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4-Amino-2,1,3-Benzothiadiazole (ABTD) as a Removable Bidentate Directing Group for the Pd(II)-Catalyzed Arylation/Oxygenation of sp^2/sp^3 β-C–H Bonds of Carboxamides

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ABSTRACT

In this paper, we report 4-amino-2,1,3-benzothiadiazole (ABTD) as a new bidentate directing group (BDG) for the Pd(II)-catalyzed sp^2/sp^3 C–H activation/functionalization of various aliphatic/alicyclic/aromatic carboxamide systems. The Pd(II)-catalyzed, ABTD-directed sp^3 C-H arylation/acetoxylation of aliphatic- and alicyclic carboxamides afforded the corresponding β-C-H arylated/acetoxylated carboxamides. The Pd(II)-catalyzed, ABTD-directed sp^3 C-H arylation of cyclobutanecarboxamide with different aryl iodides afforded the corresponding bis β-C–H arylated cyclobutanecarboxamides having all *cis* stereochemistry with a high degree of stereocontrol. The Pd(II)-catalyzed, ABTD-directed arylation/benzylation/acetoxylation/alkoxylation of *ortho* C(sp^2)–H bonds of various benzamides afforded the corresponding *ortho* C-H arylated/benzylated/oxygenated

benzamides. The observed regio- and stereoselectivity in the Pd(II)-catalyzed, ABTD-directed arylation/benzylation of aliphatic/alicyclic carboxamides and benzamides were ascertained from the X-ray structures of representative compounds **5g** (bis β-C(sp^3)–H arylated cyclobutanecarboxamide) and **7f** (*ortho* C(sp^2)–H arylated benzamide). A brief description on the efficiency, scope and limitations of bidentate directing group 4-amino-2,1,3-benzothiadiazole (ABTD) was reported.

INTRODUCTION

The transition metal-catalyzed C-H activation followed by C-C bond forming process has emerged as one of the pivotal organic transformations.[1-4] There exist numerous reports dealing on the transition metal-catalyzed, directing group-aided or directing group-free C–H activation/functionalization reactions.[1-4] The functionalization of sp^2 C-H bonds of organic molecules, sp^3 C–H bonds of benzylic systems, α-C(sp^3)-H bonds next to a heteroatom (e.g., THF and pyrrolidine systems) and diazocarbonyl compound-based C(sp^3)-H insertion reactions have been extensively studied.[1-4] Apart from these transformations, the functionalization of unactivated sp^3 C–H bonds of organic molecules was considered as an arduous task in the past decades. However, in recent years various research groups have shown that the functionalization of unactivated sp^3 C–H bonds of organic molecules is an achievable task.[1-4]

The first paper by Daugulis[5,6] dealing on the Pd(II)-catalyzed, bidentate directing group 8-aminoquinoline (**DG-a**)-assisted arylation of unactivated sp^3 C(β)–H bonds of aliphatic and aromatic carboxamides has given an inspiring direction to the research area pertaining to the sp^3 C–H activation/functionalization reactions (Figure 1).[1-4,7,8] Concurrently, Yu's work[9a] dealing on the Pd(II)-catalyzed, monodentate directing group 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (**DG-b**)-assisted functionalization of unactivated sp^3 C–H bonds of

organic molecules has provided a motivation to the synthetic organic chemists (Figure 1). Consequently, while the directing group-free C–H activation/functionalization transformation still remains as a challenging and less explored area; the directing group-assisted C–H activation/functionalization tactic has emerged as a dependable method to functionalize organic molecules with high degree of site-selectivity.[1-4]

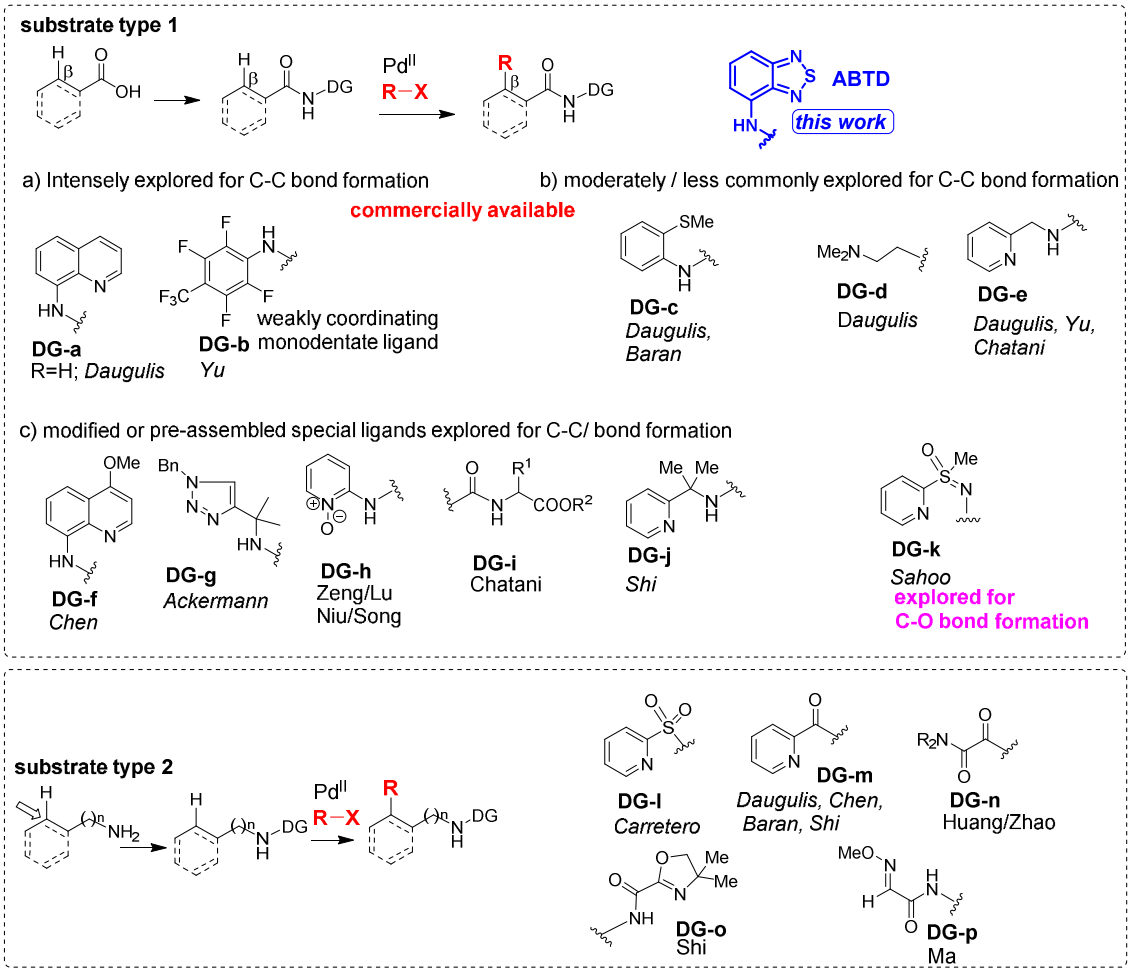


Figure 1. Bidentate directing groups explored for sp^2/sp^3 C–H activation/functionalization.

The bidentate directing group 8-aminoquinoline (**DG-a**, Figure 1)[1-4,7,8] was found to be efficient for the functionalization (e.g., arylation, alkylation, acetoxylation) of *β*-C-H bonds of carboxylic acid and amino acid systems (substrate type 1, Figure 1). However, considering the importance of the C–H activation/functionalization in organic synthesis and

to pronounce the availability of other optional bidentate directing groups,[10-13] few other auxiliaries were also identified for performing the C–H activation/functionalization of carboxylic acid derivatives and amine systems (substrate type 2, Figure 1).

With regard to the substrate type 1, several research groups showed the functionalization of sp^2/sp^3 C–H bonds of carboxylic acid derivatives using the directing group **DG-a** (Figure 1).[1-4] Apart from the popular directing group **DG-a**,[5,6] the **DG-c**[6,10a] was found to be moderately efficient directing group for the C-H activation followed by C-C bond formation and the **DG-c** was not popularly used for the C-H oxygenation reactions.[1-4] Yu's group extensively exploited the **DG-b**[6,10a] for the C-C bond formation and to the best of our knowledge, the **DG-b** was not popularly used for the C-H oxygenation reactions.[1-4] The **DG-d**[6] and **DG-e**[6,11a,b] were less commonly used and it appears that the **DG-d** and **DG-e** are relatively less efficient directing groups for the functionalization of *β*-C-H bonds of carboxylic acid derivatives (substrate type 1, Figure 1).

Chen *et al.* used the modified quinoline-type bidentate directing group **DG-f**[12a] for the *γ*-C(sp^3)-H amination reactions. Shi[13a] used the **DG-g** for performing the palladium-catalyzed substitution/cyclization reactions of amine systems. Ackermann[13b] also used the **DG-g** for performing the Fe-catalyzed, Grignard reagent-employed arylation of *β*-C-H bonds of carboxylic acid derivatives. Recently, Niu and Song[12f,g] used the pyridine *N*-oxide-type directing group **Dg-h** for the Pd(II)-catalyzed arylation of *β*-C(sp^3)-H bonds of aliphatic carboxylic acids. Concurrently, Zeng and Lu[12e] also used the pyridine *N*-oxide-type directing group **Dg-h** for the Pd(II)-catalyzed selective arylation of *β*-C(sp^3)-H bond of propionic acid system.

Recently, Chatani described[11c] the Pd(II)-catalyzed functionalization of *ortho* C-H bonds in *N*-benzoyl α-amino ester derivatives, in which both the NH-amido and the ester carbonyl groups of the **DG-i** reported to play a role in the C-H activation/functionalization

formation process. Shi[12c] and Sahoo[13c] have respectively introduced the directing groups **Dg-j** and **Dg-k** for the oxidation/oxygenation of β-C(sp^3)-H bonds of aliphatic carboxylic acids. Furthermore, Shi revealed the utility of the directing group **Dg-j** for the Pd(II)-catalyzed selective arylation of sp^3 C-H bonds of alanine and aliphatic carboxylic acid systems.[11e,f] In general, the Pd(II)-catalyzed, bidentate directing group-assisted C-H arylation/functionalization reactions have been performed using silver salts as additives.[1-4] It is to be noted that the Pd(II)-catalyzed, the **Dg-j**-directed arylations of methylene sp^3 C-H bonds aliphatic carboxylic acid systems were performed without using any silver salts.[11f]

With regard to the substrate type 2, several research groups showed the functionalization of sp^2/sp^3 C–H bonds of various amine systems using the bidentate directing group **DG-m** (picolinamide directing group, Figure 1).[4f,6,10a] Additionally, Baran[10b] and Shi[8a] showed the utility of the directing group **DG-m** for the arylation of sp^3 C-H bonds of amine/carboxylic acid systems. Carretero[12b] used the *N*-(2-pyridyl)sulfonyl directing group **DG-l** for the Pd(II)-catalyzed functionalization of sp^3 C-H bonds of amino acid derivatives. Huang and Zhao[13d] used the oxalylamide directing group **DG-n** for the functionalization of C-H bonds of amine systems. Recently, Shi[11d] revealed an oxazoline-carboxylate directing group **DG-o** for the arylation of sp^2/sp^3 C-H bonds of various amine systems. Ma[12d] reported 2-methoxyiminoacetyl directing group **DG-p** (MIA) for the Pd(II)-catalyzed functionalization of sp^3 C-H bonds of amine systems.

The reported bidentate directing groups were efficient and developed with an aim to achieve high degree of site-selectivity in the Pd(II)-catalyzed C-H activation-based C-C/C-O bond forming reactions involving the substrate type 1.[1-4,14-16] Nevertheless, some of the seminal bidentate directing groups (e.g., **DG-g**, **DG-h**, **DG-j** and **DG-k)** are not commercially available and need to be pre-assembled by involving few synthetic steps/transformations.[12c,e-g,13a-c] Additionally, Daugulis *et al.* revealed[5,6] that the attempts on

the Pd(II)-catalyzed C-H arylation of methyl group of propionic acid with the help of the typically used bidentate directing groups (e.g., **DG-a** and **DG-c**) afforded the corresponding mono arylation product (3-arylated propionamide) and bis arylation product (3,3-bis arylated propionamide).

Given that the research field pertaining to the bidentate directing group-directed site-selective sp^3 C–H activation/functionalization reactions is still emerging; the scope and limitations of the bidentate directing groups yet to be clearly scrutinized. Furthermore, given the importance of the C–H activation/functionalization tactics in organic synthesis, advancing the research area pertaining to the directing group-assisted C–H activation/functionalization reactions by developing new directing groups might (a) ensure the availability of commercially available other optional bidentate directing groups, and (b) enhance the understanding with regard to the scope and limitations of bidentate directing groups while executing the site-selective C-H functionalization of suitable substrates. Hence, with an aspiration to bolster the sp^2/sp^3 C–H activation/functionalization method,[6-16] we envisaged to report 4-amino-2,1,3-benzothiadiazole (ABTD)[17] as a new bidentate directing group for the Pd(II)-catalyzed, sp^2/sp^3 C–H activation/functionalization of various aliphatic/alicyclic/aromatic carboxamide systems. The results from our investigation on the Pd(II)-catalyzed, ABTD-directed arylation/acetoxylation of β-C(sp^3)-H bonds of aliphatic/alicyclic carboxamides and arylation/benzylation/acetoxylation/methoxylation of *ortho* C(sp^2)-H bonds of various benzamides are reported.

RESULSTS AND DISCUSSION

To explore 4-amino-2,1,3-benzothiadiazole (ABTD) as a directing group for the Pd(II)-catalyzed C–H activation and direct arylation of carboxamides, initially we assembled carboxamide **1a** from butanoyl chloride and ABTD. We then carried out the optimization reactions using carboxamide **1a** and Table 1 shows the results for the Pd(II)-catalyzed sp^3 C-

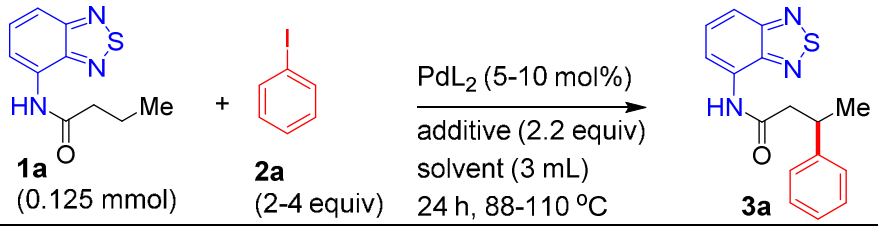
H arylation of **1a** with **2a** in the presence of various palladium catalysts and additives in different solvents. The reaction of a mixture of **1a** (1 equiv), PhI (**2a**, 4 equiv), $Pd(OAc)_2$ catalyst (5 or 10 mol%) and AgOAc additive in toluene at 110 ^oC afforded the methylene C(*β*)–H arylated product **3a** in 85-95% yields (entries 1 and 2, Table 1). The Pd(II)-catalyzed sp^3 C–H arylation of **1a** with **2a** using additional additives, such as Ag_2CO_3 or KOAc furnished the product **3a** in 75 and <10% yields, respectively (entries 3 and 4, Table 1). The usage of $PhI(OAc)_2$ as an additive failed to give the product **3a** (entry 5, Table 1). The arylation of **1a** with **2a** in the presence of other palladium catalysts, such as, $PdCl_2$ or $Pd(TFA)_2$ furnished the product **3a** in 84 and 40% yields, respectively (entries 6 and 7, Table 1). The Pd(II)-catalyzed sp^3 C–H arylation of **1a** with **2a** in other solvents, such as, *tert*-amylOH or 1,2-DCE furnished the product **3a** in 93 and 92% yields, respectively (entries 8 and 9, Table 1). The sp^3 C–H arylation of **1a** with 2 or 3 equiv of **2a** afforded the product **3a** in 70 and 87% yields, respectively (entries 10 and 11, Table 1).

We then examined the generality of the Pd(II)-catalyzed, ABTD-directed arylation of methylene C(*β*)–H bonds of various aliphatic carboxamides (Table 2). Using the optimized reaction conditions, we carried out the $Pd(OAc)_2$/AgOAc catalytic system-based, ABTD-directed C–H arylation of **1a** with different aryl iodides that possessed electron-donating or electron-withdrawing groups at the *para*/*meta* position of the aryl ring in the corresponding aryl iodides. Accordingly, a variety of corresponding *β*-C-H arylated butanamides **3a-g** were obtained in 52-97% yields (Table 2). The *β*-C-H arylated butanamides **3h** (63%) and **3i** (86%) were obtained from the Pd(II)-catalyzed, ABTD-directed arylation of methylene C(*β*)–H bond of **1a** with the corresponding disubstituted aryl iodides (Table 2).

Next, we performed the $Pd(OAc)_2$/AgOAc catalytic system-based, ABTD-directed arylation of methylene C(*β*)–H bonds of various aliphatic carboxamides **1b-f** with different aryl iodides, which furnished the corresponding *β*-C-H arylated carboxamides **3j-n** in 62-90%

yields (Table 2). Then, we performed the Pd(II)-catalyzed, ABTD-directed arylations of methylene C(*β*)–H bonds of substrates **1a,d,g** with a heteroaryl iodide (e.g., 2-fluoro-5-iodopyridine), which afforded the corresponding *β*-C-H arylated carboxamides **3o-q** in 57-90% yields (Table 2). Subsequently, we performed the Pd(II)-catalyzed, ABTD-directed C–H arylation of mono β-arylated propionamide **1h** with 1-iodo-4-methoxybenzene and 4-iodo-1,2-dimethylbenzene to afford the corresponding β′-aryl β-aryl propionamides **3r**,**s** in 52 and 53% yields, respectively (Table 2). We also performed the diastereoselective Pd(II)-catalyzed *β*-C-H arylation reactions using branched carboxamides **1aa-1ac** to obtain the corresponding *β*-C-H arylated products **3aa-3ac**, however, these reactions were not fruitful.

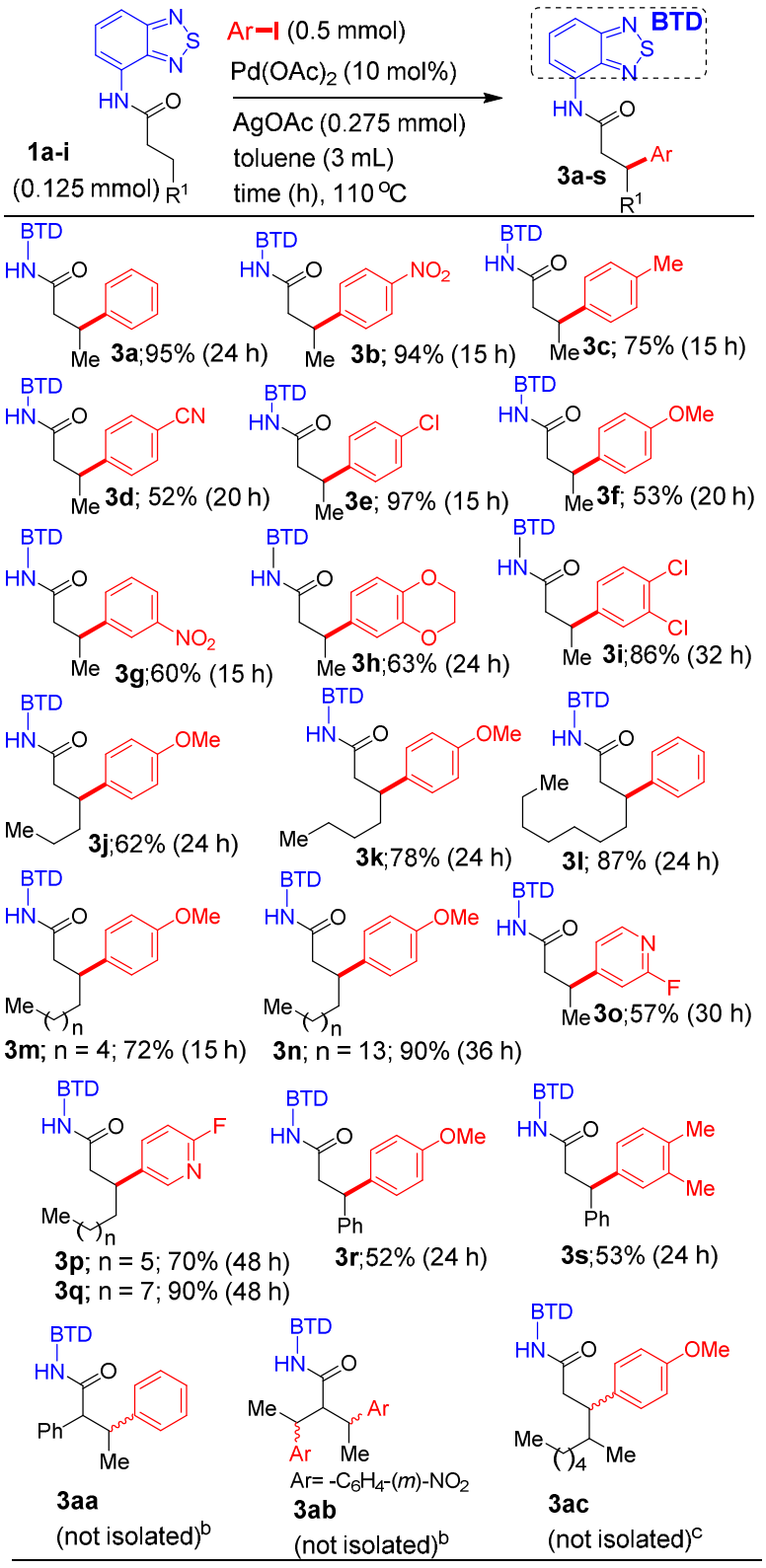
Table 1. Optimization of Reactions. Pd(II)-Catalyzed, ABTD-Directed Direct Arylation of Methylene C(*β*)–H Bond of 1a



entry	PdL_2 (mol%)	additive	solvent	*T* (°C)	yield **3a** (%)
1	$Pd(OAc)_2$ (5)	AgOAc	toluene	110	85
2	$Pd(OAc)_2$ (10)	AgOAc	toluene	110	95
3	$Pd(OAc)_2$ (10)	Ag_2CO_3	toluene	110	75
4	$Pd(OAc)_2$ (10)	KOAc	toluene	110	<10
5	$Pd(OAc)_2$ (10)	$PhI(OAc)_2$	toluene	110	0
6	$PdCl_2$ (10)	AgOAc	toluene	110	84
7	$Pd(TFA)_2$ (10)	AgOAc	toluene	110	40
8	$Pd(OAc)_2$ (10)	AgOAc	*t*-amylOH	100	93
9	$Pd(OAc)_2$ (10)	AgOAc	1,2-DCE	85	92
10[a]	$Pd(OAc)_2$ (10)	AgOAc	toluene	110	70
11[b]	$Pd(OAc)_2$ (10)	AgOAc	toluene	110	87

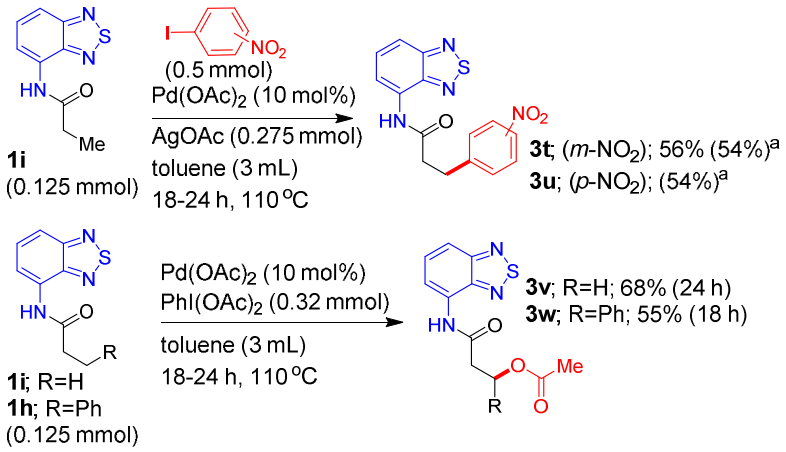
[a] 2 Equiv of **2a** was used. [b] 3 Equiv of **2a** was used.

Table 2. Scope and Generality of the Pd(II)-Catalyzed, ABTD-Directed Direct Arylation of Methylene C(*β*)–H Bonds of Various Aliphatic Carboxamides[a,14d]



[a] The *β*-C-H arylated carboxamides **3a-s** were obtained from their respective starting materials **1a-i**. [b] The reactions were carried out using the corresponding starting materials **1aa** and **1ab** and products **3aa** and **3ab** could not be isolated as the corresponding reactions gave a complex mixture. [c] The reaction was performed using the starting material **1ac** and negligible amount of product formation was observed.

