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Pd(II)-Catalyzed, Picolinamide-Assisted, *Z*-Selective *γ*-Arylation of Allylamines to Construct *Z*-Cinnamylamines

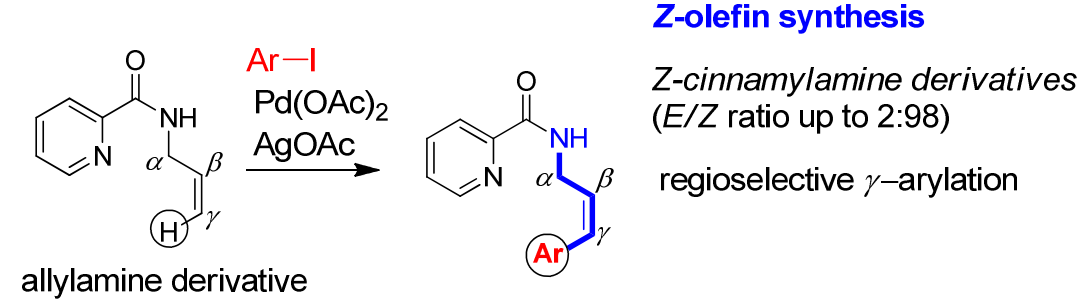
Ramarao Parella and Srinivasarao Arulananda Babu*

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

sababu@iisermohali.ac.in

ABSTRACT

bidentate directing group-assisted C-H arylation of allylamine



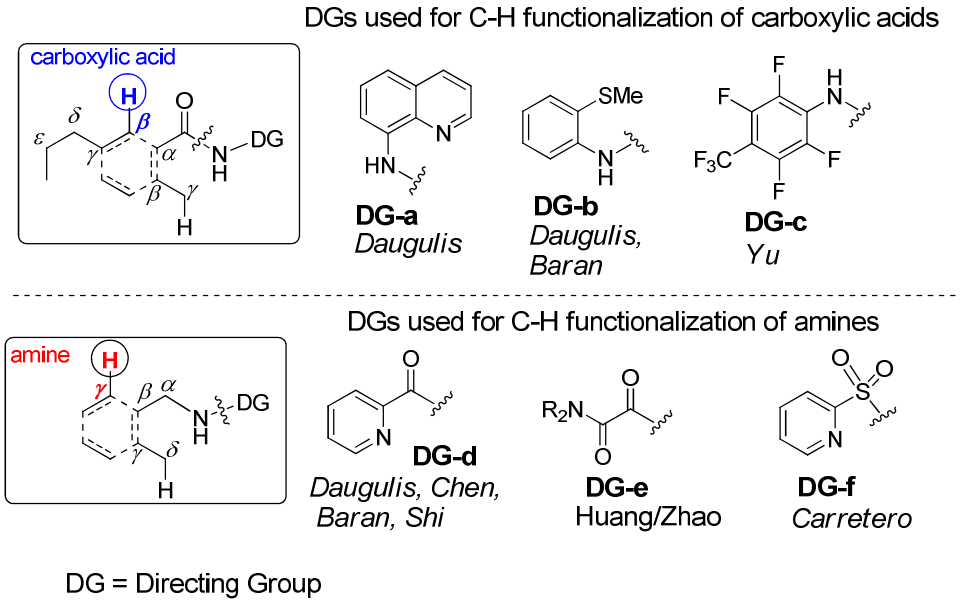
Investigations of Pd(II)-catalyzed, picolinamide-assisted, *γ*-C(sp^2)-H activation and *Z*-selective arylation of allylamines are reported. The reactions of *N*-allylpicolinamides with various aryl iodides in the presence of the catalyst $Pd(OAc)_2$ and additive AgOAc have led to the selective *γ*-arylation of allylamines to construct various cinnamylamines with moderate to good yields and good to high *E*/*Z* ratios. To obtain good *E*/*Z* ratios, the Pd(II)-catalyzed arylation reaction of *N*-allylpicolinamides was probed using different additives, directing groups and reaction conditions. The Pd(II)-catalyzed arylation of an allylamine containing both *γ*-C(sp^2)-H and *γ*-C(sp^3)-H bonds afforded moderate yields of the *γ*-C(sp^2)-H and *γ*-C(sp^3)-H bisarylated cinnamylamines. Although Heck-type *γ*-arylations of allylamines have generally afforded the *E*-cinnamylamines, the bidentate directing group picolinamide-directed arylations of allylamines

were found to be *Z*-selective. A plausible mechanism was proposed for the observed regioselectivity and *Z*-selective arylation of *N*-allylpicolinamides. Additionally, the Pd(II)-catalyzed arylation of an *N*-allyl-5-methylisoxazole-3-carboxamide afforded the *E*-cinnamylamines plausibly via a ligand-free Heck-type reaction mechanism.

INTRODUCTION

Over the past few decades, organic synthesis generously experienced the advantages of the celebrated transition-metal-catalyzed C-C bond forming cross-coupling reactions (e.g., Kumada, Negishi, Stille, Suzuki, Hiyama and Heck reactions) of suitable coupling partners.[1-3] In recent years, the construction of C-C bonds via transition-metal-catalyzed C-H bond functionalization has received special attention[4-8] because the C-H functionalization process offers additional advantages. For example, transition-metal-catalyzed C-H bond functionalization is a direct method for forming C-C bonds and does not require the preassembling of organometallic reagents. Often, C-H functionalization can be performed using commercially available starting materials (e.g., arenes, alkenes, cycloalkanes, carbonyls, and amines). The functionalization of sp^2 and sp^3 C-H bonds of organic molecules has been performed with or without the help of directing groups using transition-metal-based catalysts (e.g., Pd, Ru, Rh, Cu, and Ni).[4-10] Among the available C-H functionalization reactions, directing-group-assisted C-H functionalization reactions have received substantial attention.[9,10] This is because high levels of regioselectivity as well as stereoselectivity can be achieved.[9,10] C-H functionalization of sp^2 or sp^3 C-H bonds of organic molecules using Daugulis' bidentate directing group[11] (e.g., **DG-a** and **DG-b**), Yu's monodentate directing group[12] and other related/modified bidentate directing groups have been extensively studied (Scheme 1).[9,10,13-21]

Scheme 1. Bidentate Directing Group-Assisted C-H Functionalization of Carboxylic Acids and Amines.



Allylamine derivatives are an important class of compounds and are ubiquitous in biologically active molecules and are considered important in medicinal chemistry research and pharmaceuticals.[22,23] Allylamine derivatives or allylamine-tethered molecules are notably useful synthetic building blocks for assembling various nitrogen-containing compounds.[24-26] Various γ-arylated allylamine derivatives (cinnamylamines) have been found to exhibit a wide range of biological activities and have been identified as potential drug candidates. Notably, some cinnamylamine molecules are currently being used as medicines (Figure 1).[22,23] For example, naftifine is an antifungal drug used for the topical treatment of tinea pedis, tinea cruris and tinea corporis. Flunarizine is a calcium antagonist, and flunarizine is effective in the prophylaxis of migraine. Cinnarizine has been characterized as an antihistamine and calcium-channel blocker and is prescribed for nausea and vomiting. Additionally, the cinnamylamine derivative CP-724,714 was found to stop the growth of tumor cells.

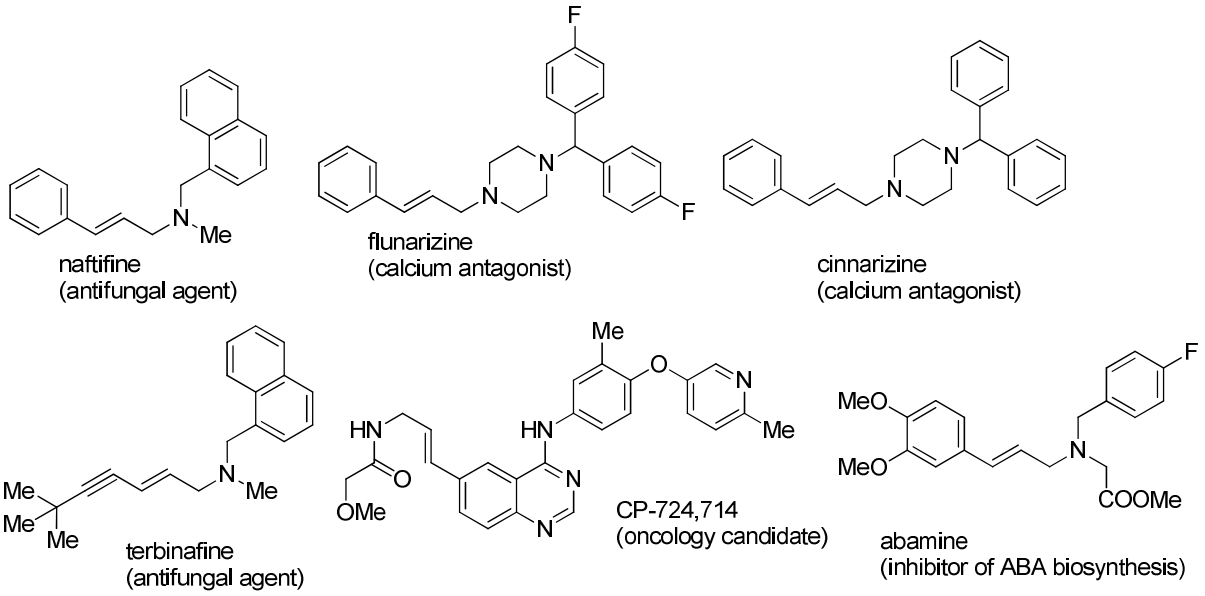
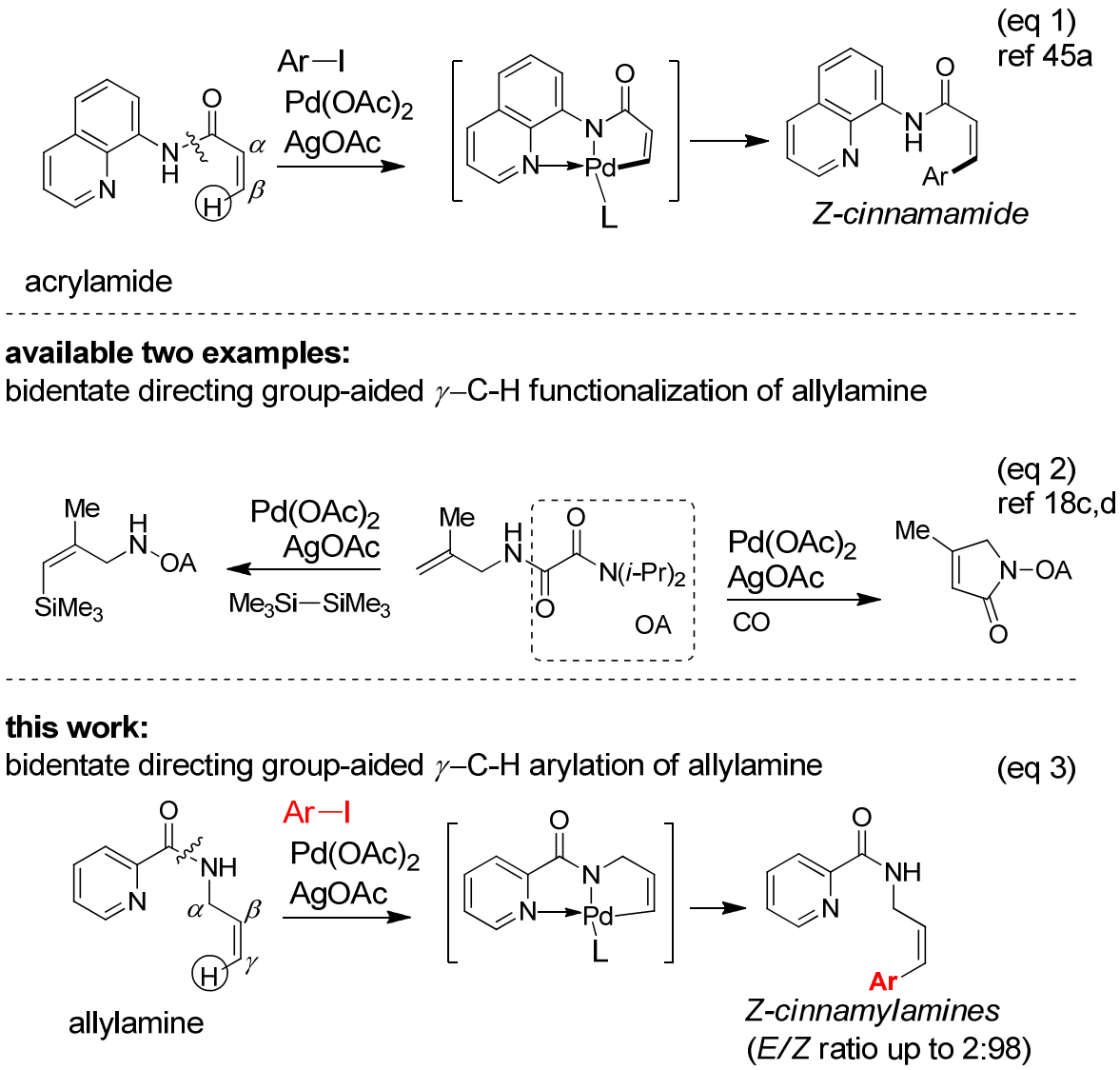


Figure 1. Biologically active allylamines/cinnamylamines (*γ*-arylated allylamine derivatives).

In general, allylamine derivatives are synthesized using various methods and, given the importance of cinnamylamines (*γ*-arylated allylamine derivatives) in medicinal chemistry research, considerable efforts have been made to assemble cinnamylamines.[27-30] Notably, the celebrated Mizoroki-Heck-type reaction[31-33] comprising allylamines and suitable coupling partners (e.g., aryl halides or pseudohalides) is well utilized to assemble cinnamylamines.[34-43] Cinnamylamines have also been prepared via the metal-catalyzed C-H functionalization of allylamines by using arenes[42,43] and the oxidative Heck-type reaction comprising allylamines and aryl boronic acids.[39,40] Typically, in these reactions, the corresponding cinnamylamines with *E*-geometries are obtained as predominant isomers. Consequently, the construction of *Z*-cinnamylamines as the predominant isomers has been less frequently encountered.[43] Furthermore, in some of the reactions, the Mizoroki-Heck-type arylation of allylamines was found to afford both the *γ*- and *β*-arylated allylamines.

Scheme 2. Bidentate Directing Group-Assisted C-H Functionalization of Acrylamide and Allylamine.



A survey of the literature revealed that noteworthy investigations have been performed to accomplish regioselectivity in the Mizoroki-Heck-type arylation of allylamines. Most of these reactions afforded *E*-cinnamylamines as the major isomers.[34-43] Apart from the report by Xu/Deng,[43] the construction of *Z*-cinnamylamines via the reaction of aryl halides and allylamines

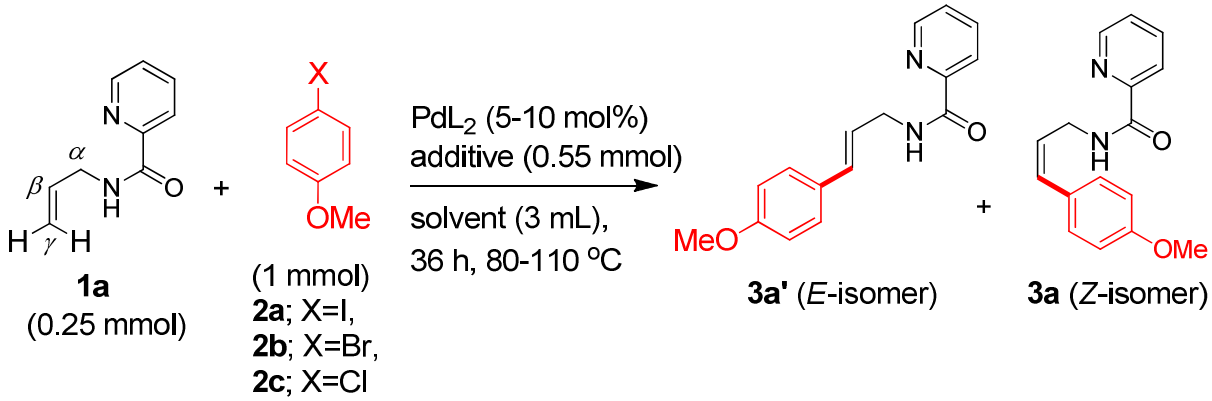
involving the transition-metal-catalyzed direct arylation technique (e.g., Heck and C-H activation reactions)[34-43] has not been explored well. Recently, Liu reported[44a] the stereoselective synthesis of *Z*-allylic amines via a Cp_2TiCl_2-catalyzed *cis*-hydroalumination of propargylic amines with Red-Al. Consequently, there exist only limited reports dealing with the construction of *Z*-cinnamylamines.

