}N_3O_4S$: 448.1331; found: 448.1335.

*4-Methyl-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26g**).* Following the general procedure, **26g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (78%, 50 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 174−176 °C; IR (DCM): 3306, 2924, 1642, 1524, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, br. s), 8.69 (1H, dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz), 8.47 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 7.94 (1H, d, J = 8.1 Hz), 7.60 (1H, s), 7.39 (1H, t, J = 8.0 Hz), 7.35−7.32 (3H, m), 7.28−7.22 (3H, m), 7.03−7.01 (3H, m), 2.41 (3H, s), 2.36 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 168.0, 148.0, 138.1, 137.7, 136.9, 136.2, 135.9, 135.7, 134.2, 131.4, 130.3, 130.1, 129.7, 127.6, 127.2, 121.6, 121.5, 120.4, 116.2, 38.4, 21.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{24}H_{22}N_3O_3S$: 432.1382; found: 432.1385.

*4′-(Butylsulfonamido)-4-methyl-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26h**).* Following the general procedure, **26h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (75%, 53 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 140−142 °C; IR (DCM): 3245, 2929, 1661, 1521, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.68 (1H, br. s), 8.69 (1H, d, J = 7.2 Hz), 8.47 (1H, br. s), 7.95 (1H, d, J = 7.6 Hz), 7.60 (1H, s), 7.42−7.35 (4H, m), 7.28−7.23 (3H, m), 7.10−7.00 (3H, m), 2.59−2.56 (2H, m), 2.36 (3H, s), 1.49−1.44 (2H, m), 1.03−0.98 (2H, m), 0.64 (3H, t, J = 7.3 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 167.9, 147.9, 138.1, 137.7, 136.6, 136.3, 136.3, 136.0, 135.7, 134.2, 131.3, 130.3, 130.1, 129.7, 127.6, 127.2, 121.5, 121.5, 120.3, 116.3, 50.7, 25.1, 21.1, 21.0, 13.3; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{27}H_{26}N_3O_3S$: 472.1695; found: 472.1680.

*4-Chloro-4′-(methylsulfonamido)-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26i**).* Following the general procedure, **26i** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 65:35) as a colorless solid (78%, 53 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 168−170 °C; IR (DCM): 3294, 2923, 1645, 1525, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (1H, br. s), 8.64 (1H, dd, J_1 = 7.2 Hz, J_2 = 1.6 Hz), 8.47 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 7.94 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.76 (1H, d, J = 2.2 Hz), 7.42−7.35 (3H, m), 7.32 (2H, d, J = 8.4 Hz), 7.27−7.22 (3H, m), 7.03 (2H, d, J = 8.5 Hz), 2.43 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.2, 148.1, 138.0, 137.5, 137.1, 136.8, 136.0, 135.5, 133.8, 131.7, 130.6, 130.0, 129.1, 127.5, 127.1, 121.9, 121.6, 120.3, 116.4, 38.5; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{23}H_{19}ClN_3O_3S$: 452.0836; found: 452.0834.

*4′-(Butylsulfonamido)-4-chloro-N-(quinolin-8-yl)-(1,1′-biphenyl)-2-carboxamide (**26j**).* Following the general procedure, **26j** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (76%, 56 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 137−139 °C; IR (DCM): 3247, 2930, 1663, 1525, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.75 (1H, d, J = 7.0 Hz), 8.58 (1H, s), 8.07 (1H, d, J = 7.9 Hz), 7.87 (1H, s), 7.53−7.37 (7H, m), 7.13 (2H, d, J = 7.4 Hz), 6.88 (1H, s), 2.73−2.69 (2H, m), 1.59−1.56 (2H, m), 1.16−1.11 (2H, m), 0.75 (3H, t, J = 7.3 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, $CDCl_3$): δ_C 166.2, 148.1, 138.1, 137.5, 137.2, 136.9, 136.0, 135.3, 133.9, 133.8, 131.8, 130.6, 130.0, 129.2, 127.6, 127.2, 121.9, 121.6, 120.1, 116.4, 50.8, 25.1, 21.1, 13.3; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{26}H_{25}ClN_3O_3S$: 494.1305; found: 494.1310.

*3-(4-(Methylsulfonamido)phenyl)-N-(quinolin-8-yl)furan-2-carboxamide (**26k**).* Following the general procedure, **26k** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (74%, 45 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 190−192 °C; IR (DCM): 3320, 2923, 1662, 1531, 759 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.73 (1H, br. s), 9.96 (1H, br. s), 8.94 (1H, d, J = 3.8 Hz), 8.71 (1H, d, J = 7.6 Hz), 8.44 (1H, d, J = 8.2 Hz), 8.10 (1H, d, J = 1.1 Hz), 7.81 (2H, d, J = 8.5 Hz), 7.71−7.65 (2H, m), 7.60 (1H, t, J = 8.0 Hz), 7.28 (2H, d, J = 8.5 Hz), 7.01 (1H, d, J = 1.2 Hz), 3.06 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 156.1, 149.1, 145.1, 140.6, 138.5, 137.8, 136.8, 133.8, 131.5, 130.5, 127.8, 127.1, 126.5, 122.4, 122.1, 118.9, 115.8, 114.8; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{21}H_{18}N_3O_4S$: 408.1018; found: 408.1017.

*3-(4-(Butylsulfonamido)phenyl)-N-(quinolin-8-yl)-thiophene-2-carboxamide (**26l**).* Following the general procedure, **26l** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (80%, 56 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 190−192 °C; IR (DCM): 3271, 2924, 1624, 1530, 738 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.05 (1H, br. s), 10.00 (1H, br. s), 8.66−8.64 (1H, m), 8.47 (1H, dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz), 8.32−8.30 (1H, m), 7.91 (1H, d, J = 5.0 Hz), 7.61 (1H, d, J = 7.4 Hz), 7.57−7.51 (4H, m), 7.31 (2H, d, J = 8.4 Hz), 7.20 (1H, d, J = 5.0 Hz), 3.03−3.00 (2H, m), 1.64−1.58 (2H, m), 1.27−1.20 (2H, m), 0.74 (3H, t, J = 7.4 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 159.8, 148.2, 142.6, 139.0, 137.5, 136.4, 134.4, 133.8, 131.6, 130.7, 130.4, 129.4, 127.6, 127.0, 122.0, 121.9, 119.5, 115.7, 50.6, 25.1, 20.6, 13.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{24}H_{24}N_3O_3S_2$: 466.1259; found: 466.1260.

*4-Chloro-N-(quinolin-8-yl)-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxamide (**27a**).* Following the general procedure, **27a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (73%, 32 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 134−136 °C; IR (DCM): 2932, 1667, 1328, 1162, 736 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.32 (1H, br. s), 8.81−8.80 (1H, m), 8.50 (1H, d, J = 7.5 Hz), 8.38 (1H, d, J = 8.3 Hz), 7.89 (1H, d, J = 2.1 Hz), 7.81 (2H, d, J = 8.2 Hz), 7.74−7.67 (4H, m), 7.60−7.54 (3H, m), 7.38 (2H, br. s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.6, 149.2, 143.4, 142.3, 138.5, 137.8, 137.3, 136.6, 134.0, 133.1, 132.5, 130.5, 129.2, 128.2, 127.9, 126.9, 125.9, 123.0, 122.3, 117.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{22}H_{17}ClN_3O_3S$: 438.0679; found: 438.0682.

*N-(Quinolin-8-yl)-3-(4-sulfamoylphenyl)benzofuran-2-carboxamide (**27c**).* Following the general procedure, **27c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (34%, 15 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; mp: 222−224 °C; IR (DCM): 2923, 1657, 1326, 1156, 748 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.91 (1H, br. s), 8.97 (1H, dd, J_1

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= 4.2 Hz, J_2 = 1.6 Hz), 8.72−8.70 (1H, m), 8.46 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.99 (2H, d, J = 8.4 Hz), 7.94−7.90 (3H, m), 7.76−7.74 (1H, m), 7.69 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.67−7.59 (3H, m), 7.55 (2H, br. s), 7.47−7.43 (1H, m); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 174.7, 156.2, 153.2, 149.4, 144.0, 142.7, 137.8, 136.9, 133.7, 133.5, 130.8, 128.5, 127.9, 127.8, 127.2, 125.8, 125.0, 124.7, 122.7, 122.6, 121.5, 116.4, 112.4; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{24}H_{18}N_3O_4S$: 444.1018; found: 444.1016.

*N-(Quinolin-8-yl)-3-(4-sulfamoylphenyl)furan-2-carboxamide (**27d**).* Following the general procedure, **27d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (61%, 24 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 216−218 °C; IR (DCM): 2930, 1730, 1325, 1173, 727 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.77 (1H, br. s), 8.96 (1H, d, J = 4.1 Hz), 8.70 (1H, d, J = 7.6 Hz), 8.45 (1H, d, J = 8.2 Hz), 8.16 (1H, d, J = 1.4 Hz), 7.97 (2H, d, J = 8.3 Hz), 7.90 (2H, d, J = 8.3 Hz), 7.71 (1H, d, J = 8.2 Hz), 7.67 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz), 7.60 (1H, t, J = 8.0 Hz), 7.47 (2H, br. s), 7.08 (1H, d, J = 1.3 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 155.8, 149.2, 145.4, 143.6, 141.4, 137.8, 136.8, 134.8, 133.6, 130.6, 130.0, 127.8, 127.1, 125.4, 122.5, 122.3, 115.9, 114.9; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{20}H_{16}N_3O_4S$: 394.0862; found: 394.0866.