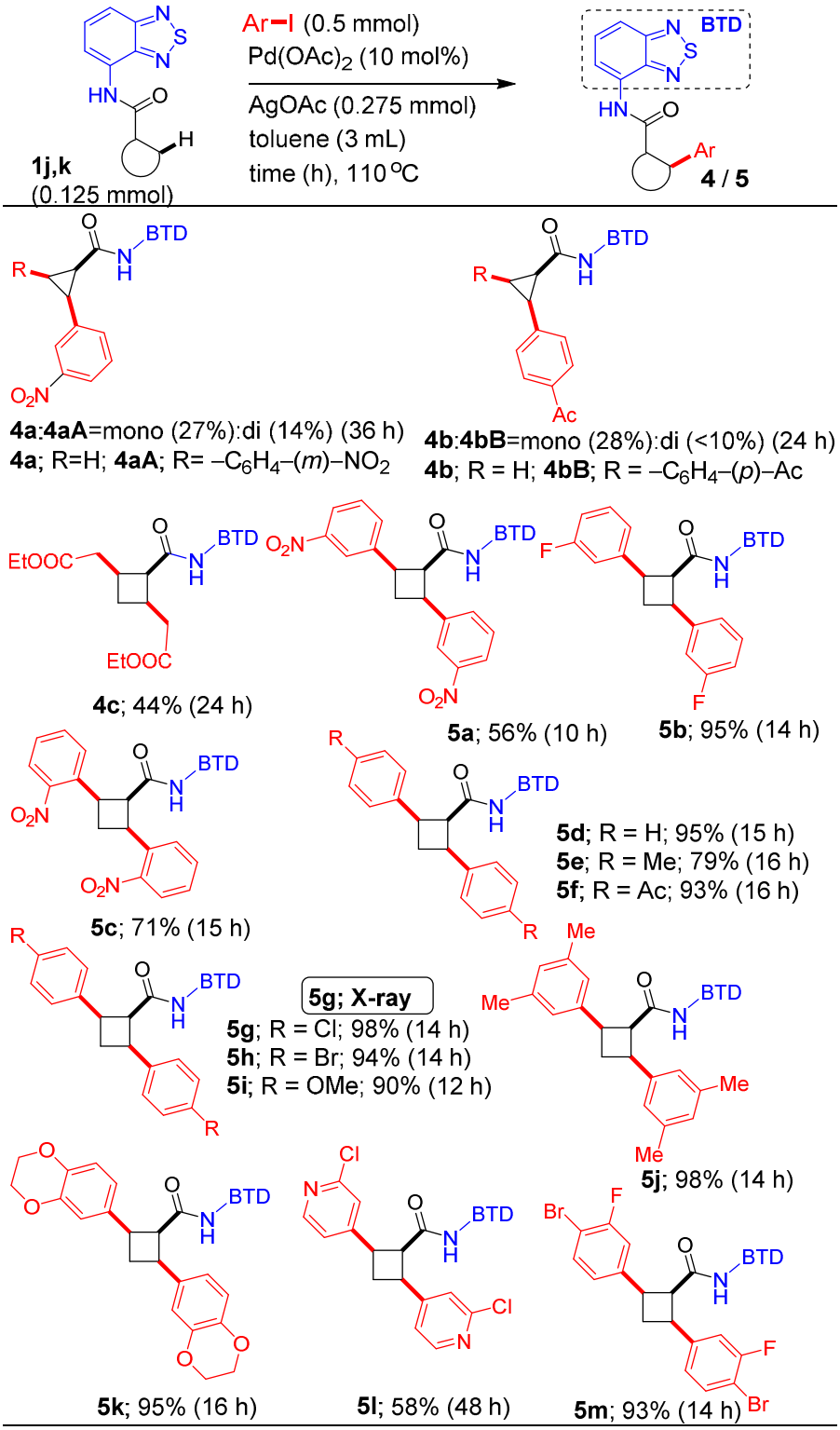
Scheme 1. Pd(II)-Catalyzed, ABTD-Directed *β*-C-H Arylation of 1i and *β*-C-H Acetoxylation of 1i,h.



[a] The reaction was performed using 0.15 mmol of 1-iodo-3-nitrobenzene for 18 h.

We also performed the $Pd(OAc)_2$/AgOAc catalytic system-based, ABTD-directed arylation of methyl C(*β*)–H bond of propionamide **1i** with 1-iodo-3-nitrobenzene and 1-iodo-4-nitrobenzene, which furnished the corresponding mono arylated propionamides **3t**,**u** in 54-56% yield, (Scheme 1). In these reactions the corresponding bis arylated propionamides were not obtained in characterizable amounts. Furthermore, we wished to attempt the acetoxylation of sp^3 C–H bond of aliphatic carboxamide system with the help of the ABTD bidentate directing group. In this regard, we performed the Pd(II)-catalyzed, ABTD-directed C-H acetoxylation of propionamides **1i**,**h** with $PhI(OAc)_2$, which gave the corresponding *β*-C–H acetoxylated propionamides **3v**,**w** in 68 and 55% yields, respectively (Scheme 1).

Table 3. Diastereoselective Pd(II)-Catalyzed, ABTD-Directed Arylation of Methylene C(*β*)–H Bonds of Cyclopropane and Cyclobutane Systems



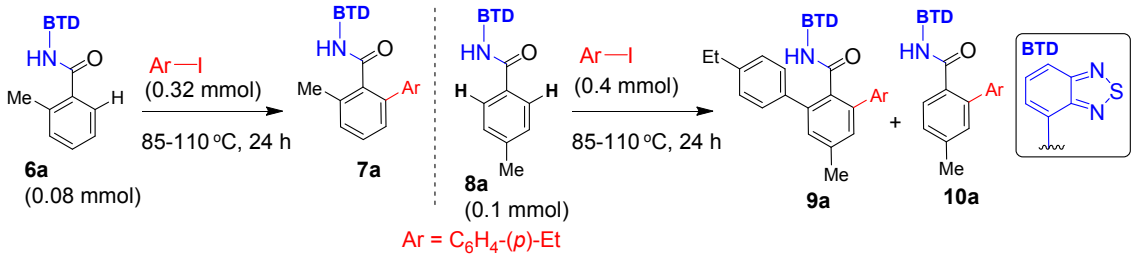
Next, we were interested to explore the diastereoselective Pd(II)-catalyzed C-H arylation of alicyclic carboxamides with the help of the ABTD bidentate directing group. In this regard, initially we performed the Pd(II)-catalyzed, ABTD-directed C–H arylation of cyclopropanecarboxamide **1j** with 1-iodo-3-nitrobenzene. This reaction gave the mono *β*-C-H arylated product **4a** in 27% yield (*cis* isomer) and bis *β*-C-H arylated product **4aA** in 14% yield (all *cis* isomer, Table 3). Similarly, the Pd(II)-catalyzed, ABTD-directed C–H arylation of cyclopropanecarboxamide **1j** with 4-iodoacetophenone furnished the corresponding mono *β*-C-H arylated product **4b** in 28% yield (*cis* isomer) and bis *β*-C-H arylated product **4bB** in <10% yield (all *cis* isomer, Table 3). Then, we envisaged to attempt the diastereoselective Pd(II)-catalyzed C–H arylation/alkylation of cyclobutanecarboxamide **1k** with the help of the ABTD bidentate directing group. Initially, we performed the Pd(II)-catalyzed, ABTD-directed C–H alkylation of cyclobutanecarboxamide **1k** with ethyl iodoacetate, which furnished the substituted cyclobutanecarboxamide **4c** in 44% yield (Table 3). Next, we performed the Pd(II)-catalyzed, ABTD-directed C–H arylation of **1k** with 1-iodo-3-nitrobenzene, 3-fluoro-1-iodobenzene and 1-iodo-2-nitrobenzene. These reactions afforded the corresponding bis *β*-C–H arylated cyclobutanecarboxamides **5a-c** having the all *cis* stereochemistry in 56-95% yields (Table 3). Similarly, the Pd(II)-catalyzed, ABTD-directed C–H arylation of **1k** with various aryl iodides that possessed electron-donating or electron-withdrawing groups at the *para* position of the aryl ring in the corresponding aryl iodides, successfully furnished the corresponding bis *β*-C–H arylated cyclobutanecarboxamides **5d-i** having the all *cis* stereochemistry in 79-98% yields (Table 3).

Furthermore, the Pd(II)-catalyzed, ABTD-directed C–H arylation of cyclobutanecarboxamide **1k** with disubstituted aryl- and heteroaryl iodides underwent smoothly to afford the corresponding bis *β*-C–H arylated cyclobutanecarboxamides **5j-m** having all *cis* stereochemistry in 58-98% yields (Table 3). It is worth to mention that the C-H

arylation of **1k** selectively occurred at both the *β*-positions of cyclobutanecarboxamide **1k** with the help of the ABTD bidentate directing group and the corresponding bis *β*-C–H arylated/alkylated carboxamides **4**/**5** were obtained with high diastereoselectivity. Notably, the double *β*-C–H arylations of cyclobutanecarboxamide **1k** have led to the assembling of various trisubstituted cyclobutanecarboxamide scaffolds having the all *cis* stereochemistry, which are analogous to the naturally occurring bioactive cyclobutanes.[10a,c] The observed *cis* stereochemistry and structure of the cyclopropanes **4a**, **4b**, **4aA** and **4bB** and cyclobutanes **5a-m** were assigned based on the similarity of the NMR spectral pattern of these compounds with the previous works dealing on the bidentate directing group-directed diastereoselective *cis* C-H arylation of cyclopropanecarboxamides[15a,e,f] and cyclobutanecarboxamides[10a,14c] systems, respectively. Additionally, the X-ray structure analysis of **5g** (see the Supporting Information for the X-ray structure of **5g**) clearly revealed that the compound **5g** has the *cis* stereochemistry in accordance with the previous reports.[10a,14c] The stereochemistry of the compound **4c**[16d,e] was assigned based on the stereochemistry of compounds **5a-m**.

Having explored the Pd(II)-catalyzed direct arylation of sp^3 C(*β*)–H bonds of aliphatic and alicyclic carboxamides using the ABTD directing group, next we wished to perform the Pd(II)-catalyzed direct arylation of *ortho* C(sp^2)–H bonds of aromatic carboxamides using the ABTD bidentate directing group. In this regard, we assembled benzamides **6a** and **8a** from their corresponding benzoyl chlorides and ABTD. We then performed the optimization reactions using benzamides **6a** and **8a**. Table 4 shows the results for the ABTD-directed mono arylation of *ortho* C(sp^2)–H bond of benzamide **6a** and bis arylation of *ortho* C(sp^2)–H bonds of benzamide **8a** in the presence of various palladium catalysts and additives in different solvents.

Table 4. Optimization Reactions. Pd(II)-Catalyzed, ABTD-Directed Arylation of *Ortho* C(sp^2)–H Bonds of Benzamides 6a/8a[a-c]



entry	**6a** (or) **8a** (1 equiv)	PdL_2 (10 mol%)	solvent (3 mL)	additive (2.2 equiv)	*t* (°C)	**7a** (or) **9a**: yield (%)
1	**6a**	nil	toluene	AgOAc	110	**7a**: 0
2	**8a**					**9a**: 0
3	**6a**	$Pd(OAc)_2$	toluene	AgOAc	110	**7a**: 70
4	**8a**					**9a**: 75
5	**6a**	$PdCl_2$	toluene	AgOAc	110	**7a**: 24
6	**8a**					**9a**: 50
7	**6a**	$Pd(PPh_3)_4$	toluene	AgOAc	110	**7a**: <5
8	**8a**					**9a**: <5
9	**6a**	$Pd(TFA)_2$	toluene	AgOAc	110	**7a**: <5
10	**8a**					**9a**: <5
11	**6a**	$Pd(OAc)_2$	toluene	Ag_2CO_3	110	**7a**: 0
12	**8a**					**9a**: 0
13	**6a**	$Pd(OAc)_2$	toluene	$PhI(OAc)_2$	110	**7a**: 0
14	**8a**					**9a**: 0
15	**6a**	$Pd(OAc)_2$	toluene	KOAc	110	**7a**: <5
16	**8a**					**9a**: <5
17	**6a**	$Pd(OAc)_2$	1,4-dioxane	AgOAc	100	**7a**: 30
18	**8a**					**9a**: <5
19	**6a**	$Pd(OAc)_2$	^{t}amylOH	AgOAc	110	**7a**: 0
20	**8a**					**9a**: 0
21	**6a**	$Pd(OAc)_2$	^{t}BuOH	AgOAc	85	**7a**: 0
22	**8a**					**9a**: 0

[a] The reaction conditions given in any row corresponds to the independent reactions carried out with **6a** and **8a**.

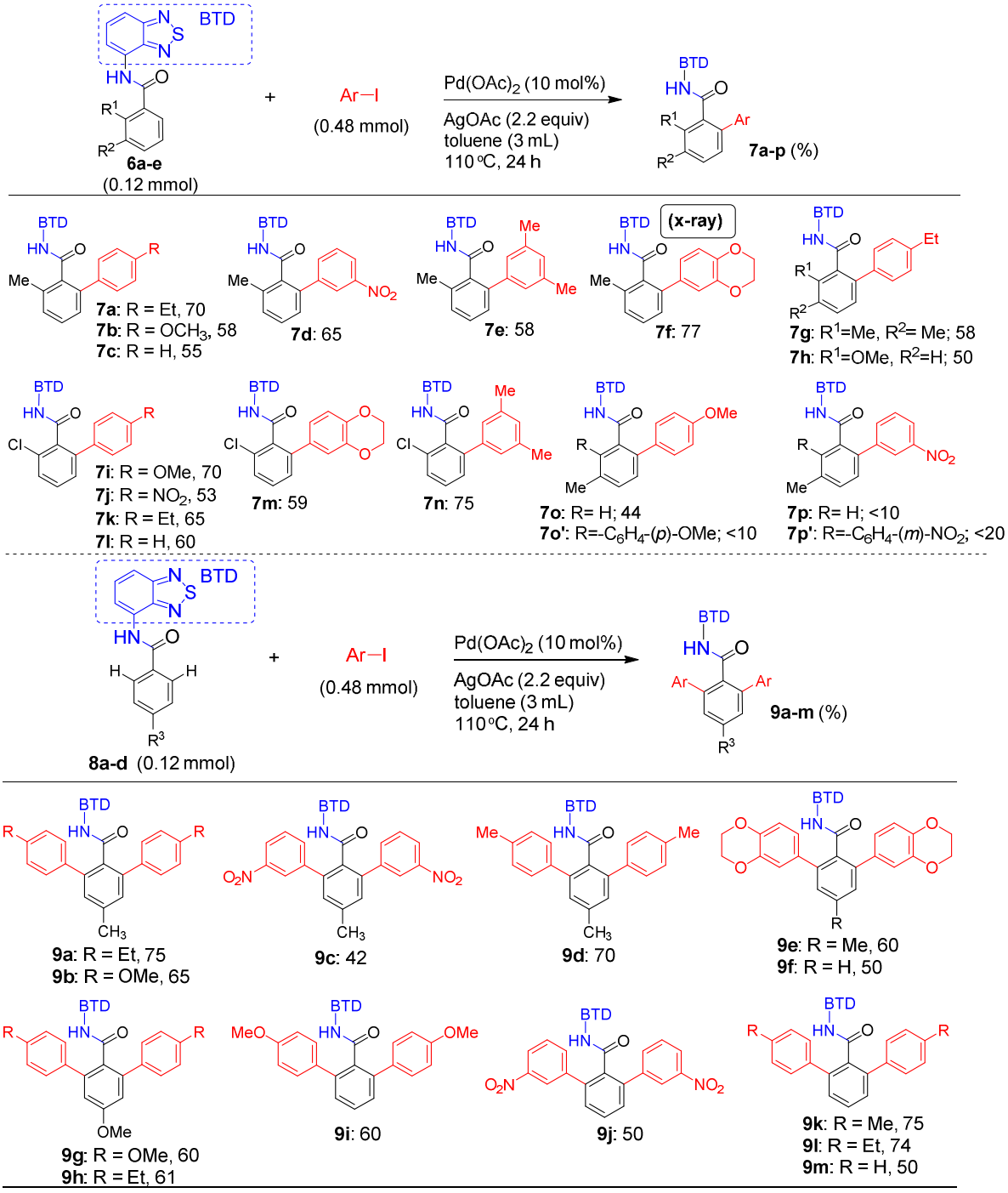
[b] The product **7a** was obtained from the corresponding reactions involving substrate **6a**.

[c] The product **9a** was obtained from the corresponding reactions involving substrate **8a**. The product **10a** was not observed in the reactions involving the substrate **8a**.

The arylation reaction of *ortho* C(sp^2)–H bond of benzamide **6a** with 1-ethyl-4-iodobenzene in the presence of 10 mol% of the $Pd(OAc)_2$ catalyst and AgOAc additive in toluene at 110 ^oC afforded the mono C-H arylated benzamide **7a** in a maximum yield of 70% (entry 2, Table 4). Similarly, the Pd(II)-catalyzed arylation of *ortho* C(sp^2)–H bonds of benzamide **8a** with 1-ethyl-4-iodobenzene afforded the bis C–H arylated benzamide **9a** in a maximum yield of 75% (entry 2, Table 4). Apart from these reactions, the other optimization reactions comprising the mono and bis arylation of *ortho* C(sp^2)–H bonds of the corresponding benzamides **6a** and **8a** in the presence of other palladium catalysts or additives or solvents were not fruitful (entries 1 and 3-11, Table 4). Next, to examine the generality of this work we planned to perform the arylation of *ortho* C(sp^2)–H bonds of various 2/3-substituted-benzamides **6a-e**, which were prepared from the ABTD directing group (Table 5). Using the optimized reaction conditions (entry 2, Table 4), we attempted the $Pd(OAc)_2$/AgOAc-catalytic system-based, ABTD-directed arylation of *ortho* C(sp^2)–H bonds of 2/3-substituted-benzamides **6a-d** with different aryl iodides that possessed electron-donating or electron-withdrawing groups at the *para/meta* position of the aryl ring in the corresponding aryl iodides. These reactions afforded a wide range of the corresponding mono C-H arylated benzamides **7a-n** in 50-77% yields (Table 5). The arylation of the *meta* substituted benzamide **6e** with 1-iodo-4-methoxybenzene afforded the corresponding mono and bis arylated benzamides **7o** and **7o′** in 44 and <10% yields. Further, the arylation of **6e**

with 1-iodo-3-nitrobenzene afforded the corresponding mono and bis arylated benzamides **7p** (<10%) and **7p′** (<20%) in low yields (Table 5).

Table 5. Substrate Scope and Generality of the Pd(II)-Catalyzed, ABTD-Directed Arylation of *Ortho* C(sp^2)–H Bond of Benzamides 6a-e and 8a-d[a,b]

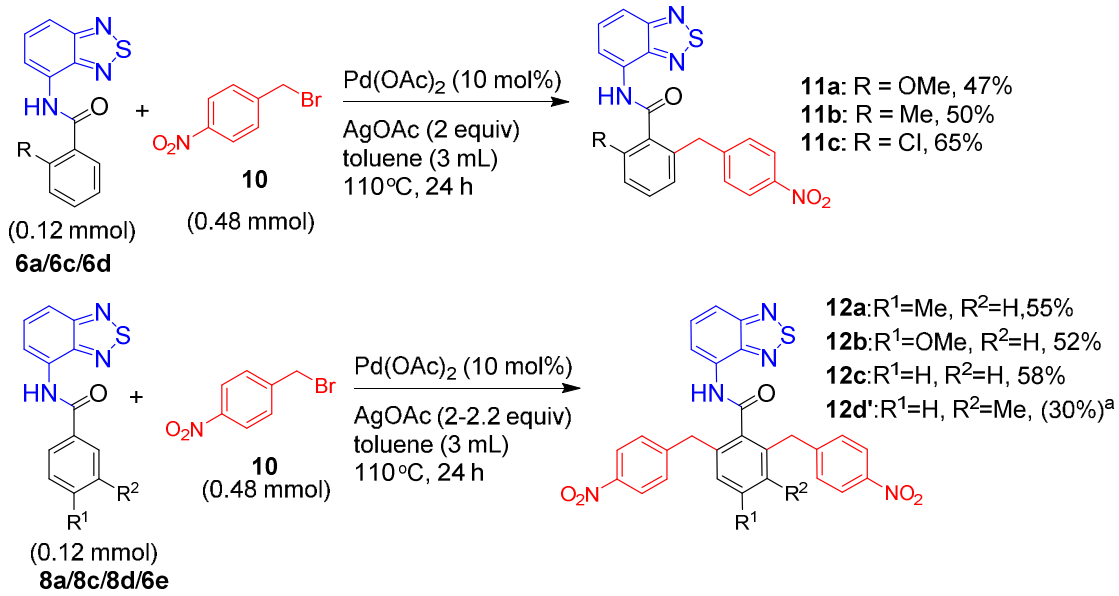


[a] The substrates used are: **6a**; R^1 = Me, R^2 = H. **6b**; R^1 = Me, R^2 = Me . **6c**; R^1 = OMe, R^2 = H. **6d**; R^1 = Cl, R^2 = H; **6e**; R^1 = H, R^2 = Me. [b] The substrates used are: **8a**; R^3 = Me. **8b**; R^3 = Cl. **8c**; R^3 = OMe. **8d**; R^3 = H.

After investigating the Pd(II)-catalyzed, ABTD-directed mono arylation of *ortho* C(sp^2)–H bonds benzamides **6a-e**, we then planned to extend the substrate scope by examining the bis arylation of *ortho* C(sp^2)–H bonds of benzamides **8a-d**. Accordingly, using the optimized reaction conditions (entry 2, Table 4), we attempted the $Pd(OAc)_2$/AgOAc-catalytic system-based, ABTD-directed arylation of *ortho* C(sp^2)–H bonds of benzamides **8a-d** with several aryl iodides that possessed electron-donating or electron-withdrawing groups at the *para/meta* position of the aryl ring in the corresponding aryl iodides. These reactions furnished a wide range of bis C-H arylated benzamides **9a-m** in 42-75% yields, respectively (Table 5).

Next, we focused our attention to explore the Pd(II)-catalyzed direct benzylation of *ortho* C(sp^2)–H bonds of benzamides with the help of the ABTD bidentate directing group. In this regard, initially, we carried out the $Pd(OAc)_2$/AgOAc-catalytic system-based, ABTD-directed *ortho* C–H benzylation of **6a**/**6c**/**6d** with 1-(bromomethyl)-4-nitrobenzene (**10**). These reactions afforded the corresponding *ortho* C–H benzylated benzamides **11a-c** in 47-65% yields, respectively (Scheme 2). Having done the Pd(II)-catalyzed mono benzylation of *ortho* C(sp^2)–H bond of **6a**/**6c**/**6d**, we then performed the Pd(II)-catalyzed, ABTD-directed bis benzylation of *ortho* C(sp^2)–H bonds of benzamides **8a**/**8c**/**8d**/**6e** with **10**. These reactions furnished the corresponding bis *ortho*-C–H benzylated benzamides **12a-c** and **12d′** in 30-58% yields, respectively (Scheme 2).

Scheme 2. The Pd(II)-Catalyzed, ABTD-Directed Mono and Bis Benzylation of *Ortho* C(sp^2)–H Bonds of Benzamides 6 and 8.[a]

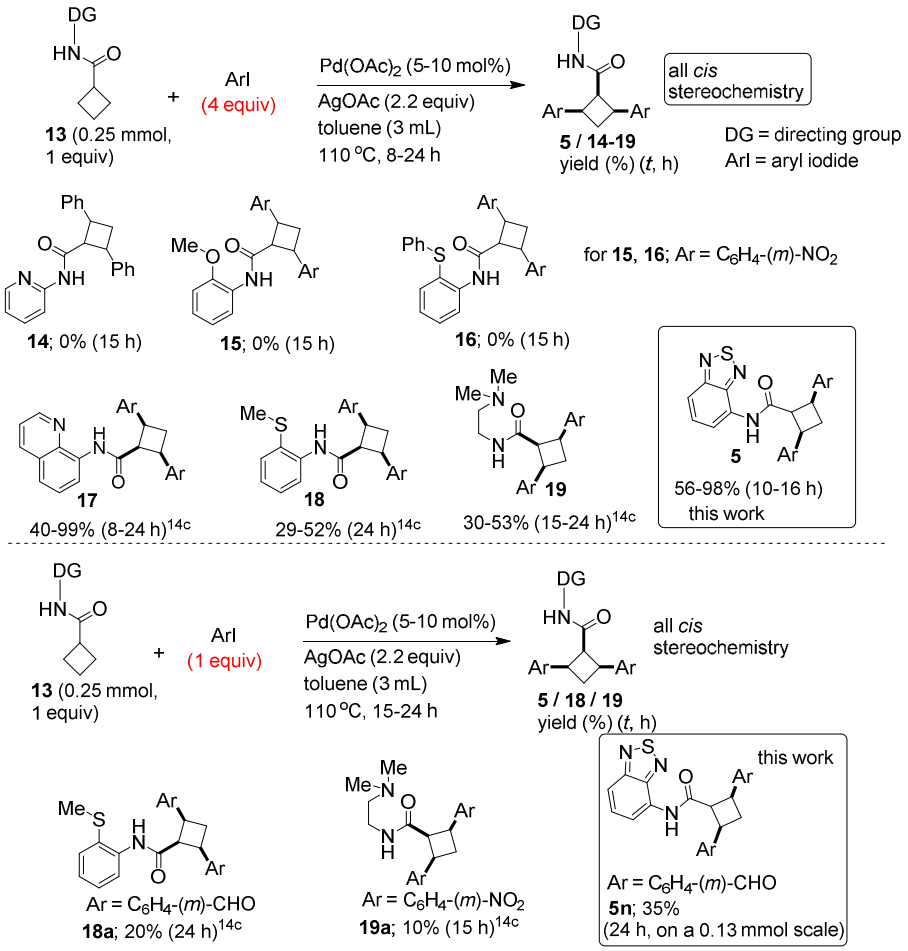


[a] The benzylation of **6e** afforded the bis benzylated product **12d′** along with the corresponding mono benzylated product **12d** in <10% yield. Our efforts to isolate the compound **12d** in pure form were not fruitful.

