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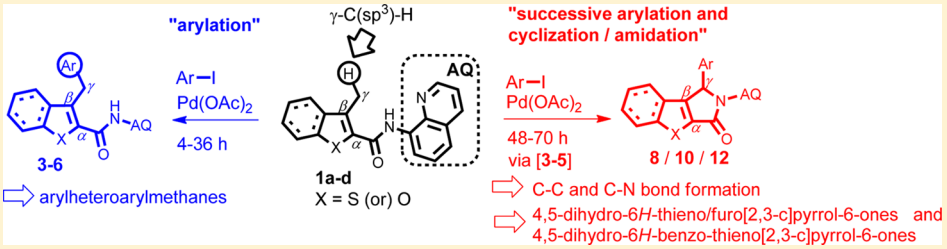
Pd(II)-Catalyzed Arylation and Intramolecular Amidation of γ-C(sp^3)−H Bonds: En Route to Arylheteroarylmethane and Pyrrolidone Ring Annulated Furan/Thiophene Scaffolds

Ramarao Parella and Srinivasarao Arulananda Babu*

Department Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, Knowledge City, Sector 81, SAS Nagar, Manauli P.O., Mohali, Punjab 140306, India

Supporting Information



ABSTRACT: We report the Pd(II)-catalyzed, bidentate directing group (BDG)-assisted arylation and successive arylation/intramolecular amidation of γ-C(sp^3)−H bonds. The Pd(II)-catalyzed BDG-assisted C−H activation and functionalization of the β-C(sp^3)−H bonds of carboxylic acids are well documented, but only a few reports are available that deal with the BDG-directed functionalization of the γ-C(sp^3)−H bonds. Various 3-methylthiophene/furan-2-carboxamides (**1a**−**e**) were derived from their corresponding carboxylic acids and bidentate directing groups. These compounds were then used as substrates to investigate the arylation and successive arylation/intramolecular amidation of the γ-C(sp^3)−H bonds. The γ-C(sp^3)−H arylation arose from the Pd(II)-catalyzed reactions of these compounds with aryl iodides with reaction periods of 4−24 h (except a few reactions which required 36 or 48 h). Notably, these reactions led to the construction of various unsymmetrical diarylmethane scaffolds, such as thiophene/furan-based arylheteroarylmethanes (**3**−**6**). Prolonging the reaction period to 48−70 h led to successive γ-C(sp^3)−H arylation/intramolecular amidation and the construction of both C−C and C−N bonds. Accordingly, these reactions led to the construction of new classes of pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds (e.g., 4,5-dihydro-6*H*-thieno[2,3-*c*]pyrrol-6-ones (**8**), 4,5-dihydro-6*H*-furo[2,3-*c*]pyrrol-6-ones (**10**), and 1-phenyl-1,2-dihydro-3*H*-benzo[4,5]thieno-[2,3-*c*]pyrrol-3-ones (**12**)), and notably, compounds **8**, **10**, and **12** resemble the skeletons of 3-phenylisoindolin-1-ones.

INTRODUCTION

The transition-metal-catalyzed sp^2/sp^3 C−H activation/functionalization process is a powerful synthesis technique for constructing C−C and C−X bonds (where X can be O, S, N, etc.).[1−5] The transition-metal-catalyzed functionalization of the sp^2/sp^3 C−H bonds of organic molecules can be performed with or without a directing group.[1−7] There are numerous reports of synthesis methods dealing with the site-selective functionalization of the C(sp^2)−H bonds of different classes of arenes and heteroarenes. Since the work by Daugulis et al.,[8a] special attention has been given to the site-selective functionalization of the C(sp^3)−H bonds of organic molecules such as alkyl chains and cyclic compounds. In 2005, Daugulis reported the Pd(II)-catalyzed direct arylation of β-C(sp^3)−H bonds of carboxylic acids with the help of a bidentate directing group (BDG), such as 8-aminoquinoline (**DG-a**) and 2-(methylthio)aniline) (**DG-b**).[8] Yu's group[9] exploited the monodentate directing group (e.g., 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (**DG-c**)) to accomplish the Pd(II)-catalyzed functionalization of the β-C(sp^3)−H bonds of carboxylic acids.

The 8-aminoquinoline-type BDGs (**DG-a**, **DG-b**, and **DG-c**, etc., Scheme 1)[6,7,10−12] have been well exploited for the functionalization of the sp^2/sp^3 C−H bonds of carboxylic acids, while picolinamide (PA)-type BDGs (**DG-d**, **Dg-e**, and **DG-f**, etc.) have been used for the functionalization of the sp^2/sp^3 C−H bonds of amines. With regard to site selectivity, there are numerous reports dealing with the PA-type BDG-assisted functionalization of the γ-C−H and remote δ- and ε-C−H bonds of amines.[1−7,13−20] Notably, the 8-aminoquinoline-type BDGs have favorably assisted the functionalization of the β-C−H bonds of carboxylic acids.[1−7,10−12]

While the functionalization of the remote γ-, δ-, and ε-C(sp^2/sp^3)−H bonds of suitable amines has been well advanced using PA-type BDGs,[6,7,13−22] similar work on suitable carboxylic acids is currently limited to the functionalization of the remote γ-C(sp^2/sp^3)−H bonds. Only a few reports deal with the BDG-assisted functionalization of the γ-C(sp^2/sp^3)−H bonds (Schemes 1 and 2).[6,7,23−27] We assembled the 3-methylfuran/

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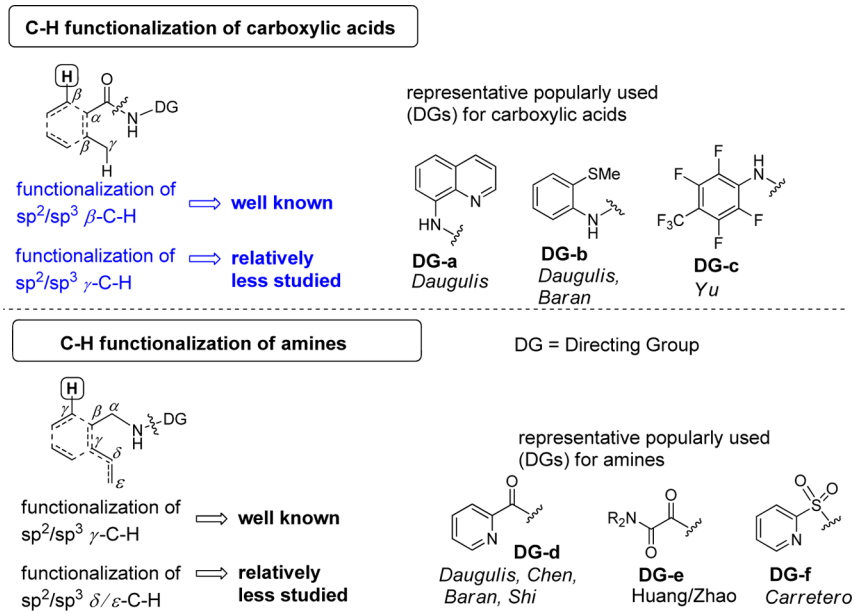
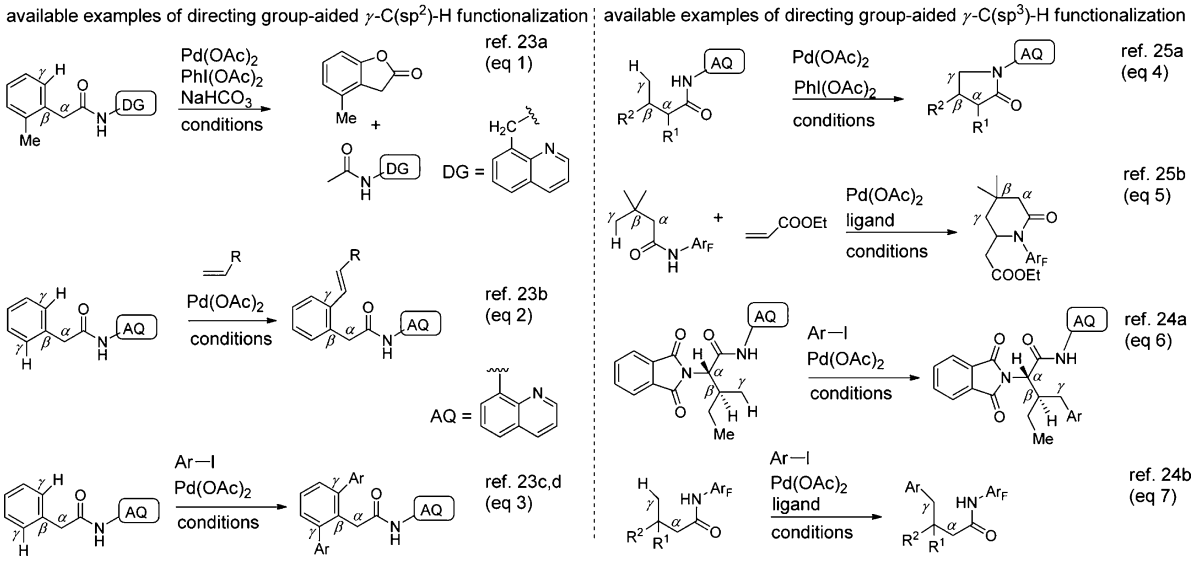
Scheme 1. Bidentate Directing Group Assisted C−H Functionalization



Scheme 2. Available Examples of Bidentate Directing Group Assisted sp^2/sp^3 γ-C−H Functionalization



thiophene-2-carboxamides **1a−e** from their corresponding carboxylic acids and BDGs, such as 8-aminoquinoline and 2-(methylthio)aniline (Schemes 3−5). The γ-C(sp^3)−H bonds of compounds **1a−e** can be subjected to the Pd(II)-catalyzed arylation and successive arylation/intramolecular amidation to afford new classes of furan/thiophene-based arylheteroarylmethane (unsymmetrical diarylmethane) scaffolds and pyrrolidone-ring annulated furan/thiophene heterocycles (Schemes 3 and 4).

Apart from the C−H functionalization reactions comprising the intermolecular arylation, alkylation, amination/amidation, and acetoxylation, the BDG-assisted or directing group-free C−H functionalization technique was also well explored for performing the intramolecular sp^2/sp^3 C−H amination/amidation reactions.[1−7,28−34] Notably, intramolecular sp^2/sp^3 C−H amination/amidation reactions have led to the assembly of various heterocyclic compounds and biologically active molecules, including azetidines, pyrrolidines, piperidines, indolines, quinolones, isoindolin-1-one cores, and other cyclic amines.[1−7,28−33,35−39] In particular, Scheme 4 shows representative reports dealing with the functionalization/intramolecular amination/amidation of benzylic γ-C(sp^3)−H bonds of the corresponding aromatic compounds affording the isoindolin-1-one cores and examples of bioactive isoindolin-1-one cores.[35]

Furan/thiophene-based molecules, arylheteroarylmethane, and isoindolin-1-one scaffolds independently have important roles in organic synthesis and pharmaceuticals. Functionalized thiophenes/furans and benzothiophenes/benzofurans are important building blocks in organic synthesis, materials, and medicinal chemistry research.[40,41] Arylheteroarylmethane scaffolds,[42−46] which are a subclass of diarylmethanes, and isoindolin-1-one scaffolds[35] both independently have an important place in medicinal chemistry due to their wide range of pharmacological activities. Representative examples of bioactive furan/thiophene-based molecules,[41] arylheteroaryl-

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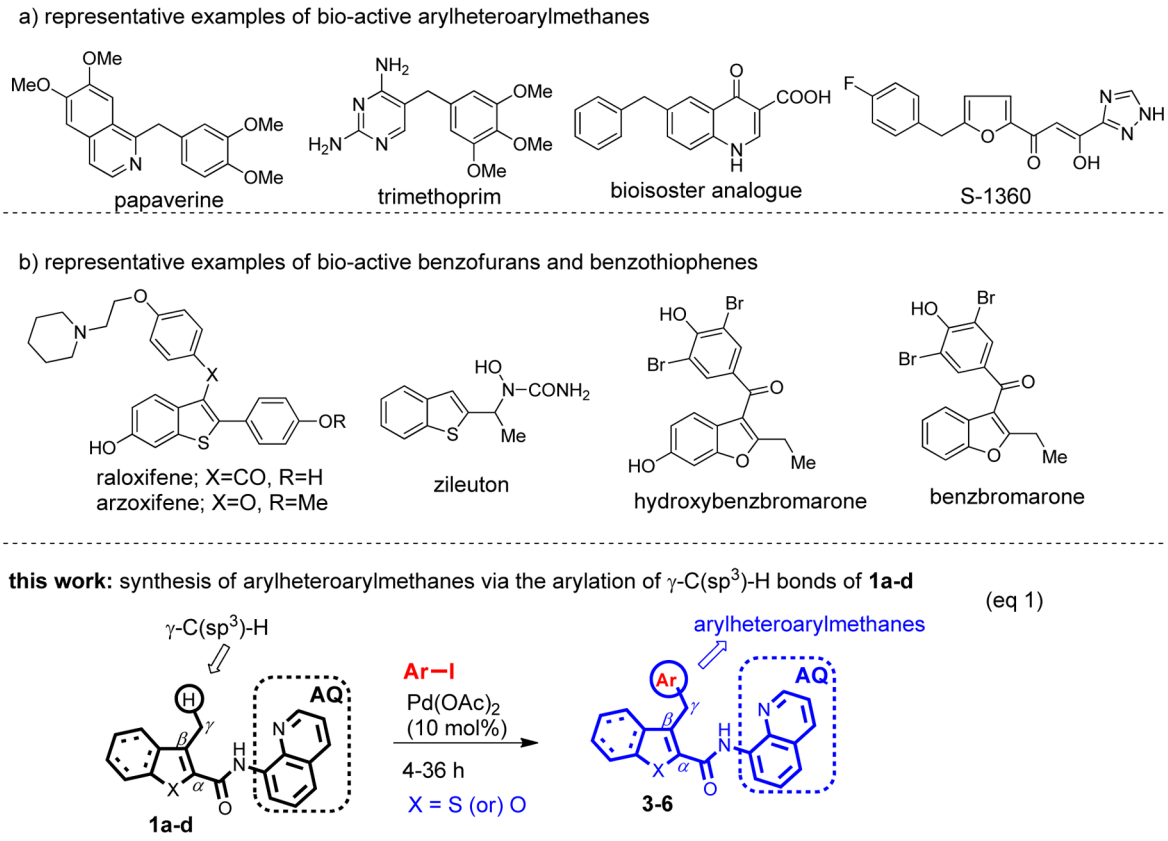
Scheme 3. Bioactive Arylheteroarylmethanes and Benzofurans/Benzothiophenes: Synthesis of Arylheteroarylmethanes via γ-C(sp^3)−H Functionalization



methane (unsymmetrical diarylmethanes),[43] and isoindolin-1-one scaffolds[35] are illustrated in Schemes 3 and 4.

In continuation of our laboratory's research program on the C−H activation reactions, herein we report our investigations on the Pd(II)-catalyzed BDG-assisted arylation and successive arylation/intramolecular amidation of γ-C(sp^3)−H bonds of 3-methylfuran/thiophene-2-carboxamides and 3-methylbenzofuran/thiophene-2-carboxamides (Schemes 3 and 4). This work reveals the construction of a wide range of new classes of furan/thiophene-based arylheteroarylmethanes (**3**−**7**) and pyrrolidone-ring annulated furan/thiophene heterocyclic frameworks (e.g., 4,5-dihydro-6*H*-thieno[2,3-*c*]pyrrol-6-ones (**8**), 4,5-dihydro-6*H*-furo[2,3-*c*]pyrrol-6-ones (**10**), and 4,5-dihydro-6*H*-benzothieno[2,3-*c*]pyrrol-6-one (**12**)).

RESULTS AND DISCUSSION

To begin our investigations, we first assembled various 3-methylthiophene/furan-2-carboxamides for use as starting materials. Accordingly, the substrates **1a**−**g** were assembled from their corresponding carboxylic acid chlorides and commonly used BDGs,[6,8a,b] such as 8-aminoquinoline and 2-(methylthio)aniline (Scheme 5). To examine the efficiency and role of the BDGs, the substrates **1h**−**m** were then assembled from their corresponding carboxylic acid chlorides and amines (Scheme 5). After assembling the required starting materials, we attempted to construct arylheteroarylmethane scaffold **3a** via the Pd(II)-catalyzed, 8-aminoquinoline-assisted arylation of γ-C(sp^3)−H bonds of the thiophene-2-carboxamide system **1a**. Table 1 shows the optimized reaction conditions with various Pd catalysts, additives, and solvents.

The γ-C(sp^3)−H arylated derivative **3a** (arylheteroarylmethane) was obtained in 14% yield from the reaction of a mixture of substrate **1a** (1 equiv), aryl iodide **2a** (4 equiv), and $Pd(OAc)_2$ catalyst without any additive in toluene at 110 °C for 24 h (entry 1, Table 1). The reaction of **1a**, **2a**, and AgOAc additive without $Pd(OAc)_2$ catalyst did not give any product (entry 2, Table 1). The arylation of **1a** with 2−4 equiv of **2a** using $Pd(OAc)_2$ catalyst and AgOAc additive afforded the arylheteroarylmethane derivative **3a** in low yields (32−45% yields, entries 3 and 4, Table 1). Next, we performed the arylation of **1a** with 6 equiv of **2a**, $Pd(OAc)_2$ catalyst, and AgOAc additive in toluene at 110 °C for 4 h. This reaction afforded the arylheteroarylmethane derivative **3a** with a maximum yield of 72% (entry 5 Table 1).

To improve the yield of **3a**, we attempted the arylation of **1a** with **2a** using various Pd catalysts, additives, and solvents. The γ-C(sp^3)−H arylation of **1a** with other palladium catalysts such as $PdCl_2$, $Pd(CH_3CN)_2Cl_2$, and $Pd(TFA)_2$ afforded the arylheteroarylmethane derivative **3a** in 41−43% yield (entries 6−8, Table 1). We also attempted the arylation of **1a** with **2a** with $Pd(OAc)_2$ catalyst and various additives, such as KOAc, K_2CO_3, and Cs_2CO_3, which afforded **3a** in 5−9% yield (entries 9−11, Table 1). The arylation of **1a** with **2a** with $Pd(OAc)_2$ catalyst and Ag_2CO_3 as an additive afforded **3a** in 41% yield (entry 12, Table 1). The arylation of **1a** with **2a** with $Pd(OAc)_2$ catalyst and AgOAc additive in solvents such as *t*BuOH and 1,2-DCE afforded **3a** in 6−15% yield (entries 13 and 14, Table 1). The arylation of **1a** with **2a** with $Pd(OAc)_2$ catalyst and AgOAc additive in 1,4-dioxane and *t*AmylOH afforded **3a** in 45−49% yield (entries 15 and 16, Table 1). Compound **3a** was not produced when coupling partners such as aryl bromide **2b**

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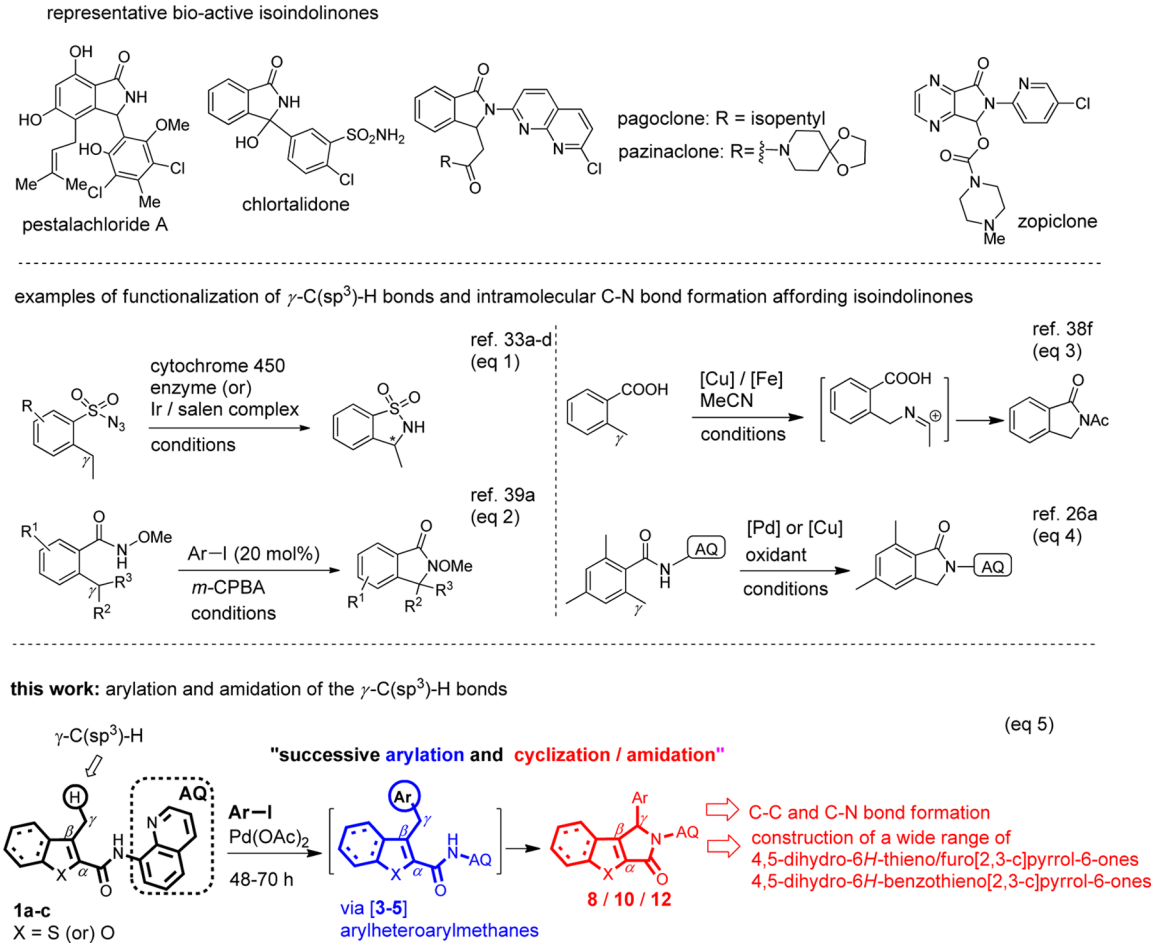
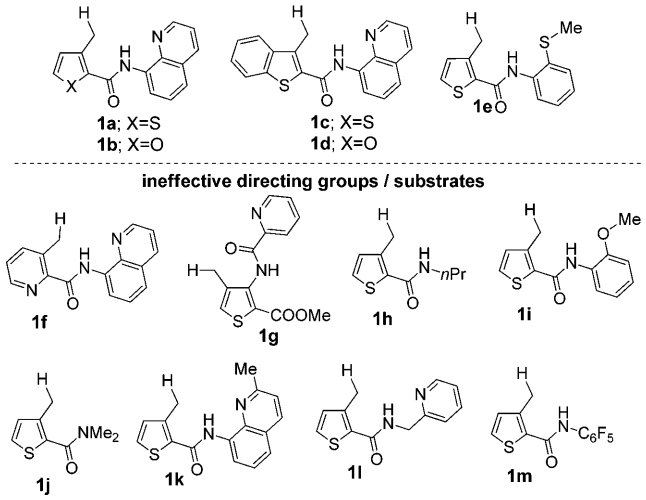
Scheme 4. Bioactive Isoindolinone Scaffolds: Synthesis of Isoindolinone Scaffolds via the Functionalization/Intramolecular Amidation of Benzylic γ-C(sp^3)−H Bonds



Scheme 5. Directing Groups and Substrates Used To Investigate the γ-C(sp^3)−H Arylation/Amidation Reactions[a47]



[a]Conditions: substrate (0.125 mmol), **2a** or ArI (0.75−1 mmol), $Pd(OAc)_2$ (10−20 mol %), AgOAc (0.27 mmol), toluene (3 mL), 24−48 h, and 110 °C.

or aryl chloride **2c** were used instead of aryl iodide **2a** for the arylation of **1a** with $Pd(OAc)_2$ catalyst and AgOAc additive (entries 17 and 18, Table 1).

