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# Pd(II)-Catalyzed Arylation and Intramolecular Amidation of $\gamma$-C($sp^3$)-H Bonds: En Route To Arylheteroarylmethane and Pyrrolidone-Ring Annulated Furan/Thiophene Scaffolds

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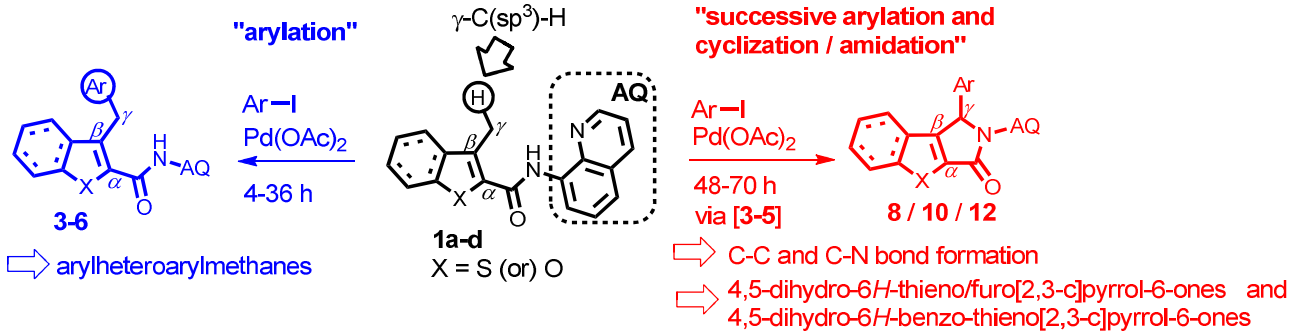
## ABSTRACT




We report the Pd(II)-catalyzed, bidentate directing group (BDG)-assisted arylation and successive arylation/intramolecular amidation of $\gamma$-C($sp^3$)-H bonds. The Pd(II)-catalyzed BDG-assisted C-H activation and functionalization of the $\beta$-C($sp^3$)-H bonds of carboxylic acids are well documented, but only a few reports are available which are dealing with the BDG-directed functionalization of the $\gamma$-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 $\gamma$-C($sp^3$)-H bonds. The $\gamma$-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 $\gamma$-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, the 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 $\beta$-C($sp^3$)-H bonds of carboxylic acids with the help 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 $\beta$-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

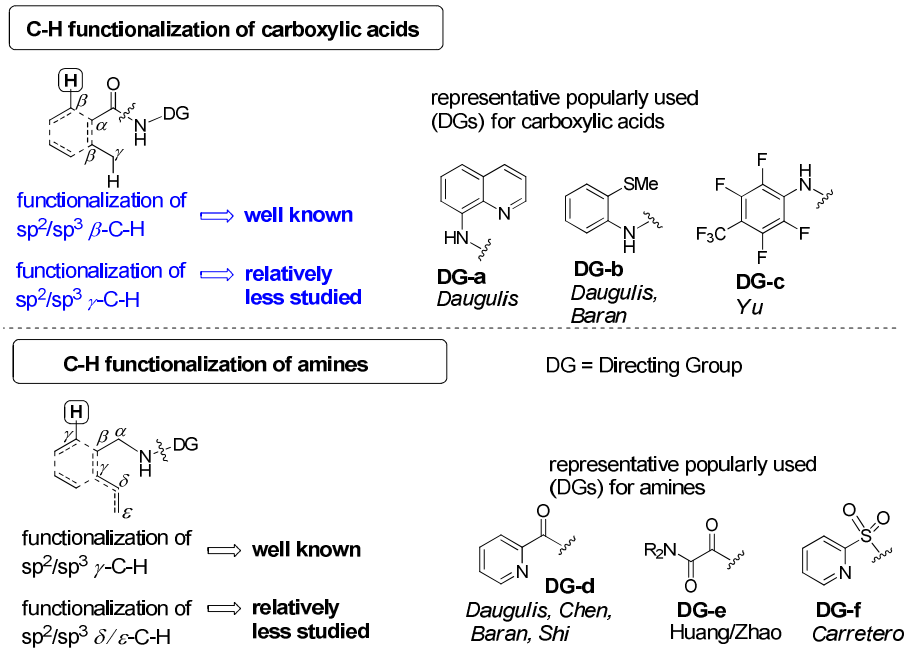
picolinamide (PA)-type BDGs (**DG-d**, **Dg-e**, and **DG-f**, etc.) have been used for the functionalization of the $sp^2/sp^3$ C-H bonds of amines. With regard to site-selectivity, there are numerous reports dealing with the PA-type BDG-assisted functionalization of the $\gamma$-C-H and remote $\delta$- and $\varepsilon$-C-H bonds of amines.[1-7,13-20] Notably, the 8-aminoquinoline-type BDGs have favorably assisted the functionalization of the $\beta$-C-H bonds of carboxylic acids.[1-7,10-12]

While the functionalization of the remote $\gamma$-, $\delta$- and $\varepsilon$-C($sp^2/sp^3$)-H bonds of suitable amines has been well advanced using PA-type BDGs,[6,7,13-22] however, similar work on suitable carboxylic acids is currently limited to the functionalization of the remote $\gamma$-C($sp^2/sp^3$)-H bonds. Only a few reports deal with the BDG-assisted functionalization of the $\gamma$-C($sp^2/sp^3$)-H bonds (Schemes 1 and 2).[6,7,23-27] We assembled the 3-methylfuran/thiophene-2-carboxamides **1a-e** from their corresponding carboxylic acids and BDGs, such as 8-aminoquinoline and 2-(methylthio)aniline (Schemes 3-5). The $\gamma$-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).

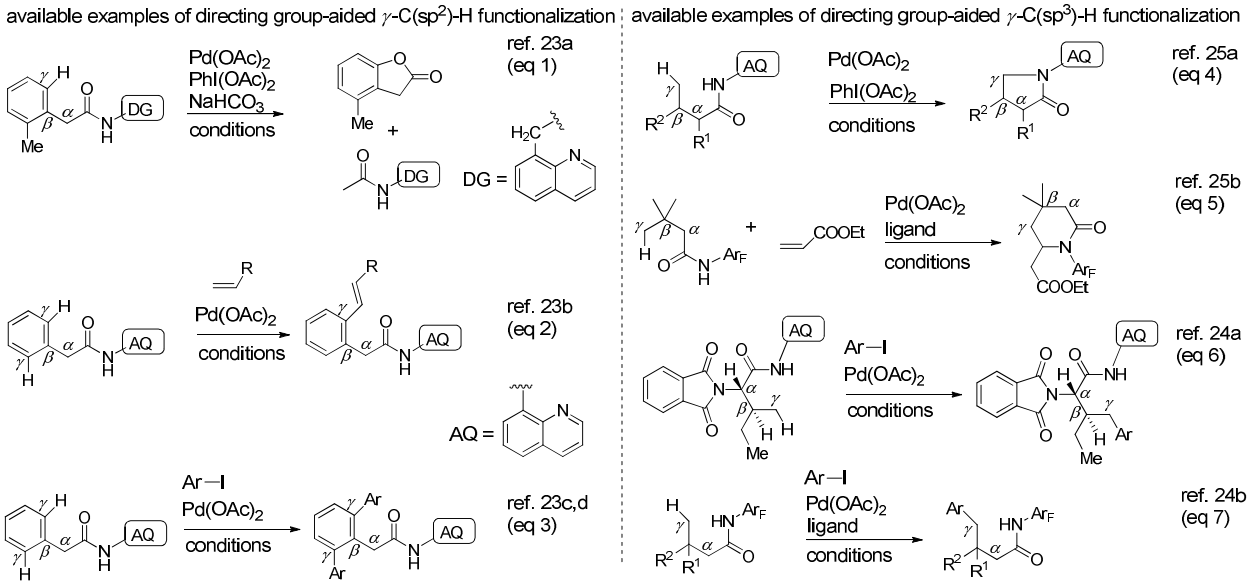
Apart from the C-H functionalization reactions comprising the intermolecular arylation, alkylation, amination/amidation, acetoxylation, the BDG-assisted or directing group-free C–H functionalization technique was also well explored for performing the intramolecular $sp^2/sp^3$ C-H amination/amidation 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 representative reports dealing with the functionalization/intramolecular amination/amidation of benzylic $\gamma$-C($sp^3$)-H

bonds of corresponding aromatic compounds affording the isoindolin-1-one cores and examples of bio-active isoindolin-1-one cores.[35]

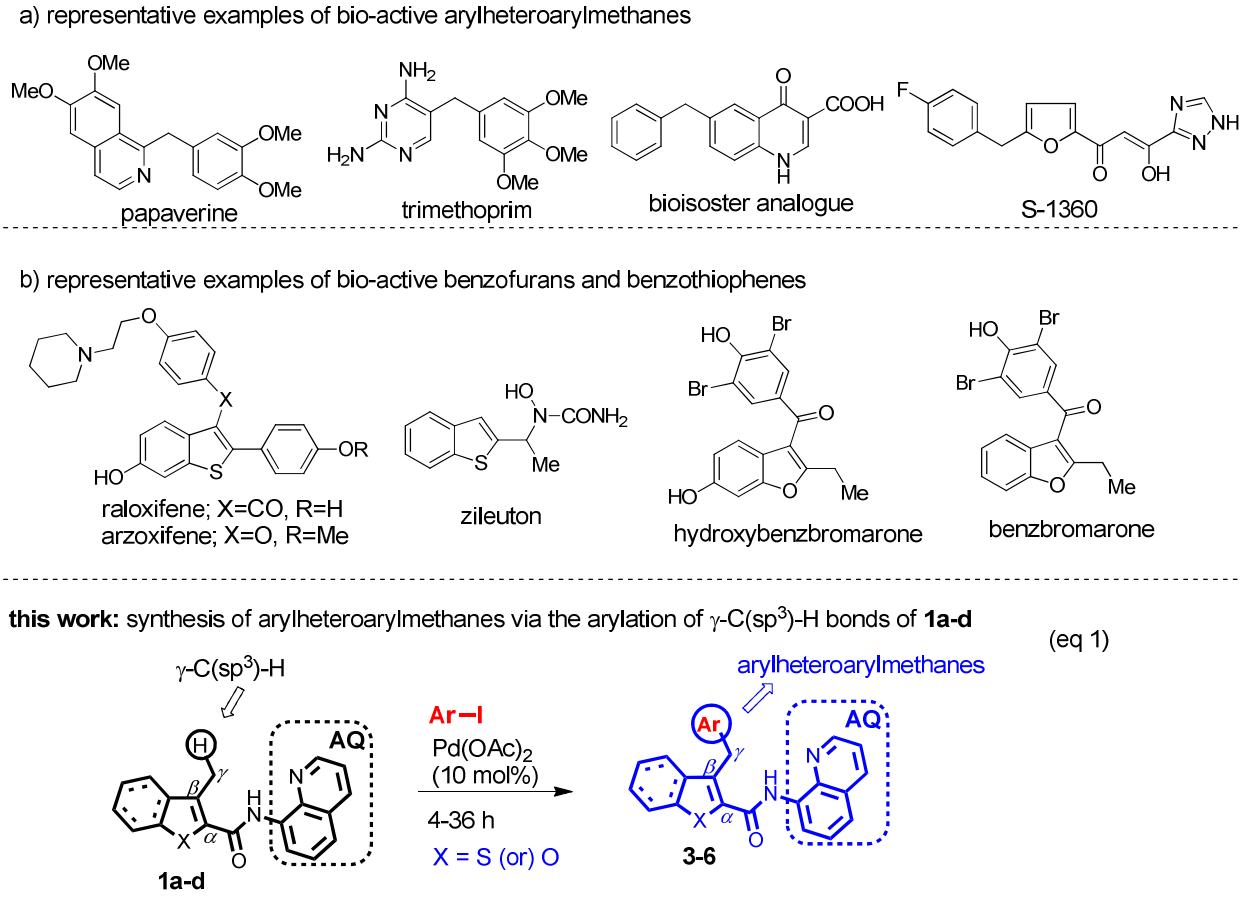
**Scheme 1. Bidentate directing group-assisted C-H functionalization.**