The C-H arylated/benzylated compounds **7a-p**, **9a-m**, **11a-c**, **12a-c** and **12d′** obtained from the Pd(II)-catalyzed, ABTD-directed arylation/benzylation of *ortho* C–H bonds of the corresponding substrates **6a-e** and **8a-d** were characterized based on their NMR spectra and HRMS analyses data. For example, a comparison the ^{1}H NMR spectra of substrate **6b** and carboxamide **7g** was performed. The corresponding distinct doublet peaks of the *meta* and *para* protons of *ortho* C-H arylated carboxamide **7g** revealed that the arylation occurred at the *ortho* C–H bond of the 2,3-dimethylbenzamide system **6b**. Similarly, a comparison the ^{1}H NMR spectra of substrate **8a** and carboxamides **9d**/**12a** was performed. The corresponding distinct singlet peak of the *meta* protons of the bis *ortho* C-H arylated/benzylated 4-methylbenzamide systems **9d**/**12a** revealed that the arylation/benzylation occurred at both the *ortho* C–H bonds of the 4-methylbenzamide system **8a**. Additionally, the observed

regioselectivity in the reactions comprising the Pd(II)-catalyzed, ABTD-directed *ortho* C(sp^2)–H arylation/benzylation of benzamides **6a-e** and **8a-d** was unambiguously confirmed from the X-ray structure of a representative *ortho* C–H arylated benzamide **7f** (see the Supporting Information for the X-ray structure of **7f**).

Scheme 3. Comparison of ABTD with the Pivotal Bidentate Directing Groups Reported for the Pd(II)-Catalyzed Arylation of Cyclobutanecarboxamide[14c]



Next, it was envisaged to carry out a brief comparison on the efficiency, scope and limitations of the 4-amino-2,1,3-benzothiadiazole (ABTD) bidentate directing group with the other seminal bidentate directing groups used for performing the Pd(II)-catalyzed arylation/acetoxylation of carboxylic acid derivatives. Accordingly, Schemes 3-6 reveal a comparison of the propensity of the ABTD directing group with the typical bidentate

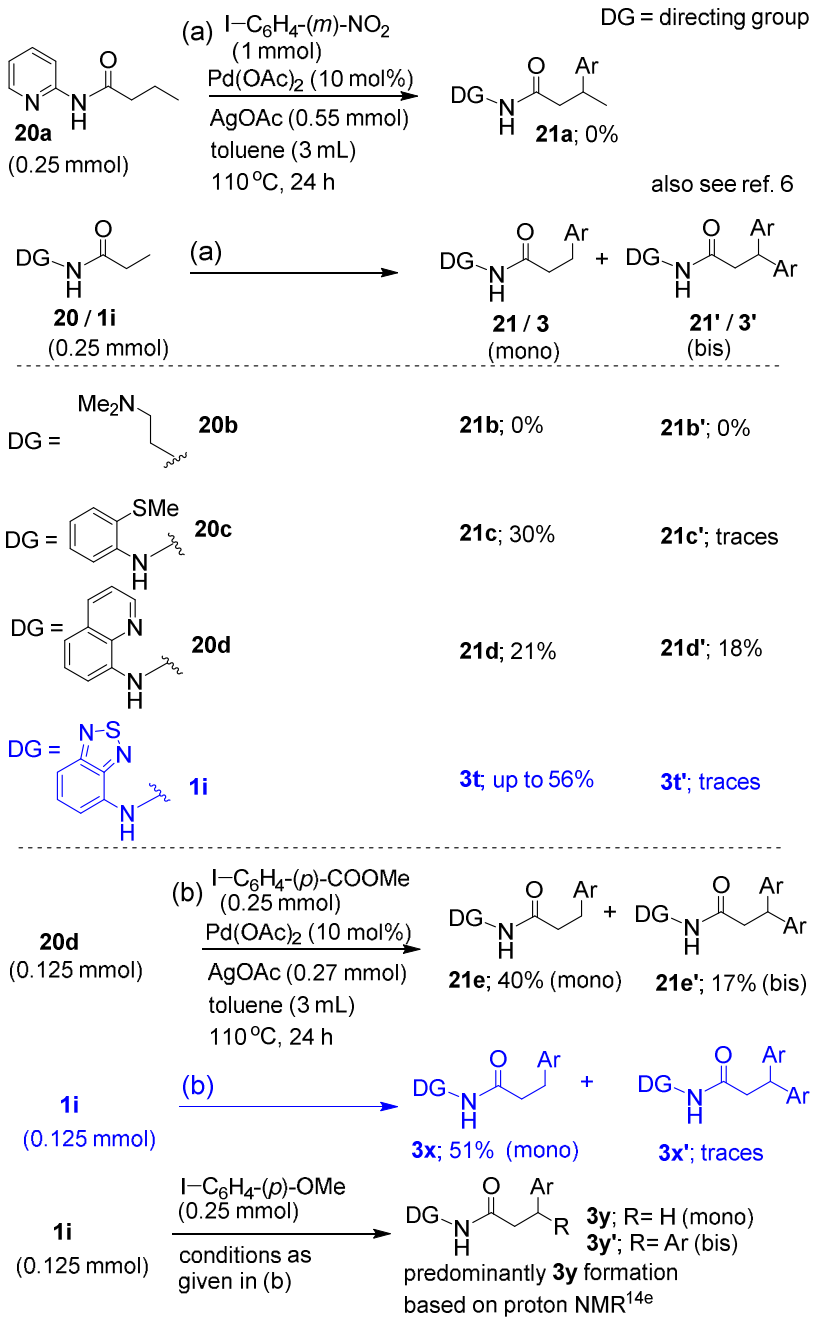
directing groups reported for the Pd(II)-catalyzed arylation of cyclobutanecarboxamide system **13** (Scheme 3). The expected bis C-H arylated cyclobutanecarboxamides **14-16** did not form in the Pd(II)-catalyzed C−H arylation of their corresponding starting materials. The reason for this may be that the respective bidentate directing groups linked with the cyclobutanecarboxamides **13** have not assisted the arylation of C−H bond of the corresponding cyclobutanecarboxamides **13**.

Typically, the Pd(II)-catalyzed C-H arylations of carboxylic acid derivatives have been performed using the 8-aminoquinoline, 2-(methylthio)aniline and N^1,N^1-dimethylethane bidentate directing groups.[3,5,6] Using these bidentate directing groups, our lab reported the Pd(II)-catalyzed diastereoselective double *β*-C-H activation and arylation of cyclobutanecarboxamides.[14c] A comparison of the efficiencies of these bidentate directing groups with the ABTD directing group with regard to the diastereoselective *β*-C-H arylation of cyclobutane system was carried out. It was found that the ABTD bidentate directing group is relatively more efficient than the 2-(methylthio)aniline and N^1,N^1-dimethylethane-1,2-diamine directing groups and the efficiency of the 4-amino-2,1,3-benzothiadiazole directing group was comparable to the 8-aminoquinoline bidentate directing group (Scheme 3).

Furthermore, the results shown in Scheme 4 provided additional inputs with regard to the assistance provided by the ABTD bidentate directing group for the selective mono *β*-C-H arylation of the methyl group of propionamide. Daugulis *et al.* revealed[5,6] that the attempts on the Pd(II)-catalyzed C-H arylation of methyl group of propionamide with the help of the typically used bidentate directing groups (e.g., 8-aminoquinoline and 2-(methylthio)aniline) afforded the corresponding 3-arylated propionamide (mono arylation product) and 3,3-bis arylated propionamide (bis arylation product).[5,6] In the present investigation, the Pd(OAc)/AgOAc-catalytic system-based C-H arylation of butyramide **20a** (assembled from the 2-aminopyridine directing group) and propionamide **20b** (assembled from the N^1,N^1-

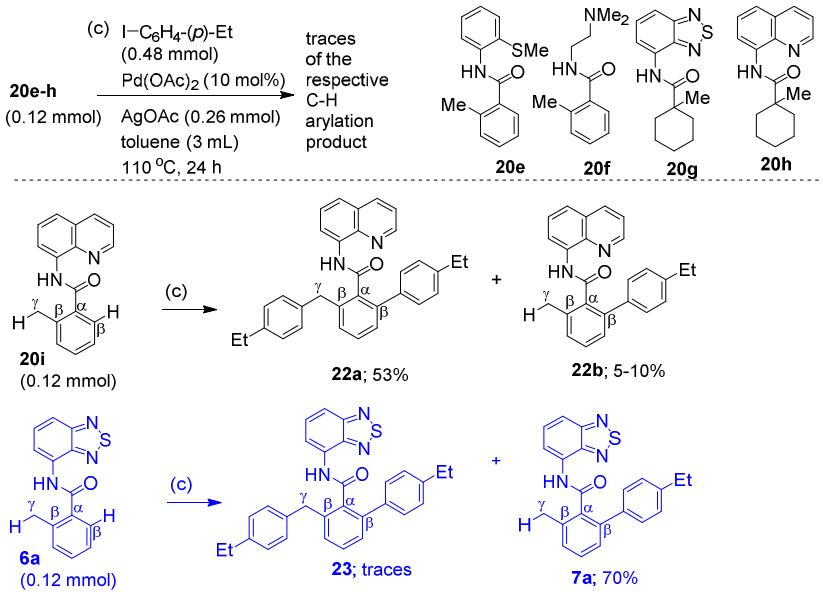
dimethylethane-1,2-diamine directing group) did not give the expected products **21a**, **21b** and **21b′** (Scheme 4).

Scheme 4. Comparison of ABTD with the Other Pivotal Directing Groups Used for the Mono *β*-C-H Arylation of Popionic Acid.[6,14d]



The Pd(II)-catalyzed C-H arylation of **20c**, which was assembled from the 2-(methylthio)aniline bidentate directing group afforded the mono arylation product **21c** in low yield (30%. Scheme 4). However, the Pd(II)-catalyzed C-H arylation of **20d**, which was assembled from the 8-aminoquinoline bidentate directing group afforded the corresponding mono arylation products **21d/21e** (21-40%) and bis arylation product **21d′/21e′** (17-18%, Scheme 4). Nonetheless, the Pd(II)-catalyzed C-H arylation of **1i**, which was assembled from the ABTD bidentate directing group selectively afforded the mono arylation products **3t/3x** in good yields (up to 56%, Schemes 1 and 4). Furthermore, we observed that the ABTD-directed C-H arylation of **6a** selectively afforded the mono arylation product **7a** in 70% yield (Scheme 5). On the other hand, the 8-aminoquinoline-directed C-H arylation of **20i** afforded the bis arylation product **22a** in 53% yield along with the compound **22b** in 5-10% yield (Scheme 5).[16f]

Scheme 5. Typical Comparison of ABTD with the Other Pivotal Directing Groups Used for the C-H Arylation Carboxamides.



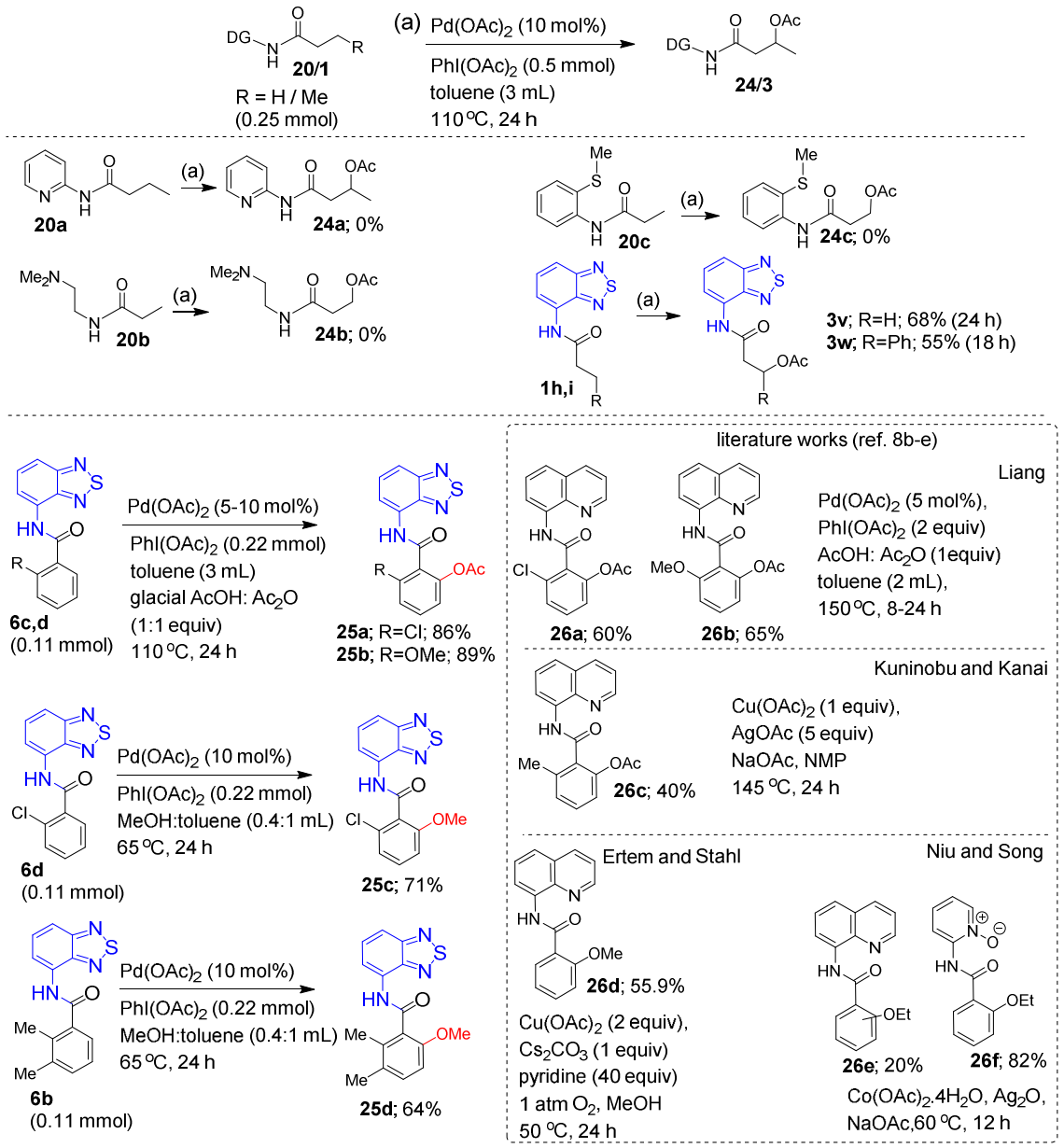
Additionally, we performed the Pd(II)-catalyzed, ABTD-directed *β*-C-H acetoxylation of substrate **1i** with $PhI(OAc)_2$, which afforded the corresponding C-H acetoxylated products

3v/3w in 55-68% yields (Scheme 6). However, the Pd(II)-catalyzed *β*-C-H acetoxylation of the corresponding carboxamides **20a-c**, directed by the respective bidentate directing groups were not fruitful (Scheme 6). We also performed the Pd(II)-catalyzed, ABTD-directed *β*-C-H acetoxylation of substrates **6c,d**, which afforded the corresponding C-H acetoxylated **25a,b** in 86-89% yields, respectively (Scheme 6). Similarly, the Pd(II)-catalyzed, ABTD-directed *β*-C-H methoxylation of **6b,d** afforded the corresponding C-H methoxylated products **25c,d** in 64-71% yields, respectively. A comparison of the Pd(II)-catalyzed ABTD directing group-based C-H acetoxylation/alkoxylation reactions with the seminal works[8b-e] dealing on the C-H acetoxylation/alkoxylation using typical bidentate directing groups was shown in Scheme 6. The ABTD directing group-based C-H acetoxylation/alkoxylation of benzamides **6b-d** afforded the products **25a-d** in good yields involving relatively simple reaction conditions. Overall, the results presented in Schemes 3-6 have afforded a brief comparison on the adeptness, scope and limitations of the ABTD bidentate directing group with regard to the other seminal bidentate directing groups used for performing the Pd(II)-catalyzed C-H arylation/benzylation/acetoxylation of carboxylic acid derivatives.

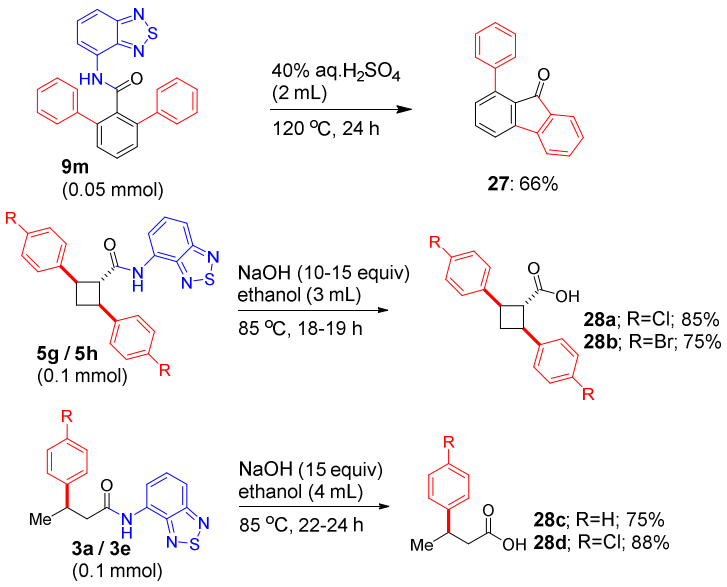
Finally, we also attempted the removal of the ABTD bidentate directing group after the C-H arylation of reactions using representative C-H arylated carboxamides (Scheme 7). Initially, we attempted the amide hydrolysis reaction of **9m** with aq. H_2SO_4, which afforded the 9-fluorenone derivative **27** (Scheme 7) and in this reaction, the corresponding carboxylic acid was not obtained in characterizable amount. After the removal of the directing group, the corresponding carboxylic acid has undergone an intramolecular Friedel-Crafts acylation to directly afford the compound **27** under the experimental condition. The base-mediated amide hydrolysis of **5g** and **5h** furnished the corresponding trisubstituted cyclobutanecarboxylic acids **28a** and **28b** (Scheme 7). The stereochemistry of carboxylic acids **28a** and **28b** was assigned by comparing the NMR spectral data of **28a** and **28b** with the previous work,[14c]

which also revealed the occurrence of epimerization at the carbonyl group containing stereocenter of **28a** and **28b**[14c] under the experimental condition. The removal of the ABTD bidentate directing group from **3a** and **3e** under the base-mediated hydrolysis reaction conditions gave the corresponding *β*-arylbutyric acids **28c** and **28d** (Scheme 7).

Scheme 6. Comparison of ABTD with the Other Seminal Works on the C-H Acetoxylation/Alkoxylation of Carboxamides.



Scheme 7. Removal of the ABTD Directing Group After the β-C-H Arylation of Carboxamides.[14e]



CONCLUSION

In summary, we have shown 4-amino-2,1,3-benzothiadiazole (ABTD) as a new bidentate directing group for the $Pd(OAc)_2$/AgOAc catalytic system-based sp^2/sp^3 C–H activation/functionalization and C-C/C-O bond formation. The ABTD directing group directed the Pd(II)-catalyzed C–H arylation/acetoxylation to occur at the *β*-position of various aliphatic/alicyclic carboxamides and benzamides. Various examples comprising the *β*-C-H arylated/acetoxylated carboxamides and trisubstituted cyclobutanecarboxamide scaffolds having the all *cis* stereochemistry were synthesized in good yields. Further, the Pd(II)-catalyzed, ABTD-directed arylation and benzylation of *ortho* $C(sp^2)$–H bonds of various benzamides afforded the corresponding mono/bis *β*-C-H arylated/benzylated benzamides in good yields. A brief description on the efficiency, scope and limitations of the ABTD bidentate directing group was presented by comparing the efficiency of ABTD with other seminal bidentate directing groups. Finally, we have also shown the removal of the ABTD directing group from representative C-H arylated compounds. It is to be noted that the

research field pertaining to the bidentate directing group-directed site-selective sp^3 C–H activation/functionalization is still emerging. Hence, advancing the research area pertaining to the directing group-assisted sp^2/sp^3 C–H activation/functionalization reactions by developing new directing groups/substrates will enhance the understanding with regard to the scope and limitations of the directing groups while exercising the site-selective C-H functionalization. Hence, we believe that ABTD might serve as an optional directing group when the site-selective C–H activation/functionalization of suitable carboxylic acid substrates is explored.

EXPERIMENTAL SECTION

General. IR spectra of compounds were recorded as thin films or KBr pellets. ^{1}H and $^{13}C\{^1H\}$ NMR spectra of all compounds were recorded on 400 MHz and 100 MHz spectrometers, respectively (using TMS as an internal standard). HRMS measurements were obtained from QTOF mass analyzer using electrospray ionization (ESI) method. Column chromatography was carried out using silica gel 100-200 mesh. Reactions were performed in anhydrous solvent under a nitrogen atmosphere. Isolated yields of all compounds were reported and yields of all compounds reported here were not optimized. Compounds **3a-i** and **3o** were obtained from substrate **1a**. Compounds **3j**, **3k**, **3l**, **3m** and **3n** were obtained from the corresponding substrates **1b**, **1c**, **1d**, **1e** and **1f**. Compounds **3p**, **3q**, **3r** and **3s** were obtained from the corresponding substrates **1d**, **1g** and **1h**. Compounds **4a/4aA** and **4b/4bB** were obtained from substrate **1j**. Compounds **5a-m** were obtained from substrate **1k**. Compounds **27**,[20a] **28a**,[14c] **28b**,[14c] **28c**,[19] **28d**,[19] **20a**,[20b] **20b**,[6] **20c**,[6] **20d**[6] and **21d**[20c] were reported in the literature. The reactions shown in Scheme 3 for comparing the efficiency of the ABTD with other popular bidentate directing groups are reported by our group.[14c] General procedures for the preparation of required carboxamide starting materials and C-H arylation/benzylation/oxygenation of carboxamides are given below. See the respective

Schemes 1-7 and Tables 1-5 for exact reaction conditions and starting materials/reagents used.

General procedure for the synthesis of carboxamides 1a-k and 1aa-1ac. A dry RB flask containing benzo[*c*][1,2,5]thiadiazol-4-amine (1 mmol), Et_3N (1.1 mmol) was stirred for 5−10 min under a nitrogen atmosphere. Then, to the reaction flask was added anhydrous DCM (4 mL) followed by dropwise addition of the corresponding acid chloride (1 mmol). Then, the reaction mixture was stirred for 12 h. After this period, the reaction mixture was diluted with dichloromethane (3-5 mL) and washed with water (5-7 mL) and twice with saturated aqueous $NaHCO_3$ solution (3-5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuum and purification of the resulting reaction mixture by column chromatography (silica gel, 100−200 mesh, EtOAc/hexanes) furnished the corresponding carboxamides **1a-k** and **1aa-1ac**.

General procedure for the C-H functionalization of carboxamides 1a-k, 1aa-1ac and 20a-h. An appropriate carboxamide (0.125 mmol, 1 equiv), $Pd(OAc)_2$ (2.8 mg, 10 mol%), an appropriate aryl iodide (0.5 mmol, 4 equiv) and AgOAc (45.9 mg, 0.275 mmol, 2.2 equiv) in anhydrous toluene (3 mL) was heated at 110 ^oC for 12-48 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in vacuum and purification of the resulting reaction mixture through column chromatography furnished the corresponding C-H arylated carboxamides **3a-3s, 4a, 4aA, 4b, 4bB**, **5a-5m** and **21** (see the corresponding Tables/Schemes for specific examples).

General procedure for the selective mono arylation of carboxamide 1i. An appropriate amide (0.125 mmol, 1 equiv), $Pd(OAc)_2$ (2.8 mg, 10 mol%), an appropriate aryl iodide (0.15 mmol, 1.2 equiv) and AgOAc (45.9 mg, 0.275 mmol, 2.2 equiv) in anhydrous toluene (3 mL) was heated at 110 ^oC for 18-24 h under nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in vacuum and purification of the resulting reaction

mixture through column chromatography furnished the corresponding C-H arylated amides **3t,u** (see the corresponding Scheme for specific examples).

General procedure for the C-H acetoxylation of carboxamides 1h,i/20a-c. An appropriate amide (0.125 mmol, 1 equiv), $Pd(OAc)_2$ (2.8 mg, 10 mol%), $PhI(OAc)_2$ (0.32 mmol, 2.5 equiv) and anhydrous toluene (3 mL) was heated at 110 ^oC for 18-24 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in vacuum and purification of the resulting reaction mixture through column chromatography furnished the corresponding β-acetoxylated amides **3v,w** (see the corresponding Schemes for specific examples).

Procedure for the alkylation of 1k and the preparation of 4c. Cyclobutanecarboxamide **1k** (0.125 mmol), $Pd(OAc)_2$ (2.8 mg, 10 mol%), ethyl iodoacetate (80 mg, 0.37 mmol), Ag_2CO_3 (75 mg, 0.27 mmol), and $(BnO)_2PO_2H$ (7 mg, 20 mol%) in anhydrous *tert*-amyl alcohol (2 mL) was heated at 110 °C for 24 h under a nitrogen atmosphere. After the reaction period, the mixture was concentrated in vacuum, purification of the crude residue by column chromatography on silica gel furnished the corresponding β-alkylated carboxamide **4c**.

General procedure for the hydrolysis of C-H arylated carboxamides 5g,h, and 3a,e. A solution of corresponding carboxamide (0.1 mmol) and NaOH (10-15 equiv) in ethanol (3-4 mL) was heated at 85 °C for 18-24 h. After this period, the reaction mixture was diluted with water (3-4 mL) and extracted with DCM (2 × 10 mL) and then, the aqueous layer was acidified with 1 N HCl to get a pH ≈ 2. The resulted aqueous layers were extracted with DCM (2 × 10 mL) and the combined organic layers were dried over Na_2SO_4 followed by the evaporation of the solvent in vacuum resulted the corresponding pure carboxylic acids **28a-d**.