Next, to determine the role of the BDG 8-aminoquinoline and to find other working directing groups in the arylation of γ-C(sp^3)−H bond, we performed the arylation of carboxamides **1g−m** using the optimized reaction conditions (entry 5, Table 1). The Pd(II)-catalyzed arylation of the γ-C(sp^3)−H bond of the substrates **1g−m** failed to afford the corresponding arylheteroarylmethane derivatives in characterizable amounts (Scheme 5).[47] These reactions indicated that the corresponding directing groups/amides did not effectively assist in the arylation of the γ-C(sp^3)−H bond of these substrates (Scheme 5). Additionally, while the 8-aminoquinoline-assisted γ-C(sp^3)-arylation of **1a** was successful, the Pd(II)-catalyzed 8-aminoquinoline-assisted γ-C(sp^3)-arylation of **1f** did not afford the corresponding arylheteroarylmethane derivative. The exact reaction for the failure of arylation of **1f** is not clear at this stage, but the presence of multiple coordinating N atoms in substrate **1f** might have hindered the C−H activation process, as suggested by Liu et al.[38a]

We next explored the generality and substrate scope of this protocol using substrates **1a−d**. Scheme 6 shows the $Pd(OAc)_2$-catalyzed, AgOAc-promoted, 8-aminoquinoline-assisted arylation of the γ-C(sp^3)−H bond of **1a** and **1b** with a variety of aryl iodides under the optimized reaction conditions (entry 5, Table 1). The arylation of **1a** with aryl iodides

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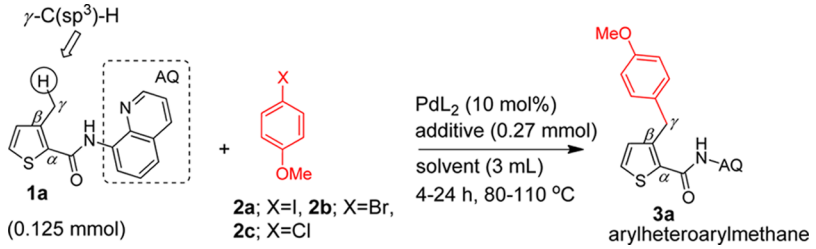
Table 1. Optimization of Reaction Conditions for the γ-C(sp^3)−H Arylation of Substrate 1a[a]



entry	PdL_2 (10 mol %)	**2a** (mmol)	additive	solvent	*T* (°C)	*t* (h)	**3a**: yield (%)
1	$Pd(OAc)_2$	0.5		toluene	110	24	14
2		0.5	AgOAc	toluene	110	24	0
3	$Pd(OAc)_2$	0.25	AgOAc	toluene	110	4	32
4	$Pd(OAc)_2$	0.5	AgOAc	toluene	110	4	45
5	**$Pd(OAc)_2$**	**0.75**	**AgOAc**	**toluene**	**110**	**4**	**72**
6	$PdCl_2$	0.75	AgOAc	toluene	110	4	41
7	$Pd(MeCN)_2Cl_2$	0.75	AgOAc	toluene	110	4	43
8	$Pd(TFA)_2$	0.75	AgOAc	toluene	110	4	42
9	$Pd(OAc)_2$	0.75	KOAc	toluene	110	4	9
10	$Pd(OAc)_2$	0.75	K_2CO_3	toluene	110	4	5
11	$Pd(OAc)_2$	0.75	Cs_2CO_3	toluene	110	4	6
12	$Pd(OAc)_2$	0.75	Ag_2CO_3	toluene	110	4	41
13	$Pd(OAc)_2$	0.75	AgOAc	*t*BuOH	85	4	6
14	$Pd(OAc)_2$	0.75	AgOAc	1,2-DCE	80	4	15
15	$Pd(OAc)_2$	0.75	AgOAc	1,4-dioxane	100	4	49
16	$Pd(OAc)_2$	0.75	AgOAc	*t*AmylOH	110	4	45
17[b]	$Pd(OAc)_2$	0.75	AgOAc	toluene	110	4	0
18[c]	$Pd(OAc)_2$	0.75	AgOAc	toluene	110	4	0

[a]All of the reactions were performed using **2a**. [b]**2b** was used instead of **2a**. [c]**2c** was used instead of **2a**.

containing a substituent at the *para* position (e.g., Ac, COOMe, Et, NO_2, and Br) and PhI afforded the corresponding arylheteroarylmethane derivatives **3b−g** in 53−72% yield (Scheme 6). We then performed the Pd(II)-catalyzed γ-C(sp^3)−H arylation of **1a** with a disubstituted aryl iodide and a variety of heteroaryl iodides, which afforded the corresponding arylheteroarylmethane derivative **3h** and the diheteroarylmethane derivatives **3i−n** in 46−96% yield (Scheme 6).

We next performed the Pd(II)-catalyzed arylation using the furan-2-carboxamide derivative **1b**. The arylation of substrate **1b** with aryl iodides containing a substituent at the *para* or *meta* position (e.g., Ac, COOR, OMe, alkyl, NO_2, CN, and Cl) afforded the corresponding arylheteroarylmethane derivatives **4a−k** in 55−93% yield (Scheme 6). We also performed the arylation of **1b** with a disubstituted aryl iodide and heteroaryl iodides, which afforded the corresponding arylheteroarylmethane derivative **4l** and diheteroarylmethane derivatives **4m−o** in 55−82% yield (Scheme 6).

We next expanded the scope of this protocol by performing the γ-C(sp^3)−H arylation of **1c** and **1d** (Scheme 7) with a variety of aryl iodides under the optimized reaction conditions (entry 5, Table 1). The arylation of **1c** with aryl iodides containing a substituent at the *para* or *meta* position (e.g., Ac, COOR, OMe, and NO_2) afforded the corresponding arylheteroarylmethane derivatives **5a−f** in 41−60% yield (Scheme 7). The arylation of **1c** with heteroaryl iodides also afforded the corresponding diheteroarylmethane derivatives **5g** and **5h** in 71−76% yield (Scheme 7). Then, the $Pd(OAc)_2$-catalyzed γ-C(sp^3)−H arylation of **1d** with aryl iodides containing a substituent at the *para* position (e.g., Ac, COOMe, OMe, and Et) afforded the corresponding arylheteroarylmethane derivatives **6a−d** in 31−66% yield (Scheme 7). The arylation of **1d** with a disubstituted aryl iodide and a heteroaryl iodide also afforded the corresponding arylheteroarylmethane derivative **6e** and diheteroarylmethane derivative **6f** in 45−57% yield (Scheme 7).

We next examined the γ-C(sp^3)−H arylation using the BDG 2-(methylthio)aniline. Scheme 8 shows the arylation of the substrate **1e** with a variety of aryl iodides under the optimized reaction conditions (entry 5, Table 1). The arylation of **1e** with aryl iodides containing a substituent at the *para* or *meta* position (e.g., OMe, Ac, COOMe, Et, and NO_2) afforded the corresponding arylheteroarylmethane derivatives **7a−e** in 50−58% yield (Scheme 8). The arylation of **1e** with disubstituted aryl iodides and heteroaryl iodides also afforded the corresponding arylheteroarylmethane derivatives **7f** and **7g** and the diheteroarylmethane derivatives **7h** and **7i** in 53−61% yield (Scheme 8). Notably, the yields of **7** (Scheme 8) obtained using the BDG 2-(methylthio)aniline were comparable with those of **3** obtained using the 8-aminoquinoline BDG (Scheme 6). We also attempted the removal of the BDG 8-aminoquinoline after the Pd(II)-catalyzed γ-C(sp^3)−H-arylation of **1a**. The NaOH-mediated amide hydrolysis of a representative arylheteroarylmethane derivative **3a** afforded the carboxylic acid **3aa** in 64% yield (Scheme 9). Additionally, treatment of **3a** with MeOH in $BF_3{\cdot}OEt_2$ afforded the methyl ester derivative **3ab** in 85% yield (Scheme 9).

The γ-C−H arylations of the methyl group in compounds **1a−e** resulted in the corresponding arylheteroarylmethanes and diheteroarylmethanes **3−7** containing the methylene γ-C−H bonds. Thus, under the experimental conditions used for the γ-C(sp^3)−H arylation of the compounds **1a−e**, we expected that

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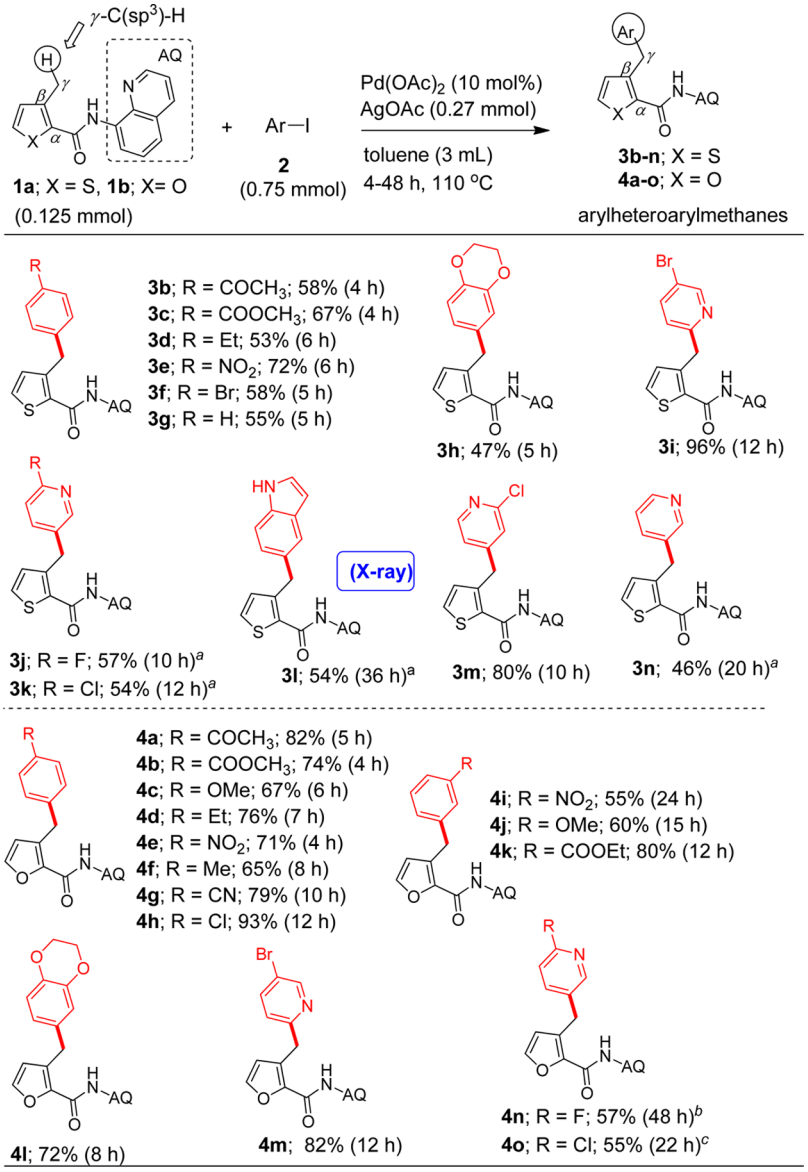
Scheme 6. γ-C(sp^3)−H Arylation of 1a,b: Construction of Thiophene/Furan-Based Arylheteroarylmethanes 3 and 4



[a]1.0 mmol of the corresponding aryl iodide was used in this reaction. [b]20 mol % of catalyst was used. [c]1.0 mmol of the corresponding aryl iodide was used in this reaction.

it would also be possible to accomplish the intramolecular C−H amidation through the methylene γ-C−H bonds in the compounds **3**−**7**. We therefore explored the possibility of successive arylation/intramolecular amidation of the remote γ-C(sp^3)−H bonds of substrates **1a**−**e** employing the Pd(OAc)$_2$ catalyst and AgOAc additive. The successive arylation and intramolecular amidation of the substrates, e.g., **1a**−**c**, are expected to afford the corresponding new classes of pyrrolidone ring annulated furan/thiophene-based heterocycles **8**, **10**, and **12** (Scheme 10).

To realize the Pd(II)-catalyzed BDG-directed successive arylation/intramolecular amidation of the remote γ-C(sp^3)−H bond, we first attempted the successive arylation/intramolecular amidation reaction using the thiophene-2-carboxamide system **1a**. Table 2 shows the optimization of the reaction conditions using various Pd catalysts, additives, and solvents. The Pd(II)-catalyzed arylation of **1a** with 4−6 equiv of **2a** in toluene at 110 °C for 4 h afforded the arylheteroarylmethane derivative **3a** in 72% yield (entry 1, Table 2). We then prolonged the reaction period to accomplish the successive arylation/intramolecular amidation of the γ-C(sp^3)−H bond of substrate **1a**. The Pd(II)-catalyzed reaction of a mixture containing **1a** (1 equiv) and aryl iodide **2a** (4 equiv) was carried out in toluene at 110 °C for 24 h. This reaction afforded **3a** in 40% yield, and the expected pyrrolidone-ring annulated thiophene heterocycle **8a** in 20% yield via the intramolecular C−H amidation (entry 2, Table 2). To improve the yield of this process, we next performed the reaction of **1a** (1 equiv) and aryl iodide **2a** (8−10 equiv) in toluene at 110 °C for 48 h with 10−20 mol % of the Pd(OAc)$_2$ catalyst. These reactions afforded **8a** in improved yields (59−71%, entries 3−5, Table 2). In these reactions, **3a** was obtained in <5% yield along with the arylheteroarylketone **9a** in 10−12% yield. It is obvious that the product **8a** was formed from the C−H arylated product **3a** via the intramolecular C−H amidation process. It is assumed that the ketone product **9a** was formed from the Pd(II)-catalyzed

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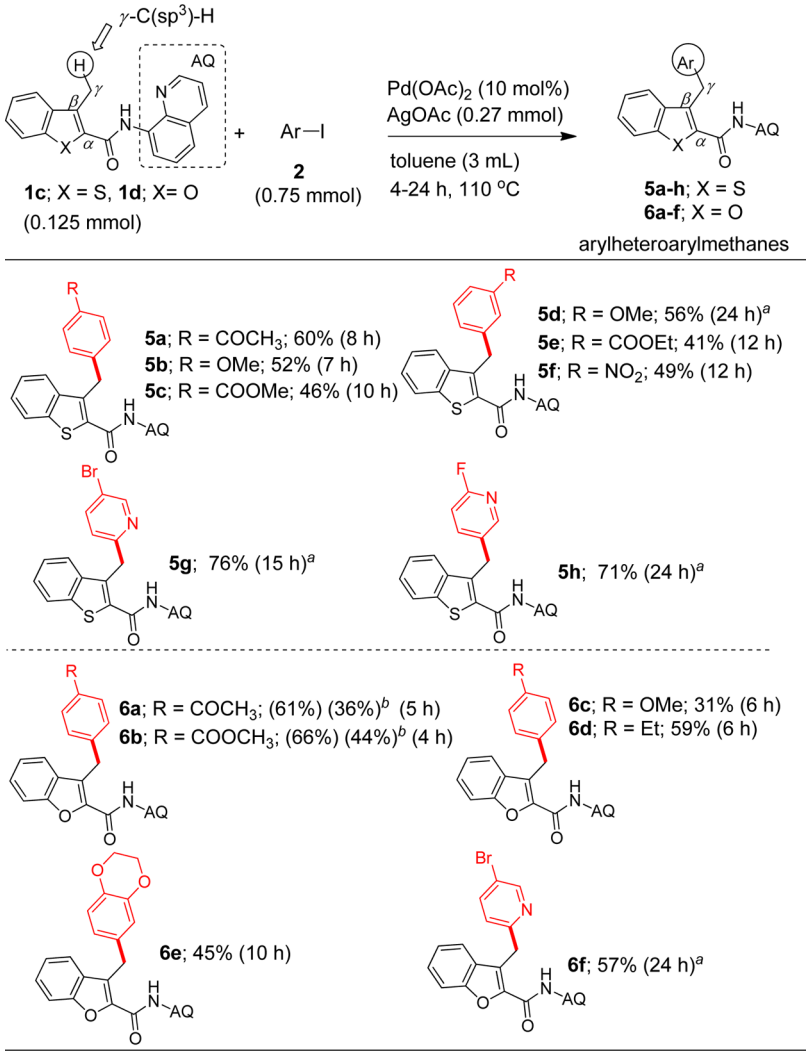
Scheme 7. γ-C(sp^3)−H Arylation of 1c,d: Construction of Benzothiophene/Furan-Based Arylheteroarylmethanes 5 and 6



[a]1.0 mmol of the corresponding aryl iodide was used in this reaction. [b]0.5 mmol of the corresponding aryl iodide was used in this reaction.

oxidation of methylene group of **3a** with adventitious oxygen in the reaction system.[45]

Next, to improve the yield of **8a** further, we attempted the arylation of **1a** with **2a** using various Pd catalysts, additives, and solvents. The reactions of **1a** with **2a** with other palladium catalysts $PdCl_2$, $Pd(CH_3CN)_2Cl_2$, and $Pd(TFA)_2$ afforded both **3a** and **8a** without any improvement in the yield for **8a** (entries 6−8, Table 2). We also attempted the Pd(II)-catalyzed reaction of **1a** with **2a** with various additives, such as, KOAc, K_2CO_3, and Cs_2CO_3, which were not fruitful, and the yield of **8a** did not improve (entries 9−11, Table 2). The reaction of **1a** with **2a** with $Pd(OAc)_2$ catalyst and Ag_2CO_3 additive gave **8a** in 43% yield (entry 12, Table 2). We also attempted the reaction of **1a** with **2a** with $Pd(OAc)_2$ catalyst and AgOAc additive in other solvents, such as 1,2-DCE, 1,4-dioxane, *t*AmylOH, and *t*BuOH. These trails were also not fruitful, and the yield of the product **8a** did not improve (entries 13−16, Table 2). The Pd(II)-catalyzed reactions of **1a** with coupling partners such as aryl bromide **2b** or aryl chloride **2c** instead of aryl iodide **2a** were ineffective (entries 17 and 18, Table 2). Additionally, to find out whether we can use lesser amounts of aryl iodide **2a** and to improve the yield of **8a** further, we attempted the Pd(II)-catalyzed arylation of **1a** with **2a** (4 equiv) using various additives/ligands such as quinoline, 2-methylquinoline, and 2-hydroxy-4-methylquinoline. These trails were also not fruitful, and the product **8a** was not formed (entries 19−21, Table 2).

We then explored the generality and substrate scope of this arylation/intramolecular amidation protocol using substrates **1a−c**. Scheme 11 shows amidation of the γ-C(sp^3)−H bond of **1a** with a variety of aryl iodides under the optimized reaction conditions (entry 5, Table 2). The Pd(II)-catalyzed successive γ-C(sp^3)−H arylation/intramolecular amidation of **1a** with aryl iodides containing a substituent at the *para* position (e.g., F, Cl, Br, I, Ac, COOMe, and alkyl) and PhI afforded the corresponding pyrrolidone-ring annulated thiophene-based heterocyclic scaffolds **8b−n** in 44−71% yield (Scheme 11). In some cases, the corresponding arylheteroaryl ketones **9g−n** were also obtained in 7−28% yield, as observed in the optimization reactions (Table 2).[45]

Next, we performed the arylation/intramolecular amidation of **1a** with aryl iodides containing a substituent at the *meta* position (e.g., OMe, COOEt, NO_2, Cl, F, Br, I, Me, and CF_3). These reactions afforded the corresponding pyrrolidone-ring annulated thiophene-based heterocyclic scaffolds **8o−w** in 51−66% yield (Scheme 11). In some cases, the corresponding arylheteroarylketones **9o** and **9p** were also obtained in 20−27%

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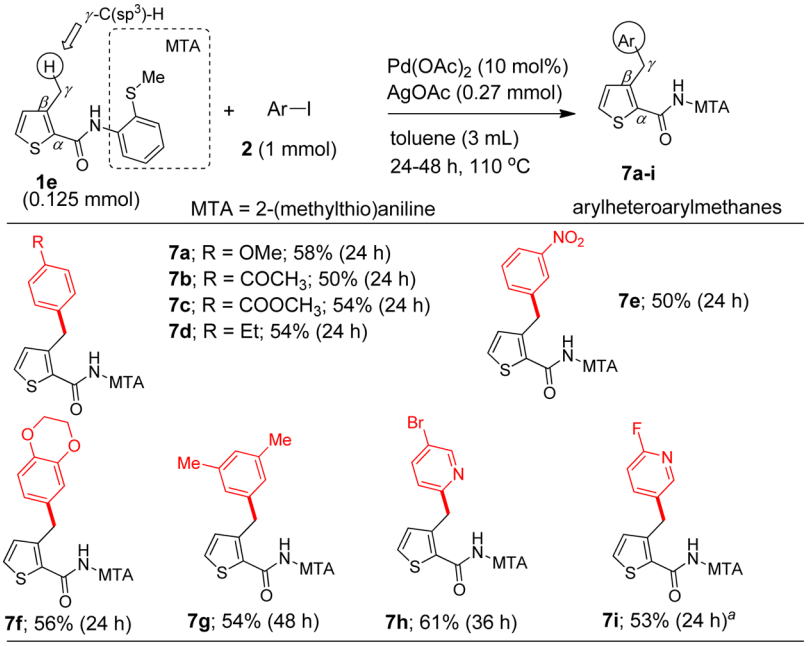
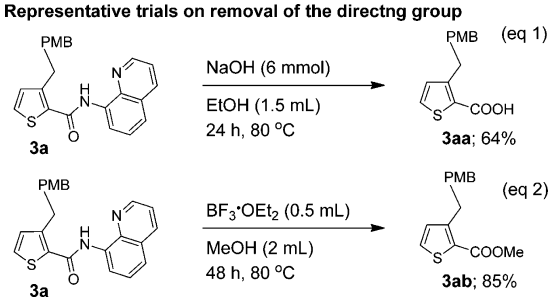
Scheme 8. MTA-Directed γ-C(sp^3)−H Arylation of 1e: Construction of Thiophene-Based Arylheteroarylmethanes 7



[a]0.75 mmol of the corresponding aryl iodide was used in this reaction.