**Scheme 2. Available examples of bidentate directing group-assisted $sp^2$ / $sp^3$ γ-C-H functionalization.**

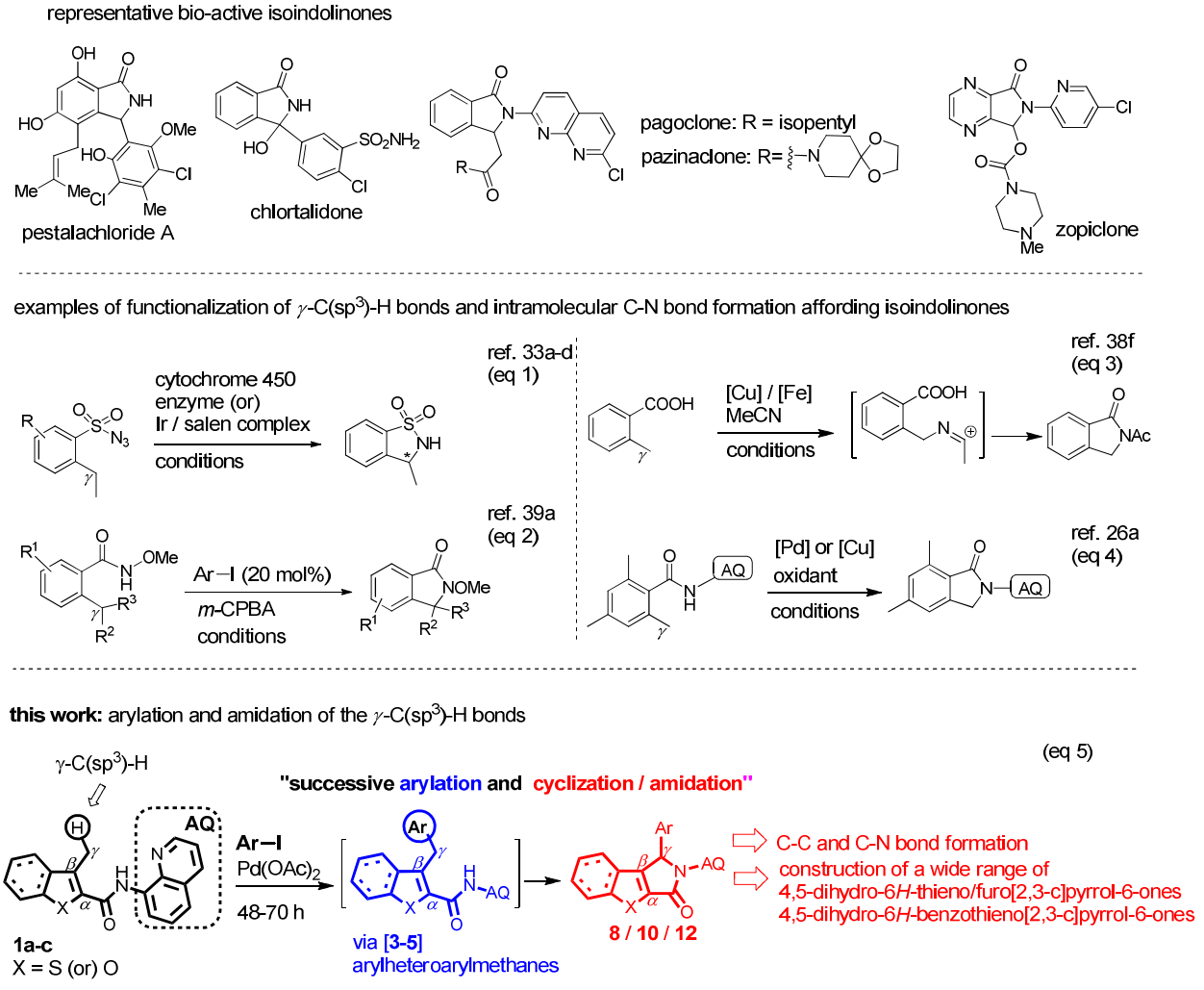


**Scheme 3. Bio-active arylheteroarylmethanes and benzofurans/benzothiophenes. Synthesis of arylheteroarylmethanes via γ-C(sp$^3$)-H functionalization.**




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 bio-active furan/thiophene-based molecules,[41] arylheteroarylmethane (unsymmetrical diarylmethanes),[43] and isoindolin-1-one scaffolds[35] are illustrated in Schemes 3 and 4.

**Scheme 4. Bio-Active isoindolinone scaffolds. Synthesis of isoindolinone scaffolds via the functionalization/intramolecular amidation of benzylic $\gamma$-C($sp^3$)-H bonds.**



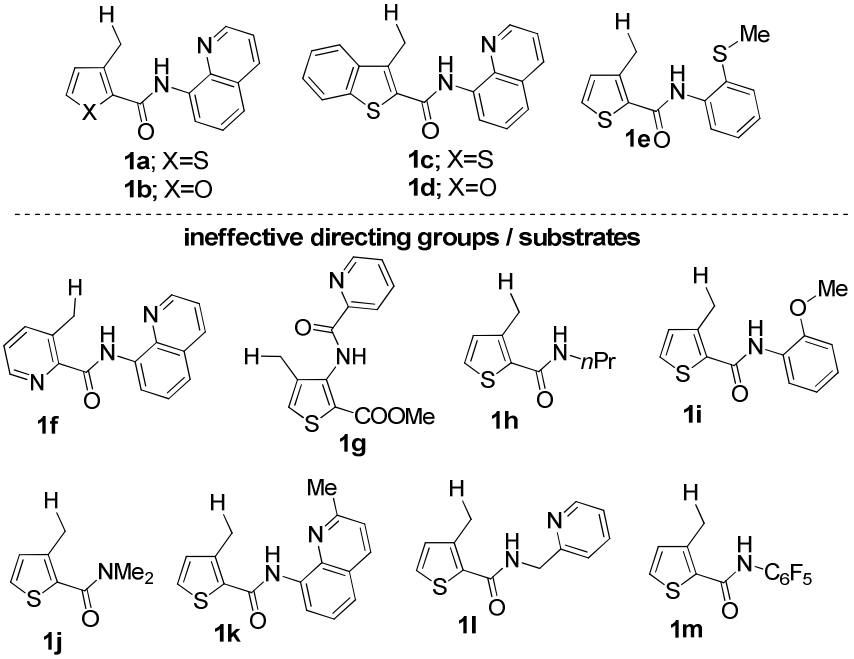

In continuation of our lab's research programme on the C-H activation reactions, herein we report our investigations on the Pd(II)-catalyzed BDG-assisted arylation and successive arylation/intramolecular amidation of $\gamma$-C($sp^3$)-H bonds of 3-methylfuran/thiophene-2-carboxamides and 3-methylbenzofuran/thiophene-2-carboxamides (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 $\gamma$-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.

**Scheme 5. Directing groups and substrates used to investigate the $\gamma$-C(sp$^3$)-H arylation/amidation reactions.**[a,47]



[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.

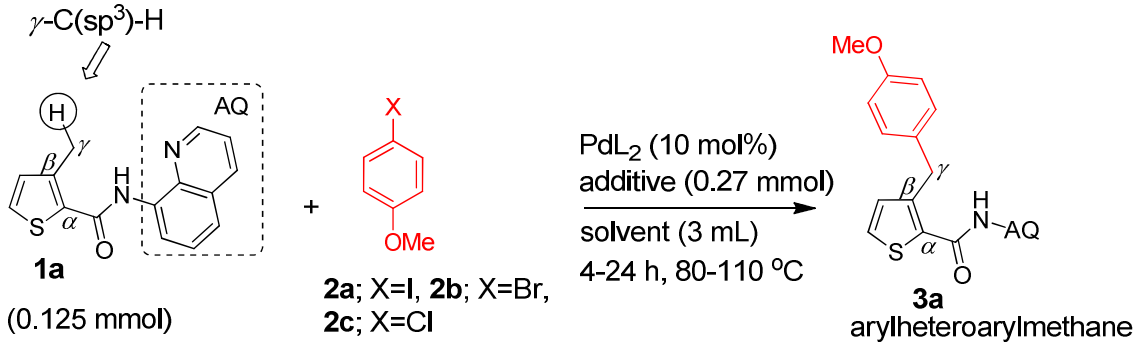
The $\gamma$-C($sp^3$)-H arylated derivative **3a** (arylheteroarylmethane) was obtained in 14% yield from the reaction of a mixture of substrate **1a** (1 equiv), aryl iodide **2a** (4 equiv), and $Pd(OAc)_2$ catalyst without any additive in toluene at 110 $^oC$ for 24 h (entry 1, Table 1). The reaction 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 $^oC$ 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 $\gamma$-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 tried 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). **3a** was not produced when using coupling partners such as aryl bromide **2b** or aryl

chloride **2c** 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 $\gamma$-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 $\gamma$-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 $\gamma$-C($sp^3$)-H bond of these substrates (Scheme 5). Additionally, while the 8-aminoquinoline-assisted $\gamma$-C($sp^3$)-arylation of **1a** was successful, the Pd(II)-catalyzed 8-aminoquinoline-assisted $\gamma$-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]