General procedure for the synthesis of benzamides/carboxamides 6d, 8a, 8b, 8d and 20a-d. A dry flask containing 4-amino-2,1,3-benzothiadiazole (1 mmol, 151 mg), Et_3N (1.1 mmol, 115 mg) was stirred for 5−10 min under a nitrogen atmosphere. Then, to the reaction

flask anhydrous DCM (4 mL) was added followed by dropwise addition of an appropriate acid chloride (1 mmol). The resulting mixture was stirred at rt for 12 h. After this period, the reaction mixture was diluted with dichloromethane and washed with water and twice with 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 (silica gel, 100−200 mesh, EtOAc/hexanes = 1:4) furnished the corresponding benzamides **6d, 8a, 8b, 8d** and **20a-d**.

General procedure for the synthesis of benzamides 6a-6c, 6e and 8c. The corresponding carboxylic acid (3 mmol) was dissolved in dry DCM (15 mL) by adding 2 to 3 drops of dry DMF, to this reaction mixture oxalyl chloride (1.5 equiv, 190 mg) was added at 0 ^oC and then, the reaction mixture was stirred and allowed to attain rt over the period of 6-8 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuum to remove excess oxalyl chloride and solvent. The resultant acid chloride was dissolved in DCM (15 mL). Then, this DCM solution was added to a separate flask containing 4-amino-2,1,3-benzothiadiazole (2 mmol, 302 mg) and Et_3N (1.5 equiv, 303 mg) in DCM (3 mL) at 0 ^oC. After this the resultant reaction mixture was stirred and allowed to attain rt over the period of 6-8 h under a nitrogen atm. After this period, the reaction mixture was diluted with dichloromethane and then washed with water followed by saturated aqueous $NaHCO_3$ solution. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuum. Purification of the resulting reaction mixture by column chromatography (silica gel, 100−200 mesh, EtOAc/hexanes = 1:4) furnished benzamides **6a-6c**, **6e** and **8c**.

General procedure for the Pd(II)-catalyzed, ABTD-directed *ortho* C(sp^2)–H arylation and benzylation of benzamides 6a-e and 8a-d. An appropriate benzamide **6/8** (0.12 mmol, 1 equiv), $Pd(OAc)_2$ (10 mol%, 2.7 mg), an appropriate aryl iodide or 1-(bromomethyl)-4-nitrobenzene (0.36 mmol-0.48 mmol, 4 equiv) and AgOAc (0.24-0.264 mmol, 2-2.2 equiv,

40-43.8 mg,) in anhydrous toluene (3 mL) was heated at 110 ^{o}C for 24 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in vacuum and purification of the resulting reaction mixture by column chromatography furnished the corresponding *ortho* C(sp^2)–H arylated/benzylated benzamides **7/9/11/12** (see the corresponding Tables/Schemes for specific examples).

Procedure for the synthesis of the compound 27. The bis-arylated benzamide **9m** (0.05 mmol, 20 mg) and 40% aq. H_2SO_4 (2 mL) were heated at 120 °C for 24 h. After this period, the reaction mixture was diluted with water and extracted with ether (2 × 10 mL), the combined organic layers were dried over Na_2SO_4 and then, the solvent was removed under vacuum. The crude reaction mixture was purified by column chromatography on silica gel to afford the compound **27**.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)butyramide (1a).** Following the general procedure described above, **1a** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a colorless solid; R_f = 0.54 (EtOAc/Hexanes = 1:5); Yield: 90% (200 mg); mp 86-88 ^{o}C; IR (KBr): 3053, 1698, 1547, 1264, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 1H, J = 7.3 Hz), 8.50 (br. s, 1H), 7.67 (d, 1H, J = 8.8 Hz), 7.60 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.3 Hz), 2.53 (t, 2H, J = 7.4 Hz), 1.90-1.81 (m, 2H), 1.07 (t, 3H, J = 7.4 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 171.8, 154.7, 147.7, 131.2, 129.9, 115.6, 114.9, 39.8, 19.0, 13.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{12}N_3OS$: 222.0701; found 222.0695. The NH proton is perhaps merged with the doublet peak at δ 8.50 in the ^{1}H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)hexanamide (1b).** Following the general procedure described above, **1b** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a colorless solid; R_f = 0.50 (EtOAc/Hexanes = 1:5); Yield: 70% (174 mg); mp 98-100 ^{o}C; IR (KBr): 3396, 1662, 1521, 1257, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, 1H, J = 7.4 Hz), 8.50 (br. s, 1H), 7.68 (dd, 1H, J_1 = 8.9 Hz, J_2 = 1.0 Hz),

7.60 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.4 Hz), 2.55 (t, 2H, J = 7.4 Hz), 1.86-1.78 (m, 2H), 1.45-1.37 (m, 4H), 0.96-0.93 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.0, 154.7, 147.7, 131.2, 130.0, 115.6, 114.9, 37.9, 31.4, 25.2, 22.4, 14.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{12}H_{16}N_3OS$: 250.1014; found 250.1017. The NH proton is perhaps merged with the doublet peak at δ 8.51 in the ^1H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)heptanamide (1c).** Following the general procedure described above, **1c** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 15:85) as a pale yellow solid; R_f = 0.52 (EtOAc/Hexanes = 1:5); Yield: 98% (258 mg); mp 79-81 ^oC; IR (KBr): 3312, 2935, 2358, 1523 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (br. s, 1H), 8.48 (d, 1H, J = 7.5 Hz), 7.64 (dd, 1H, J_1 = 8.9 Hz, J_2 = 1.0 Hz), 7.56 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.5 Hz), 2.54 (t, 2H, J = 7.5 Hz), 1.83-1.75 (m, 2H), 1.44-1.38 (m, 2H), 1.36-1.30 (m, 4H), 0.89 (t, 3H, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.9, 154.7, 147.7, 131.1, 130.0, 115.5, 114.9, 37.9, 31.6, 28.9, 25.4, 22.5, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{18}N_3OS$: 264.1171; found 264.1174. The NH proton is perhaps merged with the doublet peak at δ 8.49 in the ^1H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)decanamide (1d).** Following the general procedure described above, **1d** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a colorless solid; R_f = 0.53 (EtOAc/Hexanes = 1:5); Yield: 73% (223 mg); mp 89-91 ^oC; IR (KBr): 3307, 1666, 1522, 1407, 1276, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, 1H, J = 7.4 Hz), 8.49 (br. s, 1H), 7.68 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.0 Hz), 7.61 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 2.55 (t, 2H, J = 7.4 Hz), 1.85-1.78 (m, 2H), 1.46-1.28 (m, 12H), 0.89 (t, 3H, J = 6.7 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.9, 154.7, 147.7, 131.2, 130.0, 115.6, 114.9, 37.9, 31.9, 29.4, 29.4, 29.3, 29.2, 25.5, 22.7, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{24}N_3OS$: 306.1640; found 306.1647.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)nonanamide (1e).** Following the general procedure described above, **1e** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 15:85) as a colorless solid; R_f = 0.53 (EtOAc/Hexanes = 1:5); Yield: 81% (236 mg); mp 80-82 ^{o}C; IR (KBr): 3309, 2916, 1657, 1409 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (br. s, 1H), 8.45 (d, 1H, J = 7.3 Hz), 7.62-7.59 (m, 1H), 7.56-7.51 (m, 1H), 2.52 (t, 2H, J = 7.4 Hz), 1.81-1.74 (m, 2H), 1.41-1.24 (m, 10H), 0.85 (t, 3H, J = 6.5 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.0, 154.7, 147.7, 131.1, 129.9, 115.5, 114.9, 37.9, 31.8, 29.3, 29.2, 29.1, 25.5, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{22}N_3OS$: 292.1484; found 292.1480.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)stearamide (1f).** Following the general procedure described above, **1f** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colorless solid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 98% (409 mg); mp 99-101 ^{o}C; IR (KBr): 3054, 1548, 1422, 1265, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 1H, J = 7.5 Hz), 8.50 (br. s, 1H), 7.67 (d, 1H, J = 8.8 Hz), 7.59 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.5 Hz), 2.55 (t, 2H, J = 7.5 Hz), 1.85-1.77 (m, 2H), 1.43-1.26 (m, 28H), 0.89 (t, 3H, J = 7.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 171.9, 154.7, 147.7, 131.2, 130.0, 115.6, 114.8, 37.9, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 25.5, 22.7, 14.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{40}N_3OS$: 418.2892; found 418.2889. The NH proton is perhaps merged with the doublet peak at δ 8.50 in the ^{1}H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)dodecanamide (1g).** Following the general procedure described above, **1g** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 15:85) as a pale yellow solid; R_f = 0.51 (EtOAc/Hexanes = 1:5); Yield: 75% (249 mg); mp 83-85 ^{o}C; IR (KBr): 3054, 2305, 1421, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 1H, J = 6.8 Hz), 8.51 (br. s, 1H), 7.66 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.0 Hz), 7.59 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 2.55 (t, 2H, J = 7.5 Hz), 1.85-1.77 (m, 2H), 1.44-1.26

(m, 16H), 0.88 (t, 3H, J= 6.6 Hz); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 172.0, 154.7, 147.7, 131.2, 130.0, 115.6, 114.9, 37.9, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 25.5, 22.7, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{28}N_3OS$: 334.1953; found 334.1949. The NH proton is perhaps merged with the doublet peak at δ 8.50 in the ^{1}H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-phenylpropanamide (1h).** Following the general procedure described above, **1h** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 15:85) as a colorless solid; R_f = 0.58 (EtOAc/Hexanes = 1:5); Yield: 90% (254 mg); mp 114-116 ^{o}C; IR (KBr): 3318, 2962, 1547, 1409 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, 1H, J= 7.3 Hz), 8.44 (br. s, 1H), 7.69 (d, 1H, J= 8.7 Hz), 7.61 (dd, 1H, J_1= 8.7 Hz, J_2= 7.3 Hz), 7.35-7.29 (m, 4H), 7.25-7.22 (m, 1H), 3.15 (t, 2H, J= 7.4 Hz), 2.88 (t, 2H, J= 7.4 Hz); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 154.7, 147.7, 140.4, 131.1, 129.8, 128.7, 128.4, 126.5, 115.8, 115.0, 39.5, 31.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{14}N_3OS$: 284.0858; found 284.0850.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)propionamide (1i).** Following the general procedure described above, **1i** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 80% (166 mg); mp 129-131 ^{o}C; IR (KBr): 3323, 1667, 1524, 1278, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 1H, J= 7.2 Hz), 8.50 (br. s, 1H), 7.67 (dd, 1H, J_1= 8.8 Hz, J_2= 0.9 Hz), 7.60 (dd, 1H, J_1= 8.8 Hz, J_2= 7.2 Hz), 2.59 (q, 2H, J= 7.6 Hz), 1.34 (t, 3H, J= 7.6 Hz); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 172.5, 154.7, 147.7, 131.2, 130.0, 115.6, 114.8, 30.9, 9.5; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_9H_{10}N_3OS$: 208.0545; found 208.0541. The NH proton is perhaps merged with the doublet peak at δ 8.50 in the ^{1}H NMR spectrum.

***N*-(Benzo[c][1,2,5]thiadiazol-4-yl)cyclopropanecarboxamide (1j).** Following the general procedure described above, **1j** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a colorless solid; R_f = 0.56 (EtOAc/Hexanes = 1:5);

Yield: 70% (153 mg); mp 142-144 ^{o}C; IR (KBr): 3314, 1656, 1558, 419 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (br. s, 1H), 8.46 (dd, 1H, J_1 = 7.4 Hz, J_2 = 1.0 Hz), 7.68 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.0 Hz), 7.60 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 1.80-1.71 (m, 1H), 1.21-1.75 (m, 2H), 1.0-0.95 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.4, 154.8, 147.7, 131.2, 130.1, 115.5, 114.8, 16.1, 8.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{10}N_3OS$: 220.0545; found 220.0540.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)cyclobutanecarboxamide (1k).** Following the general procedure described above, **1k** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a colorless solid; R_f = 0.56 (EtOAc/Hexanes = 1:5); Yield: 95% (221 mg); mp 169-171 ^{o}C; IR (KBr): 3399, 1656, 1555, 1257, 1098 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 1H, J = 7.2 Hz), 8.39 (br. s, 1H), 7.66 (d, 1H, J = 8.8 Hz), 7.59 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.2 Hz), 3.41-3.32 (m, 1H), 2.53-2.43 (m, 2H), 2.37-2.29 (m, 2H), 2.11-1.97 (m, 2H) ; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.7, 154.7, 147.7, 131.2, 130.0, 115.5, 114.8, 41.0, 25.4, 18.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{11}H_{12}N_3OS$: 234.0701; found 234.0710.

***N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)-2-phenylbutanamide (1aa).** The resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **1aa** as a pale yellow coloured viscous liquid; Yield: 85% (252 mg); R_f (EtOAc:Hexanes = 1:4) 0.78; IR (DCM): 3389, 2965, 1694, 1546, 747, cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.51 (br. s, 1H), 8.50 (d, 1H, J = 6.7 Hz), 7.63 (d, 1H, J = 8.8 Hz), 7.56 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.47-7.45 (m, 2H), 7.41 (t, 2H, J = 7.2 Hz); 7.32 (t, 1H, J = 7.2 Hz), 3.61 (t, 1H, J = 7.6 Hz), 2.39-2.32 (m, 1H), 2.01-1.94 (m, 1H), 1.00 (t, 3H, J = 7.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 172.2, 154.7, 147.7, 139.1, 131.1, 129.9, 129.1, 128.0, 127.7, 115.7, 114.7, 56.4, 26.4, 12.4; HRMS (ESI) calcd for $C_{16}H_{16}N_3OS$ $[M+H]^+$ 298.1014 found 298.1002.

***N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)-2-ethylbutanamide (1ab).** The resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **1ab** as a pale yellow colour solid; Yield: 87% (656 mg); mp: 60−62 °C; R_f (EtOAc:Hexanes = 1:4) 0.75; IR (DCM): 3321, 3056, 2964, 1693,748, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.55 (d, 1H, J = 7.3 Hz), 8.50 (br. s, 1H), 7.67 (d, 1H, J = 8.8 Hz), 7.60 (dd, 1H, J_1 = 8.0, J_2 = 7.4 Hz), 2.32-2.25 (m, 1H), 1.86-1.75 (m, 2H), 1.71-1.61 (m, 2H), 1.00 (t, 6H, J = 7.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.9, 154.7, 147.8, 131.2, 129.9, 115.6, 115.0, 52.4, 25.8, 12.1; HRMS (ESI) calcd for $C_{12}H_{16}N_3OS$ $[M+H]^+$ 250.1014 found 250.1003.

***N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)-4-methylnonanamide (1ac).** The resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **1ac** as a pale yellow colour solid; Yield: 90% (274 mg); mp: 90−92 °C; R_f (EtOAc:Hexanes = 1:4) 0.80; IR (DCM): 3314, 2919, 1667, 1523, 750, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.51 (br. s, 1H), 8.42 (d, 1H, J = 7.3 Hz), 7.56 (d, 1H, J = 8.8 Hz), 7.48 (dd, 1H, J_1 = 8.0, J_2 = 7.4 Hz), 2.58-2.44 (m, 2H), 1.83-1.76 (m, 1H), 1.61-1.52 (m, 1H), 1.49-1.45 (m, 1H), 1.32-1.18 (m, 7H), 1.14-1.08 (m, 1H), 0.89 (d, 3H, J = 6.6 Hz), 0.83 (t, 3H, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 172.1, 154.7, 147.6, 131.0, 129.9, 115.4, 114.9, 36.7, 35.6, 32.5, 32.4, 32.1, 26.6, 22.7, 19.4, 14.1; HRMS (ESI) calcd for $C_{16}H_{24}N_3OS$ $[M+H]^+$ 306.1640 found 306.1627.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-phenylbutanamide (3a).** Following the general procedure described above, **3a** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a brown liquid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 95% (35 mg); IR (DCM): 3321, 1696, 1543, 1517, 1408, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, 1H, J = 7.4 Hz), 8.35 (br. s, 1H), 7.67 (d, 1H, J = 8.8 Hz), 7.58 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.34-7.32 (m, 4H), 7.25-7.19 (m, 1H), 3.53-3.44 (m, 1H), 2.87 (dd, 1H, J_1 = 14.5 Hz, J_2 = 7.1 Hz), 2.78 (dd, 1H, J_1 = 14.5 Hz, J_2 =

7.7 Hz), 1.44 (d, 3H, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 154.7, 147.6, 145.4, 131.1, 129.8, 128.8, 126.8, 126.6, 115.7, 114.9, 46.7, 36.9, 21.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{16}N_3OS$: 298.1014; found 298.1008.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-nitrophenyl)butanamide (3b).** Following the general procedure described above, **3b** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown liquid; R_f = 0.46 (EtOAc/Hexanes = 1:5); Yield: 94% (40 mg); IR (DCM): 3387, 1547, 1516, 1408, 856 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, 1H, J = 7.4 Hz), 8.38 (br. s, 1H), 8.19 (d, 2H, J = 8.8 Hz), 7.68 (d, 1H, J = 8.3 Hz), 7.59 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.50 (d, 2H, J = 8.8 Hz), 3.67-3.61 (m, 1H), 2.87 (d, 2H, J = 7.4 Hz), 1.47 (d, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.4, 154.7, 153.2, 147.6, 146.7, 131.0, 129.5, 127.8, 124.0, 116.0, 115.2, 45.8, 36.6, 21.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{15}N_4O_3S$: 343.0865; found 343.0871.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(*p*-tolyl)butanamide (3c).** Following the general procedure described above, **3c** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow solid; R_f = 0.57 (EtOAc/Hexanes = 1:5); Yield: 75% (29 mg); mp 91-93 ^oC; IR (KBr): 3398, 1695, 1546, 1408, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, 1H, J = 7.3 Hz), 8.33 (br. s, 1H), 7.67 (d, 1H, J = 8.2 Hz), 7.59 (dd, 1H, J_1 = 8.6 Hz, J_2 = 7.4 Hz), 7.22 (d, 2H, J = 8.0 Hz), 7.14 (d, 2H, J = 8.0 Hz), 3.47-3.42 (m, 1H), 2.85 (dd, 1H, J_1 = 14.5 Hz, J_2 = 7.2 Hz), 2.76 (dd, 1H, J_1 = 14.5 Hz, J_2 = 7.4 Hz), 2.32 (s, 3H), 1.42 (d, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.5, 154.7, 147.6, 142.4, 136.2, 131.2, 129.8, 129.4, 126.6, 115.7, 114.9, 46.8, 36.5, 22.0, 21.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}N_3OS$: 312.1171; found 312.1176.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-cyanophenyl)butanamide (3d).** Following the general procedure described above, **3d** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.49 (EtOAc/Hexanes = 1:5); Yield: 52% (21 mg); mp 146-148 ^oC; IR (KBr): 3392, 1609, 1546, 1408, 832 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J= 7.4 Hz), 8.35 (br. s, 1H), 7.69 (d, 1H, J= 8.8 Hz), 7.62 (d, 2H, J= 8.4 Hz), 7.58 (d, 1H, J= 8.8 Hz), 7.44 (d, 2H, J= 8.4 Hz), 3.60-3.54 (m, 1H), 2.83 (dd, 2H, J_1= 7.3 Hz, J_2= 1.4 Hz), 1.44 (d, 3H, J= 7.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 154.7, 151.0, 147.6, 132.6, 131.0, 129.5, 127.7, 118.9, 116.0, 115.1, 110.5, 45.8, 36.8, 21.5; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{15}N_4OS$: 323.0967; found 323.0960.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-chlorophenyl)butanamide (3e).** Following the general procedure described above, **3e** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 97% (40 mg); mp 98-100 ^oC; IR (KBr): 3401, 1651, 1546, 1409, 1274, 679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, J= 7.3 Hz), 8.30 (br. s, 1H), 7.68 (d, 1H, J= 8.8 Hz), 7.58 (dd, 1H, J_1= 8.8 Hz, J_2= 7.3 Hz), 7.30-7.24 (m, 4H), 3.50-3.44 (m, 1H), 2.84-2.76 (m, 2H), 1.41 (d, 3H, J= 7.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.0, 154.7, 147.6, 143.9, 132.3, 131.0, 129.6, 128.9, 128.2, 115.8, 115.0, 46.5, 36.3, 21.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{15}ClN_3OS$: 332.0624; found 332.0629.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)butanamide (3f).** Following the general procedure described above, **3f** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 53% (22 mg); mp 93-95 ^oC; IR (KBr): 3401, 1611, 1512, 1408, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, 1H, J= 7.3 Hz),

8.33 (br. s, 1H), 7.66 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.9 Hz), 7.58 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.3 Hz), 7.24 (d, 2H, J = 8.6 Hz), 6.86 (d, 2H, J = 8.6 Hz), 3.77 (s, 3H), 3.46-3.40 (m, 1H), 2.84-2.72 (m, 2H), 1.40 (d, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.6, 158.2, 154.7, 147.6, 137.5, 131.1, 129.8, 127.7, 115.7, 114.9, 114.1, 55.2, 47.0, 36.2, 22.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}N_3O_2S$: 328.1120; found 328.1131.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(3-nitrophenyl)butanamide (3g).** Following the general procedure described above, **3g** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a brown liquid; R_f = 0.47 (EtOAc/Hexanes = 1:5); Yield: 60% (26 mg); IR (DCM): 3374, 1696, 1526, 1349, 897 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, 1H, J = 7.5 Hz), 8.42 (br. s, 1H), 8.21 (t, 1H, J = 1.9 Hz), 8.09-8.06 (m, 1H), 7.67 (dd, 2H, J_1 = 8.8 Hz, J_2 = 0.8 Hz), 7.57 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.5 Hz), 7.48 (t, 1H, J = 7.9 Hz), 3.67-3.61 (m, 1H), 2.94-2.83 (m, 2H), 1.48 (d, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 154.7, 148.5, 147.6, 147.5, 133.6, 131.0, 129.6, 129.5, 121.8, 121.6, 116.0, 115.1, 45.8, 36.4, 21.7; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{15}N_4O_3S$: 343.0865; found 343.0858. The NH proton is perhaps merged with the doublet peak at δ 8.42 in the ^1H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)butanamide (3h).** Following the general procedure described above, **3h** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a colorless liquid; R_f = 0.54 (EtOAc/Hexanes = 1:4); Yield: 63% (28 mg); IR (DCM): 3404, 1683, 1546, 1408, 1068 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, 1H, J = 7.3 Hz), 8.33 (br. s, 1H), 7.66 (d, 1H, J = 8.3 Hz), 7.59 (dd, 1H, J_1 = 8.7 Hz, J_2 = 7.4 Hz), 6.83-6.79 (m, 3H), 4.24-4.21 (m, 4H), 3.39-3.34 (m, 1H), 2.81 (dd, 1H, J_1 = 14.5 Hz, J_2 = 7.4 Hz), 2.72 (dd, 1H, J_1 = 14.5 Hz, J_2 = 7.4 Hz), 1.38 (d, 3H, J = 6.9 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.5, 154.7, 147.6, 143.6, 142.2, 138.8, 131.1, 129.8, 119.7, 117.5, 115.7,

115.4, 114.9, 64.4, 64.3, 46.8, 36.3, 22.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{18}N_3O_3S$: 356.1069; found 356.1068.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(3,4-dichlorophenyl)butanamide (3i):** Following the general procedure described above, **3i** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a brown viscous liquid; R_f = 0.57 (EtOAc/Hexanes = 1:5); Yield: 86% (39 mg); IR (neat): 3400, 1421, 1265, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, 1H, J = 7.4 Hz), 8.33 (br. s, 1H), 7.68 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.7 Hz), 7.58 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.41 (d, 1H, J = 2.0 Hz), 7.37 (d, 1H, J = 8.2 Hz), 7.16 (dd, 1H, J_1 = 8.2 Hz, J_2 = 2.0 Hz), 3.46 (m, 1H), 2.80-2.77 (m, 2H), 1.41 (d, 3H, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.6, 154.6, 147.6, 145.7, 132.7, 131.0, 130.6, 130.5, 129.5, 128.9, 126.4, 115.9, 115.1, 46.1, 36.1, 21.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}Cl_2N_3OS$: 366.0235; found 366.0223.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)hexanamide (3j).** Following the general procedure described above, **3j** was obtained from the carboxamide **1b** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown liquid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 62% (28 mg); IR (DCM): 3406, 1693, 1547, 1408, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, 1H, J = 7.2 Hz), 8.27 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.9 Hz, J_2 = 0.9 Hz), 7.56 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.2 Hz), 7.20 (d, 2H, J = 8.7 Hz), 6.84 (d, 2H, J = 8.7 Hz), 3.76 (s, 3H), 3.27-3.20 (m, 1H), 2.83 (dd, 1H, J_1 = 14.5 Hz, J_2 = 6.4 Hz), 2.75 (dd, 1H, J_1 = 14.5 Hz, J_2 = 8.4 Hz), 1.79-1.62 (m, 2H), 1.30-1.19 (m, 2H), 0.89 (t, 3H, J = 7.3 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 158.2, 154.7, 147.6, 135.8, 131.1, 129.8, 128.3, 115.6, 114.8, 114.1, 55.2, 45.9, 41.7, 38.6, 20.5, 14.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{22}N_3O_2S$: 356.1433; found 356.1423.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)heptanamide (3k).** Following the general procedure described above, **3k** was obtained from the carboxamide **1c** after

purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a yellow liquid; R_f = 0.56 (EtOAc/Hexanes = 1:5); Yield: 78% (36 mg); IR (DCM): 3054, 1547, 1421, 1265, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J = 7.4 Hz), 8.26 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.8 Hz), 7.56 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.20 (d, 2H, J = 8.6 Hz), 6.85 (d, 2H, J = 8.6 Hz), 3.76 (s, 3H), 3.23-3.19 (m, 1H), 2.83 (dd, 1H, J_1 = 14.5 Hz, J_2 = 6.4 Hz), 2.75 (dd, 1H, J_1 = 14.5 Hz, J_2 = 8.4 Hz), 1.80-1.66 (m, 2H), 1.35-1.14 (m, 4H), 0.85 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 158.2, 154.7, 147.6, 135.9, 131.1, 129.8, 128.3, 115.6, 114.8, 114.1, 55.2, 46.0, 41.9, 36.1, 29.6, 22.6, 14.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}N_3O_2S$: 370.1589; found 370.1580.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-phenyldecanamide (3l).** Following the general procedure described above, **3l** was obtained from the carboxamide **1d** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a yellow viscous liquid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 87% (41 mg); IR (neat): 3393, 2928, 2366, 1546 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J = 7.3 Hz), 8.30 (br. s, 1H), 7.64 (d, 1H, J = 8.6 Hz), 7.56 (dd, 1H, J_1 = 8.6 Hz, J_2 = 7.3 Hz), 7.33-7.21 (m, 4H), 7.20-7.17 (m, 1H), 3.31-3.24 (m, 1H), 2.89-2.77 (m, 2H), 1.80-1.70 (m, 2H), 1.28-1.22 (m, 10H), 0.86 (t, 3H, J = 6.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.5, 154.7, 147.6, 144.0, 131.1, 129.8, 128.7, 127.4, 126.6, 115.6, 114.9, 45.7, 42.7, 36.3, 31.8, 29.5, 29.2, 27.4, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{28}N_3OS$: 382.1953; found 382.1960.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)nonanamide (3m).** Following the general procedure described above, **3m** was obtained from the carboxamide **1e** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a yellow viscous liquid; R_f = 0.56 (EtOAc/Hexanes = 1:5); Yield: 72% (36 mg); IR (neat): 3339, 2364, 1513, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J = 7.4 Hz), 8.26 (br. s, 1H), 7.66 (d, 1H, J = 8.8 Hz), 7.56 (t, 1H, J = 8.8 Hz, J_2 = 7.4 Hz), 7.20 (d, 2H, J = 8.7 Hz), 6.85