Our group recently reported[45a] the stereoselective construction of *Z*-cinnamamide scaffolds *via* a $Pd(OAc)_2$-catalyzed, bidentate directing group 8-aminoquinoline-assisted *Z*-selective *β*-C(sp^2)-H-arylation of acrylamides (eq 1, Scheme 2). Taking an impetus from this reaction and the existing developments regarding bidentate directing group-assisted C-H functionalization,[9,10,13-18] we envisaged the construction of *Z*-cinnamylamines *via* a Pd(II)-catalyzed, bidentate directing group- and chelation-assisted *Z*-selective C-H activation followed by a *γ*-C(sp^2)-H arylation of allylamines. To date, only two examples of bidentate directing group oxalylamide-, and chelation-assisted *Z*-selective C-H functionalization of allylamines have been reported.[18c,d] Yao/Zhao reported[18c] an example comprising the synthesis of pyrrolidones via the *γ*-C(sp^2)-H carbonylation of allylamines (eq 2, Scheme 2). Wen/Zhao reported[18d] an example comprising the *γ*-C(sp^2)-H silylation of allylamines (eq 2, Scheme 2). Herein, we report our investigations on the $Pd(OAc)_2$/AgOAc catalytic system, picolinamide- and chelation-assisted *Z*-selective *γ*-C(sp^2)-H arylation of *N*-allylpicolinamides (eq 3, Scheme 2). This work divulges a contemporary method for the regioselective *γ*-arylation of allylamines involving relatively simple reaction conditions, in which aryl iodide is a coupling partner, $Pd(OAc)_2$ is the catalyst, and AgOAc acts as an additive to regenerate the catalyst.[9,10,13-18]

RESULTS AND DISCUSSION

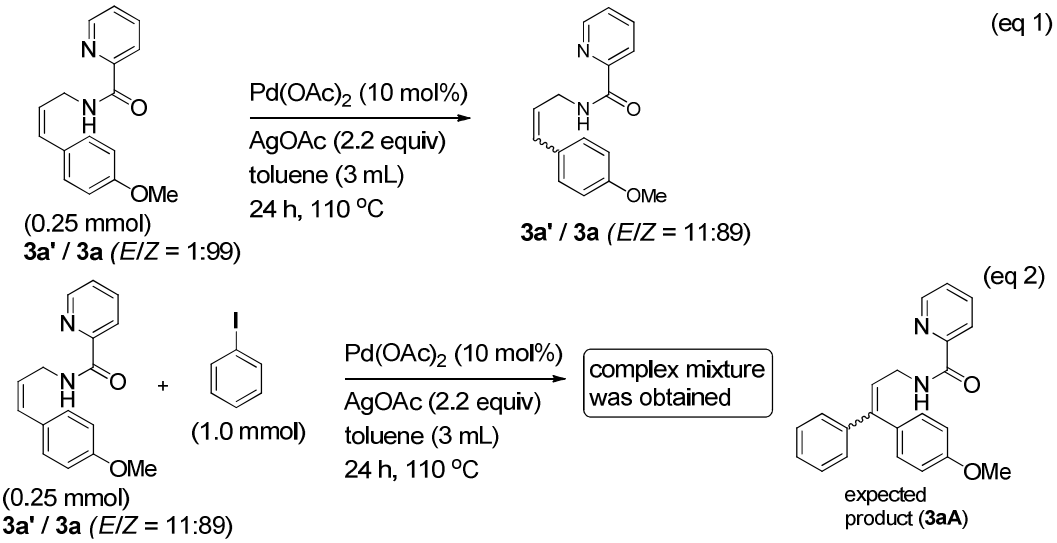
To begin our investigation on the *Z*-selective γ-C(sp^2)-H arylation of allylamines, we assembled various *N*-allylcarboxamides to use them as substrates in the $Pd(OAc)_2$/AgOAc-, bidentate directing group-assisted γ-C(sp^2)-H arylation reactions. Accordingly, the *N*-allylcarboxamide substrates **1a-m** were prepared from the corresponding allylamines and carboxylic acids (Scheme 3). After preparing the required *N*-allylcarboxamides **1a-m**, we attempted the construction of *Z*-cinnamylamine **3a** via the Pd(II)-catalyzed arylation of *N*-allylpicolinamide **1a**. Table 1 shows the optimization of the reaction conditions of the reaction of *N*-allylpicolinamide **1a** with aryl halides **2a-c** in the presence of various palladium catalysts, additives and solvents.

Table 1. Optimization of the Reaction of Allylamine 1a



Entry	PdL_2 (10 mol%)	Additive	Solvent	*T* (°C)	**3a** Yield (%)	*E*:*Z* ratio (**3a′**:**3a**)
1[b]	$Pd(OAc)_2$	AgOAc	Toluene	110	51	21:79
2	**$Pd(OAc)_2$**	**AgOAc**	**Toluene**	**110**	**64**	**11:89**
3	$Pd(OAc)_2$	Ag_2CO_3	Toluene	110	36	8:92

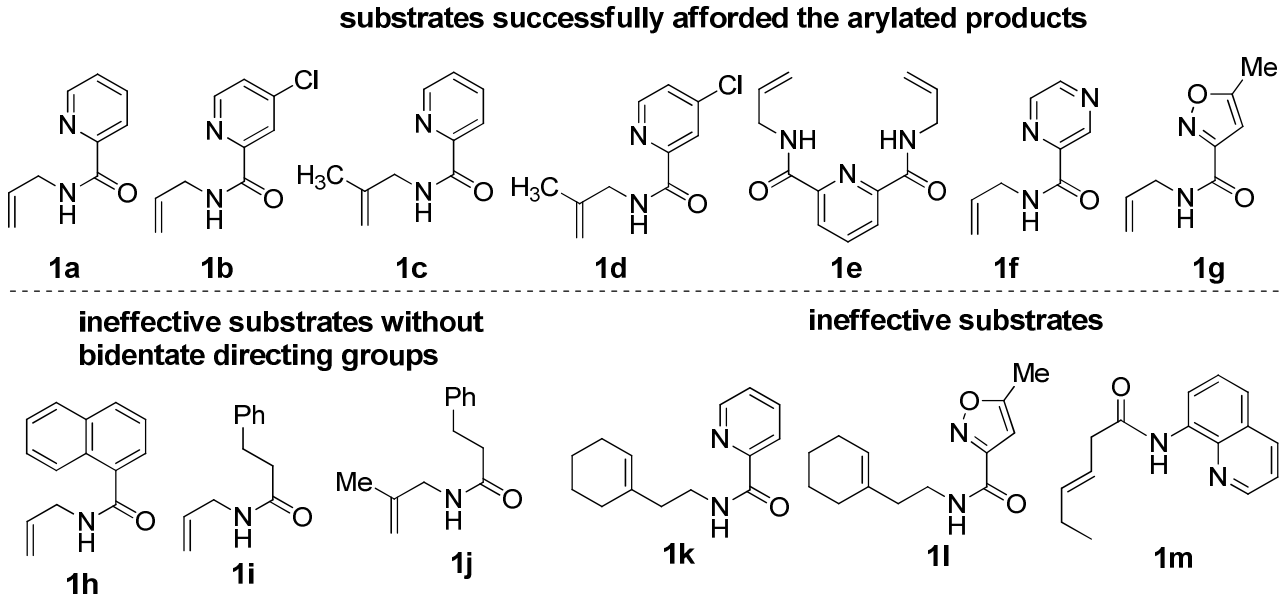
4	$Pd(OAc)_2$	$PhI(OAc)_2$	Toluene	110	0	-
5	$Pd(OAc)_2$	KOAc	Toluene	110	<10	69:31
6	$Pd(OAc)_2$	K_2CO_3	Toluene	110	29	70:30
7	$PdCl_2$	AgOAc	Toluene	110	37	11:89
8	$Pd(MeCN)_2Cl_2$	AgOAc	Toluene	110	31	11:89
9	$Pd(OAc)_2$	AgOAc	1,2-DCE	80	19	21:79
10	$Pd(OAc)_2$	AgOAc	*t*-BuOH	85	18	16:84
11	$Pd(OAc)_2$	AgOAc	*t*-AmlOH	105	37	12:88
12[c]	$Pd(OAc)_2$	AgOAc	Toluene	110	69	4:96
13[d]	$Pd(OAc)_2$	AgOAc	Toluene	110	48	16:84
14[e]	$Pd(OAc)_2$	AgOAc	Toluene	110	25	18:82
15[f]	$Pd(OAc)_2$	AgOAc	Toluene	110	0	-
16[g]	$Pd(OAc)_2$	AgOAc	Toluene	110	0	-
17[h]	$Pd(OAc)_2$ (3 mol%)	dppp (6 mol%) Et_3N (0.5 mmol)	Ethylene glycol (1.5 mL)	145	traces	-
18[i]	$Pd(OAc)_2$ (2 mol%)	PPh_3 (4 mol%) TMEDA (0.5 mmol)	DMF (1.5 mL)	120	traces	-
19[j]	$Pd(OAc)_2$ (4 mol%)	PPh_3 (8 mol%) Cs_2CO_3 (0.5 mmol)	DMF (1.5 mL)	120	traces	-
20[k]	$Pd(OAc)_2$ (10 mol%)	K_2CO_3 (1 mmol)	*t*-AmlOH (3 mL)	105	traces	-



[a] The *E*/*Z* ratios were determined from the NMR spectra of the corresponding crude reaction mixtures. All the reactions were performed using PdL_2 (5-10 mol%), additive (0.55 mmol), solvent (3 mL) for 36 h unless otherwise stated. [b] Five mol% of $Pd(OAc)_2$ was used. [c] Six equiv (1.5 mmol) of **2a** was used. [d] Three equiv (0.75 mmol) of **2a** was used. [e] Two equiv (0.5 mmol) of **2a** was used. [f] The reaction was performed using **2b** instead of **2a**. [g] The reaction was performed using **2c** instead of **2a**. [h] 0.27 mmol of **2a** and the reaction time was 5 h. [i] The reaction time was 5 h. [j] 0.83 mmol of **2a** and the reaction time was 24 h. [k] 1 mmol of **2a** and the reaction time was 24 h.

The C-H arylation reaction of a mixture of *N*-allylpicolinamide **1a** (1 equiv), 1-iodo-4-methoxybenzene (**2a**, 4 equiv), $Pd(OAc)_2$ (5 mol%) and AgOAc (2.2 equiv) in toluene at 110 °C afforded the γ-C(sp^2)-H arylated allylamine derivatives **3a′**/**3a** (*E*/*Z* isomers) with a yield of 51% and an *E*/*Z* ratio of 21:79 (entry 1, Table 1). As was envisioned, this reaction afforded the γ-C-H arylated allylamine derivative **3a** with *Z*-stereochemistry as the major isomer, and this result indicated the involvement of a chelation-assisted mechanism of *N*-allylpicolinamide **1a**. We next performed the same reaction using 10 mol% of the $Pd(OAc)_2$ catalyst, which afforded **3a′**/**3a** (*E*/*Z* isomers) with an improved yield (64%) and *E*/*Z* ratio of 11:89 (entry 2, Table 1).

Scheme 3. Directing Groups and Substrates Employed for Investigating the γ-C(sp^2)-H Arylation.[a,44b]



[a] General reaction conditions used for performing the arylations of substrates **1a-m**: substrate (0.25 mmol), **2a** or ArI (1 mmol), $Pd(OAc)_2$ (10 mol%), AgOAc (0.55 mmol), toluene (3 mL), 24 h, and 110 °C.

We then determined whether the yield and *E/Z* ratio of **3a′**/**3a** could be further improved using various palladium catalysts, additives and solvents. The Pd(II)-catalyzed γ-C(sp^2)-H arylation of **1a** with **2a** in the presence of Ag_2CO_3 afforded **3a′**/**3a** with a yield of only 36% and an *E/Z* ratio of 8:92 (entry 3, Table 1). The arylation of **1a** with **2a** in the presence of $PhI(OAc)_2$ or KOAc failed to afford **3a′**/**3a** (entries 4 and 5, Table 1). The arylation of **1a** with **2a** in the presence of K_2CO_3 afforded **3a′**/**3a** with a yield of only 29% and an *E/Z* ratio of 70:30 (entry 6, Table 1). Notably, this reaction afforded the γ-C-H arylated allylamine derivative **3a′** with *E*-stereochemistry as the major isomer, indicating the involvement of a conventional Heck-type reaction mechanism.[31,32,45a] We next attempted the arylation of **1a** with **2a** using $PdCl_2$ and

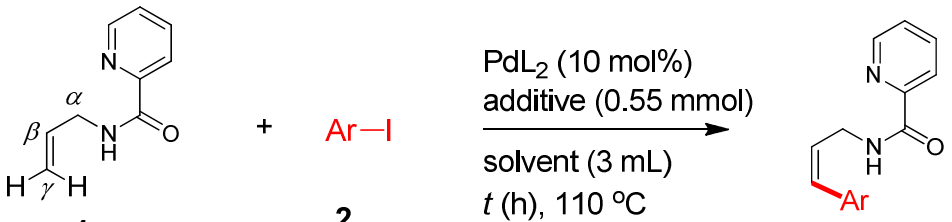
$Pd(CH_3CN)_2Cl_2$ as the catalysts instead of $Pd(OAc)_2$. The reaction of **1a** with **2a** in the presence of $PdCl_2$ or $Pd(CH_3CN)_2Cl_2$ (10 mol%) and AgOAc (2.2 equiv) afforded **3a′**/**3a** with yields of only 31-37% and an *E/Z* ratio of 11:89 (entries 7 and 8, Table 1). We also performed the arylation of **1a** with **2a** in different solvents, e.g., 1,2-dichloroethane (1,2-DCE), *tert*-butanol (*t*-BuOH) and *tert*-amyl alcohol (*t*-AmylOH). The Pd(II)-catalyzed reactions of **1a** with **2a** in 1,2-DCE and *t*-BuOH solvents were not fruitful (entries 9 and 10, Table 1). The Pd(II)-catalyzed reaction of **1a** with **2a** in *t*-AmylOH afforded **3a′**/**3a** with a yield of only 37% and an *E/Z* ratio of 12:88 (entry 11, Table 1).