**Table 1. Optimization of reaction conditions. $\gamma$-C($sp^3$)-H arylation of substrate 1a**[a]

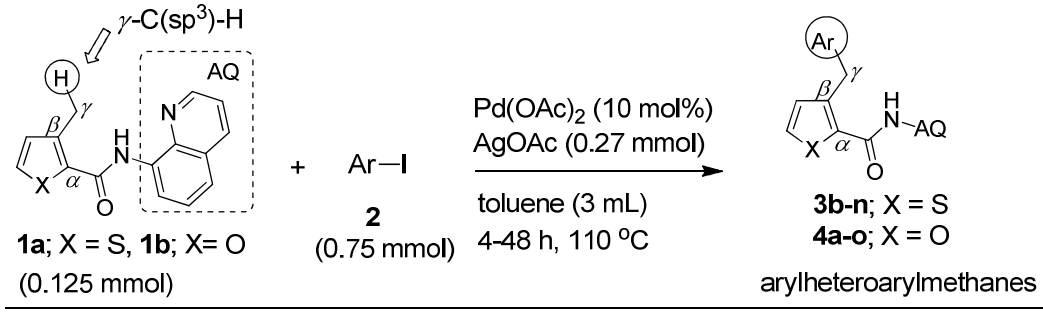


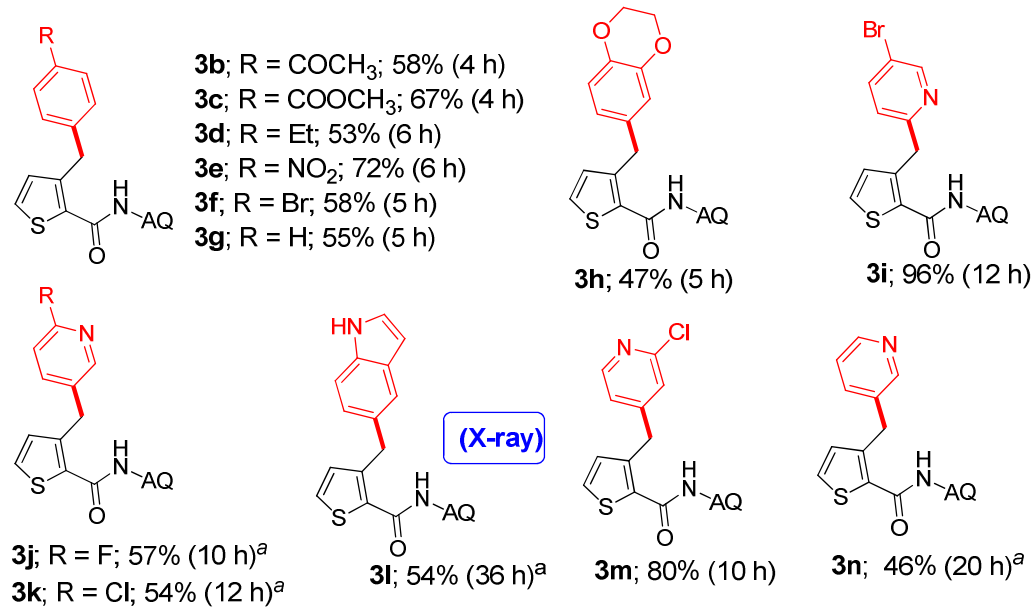

| entry | $PdL_2$ (10 mol%) | **2a** (mmol) | additive | solvent | *T* (°C) | *t* (h) | **3a**: yield (%) |
|---|---|---|---|---|---|---|---|

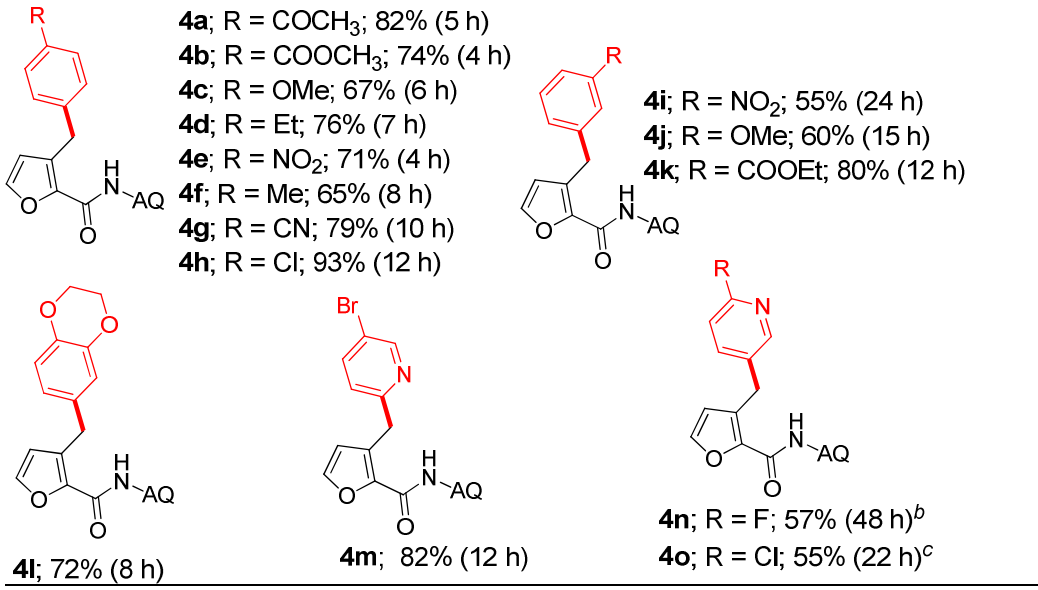
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | 0.5 | - | toluene | 110 | 24 | 14 |
| 2 | - | 0.5 | AgOAc | toluene | 110 | 24 | 0 |
| 3 | $Pd(OAc)_2$ | 0.25 | AgOAc | toluene | 110 | 4 | 32 |
| 4 | $Pd(OAc)_2$ | 0.5 | AgOAc | toluene | 110 | 4 | 45 |
| **5** | **$Pd(OAc)_2$** | **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 the reactions were performed using **2a**. [b] **2b** was used instead of **2a**. [c] **2c** was used instead of **2a**.

**Scheme 6. $\gamma$-C($sp^3$)-H arylation of 1a,b. Construction of thiophene/furan-based arylheteroarylmethanes 3/4.**



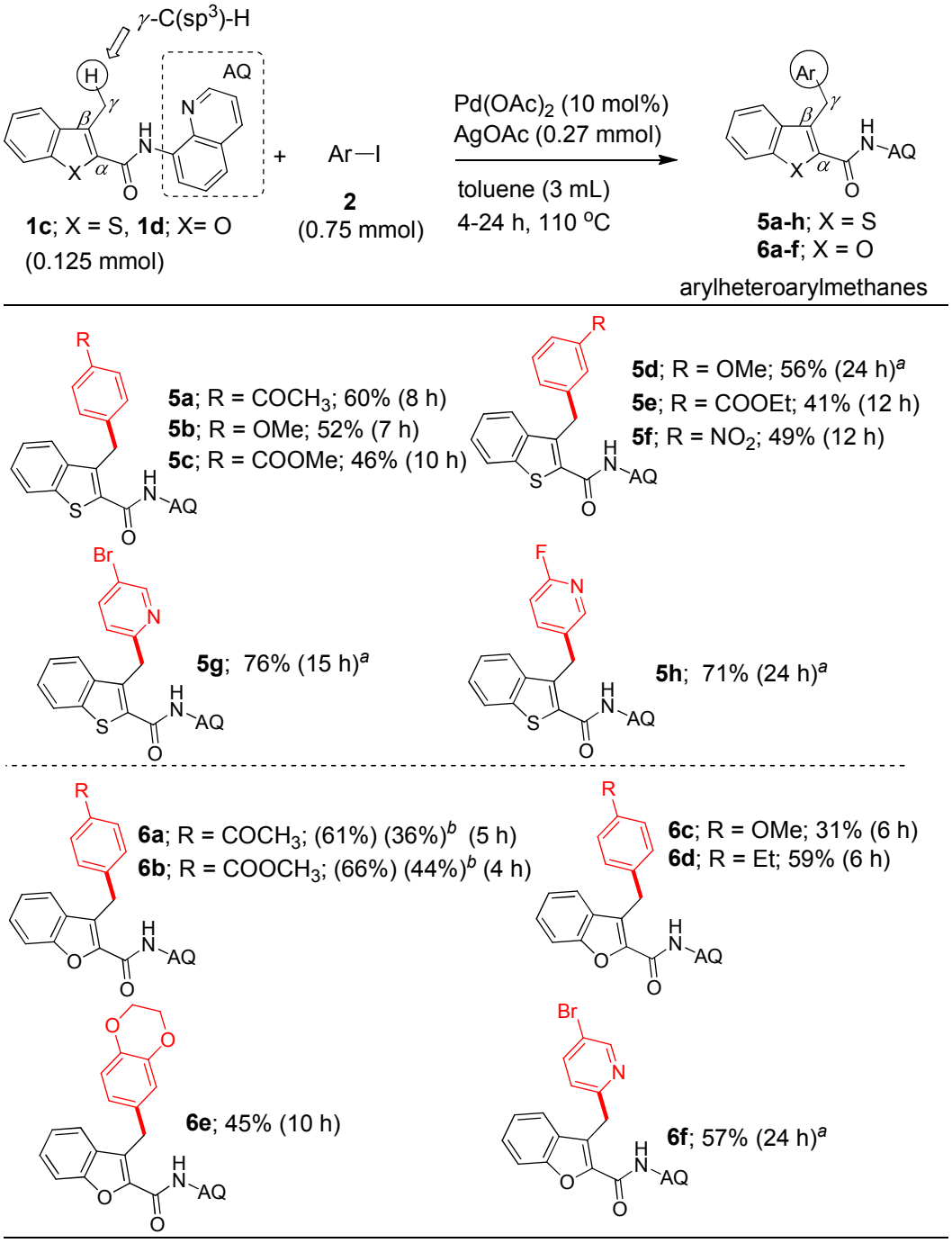



[a] 1.0 mmol of the corresponding aryl iodide was used in this reaction. [b] 20 mol% catalyst was used. [c] 1.0 mmol of the corresponding aryl iodide was used in this reaction.

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 $\gamma$-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 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 $\gamma$-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 thediheteroarylmethane derivatives **3i-n** in 46-96% yield (Scheme 6).