Scheme 9. Representative Trials To Remove the Directing Group



yield, as observed in the optimization reactions (Table 2).[45] Furthermore, the amidation of **1a** with various disubstituted aryl iodides afforded the corresponding pyrrolidone-ring annulated thiophene-based heterocyclic scaffolds **8x**, **8y**, **8z**, and **8aa** in 54−82% yield (Scheme 11). In one of the reactions, the corresponding arylheteroarylketone **9aa** was also obtained in 12% yield as observed in the optimization reactions (Table 2).[45]

We next investigated the arylation and intramolecular amidation process using substrate **1b**. Scheme 12 shows the Pd(II)-catalyzed arylation and intramolecular amidation of **1b** with aryl iodides containing a substituent at the *para* or *meta* position under the optimized reaction conditions (entry 5, Table 2). These reactions afforded the corresponding pyrrolidone ring annulated furan-based heterocyclic scaffolds **10a−c** in 33−56% yield (Scheme 12). In one of the reactions, the corresponding arylheteroaryl ketone system **11a** was also obtained in 23% yield, as observed in the optimization reactions (Table 2). We next expanded the substrate scope of this protocol by performing arylation and intramolecular amidation reaction using benzothiophene-based substrate **1c**. Scheme 13 shows the Pd(II)-catalyzed arylation and intramolecular amidation of **1c** with aryl iodides containing a substituent at the *para* position and disubstituted aryl iodides under the optimized reaction conditions (entry 5, Table 2). These reactions afforded the corresponding pyrrolidone-ring annulated benzothiophene-based heterocyclic scaffolds **12a−d** in 37−53% yield (Scheme 13).

Overall, arylheteroarylmethane and diheteroarylmethane scaffolds **3−7** were obtained in good to high yield from the Pd(II)-catalyzed γ-C(sp^3)−H arylation of **1a−e**. The pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds **8a−z**, **8aa**, **10a−c**, and **12a−d** were obtained in low to good yield from the Pd(II)-catalyzed successive γ-C(sp^3)−H arylation/intramolecular amidation of substrates **1a−c**. Some of the Pd(II)-catalyzed successive γ-C(sp^3)−H arylation/intra-

Scheme 10. Proposed Successive Arylation and Intramolecular Amidation of γ-C(sp^3)−H Bonds toward Pyrrolidone Ring Annulated Thiophene/Furan-Based Heterocycles

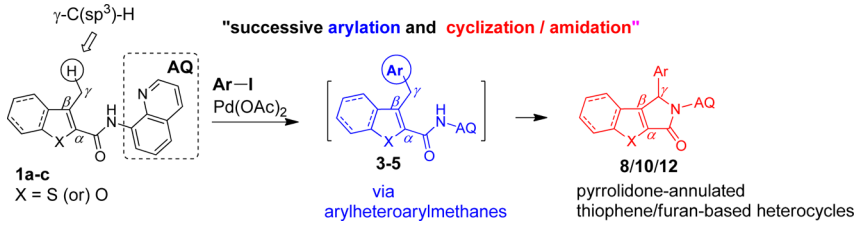


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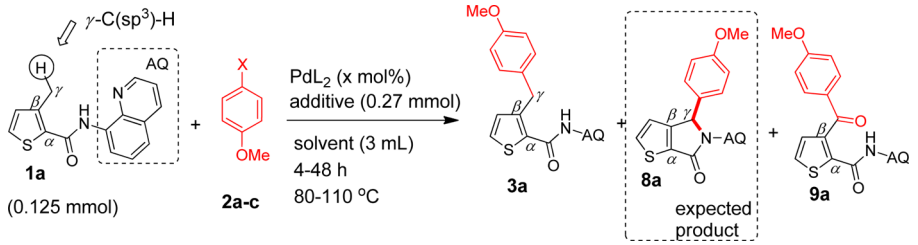
Table 2. Optimization of Reaction Conditions: Successive γ-C(sp^3)−H Arylation/Intramolecular Amidation of 1a[a]



entry	PdL_2 (*x* mol %)	**2a** (mmol)	additive	solvent	*T* (°C)	time (h)	yield (%) **3a**	**8a**	**9a**
1[b]	$Pd(OAc)_2$ (10)	0.75	AgOAc	toluene	110	4	72		
2	$Pd(OAc)_2$ (10)	0.5	AgOAc	toluene	110	24	40	20	<5
3	$Pd(OAc)_2$ (10)	1	AgOAc	toluene	110	48	<5	59	12
4	$Pd(OAc)_2$ (20)	1	AgOAc	toluene	110	48	<5	64	10
5	**$Pd(OAc)_2$ (20)**	**1.25**	**AgOAc**	**toluene**	**110**	**48**	**<5**	**71**	**12**
6	$PdCl_2$ (20)	1.25	AgOAc	toluene	110	48	49	39	<5
7	$Pd(MeCN)_2Cl_2$ (20)	1.25	AgOAc	toluene	110	48	32	45	<5
8	$Pd(TFA)_2$ (20)	1.25	AgOAc	toluene	110	48	36	21	16
9	$Pd(OAc)_2$ (20)	1.25	KOAc	toluene	110	48	64	<5	<5
10	$Pd(OAc)_2$ (20)	1.25	K_2CO_3	toluene	110	48	49	0	0
11	$Pd(OAc)_2$ (20)	1.25	Cs_2CO_3	toluene	110	48	43	0	0
12	$Pd(OAc)_2$ (20)	1.25	Ag_2CO_3	toluene	110	48	0	43	6
13	$Pd(OAc)_2$ (20)	1.25	AgOAc	1,2-DCE	80	48	30	9	<5
14	$Pd(OAc)_2$ (20)	1.25	AgOAc	1,4-dioxane	100	48	34	21	<5
15	$Pd(OAc)_2$ (20)	1.25	AgOAc	*t*AmylOH	110	48	17	15	<5
16	$Pd(OAc)_2$ (20)	1.25	AgOAc	*t*BuOH	85	48	58	<5	<5
17[c]	$Pd(OAc)_2$ (20)	1.25	AgOAc	toluene	110	48	0	0	0
18[d]	$Pd(OAc)_2$ (20)	1.25	AgOAc	toluene	110	48	0	0	0
19[e]	$Pd(OAc)_2$ (20)	0.5	AgOAc	toluene	110	24	33	0	0
20[f]	$Pd(OAc)_2$ (20)	0.5	AgOAc	toluene	110	24	19	0	0
21[g]	$Pd(OAc)_2$ (20)	0.5	AgOAc	toluene	110	24	20	<5	<5

[a]All the reactions were performed using **2a**. [b]Result of entry 5, Table 1. [c]**2b** was used instead of **2a**. [d]**2c** was used instead of **2a**. [e]Quinoline (40 mol %) was added as an additive. [f]2-Methylquinoline (40 mol %) was added as an additive. [g]2-Hydroxy-4-methylquinoline (40 mol %) was added as an additive.

molecular amidation reactions of substrates **1a−c** afforded the corresponding pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds in low to satisfactory yield. The exact reason for the low yield of some of the pyrrolidone-ring annulated thiophene/furan-based products is not clear at this stage, although some of the possible reasons are as follows. First, these processes are two-step reactions, and the pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds **8a−z**, **8aa**, **10a−c**, and **12a−d** were formed after the formation of the corresponding C−H arylated products **3−5**. Next, in some of the cases, the corresponding ketone products **9** and **11** were formed as the byproducts from the Pd(II)-catalyzed oxidation of the methylene groups of **3** and **4**.

We also performed some control experiments shown in Scheme 14 to determine a plausible mechanism for the formation of scaffolds **8a−z**, **8aa**, **10a−c**, and **12a−d** from the arylation and intramolecular amidation of substrates **1a−c**. We first performed the reaction of **1a** with the $Pd(OAc)_2$ catalyst and AgOAc additive without using any aryl iodide. Without any aryl iodide, we expected that this reaction would afford the product **14** via the Pd(II)-catalyzed intramolecular C−H amidation (eq 1, Scheme 14), but it did not.

Next, we treated **3a** with excess amounts of **2a**, the $Pd(OAc)_2$ catalyst, and AgOAc additive. This reaction successfully afforded the expected scaffold **8a** (54%, eq 2, Scheme 14) along with the arylheteroaryl ketone derivative **9a** (10%), as obtained in the optimization reactions (Table 2). Notably, the reactions using 10 mol % or 1 equiv of **2a** afforded the expected product **8a** in 12−27% yield and the byproduct **9a** in 18−20% yield (eq 2, Scheme 14). Since we have used the same aryl iodide **2a**, which was used to assemble **3a** in the reaction shown in Scheme 14 (eq 2), we then treated **3a** with a different aryl iodide to check whether the amidation is occurring or not. Accordingly, we treated **3a** with 1-chloro-4-iodobenzene, $Pd(OAc)_2$ catalyst, and AgOAc additive. Similar to the outcome of reaction of **3a** with **2a**, the reaction of **3a** with 1-chloro-4-iodobenzene also afforded the expected scaffold **8a** in 51% yield along with **9a** in 10% yield (eq 3, Scheme 14). We then performed the reaction of **3a** with the $Pd(OAc)_2$ catalyst and AgOAc additive without using any aryl iodide. We expected that this reaction would afford **8a** via the Pd(II)-catalyzed C−H amidation (eq 4, Scheme 14). However, it did not afford **8a**, and the starting material **3a** was recovered (40% recovery). The reaction did afford the arylheteroaryl ketone derivative **9a** as a byproduct in 15% yield (eq 4, Scheme 14). Then, to check whether the product **9a** was formed in the above reactions due to adventitious moisture, we performed the reaction of **3a** with **2a**, $Pd(OAc)_2$ catalyst and AgOAc additive and water. This reaction afforded the product **8a** in 11−20% yields and **9a** in only 7−8% yields (eq 5, Scheme 14). While we

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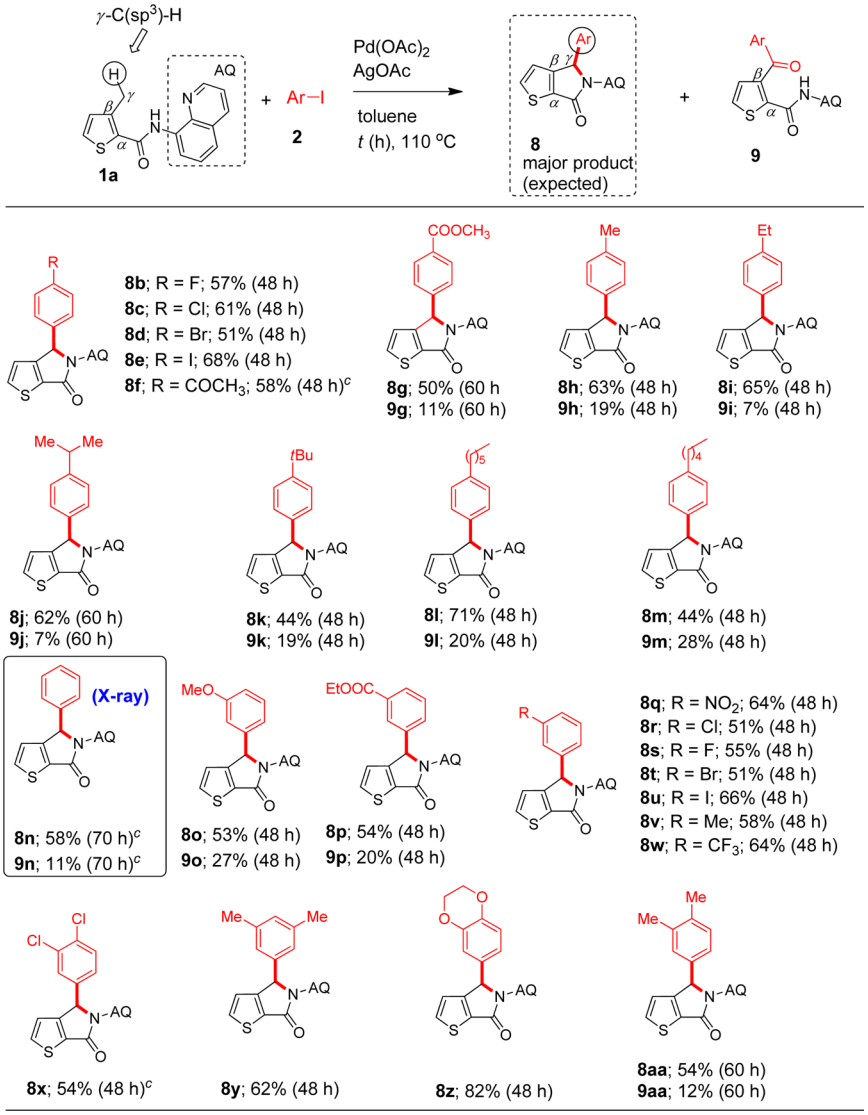
Scheme 11. Successive Arylation/Intramolecular Amidation of the γ-C(sp^3)−H Bond of 1a: Synthesis of Pyrrolidone Ring Annulated Thiophene Scaffolds 8b−z and 8aa[a,b]



[a]All reactions were performed using **1a** (0.125 mmol), ArI (1.25 mmol), $Pd(OAc)_2$ (20 mol %), and AgOAc (0.27 mmol) in toluene (2−3 mL). [b]The corresponding ketone products **9g−p** and **9aa** (minor products) were isolated in pure forms. In the rest of the cases, the corresponding ketone products **9** (minor products) were not obtained in characterizable amounts. [c]1.5 mmol of ArI was used.

expected that this reaction will afford only the product **9a** as the major isomer, however, we obtained both the products **8a** and **9a** (eq 5, Scheme 14) similar to the reactions shown in eq 2 (Scheme 14). It is assumed that the ketone **9a** was formed from the Pd(II)-catalyzed oxidation of the methylene group of **3a** with adventitious oxygen in the reaction system.[45]

These control reactions indicated that (a) the process comprising the formation of pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffold (e.g., **8a−z**, **8aa**, **10a−c**, and **12a−d**) involves two steps: C−H arylation and intramolecular C−H amidation; (b) the pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds were formed only after the formation of the corresponding C−H arylated products (e.g., arylheteroarylmethanes **3−5**); and (c) aryl iodide seems to be an important component in the intramolecular amidation step, which affords the pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds from the C−H arylated products (e.g., arylheteroarylmethanes/diheteroarylmethanes **3−5**).

The Pd(II)-catalyzed reactions of compounds **1a−d** with aryl iodides with reaction periods of 4−24 h (except a few reactions which required 36 or 48 h) afforded the corresponding diarylmethanes **3−6** (monoarylated products) in satisfactory to high yields (Table 1 and Schemes 6 and 7). In these reactions, the column chromatographic purification of the corresponding crude reaction mixtures did not afford any other corresponding byproducts, such as bis-arylated products or intramolecular C−H amidation products (e.g., **8**, **10**, and **12**) in characterizable amounts, and in most of the reactions the corresponding starting materials (**1a−c**) were also recovered. On the other hand, the Pd(II)-catalyzed reactions of compounds **1a−c** with aryl iodides with reaction periods of 48−70 h led to the corresponding successive γ-C(sp^3)−H arylation/intramolecular amidation products **8**, **10**, and **12** (Table 2 and Schemes 11−13) in satisfactory to high yields. While some of the

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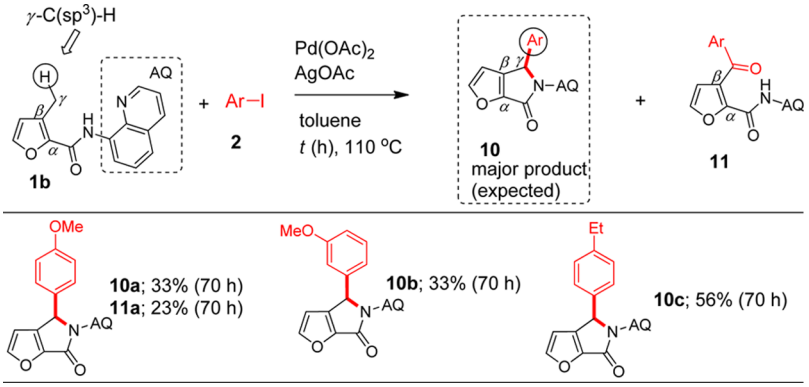
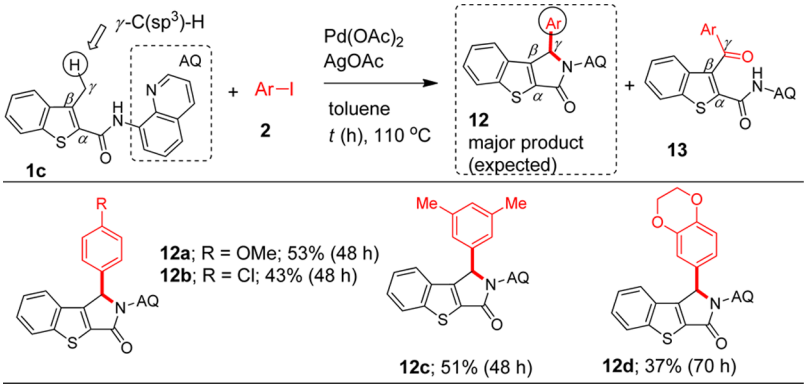
Scheme 12. Successive Arylation/Intramolecular Amidation of the γ-C(sp³)−H Bond of 1b: Synthesis of Pyrrolidone Ring Annulated Furan Scaffolds 10a−c[a,b]



[a]All reactions were performed using **1b** (0.125 mmol), ArI (1.5 mmol), $Pd(OAc)_2$ (20−30 mol %), and AgOAc (0.27 mmol) in toluene (2−3 mL). [b]The corresponding ketone products **11a** (minor product) was isolated in pure form. In the rest of the cases, the corresponding ketone products **11** (minor products) were not obtained in characterizable amounts.

Scheme 13. Successive Arylation/Intramolecular Amidation of the γ-C(sp³)−H Bond of 1c: Synthesis of Pyrrolidone Ring Annulated Benzothiophene Scaffolds 12a−f[a,b]



[a]All reactions were performed using **1c** (0.125 mmol), ArI (1.5 mmol), $Pd(OAc)_2$ (20 mol %), and AgOAc (0.27 mmol) in toluene (2−3 mL) for 48−70 h. [b]The corresponding ketone products **13** (minor products) were not obtained in characterizable amounts.

reactions gave the corresponding ketones **9** and **11** as the byproducts, the column chromatographic purification of the corresponding crude reaction mixtures also did not afford any other corresponding bis-arylated products in characterizable amounts. At this stage, an exact reason for the selective formation **8**, **10**, and **12** via the monoarylation followed by intramolecular C−H amidation over the bis arylation is not clear to us. It is proposed that the formation of a five membered-ring during the reductive elimination step (Scheme 15) might be the driving force to afford the corresponding cyclized products **8**, **10**, and **12** over the bis arylation.

On basis of the results from the control reactions (Scheme 14) and the observed products **3**−**5** and **8**/**10**/**12**, the γ-C(sp³)−H arylation and successive arylation/intramolecular amidation can be plausibly explained via a chelation- and BDG-assisted mechanism in concurrence with the proposed Pd^{II}−Pd^{IV} catalytic cycle mechanism[1−7] (Scheme 15). It is well documented that $Pd(OAc)_2$ functions as a catalyst and the AgOAc additive regenerates the $Pd(OAc)_2$ catalyst in the catalytic process.[1−7] An initial coordination of **1a** with $Pd(OAc)_2$ followed by the γ-C(sp³)−H activation generates the Pd(II) species **15**, which undergoes an oxidative addition with ArI to afford the Pd(IV) species **16**. Species **16** then undergoes reductive elimination to afford the species **17**. Species **17** then undergoes a ligand exchange followed by protonation with AcOH to afford the γ-C(sp³)−H arylated product **3a** and the Pd(II) catalyst (Scheme 15).

Subsequently, **3a** reacts with the palladium(II) catalyst to afford the Pd(II) species **18**, which undergoes an oxidative addition with ArI to afford the Pd(IV) species **19**. Species **19** then undergoes reductive elimination to afford the pyrrolidone-ring annulated thiophene-based heterocycle **8** and the palladium(II) species **20** (Scheme 15). Plausibly, species **20** then generates biaryl **21** and palladium(II) catalyst involving reductive elimination, ligand exchange, and protonation processes, respectively.[48] Given that depending on the reaction conditions used the Pd(II)-catalyzed arylation of **1a** selectively afforded either monoarylated product **3a** or the cyclized products **8**, it is believed that the formation of bis-arylated product **22** seems to be a less favored process than the formation of a five-membered ring in the reductive elimination step involving the species **19**.

The arylheteroarylmethane and diheteroarylmethane scaffolds **3**−**7** were characterized by NMR and HRMS analysis. A representative diheteroarylmethane derivative **3l** was also characterized by X-ray structure analysis (see the SI for the X-ray structure). Characteristically, the corresponding benzylic signals of **3**−**7** appeared as singlet peaks around δ 4.4−4.8 ppm

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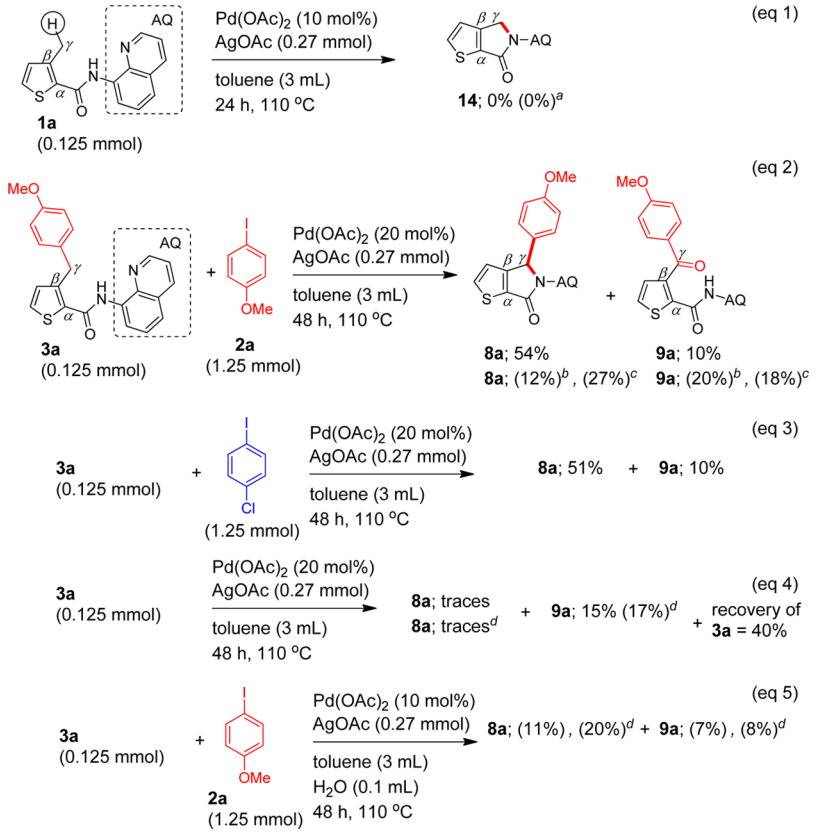
Scheme 14. Control Experiments To Explain the Proposed Mechanism of the Successive Arylation/Intramolecular Amidation Affording the Pyrrolidone Ring Annulated Scaffolds



[a]This reaction was performed without $Pd(OAc)_2$. [b]10 mol % of **2a** was used. [c]0.125 mmol of **2a** was used. [d]The reaction was performed under aerobic conditions.

in the proton NMR spectra. Similarly, the pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds **8a–z**, **8aa**, **10a–c**, and **12a–d** were characterized by NMR and HRMS analysis. Characteristically, the corresponding benzylic signals of **8**, **10**, and **12** appeared as singlet peaks around δ 6.8–7.4 ppm in the proton NMR spectra. A representative pyrrolidone-ring annulated thiophene-based heterocyclic scaffold **8n** was also characterized by X-ray structure analysis (see the SI for the X-ray structure). The arylheteroaryl ketones **9g–p**, **9aa**, and **11a** were also characterized by NMR and HRMS analysis.