To improve the yield and *E/Z* ratio of **3a′**/**3a**, we screened the Pd(II)-catalyzed arylation of **1a** using different equiv of **2a**. Accordingly, the arylation of **1a** (1 equiv) with 6 equiv of **2a** afforded **3a′**/**3a** in a marginally improved yield (69%) with an *E/Z* ratio of 4:96 (entry 12, Table 1). The arylation of **1a** (1 equiv) with 2-3 equiv of **2a** afforded low yields of **3a′**/**3a** (25-48%) with slightly decreased *E/Z* ratios (*E/Z* ratio up to 16:84, entries 13 and 14, Table 1). The arylation of **1a** with the coupling partners 1-bromo-4-methoxybenzene (**2b**) and 1-chloro-4-methoxybenzene (**2c**) instead of **2a** did not afford **3a′**/**3a** (entries 15 and 16, Table 1). We also performed the arylation of **1a** using various standard Heck-type reaction conditions, and these reactions were not fruitful (entries 17-20, Table 1). The optimization reactions revealed that the isomers **3a′**/**3a** were formed with different *E/Z* ratios under the experimental conditions. While we cannot ignore the occurrence of thermal *cis-trans* (*Z*/*E*) isomerization as discussed in our previous work,[45a] a control reaction was performed to check whether the *cis-trans* (*Z*/*E*) isomerization is occurring under the thermal condition or the *E*-isomer is formed under via a conventional Heck-type reaction pathway. Accordingly, the isomers **3a′**/**3a** (*E/Z* = 1:99) were treated with the catalyst $Pd(OAc)_2$ and additive AgOAc in the absence of **2a**. The crude NMR of

this reaction revealed a minor change in the *E/Z* ratio and the *E/Z* ratio was found to be 11:89 (eq 1, Table 1). Additionally, to check whether a second arylation of **3a′**/**3a** occurs under the experimental conditions**,** we performed the arylation of **3a′**/**3a** (*E/Z* = 11:89) with iodobenzene. This reaction afforded a complex mixture and purification of the crude mixture did not give the expected bisarylated product **3aA** (eq 2, Table 1). After successfully achieving the arylations of substrates **1a-g**, we then performed the Pd(II)-catalyzed arylations of substrates **1h-j**, which were lacking the corresponding bidentate directing groups, and these reactions did not give the corresponding arylated products in characterizable amounts (Scheme 3).[44b] These experiments indicated that, in substrates **1a-g**, the corresponding bidentate directing groups played an important role in the Pd(II)-catalyzed C-H arylation process to afford the corresponding *Z*-isomers **3-7** (major isomers).

With the reaction conditions optimized, we next wished to explore the generality and substrate scope of this protocol. Accordingly, Scheme 4 shows the arylation of **1a** with a wide range of aryl iodides under the optimized reaction conditions (entry 2, Table 1). The arylation of **1a** with aryl iodides containing an alkyl substituent at the para position afforded the corresponding γ-C-H arylated allylamines **3b-g** with yields of 50-82% and moderate to good *E/Z* ratios (*E/Z* up to 9:91). The arylation of **1a** with various disubstituted aryl iodides and an aryl iodide containing a substituent at the meta position (e.g., COOEt) afforded the corresponding allylamines **3h-k** with yields of 40-59% and low to moderate *E/Z* ratios (*E/Z* up to 22:79, Scheme 4). We also performed the arylation of **1a** using another optimized reaction conditions (entry 12, Table 1) in which 6 equiv of ArI (**2a**) was used. Accordingly, the products **3b**, **3c**, **3g** and **3h** were obtained from the arylation of **1a** with the corresponding aryl iodides with relatively good *E/Z* ratios (*E/Z* up to 15:85, Scheme 4).

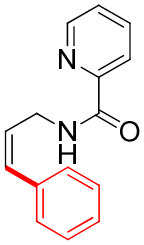
Scheme 4. Pd(II)-Catalyzed, Picolinamide-, Chelation-Assisted Construction of *Z*-Cinnamylamines 3b-m.



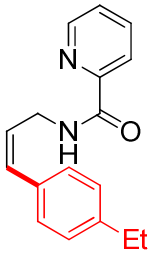
1a (0.25 mmol)

2 (1 mmol)

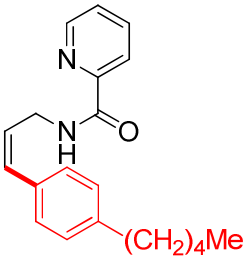
3b-m (*Z*-isomer, major)



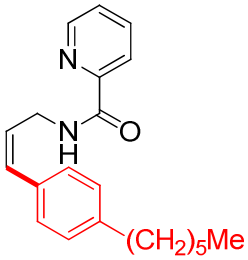
3b; 57%
E:*Z* = 25:75 (36 h)
E:*Z* = 15:85 (36 h)[b]



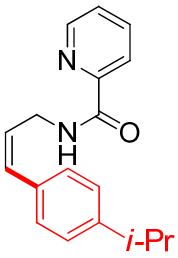
3c; 66%
E:*Z* = 25:75 (36 h)
E:*Z* = 15:85 (36 h)[b]



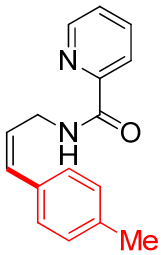
3d; 69%
E:*Z* = 9:91 (48 h)[c]



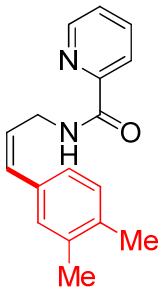
3e; 64%
E:Z = 14:86 (48 h)[c]



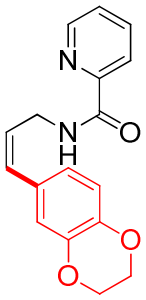
3f; 50%
E:*Z* = 20:80 (36 h)



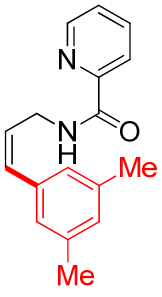
3g' = 11% (*E*)
3g = 71% (*Z*)
E:*Z* = 29:71 (36 h)[d]
E:*Z* = 15:85 (36 h)[b]



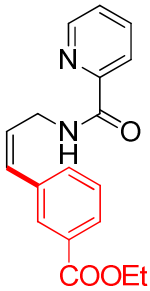
3h; 40%
E:*Z* = 29:71 (36 h)
E:*Z* = 16:84 (36 h)[b]



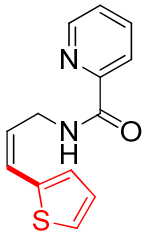
3i; 59%
E:Z = 27:73 (48 h)



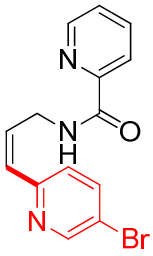
3j; 51%
E:*Z* = 38:62 (48 h)[e]



3k; 54%
E:*Z* = 21:79 (36 h)



3l; 69%
E:*Z* = 10:90 (48 h)[f]



3m; 50%
E:Z = 2:98 (48 h)

[a] The *E*/*Z* ratios were determined from the NMR spectra of the corresponding crude reaction mixtures, and in most cases, the corresponding major isomer (*Z*) was isolated in its pure form. [b] These reactions were performed using the conditions of entry 12 in Table 1, and some other trials using the conditions of entry 12 in Table 1 were not fruitful. [c] Two mmol of ArI was used. [d] In this case, compounds **3g′** (*E*-isomer) and **3g** (*Z*-isomer) were isolated in their pure forms. [e] Two mmol of ArI and 15 mol% of $Pd(OAc)_2$ were used. [f] Five mol% of $Pd(OAc)_2$ was used.

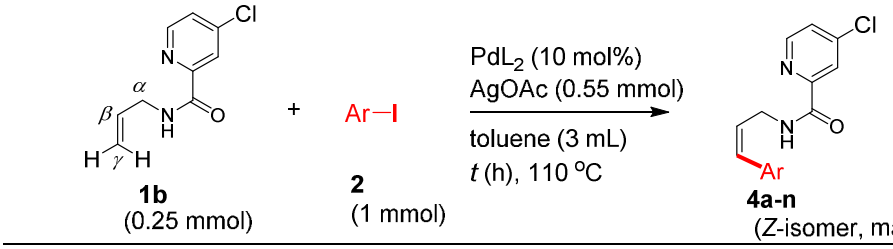
Then, we also performed the arylation of **1a** using heteroaryl iodides to afford the corresponding allylamine derivatives **3l** and **3m** with yields of 50-69% and high *E/Z* ratios (*E/Z* up to 2:98, Scheme 4). Most of the allylamines **3′**/**3** were obtained in satisfactory yields (>50% yields) and *E/Z* ratios (*E/Z* ratios ranging from 38:62 to 2:98). After performing the Pd(II)-catalyzed *γ*-C-H arylation of allylamine **1a** using picolinamide as the bidentate directing group to determine other working directing groups and obtain an improved yield and *E/Z* ratio, we attempted the *γ*-C-H arylation of allylamine **1b** by using 4-chloropicolinamide as the bidentate directing group. The arylation of **1b** with PhI, aryl iodides containing a substituent at the para or meta position (e.g., OMe, Me, Et, *n*-pentyl, *n*-hexyl, *i*-Pr and COOEt), disubstituted aryl iodides and heteroaryl iodides afforded the corresponding *γ*-C-H arylated allylamine derivatives **4a-n** with yields of 41-63% and low to good *E/Z* ratios (*E/Z* up to 12:88, Scheme 5). Most of the derivatives **4′**/**4** were obtained with satisfactory yields (>50% yields) and *E/Z* ratios (*E/Z* ratios ranging from 34:66 to 12:88). A comparison of the obtained yields and *E/Z* ratios of the products

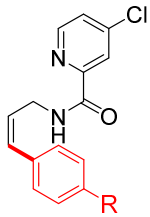
shown in Schemes 4 and 5 revealed that, except for some cases, the efficacy of the bidentate directing group 4-chloro-2-picolinamide was comparable to that of 2-picolinamide.

To extend the substrate scope of this method, we attempted the arylation of *N*-(2-methylallyl)picolinamides **1c** and **1d**, which were derived from *β*-methylallylamine and the corresponding picolinic acids. Notably, *N*-(2-methylallyl)picolinamides **1c** and **1d** contain both *γ*-C(sp^3)-H and *γ*-C(sp^2)-H bonds, which can undergo the arylation under the experimental conditions. Scheme 6 shows the arylation of **1c** and **1d** with various aryl iodides under the optimized reaction conditions. We initially performed the Pd(II)-catalyzed reaction of **1c** with aryl iodides containing a substituent at the para position (e.g., Me, Et, Cl, COOMe and *i*-Pr), which afforded the corresponding *γ*-C(sp^2)-H and *γ*-C(sp^3)-H bisarylated allylamine derivatives **5a-e** with yields of 36-50% (Scheme 6).

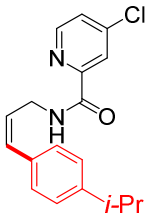
We then performed the Pd(II)-catalyzed reaction of **1c** and **1d** with various disubstituted aryl iodides, an aryl iodide containing a substituent at the meta position (e.g., COOEt) and heteroaryl iodides. These reactions also afforded the corresponding *γ*-C(sp^2)-H and *γ*-C(sp^3)-H bisarylated allylamine derivatives **5f-k** and **7a** with yields of 34-47%. It should be noted that the Pd(II)-catalyzed reaction of **1c** with 2-chloro-4-iodopyridine afforded the *γ*-C(sp^2)-H monoarylated product **6a** along with the expected *γ*-C(sp^2)-H and *γ*-C(sp^3)-H bisarylated allylamine derivative **5k**. Given this interesting result, we performed the Pd(II)-catalyzed arylation of **1c** and **1d** with various iodopyridines, which afforded the corresponding *γ*-C(sp^2)-H monoarylated products **6b-d** with yields of 40-41% (Scheme 6).

Scheme 5. Pd(II)-Catalyzed, 4-Chloropicolinamide-, Chelation-Assisted Construction of *Z*-Cinnamylamines 4a-n.[a]

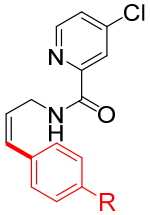




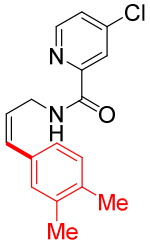
4a; R=H, 50%, *E*:*Z* = 34:66 (36 h)
4b; R=OMe, 41%, *E*:*Z* = 29:71 (36 h)



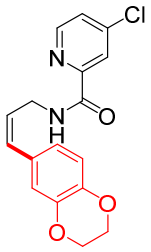
4c' = 8% (*E*)
4c = 53% (*Z*)
E:*Z* = 19:81 (36 h)[b]



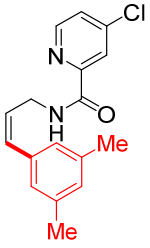
4d; R=Me, 56%, *E*:*Z* = 17:83 (36 h)[c]
4e; R=Et, 50%, *E*:*Z* = 16:84 (36 h)
4f; R=*n*-pentyl, 57%, *E*:*Z* = 20:80 (36 h)
4g; R=*n*-hexyl, 50%, *E*:*Z* = 20:80 (36 h)



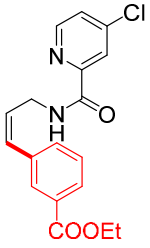
4h; 52%
E:*Z* = 12:88 (36 h)[c]



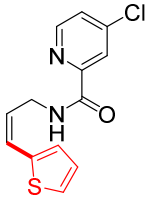
4i; 60%
E:*Z* = 28:72 (36 h)



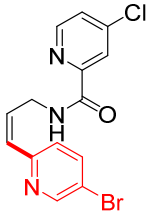
4j; 53%
E:*Z* = 28:72 (36 h)[c]



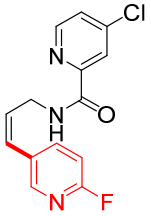
4k; 58%
E:*Z* = 23:77 (48 h)



4l; 63%
E:*Z* = 37:63 (60 h)[d]



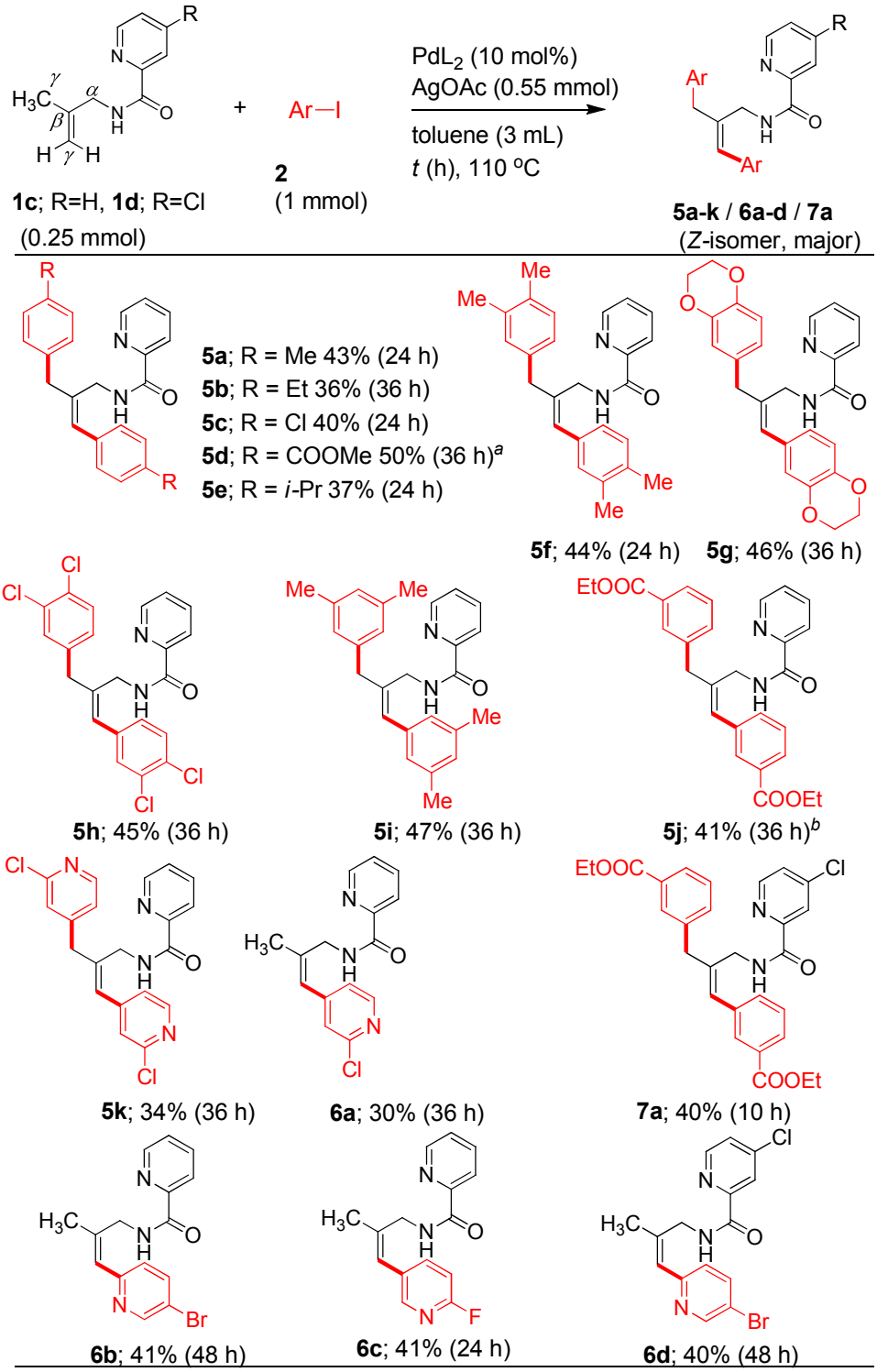
4m; 54%
E:*Z* = 23:77 (48 h)