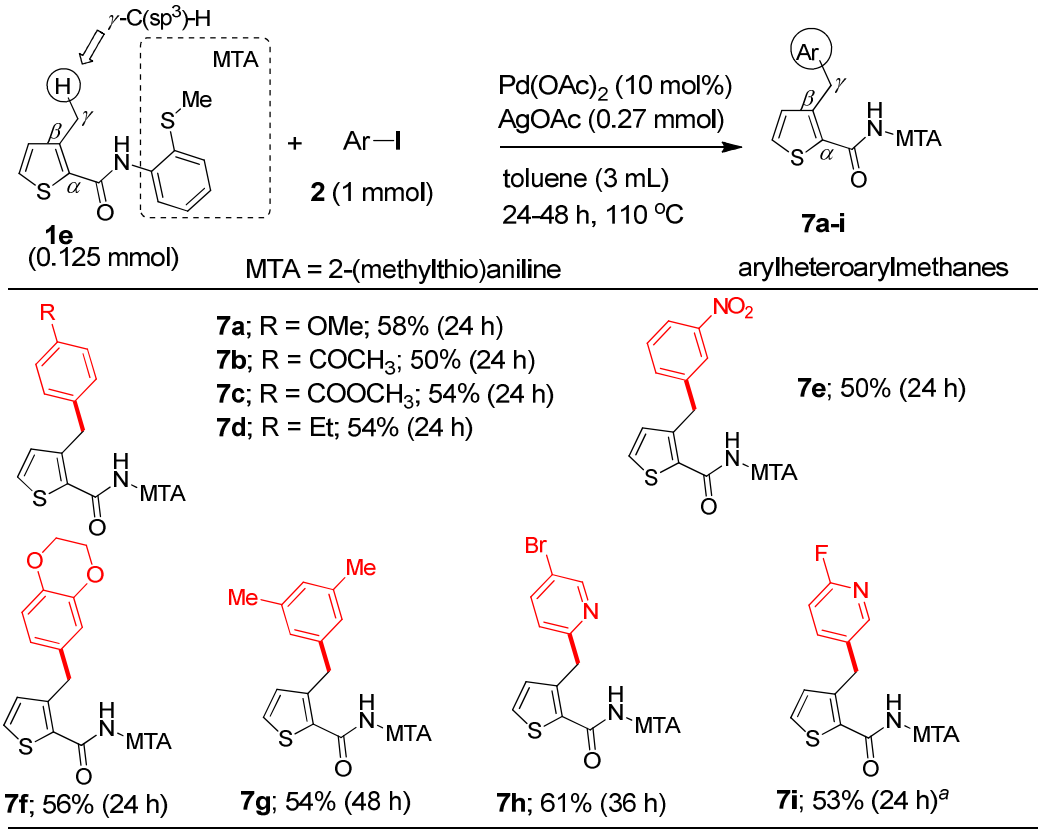
We next performed the Pd(II)-catalyzed arylation using the furan-2-carboxamide derivative **1b**. The arylation of substrate **1b** with aryl iodides containing a substituent at the *para* or *meta* position (e.g., Ac, COOR, OMe, alkyl, $NO_2$, CN, and Cl) afforded the corresponding arylheteroarylmethane 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).

**Scheme 7. $\gamma$-C(sp$^3$)-H arylation of 1c,d. Construction of benzo-thiophene/furan-based arylheteroarylmethanes 5/6.**




[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.

**Scheme 8. MTA-directed $\gamma$-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.

We next expanded the scope of this protocol by performing the $\gamma$-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 $\gamma$-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

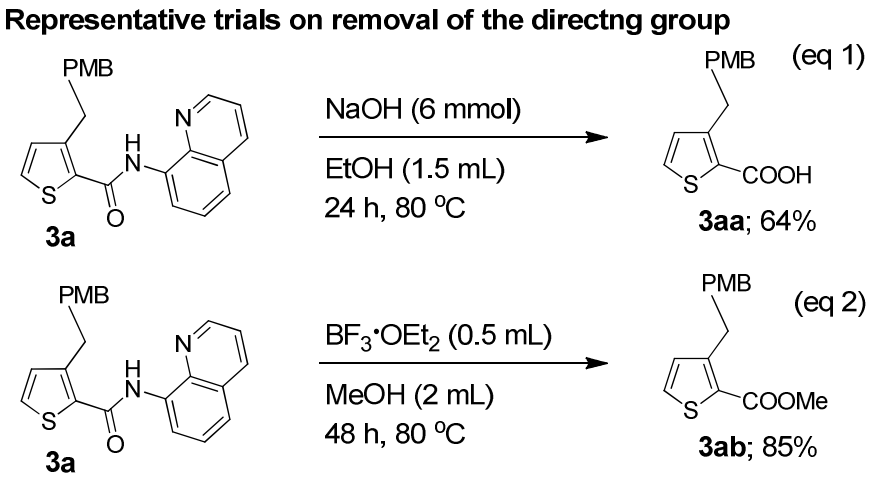
disubstituted aryl iodide and a heteroaryl iodide also afforded the corresponding arylheteroarylmethane derivative **6e** and diheteroarylmethane derivative **6f** in 45-57% yield (Scheme 7).

We next examined the $\gamma$-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 $\gamma$-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, the treatment of the **3a** with MeOH in $BF_3{\cdot}OEt_2$ afforded the methyl ester derivative **3ab** in 85% yield (Scheme 9).

The $\gamma$-C-H arylations of the methyl group in compounds **1a-e** resulted in the corresponding arylheteroarylmethanes and diheteroarylmethanes **3-7** containing the methylene $\gamma$-C-H bonds. Thus, under the experimental conditions used for the $\gamma$-C($sp^3$)-H arylation of the compounds **1a-e**, we expected that it would also possible to accomplish the intramolecular C-H amidation through the methylene $\gamma$-C-H bonds in the compounds **3-7**. We therefore explored the possibility of successive arylation/intramolecular amidation of the remote $\gamma$-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).

**Scheme 9. Representative trials to remove the directing group.**




**Scheme 10. Proposed successive arylation and intramolecular amidation of *γ*-C(sp$^3$)-H bonds towards pyrrolidone-ring annulated thiophene/furan-based heterocycles.**

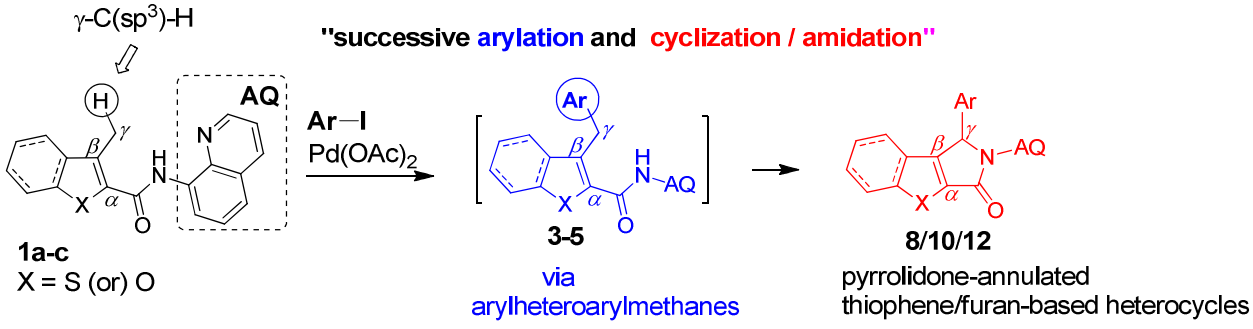
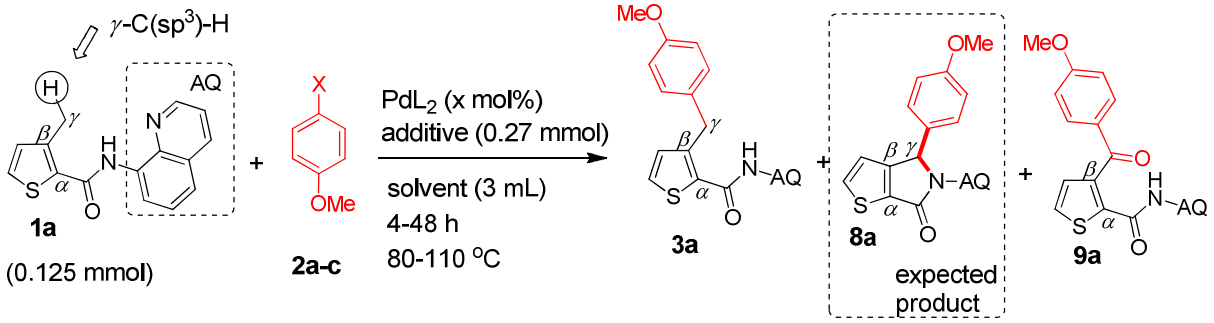


**Table 2. Optimization of reaction conditions. Successive $\gamma$-C($sp^3$)-H arylation/intramolecular amidation of 1a**[a]




| Entry | $PdL_2$ (x mol%) | **2a** (mmol) | Additive | Solvent | $T$ (°C) | $t$ (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[d] | $Pd(OAc)_2$ (20) | 0.5 | AgOAc | toluene | 110 | 24 | 33 | 0 | 0 |
| 20[e] | $Pd(OAc)_2$ (20) | 0.5 | AgOAc | toluene | 110 | 24 | 19 | 0 | 0 |
| 21[f] | $Pd(OAc)_2$ (20) | 0.5 | AgOAc | toluene | 110 | 24 | 20 | <5 | <5 |

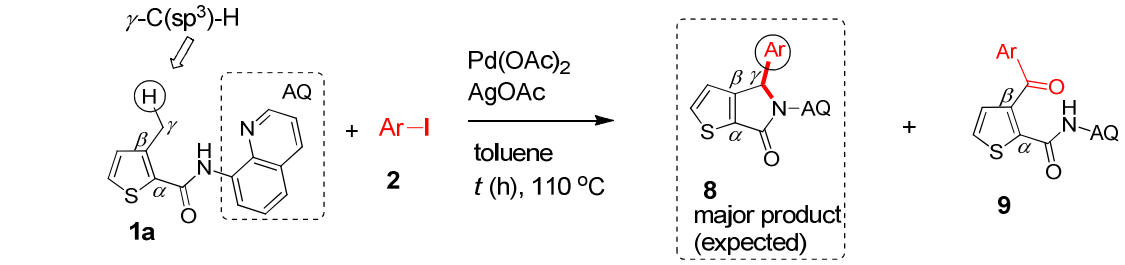
[a] All the reactions were performed using **2a**. [b] Result of entry 5, Table 1. [c] **2b** was used instead of **2a**. [d] **2c** was used instead of **2a**. [d] Quinoline (40 mol%) was added as an additive. [e] 2-Methyl quinoline (40 mol%) was added as an additive. [f] 2-Hydroxy-4-methylquinoline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

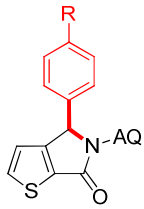
To realize the Pd(II)-catalyzed BDG-directed successive arylation/intramolecular amidation of the remote $\gamma$-C($sp^3$)-H bond, we first attempted the successive arylation/intramolecular amidation reaction using the thiophene-2-carboxamide system **1a**. Table 2 shows the optimization of the reaction 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 $^oC$ 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 $\gamma$-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 $^oC$ 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 $^{o}$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 oxidation of methylene group of **3a** with adventitious oxygen in the reaction system.[45]

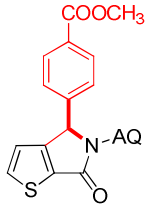
Next, to improve the yield of **8a** further, we attempted the arylation of **1a** with **2a** using various Pd catalysts, additives, and solvents. The reactions of **1a** with **2a** with other palladium catalysts $PdCl_2$, $Pd(CH_3CN)_2Cl_2$, and $Pd(TFA)_2$ afforded both **3a** and **8a** without any improvement in the yield for **8a** (entries 6-8, Table 2). We also tried 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 tried 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-methyl quinoline and 2-hydroxy-4-methylquinoline. These trails were also not fruitful, and the product **8a** was not formed (entries 19-21, Table 2).