*3-Fluoro-N-(quinolin-8-yl)-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxamide (**27e**).* Following the general procedure, **27e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (64%, 27 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 241−243 °C; IR (DCM): 2928, 1657, 1309, 1012, 746 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.70 (1H, br. s), 8.89 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.45 (1H, dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz), 8.41 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.79−7.73 (5H, m), 7.69−7.57 (3H, m), 7.46 (1H, t, J = 8.7 Hz), 7.38−7.37 (1H, m), 7.37 (2H, br. s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 162.7, 158.9 (d, J_{C-F} = 246.4), 149.4, 143.4, 142.4 (d, J_{C-F} = 2.0 Hz), 140.3 (d, J_{C-F} = 3.4 Hz), 138.6, 136.7, 133.9, 131.6 (d, J_{C-F} = 9.1 Hz), 129.1, 128.0, 126.9, 126.2 (d, J_{C-F} = 1.7 Hz), 125.8, 125.1 (d, J_{C-F} = 18.9 Hz), 123.3, 122.4, 118.1, 115.5 (d, J_{C-F} = 22.1 Hz); ^{19}F {^{1}H} NMR (∼376 MHz, $CDCl_3$): δ_F −116.04; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{22}H_{17}FN_3O_3S$: 422.0975; found: 422.0969.

*3-Bromo-N-(quinolin-8-yl)-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxamide (**27f**).* Following the general procedure, **27f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (68%, 33 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 242−244 °C; IR (DCM): 2928, 1666, 1166, 1021, 759 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.58 (1H, br. s), 8.88 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.44−8.40 (2H, m), 7.81 (1H, dd, J_1 = 7.7 Hz, J_2 = 1.4 Hz), 7.75 (4H, s), 7.73 (1H, dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz), 7.64−7.58 (2H, m), 7.54 (1H, t, J = 7.7 Hz), 7.50 (1H, dd, J_1 = 7.7 Hz, J_2 = 1.4 Hz), 7.35 (2H, br. s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 165.4, 149.2, 143.4, 142.5, 139.9, 138.7, 138.0, 136.6, 133.8, 132.1, 131.0, 129.4, 129.2, 128.2, 127.9, 126.8, 125.6, 123.1, 122.3, 119.9, 118.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{22}H_{17}BrN_3O_3S$: 482.0174; found: 482.0174.

*4-Methyl-N-(quinolin-8-yl)-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxamide (**27g**).* Following the general procedure, **27g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (60%, 25 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 180−182 °C; IR (DCM): 2928, 1667, 1322, 1161, 766 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.09 (1H, br. s), 8.77 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.55 (1H, d, J = 7.5 Hz), 8.38 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz), 7.77 (2H, d, J = 8.2 Hz), 7.70−7.56 (6H, m), 7.49 (1H, d, J = 8.0 Hz), 7.43 (1H, d, J = 7.8 Hz), 7.33 (2H, br. s), 2.45 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 166.9, 149.1, 143.3, 142.9, 138.1, 138.0, 136.6, 135.9, 135.7, 134.1, 131.4, 130.7, 129.1, 128.8, 127.8, 126.9, 125.7, 122.4, 122.3, 116.5, 20.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{23}H_{20}N_3O_3S$: 418.1225; found: 418.1216.

*5′-Methyl-N-(quinolin-8-yl)-4,4″-disulfamoyl-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**27h**).* Following the general procedure, **27h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (65%, 37 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 230−232 °C; IR (DCM): 2928, 1726, 1288, 1016, 760 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.14 (1H, br. s), 8.76 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.32 (1H, dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz), 8.07 (1H, dd, J_1 = 7.6 Hz, J_2 = 0.9 Hz), 7.73 (8H, s), 7.64 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.0 Hz), 7.55 (1H, dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.47 (1H, t, J = 8.0 Hz), 7.38 (2H, s), 7.32 (4H, br. s), 2.49 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 166.6, 149.2, 143.5, 143.1, 139.5, 138.8, 138.5, 136.5, 133.6, 133.3, 130.5, 129.2, 127.8, 126.7, 125.5, 123.1, 122.2, 118.2, 20.9; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{29}H_{23}N_4O_5S_2$: 571.1110; found: 571.1086.

*N-(Quinolin-8-yl)-4,4″-disulfamoyl-(1,1′:3′,1″-terphenyl)-2′-carboxamide (**27i**).* Following the general procedure, **27i** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (68%, 38 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 150−152 °C; IR (DCM): 2932, 1661, 1167, 1021, 754 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.31 (1H, br. s), 8.79 (1H, d, J = 2.8 Hz), 8.35−8.33 (1H, m), 8.04 (1H, d, J = 7.3 Hz), 7.79−7.74 (8H, m), 7.71 (1H, d, J = 7.7 Hz), 7.66 (1H, d, J = 8.1 Hz), 7.57−7.55 (3H, m), 7.49 (1H, t, J = 7.9 Hz), 7.34 (4H, br. s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 166.5, 149.3, 143.4, 143.1, 139.0, 138.5, 136.5, 135.9, 133.6, 130.0, 129.8, 129.2, 127.9, 126.7, 125.6, 123.3, 122.2, 118.7; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{28}H_{23}N_4O_5S_2$: 559.1110; found: 559.1113.

*2-(3-Chloro-4′-sulfamoyl-(1,1′-biphenyl)-2-yl)-N-(quinolin-8-yl)acetamide (**27j**).* Following the general procedure, **27j** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (68%, 31 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 136−138 °C; IR (DCM): 2930, 1665, 1162, 1019, 740 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.31 (1H, br. s), 8.89 (1H, dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.58−8.56 (1H, m), 8.40 (1H, dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz), 7.88 (2H, d, J = 8.4 Hz), 7.68 (1H, dd, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.64−7.55 (5H, m), 7.45 (1H, t, J = 7.9 Hz), 7.39 (2H, br. s), 7.32 (1H, dd, J_1 = 7.7 Hz, J_2 = 1.2 Hz), 3.99 (2H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 168.6, 149.0, 143.7, 143.5, 143.4, 138.2, 136.7, 135.3, 134.4, 131.4, 129.5, 129.1, 128.8, 128.7, 127.9, 127.0, 125.9, 122.2, 122.2, 117.0, 40.1; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{23}H_{19}ClN_3O_3S$: 452.0836; found: 452.0833.

*4-Chloro-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxylic Acid (**28a**).* Following the general procedure, **28a** was obtained

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after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless semisolid (61%, 19 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; IR (DCM): 2925, 2256, 1657, 1271, 1023, 762 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.85−81 (3H, m), 7.68 (1H, dd, J_1 = 8.2 Hz, J_2 = 2.0 Hz), 7.51 (2H, d, J = 8.2 Hz), 7.44−7.43 (3H, m); (The proton signal of COOH is not clearly identified); ^{13}C NMR (∼101.0 MHz, DMSO-d_6): δ_C 167.7, 143.2, 143.1, 138.8, 133.7, 132.8, 132.6, 131.0, 129.1, 128.9, 125.5; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{13}H_9ClNO_4S$: 309.9941; found: 309.9948.

*4-Methoxy-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxylic Acid (**28d**).* Following the general procedure, **28d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 90:10) as a colorless semisolid (62%, 19 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; IR (DCM): 2922, 1716, 1280, 1162, 824 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.81 (2H, d, J = 8.4 Hz), 7.46 (2H, d, J = 8.4 Hz), 7.39 (2H, br. s), 7.32 (1H, d, J = 8.5 Hz), 7.29 (1H, d, J = 2.8 Hz), 7.17 (1H, dd, J_1 = 8.5 Hz, J_2 = 2.8 Hz), 3.83 (3H, s); (The proton signal of COOH is not clearly identified); ^{13}C NMR (∼101.0 MHz, DMSO-d_6): δ_C 169.0, 158.8, 144.3, 142.4, 133.2, 132.3, 132.1, 129.0, 125.5, 117.0, 114.6, 55.6; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{14}H_{12}NO_5S$: 306.0436; found: 306.0422.

*4-Methyl-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxylic Acid (**28e**).* Following the general procedure, **28e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 90:10) as a colorless semisolid (41%, 12 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; IR (DCM): 2929, 1707, 1271, 1012, 739 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.82 (2H, d, J = 8.0 Hz), 7.61 (1H, s), 7.47−40 (5H, m), 7.28 (1H, d, J = 7.8 Hz), 2.39 (3H, s); (The proton signal of COOH is not clearly identified); ^{13}C NMR (∼101.0 MHz, DMSO-d_6): δ_C 169.2, 144.5, 142.6, 137.7, 137.2, 131.9, 131.8, 130.6, 130.0, 128.9, 125.4, 20.5; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{14}H_{12}NO_4S$: 290.0487; found: 290.0490.