4n; 50%
E:*Z* = 18:82 (36 h)[c]

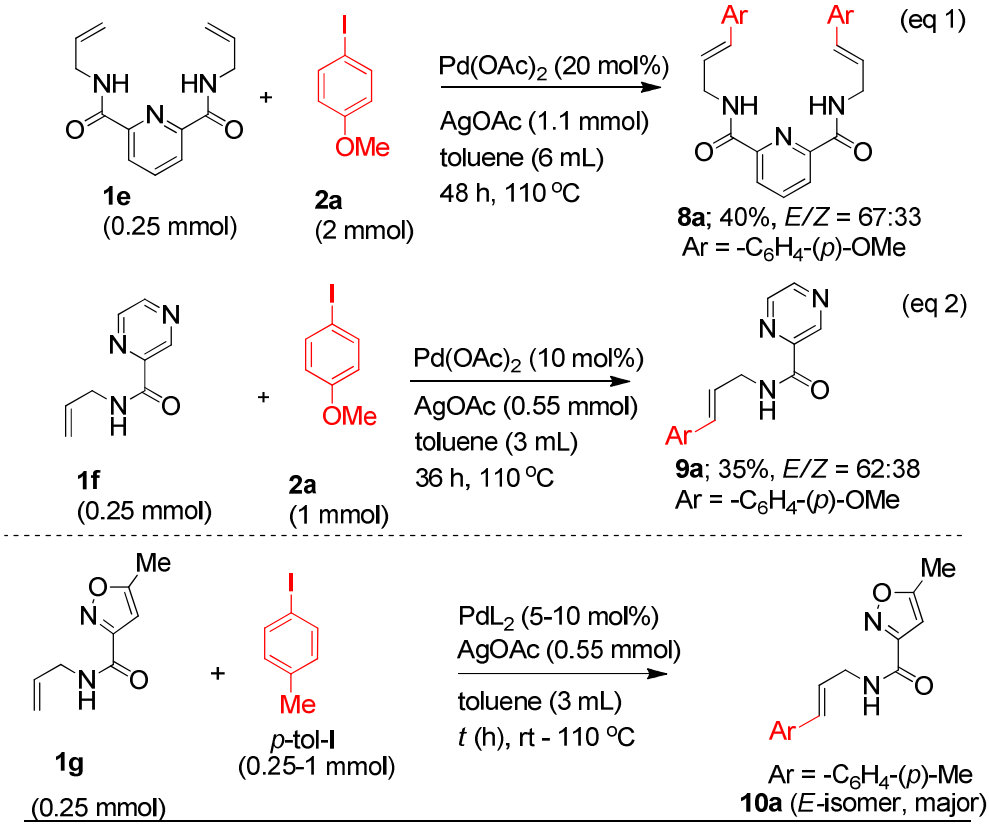
[a] The *E*/*Z* ratios were determined from the NMR spectra of the corresponding crude reaction mixtures, and in most cases, the corresponding major isomer (*Z*-isomer) was isolated in pure form. [b] In this case, compounds **4c′** (*E*-isomer) and **4c** (*Z*-isomer) were isolated in their pure forms. [c] Fifteen mol% of $Pd(OAc)_2$ was used. [d] Two mmol of ArI was used.

Scheme 6. Pd(II)-Catalyzed, Picolinamide-, Chelation-Assisted sp^2 and sp^3 γ-C-H Arylation to Construct *Z*-Cinnamylamines 5a-k, 6a-d and 7a.

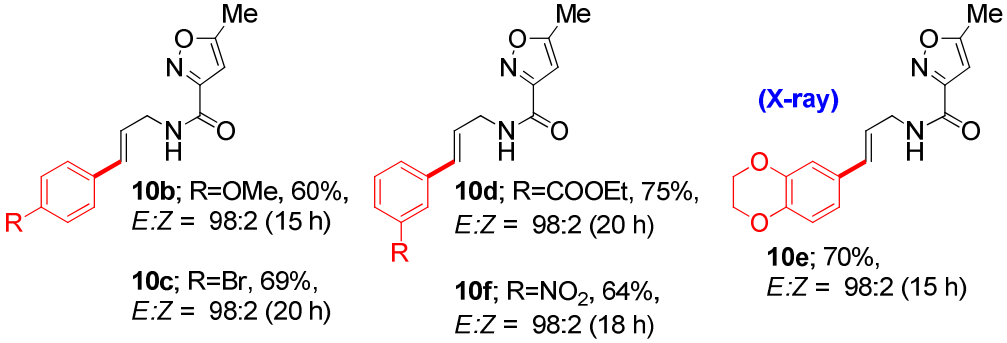


[a] Fifteen mol% of $Pd(OAc)_2$ was used. [b] Twenty mol% of $Pd(OAc)_2$ was used.

Scheme 7. $Pd(OAc)_2$/AgOAc-Catalyzed *E*-Selective *γ*-C-H Arylation of Allylamine Substrates 1e-g.[a]



Entry	PdL_2 (mol%)	*p*-Tol-I (mmol)	*T* (°C)	*t* (h)	**10a** Yield (%)	*E*:*Z* ratio
1	$Pd(OAc)_2$ (10)	0.25	110	0.5	48	98:2
2	$Pd(OAc)_2$ (5)	0.25	rt	60	33	89:11
3	$Pd(OAc)_2$ (5)	0.25	50	24	78	98:2
4[b]	$Pd(OAc)_2$ (5)	1	rt	24	-	-
5[b]	$Pd(OAc)_2$ (5)	1	50	24	-	-
6[b]	$Pd(OAc)_2$ (10)	0.5	110	48	-	-
7[b]	$Pd(OAc)_2$ (10)	1	110	48	-	-

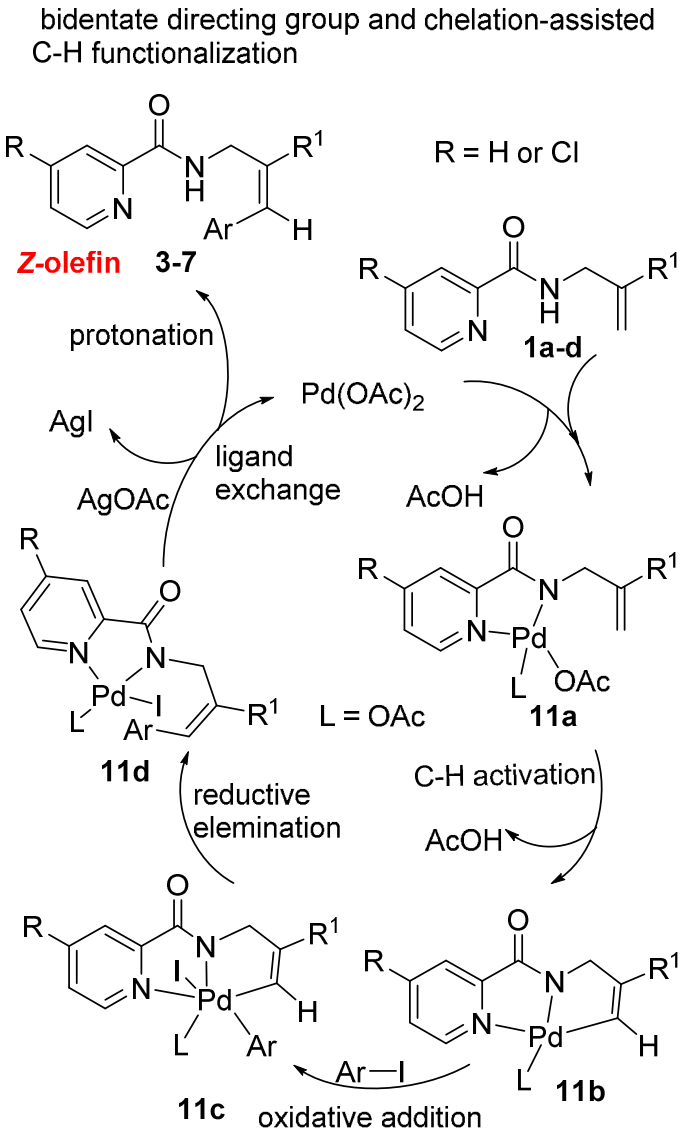


[a] The *E*/*Z* ratios were determined from the NMR spectra of the corresponding crude reaction mixtures. Compounds **10b-f** were prepared using the conditions given in entry 3. [b] A complex mixture was obtained, and purification of the crude reaction mixture did not afford the corresponding cinnamylamine in pure form.

Next, to elaborate our investigation on the $Pd(OAc)_2$/AgOAc-catalyzed γ-C-H arylation of allylamines, we performed the Pd(II)-catalyzed reaction of picolinamide **1e** with **2a**, which gave derivative **8a** with a yield of 40% with an *E/Z* ratio of 67:33 (eq 1, Scheme 7). We then performed the Pd(II)-catalyzed reaction of *N*-allylpyrazine-2-carboxamide **1f** with **2a**, and this reaction afforded the γ-C-H arylated allylamine derivative **9a** with a yield of only 35% and an *E/Z* ratio of 62:38 (eq 2, Scheme 7). An initial attempt of the reaction of isoxazole-3-carboxamide **1g** (1 equiv) with *p*-tolyl iodide (1 equiv) in the presence of $Pd(OAc)_2$ (10 mol%) and AgOAc (2.2 equiv) in toluene at 110 °C afforded the γ-C-H arylated allylamine derivative **10a** with a yield of 48% and an *E/Z* ratio of 98:2 (entry 1, Scheme 7). Surprised by this reaction, we then performed the arylation of **1g** using different reaction conditions to see whether we could obtain the *Z*-isomer as the major isomer. Accordingly, the reaction of **1g** (1 equiv) with *p*-tolyl iodide (1 equiv) in the presence of $Pd(OAc)_2$ (5 mol%) in toluene at rt afforded **10a** in 33% yield with *E/Z* ratio of 89:11 (entry 2, Scheme 7). The same reaction at 50 °C afforded **10a** in an improved yield (78%) with an *E/Z* ratio of 98:2 (entry 3, Scheme 7). Apart from these reactions, other attempts to obtain the *Z*-isomer from the arylation of **1g** under different reaction conditions were not fruitful (entries 4-7, Scheme 7). These results indicate that the arylation reactions comprising the substrates **1e-g** underwent the conventional Heck-type reaction mechanism without chelation assistance by the corresponding directing groups (Scheme 7).[31,32,45a] We were

interested to capitalize on the reaction conditions that afforded compound **10a** with *E*-stereochemistry (entry 3, Scheme 7) for synthesizing various *γ*-C-H arylated allylamine derivatives. Accordingly, treatment of **1g** with various aryl iodides in the presence of $Pd(OAc)_2$ (5 mol%) in toluene at 50 ^oC afforded a series of *γ*-C-H arylated allylamines **10b-f** with *E*-stereochemistry with yields of 60-75% (Scheme 7).

Scheme 8. Plausible Mechanism for the *Z*-Selective γ-C-H Arylation of 1a-d.



In the present work, the arylations of the picolinamide substrates **1a-d** selectively afforded the corresponding γ-C-H arylated products **3-7** with *Z*-stereochemistry as the predominant isomers (Table 1, Schemes 4-6). In concurrence with the generally proposed Pd^{II}-Pd^{IV} catalytic cycle mechanism pertaining to the $Pd(OAc)_2$/AgOAc-catalyzed, bidentate directing group-assisted C-H functionalization,[9-11,45] the observed *Z*-selective γ-C-H arylations of **1a-d** could be demonstrated *via* a plausible bidentate directing group-assisted and chelation-controlled C-H activation mechanism (Scheme 8). In this process, it is believed that AgOAc helps in the ligand-exchange step to generate the Pd^{IV} species **11d**.[9-11]

Furthermore, the picolinamide substrate **1e** and pyrazine-2-carboxamide substrate **1f** were expected to afford the corresponding products **8a** and **9a** with *Z*-stereochemistry as the predominant isomers (Scheme 7); however, the corresponding products **8a** and **9a** with *E*-stereochemistry were obtained as the predominant isomers. These results are likely due to the absence of chelation assistance by the corresponding bidentate directing groups. Substrate **1e-g** appears to only weakly coordinate with palladium, and therefore, the reactions result in a mixture of products formed through two different mechanisms, such as a Heck-type mechanism[46-49] leading to the *E*-regioisomer and a bidentate directing group-assisted, chelation-controlled mechanism leading to the *Z*-regioisomer.[45a]

CONCLUSION

We investigated the Pd(II)-catalyzed, bidentate directing group- and chelation-assisted *Z*-selective γ-C(sp^2)-H arylation of allylamines. The reactions of *N*-allylpicolinamides with various aryl and heteroaryl iodides in the presence of $Pd(OAc)_2$ and AgOAc led to the selective γ-C(sp^2)-H arylation to construct various *Z*-cinnamylamine derivatives with low to high *E*/*Z* ratios (*E*/*Z* ratios up to 2:98). Additionally, the Pd(II)-catalyzed arylation of an allylamine containing both γ-

C(sp^2)-H and γ-C(sp^3)-H bonds afforded the γ-C(sp^2)-H and γ-C(sp^3)-H arylated cinnamylamine scaffolds. Although Heck-type γ-arylations of allylamines have generally afforded *E*-cinnamylamines, the present work demonstrated the construction of *Z*-cinnamylamine scaffolds with reasonably good *E*/*Z* ratios. The Pd(II)-catalyzed γ-C(sp^2)-H arylation of *N*-allylpicolinamides was probed using different additives, directing groups and reaction conditions. In concurrence with the generally proposed mechanism pertaining to the $Pd(OAc)_2$/AgOAc-catalyzed, bidentate directing group-assisted C-H functionalization, the observed *Z*-selective γ-C(sp^2)-H arylations of **1a-d** were demonstrated *via* a plausible bidentate directing group- and chelation-assisted C-H activation mechanism. Finally, the $Pd(OAc)_2$/AgOAc-catalyzed arylation of *N*-allyl-5-methylisoxazole-3-carboxamide **1g** was found to afford the *E*-cinnamylamine derivatives **10a-f**, and it is assumed that the arylations of **1g** occurred via a ligand-free Heck-type reaction mechanism to afford the corresponding *E*-cinnamylamine derivatives **10a-f**.