**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]

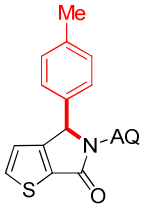


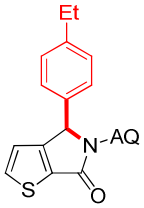
**8b**; R = F; 57% (48 h)
**8c**; R = Cl; 61% (48 h)
**8d**; R = Br; 51% (48 h)
**8e**; R = I; 68% (48 h)
**8f**; R = $COCH_3$; 58% (48 h)[c]



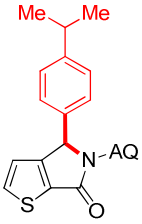
**8g**; 50% (60 h
**9g**; 11% (60 h)



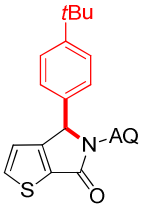
**8h**; 63% (48 h)
**9h**; 19% (48 h)



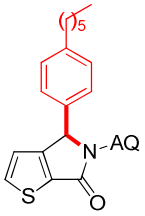
**8i**; 65% (48 h)
**9i**; 7% (48 h)



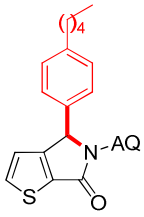
**8j**; 62% (60 h)
**9j**; 7% (60 h)



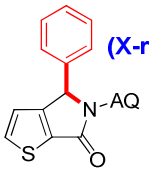
**8k**; 44% (48 h)
**9k**; 19% (48 h)



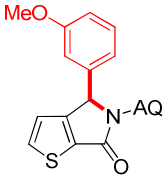
**8l**; 71% (48 h)
**9l**; 20% (48 h)



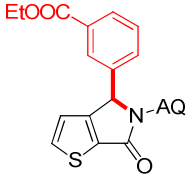
**8m**; 44% (48 h)
**9m**; 28% (48 h)



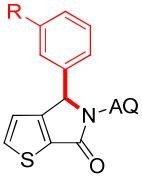
**8n**; 58% (70 h)[c]
**9n**; 11% (70 h)[c]



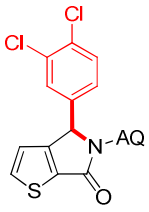
**8o**; 53% (48 h)
**9o**; 27% (48 h)



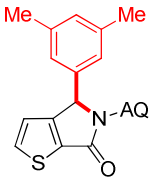
**8p**; 54% (48 h)
**9p**; 20% (48 h)



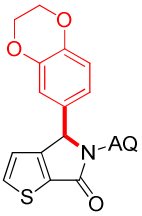
**8q**; R = $NO_2$; 64% (48 h)
**8r**; R = Cl; 51% (48 h)
**8s**; R = F; 55% (48 h)
**8t**; R = Br; 51% (48 h)
**8u**; R = I; 66% (48 h)
**8v**; R = Me; 58% (48 h)
**8w**; R = $CF_3$; 64% (48 h)



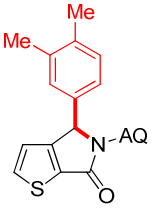
**8x**; 54% (48 h)[c]



**8y**; 62% (48 h)



**8z**; 82% (48 h)



**8aa**; 54% (60 h)
**9aa**; 12% (60 h)

[a] All reactions were performed using **1a** (0.125 mmol), ArI (1.25 mmol), $Pd(OAc)_2$ (20 mol%), 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 rest of the cases, the corresponding ketone products **9** (minor products) were not obtained in characterizable amounts.

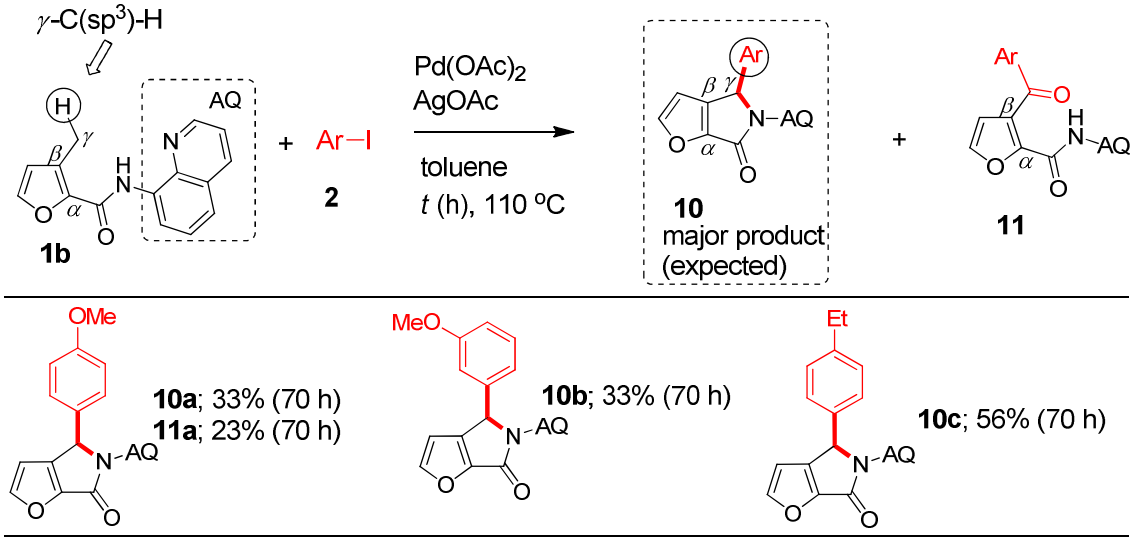
[c] 1.5 mmol of ArI was used.

We then explored the generality and substrate scope of this arylation/intramolecular amidation protocol using substrates **1a-c**. Scheme 11 shows amidation of the $\gamma$-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 $\gamma$-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 **p** were also obtained in 20-27% 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** and **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]

**Scheme 12. Successive arylation/intramolecular amidation of the γ-C(sp$^3$)-H bond of 1b. Synthesis of pyrrolidone-ring annulated furan scaffolds 10a-c.**[a,b]



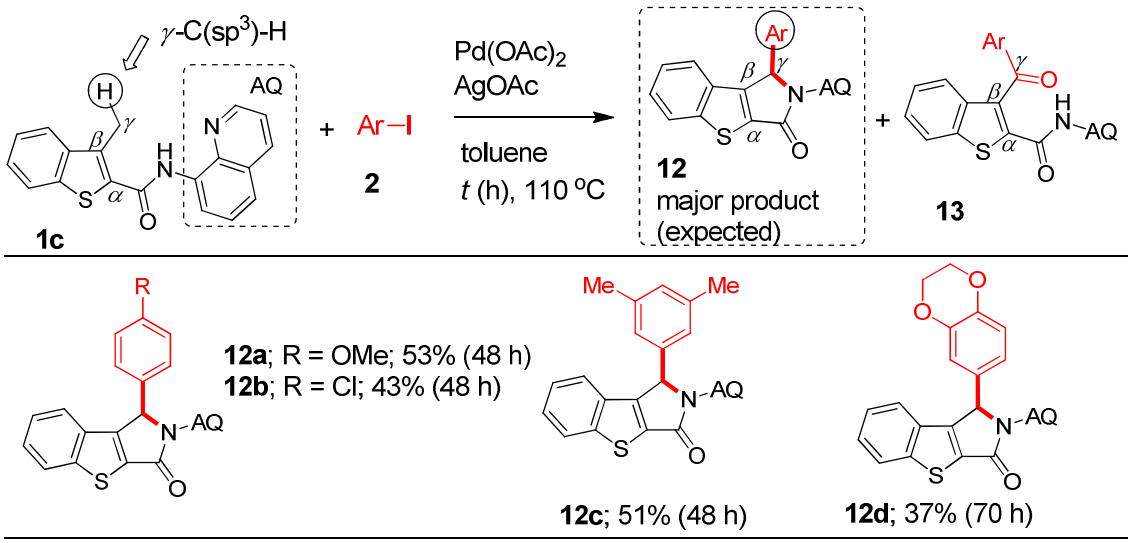

[a] All reactions were performed using **1b** (0.125 mmol), ArI (1.5 mmol), $Pd(OAc)_2$ (20-30 mol%), AgOAc (0.27 mmol) in toluene (2-3 mL).

[b] The corresponding ketone products **11a** (minor product) was isolated in pure form. In rest of the cases, the corresponding ketone products **11** (minor products) were not obtained in characterizable amounts.

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).