CONCLUSION

We investigated the Pd(II)-catalyzed, BDG-assisted C–H activation followed by the arylation and intramolecular amidation of the γ-C(sp^3)–H bonds of carboxylic acids. To this end, we used the starting materials 3-methylfuran/thiophene-2-carboxamides **1a**, **1b**, and **1e** as well as 3-methylbenzofuran-2-carboxamide **1c** and 3-methylbenzothiophene-2-carboxamide **1d** (which were derived from their corresponding carboxylic acids and BDGs). The arylation of **1a–e** with aryl iodides with reaction times of 4–36 h afforded a variety of unsymmetrical diarylmethane scaffolds, such as furan/thiophene-based arylheteroarylmethanes **3–7**. Furthermore, prolonging the reaction period of the Pd(II)-catalyzed reaction of substrates **1a–c** with aryl iodides to 48–70 h led to the successive γ-C(sp^3)–H arylation/intramolecular amidation in a single operation. This process led to the construction of several new classes of pyrrolidone-ring annulated thiophene/furan-based heterocyclic scaffolds **8**, **10**, and **12**. These scaffolds are structurally similar to the well-known 3-phenylisoindolin-1-one scaffolds. Overall, this work contributes to enriching the research area pertaining to the bidentate directing group-assisted functionalization of remote C–H bonds of carboxylic acid derivatives.

EXPERIMENTAL SECTION

General Procedures. IR spectra of samples were recorded as KBr pellets, thin films, or neat. Proton and carbon NMR spectra of all compounds were recorded using TMS as an internal standard in 400 and 100 MHz spectrometers, respectively. The HRMS measurements of all compounds were obtained from a QTOF mass analyzer using electrospray ionization (ESI) techniques. Column chromatography purification of crude reaction mixtures was carried out on silica gel (100–200 mesh) or neutral alumina. TLC analysis was performed on silica/alumina plates, and components were visualized by observation under iodine vapor. Reactions were conducted in anhydrous solvents under a nitrogen or argon atmosphere wherever required, and organic layers obtained after work up procedure were dried using anhydrous Na_2SO_4. Isolated yields of all the products are reported, and yields of the reactions/products were not optimized. Amides **1a–m** were prepared using standard literature procedures.[1−7] In all cases, after the Pd(II)-catalyzed arylation and arylation/amidation reactions, the respective crude reaction mixtures were subjected to the column chromatographic purification method. Then the fractions were collected according to the TLC, and in all cases, we focused to isolate the corresponding γ-C(sp^3)–H arylation products **3–7** and pyrrolidone-ring annulated thiophene/furan- and benzothiophene-based heterocyclic scaffolds **8**/**10**/**12**. In the reactions involving the γ-

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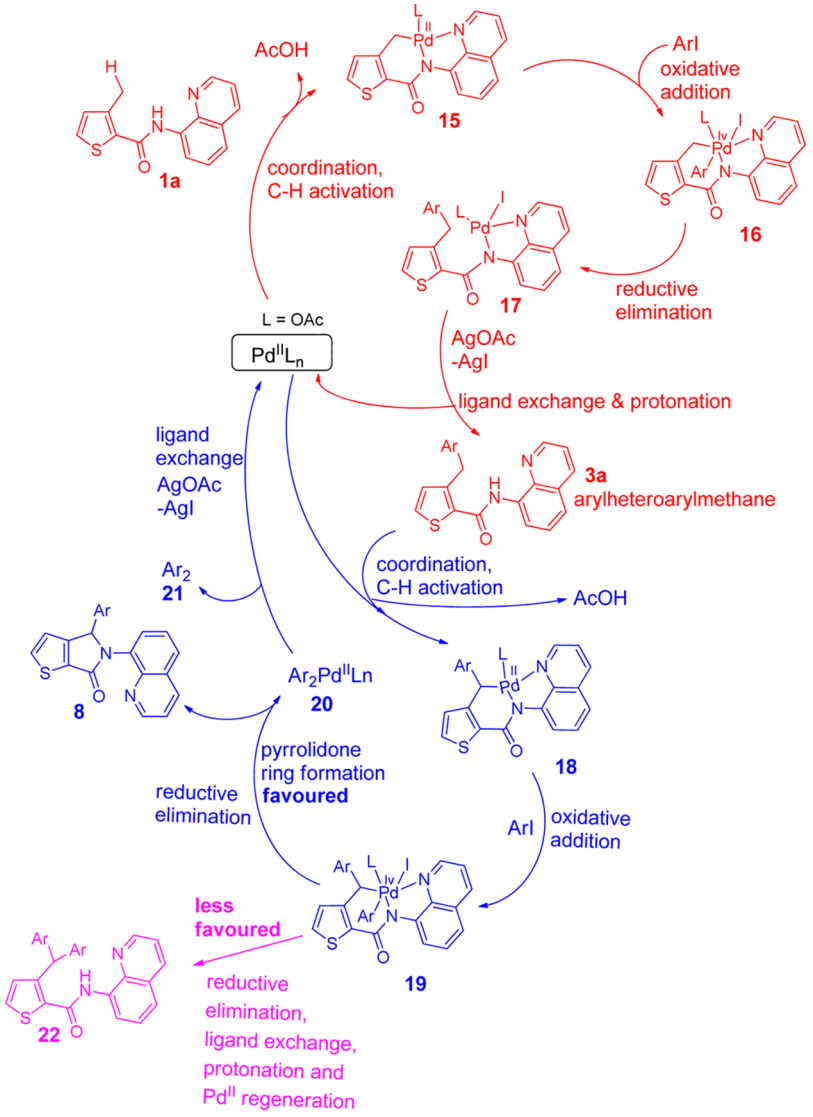
Scheme 15. Proposed Mechanism for the Pd(II)-Catalyzed γ-C(sp^3)−H Arylation of 1a−d and Successive Arylation/Intramolecular Amidation of 1a−c



C(sp^3)−H arylation and intramolecular amidation of the substrates **1a−c**, along with the expected heterocycles **8**/**10**/**12**, in some cases we isolated the corresponding ketone products **9**/**11** (minor products) as the byproducts. Specifically, the products **9a**, **9g−p**, **9aa**, and **11a** were isolated in pure form. In the rest of the cases, the corresponding ketone products **9**/**11** were not obtained in characterizable amounts. Apart from the products reported in this work, the column-chromatographic purification of the respective crude reaction mixtures did not give any other products in characterizable amounts.

General Procedure for Synthesis of Carboxamides 1a−l. An appropriate carboxylic acid (1−1.2 mmol, 1 equiv) in $SOCl_2$ (3−4 mmol, 3−4 equiv) was heated at 80 °C for 15 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuo and diluted with anhydrous DCM (3 mL) under a nitrogen atm. Then the DCM solution containing the corresponding acid chloride was added to a separate flask containing an appropriate amine (directing group, 1 mmol, 1 equiv) and Et_3N (112−123 mg, 1.1−1.2 mmol, 1.1−1.2 equiv) in anhydrous DCM (2 mL). After this, the reaction mixture was stirred at rt for 10 min, and the reaction mixture was refluxed for 12 h. After this period, the reaction mixture was diluted with DCM (5 mL) and washed with water followed by saturated aqueous $NaHCO_3$ solution. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo, and purification of the resulting reaction mixture by column chromatography (EtOAc/hexanes = 30:70) furnished the corresponding carboxamides **1a−l**.

General Procedure for the Pd(II)-Catalyzed Arylation of Carboxamides 1a−l and Preparation of Compounds 3a−n, 4a−o, 5a−h, 6a−f, and 7a−i. An appropriate carboxamide (0.125 mmol, 1 equiv), an appropriate aryl iodide (0.75−1.0 mmol, 6−8 equiv), $Pd(OAc)_2$ (2.8 mg, 10 mol %), and AgOAc (46 mg, 0.27 mmol, 2.2 equiv) in anhydrous toluene (2−3 mL) were heated at 110 °C for 4−48 h under a nitrogen atm. After the reaction period, the reaction mixture was concentrated in vacuo, and purification of the resulting reaction mixture by column chromatography on neutral alumina or silica gel (eluent = EtOAc/hexanes) furnished the corresponding arylheteroarylmethanes **3a−n**, **4a−o**, **5a−h**, **6a−f**, and **7a−i** (see the corresponding tables and schemes for specific examples).

General Procedure for the Pd(II)-Catalyzed Arylation and Intramolecular Amidation of Carboxamides 1a−c and Preparation of 8a−z, 8aa, 10a−c, and 12a−d. An appropriate carboxamide (0.125 mmol, 1 equiv), an appropriate aryl iodide (1.25 mmol, 10 equiv), $Pd(OAc)_2$ (5.6 mg, 20 mol %), and AgOAc (45.9 mg, 0.27 mmol, 2.2 equiv) in anhydrous toluene (2−3 mL) was heated at 110 °C for 48−60 h under a nitrogen atmosphere. After this reaction period, the reaction mixture was concentrated in vacuo and purification of the resulting reaction mixture by column chromatog-

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raphy on neutral alumina or silica gel (eluent = EtOAc/hexanes) furnished the corresponding heterocyclic compounds **8a−z**, **8aa**, **10a-c**, and **12a−d** (see the corresponding tables and schemes for specific examples).

Typical Procedure for the Hydrolysis of Carboxamide 3a. Preparation of the Carboxylic Acid 3aa. A solution of 3-(4-methoxybenzyl)-*N*-(quinolin-8-yl)thiophene-2-carboxamide (**3a**, 47 mg, 0.125 mmol, 1 equiv) and NaOH (240 mg, 6 mmol) in ethanol (1.5 mL) was heated at 80 °C for 24 h. After this period, the reaction mixture was diluted with water and extracted with ether (2 × 10 mL). The aqueous layer was acidified with 1 N HCl and extracted with ether (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, and then the solvent was evaporated in vacuo to afford the carboxylic acid **3aa**.

Typical Procedure for the Preparation of the Carboxylate Derivative 3ab. To a solution of 3-(4-methoxybenzyl)-*N*-(quinolin-8-yl)thiophene-2-carboxamide **3a** (47 mg, 0.125 mmol, 1 equiv) in dry methanol (3 mL) was added $BF_3{\cdot}Et_2O$ (0.5 mL) dropwise. Then the resulting mixture was stirred at 80 °C for 48 h and allowed to attain rt. Et_3N (304 mg, 3 mmol) was added dropwise to the reaction mixture with stirring, and then the solvent was evaporated in vacuo to afford the carboxylate derivative **3ab**.

*3-Methyl-N-(quinolin-8-yl)thiophene-2-carboxamide (**1a**).*[8d] Compound **1a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 70% (188 mg); R_f = 0.55 (EtOAc/hexanes = 1:4); mp 104−106 °C; IR (KBr) 3355, 1649, 1526, 1485, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.86 (dd, 1H, J_1 = 7.5 Hz, J_2 = 1.4 Hz), 8.81 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.14 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.56 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.50 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.3 Hz), 7.43 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.40 (d, 1H, J = 5.0 Hz), 6.97 (d, 1H, J = 5.0 Hz), 2.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 148.3, 141.0, 138.6, 136.3, 134.7, 132.9, 132.4, 127.9, 127.8, 127.4, 121.7, 121.6, 116.5, 16.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_2OS$ 269.0749, found 269.0742.

*3-Methyl-N-(quinolin-8-yl)furan-2-carboxamide (**1b**).*[8d] Compound **1b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 71% (179 mg); R_f = 0.52 (EtOAc/hexanes = 1:4); mp 118−120 °C; IR (KBr) 3345, 1669, 1529, 1484, 1327 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.75 (br s, 1H), 8.91−8.88 (m, 2H), 8.17 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.57 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.52 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.5 Hz), 7.50 (d, 1H, J = 1.6 Hz), 7.47 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 6.43 (d, 1H, J = 1.6 Hz), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 148.3, 142.9, 142.6, 138.7, 136.3, 134.5, 128.8, 128.0, 127.4, 121.6, 121.5, 116.3, 115.8, 11.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_2$ 253.0977, found 253.0985.

*3-Methyl-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**1c**).* Compound **1c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless solid: yield 85% (270 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); mp 133−135 °C; IR (KBr) 3303, 1649, 1526, 1423 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.62 (br s, 1H), 8.92 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 8.88 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.91−7.87 (m, 2H), 7.61 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.5 Hz), 7.51−7.46 (m, 3H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 148.5, 140.7, 139.1, 138.6, 136.4, 136.3, 134.5, 132.0, 128.0, 127.4, 126.7, 124.7, 123.4, 122.7, 121.9, 121.8, 116.6, 13.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{15}N_2OS$ 319.0905, found 319.0909.

*3-Methyl-N-(quinolin-8-yl)benzofuran-2-carboxamide (**1d**).* Compound **1d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless solid: yield 50% (151 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 178−180 °C; IR (KBr) 1648, 1527, 1486, 1354 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.99 (br s, 1H), 8.96 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.16 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.66−7.63 (m, 2H), 7.58 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.50−7.46 (m, 2H), 7.33 (t, 1H, J = 7.9 Hz), 2.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 153.5, 148.5, 143.0, 138.7, 136.3, 134.3, 129.9, 128.0, 127.3, 127.3, 123.6, 123.2, 121.9, 121.7, 120.9, 116.6, 112.0, 9.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{15}N_2O_2$ 303.1134, found 303.1129.

*3-Methyl-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**1e**).* Compound **1e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless solid: yield 70% (184 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 82−84 °C; IR (KBr) 1526, 1486, 1423, 1384, 1327 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (br s, 1H), 8.49 (d, 1H, J = 8.2 Hz), 7.55 (d, 1H, J = 7.7 Hz), 7.38 (d, 1H, J = 5.0 Hz), 7.35 (t, 1H, J = 7.6 Hz), 7.11 (t, 1H, J = 7.6 Hz), 6.97 (d, 1H, J = 5.0 Hz), 2.68 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 141.9, 138.8, 133.5, 132.5, 131.8, 129.2, 127.6, 125.2, 124.4, 120.4, 19.3, 16.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{14}NOS_2$ 264.0517, found 264.0520.

*3-Methyl-N-(quinolin-8-yl)picolinamide (**1f**).* Compound **1f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 20:80) as a colorless solid: yield 59% (157 mg); R_f = 0.35 (EtOAc/hexanes = 1:4); mp 170−172 °C; IR (KBr) 1679, 1578, 1523, 1485, 1325, 1121 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.34 (br, s, 1H), 9.01 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.64 (dd, 1H, J_1 = 4.6 Hz, J_2 = 1.0 Hz) 8.18 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.66 (dd, 1H, J_1 = 7.7 Hz, J_2 = 0.7 Hz), 7.63−7.59 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.39 (dd, 1H, J_1 = 7.7 Hz, J_2 = 4.6 Hz), 2.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.6, 147.7, 146.0, 141.1, 139.4, 136.2, 135.9, 134.9, 128.2, 127.3, 125.9, 121.7, 121.6, 116.4, 20.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{14}N_3O$ 264.1137, found 264.1130.

*Methyl 4-Methyl-3-(picolinamido)thiophene-2-carboxylate (**1g**).* Compound **1g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 70% (193 mg); R_f = 0.62 (EtOAc/hexanes = 1:4); IR (DCM) 3333, 1693, 1564, 1495, 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.0 (br, s, 1H), 8.73 (d, 1H, J = 4.4 Hz), 8.28 (d, 1H, J = 7.8 Hz), 7.91 (t, 1H, J = 7.7 Hz), 7.51 (t, 1H, J = 6.2 Hz), 7.22 (s, 1H), 3.88 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 162.1, 149.6, 148.6, 142.0, 137.4, 136.2, 127.6, 126.6, 122.7, 118.5, 52.0, 15.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{13}N_2O_3S$ 277.0647, found 277.0636.

*3-Methyl-N-propylthiophene-2-carboxamide (**1h**).* Compound **1h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless liquid: yield 89% (164 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); IR (DCM) 3369, 1717, 1636, 1521, 1281, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, 1H, J = 5.0 Hz), 6.78 (d, 1H, J = 5.0 Hz), 6.23 (br s, 1H), 3.30−3.25 (m, 2H), 2.42 (s, 3H), 1.59−1.50 (m, 2H), 0.89 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 140.3, 131.7, 131.4, 126.2, 41.6, 22.9, 15.6, 11.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_9H_{14}NOS$ 184.0796, found 184.0790.

*N-(2-Methoxyphenyl)-3-methylthiophene-2-carboxamide (**1i**).*[49b] Compound **1i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless liquid: yield 64% (160 mg); R_f = 0.43 (EtOAc/hexanes = 1:4); IR (DCM) 2927, 1656, 1522, 1460, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, 1H, J_1 = 7.9 Hz, J_2 = 1.6 Hz), 8.37 (br s, 1H), 7.37 (d, 1H, J = 5.0 Hz), 7.10 (td, 1H, J = 1.7 Hz, J_2 = 7.7 Hz), 7.03 (td, 1H, J = 1.4 Hz, J_2 = 7.8 Hz), 6.96−6.92 (m, 2H), 3.94 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 140.7, 132.6, 132.3, 127.7, 127.4, 123.8, 121.2, 119.7, 109.9, 55.9, 15.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{14}NO_2S$ 248.0745, found 248.0738.

*N,N,3-Trimethylthiophene-2-carboxamide (**1j**).* Compound **1j** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless liquid: yield 79% (135 mg); R_f = 0.65 (EtOAc/hexanes = 1:4); IR (DCM) 2927, 1622, 1547, 1392, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22−7.20 (m, 1H), 6.79−6.77 (m, 1H), 3.01 (m, 6H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 137.0, 130.7, 129.6, 125.7, 14.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_8H_{12}NOS$ 170.0640, found 170.0634. The

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N-methyl signals of amide group did not appear in the ^{13}C NMR spectrum.

*3-Methyl-N-(2-methylquinolin-8-yl)thiophene-2-carboxamide (**1k**).* Compound **1k** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless liquid: yield 67% (191 mg); R_f = 0.51 (EtOAc/hexanes = 1:4); IR (DCM) 3350, 1716, 1530, 1384, 1106 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.47 (br, s, 1H), 8.78 (dd, 1H, J_1 = 7.5 Hz, J_2 = 1.4 Hz), 7.92 (d, 1H, J = 8.4 Hz), 7.44 (dd, 1H, J_1 = 8.0 Hz, J_2 = 7.7 Hz) 7.39−7.37 (m, 2H), 7.22 (d, 1H, J = 8.4 Hz), 6.94 (d, 1H, J = 5.0 Hz), 2.73 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 157.1, 140.1, 137.8, 136.3, 134.0, 133.7, 132.4, 128.1, 126.3, 125.9, 122.4, 121.3, 116.3, 25.2, 16.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{15}N_2OS$ 283.0905, found 283.0898.

*3-Methyl-N-(pyridin-2-ylmethyl)thiophene-2-carboxamide (**1l**).* Compound **1l** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 20:80) as a colorless liquid: yield 67% (156 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); IR (DCM) 3394, 1632, 1511, 1414, 1049 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.66−7.63 (m, 1H), 7.40 (br, s, 1H), 7.30−7.25 (m, 2H), 7.19−7.18 (m, 1H), 6.87−6.86 (m, 1H), 4.70 (m, 2H), 2.55 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 156.2, 149.0, 140.7, 136.8, 132.0, 131.5, 126.8, 122.4, 122.0, 44.7, 15.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{13}N_2OS$ 233.0749, found 233.0742.

Procedure for the Preparation of Amide 1m. This compound was prepared using the literature procedure.[9c] 3-Methylthiophene-2-carboxylic acid (1 mmol, 1 equiv) in $SOCl_2$ (4 mmol, 4 equiv) was heated at 80 °C for 15 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuo and diluted with anhydrous toluene (3 mL) under a nitrogen atm. Then, the toluene solution containing the corresponding acid chloride was added to a separate flask containing 2,3,4,5,6-pentafluoroaniline (1.1 mmol, 1 equiv) in anhydrous toluene (3 mL). The reaction mixture was refluxed for 12 h and then stirred at room temperature for 4 h. The reaction mixture was concentrated under vacuum to afford the product **1m**, which was obtained as a colorless solid after recrystallization (EtOAc/hexanes = 30:70): yield 50% (154 mg); mp 113−115 °C; IR (KBr) 3019, 1523, 1215, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (br s, 1H), 7.40 (d, 1H, J = 4.8 Hz), 6.97 (d, 1H, J = 4.8 Hz), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 144.8, 144.7−144.1 (m), 141.8−141.7 (m), 141.4−141.3 (m), 139.2−138.6 (m), 136.7−136.4 (m), 132.5, 128.4, 128.1, 112.1−111.9 (m), 15.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_7F_2NOS$ 308.0169, found 308.0154.

*3-(4-Methoxybenzyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3a**).* Compound **3a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 72% (34 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); IR (DCM) 3308, 1651, 1523, 1483, 1244, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.48 (br s, 1H), 8.88 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.80 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.48 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.39 (d, 1H, J = 5.1 Hz), 7.25 (d, 2H, J = 8.7 Hz), 6.90 (d, 1H, J = 5.1 Hz), 6.87 (d, 2H, J = 8.7 Hz),), 4.48 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 158.1, 148.3, 145.6, 138.6, 136.3, 134.7, 132.2, 132.1, 131.6, 129.9, 128.0, 127.5, 127.4, 121.7, 116.6, 113.9, 55.3, 34.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_2S$ 375.1167, found 375.1180.

*3-(4-Acetylbenzyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3b**).* Compound **3b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a pale yellow solid: yield 58% (28 mg); R_f = 0.35 (EtOAc/hexanes = 1:4); mp 126−128 °C; IR (KBr)1653, 1525, 1485, 1384, 1265 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.48 (br s, 1H), 8.85 (dd, 1H, J_1 = 7.1 Hz, J_2 = 1.8 Hz), 8.80 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.92 (d, 2H, J = 8.2 Hz), 7.62−7.55 (m, 2H), 7.48 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.43−7.42 (m, 3H), 6.92 (d, 1H, J = 5.0 Hz), 4.60 (s, 2H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 160.9, 148.3, 145.9, 144.3, 138.6, 136.4, 135.3, 134.5, 132.2, 131.4, 129.1, 128.7, 128.0, 127.6, 127.4, 121.8, 121.8, 116.6, 35.2, 26.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_2S$ 387.1167, found 387.1179.

*Methyl 4-((2-(Quinolin-8-ylcarbamoyl)thiophene-3-yl)methyl)-benzoate (**3c**).* Compound **3c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a brown solid: yield 67% (34 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); mp 134−136 °C; IR (KBr) 3303, 1656, 1525, 1485, 1327, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.47 (br s, 1H), 8.85 (dd, 1H, J_1 = 7.2 Hz, J_2 = 1.7 Hz), 8.79 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.99 (d, 2H, J = 8.3 Hz), 7.59 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.9 Hz), 7.48 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.42−7.39 (m, 3H), 6.90 (d, 1H, J = 5.1 Hz), 4.59 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 161.0, 148.3, 145.6, 144.4, 138.6, 136.4, 134.5, 132.2, 131.4, 129.9, 128.9, 128.2, 128.0, 127.6, 127.4, 121.8, 121.7, 116.6, 52.0, 35.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_3S$ 403.1116, found 403.1101.