*3-Methyl-4′-sulfamoyl-(1,1′-biphenyl)-2-carboxylic Acid (**28f**).* Following the general procedure, **28f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 95:05) as a colorless semisolid (65%, 19 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.10; IR (DCM): 2924, 1660, 1163, 1024, 763 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.83 (2H, d, J = 8.4 Hz), 7.60 (2H, d, J = 8.4 Hz), 7.42 (2H, br. s), 7.33 (1H, t, J = 7.6 Hz), 7.26 (1H, d, J = 7.3 Hz), 7.18 (1H, d, J = 7.4 Hz), 2.31 (3H, s); (The proton signal of COOH is not clearly identified); ^{13}C NMR (∼101.0 MHz, DMSO-d_6): δ_C 172.6, 145.3, 142.3, 135.3, 133.3, 129.3, 128.9, 126.7, 125.5, 19.7; Carbon count: 10 (2 peak missing); HRMS (ESI): m/z (M+Na)$^+$ calcd for $C_{14}H_{13}NNaO_4S$: 314.0463; found: 314.0461.

*3′-Methoxy-(1,1′-biphenyl)-4-sulfonamide (**29b**).* Following the general procedure, **29b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (64%, 17 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 130−132 °C; IR (DCM): 2934, 1586, 1316, 1162, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.90 (2H, d, J = 8.2 Hz), 7.86 (2H, d, J = 8.3 Hz), 7.43 (2H, br. s), 7.43−7.39 (1H, m), 7.28 (1H, d, J = 7.7 Hz), 7.24 (1H, s), 6.99 (1H, d, J = 8.0 Hz), 3.82 (3H, s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 160.0, 143.5, 143.1, 140.4, 130.4, 127.5, 126.4, 119.5, 114.1, 112.6, 55.4; HRMS (ESI): m/z (M+Na)$^+$ calcd for $C_{13}H_{13}NNaO_3S$: 286.0514; found: 286.0518.

*4-(Benzofuran-3-yl)benzenesulfonamide (**29c**).* Following the general procedure, **29c** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (58%, 16 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 146−148 °C; IR (DCM): 2932, 1597, 1329, 1163, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 8.52 (1H, br. s), 8.00−7.93 (4H, m), 7.70 (1H, dd, J_1 = 7.5 Hz, J_2 = 1.2 Hz), 7.44−7.37 (4H, m); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 155.3, 144.1, 142.8, 135.0, 127.3, 126.5, 125.1, 123.7, 120.5, 120.1, 112.0; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{14}H_{10}NO_3S$: 272.0382; found: 272.0374.

*4-(Benzo(b)thiophen-3-yl)benzenesulfonamide (**29d**).* Following the general procedure, **29d** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (59%, 17 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 192−194 °C; IR (DCM): 2929, 2345, 1329, 1156, 745 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 8.12−8.09 (1H, m), 7.98−7.96 (3H, m), 7.93−7.91 (1H, m), 7.84−7.79 (2H, m), 7.49−7.45 (3H, m); ^{13}C NMR (∼101.0 MHz, DMSO-d_6): δ_C 143.1, 140.2, 138.6, 136.8, 135.7, 128.8, 126.4, 125.0, 124.9, 123.4, 122.3; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{14}H_{10}NO_2S_2$: 288.0153; found: 288.0142.

*4-(Thiophen-3-yl)benzenesulfonamide (**29e**).* Following the general procedure, **29e** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (67%, 16 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 218−220 °C; IR (DCM): 2924, 1530, 1284, 1160, 760 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 8.05 (1H, dd, J_1 = 2.8 Hz, J_2 = 1.3 Hz), 7.92 (2H, d, J = 8.5 Hz), 7.84 (2H, d, J = 8.5 Hz), 7.69 (1H, dd, J_1 = 5.0 Hz, J_2 = 2.9 Hz), 7.64 (1H, dd, J_1 = 5.0 Hz, J_2 = 1.3 Hz), 7.38 (2H, br. s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 142.4, 140.0, 138.2, 127.7, 126.4, 126.3, 126.3, 123.0; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{10}H_8NO_2S_2$: 237.9997; found: 237.9984.

*3′-Ethoxy-(1,1′-biphenyl)-4-sulfonamide (**29f**).* Following the general procedure, **29f** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 60:40) as a colorless solid (61%, 17 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.40; mp: 112−114 °C; IR (DCM): 2927, 1584, 1320, 1161, 762 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.91−7.85 (4H, m), 7.43 (2H, br. s), 7.40 (1H, t, J = 8.0 Hz), 7.27 (1H, d, J = 8.0 Hz), 7.24−7.23 (1H, m), 6.98 (1H, dd, J_1 = 8.2 Hz, J_2 = 2.0 Hz), 4.10 (2H, q, J = 7.0 Hz), 1.35 (3H, t, J = 7.0 Hz); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 159.2, 143.4, 143.1, 140.2, 130.3, 127.4, 126.3, 119.3, 114.4, 113.1, 63.2, 14.8; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{14}H_{14}NO_3S$: 276.0695; found: 276.0683.

*4-(Naphthalen-2-yl)benzenesulfonamide (**29g**).* Following the general procedure, **29g** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 90:10) as a colorless solid (63%, 18 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.10; mp: 130−132 °C; IR (DCM): 2929, 1726, 1283, 1158, 757 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 8.32 (1H, s), 8.06−8.02 (4H, m), 7.98−7.89 (4H, m), 7.58−7.55 (2H, m), 7.44 (2H, br. s); ^{13}C {^1H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 143.2, 143.0, 136.0, 133.2, 132.6, 128.7, 128.4, 127.6, 127.5, 126.7, 126.4, 126.1, 125.0;

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HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{16}H_{12}NO_2S$: 282.0589; found: 282.0576.

*4-(2,3-Dihydrobenzo(b)(1,4)dioxin-6-yl)-benzenesulfonamide (**29h**).* Following the general procedure, **29h** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (69%, 20 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 213−215 °C; IR (DCM): 2928, 1726, 1309, 1160, 715 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.84 (2H, d, J = 8.6 Hz), 7.79 (2H, d, J = 8.5 Hz), 7.37 (2H, br. s), 7.25 (1H, d, J = 2.2 Hz), 7.21 (1H, dd, J_1 = 8.4 Hz, J_2 = 2.2 Hz), 6.97 (1H, d, J = 8.4 Hz), 4.29 (4H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 143.9, 143.8, 142.8, 142.3, 131.9, 126.6, 126.2, 119.9, 117.7, 115.5, 64.2, 64.1; HRMS (ESI): m/z (M+Na)$^+$ calcd for $C_{14}H_{13}NNaO_4S$: 314.0463; found: 314.0451.

*4-(Pyren-2-yl)benzenesulfonamide (**29i**).* Following the general procedure, **29i** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a colorless solid (59%, 21 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; mp: 248−250 °C; IR (DCM): 3396, 1654, 1292, 1153, 763 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.69 (2H, s), 8.33 (2H, d, J = 7.7 Hz), 8.30−8.21 (6H, m), 8.10 (1H, t, J = 7.7 Hz), 8.03 (2H, d, J = 8.4 Hz), 7.49 (2H, br. s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 143.6, 143.2, 136.5, 131.3, 130.8, 128.2, 128.1, 127.6, 126.7, 126.6, 125.5, 123.6, 123.5, 123.5; HRMS (ESI): m/z (M)$^+$ calcd for $C_{22}H_{15}NO_2S$: 357.0823; found: 357.0818.

*5′-Methoxy-(1,1′:3′,1″-terphenyl)-4,4″-disulfonamide (**29j**).* Following the general procedure, **29j** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (60%, 25 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 222−224 °C; IR (DCM): 2922, 1733, 1328, 1153, 821 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.01−7.99 (4H, m), 7.92−7.90 (4H, m), 7.62 (1H, t, J = 1.4 Hz), 7.44 (4H, br. s), 7.33 (2H, d, J = 1.4 Hz), 3.92 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 160.5, 143.3, 143.1, 141.0, 127.7, 126.2, 118.4, 112.6, 55.6; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{19}H_{17}N_2O_5S_2$: 417.0579; found: 417.0570.

*4′-Chloro-2′-(4-methylbenzoyl)-(1,1′-biphenyl)-4-sulfonamide (**30a**).* Following the general procedure, **30a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (44%, 17 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.60; mp: 160−162 °C; IR (DCM): 3401, 2256, 1658, 1162, 762 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.75−7.71 (3H, m), 7.60−7.56 (4H, m), 7.41 (2H, d, J = 8.2 Hz), 7.38 (2H, br. s), 7.26 (2H, d, J = 8.0 Hz), 2.33 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 195.2, 144.7, 143.2, 142.0, 140.4, 137.5, 133.6, 132.9, 132.2, 130.4, 129.9, 129.5, 129.1, 127.9, 125.8, 21.3; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{20}H_{17}ClNO_3S$: 386.0618; found: 386.0618.