EXPERIMENTAL SECTION

General Considerations. IR spectra of allylamines were recorded as thin films or KBr pellets. ^{1}H and ^{13}C NMR spectra of samples were recorded on 400 MHz and 100 MHz spectrometers, respectively (using TMS as an internal standard). HRMS measurements reported in this work were obtained from QTOF mass analyzer using electrospray ionization method (ESI). Column chromatography was carried out using silica gel (100-200 mesh) or neutral alumina. Starting materials preparation and C-H functionalization reactions were performed in anhydrous solvents under a nitrogen atmosphere wherever necessary. Isolated yields of all the compounds were reported and yields were not optimized. Thin layer chromatography (TLC) analysis was performed on silica gel or alumina plates and the components were visualized by observation

under iodine vapor. Amide starting materials used in the Pd(II)-catalyzed C-H arylation reactions were prepared (from their corresponding acids and amines) using the standard literature procedures.[9-11] The *E*/*Z* ratios were determined from the NMR spectra of the corresponding crude reaction mixtures and in the cases of the Table 1 and Schemes 4, 5 and 7 the total yields of *E*/*Z* isomers were reported. With regard to the C-H arylation reactions of **1a-d**, the data given here corresponds to the corresponding major isomers (*Z*-isomers) **3a-m**, **4a-n**, **5a-k**, **7a** and **6a-d**. In some cases, the corresponding minor isomers (*E*-isomers) **3g′** and **4c′** were isolated and characterized. With regard to the C-H arylation reactions of **1e-g**, the data given here correspond to the major isomers **8a**, **9a** and **10a-f** (*E*-isomers).

In concurrence with representative literature reports, [18c,d,43,45a] the *Z*-stereochemistry of **3a-m**, **4a-n**, **5a-k**, **7a** and **6a-d** (major isomers) and the *E*-stereochemistry of **3g′** and **4c′** (minor isomers) were ascertained based on the observed characteristic coupling constant values of the corresponding doublet peaks of the olefin protons ($J = \sim 11.5$ Hz for the *Z*-isomers and $J = \sim 15.8$ Hz for the *E*-isomers). The *E*-stereochemistry of **8a**, **9a** and **10a-f** were ascertained based on the observed characteristic coupling constant values of the corresponding doublet peaks of the olefin protons ($J = \sim 15.8$ Hz). Additionally, the observed *E*-stereochemistry of a representative compound **10e** was confirmed from the X-ray structure analysis (see the SI for the X-ray structure of **10e**).

The following points are with regard to separation of *E*/*Z* isomers. After the arylation of the corresponding allylamines **1a,b**, the purification of the crude reaction mixture afforded the respective *E*/*Z* cinnamylamines as a mixture since the corresponding *E*/*Z* cinnamylamines (**3′**/**3** and **4′**/**4**) had similar/close R_f values. Hence, the respective *E*/*Z* cinnamylamines were subjected to the repetitive column chromatographic purification to obtain the corresponding pure

compounds. In some cases, we isolated the major isomers (*Z*-isomers) in pure form after the repetitive column chromatographic purification and in some other cases, we got only a few column fractions of the corresponding major isomers (*Z*-isomers) in pure forms, which were used for characterization. Despite our repeated efforts to obtain the major isomers (*Z*-isomers) in pure forms, in some cases, the *Z*-isomers were obtained with traces of corresponding minor isomers due to similar *Rf* values of both major and minor isomers. With regard to isolation of minor isomers (*E*-isomers), except the minor isomers **3g′** and **4c′** (*E*-isomers), our repeated efforts to isolate the corresponding other *E*-isomers **3′** and **4′** in pure forms for characterization were not fruitful. The Pd(II)-catalyzed arylation of **1c,d** afforded the corresponding double C-H arylated compounds **5a-k** and **7a** (*Z*-isomers) as the major isomers. Though in some reactions the corresponding crude NMRs indicated the formation of trace amounts minor compounds, except the compound **6a**, either we could not isolate any other corresponding minor isomers in pure forms or the reactions did not give any other isomers in characterizable amounts.

Procedure for the synthesis of *N*-allylamide 1a-f, 1h-k and 1m: An oven-dried round-bottom flask (25 mL capacity) was charged with an appropriate carboxylic acid (1.2 mmol, 1 equiv) and anhydrous DCM (4-6 mL) and two-three drops of DMF. To this solution oxalyl chloride (1.5 mmol, 1.5 equiv, 190 mg) was added dropwise at 0 °C. The mixture was stirred at rt for 12 h and then, the solvent was removed in vacuo and then dissolved in DCM (4-6 mL). The resulting acid chloride solution was immediately used in the next step without further purification. Another oven-dried round-bottom flask (25 mL capacity) was charged with an appropriate allylamine (1.0 mmol, 1 equiv), Et_3N (1.5 mmol, 1.5 equiv, 152 mg), DMAP (0.1 mmol, 0.1 equiv, 12 mg). To this solution, the acid chloride solution (obtained in the previous step) was added dropwise at 0 °C and after the addition the solution was warmed to rt and allow to stir overnight. Then, the

reaction mixture was quenched with sat. aq. $NaHCO_3$ solution (10-15 mL) and the organic layer was separated, dried over anhydrous MgSO4 and evaporated in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc:Hexanes = 30:70) to afford the corresponding carboxamides **1a-f**, **1h-k** and **1m**.

Procedure for the synthesis of carboxamides 1g and 1l: An oven-dried round-bottom flask (25 mL capacity) was charged with 5-methylisoxazole-3-carboxylic acid (1 mmol, 1 equiv) and DCM (6 mL) under a nitrogen atm. Then, EDCI (1.1 mmol, 1.1 equiv, 172 mg) and HOBt•H_2O (1.1 mmol, 1.1 equiv, 168 mg) were added dropwise at 0 °C and the reaction mixture was stirred for 15 min. Then, to the reaction mixture an appropriate allylamine (1 mmol, 1.1 equiv) was added dropwise at 0 °C. Then, the solution was warmed to room temperature and the stirring was continued for 12 h. After this period, water (4-7 mL) was added and extracted with DCM (4-7 mL, 2-3 times). The combined organic layers were washed with sat. aq. $NaHCO_3$ (10 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc:Hexanes = 35:65) to afford the corresponding products **1g** and **1l**.

General procedure for the Pd(II)-catalyzed arylation of *N*-allylamide derivatives 1a-m and the preparation of 3a-m/4a-n/5a-k/6a-d/7a/10a-f. An oven-dried round-bottom flask (10 mL capacity) was charged with an appropriate *N*-allylamide derivative (0.25 mmol, 1 equiv), an appropriate aryl iodide (1.0 mmol, 4.0 equiv), $Pd(OAc)_2$ (10 mol%, 5.6 mg,), AgOAc (0.55 mmol, 2.2 equiv, 91.8 mg) and toluene (3 mL). This reaction mixture was heated at 110 ^oC for 24-48 h under a nitrogen atm. After this period, the reaction mixture was concentrated in vacuo and purification of the resulting reaction mixture by column chromatography on silica gel

furnished the corresponding γ-C-H arylated allylamine derivatives **3a-m**/**4a-n**/**5a-k**/**6a-d**/**7a**/**10a-f** (see the corresponding Tables/Schemes for specific examples).

***N*-Allylpicolinamide (1a):**[50a] The compound **1a** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown colour liquid; R_f = 0.51 (EtOAc/hexane = 1:4); Yield: 77% (126 mg); IR (DCM): 3446, 2064, 1642, 1529, 1465 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (dd, 1H, J_1 = 4.8 Hz, J_2 = 0.8 Hz), 8.21 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 8.17 (br. s, 1H), 7.85 (t, 1H, J = 7.7 Hz), 7.45-7.41(m, 1H), 5.99-5.89 (m, 1H), 5.30-5.16 (m, 2H), 4.13-4.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.7, 148.0, 137.3, 134.0, 126.2, 122.2, 116.3, 41.7; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_9H_{11}N_2O$: 163.0871; found 163.0875.

***N*-Allyl-4-chloropicolinamide (1b):**[50b] The compound **1b** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow colour liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 67% (133 mg); IR (DCM): 3441, 2063, 1643, 1524, 1290 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, 1H, J = 5.2 Hz), 8.17 (d, 1H, J = 2.0 Hz), 8.10 (br. s, 1H), 7.41 (td, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 5.95-5.85 (m, 1H), 5.26-5.13 (m, 2H), 4.09-4.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.8, 133.8, 126.3, 122.9, 116.6, 41.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_9H_{10}ClN_2O$: 197.0482; found 197.0484.

***N*-(2-Methylallyl)picolinamide (1c):** The compound **1c** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.52 (EtOAc/hexane = 1:4); Yield: 69% (123 mg); IR (DCM): 3389, 1675, 1527, 1289 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32-8.31 (m, 1H), 8.17 (br. s, 1H), 8.00 (dd, 1H, J_1 = 7.8 Hz, J_2 = 0.9 Hz), 7.61 (td, 1H, J = 7.7 Hz, J = 1.8 Hz), 7.21-7.19 (m, 1H), 4.69-4.63 (m, 2H), 3.82 (d, 2H, J = 6.4 Hz), 1.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 149.6, 147.9, 141.6, 137.2, 126.1,

122.1, 110.8, 44.7, 20.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{13}N_2O$: 177.1028; found 177.1023.

4-Chloro-*N*-(2-methylallyl)picolinamide (1d): The compound **1d** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 35% (74 mg); IR (DCM): 3391, 1677, 1527, 1292 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, *J* = 5.2 Hz), 8.21 (d, 1H, *J* = 1.4 Hz), 8.14 (br. s, 1H), 7.44-7.42 (m, 1H), 4.90 (s, 1H), 4.87 (s, 1H), 4.01 (d, 2H, *J* = 6.2 Hz), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 151.3, 149.0, 145.9, 141.6, 126.3, 123.0, 111.2, 45.1, 20.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{12}ClN_2O$: 211.0638; found 211.0629.

***N*$_2$,*N*$_6$-Diallylpyridine-2,6-dicarboxamide (1e):** The compound **1e** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 65% (161 mg); IR (DCM): 3287, 1667, 1537, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.18 (t, 2H, *J* = 6.0 Hz), 8.28 (d, 2H, *J* = 7.8 Hz), 7.95 (t, 1H, *J* = 7.8 Hz), 5.69-5.59 (m, 2H), 4.96-4.91 (m, 2H), 4.83-4.81 (m, 2H), 3.86 (t, 4H, *J* = 5.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 148.8, 138.9, 133.8, 124.9, 116.1, 42.0; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{13}H_{15}N_3NaO_2$: 268.1062; found 268.1068.

***N*-Allylpyrazine-2-carboxamide (1f):** The compound **1f** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 40:60) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 70% (115 mg); IR (DCM): 3397, 1667, 1532, 1402 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.41 (dd, 1H, J_1 = 3.4 Hz, J_2 = 1.3 Hz), 8.74 (dd, 1H, J_1 = 5.1 Hz, J_2 = 2.5 Hz), 8.53 (br. s, 1H), 7.95 (br. s, 1H), 5.97-5.88 (m, 1H), 5.30-5.16 (m, 2H), 4.13-4.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 147.3, 144.4, 144.4, 142.6, 133.6, 116.8, 41.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_8H_{10}N_3O$: 164.0824; found 164.0822.

***N*-Allyl-5-methylisoxazole-3-carboxamide (1g):** The compound **1g** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 50% (83 mg); IR (DCM): 3332, 1673, 1599, 1458, 1280 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (br. s, 1H), 6.43 (s, 1H), 5.92-5.83 (m, 1H), 5.26-5.14 (m, 2H), 4.04 (t, 2H, *J* = 5.8 Hz), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 159.0, 158.7, 133.4, 116.8, 101.4, 41.7, 12.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_8H_{11}N_2O_2$: 167.0821; found 167.0815.

***N*-Allyl-1-naphthamide (1h):** The compound **1h** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 65% (138 mg); IR (KBr): 3284, 1640, 1536, 1422 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, 1H, *J* = 8.1 Hz), 7.77-7.73 (m, 2H), 7.45-7.37 (m, 2H), 7.32 (d, 1H, *J* = 7.0 Hz), 7.18 (t, 1H, *J* = 7.9 Hz), 6.99 (br. s, 1H), 5.80-5.71 (m, 1H), 5.12-5.01 (m, 2H), 3.84 (t, 2H, *J* = 5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 139.1, 134.1, 133.5, 130.3, 130.1, 128.2, 126.8, 126.2, 125.5, 125.0, 124.6, 116.1, 42.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}NO$: 212.1075; found 212.1082.

***N*-Allyl-3-phenylpropanamide (1i):**[50c] The compound **1i** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 72% (137 mg); IR (DCM): 3293, 1643, 1551, 1454, 1262 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (m, 2H), 7.22-7.19 (m, 3H), 6.28 (br. s, 1H), 5.82-5.72 (m, 1H), 5.10-5.06 (m, 2H), 3.83 (t, 2H, *J* = 5.6 Hz), 2.97 (t, 2H, *J* = 7.5 Hz), 2.52 (t, 2H, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 140.9, 134.2, 128.5, 128.3, 126.2, 116.1, 41.9, 38.3, 31.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{12}H_{16}NO$: 190.1232; found 190.1228.

***N*-(2-Methylallyl)-3-phenylpropanamide (1j):**[50d] The compound **1j** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 74% (152 mg); IR (DCM): 3294, 1648, 1553, 1454 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.27 (m, 2H), 7.22-7.20 (m, 3H), 6.00 (br. s, 1H), 4.78 (s, 1H), 4.70 (s, 1H), 3.77 (d, 2H, *J* = 5.9 Hz), 2.99 (t, 2H, *J* = 7.9 Hz), 2.54 (t, 2H, *J* = 7.9 Hz), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 141.9, 140.9, 128.5, 128.4, 126.2, 110.8, 45.0, 38.4, 31.8, 20.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{18}NO$: 204.1388; found 204.1379.

***N*-(2-(Cyclohex-1-en-1-yl)ethyl)picolinamide (1k):**[50e] The compound **1k** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 40:60) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 80% (184 mg); IR (DCM): 3392, 1665, 1590, 1433 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (dd, 1H, J_1 = 4.7 Hz, J_1 = 0.5 Hz), 8.14 (d, 1H, *J* = 7.8 Hz), 8.05 (br. s, 1H), 7.77 (td, 1H, *J* = 7.7 Hz, *J* = 1.7 Hz), 7.37-7.33 (m, 1H), 5.47 (s, 1H), 3.52-3.47 (m, 2H), 2.22-2.19 (m, 2H), 1.94-1.92 (m, 4H), 1.60-1.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 150.0, 148.0, 137.2, 134.5, 125.9, 123.4, 122.0, 37.7, 37.5, 28.0, 25.2, 22.8, 22.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{19}N_2O$: 231.1497; found 231.1491.

***N*-(2-(Cyclohex-1-en-1-yl)ethyl)-5-methylisoxazole-3-carboxamide (1l):** The compound **1l** was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.52 (EtOAc/Hexanes = 1:4); Yield: 65% (153 mg); IR (DCM): 3365, 1660, 1601, 1545, 1270 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ 6.83 (br. s, 1H), 6.42 (s, 1H), 5.51 (s, 1H), 3.52-3.47 (m, 2H), 2.47 (s, 3H), 2.22 (t, 2H, *J* = 6.8 Hz), 1.99-1.95 (m, 4H), 1.65-1.53 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 159.0, 158.9, 134.2, 123.9, 101.4,

37.4, 37.3, 27.9, 25.2, 22.8, 22.3, 12.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{19}N_2O_2$: 235.1447; found 235.1440.

(*E*)-*N*-(Quinolin-8-yl)hex-3-enamide (1m): The compound **1m** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a brown colour liquid; R_f = 0.51 (EtOAc/Hexane = 1:4); Yield: 70% (168 mg); IR (DCM): 3054, 2305, 1422, 1265 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.10 (br. s, 1H), 8.80-8.77 (m, 2H), 8.13 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.53 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.7 Hz), 7.48 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.6 Hz), 7.43 (dd, 1H, J_1 = 8.3 Hz, J_2 = 4.2 Hz), 5.92-5.72 (m, 2H), 3.28 (d, 2H, J = 7.1 Hz), 2.24-2.16 (m, 2H), 1.14 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 148.1, 138.7, 138.5, 136.3, 134.5, 127.9, 127.4, 121.6, 121.5, 121.4, 116.3, 42.1, 25.8, 13.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{17}N_2O$: 241.1341; found 241.1330.