*3-(4-Ethylbenzyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3d**).* Compound **3d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 53% (25 mg); R_f = 0.51 (EtOAc/hexanes = 1:4); IR (DCM) 2962, 1660, 1524, 1484, 1423 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.49 (br s, 1H), 8.88 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.78 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.76 Hz), 7.55 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.47 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.39 (d, 1H, J = 5.1 Hz), 7.25 (d, 2H, J = 8.1 Hz), 7.16 (d, 2H, J = 8.1 Hz), 6.91 (d, 1H, J = 5.1 Hz), 4.51 (s, 2H), 2.64 (q, 2H, J = 7.6 Hz), 1.24 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 148.3, 145.4, 142.1, 138.6, 137.3, 136.3, 134.7, 132.1, 131.7, 128.9, 128.0, 128.0, 127.4, 121.7, 116.6, 35.0, 28.5, 15.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{21}N_2OS$ 373.1375, found 373.1367.

*3-(4-Nitrobenzyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3e**).*[49a] Compound **3e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a pale yellow solid: yield 72% (35 mg); R_f = 0.43 (EtOAc/hexanes = 1:4); mp 153−155 °C; IR (KBr) 1648, 1529, 1484, 1385 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.48 (br s, 1H), 8.84−8.82 (m, 2H), 8.21 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 8.16 (d, 2H, J = 8.8 Hz), 7.62−7.56 (m, 2H), 7.52−7.49 (m, 3H), 7.45 (d, 1H, J = 5.0 Hz), 6.94 (d, 1H, J = 5.0 Hz), 4.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 148.4, 148.1, 146.5, 143.8, 138.5, 136.5, 134.4, 132.2, 131.3, 129.6, 128.0, 127.7, 127.4, 123.8, 122.0, 121.8, 116.6, 35.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{16}N_3O_3S$ 390.0912, found 390.0917.

*3-(4-Bromobenzyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3f**).* Compound **3f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 58% (31 mg); R_f = 0.41 (EtOAc/hexanes = 1:4); mp 112−114 °C; IR (KBr) 1660, 1525, 1485, 1385 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.85 (dd, 1H, J_1 = 7.2 Hz, J_2 = 1.7 Hz), 8.80 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.8 Hz), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.43 (d, 2H, J = 8.4 Hz), 7.41 (d, 1H, J = 5.1 Hz), 7.21 (d, 2H, J = 8.4 Hz), 6.90 (d, 1H, J = 5.1 Hz), 4.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 148.3, 144.7, 139.2, 138.6, 136.4, 134.5, 132.1, 131.6, 131.4, 130.7, 127.9, 127.5, 127.4, 121.8, 121.8, 120.1, 116.6, 34.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{16}BrN_2OS$ 423.0167, found 423.0164.

*3-Benzyl-N-(quinolin-8-yl)thiophene-2-carboxamide (**3g**).* Compound **3g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 55% (24 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); mp 138−140 °C; IR (KBr) 1661, 1525, 1485, 1328 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.49 (br s, 1H), 8.88 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.79 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.47 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.39 (d, 1H, J = 5.1 Hz), 7.34−7.30 (m, 4H), 7.26−7.22 (m, 1H), 6.91 (d, 1H, J = 5.1 Hz), 4.55

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(s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 148.3, 145.1, 140.1, 138.6, 136.3, 134.6, 132.2, 131.6, 128.9, 128.5, 128.0, 127.5, 127.4, 126.3, 121.7, 116.6, 35.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{17}N_2OS$ 345.1062, found 345.1048.

*3-((2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3h**).* Compound **3h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a brown solid: yield 47% (24 mg); R_f = 0.48 (EtOAc/hexanes = 1:4); mp 209−211 °C; IR (KBr) 3339, 1658, 1525, 1429, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.87 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 8.81 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.59 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.47 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.39 (d, 1H, J = 5.1 Hz), 6.93 (d, 1H, J = 5.0 Hz), 6.84 (s, 1H), 6.82−6.81 (m, 2H), 4.43 (s, 2H), 4.24 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 148.3, 145.3, 143.4, 142.0, 138.6, 136.3, 134.7, 133.4, 132.1, 131.6, 128.0, 127.5, 127.4, 121.9, 121.7, 117.6, 117.2, 116.6, 64.4, 64.3, 34.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_3S$ 403.1116, found 403.1104.

*3-((5-Bromopyridin-2-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3i**).* Compound **3i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a brown solid: yield 96% (51 mg); R_f = 0.35 (EtOAc/hexanes = 1:4); mp 150−152 °C; IR (KBr) 1654, 1524, 1485, 1382 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.74 (br s, 1H), 8.84 (dd, 1H, J_1 = 7.2 Hz, J_2 = 1.7 Hz), 8.77 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.65 (d, 1H, J = 2.3 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.73 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.4 Hz), 7.61−7.54 (m, 2H), 7.46 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.42 (d, 1H, J = 5.1 Hz), 7.30 (d, 1H, J = 8.6 Hz), 7.04 (d, 1H, J = 5.1 Hz), 4.62 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 158.5, 150.3, 148.3, 142.7, 139.3, 138.8, 136.3, 134.7, 132.9, 131.4, 128.0, 127.6, 127.3, 124.7, 121.9, 121.7, 118.4, 117.1, 37.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}BrN_3OS$ 424.0119, found 424.0114.

*3-((6-Fluoropyridin-3-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3j**).* Compound **3j** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a pale yellow solid: yield 57% (26 mg); R_f = 0.32 (EtOAc/hexanes = 1:4); mp 124−126 °C; IR (KBr) 1659, 1526, 1484, 1328, 1246 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.83 (d, 2H, J = 7.2 Hz), 8.19 (d, 2H, J = 8.6 Hz), 7.80−7.76 (m, 1H), 7.61−7.55 (m, 2H), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.43 (d, 1H, J = 5.0 Hz), 6.93 (d, 1H, J = 8.3 Hz), 6.86 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.5 Hz), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, J_{C-F} = 236.2 Hz), 160.8, 148.4, 147.3 (d, J_{C-F} = 14.4 Hz), 144.3, 141.7 (d, J_{C-F} = 7.6 Hz), 138.5, 136.4, 134.4, 133.5 (d, J_{C-F} = 4.4 Hz), 132.0, 131.2, 128.0, 127.7, 127.4, 121.9, 121.8, 116.6, 109.3 (d, J_{C-F} = 37.2 Hz), 31.5 (d, J_{C-F} = 1.1 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}FN_3OS$ 364.0920, found 364.0913.

*3-((6-Chloropyridin-3-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3k**).* Compound **3k** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 54% (26 mg); R_f = 0.34 (EtOAc/hexanes = 1:4); mp 122−124 °C; IR (KBr) 1657, 1585, 1385, 1244, 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.84−8.82 (m, 2H), 8.39 (d, 1H, J = 2.1 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.65 (dd, 1H, J_1 = 8.2 Hz, J_2 = 2.5 Hz), 7.62−7.56 (m, 2H), 7.50 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.44 (d, 1H, J = 5.1 Hz), 7.26 (d, 1H, J = 8.2 Hz), 6.94 (d, 1H, J = 5.1 Hz), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 149.8, 149.4, 148.4, 144.0, 139.4, 138.5, 136.4, 134.8, 134.4, 132.1, 131.2, 128.0, 127.8, 127.4, 124.1, 122.0, 121.8, 116.6, 31.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}ClN_3OS$ 380.0624, found 380.0611.

*3-((1H-Indol-5-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3l**).* Compound **3l** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 60:40) as a colorless liquid: yield 54% (26 mg); R_f = 0.22 (EtOAc/hexanes = 1:4); IR (DCM) 3319, 1707, 1651, 1526, 1484, 1384 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 10.48 (br s, 1H), 8.96 (br s, 1H), 8.84 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 8.67 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.13 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.57−7.49 (m, 3H), 7.40 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.32−7.30 (m, 2H), 7.16−7.11 (m, 2H), 6.87 (d, 1H, J = 5.1 Hz), 6.44−6.43 (m, 1H), 4.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 161.3, 148.3, 146.1, 138.6, 136.2, 134.7, 134.7, 132.1, 131.9, 131.0, 128.2, 127.9, 127.4, 127.3, 124.6, 123.2, 121.7, 121.7, 120.4, 116.6, 111.2, 111.0, 35.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{18}N_3OS$ 384.1171, found 384.1159.

*3-((2-Chloropyridin-4-yl)methyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3m**).* Compound **3m** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 80% (38 mg); R_f = 0.35 (EtOAc/hexanes = 1:4); IR (DCM) 1657, 1591, 1526, 1485, 1327 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.83−8.81 (m, 2H), 8.29 (d, 1H, J = 5.1 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.61−7.56 (m, 2H), 7.51−7.47 (m, 2H), 7.28 (s, 1H), 7.20−7.18 (m, 1H), 6.95 (d, 1H, J_1 = 5.1 Hz), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 152.6, 151.7, 149.6, 148.4, 142.6, 138.5, 136.4, 134.3, 132.6, 131.3, 128.0, 127.8, 127.4, 124.4, 123.0, 122.0, 121.9, 121.8, 116.6, 34.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}ClN_3OS$ 380.0624, found 380.0626.

*3-(Pyridin-3-ylmethyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**3n**).* Compound **3n** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 46% (20 mg); R_f = 0.39 (EtOAc/hexanes = 1:4); IR (DCM) 1656, 1525, 1484, 1385, 1122 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (br s, 1H), 8.85 (dd, 1H, J_1 = 7.1 Hz, J_2 = 1.8 Hz), 8.82 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.63 (d, 1H, J = 1.6 Hz), 8.48 (dd, 1H, J_1 = 4.7 Hz, J_2 = 1.1 Hz), 8.20 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.5 Hz), 7.65 (d, 1H, J = 7.8 Hz), 7.62−7.55 (m, 2H), 7.49 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.43 (d, 1H, J = 5.1 Hz), 7.23 (dd, 1H, J_1 = 7.8 Hz, J_2 = 4.8 Hz), 6.93 (d, 1H, J = 5.1 Hz), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 150.2, 148.4, 147.7, 144.3, 138.5, 136.4, 135.8, 134.5, 132.2, 131.4, 128.0, 127.7, 127.4, 123.5, 121.9, 121.9, 116.6, 32.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{16}N_3OS$ 346.1014, found 346.1001.

*3-(4-Acetylbenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4a**).* Compound **4a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a pale yellow solid: yield 82% (38 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 143−145 °C; IR (KBr) 3302, 1671, 1529, 1484, 1328 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.81 (br s, 1H), 8.89 (d, 1H, J = 1.8 Hz), 8.87 (dd, 1H, J_1 = 2.9 Hz, J_2 = 1.7 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.90 (d, 2H, J = 8.4 Hz), 7.59−7.53 (m, 2H), 7.51 (d, 1H, J = 8.3 Hz), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.42 (d, 2H, J = 8.4 Hz), 6.35 (d, 1H, J = 1.8 Hz), 4.44 (s, 2H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 157.5, 148.4, 145.7, 143.4, 142.6, 138.7, 136.4, 135.4, 134.3, 131.0, 129.1, 128.7, 128.1, 127.4, 121.8, 121.7, 116.5, 114.5, 31.5, 26.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_3$ 371.1396, found 371.1389.

*Methyl 4-((2-(Quinolin-8-ylcarbamoyl)furan-3-yl)methyl)-benzoate (**4b**).* Compound **4b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a brown solid: yield 74% (36 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 158−160 °C; IR (KBr) 3436, 1648, 1529, 1485 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br s, 1H), 8.92−8.89 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.99 (d, 2H, J = 8.4 Hz), 7.61−7.54 (m, 2H), 7.52−7.48 (m, 2H), 7.42 (d, 2H, J = 8.4 Hz), 6.35 (d, 1H, J = 1.8 Hz), 4.46 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 157.5, 148.4, 145.4, 143.4, 142.5, 138.7, 136.4, 134.3, 131.1, 129.9, 128.9, 128.3, 128.1, 127.4, 121.8, 121.7, 116.5, 114.5, 52.0, 31.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_4$ 387.1345, found 387.1337.

*3-(4-Methoxybenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4c**).* Compound **4c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a brown solid: yield 67% (30 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 125−127 °C; IR (KBr) 3341, 1668, 1530, 1484, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H), 8.94−8.90 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56

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(dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.52−7.49 (m, 2H), 7.28 (d, 2H, J = 8.7 Hz), 6.87 (d, 2H, J = 8.7 Hz), 6.36 (d, 1H, J = 1.7 Hz), 4.34 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 157.7, 148.4, 143.2, 142.1, 138.7, 136.4, 134.4, 132.7, 132.1, 129.8, 128.1, 127.4, 121.7, 121.6, 116.5, 114.6, 113.9, 55.3, 30.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3$ 359.1396, found 359.1405.

*3-(4-Ethylbenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4d**).* Compound **4d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 76% (34 mg); R_f = 0.43 (EtOAc/hexanes = 1:4); IR (DCM) 3341, 1670, 1529, 1484, 1384 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H), 8.94 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.90 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.51−7.48 (m, 2H), 7.29 (d, 2H, J = 8.1 Hz), 7.17 (d, 2H, J = 8.1 Hz), 6.38 (d, 1H, J = 1.8 Hz), 4.38 (s, 2H), 2.65 (q, 2H, J = 7.6 Hz), 1.25 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 148.4, 143.2, 142.2, 142.2, 138.7, 137.2, 136.4, 134.5, 132.5, 128.8, 128.1, 128.0, 127.4, 121.7, 121.6, 116.5, 114.7, 31.1, 28.5, 15.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{21}N_2O_2$ 357.1603, found 357.1597.

*3-(4-Nitrobenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4e**).* Compound **4e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 71% (33 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); IR (DCM) 1655, 1525, 1485, 1327 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (br s, 1H), 8.91 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.87 (dd, 1H, J_1 = 6.6 Hz, J_2 = 2.4 Hz), 8.21 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 8.17 (d, 2H, J = 8.8 Hz), 7.61−7.55 (m, 3H), 7.52−7.50 (m, 3H), 6.39 (d, 1H, J = 1.8 Hz), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 148.5, 147.7, 146.6, 143.6, 142.8, 138.7, 136.4, 134.2, 130.1, 129.6, 128.1, 127.3, 123.8, 121.9, 121.8, 116.6, 114.4, 31.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{16}N_3O_4$ 374.1141, found 374.1149.

*3-(4-Methylbenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4f**).* Compound **4f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 65% (28 mg); R_f = 0.42 (EtOAc/hexanes = 1:4); mp 118−120 °C; IR (KBr) 1665, 1596, 1384, 1247, 1094 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H), 8.93 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.6 Hz), 8.91 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.56 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.52−7.49 (m, 2H), 7.26 (d, 2H, J = 7.8 Hz), 7.14 (d, 2H, J = 7.8 Hz), 6.35 (d, 1H, J = 1.7 Hz), 4.37 (s, 2H), 2.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 148.4, 143.2, 142.2, 138.7, 136.9, 136.4, 135.8, 134.5, 132.6, 129.2, 128.8, 128.1, 127.4, 121.7, 121.6, 116.5, 114.6, 31.1, 21.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_2$ 343.1447, found 343.1434.

*3-(4-Cyanobenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4g**).* Compound **4g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 79% (35 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); mp 163−165 °C; IR (KBr) 1657, 1533, 1484, 1385, 1215 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.84 (br s, 1H), 8.90 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.88 (dd, 1H, J_1 = 6.6 Hz, J_2 = 2.4 Hz), 8.21 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.62−7.53 (m, 5H), 7.50 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.46 (d, 2H, J = 8.4 Hz), 6.37 (d, 1H, J = 1.7 Hz), 4.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 148.5, 145.6, 143.6, 142.8, 138.7, 136.4, 134.2, 132.4, 130.2, 129.6, 128.1, 127.3, 121.9, 121.8, 119.1, 116.5, 114.4, 110.2, 31.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{16}N_3O_2$ 354.1243, found 354.1231.

*3-(4-Chlorobenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4h**).* Compound **4h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as colorless solid: yield 93% (42 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); mp 108−110 °C; IR (KBr) 1593, 1502, 1384, 1122 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br s, 1H), 8.91−8.90 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.62−7.55 (m, 2H), 7.52−7.49 (m, 2H), 7.29 (s, 4H), 6.35 (d, 1H, J = 1.7 Hz), 4.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 148.4, 143.3, 142.4, 138.7, 138.5, 136.4, 134.3, 132.1, 131.6, 130.2, 128.6, 128.1, 127.4, 121.8, 121.7, 116.5, 114.5, 30.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{16}ClN_2O_2$ 363.0900, found 363.0887.

*3-(3-Nitrobenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4i**).* Compound **4i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a pale yellow solid: yield 55% (26 mg); R_f = 0.41 (EtOAc/hexanes = 1:4); mp 157−159 °C; IR (KBr) 1666, 1598, 1483, 1350, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (br s, 1H), 8.91 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.89 (dd, 1H, J_1 = 6.7 Hz, J_2 = 2.2 Hz), 8.22−8.20 (m, 2H), 8.10 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 7.72 (dd, 1H, J_1 = 7.6 Hz, J_2 = 0.3 Hz), 7.62−7.56 (m, 3H), 7.53−7.46 (m, 2H), 6.41 (d, 1H, J = 1.8 Hz), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 148.5, 143.6, 142.8, 142.0, 138.7, 136.4, 135.2, 134.2, 130.2, 129.4, 128.1, 127.4, 123.5, 121.9, 121.8, 121.5, 116.6, 114.4, 31.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{16}N_3O_4$ 374.1141, found 374.1127.

*3-(3-Methoxybenzyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4j**).* Compound **4j** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 60% (27 mg); R_f = 0.48 (EtOAc/hexanes = 1:4); IR (DCM) 1668, 1530, 1384, 1260, 1050 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H), 8.94−8.90 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.60 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.52−7.49 (m, 2H), 7.25 (t, 1H, J = 7.8 Hz), 6.95 (d, 1H, J = 7.6 Hz), 6.91 (br s, 1H), 6.79 (dd, 1H, J_1 = 8.1 Hz, J_2 = 2.4 Hz), 6.37 (d, 1H, J = 1.7 Hz), 4.39 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 157.7, 148.4, 143.2, 142.3, 141.5, 138.7, 136.4, 134.4, 132.1, 129.5, 128.1, 127.4, 121.7, 121.7, 121.3, 116.5, 114.7, 114.6, 111.7, 55.2, 31.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3$ 359.1396, found 359.1384.

*Ethyl 3-((2-(Quinolin-8-ylcarbamoyl)furan-3-yl)methyl)benzoate (**4k**).* Compound **4k** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 80% (40 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); IR (DCM) 1714, 1668, 1578, 1484, 1385 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br s, 1H), 8.93−8.90 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 8.02 (br s, 1H), 7.93 (d, 1H, J = 7.8 Hz), 7.61−7.54 (m, 3H), 7.52−7.48 (m, 2H), 7.39 (t, 1H, J = 7.7 Hz), 6.35 (d, 1H, J = 1.7 Hz), 4.46 (s, 2H), 4.38 (q, 2H, J = 7.1 Hz), 1.40 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 157.6, 148.4, 143.4, 142.4, 140.3, 138.7, 136.4, 134.4, 133.5, 131.5, 130.7, 129.8, 128.6, 127.6, 127.4, 121.7, 116.5, 114.5, 61.0, 31.3, 14.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_2O_4$ 401.1501, found 401.1486.

*3-((2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4l**).* Compound **4l** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 72% (35 mg); R_f = 0.49 (EtOAc/hexanes = 1:4); mp 100−102 °C; IR (KBr) 3345, 1668, 1532, 1288 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.81 (br s, 1H), 8.91−8.90 (m, 2H), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.59 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.55 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.8 Hz), 7.52−7.50 (m, 2H), 6.86−6.82 (m, 3H), 6.38 (d, 1H, J = 1.8 Hz), 4.29 (s, 2H), 4.26−4.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 148.4, 143.4, 143.2, 142.2, 142.0, 138.7, 136.4, 134.4, 133.3, 132.4, 128.1, 127.4, 121.8, 121.7, 121.6, 117.5, 117.2, 116.5, 114.6, 64.4, 64.3, 30.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_4$ 387.1345, found 387.1340.

*3-((5-Bromopyridin-2-yl)methyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4m**).* Compound **4m** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 82% (42 mg); R_f = 0.35 (EtOAc/hexanes = 1:4); mp 146−148 °C; IR (KBr) 3339, 1666, 1598, 1531, 1425, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br s, 1H), 8.91−8.88 (m, 2H), 8.62 (d, 1H, J = 2.2 Hz), 8.20 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.73 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 7.61−7.53 (m, 3H), 7.49 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.33 (d, 1H, J = 8.3 Hz), 6.53 (d, 1H, J = 1.7 Hz), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 157.5, 150.2, 148.4, 143.4, 143.4, 142.6, 139.3, 138.7, 136.4, 134.3, 129.9, 128.1, 127.3, 124.8, 121.8, 118.5, 116.5, 114.8, 33.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}BrN_3O_2$ 408.0348, found 408.0334.

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*3-((6-Fluoropyridin-3-yl)methyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4n**).* Compound **4n** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 57% (25 mg); R_f = 0.30 (EtOAc/hexanes = 1:4); mp 129−131 °C; IR (KBr) 1667, 1598, 1532, 1483, 1385, 1123 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.84 (br s, 1H), 8.91 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.88 (dd, 1H, J_1 = 6.8 Hz, J_2 = 2.2 Hz), 8.22−8.20 (m, 2H), 7.81 (td, 1H, J_1 = 2.5 Hz, J_2 = 8.2 Hz), 7.62−7.55 (m, 3H), 7.51 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 6.88 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.9 Hz), 6.38 (d, 1H, J = 1.7 Hz), 4.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, J_{C-F} = 236.0 Hz), 157.4, 148.5, 147.2 (d, J_{C-F} = 13.9 Hz), 143.6, 142.6, 141.7 (d, J_{C-F} = 7.8 Hz), 138.7, 136.4, 134.2, 133.2 (d, J_{C-F} = 4.4 Hz), 130.7, 128.1, 127.4, 121.9, 121.8, 116.5, 114.3, 109.4 (d, J_{C-F} = 37.5 Hz), 27.8 (d, J_{C-F} = 1.2 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}FN_3O_2$ 348.1148, found 348.1135.

*3-((6-Chloropyridin-3-yl)methyl)-N-(quinolin-8-yl)furan-2-carboxamide (**4o**).* Compound **4o** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 55% (25 mg); R_f = 0.30 (EtOAc/hexanes = 1:4); mp 148−150 °C; IR (KBr) 1666, 1597, 1531, 1459, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.83 (br s, 1H), 8.91 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.87 (dd, 1H, J_1 = 6.7 Hz, J_2 = 2.2 Hz), 8.39 (d, 1H, J = 2.2 Hz), 8.21 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.5 Hz), 7.67 (dd, 1H, J_1 = 8.2 Hz, J_2 = 2.4 Hz), 7.62−7.55 (m, 3H), 7.51 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.27 (d, 1H, J = 8.2 Hz), 6.37 (d, 1H, J = 1.6 Hz), 4.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 149.7, 149.5, 148.5, 143.6, 142.7, 139.4, 138.7, 136.4, 134.5, 134.2, 130.3, 128.1, 127.3, 124.2, 121.9, 121.8, 116.5, 114.3, 28.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{15}ClN_3O_2$ 364.0853, found 364.0840.