*4′-Chloro-2′-(3,4-dimethylbenzoyl)-(1,1′-biphenyl)-4-sulfonamide (**30b**).* Following the general procedure, **30b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 50:50) as a colorless solid (52%, 21 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 186−188 °C; IR (DCM): 2924, 2256, 1660, 1163, 762 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.75−7.73 (1H, m), 7.71 (2H, d, J = 8.3 Hz), 7.58 (1H, d, J = 8.4 Hz), 7.53 (1H, d, J = 2.1 Hz), 7.48 (1H, br. s), 7.41−7.36 (5H, m), 7.22 (1H, d, J = 7.9 Hz), 2.25 (3H, s), 2.21 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 195.2, 143.6, 143.2, 142.1, 140.5, 137.6, 137.0, 133.9, 132.8, 132.2, 130.4, 130.3, 129.9, 129.1, 127.9, 127.8, 125.7, 19.7, 19.3; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{21}H_{17}ClNO_3S$: 398.0618; found: 398.0621.

*4-(9-Oxo-9H-xanthen-1-yl)benzenesulfonamide (**31a**).* Following the general procedure, **31a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 70:30) as a colorless solid (63%, 22 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.50; mp: 270−272 °C; IR (DCM): 2928, 1729, 1333, 1167, 744 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.01 (1H, dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz), 7.90−7.83 (4H, m), 7.73 (1H, dd, J_1 = 8.4 Hz, J_2 = 1.0 Hz), 7.67 (1H, d, J = 8.0 Hz), 7.51−7.49 (2H, m), 7.45−7.41 (3H, m), 7.21 (1H, dd, J_1 = 7.4 Hz, J_2 = 1.1 Hz); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 175.9, 156.7, 154.9, 145.2, 142.5, 141.8, 135.5, 134.5, 129.2, 127.3, 126.2, 124.9, 124.4, 122.0, 118.6, 118.6, 117.8; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{19}H_{12}NO_4S$: 350.0487; found: 350.0478.

*4-(7-Methyl-9-oxo-9H-fluoren-1-yl)benzenesulfonamide (**31b**).* Following the general procedure, **31b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80:20) as a yellow colored solid (60%, 21 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.30; mp: 220−222 °C; IR (DCM): 2928, 1712, 1286, 1025, 740 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.88 (2H, d, J = 8.3 Hz), 7.77 (1H, d, J = 7.4 Hz), 7.70−7.68 (3H, m), 7.62 (1H, t, J = 7.6 Hz), 7.48 (2H, br. s), 7.41 (1H, d, J = 7.6 Hz), 7.32 (1H, s), 7.23 (1H, d, J = 7.5 Hz), 2.33 (3H, s); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 192.4, 145.3, 143.6, 140.6, 140.4, 139.7, 139.6, 135.6, 135.1, 133.6, 131.0, 129.7, 129.2, 125.2, 124.3, 120.9, 120.5, 21.0; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{20}H_{16}NO_3S$: 350.0851; found: 350.0842.

*4′-(N-Benzylsulfamoyl)-4-chloro-(1,1′-biphenyl)-2-carboxylic acid (**32a**).* Following the general procedure, **32a** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 90:10) as a colorless solid (75%, 30 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; mp: 118−120 °C; IR (DCM): 3273, 2924, 1715, 1459, 701 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.24 (1H, t, J = 6.3 Hz), 7.82−7.80 (3H, m), 7.69 (1H, dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.50 (2H, d, J = 8.2 Hz), 7.43 (1H, d, J = 8.2 Hz), 7.30−7.22 (5H, m), 4.02 (2H, d, J = 6.2 Hz); (The proton signal of COOH is not clearly identified); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 167.9, 143.9, 139.8, 138.8, 137.7, 134.0, 133.0, 132.7, 131.2, 129.3, 129.2, 128.5, 127.8, 127.4, 126.5, 46.3; HRMS (ESI): m/z (M - H)$^+$ calcd for $C_{20}H_{15}ClNO_4S$: 400.0411; found: 400.0404.

*4-Chloro-4′-(methylsulfonamido)-(1,1′-biphenyl)-2-carboxylic acid (**32b**).* Following the general procedure, **32b** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 90:10) as a colorless solid (77%, 25 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50:50) 0.20; mp: 122−124 °C; IR (DCM): 3310, 2924, 1663, 1526, 759 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 9.88 (1H, br. s), 7.72 (1H, d, J = 2.2 Hz), 7.62 (1H, dd, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.40 (1H, d, J = 8.3 Hz), 7.29 (2H, d, J = 8.5 Hz), 7.23 (2H, d, J = 8.5 Hz), 3.03 (3H, s); (The proton signal of COOH is not clearly identified); ^{13}C {^{1}H} NMR (∼101.0 MHz, DMSO-d_6): δ_C 168.4, 139.1, 137.9, 134.9, 134.1, 132.3, 131.9, 130.7, 129.3, 128.6, 119.2, 40.1; HRMS (ESI): m/z (M+Na)$^+$ calcd for $C_{14}H_{12}ClNNaO_4S$: 348.0073; found: 348.0059.

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■ ASSOCIATED CONTENT

Data Availability Statement

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

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c10558.

X-ray structure and brief X-ray structure data of the data of compound **29b**, copies of ^{1}H and ^{13}C NMR charts of isolated compounds (PDF)

X-ray structure data of the compound **29b** (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Selected reviews on sulfonamides: (a) Lesch, J. E. *The First Miracle Drugs: How the Sulfa Drugs Transformed Medicine*; Oxford University Press: Oxford, 2006. (b) Drews, J. Drug discovery: A historical perspective. *Science* **2000**, *287*, 1960−1964. (c) Supuran, C. T. Special issue: Sulfonamides. *Molecules* **2017**, *22*, 1642. (d) Ilardi, E. A.; Vitaku, E.; Njardarson, J. T. Data-mining for sulfur and fluorine: An evaluation of pharmaceuticals to reveal opportunities for drug design and discovery. *J. Med. Chem.* **2014**, *57*, 2832−2842. (e) Sarkar, D. *Sulfonamides: An Overview*; Nova Science Publishers Inc.: New York, 2020. (f) Fischer, J.; Ganellin, C. R. *Analogue-based Drug Discovery*; John Wiley-VCH Verlag GmbH & Co.: Weinheim, 2006. (g) Chinthakindi, P. K.; Naicker, T.; Thota, N.; Govender, T.; Kruger, H. G.; Arvidsson, P. I. Sulfonimidamides in medicinal and agricultural chemistry. *Angew. Chem., Int. Ed.* **2017**, *56*, 4100−4109. (h) Mujumdar, P.; Poulsen, S.-A. Natural product primary sulfonamides and primary sulfamates. *J. Nat. Prod.* **2015**, *78*, 1470−1477.

(2) Selected reviews on sulfonamides: (a) Supuran, C. T.; Casini, A.; Scozzafava, A. Protease inhibitors of the sulfonamide type: Anticancer, antiinflammatory, and antiviral agents. *Med. Res. Rev.* **2003**, *23*, 535−558. (b) Wan, Y.; Fang, G.; Chen, H.; Deng, X.; Tang, Z. Sulfonamide derivatives as potential anti-cancer agents and their SARS elucidation. *Eur. J. Med. Chem.* **2021**, *226*, 113837. (c) Jain, P.; Saravanan, C.; Singh, S. K. Sulfonamides: Deserving class as MMP inhibitors? *Eur. J. Med. Chem.* **2013**, *60*, 89−100. (d) Elgemeie, G. H.; Azzam, R. A.; Elsayed, R. E. Sulfa drug analogs: New classes of *n*-sulfonyl aminated azines and their biological and preclinical importance in medicinal chemistry (2000−2018). *Med. Chem. Res.* **2019**, *28*, 1099−1131. (e) Ovung, A.; Bhattacharyya, J. Sulfonamide drugs: Structure, antibacterial property, toxicity, and biophysical interactions. *Biophys. Rev.* **2021**, *13*, 259−272. (f) Ammazzalorso, A.; Filippis, B. E.; Giampietro, L.; Amoroso, R. *N*-Acylsulfonamides: Synthetic routes and biological potential in medicinal chemistry. *Chem. Biol. Drug. Des.* **2017**, *90*, 1094−1105. (g) Ballatore, C.; Huryn, D. M.; Smith, A. B., III Carboxylic acid (bio)isosteres in drug design. *ChemMedChem.* **2013**, *8*, 385−395. (h) Petkowski, J. J.; Bains, W.; Seager, S. Natural products containing a nitrogen−sulfur bond. *J. Nat. Prod.* **2018**, *81*, 423−446.

(3) Selected reviews on sulfonamides: (a) Apaydın, S.; Török, M. Sulfonamide derivatives as multi-target agents for complex diseases. *Bioorg. Med. Chem. Lett.* **2019**, *29*, 2042−2050. (b) Moskalik, M. Y. Sulfonamides with heterocyclic periphery as antiviral agents. *Molecules* **2023**, *28*, 51. (c) Chen, Y. Recent functionalizations of primary sulfonamides. *Synthesis* **2016**, *48*, 2483−2522. (d) Mondal, S.; Malakar, S. Synthesis of sulfonamide and their synthetic and therapeutic applications: Recent advances. *Tetrahedron* **2020**, *76*, 131662. (e) Ashfaq, M.; Shah, S. S. A.; Najjam, T.; Shaheen, S.; Rivera, G. Synthetic routes of sulfonamide derivatives: A brief review. *Mini-Rev. Org. Chem.* **2013**, *10*, 160−170. (f) Zafar, W.; Sumrra, S. H.; Hassan, A. U.; Chohan, Z. H. A review on 'sulfonamides': Their chemistry and pharmacological potentials for designing therapeutic drugs in medical science. *J. Coord. Chem.* **2023**, *76*, 546−580. (g) Smith, C. L.; Powell, K. R. Review of the sulfonamides and trimethoprim. *Pediatr. Rev.* **2000**, *21*, 368−371. (h) Ghosh, S.; Pal, P. P.; Hajra, A. *N*-Heteroarylation of sulfonamides: An overview. *Adv. Synth. Catal.* **2023**, *365*, 3020−3043. (i) Liu, W.; Chen, J.; Su, W. Recent advances in the synthesis of sulfonamides intermediates. *Pharmaceut. Fronts* **2024**, *6*, e355−e381.