(d, 2H, J = 8.7 Hz), 3.77 (s, 3H), 3.23-3.18 (m, 1H), 2.83 (dd, 1H, J_1 = 14.5 Hz, J_2 = 6.4 Hz), 2.75 (dd, 1H, J_1 = 14.5 Hz, J_2 = 8.6 Hz), 1.76-1.69 (m, 2H), 1.30-1.20 (m, 8H), 0.86 (t, 3H, J = 6.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 158.2, 154.7, 147.6, 135.9, 131.1, 129.8, 128.3, 115.6, 114.8, 114.1, 55.2, 46.0, 42.0, 36.4, 31.7, 29.2, 27.4, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{28}N_3O_2S$: 398.1902; found 398.1896.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)octadecanamide (3n).** Following the general procedure described above, **3n** was obtained from the carboxamide **1f** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.56 (EtOAc/Hexanes = 1:5); Yield: 90% (59 mg); mp 63-65 ^oC; IR (KBr): 3406, 1693, 1547, 1408, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J = 7.4 Hz), 8.26 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.9 Hz), 7.56 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.20 (d, 2H, J = 8.7 Hz), 6.84 (d, 2H, J = 8.7 Hz), 3.76 (s, 3H), 3.23-3.19 (m, 1H), 2.83 (dd, 1H, J_1 = 14.5 Hz, J_2 = 6.4 Hz), 2.74 (dd, 1H, J_1 = 14.5 Hz, J_2 = 8.5 Hz), 1.76-1.66 (m, 2H), 1.33-1.22 (m, 26H), 0.90 (t, 3H, J = 6.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 158.2, 154.7, 147.6, 135.9, 131.1, 129.8, 128.3, 115.6, 114.8, 114.1, 55.2, 46.0, 42.0, 36.4, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 27.4, 22.7, 14.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{31}H_{46}N_3O_2S$: 524.3311; found 524.3300.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(2-fluoropyridin-4-yl)butanamide (3o).** Following the general procedure described above, **3o** was obtained from the carboxamide **1a** after purification by column chromatography on silica gel (EtOAc:Hexanes = 2:3) as a yellow thick liquid; R_f = 0.48 (EtOAc/Hexanes = 1:3); Yield: 57% (22 mg); IR (neat): 3304, 2966, 1695, 1545 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, J = 7.3 Hz), 8.38 (br. s, 1H), 8.20 (d, 1H, J = 2.4 Hz), 7.78-7.74 (m, 1H), 7.70 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.9 Hz), 7.60 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.3 Hz), 6.91 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 3.59-3.54 (m, 1H), 2.83 (d, 2H, J = 7.2 Hz), 1.45 (d, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.4,

162.6 (d, $J_{C\text{-}F}$ = 236.4 Hz), 154.7, 147.6, 146.1 (d, $J_{C\text{-}F}$ = 14.5 Hz), 139.7 (d, $J_{C\text{-}F}$ = 7.6 Hz), 138.4 (d, $J_{C\text{-}F}$ = 4.5 Hz), 131.0, 129.5, 116.0, 115.2, 109.5 (d, $J_{C\text{-}F}$ = 37.1 Hz), 46.1, 33.5, 21.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{14}FN_4OS$: 317.0872; found 317.0865.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(6-fluoropyridin-3-yl)decanamide (3p).** Following the general procedure described above, **3p** was obtained from the carboxamide **1d** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow thick liquid; R_f = 0.50 (EtOAc/Hexanes = 1:3); Yield: 70% (35 mg); IR (KBr): 3054, 2349, 1547, 1265, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, 1H, J = 7.4 Hz), 8.35 (br. s, 1H), 8.15 (d, 1H, J = 2.2 Hz), 7.74-7.70 (m, 1H), 7.67 (d, 1H, J = 8.8 Hz), 7.57 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 6.90 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.9 Hz), 3.39-3.32 (m, 1H), 2.91 (dd, 1H, J_1 = 15.0 Hz, J_2 = 6.3 Hz), 2.75 (dd, 1H, J_1 = 15.0 Hz, J_2 = 8.5 Hz), 1.86-1.67 (m, 2H), 1.33-1.24 (m, 10H), 0.86 (t, 3H, J = 6.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 162.6 (d, $J_{C\text{-}F}$ = 236.5 Hz), 154.7, 147.6, 146.7 (d, $J_{C\text{-}F}$ = 14.2 Hz), 140.1 (d, $J_{C\text{-}F}$ = 7.6 Hz), 136.9 (d, $J_{C\text{-}F}$ = 4.4 Hz), 131.0, 129.5, 116.0, 115.1, 109.5 (d, $J_{C\text{-}F}$ = 37.2 Hz), 44.9, 39.1, 35.9, 31.7, 29.3, 29.1, 27.3, 22.6, 14.1; HRMS (ESI): *m/z* $[M - H]^+$ calcd for $C_{21}H_{24}FN_4OS$: 399.1655; found 399.1640.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(6-fluoropyridin-3-yl)dodecanamide (3q).** Following the general procedure described above, **3q** was obtained from the carboxamide **1g** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a yellow thick liquid; R_f = 0.51 (EtOAc/Hexanes = 1:3); Yield: 90% (48 mg); IR (KBr): 2926, 1693, 1547, 1408, 1274, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, 1H, J = 7.4 Hz), 8.33 (br. s, 1H), 8.16 (d, 1H, J = 2.2 Hz), 7.75-7.72 (m, 1H), 7.68 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.8 Hz), 7.58 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 6.90 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.9 Hz), 3.38-3.34 (m, 1H), 2.91 (dd, 1H, J_1 = 15.0 Hz, J_2 = 6.3 Hz), 2.76 (dd, 1H, J_1 = 15.0 Hz, J_2 = 8.5 Hz), 1.84-1.79 (m, 1H), 1.73-1.67 (m, 2H), 1.31-1.13 (m, 13H), 0.88 (t, 3H, J = 7.0 Hz);

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 162.6 (d, J_{C-F} = 236.4 Hz), 154.7, 147.6, 146.7 (d, J_{C-F} = 14.3 Hz), 140.1 (d, J_{C-F} = 7.8 Hz), 137.0 (d, J_{C-F} = 4.4 Hz), 131.0, 129.4, 116.0, 115.2, 109.5 (d, J_{C-F} = 37.1 Hz), 44.9, 39.1, 35.1, 31.8, 29.5, 29.4, 29.4, 29.3, 27.3, 22.7, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{30}FN_4OS$: 429.2124; found 429.2112.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-methoxyphenyl)-3-phenylpropanamide (3r).** Following the general procedure described above, **3r** was obtained from the carboxamide **1h** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown liquid; R_f = 0.54 (EtOAc/Hexanes = 1:5); Yield: 52% (26 mg); IR (DCM): 3326, 1696, 1546, 1512, 1408, 1272, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, 1H, J = 7.3 Hz), 8.38 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.9 Hz), 7.55 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.3 Hz), 7.34-7.29 (m, 4H), 7.25 (d, 2H, J = 8.6 Hz), 7.22-7.18 (m, 1H), 6.84 (d, 2H, J = 8.6 Hz), 4.71 (t, 1H, J = 7.8 Hz), 3.76 (s, 3H), 3.27 (d, 2H, J = 7.8 Hz); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.9, 158.3, 154.6, 147.6, 143.7, 135.4, 131.1, 129.7, 128.7, 128.7, 127.6, 126.6, 115.7, 115.0, 114.1, 55.2, 46.4, 44.7; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{20}N_3O_2S$: 390.1276; found 390.1268.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(3,4-dimethylphenyl)-3-phenylpropanamide (3s).** Following the general procedure described above, **3s** was obtained from the carboxamide **1h** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a reddish brown liquid; R_f = 0.56 (EtOAc/Hexanes = 1:5); Yield: 53% (25 mg); IR (neat): 3397, 2349, 1546, 1409, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, 1H, J = 7.4 Hz), 8.38 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8 Hz, J_2 = 0.8 Hz), 7.56 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.36-7.30 (m, 4H), 7.22-7.18 (m, 1H), 7.10-7.07 (m, 3H), 4.68 (t, 1H, J = 7.8 Hz), 3.29 (d, 2H, J = 7.8 Hz), 2.22 (s, 3H), 2.20 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.9, 154.7, 147.6, 143.7, 140.7, 136.9, 135.0, 131.1, 130.0, 129.8, 129.1, 128.7, 127.6, 126.6,

124.8, 115.7, 115.0, 46.9, 44.4, 19.9, 19.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{22}N_3OS$: 388.1484; found 388.1472.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(3-nitrophenyl)propanamide (3t).** Following the general procedure described above, **3t** was obtained from the carboxamide **1i** after purification by column chromatography on silica gel (EtOAc:Hexanes = 35:65) as a pale yellow solid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 56% (23 mg); mp 134-136 ^oC; IR (KBr): 3055, 2306, 1266, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, 1H, J = 7.4 Hz), 8.46 (br. s, 1H), 8.19 (s, 1H), 8.10 (d, 1H, J = 8.2 Hz), 7.71 (d, 1H, J = 8.8 Hz), 7.66 (d, 1H, J = 7.6 Hz), 7.62 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.49 (t, 1H, J = 7.9 Hz), 3.27 (t, 2H, J = 7.4 Hz), 2.95 (t, 2H, J = 7.4 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 154.7, 148.5, 147.6, 142.4, 134.9, 131.0, 129.6, 123.3, 121.7, 116.0, 115.2, 38.5, 30.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{13}N_4O_3S$: 329.0708; found 329.0699.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-(4-nitrophenyl)propanamide (3u).** Following the general procedure described above, **3u** was obtained from the carboxamide **1i** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow solid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 54% (22 mg); mp 180-182 ^oC; IR (KBr): 3384, 2342, 1516, 1344 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, 1H, J = 7.3 Hz), 8.44 (br. s, 1H), 8.19 (d, 2H, J = 8.7 Hz), 7.71 (dd, 1H, J_1 = 8.9 Hz, J_2 = 0.8 Hz), 7.62 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.3 Hz), 7.48 (d, 2H, J = 8.7 Hz), 3.26 (t, 2H, J = 8.7 Hz), 2.94 (t, 2H, J = 8.7 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.9, 154.9, 148.4, 147.8, 146.9, 131.2, 129.7, 129.6, 124.1, 116.3, 115.4, 38.6, 31.0; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{12}N_4NaO_3S$: 351.0528; found 351.0515.

3-(Benzo[*c*][1,2,5]thiadiazol-4-ylamino)-3-oxopropyl acetate (3v). Following the general procedure described above, **3v** was obtained from the carboxamide **1i** after purification by column chromatography on silica gel (EtOAc:Hexanes = 2:3) as a pale yellow solid; R_f =

0.49 (EtOAc/Hexanes = 1:3); Yield: 68% (23 mg); mp 122-124 ^{o}C; IR (KBr): 3327, 2365, 1736, 1244 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (br. s, 1H), 8.51 (d, 1H, J = 7.4 Hz), 7.71 (dd, 1H, J_1 = 8.9 Hz, J_2 = 0.9 Hz), 7.62 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.4 Hz), 4.52 (t, 1H, J = 5.9 Hz), 2.91 (t, 2H, J = 5.9 Hz), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 168.7, 154.7, 147.7, 131.1, 129.7, 116.0, 115.2, 60.2, 37.0, 21.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{11}H_{12}N_3O_3S$: 266.0599; found 266.0591.

3-(Benzo[*c*][1,2,5]thiadiazol-4-ylamino)-3-oxo-1-phenylpropyl acetate (3w). Following the general procedure described above, **3w** was obtained from the carboxamide **1h** after purification by column chromatography on silica gel (EtOAc:Hexanes = 35:65) as a yellow solid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 55% (25 mg); mp 133-135 ^{o}C; IR (KBr): 2349, 1547, 1262, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (br. s, 1H), 8.49 (d, 1H, J = 7.4 Hz), 7.72 (d, 1H, J = 8.8 Hz), 7.64-7.60 (m, 1H), 7.46-7.44 (m, 2H), 7.41-7.33 (m, 3H), 6.31 (dd, 1H, J_1 = 8.7 Hz, J_2 = 4.4 Hz), 3.20 (dd, 1H, J_1 = 15.1 Hz, J_2 = 8.7 Hz), 3.01 (dd, 1H, J_1 = 15.1 Hz, J_2 = 4.4 Hz), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.8, 167.8, 154.7, 147.7, 139.2, 131.1, 129.6, 128.8, 128.5, 126.2, 116.0, 115.3, 72.6, 44.9, 21.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{15}N_3NaO_3S$: 364.0732; found 364.0719.

Methyl 4-(3-(benzo[*c*][1,2,5]thiadiazol-4-ylamino)-3-oxopropyl)benzoate (3x). Following the general procedure described above, **3x** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a yellow viscous liquid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 51% (22 mg); IR (DCM): 3054, 1719, 1422, 1265, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.49 (d, 1H, J = 7.2 Hz), 8.43 (br. s, 1H), 7.99 (d, 2H, J = 7.5 Hz), 7.69 (d, 1H, J = 8.8 Hz), 7.61 (t, 1H, J = 7.5 Hz), 7.37 (d, 2H, J = 7.5 Hz), 3.91 (s, 3H), 3.20 (t, 2H, J = 7.4 Hz), 2.91 (t, 2H, J = 7.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 170.3, 167.0, 154.7, 147.6, 145.8, 131.1, 130.0, 129.7, 128.4, 115.9, 115.1, 52.0, 38.8, 31.2; HRMS (ESI) calcd for $C_{17}H_{16}N_3O_3S$ $[M+H]^+$ 342.0912 found 342.0897.

(*1R,2*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-(3-nitrophenyl)cyclopropanecarboxamide (4a).** Following the general procedure described above, **4a** was obtained from the carboxamide **1j** after purification by column chromatography on silica gel (EtOAc:Hexanes = 35:65) as a pale yellow solid; R_f = 0.54 (EtOAc/Hexanes = 1:5); Yield: 27% (11 mg); mp 149-151 ^{o}C; IR (KBr): 3369, 2364, 1527, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (br. s, 1H), 8.24 (t, 1H, J = 1.8 Hz), 8.20 (d, 1H, J = 7.5 Hz), 8.08-8.05 (m, 1H), 7.69-7.66 (m, 1H), 7.64 (d, 1H, J = 8.8 Hz), 7.49 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.5 Hz), 7.46-7.42 (m, 1H), 2.77 (dd, 1H, J_1 = 16.7 Hz, J_2 = 8.6 Hz), 2.40-2.34 (m, 1H), 2.03-1.99 (m, 1H), 1.64-1.58 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.6, 154.7, 148.0, 147.5, 138.5, 135.3, 131.1, 129.7, 128.9, 124.5, 121.9, 115.7, 114.9, 25.7, 24.9, 11.7; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{13}N_4O_3S$: 341.0708; found 341.0704.

(*1S*,2R*,3S)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,3-bis(3-nitrophenyl)cyclopropanecarboxamide (4aA).** Following the general procedure described above, **4aA** was obtained from the carboxamide **1j** after purification by column chromatography on silica gel (EtOAc:Hexanes = 2:3) as a red yellow solid; R_f = 0.42 (EtOAc/Hexanes = 1:4);Yield: 14% (8 mg); mp 175-177 ^{o}C; IR (KBr): 3367, 2366, 1527, 736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (br. s, 1H), 8.27 (d, 1H, J = 7.4 Hz), 8.20-8.19 (m, 2H), 8.12-8.09 (m, 2H), 7.67 (d, 1H, J = 8.8 Hz), 7.52 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.5 Hz), 7.51-7.48 (m, 2H), 7.39 (t, 2H, J = 7.9 Hz), 3.27 (d, 2H, J = 9.1 Hz), 2.88 (t, 1H, J = 9.1 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.9, 154.7, 147.8, 147.5, 136.8, 135.2, 131.0, 129.4, 128.6, 126.2, 122.1, 116.1, 115.3, 29.0, 28.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{16}N_5O_5S$: 462.0872; found 462.0858.

(*1R,2*S**)-2-(4-Acetylphenyl)-*N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)cyclopropanecarboxamide (4b).** Following the general procedure described above, **4b**

was obtained from the carboxamide **1j** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:1) as a pale yellow solid; R_f = 0.53 (EtOAc/Hexanes = 1:2); Yield: 28% (12 mg); mp 119-121 ^{o}C; IR (KBr): 3340, 2366, 1685, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (br. s, 1H), 8.24 (d, 1H, J = 7.4 Hz), 7.87 (d, 2H, J = 8.0 Hz), 7.63 (d, 1H, J = 8.8 Hz), 7.49 (t, 1H, J = 8.4 Hz), 7.44 (d, 2H, J = 8.0 Hz), 2.73 (dd, 1H, J_1 = 16.9 Hz, J_2 = 8.5 Hz), 2.56 (s, 3H), 2.36 (dd, 1H, J_1 = 14.1 Hz, J_2 = 8.0 Hz), 2.00 (dd, 1H, J_1 = 12.6 Hz, J_2 = 5.7 Hz), 1.56 (dd, 1H, J_1 = 13.6 Hz, J_2 = 8.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.8, 167.7, 154.7, 147.5, 142.1, 135.6, 131.1, 129.8, 129.3, 128.2, 115.6, 114.8, 26.6, 26.2, 25.3, 11.5; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{16}N_3O_2S$: 338.0963; found 338.0959. The corresponding diarylated compound **4bB** could not be isolated in pure form.

Diethyl 2,2'-((1*R,2*R**,3*S**)-2-(benzo[*c*][1,2,5]thiadiazol-4-ylcarbamoyl)cyclobutane-1,3-diyl)diacetate (4c):** Following the general procedure described above, **4c** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow color solid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 44% (22 mg); mp 53-55 ^{o}C; IR (KBr): 3338, 2364, 1734, 1182 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, 1H, J = 7.3 Hz), 8.50 (br. s, 1H), 7.69 (d, 1H, J = 8.8 Hz), 7.60 (t, 1H, J = 8.8 Hz), 4.05-3.93 (m, 4H), 3.62-3.58 (m, 1H), 3.07-2.96 (m, 2H), 2.82 (dd, 2H, J_1 = 16.7 Hz, J_2 = 9.6 Hz), 2.60 (dd, 2H, J_1 = 16.7 Hz, J_2 = 6.2 Hz), 2.36-2.29 (m, 1H), 2.10 (dd, 1H, J_1 = 21.4 Hz, J_2 = 10.7 Hz), 1.08 (t, 6H, J = 7.1 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.8, 171.5, 154.8, 147.7, 131.1, 129.9, 115.7, 114.8, 60.3, 48.5, 35.4, 32.6, 31.5, 14.0; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{19}H_{23}N_3NaO_5S$: 428.1256; found 428.1248.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(3-nitrophenyl)cyclobutanecarboxamide (5a).** Following the general procedure described above, **5a** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.47

(EtOAc/Hexanes = 1:4); Yield: 56% (34 mg); mp 190-192 ^{o}C; IR (KBr): 3380, 1524, 1410, 1348, 804 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (br. s, 1H), 8.21 (t, 2H, J = 1.9 Hz), 8.01-7.98 (m, 2H), 7.87 (d, 1H, J = 7.2 Hz), 7.68 (d, 2H, J = 7.8 Hz), 7.54 (dd, 1H, J_1 = 8.9 Hz, J_2 = 0.7 Hz), 7.42 (t, 2H, J = 7.9 Hz), 7.33 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.2 Hz), 4.30-4.17 (m, 3H), 3.61 (dd, 1H, J_1 = 21.7 Hz, J_2 = 10.8 Hz), 2.92-2.87 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.1, 154.4, 148.2, 147.3, 141.9, 133.1, 130.7, 129.2, 128.7, 122.0, 121.7, 116.1, 115.2, 54.0, 38.4, 29.6; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{23}H_{18}N_5O_5S$: 476.1029; found 476.1020.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(3-fluorophenyl)cyclobutanecarboxamide (5b).** Following the general procedure described above, **5b** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.47 (EtOAc/Hexanes = 1:5); Yield: 95% (50 mg); mp 181-183 ^{o}C; IR (KBr): 3054, 2306, 1265, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (br. s, 1H), 7.99 (d, 1H, J = 7.4 Hz), 7.54 (d, 1H, J = 8.8 Hz), 7.36 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.22-7.16 (m, 2H), 7.10 (br. s, 1H), 7.08 (br. s, 1H), 7.06-7.04 (m, 1H), 7.03-7.02 (m, 1H), 6.83-6.78 (m, 2H), 4.13-4.03 (m, 3H), 3.49-3.41 (m, 1H), 2.78-2.71 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.6, 162.8 (d, $J_{C\text{-}F}$ = 244.2 Hz), 154.5, 147.5, 142.7 (d, $J_{C\text{-}F}$ = 7.2 Hz), 130.9, 129.7 (d, $J_{C\text{-}F}$ = 8.2 Hz), 129.2, 122.5 (d, $J_{C\text{-}F}$ = 2.5 Hz), 115.5, 115.1, 114.0 (d, $J_{C\text{-}F}$ = 23.3 Hz), 113.3 (d, $J_{C\text{-}F}$ = 20.9 Hz), 54.1, 38.6, 29.7; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{23}H_{18}F_2N_3OS$: 422.1139; found 422.1151.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(2-nitrophenyl)cyclobutanecarboxamide (5c).** Following the general procedure described above, **5c** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow solid; R_f = 0.48

(EtOAc/Hexanes = 1:4); Yield: 71% (42 mg); mp 171-173 ^{o}C; IR (KBr): 3393, 3055, 1523, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (br. s, 1H), 7.82 (dd, 2H, J_1 = 8.1 Hz, J_2 = 1.2 Hz), 7.78 (d, 1H, J = 8.1 Hz), 7.65 (d, 2H, J = 7.8 Hz), 7.60-7.56 (m, 2H), 7.50 (d, 1H, J = 8.8 Hz), 7.31-7.26 (m, 3H), 4.68 (td, 1H, J_1 = 8.1 Hz, J_2 = 3.3 Hz), 4.42-4.35 (m, 2H), 3.57 (dd, 1H, J_1 = 21.7 Hz, J_2 = 10.9 Hz), 2.75-2.68 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.8, 154.4, 148.8, 147.4, 135.1, 133.1, 130.5, 129.7, 129.0, 127.5, 124.6, 115.6, 114.8, 55.2, 36.1, 27.9; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{23}H_{18}N_5O_5S$: 476.1029; found 476.1043.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-diphenylcyclobutanecarboxamide (5d).** Following the general procedure described above, **5d** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:5); Yield: 95% (45 mg); mp 171-173 ^{o}C; IR (KBr): 3358, 2360, 1667, 1544 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (br. s, 1H), 7.98 (d, 1H, J = 7.5 Hz), 7.52 (d, 1H, J = 8.8 Hz), 7.35-7.32 (m, 5H), 7.28-7.23 (m, 4H), 7.11 (t, 2H, J = 7.5 Hz), 4.12-4.09 (m, 3H), 3.57-3.49 (m, 1H), 2.79-2.72 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.1, 154.5, 147.6, 140.2, 131.0, 129.4, 128.2, 126.9, 126.3, 115.2, 114.9, 54.4, 39.0, 29.6; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{23}H_{20}N_3OS$: 386.1327; found 386.1320.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-di-*p*-tolylcyclobutanecarboxamide (5e).** Following the general procedure described above, **5e** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 1:4) as a pale yellow solid; R_f = 0.52 (EtOAc/Hexanes = 1:5); Yield: 79% (41 mg); mp 199-201 ^{o}C; IR (KBr): 3054, 2349, 1265, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (br. s, 1H), 8.04 (d, 1H, J = 7.4 Hz), 7.53 (d, 1H, J = 8.8 Hz), 7.36 (t, 1H, J = 8.2 Hz), 7.22 (d, 4H, J = 7.7 Hz), 7.04 (d, 4H, J = 7.7 Hz), 4.07-4.03 (m, 3H), 3.49-3.41 (m, 1H), 2.74-2.67 (m,

1H), 2.22 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.3, 154.5, 147.6, 137.1, 135.7, 131.1, 129.6 128.9, 126.9, 115.1, 114.9, 54.5, 38.8, 29.9, 21.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{24}N_3OS$: 414.1640; found 414.1632.