*3-(4-Acetylbenzyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5a**).* Compound **5a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as pale yellow solid: yield 60% (33 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 157−159 °C; IR (KBr) 1655, 1526, 1485, 1384, 1265, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.63 (br s, 1H), 8.89 (dd, 1H, J_1 = 6.5 Hz, J_2 = 2.5 Hz), 8.76 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.93 (d, 1H, J = 8.0 Hz), 7.88 (d, 2H, J = 8.4 Hz), 7.74 (d, 1H, J = 8.0 Hz), 7.62−7.56 (m, 2H), 7.51−7.47 (m, 2H), 7.44 (d, 2H, J = 8.4 Hz), 7.42−7.38 (m, 1H), 4.87 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 161.3, 148.4, 145.1, 139.9, 139.0, 138.5, 138.1, 136.4, 135.3, 134.4, 132.9, 128.7, 128.7, 128.0, 127.3, 126.9, 125.1, 123.8, 122.8, 122.1, 121.8, 116.8, 33.0, 26.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{21}N_2O_2S$ 437.1324, found 437.1329.

*3-(4-Methoxybenzyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5b**).* Compound **5b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 52% (28 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); IR (DCM) 3311, 1657, 1522, 1482, 1242 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.62 (br s, 1H), 8.91 (dd, 1H, J_1 = 7.1 Hz, J_2 = 1.8 Hz), 8.74 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.92 (d, 1H, J = 8.0 Hz), 7.81 (d, 1H, J = 8.0 Hz), 7.62−7.56 (m, 2H), 7.49−7.45 (m, 2H), 7.42−7.38 (m, 1H), 7.27 (d, 2H, J = 8.7 Hz), 6.82 (d, 2H, J = 8.7 Hz), 4.74 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 158.0, 148.4, 140.2, 139.2, 139.0, 138.6, 136.3, 134.5, 132.8, 131.3, 129.4, 127.9, 127.4, 126.6, 124.8, 124.1, 122.7, 122.0, 121.7, 116.8, 113.9, 55.2, 32.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_2S$ 425.1324, found 425.1330.

*Methyl 4-((2-(Quinolin-8-ylcarbamoyl)benzo[b]thiophen-3-yl)methyl)benzoate (**5c**).* Compound **5c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 46% (26 mg); R_f = 0.43 (EtOAc/hexanes = 1:4); mp 208−210 °C; IR (DCM) 1720, 1661, 1529, 1485 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.63 (br s, 1H), 8.89 (dd, 1H, J_1 = 6.6 Hz, J_2 = 2.4 Hz), 8.75 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.20 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.97−7.92 (m, 3H), 7.74 (d, 1H, J = 8.1 Hz), 7.62−7.57 (m, 2H), 7.54−7.47 (m, 2H), 7.43−7.35 (m, 3H), 4.87 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 161.3, 148.4, 144.8, 139.9, 139.1, 138.6, 138.0, 136.4, 134.4, 133.0, 129.9, 128.5, 128.2, 128.0, 127.4, 126.9, 125.0, 123.8, 122.8, 122.1, 121.8, 116.8, 52.0, 33.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{21}N_2O_3S$ 453.1273, found 453.1276.

*3-(3-Methoxybenzyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5d**).* Compound **5d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 56% (30 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 133−134 °C; IR (KBr) 3422, 1656, 1527, 1484, 1385, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.62 (br s, 1H), 8.92 (d, 1H, J = 7.1 Hz), 8.73 (d, 1H, J = 4.1 Hz), 8.18 (d, 1H, J = 8.2 Hz), 7.92 (d, 1H, J = 8.0 Hz), 7.82 (d, 1H, J = 8.0 Hz), 7.62−7.55 (m, 2H), 7.49−7.45 (m, 2H), 7.40 (t, 1H, J = 7.8 Hz), 7.21 (t, 1H, J = 7.8 Hz), 6.95−6.93 (m, 2H), 6.75 (d, 1H, J = 8.7 Hz), 4.80 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 159.7, 148.4, 140.9, 140.2, 139.1, 138.6, 138.4, 136.3, 134.5, 133.0, 129.5, 127.9, 127.4, 126.7, 124.9, 124.1, 122.7, 122.0, 121.7, 120.9, 116.8, 114.4, 111.4, 55.1, 32.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_2S$ 425.1324, found 425.1308.

*Ethyl 3-((2-(Quinolin-8-ylcarbamoyl)benzo[b]thiophene-3-yl)methyl)benzoate (**5e**).* Compound **5e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 41% (24 mg); R_f = 0.46 (EtOAc/hexanes = 1:4); IR (DCM) 3324, 1715, 1656, 1484, 1328, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.64 (br s, 1H), 8.90 (dd, 1H, J_1 = 6.8 Hz, J_2 = 1.8 Hz), 8.76 (d, 1H, J = 3.6 Hz), 8.19 (d, 1H, J = 8.2 Hz), 8.11 (br s, 1H), 7.93 (d, 1H, J = 8.0 Hz), 7.89 (d, 1H, J = 7.7 Hz), 7.77 (d, 1H, J = 8.1 Hz), 7.62−7.57 (m, 2H), 7.50−7.46 (m, 3H), 7.40 (t, 1H, J = 7.8 Hz), 7.33 (t, 1H, J = 7.7 Hz), 4.86 (s, 2H), 4.35 (q, 2H, J = 7.1 Hz), 1.36 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 161.4, 148.4, 140.0, 139.6, 139.1, 138.6, 138.3, 136.3, 134.4, 133.0, 132.9, 130.6, 129.6, 128.6, 128.0, 127.5, 127.4, 126.8, 125.0, 123.9, 122.8, 122.1, 121.8, 116.8, 60.9, 32.8, 14.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{23}N_2O_3S$ 467.1429, found 467.1413.

*3-(3-Nitrobenzyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5f**).* Compound **5f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 49% (27 mg); mp 220−222 °C; R_f = 0.41 (EtOAc/hexanes = 1:4); IR (KBr) 3302, 1649, 1527, 1485, 1348 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.66 (br s, 1H), 8.88 (dd, 1H, J_1 = 5.7 Hz, J_2 = 3.3 Hz), 8.83 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.27 (br s, 1H), 8.22 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 8.06 (d, 1H, J = 8.0 Hz), 7.95 (d, 1H, J = 8.0 Hz), 7.76 (d, 1H, J = 8.0 Hz), 7.69 (d, 1H, J = 7.2 Hz), 7.61−7.58 (m, 2H), 7.54−7.50 (m, 2H), 7.44 (t, 2H, J = 8.0 Hz), 4.90 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 148.5, 141.5, 139.7, 139.0, 138.6, 137.8, 136.4, 134.8, 134.3, 132.9, 129.4, 128.0, 127.3, 127.1, 125.3, 123.5, 123.4, 123.0, 122.2, 121.9, 121.5, 116.8, 32.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{18}N_3O_3S$ 440.1069, found 440.1069.

*3-((5-Bromopyridin-2-yl)methyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5g**).* Compound **5g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a pale yellow solid: yield 76% (45 mg); R_f = 0.39 (EtOAc/hexanes = 1:4); mp 178−180 °C; IR (KBr) 1650, 1594, 1385, 1261, 1092 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.07 (br s, 1H), 8.89 (dd, 1H, J_1 = 6.7 Hz, J_2 = 1.9 Hz), 8.78 (dd, 1H, J_1 = 4.1 Hz, J_2 = 1.1 Hz), 8.67 (d, 1H, J = 2.2 Hz), 8.20 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.0 Hz), 7.92 (t, 2H, J = 8.9 Hz), 7.70 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.2 Hz), 7.64−7.58 (m, 2H), 7.50−7.40 (m, 3H), 7.35 (d, 1H, J = 8.3 Hz), 4.87 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 157.8, 150.2, 148.4, 139.8, 139.3, 139.1, 138.9, 136.7, 136.3, 134.6, 133.6, 128.1, 127.3, 126.7, 125.0, 124.5, 124.0, 122.7, 122.3, 121.8, 118.5, 117.5, 35.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{17}BrN_3OS$ 474.0276, found 474.0259.

*3-((6-Fluoropyridin-3-yl)methyl)-N-(quinolin-8-yl)benzo[b]thiophene-2-carboxamide (**5h**).* Compound **5h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 71% (37 mg); R_f = 0.33 (EtOAc/hexanes = 1:4); mp 169−171 °C; IR (KBr) 1655, 1595, 1531, 1385, 1119 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.64 (br s, 1H), 8.89 (dd, 1H, J_1 = 6.1 Hz, J_2 = 2.7 Hz), 8.84 (d, 1H, J = 4.2 Hz), 8.30

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(br s, 1H), 8.21 (d, 1H, J = 4.2 Hz), 7.94 (d, 1H, J = 8.0 Hz), 7.79 (d, 2H, J = 8.1 Hz), 7.63−7.58 (m, 2H), 7.53−7.49 (m, 2H), 7.44 (t, 1H, J = 7.9 Hz), 6.82 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.7 Hz), 4.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, J_{C-F} = 236.0 Hz), 161.1, 148.5, 147.1 (d, J_{C-F} = 14.5 Hz), 141.4 (d, J_{C-F} = 7.6 Hz), 139.5, 139.0, 138.5, 138.1, 136.4, 134.3, 132.7, 132.6, (d, J_{C-F} = 10.9 Hz), 128.0, 127.3, 127.1, 125.2, 123.5, 123.0, 122.3, 121.9, 116.8, 109.4 (d, J_{C-F} = 37.2 Hz), 29.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{17}FN_3OS$ 414.1076, found 414.1060.

*3-(4-Acetylbenzyl)-N-(quinolin-8-yl)benzofuran-2-carboxamide (**6a**).* Compound **6a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a pale yellow solid: yield 61% (32 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 189−191 °C; IR (KBr) 1649, 1529, 1487, 1327, 1265 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.13 (br s, 1H), 8.98−8.95 (m, 2H), 8.23 (d, 1H, J = 8.2 Hz), 7.89 (d, 2H, J = 8.1 Hz), 7.70 (d, 1H, J = 8.4 Hz), 7.65−7.59 (m, 2H), 7.56−7.52 (m, 4H), 7.52−7.47 (m, 1H), 7.29 (t, 1H, J = 7.7 Hz), 4.77 (s, 2H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 158.1, 153.8, 148.6, 145.1, 143.5, 138.8, 136.4, 135.4, 134.2, 128.9, 128.8, 128.7, 128.1, 127.5, 127.3, 125.2, 123.5, 122.2, 121.8, 121.3, 116.9, 112.3, 30.0, 26.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{21}N_2O_3$ 421.1552, found 421.1558.

*Methyl 4-((2-(Quinolin-8-ylcarbamoyl)benzofuran-3-yl)methyl)-benzoate (**6b**).* Compound **6b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a brown solid: yield 66% (36 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 213-215 °C; IR (KBr) 1527, 1486, 1423, 1384, 1327 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.13 (br s, 1H), 8.99−8.95 (m, 2H), 8.23 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.97 (d, 2H, J = 8.4 Hz), 7.70 (d, 1H, J = 8.3 Hz), 7.65−7.59 (m, 2H), 7.54 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.52−7.50 (m, 3H), 7.47 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.2 Hz), 7.30−7.26 (m, 1H), 4.77 (s, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 158.2, 153.8, 148.6, 144.8, 143.5, 138.8, 136.4, 134.2, 129.9, 128.8, 128.8, 128.2, 128.1, 127.5, 127.4, 125.2, 123.5, 122.2, 121.8, 121.4, 116.9, 112.2, 52.0, 30.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{21}N_2O_4$ 437.1501, found 437.1494.

*3-(4-Methoxybenzyl)-N-(quinolin-8-yl)benzofuran-2-carboxamide (**6c**).* Compound **6c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a colorless solid: yield 31% (16 mg); R_f = 0.46 (EtOAc/hexanes = 1:4); mp 208−210 °C; IR (KBr) 1668, 1528, 1486, 1423, 1327 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.11 (br s, 1H), 9.00−8.97 (m, 2H), 8.23 (d, 1H, J = 8.0 Hz), 7.68 (d, 1H, J = 8.3 Hz), 7.65−7.52 (m, 4H), 7.46 (t, 1H, J = 8.0 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.29−7.25 (m, 1H), 6.83 (d, 2H, J = 8.4 Hz), 4.64 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 158.1, 153.8, 148.6, 143.1, 138.8, 136.4, 134.3, 131.5, 129.7, 129.0, 128.1, 127.4, 127.3, 126.7, 123.3, 122.0, 121.8, 121.7, 116.9, 113.9, 112.1, 55.2, 29.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{26}H_{21}N_2O_3$ 409.1552, found 409.1557.

*3-(4-Ethylbenzyl)-N-(quinolin-8-yl)benzofuran-2-carboxamide (**6d**).* Compound **6d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 20:80) as a colorless solid: yield 59% (30 mg); R_f = 0.46 (EtOAc/hexanes = 1:4); mp 150−152 °C; IR (KBr) 2961, 1668, 1529, 1487, 1326 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.11 (br s, 1H), 9.01−8.97 (m, 2H), 8.22 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.68−7.58 (m, 4H), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.47 (td, 1H, J_1 = 7.2 Hz, J_2 = 1.2 Hz), 7.38 (d, 2H, J = 8.1 Hz), 7.28 (td, 1H, J_1 = 7.3 Hz, J_2 = 0.9 Hz), 7.13 (d, 2H, J = 8.1 Hz), 4.68 (s, 2H), 2.61 (q, 2H, J = 7.6 Hz) 1.22 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 153.7, 148.5, 143.2, 142.1, 138.8, 136.6, 136.4, 134.3, 129.1, 128.7, 128.1, 128.0, 127.4, 127.2, 126.5, 123.3, 122.0, 121.8, 121.7, 116.9, 112.1, 29.6, 28.5, 15.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{23}N_2O_2$ 407.1760, found 407.1749.

*3-((2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-N-(quinolin-8-yl)benzofuran-2-carboxamide (**6e**).* Compound **6e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 45% (25 mg); mp 216−218 °C; R_f = 0.44 (EtOAc/hexanes = 1:4); IR (KBr) 1668, 1525, 1486, 1262 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.1 (br s, 1H), 8.99−8.97 (m, 2H), 8.23 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.68 (d, 1H, J = 8.3 Hz), 7.64−7.59 (m, 3H), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.47 (td, 1H, J_1 = 7.2 Hz, J_2 = 1.2 Hz), 7.31−7.27 (m, 1H), 6.96−6.93 (m, 2H), 6.79 (d, 1H, J = 8.8 Hz), 4.60 (s, 2H), 4.22 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 153.7, 148.5, 143.3, 143.2, 142.0, 138.8, 136.4, 134.3, 132.7, 129.0, 128.1, 127.4, 127.3, 126.4, 123.4, 122.0, 121.8, 121.7, 117.4, 117.2, 116.9, 112.1, 64.3, 64.3, 29.2; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{21}N_2O_4$ 437.1501, found 437.1498.

*3-((5-Bromopyridin-2-yl)methyl)-N-(quinolin-8-yl)benzofuran-2-carboxamide (**6f**).* Compound **6f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 57% (33 mg); R_f = 0.38 (EtOAc/hexanes = 1:4); mp 209−211 °C; IR (KBr) 3333, 1657, 1596, 1385, 1266, 1091 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.13 (br s, 1H), 8.97−8.95 (m, 2H), 8.62 (d, 1H, J = 2.0 Hz), 8.22 (d, 1H, J = 8.2 Hz), 7.73−7.67 (m, 3H), 7.64−7.59 (m, 2H), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.50−7.46 (m, 1H), 7.38 (d, 1H, J = 8.4 Hz), 7.31 (d, 1H, J = 7.5 Hz), 4.84 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 158.1, 153.7, 150.1, 148.6, 143.4, 139.2, 138.8, 136.4, 134.2, 128.9, 128.1, 127.5, 127.3, 124.7, 124.5, 123.5, 122.2, 122.0, 121.8, 118.6, 116.9, 112.1, 32.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{17}BrN_3O_2$ 458.0504, found 458.0489.

*3-(4-Methoxybenzyl)-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**7a**).* Compound **7a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a pale yellow solid: yield 58% (27 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); mp 104−106 °C; IR (KBr) 3312, 1578, 1510, 1433, 1247 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 8.46 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 7.55 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.39−7.37 (m, 1H), 7.35 (d, 1H, J = 5.1 Hz), 7.22 (d, 2H, J = 8.7 Hz), 7.12 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 6.90 (d, 1H, J = 5.1 Hz), 6.86 (d, 2H, J = 8.6 Hz), 4.41 (s, 2H), 3.80 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.1, 146.1, 138.7, 133.4, 132.2, 131.8, 131.1, 129.9, 129.1, 127.3, 125.5, 124.5, 120.6, 114.0, 55.3, 34.4, 19.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{20}H_{19}NNaO_2S_2$ 392.0755, found 392.0756.

*3-(4-Acetylbenzyl)-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**7b**).* Compound **7b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 50% (24 mg); R_f = 0.51 (EtOAc/hexanes = 1:4); mp 97−99 °C; IR (KBr) 3342, 1678, 1511, 1432, 1267 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (br s, 1H), 8.43 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 7.91 (d, 2H, J = 7.8 Hz), 7.55 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.41−7.34 (m, 4H), 7.12 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 6.91 (d, 1H, J = 5.1 Hz), 4.53 (s, 2H), 2.59 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 160.7, 145.9, 145.4, 138.5, 135.3, 133.4, 131.6, 131.1, 129.1, 129.1, 128.7, 127.3, 125.6, 124.6, 120.6, 35.2, 26.6, 19.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{21}H_{19}NNaO_2S_2$ 404.0755, found 404.0746.

*Methyl 4-((2-((2-(Methylthio)phenyl)carbamoyl)thiophen-3-yl)-methyl)benzoate (**7c**).* Compound **7c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 54% (27 mg); R_f = 0.52 (EtOAc/hexanes = 1:4); IR (DCM) 1719, 1667, 1610, 1578, 1279, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (br s, 1H), 8.44 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.3 Hz), 7.98 (d, 2H, J = 8.4 Hz), 7.55 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.38−7.34 (m, 4H), 7.12 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 6.89 (d, 1H, J = 5.1 Hz), 4.53 (s, 2H), 3.91 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 160.7, 145.6, 145.4, 138.5, 133.4, 131.6, 131.1, 129.9, 129.2, 128.9, 128.2, 127.3, 125.5, 124.6, 120.6, 52.0, 35.2, 19.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{21}H_{19}NNaO_3S_2$ 420.0704, found 420.0701.

*3-(4-Ethylbenzyl)-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**7d**).* Compound **7d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 54% (25 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); IR (DCM) 3312, 1667, 1578, 1511, 1432, 1304 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (br s, 1H), 8.43 (dd, 1H, J_1 = 8.3 Hz, J_2 = 0.9 Hz), 7.51 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.5 Hz), 7.35−7.31 (m, 2H), 7.18 (d, 2H, J = 8.0 Hz), 7.12 (d, 2H, J = 8.0 Hz), 7.08 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 6.87 (d, 1H, J = 5.1 Hz), 4.41 (s, 2H), 2.60 (q, 2H, J = 7.6

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Hz), 2.33 (s, 3H), 1.21 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 146.2, 142.2, 138.7, 137.2, 133.4, 131.8, 131.2, 129.2, 128.2, 128.1, 127.3, 125.5, 124.5, 120.7, 34.9, 28.5, 19.2, 15.7; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{21}H_{21}NNaOS_2$ 390.0962, found 390.0955.

*N-(2-(Methylthio)phenyl)-3-(3-nitrobenzyl)thiophene-2-carboxamide (**7e**).* Compound **7e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 50% (24 mg); mp 130−132 °C; R_f = 0.51 (EtOAc/hexanes = 1:4); IR (KBr) 3304, 1665, 1578, 1525, 1433 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (br s, 1H), 8.42 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 8.16 (br s, 1H), 8.10−8.07 (m, 1H), 7.68 (dd, 1H, J_1 = 7.6 Hz, J_2 = 0.5 Hz), 7.55 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.47 (t, 1H, J = 8.0 Hz), 7.42 (d, 1H, J = 5.0 Hz), 7.36 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 7.13 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 6.95 (d, 1H, J = 5.0 Hz), 4.58 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 148.4, 145.0, 142.3, 138.4, 135.2, 133.3, 131.5, 131.2, 129.4, 129.1, 127.6, 125.7, 124.7, 123.6, 121.5, 120.6, 34.7, 19.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{17}N_2O_3S_2$ 385.0681, found 385.0684.

*3-((2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**7f**).* Compound **7f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 25:75) as a brown solid: yield 56% (28 mg); R_f = 0.51 (EtOAc/hexanes = 1:4); mp 101−103 °C; IR (KBr) 3312, 1665, 1506, 1432, 1304, 1285 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (br s, 1H), 8.42 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.3 Hz), 7.51 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.35−7.31 (m, 2H), 7.08 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 6.88 (d, 1H, J = 5.1 Hz), 6.79−6.73 (m, 3H), 4.33 (s, 2H), 4.21 (s, 4H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 146.2, 143.4, 142.0, 138.7, 133.4, 133.3, 131.8, 131.2, 129.1, 127.3, 125.5, 124.5, 121.8, 120.7, 117.5, 117.3, 64.4, 64.3, 34.5, 19.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{20}NO_3S_2$ 398.0885, found 398.0876.

*3-(3,5-Dimethylbenzyl)-N-(2-(methylthio)phenyl)thiophene-2-carboxamide (**7g**).* Compound **7g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 54% (25 mg); R_f = 0.53 (EtOAc/hexanes = 1:4); IR (DCM) 3313, 1666, 1578, 1510, 1430, 1384 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 8.46 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.3 Hz), 7.55 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.5 Hz), 7.38 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.4 Hz), 7.35 (d, 1H, J = 5.1 Hz), 7.12 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 6.91−6.90 (m, 3H), 6.88 (br s, 1H), 4.40 (s, 2H), 2.38 (s, 3H), 2.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 146.0, 139.9, 138.7, 138.1, 133.4, 131.8, 131.3, 129.1, 128.0, 127.3, 126.7, 125.5, 124.5, 120.7, 35.1, 21.3, 19.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{21}H_{21}NNaOS_2$ 390.0962, found 390.0959.

*3-((5-Bromopyridin-2-yl)methyl)-N-(2-(methylthio)phenyl)-thiophene-2-carboxamide (**7h**).* Compound **7h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 61% (32 mg); R_f = 0.40 (EtOAc/hexanes = 1:4); IR (DCM) 1652, 1527, 1486, 1384, 1014 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (br s, 1H), 8.63 (dd, 1H, J_1 = 2.4 Hz, J_2 = 0.4 Hz), 8.07 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.3 Hz), 7.77 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.4 Hz), 7.46 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.4 Hz), 7.39 (d, 1H, J = 5.1 Hz), 7.33 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.5 Hz), 7.30 (s, 1H), 7.18 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.4 Hz), 6.98 (d, 1H, J = 5.0 Hz), 4.51 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 158.2, 150.4, 141.3, 139.7, 137.3, 134.1, 130.8, 130.7, 129.1, 128.1, 127.7, 125.5, 124.6, 123.6, 118.6, 37.1, 17.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{16}BrN_2OS_2$ 418.9887, found 418.9883.