(4) Selected papers on bioactive biaryl-based sulfonamides: (a) Chakravarty, P. K.; Naylor, E. M.; Chen, A.; Chang, R. S. L.; Chen, T.-B.; Faust, K. A.; Lotti, V. J.; Kivlighn, S. D.; Gable, R. A.; Zingaro, G. J.; Schorn, T. W.; Schaffer, L. W.; Broten, T. P.; Siegl, P. K. S.; Patchett, A. A.; Greenlee, W. J. A highly potent, orally active imidazo(4,5-b)pyridine biphenyl acylsulfonamide (MK-996; L-159,282): A new at1-selective angiotensin II receptor antagonist. *J. Med. Chem.* **1994**, *37*, 4068−4072. (b) Verhoest, P. R.; Basak, A. S.; Parikh, V.; Hayward, M.; Kauffman, G. W.; Paradis, V.; McHardy, S. F.; McLean, S.; Grimwood, S.; Schmidt, A. W.; Frawley, M. V.; Freeman, J.; Deusen, J. V.; Cox, L.; Wong, D.; Liras, S. Design and discovery of a selective small molecule κ opioid antagonist (2-methyl-N-((2′-(pyrrolidin-1-ylsulfonyl)biphenyl-4-yl)methyl)propan-1-amine, PF-4455242). *J. Med. Chem.* **2011**, *54*, 5868−5877. (c) Eijkelkamp, N.; Linley, J. E.; Baker, M. D.; Minett, M. S.; Cregg, R.; Werdehausen, R.; Rugiero, F.; Wood, J. N. Neurological perspectives on voltage-gated sodium channels. *Brain* **2012**, *135*, 2585−2612. (d) Chen, Q.-H.; Rao, P. N. P.; Knaus, E. K. Design, synthesis, and biological evaluation of *n*-acetyl-2-(or 3-)-carboxymethylbenzenesulfonamides as cyclooxygenase isozyme inhibitors. *Bioorg. Med. Chem.* **2005**, *13*, 4694−4703. (e) Yamamoto, H.; Kondo, M.; Nakamori, S.; Nagano, H.; Wakasa, K.-I.; Sugita, Y.; Chang-de, J.; Kobayashi, S.; Damdinsuren, B.; Dono, K.; Umeshita, K.; Sekimoto, M.; Sakon, M.; Matsuura, N.; Monden, M. JTE-522, A cyclooxygenase-2 inhibitor, is an effective chemopreventive agent against rat experimental liver fibrosis. *Gastoenterology* **2003**, *125*, 556−571.

(5) Selected papers on bioactive biaryl-based sulfonamides: (a) Murugesan, N.; Gu, Z.; Spergel, S.; Young, M.; Chen, P.; Mathur, A.; Leith, L.; Hermsmeier, M.; Liu, E. C.-K.; Zhang, R.; Bird, E.; Waldron, T.; Marino, A.; Koplowitz, B.; Humphreys, W. G.;

Chong, S.; Morrison, R. A.; Webb, M. L.; Moreland, S.; Trippodo, N.; Barrish, J. C. Biphenylsulfonamide endothelin receptor antagonists. 4. Discovery of *N*-((2′-(((4,5-dimethyl-3-isoxazolyl)amino)sulfonyl)-4-(2-oxazolyl)(1,1′-biphenyl)- 2-yl)methyl)-n,3,3-trimethylbutanamide (BMS-207940), a highly potent and orally active ET_A selective antagonist. *J. Med. Chem.* **2003**, *46*, 125−137. (b) Murugesan, N.; Gu, Z.; Stein, P. D.; Bisaha, S.; Spergel, S.; Girotra, R.; Lee, V. G.; Lloyd, J.; Misra, R. N.; Schmidt, J.; Mathur, A.; Stratton, L.; Kelly, Y. F.; Bird, E.; Waldron, T.; Liu, E. C.-K.; Zhang, R.; Lee, H.; Serafino, R.; Abboa-Offei, B.; Mathers, P.; Giancarli, M.; Seymour, A. A.; Webb, M. L.; Moreland, S.; Barrish, J. C.; Hunt, J. T. Biphenylsulfonamide endothelin antagonists: Structure−activity relationships of a series of mono- and disubstituted analogues and pharmacology of the orally active endothelin antagonist 2′-amino-*N*- (3,4-dimethyl-5-isoxazolyl)-4′-(2-methylpropyl)(1,1′-biphenyl)-2-sulfonamide (BMS-187308). *J. Med. Chem.* **1998**, *41*, 5198−5218. (c) Leśniak, R. K.; Nichols, R. J.; Schonemann, M.; Zhao, J.; Gajera, C. R.; Lam, G.; Nguyen, K. C.; Langston, J. W.; Smith, M.; Montine, T. J. Discovery of 1*H*-pyrazole biaryl sulfonamides as novel G2019S-LRRK2 kinase inhibitors. *ACS Med. Chem. Lett.* **2022**, *37*, 981−988. (d) Peter, K.; Olaf, T.; Reinhard, D. Development of encorafenib for BRAF-mutated advanced melanoma. *Curr. Opin. Oncol.* **2018**, *30*, 125. (e) DiMauro, E. F.; Altmann, S.; Berry, L. M.; Bregman, H.; Chakka, N.; Chu-Moyer, M.; Bojic, E. F.; Foti, R. S.; Fremeau, R.; Gao, H.; Gunaydin, H.; Guzman-Perez, A.; Hall, B. E.; Huang, H.; Jarosh, M.; Kornecook, T.; Lee, J.; Ligutti, J.; Liu, D.; Moyer, B. D.; Ortuno, D.; Rose, P. E.; Schenkel, L. B.; Taborn, K.; Wang, J.; Wang, Y.; Yu, V.; Weiss, M. M. Application of a parallel synthetic strategy in the discovery of biaryl acyl sulfonamides as efficient and selective NaV1.7 inhibitors. *J. Med. Chem.* **2016**, *59*, 7818−7839. (f) Lai, M.-J.; Lee, H.-Y.; Chuang, H.-Y.; Chang, L.-H.; Tsai, A.-C.; Chen, M.-C.; Huang, H.-L.; Wu, Y.-W.; Teng, C.-M.; Pan, S.-L.; Liu, Y.-M.; Mehndiratta, S.; Liou, J.-P. N-Sulfonyl-aminobiaryls as antitubulin agents and inhibitors of signal transducers and activators of transcription 3 (STAT3) signaling. *J. Med. Chem.* **2015**, *58*, 6549−6558. (g) Xie, Z.; Tian, Y.; Lv, X.; Xiao, X.; Zhan, M.; Cheng, K.; Li, S.; Liao, C. The selectivity and bioavailability improvement of novel oral anticoagulants: An overview. *Eur. J. Med. Chem.* **2018**, *146*, 299−317. (h) Gaulier, S. M.; McKay, R.; Swain, N. A. A Novel three-step synthesis of celecoxib *via* palladium-catalyzed direct arylation. *Tetrahedron Lett.* **2011**, *52*, 6000−6002.

(6) Selected papers on bioactive biaryl-based sulfonamides: (a) Brand, S.; Cleghorn, L. A. T.; McElroy, S. P.; Robinson, D. A.; Smith, V. C.; Hallyburton, I.; Harrison, J. R.; Norcross, N. R.; Spinks, D.; Bayliss, T.; Norval, S.; Stojanovski, L.; Torrie, L. S.; Frearson, J. A.; Brenk, R.; Fairlamb, A. H.; Ferguson, M. A. J.; Read, K. D.; Wyatt, P. G.; Gilbert, I. H. Discovery of a novel class of orally active trypanocidal *N*-myristoyltransferase inhibitors. *J. Med. Chem.* **2012**, *55*, 140. (b) Ehmann, D. E.; Demeritt, J. E.; Hull, K. G.; Fisher, S. L. *Biochim. Biophys. Acta* **2004**, *1698*, 167. (c) Liin, S. I.; Lund, P.-E.; Larsson, J. E.; Brask, J.; Wallner, B.; Elinder, F. Biaryl sulfonamide motifs up- or down-regulate ion channel activity by activating voltage sensors. *J. Gen. Physiol.* **2018**, *150*, 1215−1230. (d) Nair, S. K.; Matthews, J. J.; Cripps, S. J.; Cheng, H.; Hoffman, J. E.; Smith, C.; Kupchinsky, S.; Siu, M.; Taylor, W. D.; Wang, Y.; Johnson, T. O.; Dress, K. R.; Edwards, M. P.; Zhou, S.; Hosea, N. A.; LaPaglia, A.; Kang, P.; Castro, A.; Ermolieff, J.; Fanjul, A.; Vogel, J. E.; Rejto, P.; Dalvie, D. *N*-(Pyridin-2-yl) arylsulfonamide inhibitors of 11β-hydroxysteroid dehydrogenase type 1: Strategies to eliminate reactive metabolites. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 2344−2348.