(*1S,2*R**,4*S**)-2,4-Bis(4-acetylphenyl)-*N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)cyclobutanecarboxamide (5f).** Following the general procedure described above, **5f** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 2:3) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:1); Yield: 93% (54 mg); mp 226-228 ^{o}C; IR (KBr): 3338, 2366, 1677, 1543 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (br. s, 1H), 7.94 (d, 1H, J = 7.5 Hz), 7.84 (d, 4H, J = 8.4 Hz), 7.56 (d, 1H, J = 8.9 Hz), 7.40 (d, 4H, J = 8.4 Hz), 7.33 (dd, 1H, J_1 = 8.9 Hz, J_2 = 7.5 Hz), 4.25-4.11 (m, 3H), 3.57 (dd, 1H, J_1 = 21.7 Hz, J_2 = 11.0 Hz), 2.85-2.78 (m, 1H), 2.51 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 197.8, 168.5, 154.5, 147.5, 145.8, 135.3, 130.9, 129.1, 128.4, 127.0, 115.7, 115.1, 54.3, 39.0, 29.6, 26.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{24}N_3O_3S$: 470.1538; found 470.1545.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(4-chlorophenyl)cyclobutanecarboxamide (5g).** Following the general procedure described above, **5g** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:4); Yield: 98% (55 mg); mp 189-191 ^{o}C; IR (KBr): 3297, 1661, 1549, 816 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (br. s, 1H), 7.99 (d, 1H, J = 7.4 Hz), 7.56 (d, 1H, J = 8.8 Hz), 7.37 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 7.25 (d, 4H, J = 8.6 Hz). 7.21 (d, 4H, J = 8.6 Hz), 4.07-3.99 (m, 3H), 3.48-3.40 (m, 1H), 2.76-2.68 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 168.7, 154.6, 147.5, 138,5, 132.2, 131.0, 129.2, 128.4, 128.3, 115.7, 115.1, 54.2, 38.4, 29.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{18}Cl_2N_3OS$: 454.0548; found 454.0536.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(4-bromophenyl)cyclobutanecarboxamide (5h).** Following the general procedure described above, **5h** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.55 (EtOAc/Hexanes = 1:4); Yield: 94% (63 mg); mp 202-204 ^{o}C; IR (KBr): 3293, 2366, 1547, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (br. s, 1H), 7.99 (d, 1H, J= 7.2 Hz), 7.57 (d, 1H, J= 8.9 Hz), 7.38 (dd, 1H, J_1= 8.9 Hz, J_2= 7.2 Hz), 7.36 (d, 4H, J= 8.5 Hz), 7.19 (d, 4H, J= 8.5 Hz), 4.09-3.97 (m, 3H), 3.42 (dd, 1H, J_1= 21.5 Hz, J_2= 10.6 Hz), 2.75-2.68 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.6, 154.6, 147.5, 139.0, 131.3, 130.9, 129.1, 128.7, 120.3, 115.7, 115.1, 54.1, 38.5, 29.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{18}Br_2N_3OS$: 541.9537; found 541.9549.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(4-methoxyphenyl)cyclobutanecarboxamide (5i).** Following the general procedure described above, **5i** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown liquid; R_f = 0.52 (EtOAc/Hexanes = 1:5); Yield: 90% (50 mg); IR (DCM): 2933, 1545, 1512, 1247, 828 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (br. s, 1H), 8.04 (dd, 1H, J_1= 7.4 Hz, J_2= 0.5 Hz), 7.52 (dd, 1H, J_1= 8.8 Hz, J_2= 0.5 Hz), 7.37 (dd, 1H, J_1= 8.8 Hz, J_2= 7.4 Hz), 7.27 (d, 4H, J= 8.7 Hz), 6.78 (d, 4H, J= 8.7 Hz), 4.05-3.99 (m, 3H), 3.71 (s, 6H), 3.47-3.39 (m, 1H), 2.73-2.68 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.4, 158.0, 154.6, 147.6, 132.2, 131.1, 129.6, 128.1, 115.2, 114.9, 113.6, 55.2, 54.6, 38.5, 30.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{23}N_3NaO_3S$: 468.1358; found 468.1381.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(3,5-dimethylphenyl)cyclobutanecarboxamide (5j).** Following the general procedure described above, **5j** was obtained from the carboxamide **1k** after purification by column

chromatography on silica gel (EtOAc:Hexanes = 1:4) as a pale yellow solid; R_f = 0.57 (EtOAc/Hexanes = 1:5); Yield: 98% (54 mg); mp 98-100 ^oC; IR (KBr): 3338, 2918, 2365, 1546 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (br. s, 1H), 8.05 (d, 1H, J= 7.4 Hz), 7.54 (d, 1H, J = 8.8 Hz), 7.39 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 6.94 (br. s, 4H), 6.71 (br. s, 2H), 4.09-3.98 (m, 3H), 3.41 (dd, 1H, J_1 = 21.6 Hz, J_2 = 10.8 Hz), 2.73-2.66 (m, 1H), 2.19 (s, 12H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 154.5, 147.6, 140.0, 137.6, 131.1, 129.6, 128.0, 124.7, 115.0, 114.7, 54.5, 38.9, 29.7, 21.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{28}N_3OS$: 442.1953; found 442.1941.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)cyclobutanecarboxamide (5k).** Following the general procedure described above, **5k** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 2:3) as a reddish yellow solid; R_f = 0.46 (EtOAc/Hexanes = 1:2); Yield: 95% (59 mg); mp 203-205 ^oC; IR (KBr): 3367, 2365, 1508, 1286 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (br. s, 1H), 8.08 (d, 1H, J= 7.4 Hz), 7.55 (d, 1H, J= 8.8 Hz), 7.40 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.4 Hz), 6.83 (d, 2H, J = 2.0 Hz), 6.79 (2H, dd, J_1 = 8.3 Hz, J_2 = 2.0 Hz), 6.71 (d, 2H, J = 8.3 Hz), 4.14 (s, 8H), 4.01-3.90 (m, 3H), 3.31 (dd, 1H, J_1 = 21.7 Hz, J_2 = 10.7 Hz), 2.68-2.61 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.2, 154.6, 147.6, 143.2, 142.0, 133.4, 131.1, 129.6, 120.0, 117.0, 115.9, 115.1, 114.8, 64.2, 64.2, 54.4, 38.4, 30.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{24}N_3O_5S$: 502.1437; found 502.1425.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(2-chloropyridin-4-yl)cyclobutanecarboxamide (5l).** Following the general procedure described above, **5l** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 70:30) as a pale yellow solid; R_f = 0.45 (EtOAc/Hexanes = 1:1); Yield: 58% (33 mg); mp 169-171 ^oC; IR (KBr): 3287, 2366, 1545, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (br. s, 1H), 8.23 (d, 2H, J= 5.1 Hz), 7.96 (d, 1H, J= 7.4 Hz), 7.63 (d, 1H, J=

8.8 Hz), 7.43 (dd, 1H, J_1 = 8.8 Hz, J_2 = 7.5 Hz), 7.26 (s, 2H), 7.13 (d, 2H, J = 5.0 Hz), 4.22-4.17 (m, 1H), 4.07-4.00 (m, 2H), 3.45 (dd, 1H, J_1 = 21.7 Hz, J_2 = 10.9 Hz), 2.80-2.74 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.4, 154.6, 152.1, 151.8, 149.5, 147.5, 130.8, 128.5, 122.7, 120.8, 116.5, 115.7, 53.5, 37.8, 28.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{16}Cl_2N_5OS$: 456.0453; found 456.0440.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(4-bromo-3-fluorophenyl)cyclobutanecarboxamide (5m).** Following the general procedure described above, **5m** was obtained from the carboxamide **1k** after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a pale yellow solid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 93% (67 mg); mp 163-165 ^oC; IR (KBr): 3293, 2364, 1413, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (br. s, 1H), 8.01 (d, 1H, J = 7.4 Hz), 7.60 (d, 1H, J = 8.8 Hz), 7.44-7.37 (m, 3H), 7.09 (dd, 2H, J_1 = 9.6 Hz, J_2 = 1.9 Hz), 6.97 (dd, 2H, J_1 = 8.2 Hz, J_2 = 1.9 Hz), 4.10-3.97 (m, 3H), 3.38 (dd, 1H, J_1 = 21.7 Hz, J_2 = 10.6 Hz), 2.76-2.69 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.2, 159.0 (d, $J_{C\text{-}F}$ = 250.0 Hz), 154.6, 147.5, 141.8 (d, $J_{C\text{-}F}$ = 6.4 Hz), 133.2, 130.9, 128.9, 123.8 (d, $J_{C\text{-}F}$ = 3.4 Hz), 116.0, 115.3 (d, $J_{C\text{-}F}$ = 22.1 Hz), 115.1, 106.8 (d, $J_{C\text{-}F}$ = 20.8 Hz), 54.0, 38.2, 29.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{16}Br_2F_2N_3OS$: 577.9349; found 577.9314.

(*1S,2*R**,4*S**)-*N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,4-bis(3-formylphenyl)cyclobutanecarboxamide (5n)**. The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **5n** as a brown colour solid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 35% (20 mg); mp 132-134 ^oC; IR (DCM): 3054, 2987, 1697, 1265, 741; cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.94 (s, 2H), 8.20 (br. s, 1H), 7.88 (d, 1H, J = 7.8 Hz), 7.85 (s, 2H), 7.64-7.60 (m, 4H), 7.52 (d, 1H, J = 8.8 Hz), 7.41 (t, 2H, J = 7.6 Hz), 7.31 (t, 1H, J = 7.9 Hz), 4.21-4.15 (m, 3H), 3.65-3.58 (m, 1H), 2.87-2.80 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 192.4, 168.5, 154.5, 147.4, 141.1, 136.3, 133.0, 130.8, 129.0,

128.9, 128.2, 128.0, 115.8, 115.0, 54.2, 38.6, 29.5; HRMS (ESI) calcd for $C_{25}H_{20}N_3O_3S$ $[M+H]^+$ 442.1225 found 442.1208.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-methylbenzamide (6a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **6a** as a pale yellow colour solid; R_f = 0.68 (EtOAc/Hexanes = 1:4); Yield: 60% (326 mg); mp: 147−149 °C; IR (DCM): 3054, 2305, 1265, 895, 743, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.88 (br. s, 1H), 8.68 (d, 1H, J = 7.2 Hz), 7.75 (d, 1H, J = 8.8 Hz), 7.70-7.66 (m, 2H), 7.46 (t, 1H, J = 7.1 Hz), 7.37-7.34 (m, 2H), 2.61.(s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.2, 154.8, 147.9, 136.9, 135.6, 131.6, 131.2, 130.9, 130.1, 127.1, 126.2, 116.0, 115.0, 20.2; HRMS (ESI) calcd for $C_{14}H_{12}N_3OS$ $[M+H]^+$ 270.0701 found 270.0708.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,3-dimethylbenzamide (6b)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **6b** as a yellow color solid; R_f = 0.70 (EtOAc/Hexanes = 1:4); Yield: 35% (100 mg); mp: 147−149 °C; IR (DCM): 3054, 2986, 1421, 895, 739, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.83 (br. s, 1H), 8.79 (d, 1H, J = 7.3 Hz), 7.75 (dd, 1H, J_1 = 8.8, J_2 = 0.8 Hz), 7.69 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.45 (d, 1H, J = 7.4 Hz), 7.33 (d, 1H, J = 7.4 Hz), 7.24 (t, 1H, J = 7.6 Hz), 2.46 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.0, 154.8, 147.9, 138.5, 136.6, 134.8, 132.1, 131.2, 130.1, 125.9, 124.6, 116.0, 115.1, 204, 16.5; HRMS (ESI) calcd for $C_{15}H_{14}N_3OS$ $[M+H]^+$ 284.0858 found 284.0862.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-methoxybenzamide (6c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **6c** as a yellow colour solid; R_f = 0.54

(EtOAc/Hexanes = 1:4); Yield: 25% (100 mg); mp: 144−146 °C; IR (DCM): 3054, 2986, 1550, 895, 747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 11.50 (br. s, 1H), 8.71 (dd, 1H, J_1 = 7.1, J_2 = 1.2 Hz), 8.35 (dd, 1H, J_1 = 7.8, J_2 = 1.8 Hz), 7.69 (dd, 1H, J_1 = 8.8, J_2 = 1.2 Hz), 7.66-7.62 (m, 1H), 7.57-7.53 (m, 1H), 7.19-7.15 (m, 1H), 7.10 (d, 1H, J = 8.3 Hz), 4.22 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 163.7, 157.7, 154.9, 148.5, 133.7, 132.5, 131.4, 130.9, 121.6, 121.2, 115.4, 115.3, 111.7, 56.3; HRMS (ESI) calcd for $C_{14}H_{12}N_3O_2S$ $[M+H]^+$ 286.0650 found 286.0659.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-chlorobenzamide (6d)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **6d** as a yellow color solid; R_f = 0.60 (EtOAc/Hexanes = 1:4); Yield: 86% (250 mg); mp: 141-143 °C**;** IR (DCM); 3053, 1699, 1456, 895, 747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.42 (br. s, 1H), 8.69 (d, 1H, J = 7.3 Hz), 7.90 (dd, 1H, J_1 = 7.4 J_2 = 1.9 Hz), 7.76 (dd, 1H, J_1 = 8.8 J_2 = 0.8 Hz), 7.70-7.66 (m, 1H), 7.55-7.43 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 164.6, 154.8, 147.9, 134.4, 132.2, 131.1, 131.0, 130.7, 130.7, 129.8, 127.4, 116.4, 115.5; HRMS (ESI) calcd for $C_{13}H_9ClN_3OS$ $[M+H]^+$ 290.0155 found 290.0150.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-methylbenzamide (6e)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to afford **6e** as a pale yellow solid; Yield: 51% (274 mg); R_f = 0.68 (EtOAc/Hexanes = 1:4); mp: 145−147 °C; IR (DCM): 3054, 1653, 1411, 1265,746, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.26 (br. s, 1H), 8.67 (d, 1H, J = 7.2 Hz), 7.84 (br. s, 1H), 7.82 (d, 1H, J = 6.7, Hz), 7.74 (d, 1H, J = 8.8, Hz), 7.70-7.66 (m, 1H), 7.48-7.49 (m, 2H), 2.50 (s, 3H) $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.8, 154.8, 148.1, 139.0, 134.2, 133.2, 131.2, 130.1, 128.9, 127.9, 124.2, 115.9, 115.0, 21.5, HRMS (ESI) calcd for $C_{14}H_{12}N_3OS$ $[M+H]^+$ 270.0701 found 270.0689.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4-methylbenzamide (8a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **8a** as a pale yellow color solid; R_f = 0.68 (EtOAc/Hexanes = 1:4); Yield: 94% (255 mg); mp: 118−120 °C; IR (DCM): 3053, 2986, 1548, 895, 741, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.27 (br. s, 1H), 8.67 (dd, 1H, J_1 = 7.2, J_2 = 1.0 Hz), 7.94 (d, 2H, J = 8.2 Hz), 7.74 (dd, 1H, J_1 = 8.8, J_2 = 1.1 Hz), 7.68 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.38 (d, 2H, J = 7.9 Hz), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.6, 154.8, 148.1, 143.1, 131.3, 130.2, 129.7, 129.2, 127.2, 115.8, 115.0, 21.6; HRMS (ESI) calcd for $C_{14}H_{12}N_3OS$ $[M+H]^+$ 270.0701 found 270.0711.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4-chlorobenzamide (8b)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **8b** as a pale yellow color solid; R_f = 0.60 (EtOAc/Hexanes = 1:4); Yield: 60% (174 mg); mp: 151−153 °C**;** IR (DCM): 3054, 2986, 1548, 1265, 741, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.21 (br. s, 1H), 8.64 (dd, 1H, J_1 = 7.3, J_2 = 0.8 Hz), 7.97 (d, 2H, J= 8.7 Hz), 7.75 (dd, 1H, J_1 = 8.8, J_2 = 1.0 Hz), 7.68 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.55 (d, 2H, J= 8.7 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 164.5, 154.8, 148.0, 138.8, 132.5, 131.2, 129.8, 129.3, 128.6, 116.2, 115.2; HRMS (ESI) calcd for $C_{13}H_9ClN_3OS$ $[M+H]^+$ 290.0155 found 290.0161.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4-methoxybenzamide (8c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **8c** as a pale yellow solid; R_f = 0.54 (EtOAc/Hexanes = 1:4); Yield: 35% (100 mg); mp: 150−152 °C**;** IR (DCM): 3054, 2986, 2305, 895, 741, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.22 (br. s, 1H), 8.65 (dd, 1H, J_1 = 7.2, J_2= 1.0 Hz), 8.01 (d, 2H, J= 8.8 Hz), 7.72 (dd, 1H, J_1 = 8.8, J_2= 1.1 Hz), 7.67 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.06 (d, 2H, J= 8.8 Hz), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ

165.1, 162.9, 154.8, 148.1, 131.3, 129.2, 126.4, 115.7, 114.8, 114.2, 55.6; HRMS (ESI) calcd for $C_{14}H_{12}N_3O_2S$ $[M+H]^+$ 286.0650 found 286.0644.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)benzamide (8d)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **8d** as a pale yellow color solid; R_f = 0.70 (EtOAc/Hexanes = 1:4); Yield: 70% (177 mg); mp: 124−126 °C; IR (DCM): 3054, 2986, 1681, 895, 747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.27 (br. s, 1H), 8.66 (dd, 1H, J_1 = 7.2, J_2 = 0.6 Hz), 8.03 (d, 2H, J = 7.0 Hz), 7.73 (dd, 1H, J_1 = 8.8, J_2 = 0.9 Hz), 7.67 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.62 (d, 1H, J = 7.2 Hz), 7.57 (t, 1H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.6, 154.8, 148.0, 134.2, 132.4, 131.2, 130.0, 129.0, 127.2, 116.0, 115.1; HRMS (ESI) calcd for $C_{13}H_{10}N_3OS$ $[M+H]^+$ 256.0545 found 256.0547.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-ethyl-3-methyl-[1,1'-biphenyl]-2-carboxamide (7a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7a** as a pale yellow semi-solid; R_f = 0.72 (EtOAc/Hexanes = 1:4); Yield: 70% (21 mg); IR (DCM): 3054, 2986, 1421, 1265, 895 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.50 (dd, 1H, J_1 = 7.2, J_2 = 0.8 Hz), 8.26 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8, J_2 = 0.9 Hz), 7.59 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.46 (d, 1H, J = 7.6 Hz), 7.41 (d, 2H, J = 8.3 Hz), 7.32 (t, J = 2H, 7.5 Hz), 7.06 (d, 2H, J = 8.0 Hz), 2.55 (s, 3H), 2.46 (q, 2H, J = 7.6 Hz), 0.98 (t, 3H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.6, 154.6, 147.6, 143.6, 139.8, 137.4, 136.2, 135.7, 131.0, 129.9, 129.7, 129.5, 128.5, 127.9, 127.6, 115.8, 114.8, 28.3, 19.8, 15.3; HRMS (ESI) calcd for $C_{22}H_{20}N_3OS$ $[M+H]^+$ 374.1327 found : 374.1319.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-methoxy-3-methyl-[1,1'-biphenyl]-2-carboxamide (7b)**. Following the general procedure described above, the resultant crude mixture was

purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7b** as a pale yellow solid; R_f = 0.46 (EtOAc/Hexanes = 1:4); Yield: 58% (25 mg); mp: 112−114 °C; IR (DCM): 3054, 2987, 2305, 1683, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.53 (d, 1H *J* = 7.3 Hz), 8.30 (br. s, 1H), 7.66 (d, 1H, *J* = 8.8 Hz), 7.60 (dd, 1H J_1 = 8.8, J_2 = 7.3 Hz), 7.45 (d, 2H, *J* = 8.6 Hz), 7.46-7.42 (m, 1H), 7.31 (d, 1H, *J* = 7.6 Hz), 7.29 (d, 1H, *J* = 7.6 Hz), 6.80 (d, 2H, *J* = 8.6 Hz), 3.68 (s, 3H), 2.54 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.7, 159.1, 154.6, 147.6, 139.3, 136.1, 135.8, 132.5, 131.0, 129.8, 129.7, 129.3, 127.6, 115.9, 114.9, 113.9, 55.1, 19.8; HRMS (ESI) calcd for $C_{21}H_{18}N_3O_2S$ $[M+H]^+$ 376.1120 found 376.1130.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-methyl-[1,1'-biphenyl]-2-carboxamide (7c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7c** as a pale yellow solid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 55% (22 mg); mp: 154−156 °C**;** IR (DCM): 2987, 2306, 1422, 1265, 743 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.36 (d, 1H, *J* = 7.5 Hz), 8.31 (d, 1H, *J* = 8.2 Hz), 8.22 (d, 1H, *J* = 8.9 Hz), 7.85 (dd, 1H, J_1 = 8.8, J_2 = 7.0 Hz), 7.72-7.69 (m, 2H), 7.44 (d, 1H, *J* = 7.4 Hz), 7.30-7.21 (m, 3H), 6.49 (d, 1H, *J* = 8.1 Hz), 2.92 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 162.5, 156.3, 152.1, 143.3, 138.6, 135.9, 132.3, 132.0, 131.0, 130.5, 129.6, 129.2, 123.8, 122.8, 122.6, 120.3, 119.5, 115.9, 24.5; HRMS (ESI) calcd for $C_{20}H_{16}N_3OS$ $[M+H]^+$ 346.1014 found 346.1015. The NH proton was detected in the ^1H NMR spectrum.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-methyl-3'-nitro-[1,1'-biphenyl]-2-carboxamide (7d)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7d** as a pale yellow solid; R_f = 0.40 (EtOAc/Hexanes = 1:4); Yield: 65% (30 mg); mp: 133−135 °C**;** IR (DCM): 3055, 2987, 2305, 1422, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, 1H, *J* = 7.4 Hz), 8.42 (br. s, 1H), 8.34 (br. s, 1H), 8.03 (dd, 1H, J_1 = 8.2, J_2 = 0.9 Hz), 7.85 (d, 1H, *J* = 7.7 Hz), 7.69 (d,

1H, J = 8.9 Hz), 7.59 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.52 (t, 1H, J = 7.6 Hz), 7.43 (t, 2H, J = 7.8 Hz), 7.36 (d, 1H, J = 7.6 Hz), 2.57 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.7, 154.6, 148.2, 147.5, 141.7, 137.1, 136.4, 135.9, 134.6, 130.9, 130.8, 130.1, 129.4, 129.2, 127.5, 123.6, 122.5, 116.5, 115.4, 19.7; HRMS (ESI) calcd for $C_{20}H_{15}N_4O_3S$ $[M+H]^+$ 391.0865 found 391.0857.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3,3',5'-trimethyl-[1,1'-biphenyl]-2-carboxamide (7e)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7e** as a pale yellow solid; R_f = 0.64 (EtOAc/Hexanes = 1:4); Yield: 58% (26 mg); mp: 118−120 °C**;** IR (DCM): 3055, 2987, 2305, 1422, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.49 (dd, 1H, J_1 = 7.2, J_2 = 0.9 Hz), 8.26 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8, J_2 = 1.1 Hz), 7.59 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.44 (t, 1H, J = 7.6 Hz), 7.32 (d, 1H, J = 7.7 Hz), 7.31 (d, 1H, J = 7.7 Hz), 7.10 (br. s, 2H), 6.69 (br. s, 1H), 2.55 (s, 3H), 2.15 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.6, 154.6, 147.6, 140.1, 140.0, 137.9, 136.2, 135.7, 131.0, 130.0, 129.7, 129.5, 129.0, 127.5, 126.4, 115.7, 114.6, 21.1, 19.9; HRMS (ESI) calcd for $C_{22}H_{20}N_3OS$ $[M+H]^+$ 374.1327 found 374.1322.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-6-methylbenzamide (7f).** Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7f** as a pale yellow colour solid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 77% (37 mg); mp: 159−161 °C**;** IR (DCM): 3055, 2987, 2305, 1422, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.52 (dd, 1H, J_1 = 7.2, J_2 = 0.8 Hz), 8.32 (br. s, 1H), 7.67 (dd, 1H, J_1 = 8.8, J_2 = 1.0 Hz), 7.61 (dd, 1H, J_1 = 8.8, J_2 = 7.3 Hz), 7.42 (dd, 1H, J_1 = 8.0, J_2 = 7.8 Hz), 7.29 (d, 2H, J = 7.0 Hz), 7.04 (d, 1H, J = 2.2 Hz), 6.97 (dd, 1H, J_1 = 8.4, J_2 = 2.2 Hz), 6.71 (d, 1H, J = 8.3 Hz), 4.13-4.10 (m, 4H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.5, 154.7, 147.7, 143.4,