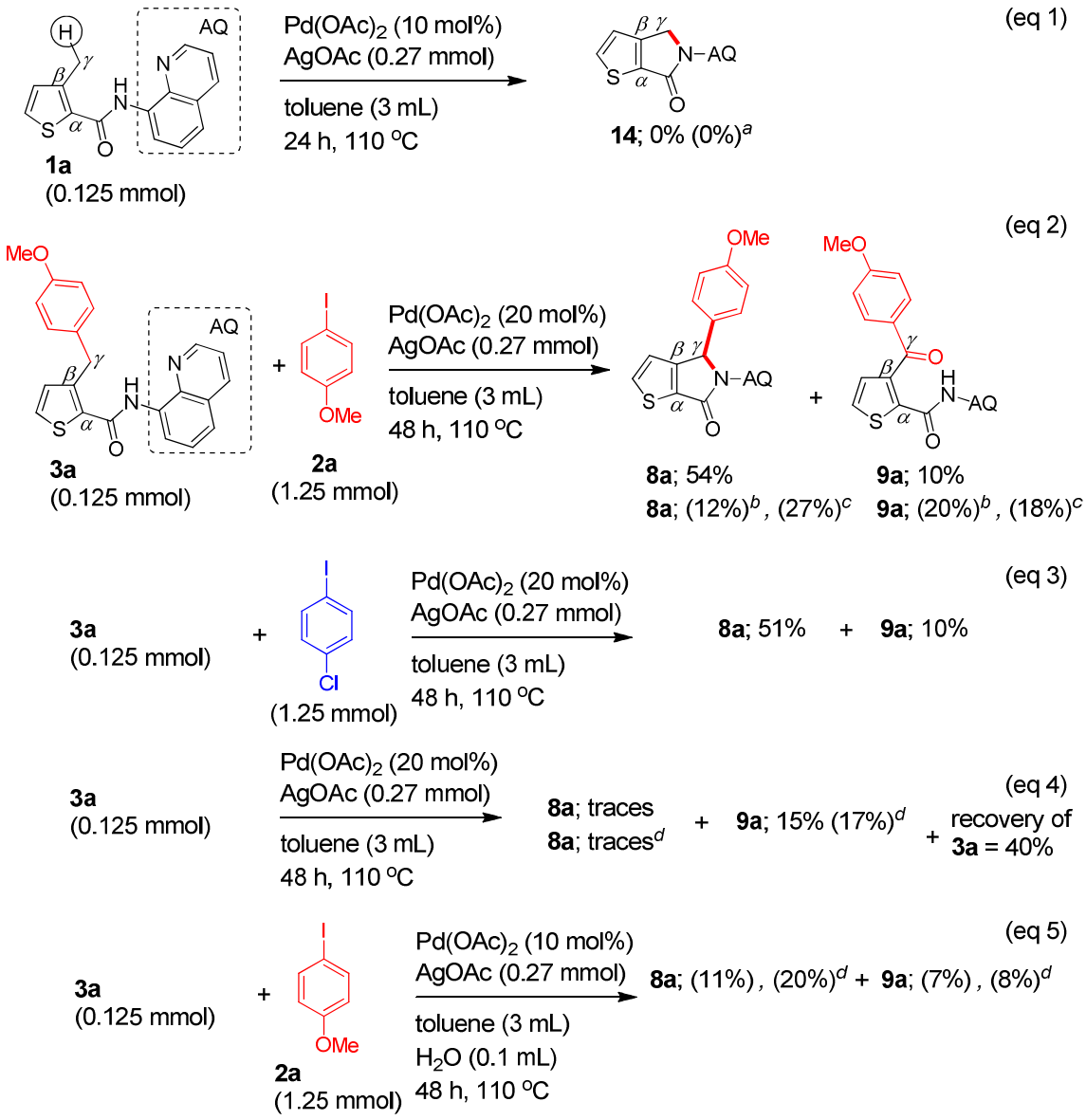
**Scheme 13. Successive arylation/intramolecular amidation of the γ-C(sp$^3$)-H bond of 1c. Synthesis of pyrrolidone-ring annulated benzothiophene scaffolds 12a-f.**[a,b]




[a] All reactions were performed using **1c** (0.125 mmol), ArI (1.5 mmol), $Pd(OAc)_2$ (20 mol%), 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.

**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 in aerobic condition.

Overall, arylheteroarylmethane and diheteroarylmethane scaffolds **3-7** were obtained in good to high yield from the Pd(II)-catalyzed $\gamma$-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 $\gamma$-C($sp^3$)-H arylation/intramolecular amidation of substrates **1a-c**. Some of the Pd(II)-catalyzed successive $\gamma$-C($sp^3$)-H arylation/intramolecular 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. Firstly, 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 by-product **9a** in 18-20% yield (eq 2, Scheme 14). Since we

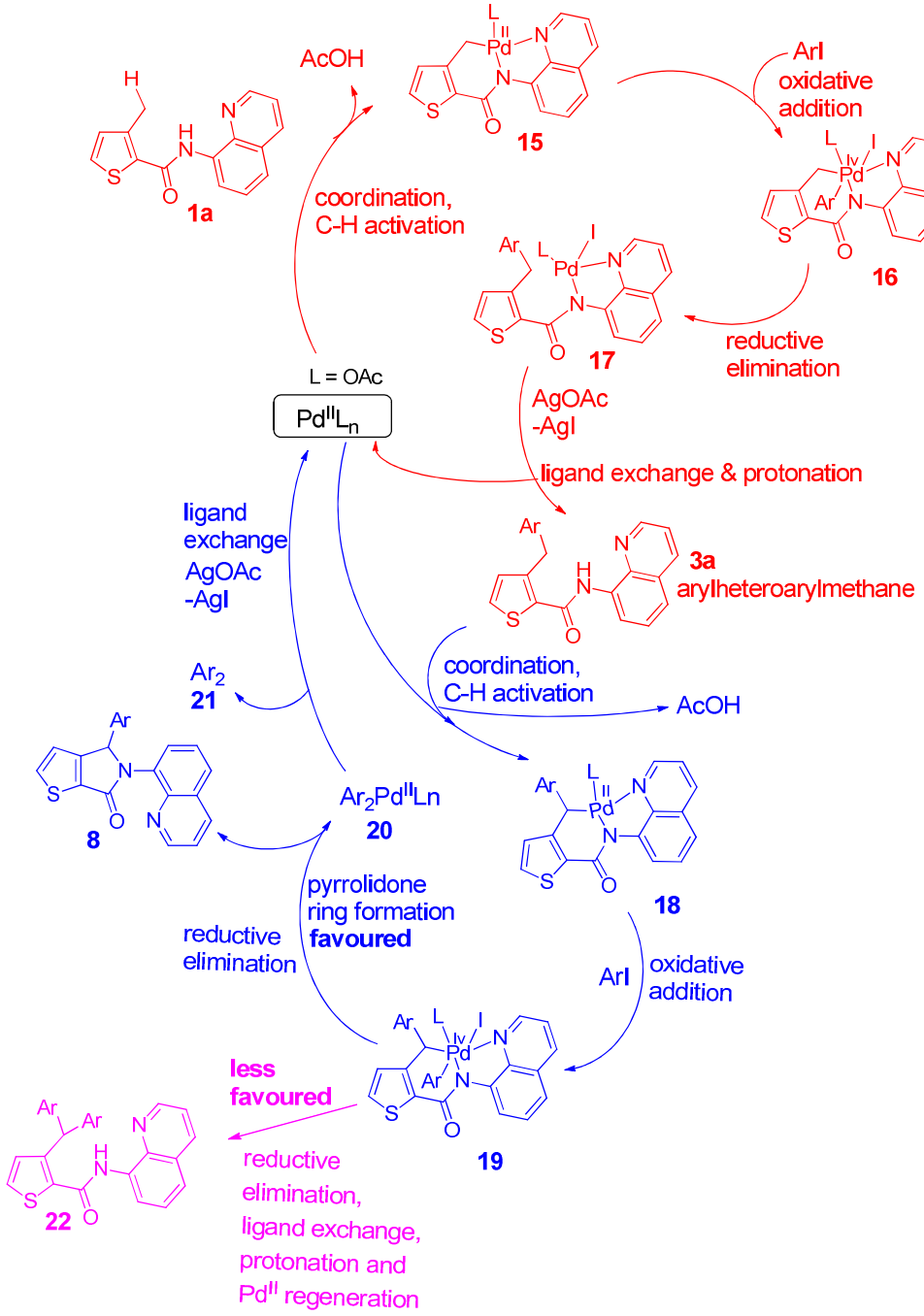
have used the same aryl iodide **2a**, which was used to assemble **3a** in the reaction shown in Scheme 14 (eq 2), we then treated **3a** with a different aryl iodide to check whether the amidation is occurring or not. Accordingly, we treated **3a** with 1-chloro-4-iodobenzene, $Pd(OAc)_2$ catalyst, 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 by-product 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 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** (mono arylated products) in satisfactory to high yields (Table 1 and Schemes 6,7). In these reactions the column chromatographic purification of the corresponding crude reaction mixtures did not afford any other corresponding by-products, 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 $\gamma$-C($sp^3$)-H arylation/intramolecular amidation products **8**, **10**, and **12** (Table 2, Schemes 11-13) in satisfactory to high yields. While some of the reactions gave the corresponding ketones **9**, and **11** as the by-products, 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 mono arylation followed by intramolecular C-H amidation over the bis arylation is not clear to us. It is proposed that the formation of 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.

**Scheme 15. Proposed mechanism for the Pd(II)-catalyzed $\gamma$-C($sp^3$)-H arylation of 1a-d and successive arylation/intramolecular amidation of 1a-c.**




On basis of the results from the control reactions (Scheme 14) and the observed products **3-5**, and **8**/**10**/**12**, the $\gamma$-C($sp^3$)-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 $\gamma$-C($sp^3$)-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 $\gamma$-C($sp^3$)-H arylated product **3a** and the $Pd(OAc)_2$ 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 mono arylated product **3a** or the cyclized products **8**, hence, it is believed that the formation of bis-arylated product **22** seems to be a less favoured 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 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 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 $\gamma$-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 periods 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 $\gamma$-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.** IR spectra of samples were recorded as KBr pellets or 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 the compounds were obtained from QTOF mass analyzer using electrospray ionization (ESI) technique. Column chromatography purification of crude reaction mixtures were 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 the 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 the cases we focused to isolate the corresponding $\gamma$-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 $\gamma$-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 by-products. Specifically, the products **9a**, **9g-p**, **9aa** and **11a** were isolated in pure form. In 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 $^oC$, for 15 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuum 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 $Na_2SO_4$, concentrated in vacuum 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 the 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) was heated at 110 $^oC$ for 4-48 h under a nitrogen atm. After the reaction period, the reaction mixture was concentrated in vacuum 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/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%), AgOAc (45.9 mg, 0.27 mmol, 2.2 equiv) in anhydrous toluene (2-3 mL) was heated at 110 $^oC$ for 48-60 h under a nitrogen atm. After this reaction period, the reaction

mixture was concentrated in vacuum and purification of the resulting reaction mixture by column chromatography 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/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 vacuum 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. Then, the reaction mixture was allowed to attain rt. Next, $Et_3N$ (304 mg, 3 mmol) was added dropwise to the reaction mixture with stirring. After this, the solvent was evaporated in vacuum to afford the carboxylate derivative **3ab**.