(7) Selected papers dealing with synthetic methods toward sulfonamides: (a) Wen, W.; Ai, Z.-P.; Wu, Z.-L.; Cai, T.; Guo, Q.-X. Stereoselective synthesis of Δ(1)-pyrroline sulfonamides *via* a chiral aldehyde mediated cascade reaction. *Org. Chem. Front.* **2023**, *11*, 156−163. (b) Feng, J.-B.; Wu, X.-F. A general iodine-mediated synthesis of primary sulfonamides from thiols and aqueous ammonia. *Org. Biomol. Chem.* **2016**, *14*, 6951−6954. (c) Wang, M.; Fan, Q.; Jiang, X. Metal-free construction of primary sulfonamides through three diverse salts. *Chem. Commun.* **2018**, *20*, 5469−5473. (d) Mukherjee, P.; Woroch, C. P.; Cleary, L.; Rusznak, M.; Franzese, R. W.; Reese, M. R.; Tucker, J. W.; Humphrey, J. M.; Etuk, S. M.; Kwan, S. C.; Am Ende, C. W.; Ball, N. D. Sulfonamide synthesis *via* calcium triflimide activation of sulfonyl fluorides. *Org. Lett.* **2018**, *20*, 3943−3947. (e) Lam, L. Y.; Chan, K. H.; Ma, C. Copper-catalyzed synthesis of functionalized aryl sulfonamides from sodium sulfinates in green solvents. *J. Org. Chem.* **2022**, *87*, 8802−8810. (f) Wakeham, R. J.; Taylor, J. E.; Bull, S. D.; Morris, J. A.; Willams, J. M. J. Iodide as an activating agent for acid chlorides in acylation reactions. *Org. Lett.* **2013**, *15*, 702−705. (g) Gómez-Palomino, A.; Cornella, J. Selective late-stage sulfonyl chloride formation from sulfonamides enabled by Pyry-BF_4. *Angew. Chem., Int. Ed.* **2019**, *58*, 18235−18239.

(8) Selected papers dealing with synthetic methods toward sulfonamides: (a) Ozaki, T.; Yorimitsu, H.; Perry, G. J. P. Primary sulfonamide functionalization *via* sulfonyl pyrroles: Seeing the *N*−Ts bond in a different light. *Chem.—Eur. J.* **2021**, *27*, 15387−15391. (b) Moon, S.-Y.; Nam, J.; Rathwell, K.; Kim, W.-S. Copper-catalyzed Chan−Lam coupling between sulfonyl azides and boronic acids at room temperature. *Org. Lett.* **2014**, *16*, 338−341. (c) Zhang, F.; Zheng, D.; Lai, L.; Cheng, J.; Sun, J.; Wu, J. Synthesis of aromatic sulfonamides through a copper-catalyzed coupling of aryldiazonium tetrafluoroborates, DABCO·$(SO_2)_2$, and *N*-chloroamines. *Org. Lett.* **2018**, *20*, 1167−1170. (d) Davies, T. Q.; Tilby, M. J.; Skolc, D.; Hall, A.; Wills, M. C. Primary Sulfonamide synthesis using the sulfinylamine reagent *N*-sulfinyl-*O*-(*tert*-butyl)hydroxylamine, *t*-BuONSO. *Org. Lett.* **2020**, *22*, 9495−9499.

(9) Selected reviews/articles on biaryls: (a) Corbet, J.-P.; Mignani, G. Selected patented cross-coupling reaction technologies. *Chem. Rev.* **2006**, *106*, 2651−2710. (b) Dieterich, F.; Stang, P. J. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: New York, 1998. (c) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed. Vol. *1*−*2*; Weinheim: Wiley-VCH, 2004. (d) Seechurn, C. C. C. J.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. Palladium-catalyzed cross-coupling: A historical contextual perspective to the 2010 Nobel Prize. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062−5085. (e) Horton, D. A.; Bourne, G. T.; Smythe, M. L. The combinatorial synthesis of bicyclic privileged structures or privileged substructures. *Chem. Rev.* **2003**, *103*, 893−930. (f) Klekota, J.; Roth, F. P. Chemical substructures that enrich for biological activity. *Bioinformatics* **2008**, *24*, 2518−2525. (g) Hajduk, P. J.; Bures, M.; Praestgaard, J.; Fesik, S. W. Privileged molecules for protein binding identified from NMR-based screening. *J. Med. Chem.* **2000**, *43*, 3443−3447. (h) Kloss, F.; Neuwirth, T.; Haensch, V. G.; Hertweck, C. Metal-free synthesis of pharmaceutically important biaryls by photosplicing. *Angew. Chem., Int. Ed.* **2018**, *57*, 14476−14481.

(10) Selected papers on synthesis of bioactive biaryl-based sulfonamides *via* cross-coupling method: (a) See ref 4d, 5a, b. (b) Schneider, C.; Broda, E.; Snieckus, V. Directed *ortho*-metalation−cross-coupling strategies. One-pot Suzuki reaction to biaryl and heterobiaryl sulfonamides. *Org. Lett.* **2011**, *13*, 3588−3591. (c) Covel, J. A.; Santora, V. J.; Smith, J. M.; Hayashi, R.; Gallardo, C.; Weinhouse, M. I.; Ibarra, J. B.; Schultz, J. A.; Park, D. M.; Estrada, S. A.; Hofilena, B. J.; Pulley, M. D.; Smith, B. M.; Ren, A.; Suarez, M.; Frazer, J.; Edwards, J.; Hauser, E. K.; Lorea, J.; Semple, G.; Grottick, A. J. design and evaluation of novel biphenyl sulfonamide derivatives with potent histamine H_3 receptor inverse agonist activity. *J. Med. Chem.* **2009**, *52*, 5603−5611. (d) Murai, N.; Miyano, M.; Yonaga, M.; Tanaka, K. One-pot primary aminomethylation of aryl and heteroaryl halides with sodium phthalimidomethyltrifluoroborate. *Org. Lett.* **2012**, *14*, 2818−2821. (e) Zhao, Z.; Snieckus, V. Directed *ortho* metalation-based methodology. Halo-, nitroso-, and boro-induced *ipso*-desilylation. Link to an *in situ* Suzuki reaction. *Org. Lett.* **2005**, *7*, 2523−2526. (f) Blanchet, J.; Macklin, T.; Ang, P.; Metallinos, C.; Snieckus, V. Directed *ortho* metalation−cross coupling strategies. *N*-cumyl arylsulfonamides. Facile deprotection and expedient route to 7- and 4,7-substituted saccharins. *J. Org. Chem.* **2007**, *72*, 3199−3206.

(11) Selected reviews on C-H functionalization: (a) Kakiuchi, F.; Murai, S. Catalytic C−H/olefin coupling. *Acc. Chem. Res.* **2002**, *35*,

https://doi.org/10.1021/acsomega.4c10558
ACS Omega 2025, 10, 17361−17393

826−834. (b) Lu, M.-Z.; Goh, J.; Maraswami, M.; Jia, Z.; Tian, J.-S.; Loh, T.-P. Recent advances in alkenyl sp^2 C−H and C−F bond functionalizations: Scope, mechanism, and applications. *Chem. Rev.* **2022**, *122*, 17479−17646. (c) Rej, S.; Das, A.; Chatani, N. Strategic evolution in transition metal-catalyzed directed C−H bond activation and future directions. *Coord. Chem. Rev.* **2021**, *431*, 213683. (d) Colby, D. A.; Bergman, R. G.; Ellman, J. A. Rhodium-catalyzed C−C bond formation *via* heteroatom-directed C−H bond activation. *Chem. Rev.* **2010**, *110*, 624−655. (e) Li, B.; Dixneuf, P. H. sp^2 C−H bond activation in water and catalytic cross-coupling reactions. *Chem. Soc. Rev.* **2013**, *42*, 5744−5767. (f) Miura, M.; Satoh, T.; Hirano, K. Development of direct aromatic coupling reactions by transition-metal catalysis. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 751−764. (g) Lyons, T. W.; Sanford, M. S. Palladium-catalyzed ligand-directed C−H functionalization reactions. *Chem. Rev.* **2010**, *110*, 1147−1169. (h) de Carvalho, R. L.; Diogo, E. B. T.; Homölle, S. L.; Dana, S.; da Silva Júnior, E. N.; Ackermann, L. The crucial role of silver(I)-salts as additives in C−H activation reactions: Overall analysis of their versatility and applicability. *Chem. Soc. Rev.* **2023**, *52*, 6359−6378.