*3-((6-Fluoropyridin-3-yl)methyl)-N-(2-(methylthio)phenyl)-thiophene-2-carboxamide (**7i**).* Compound **7i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a brown solid: yield 53% (24 mg); R_f = 0.45 (EtOAc/hexanes = 1:4); mp 146−148 °C; IR (KBr) 3306, 1663, 1523, 1483, 1244 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (br s, 1H), 8.41 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.1 Hz), 8.17−817 (m, 1H), 7.78 (td, 1H, J_1 = 8.2 Hz, J_2 = 2.5 Hz), 7.56 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.4 Hz), 7.40 (d, 1H, J = 5.1 Hz), 7.39−7.35 (m, 1H), 7.14 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 6.93 (d, 1H, J = 5.0 Hz), 6.86 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.9 Hz), 4.45 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, J_{C-F} = 236.2 Hz), 160.6, 147.2 (d, J_{C-F} = 14.4 Hz), 145.5, 141.8 (d, J_{C-F} = 7.6 Hz), 138.4, 133.5 (d, J_{C-F} = 4.7 Hz), 133.4, 131.4, 130.9, 129.2, 127.5, 125.6, 124.7, 120.5, 109.3 (d, J_{C-F} = 37.1 Hz), 31.4 (d, J_{C-F} = 1.1 Hz), 19.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{16}FN_2OS_2$ 359.0688, found 359.0692.

*3-(4-Methoxybenzyl)thiophene-2-carboxylic Acid (**3aa**).* Following the general procedure, the compound **3aa** was obtained as a brown viscous liquid (the crude material obtained was almost pure): yield 64% (20 mg); IR (DCM) 2922, 1665, 1533, 1427, 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.48 (m, 1H), 7.18 (d, 2H, J = 8.5 Hz), 6.89−6.85 (m, 3H), 4.37 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 158.1, 151.3, 132.1, 132.0, 131.4, 129.9, 126.1, 113.9, 55.3, 34.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{13}O_3S$ 249.0585, found 249.0585.

*Methyl 3-(4-Methoxybenzyl)thiophene-2-carboxylate (**3ab**).* Compound **3ab** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 20:80) as a colorless liquid: yield 85% (28 mg); R_f = 0.50 (EtOAc/hexanes = 1:4); IR (DCM) 1709, 1610, 1511, 1413, 1074 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 1H, J = 5.1 Hz), 7.18 (d, 2H, J = 8.6 Hz), 6.86−6.84 (m, 3H), 4.36 (s, 2H), 3.90 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 158.0, 149.7, 132.3, 131.0, 130.4, 129.8, 126.4, 113.8, 55.2, 51.9, 34.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{15}O_3S$ 263.0742, found 263.0736.

*4-(4-Methoxyphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8a**).* Compound **8a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a brown liquid: yield 71% (33 mg); R_f = 0.24 (EtOAc/hexanes = 2:3); IR (DCM) 1692, 1527, 1486, 1384, 1245 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.74−7.72 (m, 1H), 7.70 (d, 1H, J = 4.8 Hz), 7.59 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49−7.43 (m, 2H), 6.96−6.93 (m, 4H), 6.68 (d, 2H, J = 8.7 Hz), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 159.4, 157.4, 150.0, 144.6, 136.4, 135.4, 134.9, 134.0, 130.3, 129.3, 128.9, 128.7, 127.5, 126.3, 121.3, 121.2, 113.9, 65.8, 55.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_2S$ 373.1011, found 373.1017.

*4-(4-Fluorophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8b**).* Compound **8b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 57% (26 mg); R_f = 0.24 (EtOAc/hexanes = 2:3); IR (DCM) 3451, 1694, 1508, 1389 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.0 Hz, J_2 = 1.1 Hz), 8.18 (d, 1H, J = 8.4 Hz), 7.75−7.72 (m, 2H), 7.61 (d, 1H, J = 7.3 Hz), 7.51−7.44 (m, 2H), 7.04 (s, 1H), 7.03−7.00 (m, 2H), 6.93 (d, 1H, J = 4.8 Hz,) 6.86−6.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 162.5 (d, J_{C-F} = 245.6 Hz), 156.9, 150.0, 144.5, 136.5, 135.7, 135.0, 133.8, 132.6 (d, J_{C-F} = 3.3 Hz), 130.2, 129.4, 129.4 (d, J_{C-F} = 13.5 Hz), 127.6, 126.3, 121.4, 121.1, 115.6 (d, J_{C-F} = 21.6 Hz), 65.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}FN_2OS$ 361.0811, found 361.0819.

*4-(4-Chlorophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8c**).* Compound **8c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 61% (29 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 3353, 1694, 1490, 1389, 1221 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75−7.73 (m, 2H), 7.64 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.51−7.43 (m, 2H), 7.13 (d, 2H, J = 8.5 Hz), 7.06 (s, 1H), 7.00 (d, 2H, J = 8.5 Hz) 6.93 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 156.7, 150.0, 144.4, 136.5, 135.8, 135.4, 135.0, 134.1, 133.7, 130.1, 129.3, 129.0, 128.9, 127.6, 126.3, 121.4, 121.0, 65.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}ClN_2OS$ 377.0515, found 377.0519.

*4-(4-Bromophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8d**).* Compound **8d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 51% (27 mg); R_f = 0.32 (EtOAc/

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hexanes = 2:3); IR (DCM) 3418, 1694, 1500, 1472, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75−7.71 (m, 2H), 7.64 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.51−7.43 (m, 2H), 7.29 (d, 2H, J = 8.4 Hz), 7.06 (s, 1H), 6.94 (d, 2H, J = 8.5 Hz), 6.93 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 156.7, 150.0, 144.4, 136.5, 136.0, 135.8, 135.0, 133.7, 131.9, 130.1, 129.3, 127.6, 126.4, 122.3, 121.4, 121.0, 65.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}BrN_2OS$ 421.0010, found 421.0000.

*4-(4-Iodophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8e**).* Compound **8e** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a brown liquid: yield 68% (40 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); IR (DCM) 1692, 1500, 1389, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75−7.71 (m, 2H), 7.65 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.3 Hz), 7.52−7.48 (m, 3H), 7.13 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.04 (s, 1H), 6.92 (d, 1H, J = 4.8 Hz) 6.82 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 156.6, 150.0, 144.4, 137.8, 136.7, 136.5, 135.8, 134.9, 133.7, 130.1, 129.5, 129.3, 127.6, 126.4, 121.4, 121.0, 94.1, 65.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}IN_2OS$ 468.9872, found 468.9857.

*4-(4-Acetylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8f**).* Compound **8f** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a pale yellow liquid: yield 58% (28 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); IR (DCM) 2924, 1683, 1526, 1487, 1387 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.18 (dd, 1H, J_1 = 8.4 Hz, J_2 = 1.7 Hz), 7.77−7.72 (m, 4H), 7.68 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.51−7.44 (m, 2H), 7.19 (d, 2H, J = 8.4 Hz), 7.18 (s, 1H), 6.93 (d, 1H, J = 4.8 Hz), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 164.6, 156.4, 150.0, 144.3, 142.3, 137.0, 136.5, 136.0, 135.0, 133.7, 130.1, 129.3, 128.8, 127.8, 127.6, 126.3, 121.4, 121.0, 65.7, 26.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{17}N_2O_2S$ 385.1011, found 385.1008.

*Methyl 4-(6-Oxo-5-(quinolin-8-yl)-5,6-dihydro-4H-thieno[2,3-c]-pyrrol-4-yl)benzoate (**8g**).* Compound **8g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless solid: yield 50% (25 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); mp 162−164 °C; IR (KBr) 1721, 1698, 1282, 1107 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.83 (d, 2H, J = 8.4 Hz), 7.74−7.13 (m, 2H), 7.65 (dd, 1H, J_1 = 6.0 Hz, J_2 = 1.4 Hz), 7.49−7.44 (m, 2H), 7.16 (d, 2H, J = 8.4 Hz), 7.14 (s, 1H), 6.93 (d, 1H, J = 4.8 Hz), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.6, 156.5, 150.0, 144.4, 142.0, 136.5, 135.9, 135.0, 133.7, 130.1, 130.1, 130.0, 129.3, 127.7, 126.3, 121.4, 121.0, 65.7, 52.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{17}N_2O_3S$ 401.0960, found 401.0949.

*5-(Quinolin-8-yl)-4-(p-tolyl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8h**).* Compound **8h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless solid: yield 63% (28 mg); R_f = 0.34 (EtOAc/hexanes = 2:3); mp 126−128 °C; IR (KBr) 2923, 1693, 1526, 1472, 1387 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.72 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.62 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49−7.42 (m, 2H), 6.99−6.93 (m, 6H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 157.4, 149.9, 144.6, 138.0, 136.4, 135.4, 134.8, 134.0, 133.8, 130.3, 129.3, 129.3, 127.5, 127.5, 126.3, 121.3, 121.2, 66.1, 21.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2OS$ 357.1062, found 357.1069.

*4-(4-Ethylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8i**).* Compound **8i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 65% (30 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); IR (DCM) 2963, 1693, 1526, 1485, 1387 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.1 Hz, J_2 = 1.5 Hz), 8.17 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.72 (d, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.63 (d, 1H, J = 7.3 Hz), 7.49−7.42 (m, 2H), 7.00−6.93 (m, 6H), 2.53 (q, 2H, J = 7.6 Hz), 1.42 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 157.5, 149.9, 144.7, 144.2, 136.4, 135.4, 134.8, 134.1, 134.0, 130.4, 129.3, 128.1, 127.5, 127.5, 126.3, 121.3, 121.3, 66.1, 28.4, 15.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2OS$ 371.1218, found 371.1220.

*4-(4-Isopropylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8j**).* Compound **8j** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 62% (30 mg); R_f = 0.34 (EtOAc/hexanes = 2:3); IR (DCM) 2959, 1694, 1527, 1387 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.72 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.68 (d, 1H, J = 4.8 Hz), 7.62 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49−7.41 (m, 2H), 7.03−6.97 (m, 5H), 6.95 (d, 1H, J = 4.8 Hz), 2.82−2.75 (m, 1H), 1.15 (d, 3H, J = 2.8 Hz), 1.14 (d, 3H, J = 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 157.5, 150.0, 148.8, 144.7, 136.4, 135.4, 134.7, 134.1, 130.4, 129.3, 127.5, 127.5, 126.7, 126.3, 121.3, 121.3, 66.1, 33.7, 23.8, 23.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_2OS$ 385.1375, found 385.1384.

*4-(4-tert-Butylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8k**).* Compound **8k** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 85:15) as a colorless liquid: yield 44% (22 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); IR (DCM) 1692, 1594, 1385, 1122 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, J_1 = 4.0 Hz, J_2 = 0.6 Hz), 8.17 (d, 1H, J = 8.0 Hz), 7.73 (d, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.65 (d, 1H, J = 7.3 Hz), 7.50−7.42 (m, 2H), 7.18 (d, 2H, J = 8.0 Hz), 7.01 (s, 1H), 6.99 (d, 2H, J = 8.2 Hz), 6.95 (d, 1H, J = 4.8 Hz), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 157.5, 151.1, 150.0, 144.7, 136.4, 135.3, 134.1, 133.7, 130.5, 129.3, 127.5, 127.1, 126.3, 125.5, 121.3, 121.3, 66.0, 34.5, 31.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{23}N_2OS$ 399.1531, found 399.1516.

*4-(4-Hexylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8l**).* Compound **8l** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless liquid: yield 71% (38 mg); R_f = 0.32 (EtOAc/hexanes = 2:3); IR (DCM) 1693, 1594, 1385, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, 1H, J = 3.9 Hz), 8.16 (d, 1H, J = 8.2 Hz), 7.71 (d, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.61 (d, 1H, J = 7.3 Hz), 7.48−7.41 (m, 2H), 6.98−6.94 (m, 6H), 2.48 (t, 2H, J = 7.6 Hz), 1.52−1.46 (m, 2H), 1.30−1.25 (m, 6H), 0.86 (t, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 157.4, 150.0, 144.7, 143.1, 136.4, 135.4, 134.8, 134.1, 133.9, 130.4, 129.3, 128.6, 127.5, 126.3, 121.3, 66.1, 35.6, 31.6, 31.1, 28.9, 22.6, 14.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{27}N_2OS$ 427.1844, found 427.1828.

*4-(4-Pentylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8m**).* Compound **8m** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless liquid: yield 44% (23 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 3385, 1595, 1385, 1215 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, 1H, J = 4.0 Hz), 8.17 (d, 1H, J = 8.2 Hz), 7.72 (d, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.61 (d, 1H, J = 7.4 Hz), 7.49−7.42 (m, 2H), 6.98−6.93 (m, 6H), 2.47 (t, 2H, J = 7.7 Hz), 1.53−1.47 (m, 2H), 1.31−1.21 (m, 4H), 0.86 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 157.4, 150.0, 144.7, 143.1, 136.4, 135.4, 134.8, 134.1, 133.9, 130.4, 129.3, 128.6, 127.5, 126.3, 121.3, 66.1, 35.5, 31.5, 30.9, 22.5, 14.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{25}N_2OS$ 413.1688, found 413.1673.

*4-Phenyl-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8n**).* Compound **8n** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 85:15) as a brown solid: yield 58% (25 mg); mp 218−220 °C; R_f = 0.31 (EtOAc/hexanes = 2:3); IR (KBr) 1694, 1500, 1390, 1351 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.8 Hz), 7.73−7.70 (m, 2H), 7.62 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49−7.43 (m, 2H), 7.18−7.15 (m, 3H), 7.07−7.05 (m, 2H), 7.03 (s, 1H), 6.94 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 157.2, 150.0, 144.6, 136.8, 136.4, 135.5, 134.9, 134.0, 130.3, 129.3, 128.6, 128.3, 127.6, 127.5, 126.3, 121.3, 121.2, 66.3;

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HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{15}N_2OS$ 343.0905, found 343.0891.

*4-(3-Methoxyphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8o**).* Compound **8o** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 53% (25 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); IR (DCM) 1694, 1598, 1472, 1390 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.73 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.70 (d, 1H, J = 4.8 Hz), 7.67 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50−7.42 (m, 2H), 7.09 (t, 1H, J = 7.9 Hz), 7.00 (s, 1H), 6.95 (d, 1H, J = 4.8 Hz), 6.72−6.67 (m, 2H), 6.62 (t, 1H, J = 1.8 Hz), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 159.7, 157.2, 150.0, 144.6, 138.4, 136.4, 135.6, 134.7, 134.0, 130.2, 129.7, 129.3, 127.5, 126.3, 121.3, 121.2, 119.9, 113.6, 113.1, 66.2, 55.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_2S$ 373.1011, found 373.1002.

*Ethyl 3-(6-Oxo-5-(quinolin-8-yl)-5,6-dihydro-4H-thieno[2,3-c]pyrrol-4-yl)benzoate (**8p**).* Compound **8p** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 54% (28 mg); R_f = 0.32 (EtOAc/hexanes = 2:3); IR (DCM) 2982, 1701, 1500, 1283 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.85 (d, 1H, J = 7.2 Hz), 7.78 (s, 1H), 7.73−7.71 (m, 2H), 7.67 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50−7.43 (m, 2H), 7.31−7.24 (m, 2H), 7.12 (s, 1H), 6.92 (d, 1H, J = 4.8 Hz), 4.32 (q, 2H, J = 7.2 Hz), 1.34 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 164.7, 156.8, 150.1, 144.5, 137.4, 136.5, 135.9, 134.9, 133.7, 131.8, 131.0, 130.2, 129.5, 129.3, 128.8, 128.8, 127.7, 126.3, 121.4, 121.0, 65.8, 61.1, 14.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{19}N_2O_3S$ 415.1116, found 415.1110.

*4-(3-Nitrophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8q**).* Compound **8q** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a brown liquid: yield 64% (31 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 3453, 1698, 1530, 1438, 1350 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 8.04−7.99 (m, 2H), 7.77−7.72 (m, 3H), 7.52−7.44 (m, 3H), 7.39−7.33 (m, 1H), 7.27 (s, 1H), 6.95 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 155.9, 150.1, 148.3, 144.2, 139.4, 136.6, 136.4, 135.2, 133.6, 133.4, 129.9, 129.8, 129.4, 127.8, 126.4, 123.4, 122.7, 121.6, 120.8, 65.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}N_3O_3S$ 388.0756, found 388.0764.

*4-(3-Chlorophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8r**).* Compound **8r** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless solid: yield 51% (24 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); mp 180−182 °C; IR (KBr) 3302, 1695, 1472, 1388 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.76−7.72 (m, 2H), 7.66 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.45 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.16−7.08 (m, 3H), 7.04 (s, 1H), 6.96 (dt, 1H, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 6.94 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 156.6, 150.0, 144.4, 139.0, 136.5, 135.9, 134.9, 134.5, 133.7, 130.2, 130.0, 129.4, 128.5, 127.7, 127.7, 126.3, 125.8, 121.4, 121.1, 65.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}ClN_2OS$ 377.0515, found 377.0523.

*4-(3-Fluorophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8s**).* Compound **8s** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 55% (25 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 1696, 1500, 1472, 1130 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75−7.72 (m, 2H), 7.67 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.51−7.44 (m, 2H), 7.16−7.11 (m, 1H), 7.08 (s, 1H), 6.94 (d, 1H, J = 4.8 Hz), 6.89−6.84 (m, 2H), 6.81−6.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 162.8 (d, J_{C-F} = 245.6 Hz), 156.6, 150.0, 144.4, 139.5 (d, J_{C-F} = 6.7 Hz), 136.5, 135.8, 134.9, 133.7, 130.3, 130.2, 129.3, 127.6, 126.3, 123.3 (d, J_{C-F} = 2.8 Hz), 121.4, 121.1, 115.3 (d, J_{C-F} = 21.5 Hz), 114.5 (d, J_{C-F} = 21.8 Hz), 65.6 (d, J_{C-F} = 1.6 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}FN_2OS$ 361.0811, found 361.0812.

*4-(3-Bromophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8t**).* Compound **8t** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 51% (27 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); IR (DCM) 1694, 1527, 1486, 1327 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.72 (d, 1H, J = 4.8 Hz), 7.66 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.51 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.8 Hz), 7.46 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.31−7.29 (m, 1H), 7.25 (br s, 1H), 7.07−7.01 (m, 3H), 6.94 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 156.6, 150.0, 144.3, 139.3, 136.6, 135.9, 134.9, 133.6, 131.5, 130.6, 130.3, 130.2, 129.4, 127.7, 126.4, 126.3, 122.7, 121.4, 121.1, 65.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}BrN_2OS$ 421.0010, found 421.0001.

*4-(3-Iodophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8u**).* Compound **8u** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a brown liquid: yield 66% (39 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 1692, 1592, 1471, 1388, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 7.72 (d, 1H, J = 4.8 Hz), 7.66 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.3 Hz), 7.53−7.43 (m, 4H), 7.06 (d, 1H, J = 7.8 Hz), 6.97 (s, 1H), 6.94 (d, 1H, J = 4.8 Hz) 6.91 (t, 1H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 156.6, 150.1, 144.4, 139.3, 137.4, 136.5, 136.5, 135.9, 134.9, 133.7, 130.4, 130.2, 129.4, 127.8, 126.9, 126.3, 121.4, 121.1, 94.4, 65.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{14}IN_2OS$ 468.9872, found 468.9855.

*5-(Quinolin-8-yl)-4-(m-tolyl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8v**).* Compound **8v** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 58% (26 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); IR (DCM) 1694, 1501, 1472, 1390 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.73 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.70 (d, 1H, J = 4.8 Hz), 7.63 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50−7.42 (m, 2H), 7.06 (t, 1H, J = 7.4 Hz), 6.98−6.94 (m, 3H), 6.87 (d, 2H, J = 8.7 Hz), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 157.4, 150.0, 144.6, 138.4, 136.7, 136.4, 135.5, 134.7, 134.1, 130.3, 129.3, 128.5, 128.1, 127.5, 126.3, 124.7, 121.3, 121.2, 66.3, 21.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2OS$ 357.1062, found 357.1046.

*5-(Quinolin-8-yl)-4-(3-(trifluoromethyl)phenyl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8w**).* Compound **8w** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a brown solid: yield 64% (33 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); mp 175−177 °C; IR (KBr) 1698, 1501, 1390, 1331, 1129 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.75−7.73 (m, 2H), 7.65 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50 (d, 1H, J = 8.0 Hz), 7.47−7.41 (m, 2H), 7.35 (br s, 1H), 7.33−7.28 (m, 2H), 7.13 (s, 1H), 6.94 (d, 1H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 156.4, 150.1, 144.4, 138.1, 136.5, 136.1, 135.0, 133.6, 131.0 (q, *JC-F* = 32.2 Hz), 130.9, 129.4, 129.2, 126.4 (q, *JC-F* = 271.5 Hz), 126.3, 125.2 (q, *JC-F* = 3.4 Hz), 124.5 (q, *JC-F* = 3.7 Hz), 121.5, 121.0, 65.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{14}F_3N_2OS$ 411.0779, found 411.0773.

*4-(3,4-Dichlorophenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8x**).* Compound **8x** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless solid: yield 54% (28 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); mp 218−220 °C; IR (KBr) 1697, 1472, 1391, 1131 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.77−74 (m, 2H), 7.68 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.47 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.24 (d, 1H, J = 8.3 Hz), 7.19 (d, 1H, J = 2.1 Hz), 7.07 (s, 1H), 6.95−6.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 156.2, 150.0, 144.3, 137.3, 136.5, 136.1, 135.0, 133.5, 132.8, 132.4, 130.7, 130.0, 129.6, 129.4, 127.8,

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126.9, 126.4, 121.5, 120.9, 64.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{13}Cl_2N_2OS$ 411.0126, found 411.0114.

*4-(3,5-Dimethylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8y**).* Compound **8y** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 62% (29 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); IR (DCM) 3406, 1694, 1597, 1439, 1349, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.8 Hz), 7.73 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.68 (d, 1H, J = 4.8 Hz), 7.63 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50−7.42 (m, 2H), 6.93 (d, 1H, J = 4.8 Hz), 6.88 (s, 1H), 6.79 (br s, 1H), 6.70 (br s, 1H), 2.16 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 157.6, 150.0, 144.7, 138.1, 136.7, 136.4, 135.4, 134.6, 134.2, 130.3, 129.9, 129.3, 127.5, 126.3, 125.3, 121.3, 121.3, 66.4, 21.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2OS$ 371.1218, found 371.1229.

*4-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8z**).* Compound **8z** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 82% (41 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 1693, 1506, 1472, 1285, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.72 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.68 (d, 1H, J = 4.8 Hz), 7.65 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49 (dd, 1H, J_1 = 8.0 Hz, J_2 = 7.7 Hz), 7.42 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 6.95−6.94 (m, 2H), 6.63 (d, 1H, J = 4.8 Hz), 6.56 (d, 1H, J = 2.0 Hz), 6.51 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.1 Hz), 4.17−4.09 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 157.4, 150.0, 144.6, 143.5, 143.4, 136.4, 135.5, 134.7, 133.9, 130.4, 129.9, 129.3, 127.5, 126.4, 121.3, 121.2, 120.7, 117.4, 116.4, 65.7, 64.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{17}N_2O_3S$ 401.0960, found 401.0952.