(*Z*)-*N*-(3-(4-Methoxyphenyl)allyl)picolinamide (3a): The compound **3a** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 25:75) as a brown colour liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 64% (43 mg, *E:Z* = 11:89); IR (DCM): 3441, 1667, 1511, 1251, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.24-8.22 (m, 1H), 8.16 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.26 (d, 2H, J = 8.6 Hz), 6.92 (d, 2H, J = 8.8 Hz), 6.59 (d, 1H, J = 11.5 Hz), 5.71 (dt, 1H, J_1 = 11.5 Hz, J_2= 6.7 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 158.8, 149.8, 148.1, 137.4, 131.3, 130.1, 129.0, 126.2, 122.3, 113.8, 55.3, 37.9; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}N_2NaO_2$: 291.1109; found 291.1099.

(*Z*)-*N*-(3-Phenylallyl)picolinamide (3b): The compound **3b** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/hexane = 1:4); Yield: 57% (34 mg, *E:Z* = 25:75); IR (DCM):

3441, 1659, 1524, 1383, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.25-8.22 (m, 1H), 8.17 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.41-7.37 (m, 2H), 7.33-7.28 (m, 3H), 6.67 (d, 1H, J = 11.6 Hz), 5.81 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.87 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.8, 148.1, 137.4, 136.4, 131.8, 128.8, 128.4, 127.9, 127.3, 126.2, 122.3, 37.8; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{14}N_2NaO$: 261.1004; found 261.0995.

(*Z*)-*N*-(3-(4-Ethylphenyl)allyl)picolinamide (3c): The compound **3c** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 66% (44 mg, *E:Z* = 25:75); IR (DCM): 3441, 1735, 1623, 1383, 1046 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.25-8.22 (m, 1H), 8.16 (br. s, 1H), 7.88 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.47-7.43 (m, 1H), 7.26-7.20 (m, 4H), 6.63 (d, 1H, J = 11.6 Hz), 5.76 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.67 (q, 2H, J = 7.6 Hz), 1.26 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.8, 148.1, 143.5, 137.4, 133.7, 131.8, 128.8, 127.9, 127.1, 126.2, 122.3, 37.9, 28.6, 15.6; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO$: 289.1317; found 289.1309.

(*Z*)-*N*-(3-(4-Pentylphenyl)allyl)picolinamide (3d): The compound **3d** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 69% (53 mg, *E:Z* = 9:91); IR (DCM): 3442, 2921, 1643, 1390 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, 1H, J = 4.7 Hz), 8.23 (d, 1H, J = 7.8 Hz), 8.15 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.23 (d, 2H, J = 8.2 Hz), 7.20 (d, 2H, J = 8.2 Hz), 6.63 (d, 1H, J = 11.6 Hz), 5.76 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.7 Hz), 2.62 (t, 2H, J = 7.6 Hz), 1.67-1.60

(m, 2H), 1.36-1.27 (m, 4H), 0.92 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.1, 142.2, 137.4, 133.7, 131.8, 128.8, 128.4, 127.1, 126.2, 122.3, 37.9, 35.7, 31.5, 31.2, 22.6, 14.1; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{24}N_2NaO$: 331.1786; found 331.1776.

(*Z*)-*N*-(3-(4-Hexylphenyl)allyl)picolinamide (3e): The compound **3e** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 64% (52 mg, *E:Z* = 14:86); IR (DCM): 2928, 1678, 1523, 1434 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.23 (d, 1H, J = 7.8 Hz), 8.15 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.23 (d, 2H, J = 8.2 Hz), 7.20 (d, 2H, J = 8.2 Hz), 6.64 (d, 1H, J = 11.6 Hz), 5.76 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.7 Hz), 2.62 (t, 2H, J = 7.6 Hz), 1.68-1.59 (m, 2H), 1.38-1.27 (m, 6H), 0.91 (t, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.1, 142.2, 137.4, 133.7, 131.8, 128.8, 128.4, 127.1, 126.2, 122.3, 37.9, 35.7, 31.8, 31.4, 29.0, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{27}N_2O$: 323.2123; found 323.2111.

(*Z*)-*N*-(3-(4-Isopropylphenyl)allyl)picolinamide (3f): The compound **3f** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 50% (35 mg, *E:Z* = 20:80); IR (DCM): 3390, 1672, 1523, 1464 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.23 (d, 1H, J = 7.8 Hz), 8.15 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.25 (s, 4H), 6.63 (d, 1H, J = 11.6 Hz), 5.76 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.8 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.97-2.90 (m, 1H), 1.27 (d, 6H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.1, 137.4, 133.9, 131.8, 128.8, 127.1, 126.4, 126.2, 122.3, 37.9, 33.9, 24.0; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{20}N_2NaO$: 303.1473; found 303.1462.

(*E*)-*N*-(3-(*p*-Tolyl)allyl)picolinamide (3g'): The compound **3g'** ((*E*) minor isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/hexane = 1:4); Yield: 11% (7 mg, *E:Z* = 29:71); IR (DCM): 3442, 1738, 1642, 1365, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.59-8.57 (m, 1H), 8.26-8.24 (m, 1H), 8.21 (br. s, 1H), 7.88 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.47-7.44 (m, 1H), 7.30 (d, 2H, J = 8.8 Hz), 7.13 (d, 2H, J = 8.8 Hz), 6.61 (d, 1H, J = 15.8 Hz), 6.27 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.3 Hz), 4.28 (td, 2H, J_1 = 6.3 Hz, J_2 = 1.4 Hz), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.1, 137.5, 137.4, 133.8, 132.2, 129.3, 126.3, 126.2, 124.3, 122.3, 41.5, 21.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}N_2NaO$: 275.1160; found 275.1147.

(*Z*)-*N*-(3-(*p*-Tolyl)allyl)picolinamide (3g): The compound **3g** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 71% (45 mg, *E:Z* = 29:71); IR (DCM): 3386, 1668, 1525, 1463, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.25-8.22 (m, 1H), 8.16 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.23-7.12 (m, 4H), 6.63 (d, 1H, J = 11.5 Hz), 5.75 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.8, 148.1, 137.4, 137.1, 133.5, 131.7, 129.1, 128.8, 127.2, 126.2, 122.3, 37.9, 21.2; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}N_2NaO$: 275.1160; found 275.1148.

(*Z*)-*N*-(3-(3,4-Dimethylphenyl)allyl)picolinamide (3h): The compound **3h** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 40% (27 mg, *E:Z* = 29:71); IR (DCM): 3441, 1643, 1367, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.25-8.22 (m, 1H), 8.15 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.6 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m,

1H), 7.15 (d, 1H, J = 7.6 Hz), 7.08-7.05 (m, 2H), 6.60 (d, 1H, J = 11.6 Hz), 5.74 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.1, 137.4, 136.5, 135.8, 134.0, 131.8, 130.1, 129.6, 127.0, 126.3, 126.2, 122.3, 37.9, 19.9, 19.5; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO$: 289.1317; found 289.1308.

(*Z*)-*N*-(3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)allyl)picolinamide (3i): The compound **3i** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 59% (44 mg, *E:Z* = 27:73); IR (DCM): 3442, 1671, 1506, 1433 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56-8.55 (m, 1H), 8.23 (d, 1H, J = 7.8 Hz), 8.16 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.42 (m, 1H), 6.87 (d, 1H, J = 8.3 Hz), 6.83 (d, 1H, J = 2.0 Hz), 6.80 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.0 Hz), 6.53 (d, 1H, J = 11.5 Hz), 5.70 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.40 (td, 2H, J_1 = 6.6 Hz, J_2 = 1.8 Hz), 4.29 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.8, 148.1, 143.2, 142.9, 137.4, 131.1, 130.0, 126.8, 126.2, 122.3, 122.2, 117.6, 117.1, 64.4, 64.3, 37.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{17}N_2O_3$: 297.1239; found 297.1248.

(*Z*)-*N*-(3-(3,5-Dimethylphenyl)allyl)picolinamide (3j): The compound **3j** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 51% (34 mg, *E:Z* = 38:62); IR (DCM): 1717, 1679, 1521, 1203 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.25-8.22 (m, 1H), 8.15 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 6.94-6.93 (m, 3H), 6.60 (d, 1H, J = 11.6 Hz), 5.76 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.9 Hz), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9,

148.1, 137.9, 137.4, 136.3, 132.0, 129.0, 127.6, 126.6, 126.2, 122.3, 37.9, 21.4; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO$: 289.1317; found 289.1317.

(*Z*)-Ethyl 3-(3-(picolinamido)prop-1-en-1-yl)benzoate (3k): The compound **3k** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 54% (42 mg, *E:Z* = 21:79); IR (DCM): 3380, 1717, 1523, 1282 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56-8.55 (m, 1H), 8.22 (d, 1H, *J* = 7.8 Hz), 8.19 (br. s, 1H), 7.97 (dd, 2H, J_1 = 6.4 Hz, J_2 = 1.4 Hz), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.53-7.42 (m, 3H), 6.68 (d, 1H, *J* = 11.6 Hz), 5.87 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.43-4.36 (m, 4H), 1.41 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 164.2, 149.7, 148.1, 137.4, 136.6, 133.0, 130.9, 130.6, 129.8, 129.2, 128.5, 128.4, 126.3, 122.3, 61.1, 37.7, 14.3 ; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{19}N_2O_3$: 311.1396; found 311.1410.

(*Z*)-*N*-(3-(Thiophen-2-yl)allyl)picolinamide (3l): The compound **3l** ((*Z*) major isomer)was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as pale yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 69% (42 mg, *E:Z* = 10:90); IR (DCM): 3442, 1662, 1532, 1386 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.24 (d, 1H, *J* = 7.8 Hz), 8.24 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.43 (m, 1H), 7.34 (t, 1H, *J* = 3.0 Hz), 7.06 (t, 2H, *J* = 3.5 Hz), 6.70 (d, 1H, *J* = 11.6 Hz), 5.71 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.51 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.8, 148.1, 139.3, 137.4, 128.1, 127.2, 126.2, 126.1, 126.1, 124.0, 122.3, 38.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}N_2OS$: 245.0749; found 245.0749.

(*Z*)-*N*-(3-(5-Bromopyridin-2-yl)allyl)picolinamide (3m): The compound **3m** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel

(EtOAc:Hexanes = 30:70) as a pale yellow colour liquid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 50% (40 mg, *E:Z* = 2:98); IR (DCM): 3337, 1651, 1521 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (d, 1H, *J* = 2.2 Hz), 8.67 (br. s, 1H), 8.58-8.56 (m, 1H), 8.22 (d, 1H, *J* = 7.8 Hz), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.80 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 7.45-7.41 (m, 1H), 7.15 (d, 1H, *J* = 8.3 Hz), 6.50 (d, 1H, *J* = 11.7 Hz), 6.09 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.66 (td, 2H, J_1 = 6.5 Hz, J_2 = 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 154.1, 150.4, 150.1, 148.1, 138.9, 137.3, 133.7, 129.0, 126.1, 125.5, 122.3, 118.7, 37.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}BrN_3O$: 318.0242; found 318.0244.

(*Z*)-4-Chloro-*N*-(3-phenylallyl)picolinamide (4a): The compound **4a** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 50% (34 mg, *E:Z* = 34:66); IR (DCM): 3382, 1674, 1525, 1262 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 1.9 Hz), 8.08 (br. s, 1H), 7.46 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.41-7.37 (m, 2H), 7.32-7.28 (m, 3H), 6.68 (d, 1H, *J* = 11.6 Hz), 5.79 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.8 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 136.3, 132.1, 128.8, 128.4, 127.5, 127.4, 126.4, 122.9, 37.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{14}ClN_2O$: 273.0795; found 273.0782.

(*Z*)-4-Chloro-*N*-(3-(4-methoxyphenyl)allyl)picolinamide (4b): The compound **4b** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 41% (31 mg, *E:Z* = 29:71); IR (DCM): 3442, 1670, 1511, 1383 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 2.0 Hz), 8.07 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.25 (d, 2H, *J* = 8.6 Hz), 6.92 (d, 2H, *J* = 8.8 Hz), 6.60 (d, 1H, *J* = 11.5 Hz),

5.69 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.40 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 158.8, 151.3, 149.0, 145.9, 131.6, 130.1, 128.9, 126.4, 125.8, 122.9, 113.8, 55.3, 38.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{16}ClN_2O_2$: 303.0900; found 303.0889.

(*E*)-4-Chloro-*N*-(3-(4-isopropylphenyl)allyl)picolinamide (4c'): The compound **4c'** ((*E*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 8% (7 mg, *E:Z* = 19:81); IR (DCM): 3412, 1670, 1520, 1386 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, 1H, *J* = 5.2 Hz), 8.25 (d, 1H, *J* = 2.0 Hz), 8.12 (d, 1H, *J* = 0.5 Hz), 7.46 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.33 (d, 2H, *J* = 8.2 Hz), 7.19 (d, 2H, *J* = 8.2 Hz), 6.61 (d, 1H, *J* = 15.8 Hz), 6.25 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.27 (t, 2H, *J* = 6.0 Hz), 2.94-2.87 (m, 1H), 1.25 (d, 6H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.4, 149.0, 148.7, 145.9, 134.1, 132.4, 126.7, 126.4, 126.4, 124.1, 123.0, 41.6, 33.9, 23.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{20}ClN_2O$: 315.1264; found 315.1266.

(*Z*)-4-Chloro-*N*-(3-(4-isopropylphenyl)allyl)picolinamide (4c): The compound **4c** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 53% (42 mg, *E:Z* = 19:81); IR (DCM): 3385, 1673, 1532, 1266 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (s, 1H), 8.06 (br. s, 1H), 7.45 (d, 1H, *J* = 5.2 Hz), 7.25 (s, 4H), 6.64 (d, 1H, *J* = 11.6 Hz), 5.74 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.7 Hz), 4.42 (t, 2H, *J* = 6.4 Hz), 2.97-2.90 (m, 1H), 1.28 (d, 6H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 148.2, 145.9, 133.8, 132.0, 128.8, 126.7, 126.5, 126.3, 122.9, 38.0, 33.9, 23.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{20}ClN_2O$: 315.1264; found 315.1252.

(*Z*)-4-Chloro-*N*-(3-(*p*-tolyl)allyl)picolinamide (4d): The compound **4d** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 56% (40 mg, *E:Z* = 17:83); IR (DCM): 2926, 1677, 1525, 1260 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.23 (d, 1H, *J* = 2.0 Hz), 8.07 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.20 (s, 4H), 6.63 (d, 1H, *J* = 11.5 Hz), 5.73 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 137.2, 133.4, 132.0, 129.1, 128.7, 126.8, 126.4, 122.9, 38.0, 21.3; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{15}ClN_2NaO$: 309.0771; found 309.0772.

(*Z*)-4-Chloro-*N*-(3-(4-ethylphenyl)allyl)picolinamide (4e): The compound **4e** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 50% (38 mg, *E:Z* = 16:84); IR (DCM): 2964, 1675, 1525 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 2.0 Hz), 8.07 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.25 (s, 4H), 6.65 (d, 1H, *J* = 11.5 Hz), 5.74 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.41(td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 2.67 (q, 2H, *J* = 7.6 Hz), 1.26 (t, 3H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 143.6, 133.6, 132.0, 128.8, 127.9, 126.8, 126.4, 122.9, 38.0, 28.6, 15.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}ClN_2O$: 301.1108; found 301.1100.