(12) Selected reviews on C-H functionalization: (a) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J.-Q. Palladium(II)-catalyzed C-H activation/C-C cross-coupling reactions: Versatility and practicality. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115. (b) Yang, Y.; Lan, J.; You, J. Oxidative C−H/C−H coupling reactions between two (hetero)arenes. *Chem. Rev.* **2017**, *117*, 8787−8863. (c) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem.* **2010**, *2*, 20. (d) McMurray, L.; O'hara, F.; Gaunt, M. J. Recent developments in natural product synthesis using metal-catalysed C−H bond functionalisation. *Chem. Soc. Rev.* **2011**, *40*, 1885−1898. (e) Sinha, S. K.; Guin, S.; Maiti, S.; Biswas, J. P.; Porey, S.; Maiti, D. Toolbox for distal C−H bond functionalizations in organic molecules. *Chem. Rev.* **2022**, *122*, 5682−5841. (f) Manoharan, R.; Jeganmohan, M. Alkylation, annulation, and alkenylation of organic molecules with maleimides by transition-metal-catalyzed C-H bond activation. *Asian J. Org. Chem.* **2019**, *8*, 1949−1969. (g) Babu, S. A.; Aggarwal, Y.; Patel, P.; Tomar, R. Diastereoselective palladium-catalyzed functionalization of prochiral $C(sp^3)$−H bonds of aliphatic and alicyclic compounds. *Chem. Commun.* **2022**, *58*, 2612−2633. (h) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. C-H bond functionalization: Emerging synthetic tools for natural products and pharmaceuticals. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960−9009.

(13) Selected reviews on bidentate directing group-assisted C-H functionalization: (a) Rej, S.; Ano, Y.; Chatani, N. Bidentate directing groups: an efficient tool in C−H bond functionalization chemistry for the expedient construction of C−C bonds. *Chem. Rev.* **2020**, *120*, 1788−1887. (b) Daugulis, O.; Roane, J.; Tran, L. D. Bidentate, monoanionic auxiliary-directed functionalization of carbon−hydrogen bonds. *Acc. Chem. Res.* **2015**, *48*, 1053−1064. (c) Sambiagio, C.; Schönbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnürch, M. A comprehensive overview of directing groups applied in metal-catalysed C−H functionalisation chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603−6743. (d) He, G.; Wang, B.; Nack, W. A.; Chen, G. Syntheses and transformations of α-amino acids *via* palladium-catalyzed auxiliary-directed sp^3 C−H functionalization. *Acc. Chem. Res.* **2016**, *49*, 635−645. (e) Rit, R. K.; Yadav, M. R.; Ghosh, K.; Sahoo, A. K. Reusable directing groups (8-aminoquinoline, picolinamide, sulfoximine) in $C(sp^3)$−H bond activation: Present and future. *Tetrahedron* **2015**, *71*, 4450−4459. (f) Li, H.; Li, B.-J.; Shi, Z.-J. Challenge and progress: Palladium-catalyzed sp^3 C−H activation. *Catal. Sci. Technol.* **2011**, *1*, 191−206. (g) Liu, B.; Romine, A. M.; Rubel, C. Z.; Engle, K. M.; Shi, B.-F. Transition-metal-catalyzed, coordination-assisted functionalization of nonactivated $C(sp^3)$−H bonds. *Chem. Rev.* **2021**, *121*, 14957−15074. (h) Ni, S.-F.; Huang, G.; Chen, Y.; Wright, J. S.; Li, M.; Dang, L. Recent advances in γ-$C(sp^3)$−H bond activation of amides, aliphatic amines, sulfanilamides and amino acids. *Coord. Chem. Rev.* **2022**, *455*, No. 214255.

(14) Selected reports on bidentate directing group-assisted C-H functionalization: (a) Shabashov, D.; Daugulis, O. Auxiliary-assisted palladium-catalyzed arylation and alkylation of sp^2 and sp^3 carbon−hydrogen bonds. *J. Am. Chem. Soc.* **2010**, *132*, 3965−3972. (b) Reddy, C.; Bisht, N.; Parella, R.; Babu, S. A. 4-Amino-2,1,3-benzothiadiazole as a removable bidentate directing group for the pd(ii)-catalyzed arylation/oxygenation of sp^2/sp^3 β-C−H bonds of carboxamides. *J. Org. Chem.* **2016**, *81*, 12143−12168. (c) Bolsakova, J.; Lukasevics, L.; Grigorjeva, L. Cobalt-catalyzed, directed C−H functionalization/annulation of phenylglycinol derivatives with alkynes. *J. Org. Chem.* **2020**, *85*, 4482−4499. (d) Martínez-Flores, S.; Mujica-Martinez, C. A.; Polindara-García, L. A. Palladium-catalyzed $C(sp^2/sp^3)$−H arylation of aryl glycinamide derivatives using picolinamide as directing group. *Eur. J. Org. Chem.* **2022**, *2022*, No. e202101517. (e) Zhao, Y.; He, G.; Nack, W. A.; Chen, G. Palladium-catalyzed alkenylation and alkynylation of *ortho*-$C(sp^2)$−H bonds of benzylamine picolinamides. *Org. Lett.* **2012**, *14*, 2948−2951. (f) Kuai, C.; Wang, L.; Li, B.; Yang, Z.; Cui, X. Cobalt-catalyzed selective synthesis of isoquinolines using picolinamide as a traceless directing group. *Org. Lett.* **2017**, *19*, 2102−2105. (g) Seki, A.; Takahashi, Y. Pd-catalyzed methylene γ-$C(sp^3)$—H alkenylation of *N*-picolinoylcycloalkylamines with alkenyl iodides promoted by 2-*tert*-butyl-1,4-benzoquinone. *Tetrahedron Lett.* **2021**, *74*, 153130. (h) Xu, J.; Qiao, L.; Shen, J.; Chai, K.; Shen, C.; Zhang, P. Nickel(II)-catalyzed site-selective C−H bond trifluoromethylation of arylamine in water through a coordinating activation strategy. *Org. Lett.* **2017**, *19*, 5661−5664.

(15) Selected reports on bidentate directing group-assisted C-H functionalization: (a) Kanyiva, K. S.; Kuninobu, Y.; Kanai, M. Palladium-catalyzed direct C−H silylation and germanylation of benzamides and carboxamides. *Org. Lett.* **2014**, *16*, 1968−1971. (b) Han, J.; Liu, P.; Wang, C.; Wang, Q.; Zhang, J.; Zhao, Y.; Shi, D.; Huang, Z.; Zhao, Y. Oxalyl amide assisted palladium-catalyzed arylation of $C(sp^2)$−H bond at the δ position. *Org. Lett.* **2014**, *16*, 5682−5685. (c) García-Rubia, A.; Laga, E.; Cativiela, C.; Urriolabeitia, E. P.; Gomez-Arrayás, R.; Carretero, J. C. Pd-catalyzed directed *ortho*-C−H alkenylation of phenylalanine derivatives. *J. Org. Chem.* **2015**, *80*, 3321−3331. (d) Wang, Z.-K.; Wu, Y.-J.; Yao, Q.-J.; Shi, B.-F. Synthesis of chiral diarylmethylamines by cobalt-catalyzed enantioselective C-H alkoxylation. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202304706. (e) Parella, R.; Babu, S. A. Pd(II)-catalyzed, picolinamide-assisted, *Z*-selective γ-arylation of allylamines to construct *Z*-cinnamylamines. *J. Org. Chem.* **2017**, *82*, 6550−6567. (f) Singh, P.; Babu, S. A. Pd-catalyzed arylation and benzylation of tyrosine at the δ−$C(sp^2)$−H and C(2) positions: Expanding the library of unnatural tyrosines. *Eur. J. Org. Chem.* **2023**, *26*, No. e22602300440.

(16) Selected reports on bidentate directing group-assisted C-H functionalization: (a) Uemura, T.; Yamaguchi, M.; Chatani, N. phenyltrimethylammonium salts as methylation reagents in the nickel-catalyzed methylation of C−H bonds. *Angew. Chem., Int. Ed.* **2016**, *55*, 3162−3165. (b) Asako, S.; Ilies, L.; Nakamura, E. Iron-catalyzed *ortho*-allylation of aromatic carboxamides with allyl ethers. *J. Am. Chem. Soc.* **2013**, *135*, 17755−17757. (c) Wang, X.; Niu, S.; Xu, L.; Zhang, C.; Meng, L.; Zhang, X.; Ma, D. Pd-catalyzed dimethylation of tyrosine-derived picolinamide for synthesis of (*S*)-*N*-boc-2,6-dimethyltyrosine and its analogues. *Org. Lett.* **2017**, *19*, 246−249. (d) Zeng, W.; Nukeyeva, M.; Wang, Q.; Jiang, C. synthesis of unnatural α-amino acid derivatives *via* selective *o*-C−H functionalization. *Org. Biomol. Chem.* **2018**, *16*, 598−608. (e) Odani, R.; Hirano, K.; Satoh, T.; Miura, M. Copper-mediated dehydrogenative biaryl coupling of naphthylamines and 1,3-azoles. *J. Org. Chem.* **2013**, *78*, 11045−11052. (f) Roy, S.; Pradhan, S.; Punniyamurthy, T. Copper-mediated regioselective C−H etherification of naphthylamides with arylboronic acids using water as an oxygen source. *Chem. Commun.* **2018**, *54*, 3899−3902. (g) Narang, U.; Singh, P.; Babu, S. A. Construction of β-phenylalanine derivatives through Pd-catalyzed, $C(sp^2)$−H (*ortho*) functionalization. *Eur. J. Org. Chem.* **2023**, *26*, No. e202300463. (h) Dalal, A.; Bodak, S.; Babu, S. A. Picolinamide-assisted *ortho*-C−H functionalization of pyrenylglycine derivatives using aryl iodides. *Org. Biomol. Chem.* **2024**, *22*, 1279−1298.