*4-(3,4-Dimethylphenyl)-5-(quinolin-8-yl)-4H-thieno[2,3-c]pyrrol-6(5H)-one (**8aa**).* Compound **8aa** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 54% (25 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 3396, 1693, 1504, 1391, 1137, 1021 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.72 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.69 (d, 1H, J = 4.8 Hz), 7.63 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.49−7.42 (m, 2H), 6.94−6.91 (m, 3H), 6.83 (br s, 1H), 6.79 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.6 Hz), 2.13 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 157.6, 150.0, 144.7, 136.9, 136.7, 136.4, 135.4, 134.6, 134.1, 130.4, 129.8, 129.3, 128.6, 127.5, 126.3, 125.1, 121.3, 121.3, 66.2, 19.7, 19.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2OS$ 371.1218, found 371.1206.

*3-(4-Methoxybenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9a**).* Compound **9a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 16% (8 mg); R_f = 0.45 (EtOAc/hexanes = 2:3); IR (DCM) 3306, 1653, 1531, 1261, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.38 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.77 (dd, 1H, J_1 = 6.1 Hz, J_2 = 2.9 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.92 (d, 2H, J = 9.0 Hz), 7.57 (d, 1H, J = 5.2 Hz), 7.54−7.53 (m, 2H), 7.48 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.25 (d, 1H, J = 5.2 Hz), 6.93 (d, 2H, J = 9.0 Hz), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 164.0, 159.7, 148.6, 142.3, 140.2, 139.2, 136.1, 134.6, 132.7, 130.5, 130.4, 128.5, 128.0, 127.1, 122.4, 121.6, 117.9, 113.7, 55.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_3S$ 389.0960, found 389.0948.

*Methyl 4-(2-(Quinolin-8-ylcarbamoyl)thiophene-3-carbonyl)-benzoate (**9g**).* Compound **9g** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 11% (6 mg); R_f = 0.46 (EtOAc/hexanes = 2:3); IR (DCM) 1722, 1661, 1531, 1486 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.40 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.73 (dd, 1H, J_1 = 7.2 Hz, J_2 = 1.8 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 8.10 (d, 2H, J = 8.6 Hz), 7.95 (d, 2H, J = 8.6 Hz), 7.59 (d, 1H, J = 5.2 Hz), 7.58−7.49 (m, 3H), 7.27 (d, 1H, J = 5.2 Hz), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 166.2, 159.3, 148.7, 143.4, 141.1, 139.5, 139.1, 136.3, 134.4, 133.9, 130.5, 129.7, 129.6, 128.7, 128.0, 127.2, 122.5, 121.7, 117.8, 52.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{17}N_2O_4S$ 417.0909, found 417.0906.

*3-(4-Methylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9h**).* Compound **9h** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 19% (9 mg); R_f = 0.47 (EtOAc/hexanes = 2:3); IR (DCM) 3302, 1651, 1530, 1485, 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.45 (br s, 1H), 8.93 (d, 1H, J = 3.9 Hz), 8.77 (dd, 1H, J_1 = 6.2 Hz, J_2 = 2.6 Hz), 8.17 (d, 1H, J = 8.4 Hz), 7.82 (d, 2H, J = 8.0 Hz), 7.57−7.53 (m, 3H), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.26−7.24 (m, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 159.7, 148.6, 144.5, 142.8, 140.0, 139.2, 136.1, 135.1, 134.6, 130.6, 130.3, 129.2, 128.4, 128.0, 127.1, 122.4, 121.6, 117.9, 21.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_2S$ 373.1011, found 373.1023.

*3-(4-Ethylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9i**).* Compound **9i** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 50:50) as a colorless liquid: yield 7% (4 mg); R_f = 0.46 (EtOAc/hexanes = 2:3); IR (DCM) 1655, 1528, 1486, 1327, 1272 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.45 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.76 (dd, 1H, J_1 = 6.4 Hz, J_2 = 2.6 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.84 (d, 2H, J = 8.3 Hz), 7.56 (d, 1H, J = 5.2 Hz), 7.54−7.46 (m, 2H), 7.49 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.28−7.26 (m, 3H), 2.69 (q, 2H, J = 7.6 Hz), 1.23 (d, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 159.7, 150.7, 148.6, 142.9, 140.0, 139.2, 136.1, 135.3, 134.6, 130.6, 130.4, 128.4, 128.0, 128.0, 127.1, 122.4, 121.6, 117.9, 29.0, 15.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_2S$ 387.1167, found 387.1163.

*3-(4-Isopropylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9j**).* Compound **9j** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 7% (4 mg); R_f = 0.46 (EtOAc/hexanes = 2:3); IR (DCM) 3435, 1650, 1528, 1486, 1327 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.44 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.76 (dd, 1H, J_1 = 6.5 Hz, J_2 = 2.5 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.85 (d, 2H, J = 8.4 Hz), 7.56 (d, 1H, J = 5.2 Hz), 7.54−7.52 (m, 1H), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.30−7.27 (m, 3H), 2.98−2.91 (m, 1H), 1.24 (d, 6H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 159.7, 155.2, 148.6, 142.9, 140.0, 139.2, 136.1, 135.4, 134.6, 130.6, 130.4, 128.4, 128.0, 127.1, 126.6, 122.4, 121.6, 117.9, 34.3, 23.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_2O_2S$ 401.1324, found 401.1316.

*3-(4-tert-Butylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9k**).* Compound **9k** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 19% (10 mg); R_f = 0.47 (EtOAc/hexanes = 2:3); IR (DCM) 1655, 1596, 1384, 1273, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.42 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.5 Hz), 8.75 (dd, 1H, J_1 = 6.5 Hz, J_2 = 2.4 Hz), 8.16 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.5 Hz), 7.85 (d, 2H, J = 8.4 Hz), 7.56 (d, 1H, J = 5.1 Hz), 7.54−7.52 (m, 2H), 7.49 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.44 (d, 2H, J = 8.4 Hz), 7.29 (d, 1H, J = 5.1 Hz), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 159.7, 157.4, 148.6, 143.0, 140.0, 139.2, 136.1, 135.0, 134.6, 130.7, 130.1, 128.4, 128.0, 127.1, 125.4, 122.4, 121.6, 117.9, 35.2, 31.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{23}N_2O_2S$ 415.1480, found 415.1465.

*3-(4-Hexylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9l**).* Compound **9l** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 20% (11 mg); R_f = 0.44 (EtOAc/hexanes = 2:3); IR (DCM) 1654, 1533, 1422, 1384, 1261 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.44 (br s, 1H), 8.94 (dd, 1H, J_1 = 4.1 Hz, J_2 = 1.1 Hz), 8.76 (d, 1H, J = 6.2 Hz), 8.16 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.0 Hz), 7.83 (d, 2H, J = 8.1 Hz), 7.57 (d, 1H, J = 5.2 Hz), 7.54−7.53 (m, 2H), 7.47 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.27−7.23 (m, 3H), 2.64 (t, 2H, J = 7.6 Hz), 1.64−1.57 (m, 2H), 1.29−1.29 (m, 6H), 0.89 (t, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 159.7, 149.5, 148.6, 142.9, 140.0, 139.2, 136.1, 135.3, 134.6, 130.7, 130.3, 128.5, 128.4, 128.0, 127.1, 122.4, 121.6, 117.9, 36.1, 31.6, 31.0, 28.9, 22.6, 14.1; HRMS

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(ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{27}N_2O_2S$ 443.1793, found 443.1777.

*3-(4-Pentylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9m**).* Compound **9m** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 28% (15 mg); R_f = 0.45 (EtOAc/hexanes = 2:3); IR (DCM) 1658, 1603, 1532, 1119, 1044 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.44 (br s, 1H), 8.93 (d, 1H, J = 4.0 Hz), 8.76 (dd, 1H, J_1 = 6.3 Hz, J_2 = 2.6 Hz), 8.17 (d, 1H, J = 8.3 Hz), 7.84 (d, 2H, J = 8.0 Hz), 7.56 (d, 1H, J = 5.2 Hz), 7.54−7.52 (m, 2H), 7.47 (dd, 1H, J_1 = 8.5 Hz, J_2 = 4.4 Hz), 7.26−7.23 (m, 3H), 2.64 (t, 2H, J = 7.6 Hz), 1.63−1.56 (m, 2H), 1.34−1.28 (m, 4H), 0.89 (t, 3H, J = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 159.7, 149.5, 148.6, 142.9, 140.0, 139.2, 136.1, 135.3, 134.6, 130.6, 130.3, 128.5, 128.4, 128.0, 127.1, 122.4, 121.6, 117.9, 36.0, 31.4, 30.8, 22.5, 14.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_2S$ 429.1637, found 429.1621.

*3-Benzoyl-N-(quinolin-8-yl)thiophene-2-carboxamide (**9n**).* Compound **9n** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 50:50) as a brown solid: yield 11% (5 mg); R_f = 0.43 (EtOAc/hexanes = 2:3); mp 138−140 °C; IR (DCM) 3311, 1659, 1532, 1425, 1272 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.47 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.76 (dd, 1H, J_1 = 6.6 Hz, J_2 = 2.4 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.92−7.90 (m, 2H), 7.59−7.43 (m, 7H), 7.27 (d, J = 5.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 159.6, 148.7, 143.2, 139.7, 139.2, 137.7, 136.2, 134.6, 133.5, 130.7, 130.1, 128.4, 128.0, 127.1, 122.4, 121.6, 117.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{15}N_2O_2S$ 359.0854, found 359.0852.

*3-(3-Methoxybenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9o**).* Compound **9o** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless solid: yield 27% (13 mg); R_f = 0.44 (EtOAc/hexanes = 2:3); mp 136−138 °C; IR (KBr) 3312, 1658, 1532, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.40 (br s, 1H), 8.93 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.76 (dd, 1H, J_1 = 6.7 Hz, J_2 = 2.3 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.57 (d, 1H, J = 5.2 Hz), 7.55−7.53 (m, 2H), 7.51−7.47 (m, 2H), 7.41 (dt, 1H, J_1 = 7.6 Hz, J_2 = 1.2 Hz), 7.34 (t, 1H, J = 8.0 Hz), 7.28 (d, 1H, J = 5.2 Hz), 7.12−7.09 (m, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 159.6, 159.6, 148.6, 143.0, 139.9, 139.1, 139.0, 136.2, 134.5, 130.6, 129.4, 128.4, 128.0, 127.2, 123.1, 122.4, 121.6, 120.2, 117.9, 113.7, 55.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_3S$ 389.0960, found 389.0962.

*Ethyl 3-(2-(Quinolin-8-ylcarbamoyl)thiophene-3-carbonyl)-benzoate (**9p**).* Compound **9p** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 50:50) as a colorless solid: yield 20% (11 mg); R_f = 0.40 (EtOAc/hexanes = 2:3); mp 113−115 °C; IR (KBr) 2985, 1719, 1660, 1532, 1241 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.40 (br s, 1H), 8.94 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.75 (dd, 1H, J_1 = 7.0 Hz, J_2 = 1.9 Hz), 8.56 (br s, 1H), 8.23 (d, 1H, J = 7.8 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 8.08 (d, 1H, J = 7.8 Hz), 7.60 (d, 1H, J = 5.2 Hz), 7.57−7.53 (m, 3H), 7.49 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.28 (d, 1H, J = 5.2 Hz), 4.38 (q, 2H, J = 7.1 Hz), 1.39 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 165.6, 159.4, 148.7, 143.3, 139.5, 139.1, 138.0, 136.2, 134,4, 134.1, 133.9, 130.9, 130.9, 130.5, 128.7, 128.7, 128.0, 127.2, 122.5, 121.7, 117.8, 61.4, 14.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{19}N_2O_4S$ 431.1066, found 431.1058.

*3-(3,4-Dimethylbenzoyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (**9aa**).* Compound **9aa** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 12% (6 mg); R_f = 0.40 (EtOAc/hexanes = 2:3); IR (DCM) 3317, 1654, 1529, 1486 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.45 (br s, 1H), 8.94 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.76 (dd, 1H, J_1 = 6.3 Hz, J_2 = 2.8 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.71 (br s, 1H), 7.61 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.7 Hz), 7.56 (d, 1H, J = 5.1 Hz), 7.55−7.53 (m, 2H), 7.48 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.26 (d, 1H, J = 5.1 Hz), 7.19 (d, 1H, J = 7.9 Hz), 2.30 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 159.8, 148.7, 143.3, 142.9, 140.1, 139.2, 136.9, 136.1, 135.5, 134.6, 131.1, 130.7, 129.5, 128.3, 128.1, 128.0, 127.1, 122.4, 121.6, 117.9, 20.1, 19.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_2S$ 387.1167, found 387.1152.

*4-(4-Methoxyphenyl)-5-(quinolin-8-yl)-4H-furo[2,3-c]pyrrol-6(5H)-one (**10a**).* Compound **10a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless liquid: yield 33% (15 mg); R_f = 0.35 (EtOAc/hexanes = 2:3); IR (DCM) 1595, 1385, 1258, 1093, 1245 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.6 Hz), 8.18 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.74−7.71 (m, 2H), 7.51 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.47−7.43 (m, 2H), 6.93 (d, 2H, J = 8.7 Hz), 6.83 (s, 1H), 6.68 (d, 2H, J = 8.7 Hz), 6.50 (d, 1H, J = 1.7 Hz), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 150.2, 150.2, 150.0, 144.7, 141.4, 136.5, 133.8, 130.4, 129.3, 129.0, 127.8, 127.6, 126.3, 121.3, 113.9, 107.4, 62.3, 55.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_3$ 357.1239, found 357.1227.

*4-(3-Methoxyphenyl)-5-(quinolin-8-yl)-4H-furo[2,3-c]pyrrol-6(5H)-one (**10b**).* Compound **10b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless liquid: yield 33% (15 mg); R_f = 0.34 (EtOAc/hexanes = 2:3); IR (DCM) 1702, 1597, 1471, 1386, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.74−7.72 (m, 2H), 7.58 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.8 Hz), 7.48 (d, 1H, J = 7.9 Hz), 7.45 (dd, 1H, J_1 = 4.0 Hz, J_2 = 1.6 Hz), 7.09 (t, 1H, J = 7.9 Hz), 6.87 (s, 1H), 6.71 (dd, 1H, J_1 = 8.2 Hz, J_2 = 2.1 Hz), 6.65 (d, 1H, J = 7.6 Hz), 6.59 (t, 1H, J = 1.9 Hz), 6.51 (d, 1H, J = 1.7 Hz), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 159.3, 150.3, 150.1, 150.0, 144.6, 141.4, 137.6, 136.5, 133.8, 130.3, 129.6, 129.3, 127.6, 126.3, 121.4, 120.0, 113.9, 113.0, 107.4, 62.7, 55.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_3$ 357.1239, found 357.1226.

*4-(4-Ethylphenyl)-5-(quinolin-8-yl)-4H-furo[2,3-c]pyrrol-6(5H)-one (**10c**).* Compound **10c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 90:10) as a colorless solid: yield 56% (25 mg); R_f = 0.33 (EtOAc/hexanes = 2:3); mp 186−188 °C; IR (KBr) 3301, 1711, 1648, 1529, 1388 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.7 Hz), 8.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.73−7.71 (m, 2H), 7.53 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.5 Hz), 7.47−7.43 (m, 2H), 6.99 (d, 2H, J = 8.2 Hz), 6.94 (d, 2H, J = 8.2 Hz), 6.87 (s, 1H), 6.50 (d, 1H, J = 1.8 Hz), 2.54 (q, 2H, J = 7.6 Hz), 1.15 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 150.2, 150.1, 150.0, 144.7, 144.3, 141.5, 136.4, 133.9, 133.2, 130.4, 129.3, 128.1, 127.6, 127.6, 126.3, 121.3, 107.4, 62.6, 28.4, 15.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_2$ 355.1447, found 355.1443.

*3-(4-Methoxybenzoyl)-N-(quinolin-8-yl)furan-2-carboxamide (**11a**).* Compound **11a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 30:70) as a colorless liquid: yield 23% (11 mg); R_f = 0.45 (EtOAc/hexanes = 2:3); IR (DCM) 1597, 1482, 1385, 1215, 1094 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.23 (br s, 1H), 8.95 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.4 Hz), 8.81 (dd, 1H, J_1 = 7.3 Hz, J_2 = 1.4 Hz), 8.19 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.98 (d, 2H, J = 8.8 Hz), 7.71 (d, 1H, J = 1.6 Hz), 7.57−7.50 (m, 3H), 6.97 (d, 2H, J = 8.8 Hz), 6.75 (d, 1H, J = 1.6 Hz), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 164.1, 155.5, 148.6, 146.0, 143.7, 138.9, 136.3, 134.1, 132.3, 130.1, 128.5, 128.0, 127.3, 122.3, 121.7, 117.5, 113.9, 113.6, 55.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_4$ 373.1188, found 373.1175.

*1-(4-Methoxyphenyl)-2-(quinolin-8-yl)-1H-benzo[4,5]thieno[2,3-c]pyrrol-3(2H)-one (**12a**).* Compound **12a** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 85:15) as a colorless liquid: yield 53% (28 mg); R_f = 0.30 (EtOAc/hexanes = 2:3); IR (DCM) 3452, 1694, 1512, 1472, 1388 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.98 (dd, 1H, J_1 = 8.2 Hz, J_2 = 0.8 Hz), 7.75 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.9 Hz), 7.63 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.50 (d, 1H, J = 7.6 Hz), 7.48−7.41 (m, 3H), 7.32 (td, 1H, J_1 = 7.2 Hz, J_2 = 1.0 Hz), 7.18 (s, 1H), 7.02 (d, 2H, J = 8.7 Hz), 6.69 (d, 2H, J = 8.7 Hz), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 159.5, 151.8, 150.0, 146.6, 144.6, 136.4, 135.4, 133.8, 132.6, 130.3, 129.3, 129.1, 127.9, 127.6, 126.4, 126.4, 125.0, 124.3,

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122.8, 121.4, 114.1, 65.9, 55.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{19}N_2O_2S$ 423.1167, found 423.1175.

*1-(4-Chlorophenyl)-2-(quinolin-8-yl)-1H-benzo[4,5]thieno[2,3-c]-pyrrol-3(2H)-one (**12b**).* Compound **12b** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless liquid: yield 43% (23 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); IR (DCM) 3406, 1698, 1529, 1472, 1388 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, 1H, J = 3.7 Hz), 8.20 (d, 1H, J = 8.0 Hz), 7.99 (d, 1H, J = 8.0 Hz), 7.77 (d, 1H, J = 8.0 Hz), 7.66 (d, 1H, J = 8.4 Hz), 7.52 (d, 1H, J = 8.0 Hz), 7.49−7.42 (m, 3H), 7.34 (t, 1H, J = 7.7 Hz), 7.27 (s, 1H), 7.15 (d, 2H, J = 8.0 Hz), 7.07 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 151.1, 150.0, 146.6, 144.4, 136.5, 135.6, 134.7, 134.3, 133.4, 132.3, 130.1, 129.3, 129.3, 129.1, 127.7, 126.6, 126.4, 125.1, 124.4, 122.6, 121.5, 65.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{16}ClN_2OS$ 427.0672, found 427.0676.

*1-(3,5-Dimethylphenyl)-2-(quinolin-8-yl)-1H-benzo[4,5]thieno-[2,3-c]pyrrol-3(2H)-one (**12c**).* Compound **12c** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 85:15) as a pale green solid: yield 51% (27 mg); R_f = 0.32 (EtOAc/hexanes = 2:3); mp 249−251 °C; IR (KBr) 3436, 1646, 1527, 1486 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.0 Hz, J_2 = 1.4 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.3 Hz), 7.98 (d, 1H, J = 8.2 Hz), 7.75 (d, 1H, J = 8.0 Hz), 7.65 (d, 1H, J = 8.0 Hz), 7.52−7.42 (m, 4H), 7.33 (t, 1H, J = 8.0 Hz), 7.07 (s, 1H), 6.80 (br s, 1H), 6.77 (br s, 2H), 2.16 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 151.9, 150.0, 146.6, 144.7, 138.2, 136.4, 135.8, 135.2, 133.9, 132.6, 130.4, 130.2, 129.3, 127.7, 126.4, 126.3, 125.5, 125.0, 124.2, 122.8, 121.4, 66.6, 21.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{21}N_2OS$ 421.1375, found 421.1387.

*1-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-2-(quinolin-8-yl)-1H-benzo[4,5]thieno[2,3-c]pyrrol-3(2H)-one (**12d**).* Compound **12d** was obtained after purification by column chromatography on neutral alumina (EtOAc/hexanes = 80:20) as a colorless liquid: yield 37% (21 mg); R_f = 0.31 (EtOAc/hexanes = 2:3); IR (DCM) 1694, 1506, 1390, 1285 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, 1H, J_1 = 4.2 Hz, J_2 = 1.8 Hz), 8.19 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.7 Hz), 7.97 (d, 1H, J = 8.2 Hz), 7.76 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.4 Hz), 7.68 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.4 Hz), 7.54−7.50 (m, 2H), 7.47−7.42 (m, 2H), 7.34 (td, 1H, J_1 = 7.2 Hz, J_2 = 1.0 Hz), 7.15 (s, 1H), 6.66−6.60 (m, 3H), 4.19−4.10 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 151.7, 150.0, 146.6, 144.6, 143.6, 143.6, 136.5, 135.3, 133.7, 132.6, 130.3, 129.3, 1291.1, 127.6, 126.5, 126.4, 125.0, 124.3, 122.9, 121.4, 121.0, 117.5, 116.6, 65.8, 64.1, 64.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{19}N_2O_3S$ 451.1116, found 451.1121.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00582.

X-ray structure and brief X-ray structure data of compounds **3l** and **8n**, ^1H and ^{13}C NMR spectra of isolated compounds, and HRMS analysis chart of arylation of **3a** with **2a** (PDF)

X-ray structure data for compound **3l** (CIF)

X-ray structure data for compound **8n** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sababu@iisermohali.ac.in.

ORCID

Srinivasarao Arulananda Babu: 0000-0002-1795-8843

Notes

The authors declare no competing financial interest.

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(47) Reactions involving **1f−m** were not fruitful. Complex mixtures were obtained in some cases, and in other cases, the reactions did not yield the corresponding products in characterizable amounts. The trial reactions involving substrate **1m** were performed using additives such as quinoline or 2-methylquinoline using the literature procedures reported by Yu et al.; see refs 9 and 24b.

(48) The analysis of the HRMS (ESI) data of the crude reaction mixture of the Pd(II)-catalyzed arylation of **3a** with **2a** (eq 2, Scheme 14) indicated the following information in support of the proposed formation of biaryl compound **21**. At first, the formation of the expected product **8a** was corroborated based on its mass data, *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_2S$ 373.1011, found 373.1053. Then the formation of 4,4′-dimethoxy-1,1′-biphenyl (**21**) was corroborated based on its mass data, *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{14}NaO_2$ 237.0891, found 237.0930 (see the SI for the copy of the HRMS analysis chart).

(49) (a) Padmavathi, R.; Sankar, R.; Gopalakrishnan, B.; Parella, R.; Babu, S. A. *Eur. J. Org. Chem.* **2015**, 3727. (b) Micheal, U.; Hornfeldt, A. B. *Tetrahedron Lett.* **1970**, *11*, 5219.

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