139.1, 136.1, 135.7, 133.5, 131.1, 129.9, 129.7, 129.4, 127.6, 121.8, 117.5, 117.2, 115.9, 115.0, 64.3, 64.2, 19.8; HRMS (ESI) calcd for $C_{22}H_{18}N_3O_3S$ $[M+H]^+$ 404.1069 found 404.1065.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-ethyl-3,4-dimethyl-[1,1'-biphenyl]-2-carboxamide (7g)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7g** as a pale yellow colour semi-solid; R_f = 0.65 (EtOAc/Hexanes = 1:4); Yield: 58% (27 mg); IR (DCM): 3054, 2987, 2686, 1547, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.51 (dd, 1H, J_1 = 7.2, J_2 = 1.0 Hz), 8.31 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.9, J_2 = 1.0 Hz), 7.59 (dd, 1H, J_1 = 8.8, J_2 = 7.2 Hz), 7.40 (d, 2H, J = 8.2 Hz), 7.34 (d, 1H, J = 7.8 Hz), 7.24 (d, 1H, J = 7.8 Hz), 7.05 (d, 2H, J = 8.2 Hz), 2.46 (q, 2H, J = 7.6 Hz), 2.43 (s, 3H), 2.40 (s, 3H), 0.99 (t, 3H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.2, 154.6, 147.6, 143.3, 137.5, 137.4, 136.6, 136.2, 134.2, 131.1, 131.0, 129.9, 128.5, 127.8, 127.4, 115.8, 114.9, 28.3, 20.2, 16.7, 15.3; HRMS (ESI) calcd for $C_{23}H_{22}N_3OS$ $[M+H]^+$ 388.1484 found 388.1484.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-ethyl-3-methoxy-[1,1'-biphenyl]-2-carboxamide (7h)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7h** as a pale yellow colour solid; R_f = 0.64 (EtOAc/Hexanes = 1:4); Yield: 50% (21 mg); mp: 152−154 °C; IR (DCM): 3054, 2986, 1421, 895, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.63 (br. s, 1H), 8.53 (d, 1H, J = 7.3 Hz), 7.66 (d, 1H, J = 8.8 Hz), 7.59 (dd, 1H, J_1 = 8.6, J_2 = 7.6 Hz), 7.49 (t, 1H, J = 8.0 Hz), 7.42 (d, 2H, J = 7.9 Hz), 7.13-7.08 (m, 3H), 7.03 (d, 1H, J = 8.4 Hz), 3.93 (s, 3H), 2.54 (q, 2H, J = 7.6 Hz), 1.10 (t, 3H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.2, 156.8, 154.7, 147.7, 143.7, 141.9, 137.0, 131.2, 130.9, 130.1, 128.4, 127.9, 125.2, 122.7, 115.6, 115.0, 109.9, 56.1, 28.4, 15.3; HRMS (ESI) calcd for $C_{22}H_{19}N_3NaO_2S$ $[M+Na]^+$ 412.1096 found 412.1087.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-chloro-4'-methoxy-[1,1'-biphenyl]-2-carboxamide (7i)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7i** as a green colour semi-solid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 70% (33 mg); IR (DCM): 3054, 2987, 1689, 1422, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (d, 1H, J = 7.3, Hz), 8.45 (br. s, 1H), 7.70 (d, 1H, J = 8.8 Hz), 7.61 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.50-7.44 (m, 4H), 7.38 (dd, 1H, J_1 = 6.0, J_2 = 6.0 Hz), 6.84 (d, 2H, J = 8.7 Hz), 3.72 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.5, 159.5, 154.7, 147.6, 141.5, 135.1, 131.8, 131.1, 131.0, 130.7, 129.7, 129.5, 128.7, 128.4, 116.3, 115.4, 114.0, 55.2; HRMS (ESI) calcd for $C_{20}H_{15}ClN_3O_2S$ $[M+H]^+$ 396.0574 found 396.0554.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-chloro-3'-nitro-[1,1'-biphenyl]-2-carboxamide (7j)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7j** as a pale yellow colour solid; R_f = 0.39 (EtOAc/Hexanes = 1:4); Yield: 53% (26 mg); mp: 198−200 °C**;** IR (DCM): 3055, 2987, 1422, 1265, 741 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.57 (br. s, 1H), 8.44 (d, 1H J = 7.4 Hz), 8.41 (br. s, 1H), 8.12 (d, 1H, J = 8.2 Hz), 7.87 (d, 1H, J = 7.6 Hz), 7.71 (d, 1H, J = 8.8 Hz), 7.61-7.54 (m, 3H,), 7.49 (t, 1H, J = 8.0 Hz), 7.43 (d, 1H, J = 7.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 164.5, 154.6, 148.2, 147.5, 140.4, 139.4, 135.3, 134.6, 132.1, 131.2, 130.9, 130.0, 129.6, 129.0, 128.6, 123.6, 123.1, 116.8, 115.8; HRMS (ESI) calcd for $C_{19}H_{12}ClN_4O_3S$ $[M+H]^+$ 411.0319 found 411.0311.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-chloro-4'-ethyl-[1,1'-biphenyl]-2-carboxamide (7k)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7k** as a greenish yellow colour semi-solid; R_f = 0.64 (EtOAc/Hexanes = 1:4); Yield: 65% (30 mg); IR (DCM): 3054, 2305, 1422, 896, 741 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.51 (d, 1H, J = 7.3 Hz), 8.44 (br. s,

1H), 7.68 (d, 1H, J = 8.8 Hz), 7.60 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.50-7.46 (m, 2H), 7.43 (d, 2H, J = 8.1 Hz), 7.41-7.39 (m, 1H), 7.12 (d, 2H, J = 8.1 Hz), 2.53 (q, 2H, J = 7.6 Hz), 1.07 (t, 3H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.4, 154.6, 147.6, 144.3, 141.9, 136.1, 135.1, 131.8, 131.0, 130.7, 129.5, 128.7, 128.6, 128.4, 128.1, 116.2, 115.3, 28.4, 15.2; HRMS (ESI) calcd for $C_{21}H_{17}ClN_3OS$ $[M+H]^+$ 394.0781 found 394.0783.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-chloro-[1,1'-biphenyl]-2-carboxamide (7l)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7l** as a pale yellow colour semi-solid; R_f = 0.59 (EtOAc/Hexanes = 1:4); Yield: 60% (26 mg); IR (DCM): 3384, 2923, 1688, 1547, 784 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.51 (dd, 1H, J_1 = 7.4, J_2 = 0.6 Hz), 8.45 (br. s, 1H), 7.69 (dd, 1H, J_1 = 8.9, J_2 = 0.9 Hz), 7.60 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.54-7.48 (m, 4H), 7.41 (dd, 1H, J_1 = 6.9, J_2 = 6.9 Hz), 7.31 (t, 2H, J = 7.4 Hz), 7.25-7.20 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.2, 154.6, 147.6, 141.9, 138.8, 135.2, 131.8, 131.0, 130.8, 129.4, 128.8, 128.7, 128.6, 128.5, 128.1, 116.3, 115.3; HRMS (ESI) calcd for $C_{19}H_{13}ClN_3OS$ $[M+H]^+$ 366.0468 found 366.0454.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-chloro-6-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)benzamide (7m)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7m** as a greenish yellow colour semi-solid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 59% (30 mg); mp: 98−100 °C**;** IR (DCM): 2987, 2305, 1422, 896, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (d, 1H, J = 7.3 Hz), 8.48 (br. s, 1H), 7.70 (d, 1H, J = 8.8 Hz), 7.62 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.49-7.44 (m, 2H), 7.36 (dd, 1H, J_1 = 6.8, J_2 = 6.8 Hz), 7.03 (d, 1H, J = 2.0 Hz), 6.99 (dd, 1H, J_1 = 8.3, J_2 = 2.0 Hz), 6.76 (d, 1H, J = 8.3 Hz), 4.16 (s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.4, 154.7, 147.7, 143.6, 143.5, 141.3, 135.0, 132.1, 131.8, 131.1, 130.7,

129.6, 128.6, 128.5, 121.7, 117.6, 117.4, 116.2, 115.4, 64.3, 64.2; HRMS (ESI) calcd for $C_{21}H_{15}ClN_3O_3S$ $[M+H]^+$ 424.0523 found 424.0529.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-chloro-3',5'-dimethyl-[1,1'-biphenyl]-2-carboxamide (7n)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **7n** as a pale yellow colour solid; R_f = 0.65 (EtOAc/Hexanes = 1:4); Yield: 75% (35 mg); mp: 116−118 °C**;** IR (DCM): 3054, 2986, 1421, 895, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.49 (dd, 1H, J_1 = 7.3, J_2 = 0.6 Hz), 8.43 (br. s, 1H), 7.69 (dd, 1H, J_1 = 8.9, J_2 = 0.9 Hz), 7.61 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.51-7.45 (m, 2H), 7.39 (dd, 1H, J_1 = 7.1, J_2 = 7.1 Hz), 7.11 (s, 2H), 6.80 (s, 1H), 2.19 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.3, 154.6, 147.6, 142.2, 138.7, 138.1, 135.1, 131.8, 131.0, 130.7, 129.7, 129.6, 128.6, 128.6, 126.3, 116.1, 115.2, 21.2; HRMS (ESI) calcd for $C_{21}H_{17}ClN_3OS$ $[M+H]^+$ 394.0781 found 394.0770.

***N*-(benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-methoxy-4-methyl-[1,1'-biphenyl]-2-carboxamide (7o)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to afford **7o** as a pale yellow viscous liquid; Yield: 44% (20 mg); R_f = 0.52 (EtOAc/Hexanes = 1:4); IR (DCM): 3385, 3057, 1545, 1265, 744, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (d, 1H, J= 7.1 Hz), 8.43 (br. s, 1H), 7.72 (br. s, 1H), 7.65 (dd, 1H, J_1 = 8.8, J_2= 1.0, Hz), 7.60 (dd, 1H, J_1 = 8.8, J_2= 7.2, Hz), 7.42 (d, 2H, J = 8.6, Hz), 7.39-7.36 (m, 2H), 6.85 (d, 2H, J = 8.6, Hz), 3.71 (s, 3H) 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.2, 159.5, 154.6, 147.5, 137.4, 137.0, 134.6, 131.9, 131.8, 131.1, 130.6, 130.1, 130.0, 115.7, 114.5, 114.3, 55.2, 21.0; HRMS (ESI) calcd for $C_{21}H_{18}N_3O_2S$ $[M+H]^+$ 376.1120 found 376.1106.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4''-dimethoxy-4'-methyl-[1,1':3',1''-terphenyl]-2'-carboxamide (7o′)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to afford **7o′**as a pale yellow viscous liquid; Yield: <10% (6 mg); R_f =

0.45 (EtOAc/Hexanes = 1:4); IR (DCM): 3385, 3057, 1545, 1265, 744, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.25 (br. s, 1H), 8.17 (d, 1H, *J* = 7.4 Hz), 7.58 (d, 1H, *J* = 8.8, Hz), 7.47-7.43 (m, 4H), 7.36 (d, 1H, *J* = 7.8 Hz), 7.26 (d, 2H, *J* = 7.4 Hz), 6.81 (d, 4H, *J* = 8.6, Hz), 3.71 (s, 3H), 3.70 (s, 3H), 2.21 (s, 3H); HRMS (ESI) calcd for $C_{28}H_{24}N_3O_3S$ $[M+H]^+$ 482.1538 found 482.1521. This compound contains residual grease impurity and purity of this compound is about 90-95% and for this compound only a representable proton NMR was recorded.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4-methyl-3'-nitro-[1,1'-biphenyl]-2-carboxamide (7p)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to afford **7p** as a pale yellow solid; Yield: <10% (6 mg); R_f = 0.42 (EtOAc/Hexanes = 1:4); mp: 161−163 °C; IR (DCM): 3054, 2987, 1526, 1265, 747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.48 (br. s, 1H), 8.48 (d, 1H, *J* = 6.9, Hz), 8.42 (br. s, 1H), 8.10 (d, 1H, *J* = 8.7, Hz), 7.77 (d, 1H, *J* = 8.6, Hz), 7.72 (br. s, 1H), 7.68 (d, 1H, *J* = 8.8, Hz), 7.60 (dd, 1H, J_1 = 7.8, J_2 = 7.6, Hz), 7.49-7.42 (m, 3H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.2, 154.6, 148.5, 147.5, 141.6, 139.2, 135.1, 135.0, 132.1, 131.0, 130.7, 129.6, 129.5, 129.5, 123.6, 122.5, 116.2, 115.0, 21.2; HRMS (ESI) calcd for $C_{20}H_{15}N_4O_3S$ $[M+H]^+$ 391.0865 found 391.0852. This compound contains residual grease impurity and purity of this compound is about 95%.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4'-methyl-3,3''-dinitro-[1,1':3',1''-terphenyl]-2'-carboxamide (7p′)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to afford **7p′**as a pale yellow solid; Yield: <20% (13 mg); R_f = 0.36 (EtOAc/Hexanes = 1:4); mp: 159−161 °C; IR (DCM): 3054, 2987, 1526, 1265, 747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.45 (br. s, 1H), 8.32 (br. s, 1H), 8.24 (br. s, 1H), 8.09 (d, 2H, *J* = 8.1, Hz), 8.00 (d, 1H, *J* = 7.4, Hz), 7.86 (d, 1H, *J* = 7.8, Hz), 7.71 (d, 1H, *J* = 7.6, Hz), 7.62-7.58 (m, 2H), 7.53-7.49 (m, 2H), 7.46 (d, 1H, *J* = 7.5, Hz), 7.42 (d, 1H, *J* = 8.6, Hz), 2.26 (s,

3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.3, 154.4, 148.3, 148.1, 147.2, 141.2, 139.9, 137.7, 137.3, 136.2, 135.4, 134.6, 132.2, 130.7, 130.1, 129.6, 129.5, 128.6, 124.3, 123.6, 122.8, 122.7, 116.6 115.3, 20.7 HRMS (ESI) calcd for $C_{26}H_{18}N_5O_5S$ $[M+H]^+$ 512.1029 found 512.1015. This compound contains residual grease impurity and purity of this compound is about 90-95%.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4''-diethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-carboxamide (9a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9a** as a pale yellow colour solid; R_f = 0.75 (EtOAc/Hexanes = 1:4); Yield: 75% (33 mg); mp: 145−147 °C; IR (DCM): 3055, 2987, 2306, 1265, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.29 (br. s, 1H), 8.27 (br. s, 1H), 7.58 (d, 1H, J = 8.4 Hz), 7.50 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.43 (d, 4H, J = 8.0 Hz), 7.29 (s, 2H), 7.11 (d, 4H, J = 8.0 Hz), 2.53 (q, 4H, J = 7.6 Hz), 2.50 (s, 3H), 1.07 (t, 6H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.1, 154.5, 147.5, 143.5, 140.8, 139.8, 137.6, 132.5, 131.1, 130.0, 130.0, 128.5, 127.9, 115.4, 114.4, 28.4, 21.4, 15.3; HRMS (ESI) calcd for $C_{30}H_{28}N_3OS$ $[M+H]^+$ 478.1953 found 478.1944.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4''-dimethoxy-5'-methyl-[1,1':3',1''-terphenyl]-2'-carboxamide (9b)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9b** as a pale yellow colour solid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 65% (39 mg); mp: 145−147 °C; IR (DCM): 3054, 2987, 1609, 1422, 744 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.32 (br. s, 1H), 8.31 (d, 1H, J = 6.7 Hz), 7.60 (d, 1H, J = 8.8 Hz), 7.51 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.45 (d, 4H, J = 8.7 Hz), 7.26 (s, 2H), 6.83(d, 4H, J = 8.7 Hz), 3.72 (s, 6H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.2, 159.0, 154.6, 147.5, 140.3, 139.7, 132.7, 132.5, 131.1, 129.9, 129.7, 115.6, 114.6, 113.8, 55.2, 21.4; HRMS (ESI) calcd for $C_{28}H_{23}N_3NaO_3S$ $[M+Na]^+$ 504.1358 found 504.1370.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-5'-methyl-3,3''-dinitro-[1,1':3',1''-terphenyl]-2'-carboxamide (9c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9c** as a pale yellow colour solid; R_f = 0.35 (EtOAc/Hexanes = 1:4); Yield: 42% (25 mg); mp: 225−227 °C**;** IR (DCM): 2918, 1647, 1529, 1351, 805 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.45 (br. s, 2H), 8.28 (br. s, 1H), 8.15 (d, 1H, J = 7.4 Hz), 8.10 (dd, 2H, J_1 = 8.2, J_2 = 1.2 Hz), 7.85 (d, 2H, J = 7.7 Hz), 7.63 (d, 1H, J = 8.8 Hz), 7.50-7.45 (m, 3H), 7.41 (s, 2H), 2.58 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.5, 154.5, 148.2, 147.3, 141.4, 141.0, 138.5, 134.7, 132.7, 131.0, 130.7, 129.4, 128.8, 123.7, 122.7, 116.6, 115.4, 21.47; HRMS (ESI) calcd for $C_{26}H_{18}N_5O_5S$ $[M+H]^+$ 512.1029 found 512.1008.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4'',5'-trimethyl-[1,1':3',1''-terphenyl]-2'-carboxamide (9d)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9d** as a pale yellow colour solid; R_f = 0.72 (EtOAc/Hexanes = 1:4); Yield: 70% (37 mg); mp: 139−141 °C; IR (DCM): 3055, 2987, 2306, 1422, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.30 (br. s, 1H), 8.29 (d, 1H, J = 7.5 Hz), 7.59 (dd, 1H, J_1 = 8.8, J_2 = 0.8 Hz), 7.50 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.41 (d, 4H, J = 8.0 Hz), 7.27 (s, 2H), 7.09 (d, 4H, J = 8.0 Hz), 2.50 (s, 3H), 2.24 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.1, 154.6, 147.5, 140.8, 139.7, 137.4, 137.2, 132.5, 131.1, 130.0, 129.9, 129.1, 128.4, 115.5, 114.6, 21.4, 21.1; HRMS (ESI) calcd for $C_{28}H_{24}N_3OS$ $[M+H]^+$ 450.1640 found 450.1644.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,6-bis(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-4-methylbenzamide (9e)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9e** as a yellow colour semi-solid; R_f = 0.43 (EtOAc/Hexanes = 1:4); Yield: 60% (40 mg); IR (DCM): 2986, 2305, 1421, 895, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.33 (br. s, 1H), 8.31 (br. s,

1H), 7.62 (d, 1H, J = 8.7 Hz), 7.53 (dd, 1H, J_1 = 8.7, J_2 = 7.3 Hz), 7.23 (s, 2H), 7.04 (d, 2H, J = 2.0 Hz), 6.96 (dd, 2H, J_1 = 8.3, J_2 = 2.1 Hz), 6.73 (d, 2H, J = 8.3 Hz), 4.16 (s, 8H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.9, 148.2, 144.8, 143.8, 141.0, 138.2, 136.3, 134.4, 131.7, 131.1, 130.3, 130.0, 129.7, 129.4, 128.1, 127.8, 127.3, 127.2, 126.2, 122.9, 122.2, 121.6, 116.5, 58.9, 53.9, 45.0, 30.1, 22.3; HRMS (ESI) calcd for $C_{30}H_{23}N_3NaO_5S$ $[M+Na]^+$ 560.1256 found 560.1276.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,6-bis(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)benzamide (9f)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9f** as a pale yellow colour solid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 50% (31 mg); mp: 178−180 °C; IR (DCM): 3054, 2986, 2305, 1687,730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.34 (br. s, 1H), 8.32 (d, 1H, J = 7.3 Hz), 7.63 (dd, 1H, J_1 = 8.8, J_2 = 0.7 Hz), 7.56-7.51 (m, 2H), 7.42 (d, 2H, J = 7.6 Hz), 7.05 (d, 2H, J = 2.1 Hz), 6.98 (dd, 2H, J_1 = 8.4, J_2 = 2.2 Hz), 6.74 (d, 2H, J = 8.3 Hz), 4.16 (s, 8H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.8, 154.6, 147.6, 143.3, 143.2, 140.1, 134.9, 133.5, 131.1, 129.9, 129.7, 129.2, 121.8, 117.6, 117.2, 115.6, 114.8, 64.3, 64.2; HRMS (ESI) calcd for $C_{29}H_{22}N_3O_5S$ $[M+H]^+$ 524.1280 found 524.1282.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4'',5'-trimethoxy-[1,1':3',1''-terphenyl]-2'-carboxamide (9g)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9g** as a pale yellow colour solid; R_f = 0.38 (EtOAc/Hexanes = 1:4); Yield: 60% (35 mg); mp: 68−70 °C; IR (DCM): 2987, 2686, 2305, 896, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.30 (br. s, 1H), 8.28 (br. s, 1H), 7.60 (d, 1H, J = 8.8 Hz), 7.50 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.45 (d, 4H, J = 8.7 Hz), 6.94 (s, 2H), 6.83 (d, 4H, J = 8.7 Hz), 3.93 (s, 3H), 3.71 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.0, 159.9, 159.2, 154.6, 147.5, 142.2, 132.6, 131.1, 129.9,

129.6, 128.2, 115.5, 114.5, 113.8, 55.6, 55.2; HRMS (ESI) calcd for $C_{28}H_{24}N_3O_4S$ $[M+H]^+$ 498.1488 found 498.1497.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4''-diethyl-5'-methoxy-[1,1':3',1''-terphenyl]-2'-carboxamide (9h)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9h** as a yellow colour solid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 61% (36 mg); mp: 105−107 °C**;** IR (DCM): 2987, 2411, 2306, 1422,748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 1H, J_1 = 7.3 Hz), 8.24 (br. s, 1H), 7.58 (d, 1H, J = 8.6 Hz), 7.49 (dd, 1H, J_1 = 8.8, J_2 = 7.4Hz), 7.44 (d, 4H, J = 8.0 Hz), 7.11 (d, 4H, J = 8.0 Hz), 6.99 (s, 2H), 3.93 (s, 3H), 2.53 (q, 4H, J = 7.6 Hz), 1.06 (t, 6H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.9, 159.9, 154.5, 147.4, 143.8, 142.7, 137.6, 131.1, 130.1, 128.4, 128.2, 127.9, 115.3, 114.7, 114.3, 55.6, 28.4, 15.3; HRMS (ESI) calcd for $C_{30}H_{28}N_3O_2S$ $[M+H]^+$ 494.1902 found 494.1890.

***N*-(Benzo[c][1,2,5]thiadiazol-4-yl)-4,4''-dimethoxy-[1,1':3',1''-terphenyl]-2'-carboxamide (9i)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9i** as a pale yellow colour solid; R_f = 0.41 (EtOAc/Hexanes = 1:4); Yield: 60% (33 mg); mp: 148−150 °C; IR (DCM): 3055, 2987, 2306, 1547, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.33 (br. s, 1H), 8.31 (d, 1H J = 7.5 Hz), 7.61 (d, 1H, J = 8.8 Hz), 7.59-7.49 (m, 2H), 7.46 (d, 4H J = 8.8 Hz), 7.45-7.43 (m, 2H), 6.84 (d, 4H, J = 8.8 Hz), 3.72 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.0, 159.1, 154.6, 147.5, 140.2, 135.1, 132.5, 131.0, 129.8, 129.8, 129.7, 129.2, 115.7, 114.8, 113.9, 55.2; HRMS (ESI) calcd for $C_{27}H_{22}N_3O_3S$ $[M+H]^+$ 468.1382 found 468.1370.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3,3''-dinitro-[1,1':3',1''-terphenyl]-2'-carboxamide (9j)**. Following the general procedure described above, the resultant crude mixture was

purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9j** as a pale yellow colour solid; R_f = 0.33 (EtOAc/Hexanes = 1:4); Yield: 50% (30 mg); mp: 227−229 °C; IR (DCM): 3055, 2308, 1422, 1265, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.46 (br. s, 2H), 8.32 (br. s, 1H), 8.15-8.11 (m, 3H), 7.87 (d, 2H, J = 7.7 Hz), 7.75 (t, 1H, J = 7.7 Hz), 7.65-7.60 (m, 3H), 7.51-7.47 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.2, 154.5, 148.3, 147.3, 141.2, 138.5, 135.3, 134.7, 130.7, 130.7, 130.4, 129.5, 128.7, 123.7, 122.9, 116.7, 115.5; HRMS (ESI) calcd for $C_{25}H_{16}N_5O_5S$ $[M+H]^+$ 498.0872 found 498.0855.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4,4''-dimethyl-[1,1':3',1''-terphenyl]-2'-carboxamide (9k)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9k** as a pale yellow solid; R_f = 0.68 (EtOAc/Hexanes = 1:4); Yield: 75% (39 mg); mp: 189−191 °C**;** IR (DCM): 3055, 2987, 2306, 1422,748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.22 (br. s, 1H), 8.18 (dd, 1H, J_1 = 7.4, J_2 = 0.7 Hz), 7.51-7.45 (m, 2H), 7.40 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.35 (d, 2H, J = 7.4 Hz), 7.31 (d, 4H, J = 8.0 Hz), 7.00 (d, 4H, J = 8.0 Hz), 2.14 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.9, 154.6, 147.5, 140.6, 137.3, 137.2, 135.1, 131.1, 129.8, 129.7, 129.4, 129.1, 128.5, 115.6, 114.8, 21.1; HRMS (ESI) calcd for $C_{27}H_{22}N_3OS$ $[M+H]^+$ 436.1484 found 436.1506.