https://doi.org/10.1021/acsomega.4c10558
ACS Omega 2025, 10, 17361−17393

(17) Selected reports on bidentate directing group-assisted C-H functionalization: (a) Verma, A.; Elias, A. J. C−H bond functionalization of aryl acids and amines by 'on-water' reaction: bi-dentate directing group enabled synthesis of biaryl and *m*-teraryl carboxamides. *Chem.—Asian J.* **2023**, *18*, No. e202300191. (b) Xiang, T.; Liu, Y.; Xu, Q.; He, K.; Pan, F. Palladium-catalyzed regio- and diastereoselective olefinic C−H difluoromethylthiolation at room temperature. *J. Org. Chem.* **2022**, *87*, 3135−3144. (c) Li, C.; Zhang, D.; Zhu, W.; Wan, P.; Liu, H. Pd(II)-catalyzed direct functionalization of C−H bonds of benzamides for synthesis of 1,1-difluoro-1-alkenes. *Org. Chem. Front.* **2016**, *3*, 1080−1083. (d) Parella, R.; Babu, S. A. $Pd(OAc)_2$-catalyzed, AgOAc-promoted *Z* selective directed *β*-arylation of acrylamide systems and stereoselective construction of *Z*-cinnamamide scaffolds. *J. Org. Chem.* **2015**, *80*, 12379−12396. (e) Padmavathi, R.; Babu, S. A. Pd(II)-catalyzed selective *β*-C−H functionalization of azobenzene carboxamides. *Org. Biomol. Chem.* **2023**, *21*, 2689−2694. (f) Gopalakrishnan, B.; Mohan, S.; Parella, R.; Babu, S. A. Diastereoselective Pd(II)-catalyzed sp^3 C−H arylation followed by ring opening of cyclopropanecarboxamides: construction of anti *β*-acyloxy carboxamide derivatives. *J. Org. Chem.* **2016**, *81*, 8988−9005. (g) Antermite, D.; White, A. J. P.; Casarrubios, L.; Bull, J. A. On the mechanism and selectivity of palladium-catalyzed C(sp^3)−H arylation of pyrrolidines and piperidines at unactivated C4 positions: Discovery of an improved dimethylaminoquinoline amide directing group. *ACS Catal.* **2023**, *13*, 9597−9615.

(18) Selected papers on synthesis of biaryl-based sulfonamides *via* C-H functionalization: (a) Vanjari, R.; Guntreddi, T.; Singh, K. N. Palladium-catalyzed site-selective C−H functionalization of weakly coordinating sulfonamides: Synthesis of biaryl sulfonamides. *Chem.—Asian J.* **2016**, *11*, 696−699. (b) Liu, W.; Wang, D.; Zhao, Y.; Yi, F.; Chen, J. Palladium-catalyzed mono-selective *ortho* C-H arylation of aryl sulfonamides in water: A concise access to biaryl sulfonamide derivatives. *Adv. Synth. Catal.* **2016**, *358*, 1968−1974. (c) Liu, W.; Zhao, Y.; Yi, F.; Chen, J. Palladium(II)/copper(I)-catalyzed sequential C-H arylation and oxidative C-N bond cleavage of aryl sulfonamino acids: Efficient one-pot synthesis of primary biaryl sulfonamides. *Tetrahedron* **2016**, *72*, 8382−8386. (d) Ran, Y.; Yang, Y.; You, H.; You, J. $RhCl_3$-catalyzed oxidative C−H/C−H cross-coupling of (hetero)aromatic sulfonamides with (hetero)arenes. *ACS Catal.* **2018**, *8*, 1796−1801. (e) Dai, H.-X.; Stepan, A. F.; Plummer, M. S.; Zhang, Y.-H.; Yu, J.-Q. Divergent C−H functionalizations directed by sulfonamide pharmacophores: Late-stage diversification as a tool for drug discovery. *J. Am. Chem. Soc.* **2011**, *133*, 7222−7222. (f) Laha, J. K.; Dayal, N.; Jethava, K. P.; Prajapati, D. V. Access to biaryl sulfonamides by palladium-catalyzed intramolecular oxidative coupling and subsequent nucleophilic ring opening of heterobiaryl sultams with amines. *Org. Lett.* **2015**, *17*, 1296−1299. (g) Dong, Y.; Zhang, X.; Chen, J.; Zou, W.; Lina, S.; Xu, H. Switching the site-selectivity of C−H activation in aryl sulfonamides containing strongly coordinating *N*-heterocycles. *Chem. Sci.* **2019**, *10*, 8744−8751.

(19) Selected reviews dealing on synthesis of arylsulfonamides *via* C-H functionalization: (a) Zhang, Y.-J.; Li, M.-L.; Hu, H.-X.; Teng, F. Recent advances in palladium-catalyzed sulfonylation *via* SO_2 insertion. *Org. Biomol. Chem.* **2024**, *22*, 5868−5885. (b) Kurbonovich, K. J.; Nasiriddinovich, T. J.; Ibodullayevich, N. K.; Qizi, J. M. I.; Muhammedova, M. B.; Qurvonnazarovich, B. I.; Ergashovich, Y. K. Recent progress in cross-dehydrogenative sulfonamidation of (hetero)arenes. *Chem. Rev. Lett.* **2024**, *7*, 263−276.

(20) Selected reviews dealing on synthesis of arylsulfonamides *via* C-H functionalization: (a) Dong, Y.; Chen, J.; Cui, Y.; Bao, L.; Xu, H. Cp^*Rh^{III}-Catalyzed sulfonamide-directed *ortho* arene C−H carbenoid functionalization with pyridotriazoles. *Org. Lett.* **2020**, *22*, 772−775. (b) Hou, H.; Zhao, Y.; Sheng, S.; Chen, J. Iridium-catalyzed *ortho*-C−H amidation of benzenesulfonamides with sulfonyl azides. *Adv. Synth. Catal.* **2019**, *361*, 4393−4398. (c) Lan, T.; Wang, L.; Rao, Y. Regioselective annulation of aryl sulfonamides with allenes through cobalt-promoted C−H functionalization. *Org. Lett.* **2017**, *19*, 972−975. (d) Hou, H.; Zhao, Y.; Pub, S.; Chen, J. Rhodium-catalyzed direct C−H bond alkynylation of aryl sulfonamides with bromoalkynes. *Org. Biomol. Chem.* **2019**, *17*, 2948−2953. (e) Wu, G.; Ouyang, W.; Chen, Q.; Huo, Y.; Li, X. Cross-dehydrogenative alkynylation of sulfonamides and amides with terminal alkynes *via* Ir(III) catalysis. *Org. Chem. Front.* **2019**, *6*, 284−289. (f) Zhang, P.; Ma, Q.; Jiang, Z.; Xu, X.; Jin, Z. Transition-metal-catalyzed remote *meta*-C-H alkylation and alkynylation of aryl sulfonic acids enabled by an indolyl template. *Chin. Chem. Lett.* **2024**, *35*, 109361. (g) Ojhaa, S.; Panda, N. Palladium-catalyzed *ortho*-benzoylation of sulfonamides through C−H activation: Expedient synthesis of cyclic *N*-sulfonyl ketimines. *Adv. Synth. Catal.* **2020**, *362*, 561−571. (h) Dong, Y.; Chen, J.; Xu, H. Rhodium(III)-catalyzed sulfonamide directed *ortho* C−H carbenoid functionalization *via* metal carbene migratory insertion. *Chem. Commun.* **2019**, *55*, 2027−2030.

(21) Howe, G. W.; Vandersteen, A. A.; Kluger, R. How acid-catalyzed decarboxylation of 2,4-dimethoxybenzoic acid avoids formation of protonated CO_2. *J. Am. Chem. Soc.* **2016**, *138*, 7568−7573.

(22) (a) Tachrim, Z. P.; Wang, L.; Murai, Y.; Yoshida, T.; Kurokawa, N.; Ohashi, F.; Hashiodoko, Y.; Hashimoto, M. Trifluoromethanesulfonic acid as acylation catalyst: Special feature for *C*- and/or *O*-acylation reactions. *Catalysts* **2017**, *7*, 40. (b) Hwang, J. P.; Prakash, G. K. S.; Olah, G. A. Trifluoromethanesulfonic acid catalyzed novel Friedel−Crafts acylation of aromatics with methyl benzoate. *Tetrahedron* **2000**, *56*, 7199−7203. (c) Wang, J.; Liu, J.; Lan, H.; Chu, W.; Sun, Z. Selective Friedel−Crafts acylation reactions of 2-arylphenoxyacetic acids: A simple and efficient methodology to synthesize dibenzoxepine and arylcoumaranone derivatives. *Synthesis* **2015**, *47*, 3049−3060. (d) Anderson, K. W.; Tepe, J. J. Trifluoromethanesulfonic acid catalyzed Friedel−Crafts acylation of aromatics with *β*-lactams. *Tetrahedron* **2002**, *58*, 8475−8481.

https://doi.org/10.1021/acsomega.4c10558
ACS Omega 2025, 10, 17361−17393