(*Z*)-4-Chloro-*N*-(3-(4-pentylphenyl)allyl)picolinamide (4f): The compound **4f** ((*Z*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 57% (49 mg, *E:Z* = 20:80); IR (DCM): 2928, 1679, 1523 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 2.0 Hz), 8.07 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1

Hz), 7.23 (d, 2H, *J* = 8.5 Hz), 7.20 (d, 2H, *J* = 8.5 Hz), 6.64 (d, 1H, *J* = 11.6 Hz), 5.74 (dt, 1H, *J* = 11.6 Hz, *J* = 6.7 Hz), 4.41 (td, 2H, *J* = 1.8 Hz, *J* = 6.7 Hz), 2.62 (t, 2H, *J* = 7.6 Hz), 1.67-1.60 (m, 2H), 1.39-1.32 (m, 4H), 0.92 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 142.3, 137.2, 133.6, 132.0, 130.6, 128.7, 128.5, 126.7, 126.3, 122.9, 38.0, 35.7, 31.5, 31.1, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}ClN_2O$: 343.1577; found 343.1562.

(*Z*)-4-Chloro-*N*-(3-(4-hexylphenyl)allyl)picolinamide (4g): The compound **4g** ((*Z*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 50% (45 mg, *E:Z* = 20:80); IR (DCM): 2929, 1674, 1508, 1458 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 1.9 Hz), 8.07 (br. s, 1H), 7.44 (dd, 1H, J_1 = 5.2 Hz, J_2 = 1.9 Hz), 7.22 (d, 2H, *J* = 8.4 Hz), 7.20 (d, 1H, *J* = 8.4 Hz), 6.63 (d, 1H, *J* = 11.5 Hz), 5.73 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.41 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.5 Hz), 2.62 (t, 2H, *J* = 7.6 Hz), 1.65-1.59 (m, 2H), 1.38-1.28 (m, 6H), 0.91 (t, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 142.3, 133.6, 132.0, 128.7, 128.4, 126.7, 126.3, 122.9, 38.0, 35.7, 31.7, 31.4, 29.0, 22.6, 14.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{26}ClN_2O$: 357.1734; found 357.1718.

(*Z*)-4-Chloro-*N*-(3-(3,4-dimethylphenyl)allyl)picolinamide (4h): The compound **4h** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 52% (39 mg, *E:Z* = 12:88); IR (DCM): 1717, 1522, 1281, 1106 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 2.0 Hz), 8.07 (br. s, 1H), 7.44 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.15 (d, 1H, *J* = 7.6 Hz), 7.07-7.04 (m, 2H), 6.61 (d, 1H, *J* = 11.6 Hz), 5.72 (dt, 1H, J_1 =

11.6 Hz, J_2 = 6.6 Hz), 4.41 (td, 2H, J_1 = 6.6 Hz, J_2 = 1.4 Hz), 2.29 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 136.6, 135.9, 133.9, 132.0, 130.1, 129.6, 126.6, 126.3, 126.2, 122.9, 38.0, 19.9, 19.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}ClN_2O$: 301.1108; found 301.1100.

(*Z*)-4-Chloro-*N*-(3-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)allyl)picolinamide (4i): The compound **4i** ((*Z*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 60% (50 mg, *E:Z* = 28:72); IR (DCM): 3377, 1674, 1580, 1293 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.3 Hz), 8.23 (d, 1H, *J* = 2.1 Hz), 8.07 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 6.87 (d, 1H, *J* = 8.2 Hz), 6.83-6.77 (m, 2H), 6.53 (d, 1H, *J* = 11.5 Hz), 5.67 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.39 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz), 4.28 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 143.2, 143.0, 131.4, 129.8, 126.4, 126.3, 122.9, 122.2, 117.6, 117.2, 64.4, 64.3, 38.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{16}ClN_2O_3$: 331.0849; found 331.0839.

(*Z*)-4-Chloro-*N*-(3-(3,5-dimethylphenyl)allyl)picolinamide (4j): The compound **4j** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.51 (EtOAc/Hexanes = 1:4); Yield: 53% (40 mg, *E:Z* = 28:72); IR (DCM): 3391, 1675, 1523, 1289 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.24 (d, 1H, *J* = 1.8 Hz), 8.06 (br. s, 1H), 7.44 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 6.94-6.92 (m, 3H), 6.61 (d, 1H, *J* = 11.6 Hz), 5.73 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.6 Hz), 4.41 (td, 2H, J_1 = 6.6 Hz, J_2 = 1.8 Hz), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 151.3, 149.0, 145.9, 137.9, 136.2, 132.2, 129.0, 127.2, 126.6, 126.3, 122.9, 38.0, 21.4; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{17}ClN_2NaO$: 323.0927; found 323.0923.

(*Z*)-Ethyl 3-(3-(4-chloropicolinamido)prop-1-en-1-yl)benzoate (4k): The compound **4k** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 58% (50 mg, *E:Z* = 23:77); IR (DCM): 3319, 1718, 1531, 1487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 1H, *J* = 5.2 Hz), 8.23 (d, 1H, *J* = 2.0 Hz), 8.10 (br. s, 1H), 7.99-7.97 (m, 2H), 7.51-7.42 (m, 3H), 6.69 (d, 1H, *J* = 11.5 Hz), 5.86 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.43-4.37 (m, 4H), 1.42 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 163.1, 151.2, 149.0, 145.9, 136.5, 132.9, 131.1, 130.7, 129.8, 128.8, 128.5, 128.4, 126.4, 122.9, 61.1, 37.8, 14.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{18}ClN_2O_3$: 345.1006; found 345.0994.

(*Z*)-4-Chloro-*N*-(3-(thiophen-2-yl)allyl)picolinamide (4l): The compound **4l** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 63% (44 mg, *E:Z* = 37:63); IR (DCM): 3369, 1674, 1526, 1287 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, 1H, *J* = 5.0 Hz), 8.24 (d, 1H, *J* = 1.8 Hz), 8.17 (br. s, 1H), 7.45 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.36-7.34 (m, 1H), 7.08-7.06 (m, 2H), 6.71 (d, 1H, *J* = 11.5 Hz), 5.69 (dt, 1H, J_1 = 11.5 Hz, J_2 = 6.7 Hz), 4.49 (td, 2H, J_1 = 6.7 Hz, J_2 = 1.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 151.2, 149.0, 145.9, 139.2, 128.2, 127.2, 126.4, 126.2, 125.7, 124.2, 122.9, 38.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{12}ClN_2OS$: 279.0359; found 279.0348.

(*Z*)-*N*-(3-(5-Bromopyridin-2-yl)allyl)-4-chloropicolinamide (4m): The compound **4m** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a pale yellow colour liquid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 54% (48 mg, *E:Z* = 23:77); IR (DCM): 3386, 1663, 1524, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, 1H, *J* = 2.2 Hz), 8.69 (br. s, 1H), 8.47 (d, 1H, *J* = 5.2 Hz), 8.23 (dd, 1H, J_1 =

2.0 Hz, J_2 = 0.4 Hz), 7.81 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.4 Hz), 7.44 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.0 Hz), 7.15 (d, 1H, J = 8.3 Hz), 6.52 (d, 1H, J = 11.6 Hz), 6.10 (dt, 1H, J_1 = 11.6 Hz, J_2 = 6.8 Hz), 4.64 (td, 2H, J_1 = 6.8 Hz, J_2 = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 154.0, 151.7, 150.4, 149.1, 145.8, 139.0, 133.3, 129.3, 126.2, 125.6, 123.0, 118.8, 37.9; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}BrClN_3O$: 351.9852; found 351.9844.

(*Z*)-4-Chloro-*N*-(3-(6-fluoropyridin-3-yl)allyl)picolinamide (4n): The compound **4n** ((*Z*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 50% (37 mg, *E:Z* = 18:82); IR (DCM): 3381, 1717, 1678, 1522 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47-8.45 (m, 1H), 8.22 (br. s, 1H), 8.16 (br. s, 1H), 8.13 (br. s, 1H), 7.78 (t, 1H, J = 8.0 Hz), 7.47-7.46 (m, 1H), 6.98 (dd, 1H, J_1 = 8.0 Hz, J_2 = 2.8 Hz), 6.58 (d, 1H, J = 11.6 Hz), 5.95-5.90 (m, 1H), 4.35-4.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 162.6 (d, J_{C-F} = 238.6 Hz), 151.0, 149.0, 147.6 (d, J_{C-F} = 14.6 Hz), 146.0, 141.1 (d, J_{C-F} = 7.8 Hz), 130.1, 130.0 (d, J_{C-F} = 4.7 Hz), 127.0, 126.5, 123.0, 109.3 (d, J_{C-F} = 37.2 Hz), 37.7; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}ClFN_3O$: 292.0653; found 292.0644.

(*Z*)-*N*-(2-(4-Methylbenzyl)-3-(*p*-tolyl)allyl)picolinamide (5a): The compound **5a** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 43% (39 mg); IR (DCM): 3442, 1675, 1521, 1433 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54-8.52 (m, 1H), 8.21 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.99 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.42 (m, 1H), 7.21-7.19 (m, 4H), 7.16 (d, 2H, J = 7.8 Hz), 7.11 (d, 2H, J = 7.8 Hz), 6.56 (s,1H), 4.26 (d, 2H, J = 5.8 Hz), 3.55 (s, 2H), 2.36 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.8, 148.0,

137.4, 137.3, 136.6, 136.1, 135.8, 134.0, 130.4, 129.2, 129.0, 129.0, 128.7, 126.1, 122.2, 42.1, 39.3, 21.2, 21.1; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}N_2O$: 357.1967; found 357.1982.

(*Z*)-*N*-(2-(4-Ethylbenzyl)-3-(4-ethylphenyl)allyl)picolinamide (5b): The compound **5b** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 36% (29 mg); IR (DCM): 3389, 1679, 1512, 1463 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54-8.52 (m, 1H), 8.21 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.99 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.42 (m, 1H), 7.25-7.18 (m, 6H), 7.14 (d, 2H, J = 8.1 Hz), 6.59 (s, 1H), 4.27 (d, 2H, J = 5.8 Hz), 3.56 (s, 2H), 2.69-2.60 (m, 4H), 1.27-1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.8, 148.0, 143.0, 142.2, 137.4, 137.3, 136.3, 134.3, 130.5, 129.0, 128.8, 128.0, 127.9, 126.1, 122.2, 42.2, 39.3, 28.6, 28.5, 15.6, 15.6; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{29}N_2O$: 385.2280; found 385.2290.

(*Z*)-*N*-(2-(4-Chlorobenzyl)-3-(4-chlorophenyl)allyl)picolinamide (5c): The compound **5c** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 40% (40 mg); IR (DCM): 3443, 1637, 1489 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54-8.52 (m, 1H), 8.18 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.96 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.46-7.44 (m, 1H), 7.33 (d, 2H, J = 8.5 Hz), 7.27-7.21 (m, 6H), 6.50 (s, 1H), 4.23 (d, 2H, J = 6.0 Hz), 3.55 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.5, 148.1, 138.4, 137.4, 137.4, 135.1, 132.9, 132.3, 130.4, 130.1, 129.6, 128.7, 128.6, 126.3, 122.2, 41.8, 39.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{19}Cl_2N_2O$: 397.0874; found 397.0865.

(*Z*)-Dimethyl 4,4'-(2-(picolinamidomethyl)prop-1-ene-1,3-diyl)dibenzoate (5d): The compound **5d** was obtained after purification by column chromatography on silica gel

(EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 50% (56 mg); IR (DCM): 3377, 1718, 1678, 1522 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.51-8.49 (m, 1H), 8.17 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 8.03 (d, 2H, J = 8.3 Hz), 7.99 (br. s, 1H), 7.97 (d, 2H, J = 8.3 Hz), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.38 (m, 1H), 7.37 (d, 4H, J = 8.2 Hz), 6.56 (s, 1H), 4.27 (d, 2H, J = 5.9 Hz), 3.92 (s, 3H), 3.91 (s, 3H), 3.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 166.8, 164.3, 149.4, 148.0, 144.3, 141.4, 139.5, 137.4, 130.1, 129.9, 129.7, 129.1, 128.8, 128.6, 128.4, 126.3, 122.2, 52.1, 52.1, 42.3, 39.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_5$: 445.1763; found 445.1748.

(*Z*)-*N*-(2-(4-Isopropylbenzyl)-3-(4-isopropylphenyl)allyl)picolinamide (5e): The compound **5e** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 37% (39 mg), IR (DCM): 3390, 1680, 1518, 1433 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54-8.52 (m, 1H), 8.21 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.99 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.42 (m, 1H), 7.28-7.19 (m, 6H), 7.16 (d, 2H, J = 8.1 Hz), 6.59 (s, 1H), 4.28 (d, 2H, J = 5.7 Hz), 3.56 (s, 1H), 2.98-2.85 (m, 2H), 1.26 (d, 6H, J = 6.9 Hz), 1.24 (d, 6H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.8, 148.0, 147.6, 146.8, 137.3, 137.3, 136.4, 134.4, 130.6, 128.9, 128.7, 126.5, 126.4, 126.1, 122.2, 42.3, 39.3, 33.8, 33.7, 24.1, 24.0; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{33}N_2O$: 413.2593; found 413.2594.

(*Z*)-*N*-(2-(3,4-Dimethylbenzyl)-3-(3,4-dimethylphenyl)allyl)picolinamide (5f): The compound **5f** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a yellow colour liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 44% (43 mg); IR (DCM): 3396, 1678, 1520, 1433 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.53-8.51 (m, 1H), 8.20 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.97 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2

= 1.7 Hz), 7.45-7.42 (m, 1H), 7.13-7.03 (m, 6H), 6.55 (s, 1H), 4.28 (d, 2H, J = 5.7 Hz), 3.52 (s, 2H), 2.27 (s, 6H), 2.22 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 148.0, 137.2, 136.6, 136.6, 136.4, 135.3, 134.5, 134.4, 130.4, 130.4, 130.1, 129.7, 129.6, 126.4, 126.1, 126.0, 122.1, 42.3, 39.4, 19.8, 19.8, 19.5, 19.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{29}N_2O$: 385.2280; found 385.2292

(*Z*)-*N*-(3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)allyl)picolinamide (5g): The compound **5g** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 46% (52 mg); IR (DCM): 3441, 1637, 1505, 1284, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55-8.53 (m, 1H), 8.20 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.98 (br. s, 1H), 7.85 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.42 (m, 1H), 6.85-6.83 (m, 2H), 6.81-6.78 (m, 3H), 6.75 (dd, 1H, J_1 = 8.3 Hz, J_2 = 1.8 Hz), 6.47 (s, 1H), 4.30-4.22 (m, 10H), 3.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.8, 148.0, 143.4, 143.2, 142.6, 142.1, 137.3, 136.9, 132.4, 130.4, 129.9, 126.1, 122.2, 122.1, 122.0, 117.6, 117.6, 117.2, 117.1, 64.5, 64.4, 64.3, 64.3, 41.8, 39.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_5$: 445.1763; found 445.1775.

(*Z*)-*N*-(2-(3,4-Dichlorobenzyl)-3-(3,4-dichlorophenyl)allyl)picolinamide (5h): The compound **5h** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 45% (53 mg); IR (DCM): 3384, 1738, 1676, 1468 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53-8.51 (m, 1H), 8.17 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.96 (br. s, 1H), 7.87 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.47-7.45 (m, 1H), 7.44 (d, 1H, J = 8.2 Hz), 7.40 (d, 1H, J = 1.7 Hz), 7.35 (d, 2H, J = 8.3 Hz), 7.17 (dd, 1H, J_1 = 8.3 Hz, J_2 = 2.0 Hz), 7.12 (dd, 1H, J_1 = 8.1 Hz, J_2 = 2.0 Hz), 6.45 (s, 1H), 4.24 (dd, 2H, J_1 = 6.1 Hz, J_2 = 0.7 Hz), 3.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.3, 148.1, 139.2, 139.0,

137.4, 136.5, 132.6, 132.5, 131.2, 130.9, 130.7, 130.6, 130.5, 130.4, 128.7, 128.4, 128.1, 126.4, 122.2, 41.5, 39.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{17}Cl_4N_2O$: 465.0095; found 465.0081.