***N*-(Benzo[c][1,2,5]thiadiazol-4-yl)-4,4''-diethyl-[1,1':3',1''-terphenyl]-2'-carboxamide (9l)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9l** as a pale yellow colour solid; R_f = 0.69 (EtOAc/Hexanes = 1:4); Yield: 74% (41 mg); mp: 152−154 °C**;** IR (DCM): 3055, 2987, 2305, 1546, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.28 (br. s, 1H), 8.26 (br. s, 1H), 7.61-7.57 (m, 2H), 7.52-7.46 (m, 3H), 7.44 (d, 4H, J = 8.0 Hz), 7.11 (d, 4H, J = 8.0 Hz), 2.53 (q, 4H, J = 7.6 Hz), 1.07 (t, 6H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.0, 154.5, 147.5, 143.6, 140.7, 137.5, 135.1, 131.1, 129.9, 129.8, 129.3, 128.6,

127.9, 115.5, 114.6, 28.4, 15.3; HRMS (ESI) calcd for $C_{29}H_{26}N_3OS$ $[M+H]^+$ 464.1797 found 464.1784.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-[1,1':3',1''-terphenyl]-2'-carboxamide (9m)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **9m** as a pale yellow colour solid; R_f = 0.61 (EtOAc/Hexanes = 1:4); Yield: 50% (24 mg); mp: 175−177 °C**;** IR (DCM): 3054, 2685, 2305, 895, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.30 (br. s, 1H), 8.26 (dd, 1H, J_1 = 7.4, J_2 = 0.4 Hz), 7.64-7.58 (m, 2H), 7.55-7.47 (m, 7H), 7.31 (t, 4H, J = 7.3 Hz), 7.24-7.20 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.6, 154.5, 147.4, 140.7, 140.1, 135.2, 131.0, 129.8, 129.6, 129.5, 128.6, 128.4, 127.6, 115.7, 114.7; HRMS (ESI) calcd for $C_{25}H_{18}N_3OS$ $[M+H]^+$ 408.1171 found 408.1166.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-methoxy-6-(4-nitrobenzyl)benzamide (11a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **11a** as a yellow colour solid; R_f = 0.38 (EtOAc/Hexanes = 1:4); Yield: 47% (23 mg); mp: 157−159 °C; IR (DCM): 3054, 2986, 2305, 895, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.92 (br. s, 1H), 8.61 (d, 1H, J = 7.3 Hz), 7.98 (d, 2H, J = 8.6 Hz), 7.73 (d, 1H, J = 8.8 Hz), 7.66 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.42 (t, 1H, J = 8.0 Hz), 7.36 (d, 2H, J = 8.6 Hz), 6.98 (d, 1H, J = 8.4 Hz), 6.91 (d, 1H, J = 7.7 Hz), 4.29 (s, 2H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.7, 156.8, 154.8, 148.3, 147.7, 146.3, 139.7, 131.4, 131.1, 129.8, 129.8, 125.4, 123.6, 123.3, 116.1, 115.1, 110.0, 56.0, 39.2; HRMS (ESI) calcd for $C_{21}H_{17}N_4O_4S$ $[M+H]^+$ 421.0971 found 421.0963.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-methyl-6-(4-nitrobenzyl)benzamide (11b)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **11b** as a pale yellow colour solid;

R_f = 0.35 (EtOAc/Hexanes = 1:4); Yield: 50% (24 mg); mp: 179−181 °C; IR (DCM): 2987, 2306, 1422, 1265, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.64 (d, 1H, J = 7.3 Hz), 8.37 (br. s, 1H), 7.94 (d, 2H, J = 8.4 Hz), 7.76 (d, 1H, J = 8.8 Hz), 7.67 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.37 (t, 1H J = 7.6 Hz), 7.31 (d, 2H, J = 8.4 Hz), 7.25 (d, 1H J = 7.6 Hz), 7.15 (d, 1H J = 7.6 Hz), 4.19 (s, 2H); 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.3, 154.7, 148.0., 147.4, 146.4, 137.1, 136.1, 135.2, 130.9, 130.0, 129.6, 129.3 128.0, 123.6, 116.6, 115.3, 39.3, 19.5; HRMS (ESI) calcd for $C_{21}H_{17}N_4O_3S$ $[M+H]^+$ 405.1021 found 405.1019.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-chloro-6-(4-nitrobenzyl)benzamide (11c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **11c** as a pale yellow colour solid; R_f = 0.38 (EtOAc/Hexanes = 1:4); Yield: 65% (33 mg); mp: 172−174 °C; IR (DCM): 3055, 2987, 2307, 896, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.62 (dd, 1H, J_1 = 7.4, J_2 = 0.6 Hz), 8.45 (br. s, 1H), 7.96 (d, 2H, J = 8.8 Hz), 7.78 (dd, 1H, J_1 = 8.9, J_2 = 0.9 Hz), 7.68 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.45-7.39 (m, 2H), 7.33 (d, 2H, J = 8.8 Hz), 7.23 (dd, 1H, J_1 = 6.8, J_2 = 2.0 Hz), 4.22 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.1, 154.7, 147.4, 147.0, 146.5, 139.1, 136.1, 131.5, 131.1, 130.9, 129.8, 129.1, 129.0, 128.5, 123.7, 116.8, 115.6, 39.2; HRMS (ESI) calcd for $C_{20}H_{14}ClN_4O_3S$ $[M+H]^+$ 425.0475 found 425.0471.

***N*-(Benzo[c][1,2,5]thiadiazol-4-yl)-4-methyl-2,6-bis(4-nitrobenzyl)benzamide (12a)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **12a** as a pale yellow colour solid; R_f = 0.31 (EtOAc/Hexanes = 1:4); Yield: 55% (35 mg); mp: 165−167 °C; IR (DCM): 3055, 2987, 1422, 1265, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (d, 1H, J = 7.4 Hz), 8.13 (br. s, 1H), 7.97 (d, 4H, J = 8.5 Hz), 7.75 (d, 1H, J = 8.8 Hz), 7.65 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.30 (d, 4H, J = 8.5 Hz), 7.03 (s, 2H), 4.16 (s, 4H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.9, 154.6, 147.6, 147.1, 146.5, 140.6, 136.7, 134.6, 130.8, 129.9, 129.6,

129.0, 123.7, 116.8, 115.2, 39.5, 21.4; HRMS (ESI) calcd for $C_{28}H_{20}N_5O_5S$ $[M-H]^-$ 538.1185 found 538.1163.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-4-methoxy-2,6-bis(4-nitrobenzyl)benzamide (12b)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **12b** as a pale yellow colour solid; R_f = 0.30 (EtOAc/Hexanes = 1:4); Yield: 52% (24 mg); mp: 240−242 °C; IR (DCM): 3054, 2987, 1422, 896, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.53 (dd, 1H, J_1 = 7.4, J_2 = 0.6 Hz), 8.14 (br. s, 1H), 7.98 (d, 4H, J = 8.8 Hz), 7.75 (dd, 1H, J_1 = 8.8, J_2 = 0.8 Hz), 7.64 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.31 (d, 4H, J = 8.7 Hz), 6.72 (s, 2H), 4.18 (s, 4H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.7, 160.6, 154.5, 147.3, 146.5, 138.6, 130.8, 130.1, 129.6, 129.0, 123.8, 116.7, 115.1, 114.6, 55.5, 39.5; HRMS (ESI) calcd for $C_{28}H_{22}N_5O_6S$ $[M+H]^+$ 556.1291 found 556.1298.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2,6-bis(4-nitrobenzyl)benzamide (12c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **12c** as a yellow colour solid; R_f = 0.33 (EtOAc/Hexanes = 1:4); Yield: 58% (36 mg); mp: 188−190 °C; IR (DCM): 3055, 2306, 1348, 1265, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.56 (d, 1H J = 7.3 Hz), 8.15 (br. s, 1H), 7.96 (d, 4H, J = 8.6 Hz), 7.76 (d, 1H, J = 8.8 Hz), 7.66 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.45 (t, 1H, J = 7.7 Hz), 7.30 (d, 4H, J = 8.6 Hz), 7.24 (d, 2H, J = 7.7 Hz), 4.20 (s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.6, 154.5, 147.5, 147.1, 146.5, 137.2, 136.7, 130.8, 130.4, 129.6, 129.3, 128.9, 123.8, 116.9, 115.3, 39.2; HRMS (ESI) calcd for $C_{27}H_{20}N_5O_5S$ $[M+H]^+$ 526.1185 found 526.1197.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-3-methyl-2,6-bis(4-nitrobenzyl)benzamide (12d′)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 20:80) to

afford **12d′** as a pale yellow solid; Yield: 30% (19 mg); R_f = 0.33 (EtOAc/Hexanes = 1:4); mp: 144−146 °C; IR (DCM): 3054, 2987, 1421, 1265,747, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (d, 1H, *J* = 7.4 Hz), 8.16 (br. s, 1H), 8.01 (d, 2H, *J* = 8.6 Hz), 7.96 (d, 2H, *J* = 8.6, Hz), 7.72 (d, 1H, *J* = 8.8, Hz), 7.61 (dd, 1H, J_1 = 8.7, J_2 = 7.6, Hz), 7.35 (d, 1H, *J* = 7.9 Hz), 7.32 (d, 2H, *J* = 8.6, Hz), 7.23 (d, 2H, *J* = 8.6, Hz), 7.19 (d, 1H, *J* = 7.8, Hz), 4.19 (s, 4H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.2, 154.5, 147.8, 147.1, 147.1, 146.4, 138.2, 136.9, 134.1, 134.1, 132.4, 130.8, 129.6, 129.5, 128.9, 128.9, 123.8, 123.7, 116.8, 115.2, 39.1, 36.4, 19.9 HRMS (ESI) calcd for $C_{28}H_{22}N_5O_5S$ $[M+H]^+$ 540.1342 found 540.1360.

***N*-(2-(Methylthio)phenyl)-3-(3-nitrophenyl)propanamide (21c)**. Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **21c** as a brown colour semi-solid; R_f = 0.40 (EtOAc/Hexanes = 1:4); Yield: 30% (24 mg); IR (DCM): 3333, 2923, 1682, 1530, 735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.28 (d, 1H, *J* = 8.2 Hz), 8.24 (br. s, 1H), 8.16 (br. s, 1H), 8.09 (d, 1H, *J* = 8.2 Hz), 7.63 (d, 1H, *J* = 7.6 Hz), 7.48 (t, 2H, *J* = 8.0 Hz), 7.31 (d, 1H, *J* = 7.5 Hz), 7.09 (t, 1H, *J* = 7.4 Hz), 3.21 (t, 2H, *J* = 7.4 Hz), 2.82 (t, 2H, *J* = 7.4 Hz), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.4, 148.4, 142.6, 137.8, 135.0, 132.7, 129.5, 128.8, 125.4, 124.7, 123.2, 121.6, 120.8, 38.7, 30.8, 18.9; HRMS (ESI) calcd for $C_{16}H_{17}N_2O_3S$ $[M+H]^+$ 317.0960 found 317.0946.

3-(3-Nitrophenyl)-*N*-(quinolin-8-yl)propanamide (21d).[20c] Following the general procedure described above, resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **21d** as a pale gray colour solid; R_f = 0.43 (EtOAc/Hexanes = 1:4); Yield: 21% (17 mg); mp 148-150 °C; IR (DCM): 3347, 2987, 1687, 1525, 737; cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.81 (br. s, 1H), 8.79-8.76 (m, 2H), 8.20-8.17 (m, 2H), 8.18 (d, 1H, *J* = 8.3 Hz), 8.08 (d, 1H, *J* = 8.2 Hz), 7.67 (d, 1H, *J* = 7.6 Hz), 7.57-7.51 (m, 2H), 7.47 (t,

2H, J = 7.8 Hz), 3.27 (t, 2H, J = 7.5 Hz), 2.97 (t, 2H, J = 7.5 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.7, 148.2, 142.8, 138.2, 136.4, 135.0, 134.2, 129.5, 127.9, 127.4, 123.3, 121.7, 121.7, 121.5, 116.6, 38.8, 30.9; HRMS (ESI) calcd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1192 found 322.1178.

3,3-Bis(3-nitrophenyl)-*N*-(quinolin-8-yl)propanamide (21d′). Following the general procedure described above, resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **21d′** as a pale gray colour solid; R_f = 0.29 (EtOAc/Hexanes = 1:4); Yield: 18% (20 mg); mp 201-203 °C; IR (DCM): 3347, 2987, 1527, 1265, 739; cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.86 (br. s, 1H), 8.78 (d, 1H, J = 4.2 Hz), 8.65 (dd, 1H, J_1 = 6.0, J_2 = 2.6 Hz), 8.23 (br. s, 2H), 8.17 (d, 1H, J = 8.2 Hz), 8.11 (d, 1H, J = 8.2 Hz), 8.72 (d, 2H, J = 7.5 Hz), 7.72 (d, 2H, J = 7.7 Hz), 7.56-7.50 (m, 4H), 7.47 (dd, 1H, J_1 = 8.0, J_2 = 3.4 Hz), 5.07 (t, 1H, J = 7.6 Hz), 3.45 (d, 2H, J = 7.7 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.8, 148.6, 148.3, 144.5, 138.1, 136.4, 134.2, 133.8, 130.0, 127.9, 127.3, 122.5, 122.4, 122.0, 121.8, 116.6, 46.2, 43.3; HRMS (ESI) calcd for $C_{24}H_{19}N_4O_5$ $[M+H]^+$ 443.1355 found 443.1337.

Methyl 4-(3-oxo-3-(quinolin-8-ylamino)propyl)benzoate (21e): Following the general procedure described above, **21e** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a colourless viscous liquid; R_f = 0.44 (EtOAc/Hexanes = 1:4); Yield: 40% (17 mg); IR (DCM): 3350, 1720, 1526, 1282, 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.80 (br. s, 1H), 8.79-8.78 (m, 2H), 8.18 (d, 1H, J = 8.2 Hz), 7.99 (d, 2H, J = 8.0 Hz), 7.58-7.51 (m, 2H), 7.46 (dd, 1H, J_1 = 8.2 Hz, J_2 = 4.2 Hz), 7.39 (d, 2H, J = 8.0 Hz), 3.91 (s, 3H), 3.22 (t, 2H, J = 7.6 Hz), 2.93 (t, 2H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 170.3, 167.1, 148.1, 146.3, 138.3, 136.4, 134.3, 129.9, 128.5, 128.2, 127.9, 127.4, 121.6, 121.6, 116.5, 52.0, 39.1, 31.4; HRMS (ESI) calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$ 335.1396 found 335.1381.

Dimethyl 4,4'-(3-oxo-3-(quinolin-8-ylamino)propane-1,1-diyl)dibenzoate (21e′): Following the general procedure described above, **21e′** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a colourless viscous liquid; R_f = 0.30 (EtOAc/Hexanes = 1:4); Yield: 17% (10 mg); IR (DCM): 3054, 1721, 1526, 1265, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.79 (br. s, 1H), 8.77 (d, 1H, *J* = 4.1 Hz), 8.68 (t, 1H, *J* = 4.4 Hz), 8.16 (d, 1H, *J* = 8.2 Hz), 7.98 (d, 4H, *J* = 8.1 Hz), 7.50 (d, 2H, *J* = 4.6 Hz), 7.45 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 7.42 (d, 4H, *J* = 8.1 Hz), 4.93 (t, 1H, *J* = 7.7 Hz), 3.91 (s, 6H), 3.37 (d, 2H, *J* = 7.7 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.6, 166.8, 148.1, 138.2, 136.4, 134.0, 130.1, 128.7, 127.9, 127.9, 127.3, 121.7, 121.6, 116.6, 52.1, 47.0, 43.7; HRMS (ESI) calcd for $C_{28}H_{25}N_2O_5$ $[M+H]^+$ 469.1763 found 469.1745.

4'-Ethyl-3-(4-ethylbenzyl)-*N*-(quinolin-8-yl)-[1,1'-biphenyl]-2-carboxamide (22a): The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **22a** as a colourless solid; R_f = 0.53 (EtOAc/Hexanes = 1:4); Yield: 53% (30 mg); mp 138-140 ^oC; IR (DCM): 3054, 2928, 1422, 1265, 747 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.50 (br. s, 1H), 8.77 (d, 1H, *J* = 7.6 Hz), 8.55 (d, 1H, *J* = 4.1 Hz), 8.07 (d, 1H, *J* = 8.4 Hz), 7.54-7.41 (m, 5H), 7.35 (d, 2H, *J* = 7.8 Hz), 7.26 (d, 1H, *J* = 8.0 Hz), 7.16 (d, 2H, *J* = 7.5 Hz), 7.05 (d, 2H, *J* = 7.6 Hz), 6.95 (d, 2H, *J* = 7.5 Hz), 4.22 (s, 2H), 2.44 (q, 4H, *J* = 7.6 Hz), 1.07 (t, 3H, *J* = 7.6 Hz), 0.99 (t, 3H, *J* = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.3, 147.8, 143.2, 141.8, 139.8, 139.5, 137.6, 136.7, 135.9, 134.4, 129.3, 129.1, 129.0, 128.6, 128.6, 128.1, 127.8, 127.7, 127.7, 127.2, 121.5, 121.3, 116.5, 38.8, 28.3, 28.3, 15.5, 15.2; HRMS (ESI) calcd for $C_{33}H_{31}N_2O$ $[M+H]^+$ 471.2436 found 471.2422

Typical procedure for the β-acetoxylation of 6c,d: An appropriate amide **6c** or **6d** (0.11 mmol, 30 mg), $Pd(OAc)_2$ (10 mol%, 2.3 mg), $PhI(OAc)_2$ (0.22 mmol, 70 mg), glacial AcOH (7 mg) and AC_2O (13 mg) in anhydrous toluene (3 mL) was heated at 110 ^oC for 24 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in

vacuum and purification of the resulting reaction mixture through column chromatography furnished the corresponding acetoxylated amides **25a**,**b**.

2-(Benzo[*c*][1,2,5]thiadiazol-4-ylcarbamoyl)-3-chlorophenyl acetate (25a): The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **25a** as a pale yellow solid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 86% (33 mg); mp: 129−131 °C**;** IR (DCM): 3314, 1771, 1692, 1548 and 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.83 (br. s, 1H), 8.64 (d, 1H, J = 7.3 Hz), 7.77 (d, 1H, J = 8.8 Hz), 7.67 (dd, 1H, J_1 = 8.7, J_2 = 7.4 Hz), 7.46 (t, 1H, J = 7.3 Hz), 7.41 (dd, 1H, J_1 = 8.1, J_2 = 1.0 Hz), 7.17 (dd, 1H, J_1 = 8.0, J_2 = 1.1 Hz), 2.21 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.4, 162.0, 154.8, 148.5, 147.7, 132.1, 131.4, 130.9, 129.8, 129.3, 127.7, 121.9, 116.7, 115.8, 20.8; HRMS (ESI) calcd for $C_{15}H_{10}ClNaN_3O_3S$ $[M+Na]^+$ 370.0029 found 370.0014.

2-(Benzo[*c*][1,2,5]thiadiazol-4-ylcarbamoyl)-3-methoxyphenyl acetate (25b): The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **25b** as a yellow solid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 89% (33 mg); mp: 130−132 °C; IR (DCM): 3055, 2987, 1679, 1266 and 744 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.67 (br. s, 1H), 8.64 (d, 1H, J = 7.2 Hz), 7.72 (d, 1H, J = 8.7 Hz), 7.65 (dd, 1H, J_1 = 8.7, J_2 = 7.4 Hz), 7.49 (t, 1H, J = 8.3 Hz), 6.97 (d, 1H, J = 8.5 Hz), 6.84 (d, 1H, J = 8.2 Hz), 4.01 (s, 3H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.8, 162.2, 157.6, 154.8, 150.4, 148.0, 132.0, 131.2, 130.2, 117.9, 116.3, 115.9, 115.3, 109.3, 56.5, 21.1; HRMS (ESI) calcd for $C_{16}H_{13}N_3NaO_4S$ $[M+Na]^+$ 366.0524 found 366.0511.

Typical procedure for the β-alkoxylation of 6d,b. An appropriate amide **6b** or **6d** (0.11 mmol, 30 mg), $Pd(OAc)_2$ (10 mol%, 2.3 mg), $PhI(OAc)_2$ (0.22 mmol, 70 mg) and MeOH (0.4 mL) and anhydrous toluene (1 mL) was heated at 65 °C for 24 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated in vacuum and purification

of the resulting reaction mixture through column chromatography furnished the corresponding alkoxylated amides **25c**,**d**.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-2-chloro-6-methoxybenzamide (25c)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **25c** as a yellow solid; R_f = 0.44 (EtOAc/Hexanes = 1:4); Yield: 71% (25 mg); mp: 173−175 °C; IR (DCM): 3054, 2987, 1689, 1574 and 744 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.86 (br. s, 1H), 8.73 (d, 1H, J = 6.9 Hz), 7.75 (dd, 1H, J_1 = 8.8, J_2 = 0.8 Hz), 7.68 (dd, 1H, J_1 = 8.8, J_2 = 7.4 Hz), 7.35 (t, 1H, J = 8.3 Hz), 7.08 (dd, 1H, J_1 = 8.0, J_2 = 0.5 Hz), 6.90 (d, 1H, J = 8.4 Hz), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 163.5, 157.5, 154.8, 147.8, 132.4, 131.4, 131.2, 129.9, 125.6, 122.0, 116.2, 115.5, 109.7, 56.2; HRMS (ESI) calcd for $C_{14}H_{11}ClN_3O_2S$ $[M+H]^+$ 320.0261 found 320.0249.

***N*-(Benzo[*c*][1,2,5]thiadiazol-4-yl)-6-methoxy-2,3-dimethylbenzamide (25d)**: The resultant crude mixture was purified by column chromatography (EtOAc/hexane, 1:4) to afford **(25d)** as a yellow viscous liquid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 64% (22 mg); IR (DCM): 2965, 1651, 1587, 1462 and 736 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.89 (br. s, 1H), 8.74 (dd, 1H, J_1 = 7.2, J_2 = 0.8 Hz), 7.73 (dd, 1H, J_1 = 8.8, J_2 = 1.0 Hz), 7.68 (dd, 1H, J_1 = 8.8, J_2 = 7.2 Hz), 7.20 (d, 1H, J = 8.4 Hz), 6.76 (d, 1H, J = 8.4 Hz), 3.83 (s, 3H), 2.33 (s, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.2, 154.9, 154.5, 147.9, 135.6, 131.6, 131.3, 130.2, 129.7, 126.4, 115.8, 115.1, 108.4, 55.9, 19.4, 16.7; HRMS (ESI) calcd for $C_{16}H_{16}N_3O_2S$ $[M+H]^+$ 314.0963 found 314.0951.

***1*-Phenyl-9*H*-fluoren-9-one (27)**.[20a] Following the general procedure described above, the resultant crude mixture was purified by column chromatography (EtOAc:Hexanes = 1:4) to afford **27** as a greenish-black colour semi-solid; R_f = 0.80 (EtOAc/Hexanes = 1:4); Yield: 66% (8 mg); IR (DCM): 3054, 1711, 1608, 916, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.62-7.59 (m, 2H), 7.57-7.49 (m, 6H), 7.47 (d, 2H, J = 7.5 Hz), 7.31 (t, 1H, J = 7.4 Hz), 7.23

(dd, 1H, J_1 = 7.0, J_2 = 1.5 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 193.1, 145.5, 143.6, 142.3, 137.4, 134.5, 134.2, 131.6, 129.7, 129.2, 129.2, 129.0, 128.2, 127.9, 127.2, 124.1, 120.0, 119.2; HRMS (ESI) calcd for $C_{19}H_{13}O$ $[M+H]^+$ 257.0966 found 257.0956.

2-Phenylpropanoic acid (28c).[19] Following the general procedure described above, **28c** was obtained as a pale yellow oil; Yield: 75% (11 mg); IR (neat): 2968, 1709, 1420, 1265, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.22 (m, 5H), 3.32-3.27 (m, 1H), 2.70 (dd, 2H, J_1 = 15.5 Hz, J_2 = 6.8 Hz), 2.61 (dd, 1H, J_1 = 15.5 Hz, J_2 = 8.2 Hz), 1.35 (d, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.5, 145.4, 128.6, 126.7, 126.5, 42.6, 36.2, 21.9; HRMS (ESI): *m/z* $[M - H]^+$ calcd for $C_{10}H_{11}O_2$: 163.0759; found 163.0756.

3-(4-Chlorophenyl)butanoic acid (28d).[19] Following the general procedure described above, **28d** was obtained as a colorless solid; Yield: 88% (17 mg); mp 90-92 ^oC; IR (KBr): 2963, 1705, 1494, 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, 2H, J = 8.2 Hz), 7.18 (d, 2H, J = 8.2 Hz), 3.30-3.24 (m, 1H), 2.68-2.56 (m, 2H), 1.32 (d, 3H, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.4, 143.8, 132.2, 128.7, 128.2, 42.5, 35.6, 21.9; HRMS (ESI): *m/z* $[M - H]^+$ calcd for $C_{10}H_{10}ClO_2$: 197.0369; found 197.0365.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

X-ray structures and brief X-ray structure data of the compounds **5g** and **7f**, copies of ^1H and ^{13}C NMR charts (PDF)

X-ray structure data of the compounds **5g** and **7f** (CIF)

Notes

The authors declare no competing financial interest.

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(17) When compared to the other existing bidentate directing groups (Figure 1), 4-amino-2,1,3-benzothiadiazole (ABTD) has a skeleton similar to the 8-aminoquinoline (AQ) bidentate directing group. Furthermore, 2,1,3-benzothiadiazole substrates are known to exhibit notable biological activities and the 2,1,3-benzothiadiazole (BTD) skeleton considered as one of the important moiety in the chemistry of photoluminescent compounds, functional materials and light technology. For selected articles, see: (a) Neto, B. A. D.; Lapis, A. A. M.; da Silva Júnior E. N.; Dupont, J. *Eur. J. Org. Chem.* **2013**, 228. (b) Watanabe, M.; Goto, K.; Shibahara, M.; Shinmyozu, T. *J. Org. Chem.* **2010**, *75*, 6104.

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depicted in concurrence with the generally proposed Pd^{II}-Pd^{IV} catalytic cycle mechanism involving the Pd^{II}/AgOAc catalytic system-based C-H activation of carboxamides aided by the bidentate directing groups. For selected papers, see: (a) See Refs. 1-6. (b) Tran, L. D.; Daugulis, O. *Angew. Chem. Int. Ed.* **2012**, *51*, 5188. (c) Arroniz, C.; Denis, J. G.; Ironmonger, A.; Rassias, G.; Larrosa, I. *Chem. Sci.* **2014**, *5*, 3509. (d) Tang, H.; Huang, X.-R.; Yao, J.; Chen, H. *J. Org. Chem.* **2015**, *80*, 4672.

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