**3-Methyl-*N*-(quinolin-8-yl)thiophene-2-carboxamide (1a):**[8d] The compound **1a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 70% (188 mg); $R_f$ = 0.55 (EtOAc:Hexanes = 1:4); mp 104-106 $^oC$; 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] The compound **1b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 71% (179 mg); $R_f$ = 0.52 (EtOAc:Hexanes = 1:4); mp 118-120 $^o$C; IR (KBr): 3345, 1669, 1529, 1484, 1327 cm$^{-1}$; $^1$H 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):** The compound **1c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless solid; Yield: 85% (270 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 1:4); mp 133-135 $^o$C; IR (KBr): 3303, 1649, 1526, 1423 cm$^{-1}$; $^1$H 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):** The compound **1d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless solid; Yield: 50% (151 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 178-180 $^{o}$C; IR (KBr): 1648, 1527, 1486, 1354 cm$^{-1}$; $^{1}$H 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):** The compound **1e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless solid; Yield: 70% (184 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 82-84 $^{o}$C; IR (KBr): 1526, 1486, 1423, 1384, 1327 cm$^{-1}$; $^{1}$H 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):** The compound **1f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 20:80) as a colourless solid; Yield: 59% (157 mg); $R_f$ = 0.35 (EtOAc:Hexanes = 1:4); mp 170-172 $^{o}$C; IR (KBr): 1679, 1578, 1523, 1485, 1325, 1121 cm$^{-1}$; $^{1}$H 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):** The compound **1g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 70% (193 mg); $R_f$ = 0.62 (EtOAc:Hexanes = 1:4); IR (DCM): 3333, 1693, 1564, 1495, 1274 $cm^{-1}$; $^1$H 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):** The compound **1h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless liquid; Yield: 89% (164 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); IR (DCM): 3369, 1717, 1636, 1521, 1281, 1105 $cm^{-1}$; $^1$H 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] The compound **1i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless 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):** The compound **1j** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless 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 *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):** The compound **1k** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless 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):** The compound **1l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes =

20:80) as a colourless 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 $^oC$ for 15 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuum 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 colourless solid after recrystallization (EtOAc:Hexanes = 30:70). Yield: 50% (154 mg); mp 113-115 $^oC$; 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):** The compound **3a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **3b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a pale yellow colour solid; Yield: 58% (28 mg); $R_f$ = 0.35 (EtOAc:Hexanes = 1:4); mp 126-128 $^oC$; 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)thiophen-3-yl)methyl)benzoate (3c):** The compound **3c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a brown colour solid; Yield: 67% (34 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); mp 134-136 $^oC$; 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):** The compound **3d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 53% (25 mg); $R_f$ = 0.51 (EtOAc:Hexanes = 1:4); IR (DCM): 2962, 1660, 1524, 1484, 1423 cm$^{-1}$; $^1$H 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] The compound **3e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a pale yellow colour solid; Yield: 72% (35 mg); $R_f$ = 0.43 (EtOAc:Hexanes = 1:4); mp 153-155 $^o$C; IR (KBr): 1648, 1529, 1484, 1385 cm$^{-1}$; $^1$H 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):** The compound **3f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 58% (31 mg); $R_f$ = 0.41 (EtOAc:Hexanes = 1:4); mp 112-114 $^oC$; IR (KBr): 1660, 1525, 1485, 1385 $cm^{-1}$; $^1$H 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):** The compound **3g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 55% (24 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); mp 138-140 $^oC$; IR (KBr): 1661, 1525, 1485, 1328 $cm^{-1}$; $^1$H 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 (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):** The compound **3h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a brown colour solid; Yield: 47% (24 mg); $R_f$ = 0.48 (EtOAc:Hexanes = 1:4); mp 209-211 $^oC$; IR (KBr): 3339, 1658, 1525, 1429, 1068 $cm^{-1}$; $^1H$ 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):** The compound **3i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a brown colour solid; Yield: 96% (51 mg); $R_f$ = 0.35 (EtOAc:Hexanes = 1:4); mp 150-152 $^oC$; IR (KBr): 1654, 1524, 1485, 1382 $cm^{-1}$; $^1H$ 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):** The compound **3j** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a pale yellow colour solid; Yield: 57% (26 mg); $R_f$ = 0.32 (EtOAc:Hexanes = 1:4); mp 124-126 $^oC$; IR (KBr): 1659, 1526, 1484, 1328, 1246 $cm^{-1}$; $^1H$ 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):** The compound **3k** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 54% (26 mg); $R_f$ = 0.34 (EtOAc:Hexanes = 1:4); mp 122-124 $^oC$; IR (KBr): 1657, 1585, 1385, 1244, 1100 $cm^{-1}$; $^1H$ 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-((1*H*-Indol-5-yl)methyl)-*N*-(quinolin-8-yl)thiophene-2-carboxamide (3l):** The compound **3l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 60:40) as a colourless liquid; Yield: 54% (26 mg); $R_f$ = 0.22 (EtOAc:Hexanes = 1:4); IR (DCM): 3319, 1707, 1651, 1526, 1484, 1384 $cm^{-1}$; $^1H$ 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):** The compound **3m** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 80% (38 mg); $R_f$ = 0.35 (EtOAc:Hexanes = 1:4); IR (DCM): 1657, 1591, 1526, 1485, 1327 $cm^{-1}$; $^1H$ 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):** The compound **3n** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 46% (20 mg); $R_f$ = 0.39 (EtOAc:Hexanes = 1:4); IR

(DCM): 1656, 1525, 1484, 1385, 1122 $cm^{-1}$; $^1H$ 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), 8.82 (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):** The compound **4a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a pale yellow colour solid; Yield: 82% (38 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 143-145 $^oC$; IR (KBr): 3302, 1671, 1529, 1484, 1328 $cm^{-1}$; $^1H$ 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):** The compound **4b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a brown colour solid; Yield: 74% (36 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 158-160 $^oC$; IR (KBr): 3436, 1648, 1529, 1485 $cm^{-1}$; $^1H$ 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):** The compound **4c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a brown colour solid; Yield: 67% (30 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 125-127 $^o$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 (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):** The compound **4d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **4e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 71% (33 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 1:4); IR (DCM): 1655, 1525, 1485, 1327 $cm^{-1}$; $^1H$ 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):** The compound **4f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 65% (28 mg); $R_f$ = 0.42 (EtOAc:Hexanes = 1:4); mp 118-120 $^oC$; IR (KBr): 1665, 1596, 1384, 1247, 1094 $cm^{-1}$; $^1H$ 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):** The compound **4g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes =

30:70) as a colourless solid; Yield: 79% (35 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 1:4); mp 163-165 $^oC$; IR (KBr): 1657, 1533, 1484, 1385, 1215 $cm^{-1}$; $^1H$ 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):** The compound **4h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as colourless solid; Yield: 93% (42 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 1:4); mp 108-110 $^oC$; IR (KBr): 1593, 1502, 1384, 1122 $cm^{-1}$; $^1H$ 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):** The compound **4i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a pale yellow colour solid; Yield: 55% (26 mg); $R_f$ = 0.41 (EtOAc:Hexanes = 1:4); mp 157-159 $^oC$; IR (KBr): 1666, 1598, 1483, 1350, 1093 $cm^{-1}$; $^1H$ 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):** The compound **4j** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **4k** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **4l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 72% (35 mg); $R_f$ = 0.49 (EtOAc:Hexanes = 1:4); mp 100-102 $^oC$; IR (KBr): 3345, 1668, 1532, 1288 $cm^{-1}$; $^1H$ 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):** The compound **4m** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 82% (42 mg); $R_f$ = 0.35 (EtOAc:Hexanes = 1:4); mp 146-148 $^oC$; IR (KBr): 3339, 1666, 1598, 1531, 1425, 1090 $cm^{-1}$; $^1H$ 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.

**3-((6-Fluoropyridin-3-yl)methyl)-*N*-(quinolin-8-yl)furan-2-carboxamide (4n):** The compound **4n** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 57% (25 mg); $R_f$ = 0.30 (EtOAc:Hexanes = 1:4); mp 129-131 $^{o}$C; IR (KBr): 1667, 1598, 1532, 1483, 1385, 1123 cm$^{-1}$; $^{1}$H 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):** The compound **4o** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 55% (25 mg); $R_f$ = 0.30 (EtOAc:Hexanes = 1:4); mp 148-150 $^{o}$C; IR (KBr): 1666, 1597, 1531, 1459, 1093 cm$^{-1}$; $^{1}$H 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):** The compound **5a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as pale yellow colour solid; Yield: 60% (33 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 157-159 $^oC$; 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):** The compound **5b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **5c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 46% (26 mg); $R_f$ = 0.43 (EtOAc:Hexanes = 1:4); mp 208-210 $^{o}$C; IR (DCM): 1720, 1661, 1529, 1485 cm$^{-1}$; $^{1}$H 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):** The compound **5d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 56% (30 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 133-134 $^{o}$C; IR (KBr): 3422, 1656, 1527, 1484, 1385, 1093 cm$^{-1}$; $^{1}$H 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]thiophen-3-yl)methyl)benzoate (5e):** The compound **5e** was obtained after purification by column chromatography on neutral alumina

(EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **5f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 49% (27 mg); mp 220-222 $^oC$; $R_f$ = 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):** The compound **5g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a pale yellow colour solid; Yield: 76% (45 mg); $R_f$ = 0.39

(EtOAc:Hexanes = 1:4); mp 178-180 $^{o}$C; IR (KBr): 1650, 1594, 1385, 1261, 1092 cm$^{-1}$; $^{1}$H 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):** The compound **5h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 71% (37 mg); $R_f$ = 0.33 (EtOAc:Hexanes = 1:4); mp 169-171 $^{o}$C; IR (KBr): 1655, 1595, 1531, 1385, 1119 cm$^{-1}$; $^{1}$H 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 (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):** The compound **6a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a pale yellow colour solid; Yield: 61% (32 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp

189-191 $^{o}$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):** The compound **6b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a brown colour solid; Yield: 66% (36 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 213-215 $^{o}$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):** The compound **6c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 25:75) as a colourless solid; Yield: 31% (16 mg); $R_f$ = 0.46 (EtOAc:Hexanes = 1:4); mp 208-210 $^{o}$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):** The compound **6d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 20:80) as a colourless solid; Yield: 59% (30 mg); $R_f$ = 0.46 (EtOAc:Hexanes = 1:4); mp 150-152 $^o$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):** The compound **6e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 45% (25 mg); mp 216-218 $^o$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):** The compound **6f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 57% (33 mg); $R_f$ = 0.38 (EtOAc:Hexanes = 1:4); mp 209-211 $^{o}$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):** The compound **7a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a pale yellow colour solid; Yield: 58% (27 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); mp 104-106 $^{o}$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):** The compound **7b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 50% (24 mg); $R_f$ = 0.51 (EtOAc:Hexanes = 1:4); mp 97-99 $^oC$; IR (KBr): 3342, 1678, 1511, 1432, 1267 $cm^{-1}$; $^1H$ 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):** The compound **7c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 54% (27 mg); $R_f$ = 0.52 (EtOAc:Hexanes = 1:4); IR (DCM): 1719, 1667, 1610, 1578, 1279, 757 $cm^{-1}$; $^1H$ 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):** The compound **7d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 54% (25 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); IR (DCM): 3312, 1667, 1578, 1511, 1432, 1304 $cm^{-1}$; $^1H$ 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 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):** The compound **7e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 50% (24 mg); mp 130-132 $^oC$; $R_f$ = 0.51 (EtOAc:Hexanes = 1:4); IR (KBr): 3304, 1665, 1578, 1525, 1433 $cm^{-1}$; $^1H$ 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):** The compound **7f** was obtained after purification by column chromatography

on neutral alumina (EtOAc:Hexanes = 25:75) as a brown colour solid; Yield: 56% (28 mg); $R_f$ = 0.51 (EtOAc:Hexanes = 1:4); mp 101-103 $^oC$; IR (KBr): 3312, 1665, 1506, 1432, 1304, 1285 $cm^{-1}$; $^1H$ 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):** The compound **7g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 54% (25 mg); $R_f$ = 0.53 (EtOAc:Hexanes = 1:4); IR (DCM): 3313, 1666, 1578, 1510, 1430, 1384 $cm^{-1}$; $^1H$ 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):** The compound **7h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 61% (32 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 1:4); IR (DCM): 1652, 1527, 1486, 1384, 1014 $cm^{-1}$; $^1H$ 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):** The compound **7i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a brown colour solid; Yield: 53% (24 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 1:4); mp 146-148 $^{o}$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 **3ac** was obtained as a brown colour 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):** The compound **3ab** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 20:80) as a colourless liquid; Yield: 85% (28 mg); $R_f$ = 0.50 (EtOAc:Hexanes = 1:4); IR (DCM): 1709, 1610, 1511, 1413, 1074 $cm^{-1}$; $^1H$ 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):** The compound **8a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a brown colour liquid; Yield: 71% (33 mg); $R_f$ = 0.24 (EtOAc:Hexanes = 2:3); IR (DCM): 1692, 1527, 1486, 1384, 1245 $cm^{-1}$; $^1H$ 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), 7.74-7.72 (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):** The compound **8b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 57% (26 mg); $R_f$ = 0.24 (EtOAc:Hexanes = 2:3); IR (DCM): 3451, 1694, 1508, 1389 $cm^{-1}$; $^1H$ 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):** The compound **8c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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):** The compound **8d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 51% (27 mg); $R_f$ = 0.32 (EtOAc:Hexanes = 2:3); IR (DCM): 3418, 1694, 1500, 1472, 1220 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.96 (dd, 1H, $J_1$ = 4.2 Hz, $J_2$ = 1.7 Hz), 8.18 (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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8e):** The compound **8e** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a brown colour 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):** The compound **8f** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a pale yellow colour 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-4*H*-thieno[2,3-*c*]pyrrol-4-yl)benzoate (8g):** The compound **8g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless solid; Yield: 50% (25 mg); $R_f$ = 0.33 (EtOAc:Hexanes = 2:3); mp 162-164 $^oC$; 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):** The compound **8h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless solid; Yield: 63% (28 mg); $R_f$ = 0.34 (EtOAc:Hexanes = 2:3); mp 126-128 $^oC$; 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):** The compound **8i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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):** The compound **8j** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 62% (30 mg); $R_f$ = 0.34 (EtOAc:Hexanes = 2:3); IR (DCM): 2959, 1694, 1527, 1387 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.95 (dd, 1H, $J_1$ = 4.2 Hz, $J_2$ = 1.8 Hz), 8.16 (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*-butyl)phenyl)-5-(quinolin-8-yl)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8k):** The compound **8k** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 85:15) as a colourless liquid; Yield: 44% (22 mg); $R_f$ = 0.33 (EtOAc:Hexanes = 2:3); IR (DCM): 1692, 1594, 1385, 1122 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.95 (dd, 1H, $J_1$ = 4.0 Hz, $J_2$ = 0.6Hz), 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8l):** The compound **8l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8m):** The compound **8m** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8n):** The compound **8n** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 85:15) as a brown colour solid; Yield: 58% (25 mg); mp 218-220 $^{o}$C; $R_f$ = 0.31 (EtOAc:Hexanes = 2:3); IR (KBr): 1694, 1500, 1390, 1351 cm$^{-1}$; $^{1}$H 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; 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8o):** The compound **8o** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 53% (25 mg); $R_f$ = 0.33 (EtOAc:Hexanes = 2:3); IR (DCM): 1694, 1598, 1472, 1390 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.96 (dd, 1H, $J_1$ = 4.2 Hz, $J_2$ = 1.7 Hz), 8.16 (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-4*H*-thieno[2,3-*c*]pyrrol-4-yl)benzoate (8p):** The compound **8p** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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):** The compound **8q** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a brown colour 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):** The compound **8r** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless solid; Yield: 51% (24 mg); $R_f$ = 0.31 (EtOAc:Hexanes = 2:3); mp 180-182 $^oC$; 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):** The compound **8s** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 55% (25 mg); $R_f$ = 0.30 (EtOAc:Hexanes = 2:3); IR (DCM): 1696, 1500, 1472, 1130 cm$^{-1}$; $^1$H 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):** The compound **8t** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless liquid; Yield: 51% (27 mg); $R_f$ = 0.31 (EtOAc:Hexanes = 2:3); IR (DCM): 1694, 1527, 1486, 1327 cm$^{-1}$; $^1$H 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8u):** The compound **8u** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a brown colour 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8v):** The compound **8v** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8w):** The compound **8w** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a brown colour solid; Yield: 64% (33 mg); $R_f$ = 0.30 (EtOAc:Hexanes = 2:3); mp 175-177 $^{o}$C; IR (KBr): 1698, 1501, 1390, 1331, 1129 cm$^{-1}$; $^{1}$H 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)-4*H*-thieno[2,3-*c*]pyrrol-6(5*H*)-one (8x):** The compound **8x** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless solid; Yield: 54% (28 mg); $R_f$ = 0.31 (EtOAc:Hexanes = 2:3); mp 218-220 $^{o}$C; IR (KBr): 1697, 1472, 1391, 1131 cm$^{-1}$; $^{1}$H 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, 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):** The compound **8y** was obtained after purification by column chromatography on neutral alumina

(EtOAc:Hexanes = 90:10) as a colourless 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)-4*H*-thieno[2,3-c]pyrrol-6(5*H*)-one (8z):** The compound **8z** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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):** The compound **8aa** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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):** The compound **9a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 16% (8 mg); $R_f$ = 0.45 (EtOAc:Hexanes = 2:3); IR (DCM): 3306, 1653, 1531, 1261, 1028 $cm^{-1}$; $^1$H 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):** The compound **9g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 11% (6 mg); $R_f$ = 0.46 (EtOAc:Hexanes = 2:3); IR (DCM): 1722, 1661, 1531, 1486 $cm^{-1}$; $^1$H 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):** The compound **9h** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; Yield: 19% (9 mg); $R_f$ = 0.47 (EtOAc:Hexanes = 2:3); IR (DCM): 3302, 1651, 1530, 1485, 1274 cm$^{-1}$; $^1$H 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):** The compound **9i** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 50:50) as a colourless liquid; Yield: 7% (4 mg); $R_f$ = 0.46 (EtOAc:Hexanes = 2:3); IR (DCM): 1655, 1528, 1486, 1327, 1272 cm$^{-1}$; $^1$H 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):** The compound **9j** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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*-butyl)benzoyl)-*N*-(quinolin-8-yl)thiophene-2-carboxamide (9k):** The compound **9k** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **9l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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 (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):** The compound **9m** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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):** The compound **9n** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 50:50) as a brown colour solid; Yield: 11% (5 mg); $R_f$ = 0.43 (EtOAc:Hexanes = 2:3); mp 138-140 $^oC$; 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):** The compound **9o** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless solid; Yield: 27% (13 mg); $R_f$ = 0.44 (EtOAc:Hexanes = 2:3); mp 136-138 $^o$C; IR (KBr): 3312, 1658, 1532, 1275 cm$^{-1}$; $^1$H 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):** The compound **9p** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 50:50) as a colourless solid; Yield: 20% (11 mg); $R_f$ = 0.40 (EtOAc:Hexanes = 2:3); mp 113-115 $^o$C; IR (KBr): 2985, 1719, 1660, 1532, 1241 cm$^{-1}$; $^1$H 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):** The compound **9aa** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless 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)-4*H*-furo[2,3-*c*]pyrrol-6(5*H*)-one (10a):** The compound **10a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless 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)-4*H*-furo[2,3-*c*]pyrrol-6(5*H*)-one (10b):** The compound **10b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless 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)-4*H*-furo[2,3-*c*]pyrrol-6(5*H*)-one (10c):** The compound **10c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 90:10) as a colourless solid; Yield: 56% (25 mg); $R_f$ = 0.33 (EtOAc:Hexanes = 2:3); mp 186-188 $^oC$; 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):** The compound **11a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes =

30:70) as a colourless 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)-1*H*-benzo[4,5]thieno[2,3-*c*]pyrrol-3(2*H*)-one (12a):** The compound **12a** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 85:15) as a colourless 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, 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)-1*H*-benzo[4,5]thieno[2,3-*c*]pyrrol-3(2*H*)-one (12b):** The compound **12b** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless 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)-1*H*-benzo[4,5]thieno[2,3-*c*]pyrrol-3(2*H*)-one (12c):** The compound **12c** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 85:15) as a pale green colour solid; Yield: 51% (27 mg); $R_f$ = 0.32 (EtOAc:Hexanes = 2:3); mp 249-251 $^o$C; IR (KBr): 3436, 1646, 1527, 1486 cm$^{-1}$; $^1$H 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)-1*H*-benzo[4,5]thieno[2,3-*c*]pyrrol-3(2*H*)-one (12d):** The compound **12d** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 80:20) as a colourless liquid; Yield: 37% (21 mg); $R_f$ = 0.31 (EtOAc:Hexanes = 2:3); IR (DCM): 1694, 1506, 1390, 1285 cm$^{-1}$; $^1$H 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.

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

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

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

### 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 9,24b.

(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).

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