(*Z*)-*N*-(2-(3,5-Dimethylbenzyl)-3-(3,5-dimethylphenyl)allyl)picolinamide (5i): The compound **5i** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 47% (46 mg); IR (DCM): 3388, 1679, 1520, 1464 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54-8.52 (m, 1H), 8.21 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 7.97 (br. s, 1H), 7.86 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.45-7.42 (m, 1H), 6.94-6.91 (m, 5H), 6.83 (s, 1H), 6.54 (s, 1H), 4.30 (d, 2H, J = 5.8 Hz), 3.51 (s, 2H), 2.33 (s, 6H), 2.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 149.9, 147.9, 139.1, 137.9, 137.8, 137.6, 137.2, 136.9, 130.6, 128.5, 127.9, 126.9, 126.6, 126.0, 122.1, 42.5, 39.5, 21.3, 21.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{29}N_2O$: 385.2280; found 385.2289.

(*Z*)-Diethyl 3,3'-(2-(picolinamidomethyl)prop-1-ene-1,3-diyl)dibenzoate (5j): The compound **5j** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 41% (49 mg); IR (DCM): 1716, 1680, 1521, 1204 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.52-8.50 (m, 1H), 8.18 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 8.02 (br. s, 1H), 7.97-7.91 (m, 3H,), 7.89-7.83 (m, 2H), 7.51 (d, 2H, J = 7.7 Hz), 7.45-7.37 (m, 3H), 6.56 (s, 1H), 4.39 (q, 2H, J = 7.1 Hz), 4.37 (q, 2H, J = 7.1 Hz), 4.27 (d, 2H, J = 5.9 Hz), 3.66 (s, 2H), 1.41 (t, 3H, J = 7.1 Hz), 1.38 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 166.5, 164.3, 149.5, 148.0, 139.1, 138.9, 137.3, 137.0, 133.7, 133.0, 130.8, 130.6, 130.2, 130.0, 129.9, 128.6, 128.5, 128.1, 127.8, 126.2, 122.2, 61.1, 61.0, 41.9, 39.3, 14.4, 14.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{29}N_2O_5$: 473.2076; found 473.2093.

(*Z*)-*N*-(3-(2-Chloropyridin-4-yl)-2-((2-chloropyridin-4-yl)methyl)allyl)picolinamide (5k): The compound **5k** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.45 (EtOAc/Hexanes = 1:4); Yield: 34% (34 mg); IR (DCM): 3371, 1672, 1527, 1465, 1386 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.52-8.51 (m, 1H), 8.39 (d, 1H, J = 5.1 Hz), 8.27 (d, 1H, J = 5.1 Hz), 8.16 (dt, 1H, J_1 = 7.8 Hz, J_2 = 1.0 Hz), 8.03 (br. s, 1H), 7.88 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.49-7.45 (m, 1H), 7.29 (br. s, 1H), 7.23 (br. s, 1H), 7.21 (dd, 1H, J_1 = 5.1 Hz, J_2 = 0.9 Hz), 7.14 (dd, 1H, J_1 = 5.1 Hz, J_2 = 1.4 Hz), 6.42 (s, 1H), 4.27 (d, 2H, J = 5.6 Hz), 3.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 152.0, 150.8, 149.8, 148.9, 148.2, 147.1, 141.3, 137.6, 127.8, 126.6, 124.6, 124.0, 122.9, 122.3, 122.2, 41.1, 39.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{17}Cl_2N_4O$: 399.0779; found 399.0765.

(*Z*)-*N*-(3-(2-Chloropyridin-4-yl)-2-methylallyl)picolinamide (6a): The compound **6a** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.48 (EtOAc/Hexanes = 1:4); Yield: 30% (22 mg); IR (DCM): 2925, 1713, 1423, 1364 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.35 (d, 1H, J = 5.1 Hz), 8.22 (d, 1H, J = 7.8 Hz), 8.16 (br. s, 1H), 7.89 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.49-7.45 (m, 1H), 7.25 (br. s, 1H), 7.18 (dd, 1H, J_1 = 5.1 Hz, J_2 = 0.9 Hz), 6.38 (s, 1H), 4.30 (d, 2H, J = 6.1 Hz), 2.01 (d, 3H, J = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 151.8, 149.6, 149.4, 148.1, 148.0, 140.6, 137.5, 126.4, 124.9, 123.9, 122.3, 40.6, 22.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{15}ClN_3O$: 288.0904; found 288.0895.

(*Z*)-Diethyl 3,3'-(2-((4-chloropicolinamido)methyl)prop-1-ene-1,3-diyl)dibenzoate (7a): The compound **7a** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 40% (51 mg); IR (DCM): 1716, 1679, 1521, 1282 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, 1H, *J*

= 5.2 Hz), 8.17 (d, 1H, *J* = 1.9 Hz), 7.95-7.94 (m, 3H), 7.91-7.89 (m, 2H,), 7.50 (dd, 2H, J_1 = 7.7 Hz, J_2 = 1.3 Hz), 7.46-7.36 (m, 3H), 6.58 (s,1H), 4.39 (q, 4H, *J* = 7.1 Hz), 4.27 (d, 2H, *J* = 6.0 Hz), 3.65 (s, 2H), 1.40 (t, 6H, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 166.4, 163.1, 151.0, 148.9, 145.8, 139.1, 138.5, 136.9, 133.5, 133.0, 130.8, 130.6, 130.2, 130.1, 129.8, 128.6, 128.5, 128.2, 127.8, 126.3, 122.8, 61.1, 61.0, 42.0, 39.4, 14.4, 14.3; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{28}ClN_2O_5$: 507.1687; found 507.1669.

(*Z*)-*N*-(3-(5-Bromopyridin-2-yl)-2-methylallyl)picolinamide (6b): The compound **6b** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.43 (EtOAc/Hexanes = 1:4); Yield: 41% (34 mg); IR (DCM): 2929, 1716, 1674, 1520 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (br. s, 1H), 8.72 (d, 1H, *J* = 2.3 Hz), 8.56 (d, 1H, *J* = 4.8 Hz), 8.22 (d, 1H, *J* = 7.8 Hz), 7.85 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.77 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 7.43-7.40 (m, 1H), 7.10 (d, 1H, *J* = 8.4 Hz), 6.39 (s, 1H), 4.49 (d, 2H, *J* = 6.6 Hz), 2.08 (d, 3H, *J* = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 154.5, 150.3, 150.2, 148.2, 142.5, 138.9, 137.2, 126.1, 126.0, 125.2, 122.3, 118.0, 40.6, 24.8; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{15}BrN_3O$: 332.0398; found 332.0388.

(*Z*)-*N*-(3-(6-Fluoropyridin-3-yl)-2-methylallyl)picolinamide (6c): The compound **6c** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.43 (EtOAc/Hexanes = 1:4); Yield: 41% (28 mg); IR (DCM): 2927, 1672, 1526, 1483 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.55 (m, 1H), 8.22 (d, 1H, *J* = 7.8 Hz), 8.12 (d, 1H, *J* = 1.8 Hz), 8.12 (br. s, 1H), 7.89 (td, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz), 7.78 (td, 1H, J_1 = 8.1 Hz, J_2 = 2.4 Hz), 7.48-7.45 (m, 1H), 6.93 (dd, 1H, J_1 = 8.4 Hz, J_2 = 3.0 Hz), 6.43 (s, 1H), 4.24 (d, 2H, *J* = 6.0 Hz), 2.01 (d, 3H, *J* = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 162.3 (d, J_{C-F} = 237.8 Hz), 149.5, 148.1, 147.4 (d, J_{C-F} = 14.5 Hz), 141.2 (d, J_{C-F} = 7.8 Hz), 137.8,

137.5, 130.8 (d, J_{C-F} = 4.6 Hz), 126.4, 123.7, 122.3, 109.1 (d, J_{C-F} = 37.1 Hz), 40.5, 22.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{15}FN_3O$: 272.1199; found 272.1188.

(*Z*)-*N*-(3-(5-Bromopyridin-2-yl)-2-methylallyl)-4-chloropicolinamide (6d): The compound **6d** was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.40 (EtOAc/Hexanes = 1:4); Yield: 40% (37 mg); IR (DCM): 3384, 1675, 1515, 1464 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.95 (br. s, 1H), 8.72 (d, 1H, *J* = 2.3 Hz), 8.46 (d, 1H, *J* = 5.2 Hz), 8.23 (d, 1H, *J* = 2.0 Hz), 7.78 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 7.43 (dd, 1H, J_1 = 5.2 Hz, J_2 = 2.1 Hz), 7.09 (d, 1H, *J* = 8.2 Hz), 6.39 (s, 1H), 4.48 (d, 2H, *J* = 6.7 Hz), 2.08 (d, 3H, *J* = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 154.4, 151.8, 150.2, 149.1, 145.7, 142.3, 139.0, 126.2, 126.1, 125.2, 123.0, 118.1, 40.7, 24.9; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{14}BrClN_3O$: 366.0009; found 366.0021.

N_2,N_6-Bis((*E*)-3-(4-methoxyphenyl)allyl)pyridine-2,6-dicarboxamide (8a): The compound **8a** ((*E*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 40% (46 mg, *E*:*Z* = 67:33); IR (DCM): 3441, 1643, 1524, 1241 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, 2H, *J* = 7.8 Hz), 8.05 (t, 1H, *J* = 7.8 Hz), 8.00 (t, 1H, *J* = 6.1 Hz), 7.26 (d, 4H, *J* = 8.8 Hz), 6.82 (d, 4H, *J* = 8.8 Hz), 6.52 (d, 2H, *J* = 15.8 Hz), 6.13 (dt, 2H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.27 (td, 4H, J_1 = 6.3 Hz, J_2 = 1.2 Hz), 3.81 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 159.3, 148.8, 139.0, 132.0, 129.1, 127.5, 125.3, 122.8, 114.0, 55.3, 41.8; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{27}H_{27}N_3NaO_4$: 480.1899; found 480.1916.

(*E*)-*N*-(3-(4-Methoxyphenyl)allyl)pyrazine-2-carboxamide (9a): The compound **9a** ((*E*) major isomer) was obtained after purification by column chromatography on silica gel (EtOAc:Hexanes = 30:70) as a colourless liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 35%

(24 mg, *E:Z* = 62:38); IR (DCM): 3447, 1637, 1511 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.46 (d, 1H, *J* = 1.5 Hz), 8.78 (d, 1H, *J* = 2.5 Hz), 8.55 (dd, 1H, J_1 = 2.5 Hz, J_2 = 1.5 Hz), 7.96 (br. s, 1H), 7.33 (d, 2H, *J* = 8.8 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 6.59 (d, 1H, *J* = 15.8 Hz), 6.17 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.28 (td, 2H, J_1 = 6.4 Hz, J_2 = 1.4 Hz), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 159.4, 147.3, 144.5, 142.6, 132.3, 129.2, 127.6, 122.5, 114.0, 55.3, 41.6; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{15}N_3NaO_2$: 292.1062; found 292.1051.

(*E*)-5-Methyl-*N*-(3-(*p*-tolyl)allyl)isoxazole-3-carboxamide (10a): The compound **10a** ((*E*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.50 (EtOAc/Hexane = 1:4); Yield: 78% (50 mg, *E:Z* = 98:2); IR (DCM): 3294, 1660, 1558, 1304 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, 2H, *J* = 8.0 Hz), 7.14 (d, 2H, *J* = 8.0 Hz), 7.02 (br. s, 1H), 6.58 (d, 1H, *J* = 15.8 Hz), 6.48 (d, 1H, *J* = 0.7 Hz), 6.20 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.22 (td, 2H, J_1 = 6.4 Hz, J_2 = 1.4 Hz), 2.49 (d, 3H, *J* = 0.7 Hz), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 159.0, 158.7, 137.7, 133.6, 132.6, 129.3, 126.3, 123.5, 101.5, 41.5, 21.2, 12.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{17}N_2O_2$: 257.1290; found 257.1281.

(*E*)-*N*-(3-(4-Methoxyphenyl)allyl)-5-methylisoxazole-3-carboxamide (10b): The compound **10b** ((*E*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as colourless liquid; R_f = 0.50 (EtOAc/hexane = 1:4); Yield: 60% (41 mg, *E:Z* = 98:2); IR (DCM): 3290, 1659, 1553, 1455 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, 2H, *J* = 8.7 Hz), 6.96 (br. s, 1H), 6.87 (d, 2H, *J* = 8.7 Hz), 6.56 (d, 1H, *J* = 15.8 Hz), 6.48 (br. s, 1H), 6.12 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.21 (td, 2H, J_1 = 6.2 Hz, J_2 = 1.4 Hz), 3.83 (s, 3H) 2.50 (d, 3H, *J* = 0.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 159.4, 159.0, 158.7,

132.3, 129.1, 127.6, 122.2, 114.0, 101.5, 55.3, 41.5, 12.4; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{16}N_2NaO_3$: 295.1059; found 295.1048.

(*E*)-*N*-(3-(4-Bromophenyl)allyl)-5-methylisoxazole-3-carboxamide (10c): The compound **10c** ((*E*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 69% (56 mg, *E:Z* = 98:2); IR (DCM): 3288, 1656, 1552, 1453, cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, 2H, *J* = 8.5 Hz), 7.24 (d, 2H, *J* = 8.5 Hz), 7.05 (br. s, 1H), 6.54 (d, 1H, *J* = 15.8 Hz), 6.48 (d, 1H, *J* = 0.9 Hz), 6.25 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.2 Hz), 4.22 (td, 2H, J_1 = 6.1 Hz, J_2 = 1.5 Hz), 2.49 (d, 3H, *J* = 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 159.0, 158.6, 135.3, 131.7, 131.3, 128.0, 125.5, 121.6, 101.5, 41.2, 12.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}BrN_2O_2$: 321.0239; found 321.0227.

(*E*)-Ethyl 3-(3-(5-methylisoxazole-3-carboxamido)prop-1-en-1-yl)benzoate (10d): The compound **10d** ((*E*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 75% (59 mg, *E:Z* = 98:2); IR (DCM): 3335, 1716, 1681, 1546 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.93 (d, 1H, *J* = 7.8 Hz), 7.55 (d, 1H, *J* = 7.8 Hz), 7.40 (t, 1H, *J* = 7.7 Hz), 7.06 (br. s, 1H), 6.64 (d, 1H, *J* = 15.9 Hz), 6.48 (d, 1H, *J* = 0.7 Hz), 6.34 (dt, 1H, J_1 = 15.9 Hz, J_2 = 6.1 Hz), 4.39 (q, 2H, *J* = 7.1 Hz) 4.25 (td, 2H, J_1 = 6.1 Hz, J_2 = 1.4 Hz), 2.50 (s, 3H), 1.41 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 166.4, 159.1, 158.7, 136.7, 131.5, 130.9, 130.6, 128.8, 128.6, 127.5, 126.0, 101.5, 61.1, 41.2, 14.4, 12.4; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO_4$: 337.1164; found 337.1152.

(*E*)-*N*-(3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)allyl)-5-methylisoxazole-3-carboxamide (10e): The compound **10e** ((*E*) major isomer) was obtained after purification by column

chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless solid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 70% (53 mg, *E:Z* = 98:2); mp 115-117 ^oC; IR (DCM): 3434, 1673, 1508, 1308 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ 7.00 (br. s, 1H), 6.90-6.85 (m 2H), 6.81 (d, 1H, *J* = 8.3 Hz), 6.48 (d, 1H, *J* = 15.8 Hz), 6.47 (s, 1H), 6.09 (dt, 1H, J_1 = 15.8 Hz, J_2 = 6.4 Hz), 4.26 (s, 4H), 4.19 (td, 2H, J_1 = 6.2 Hz, J_2 = 1.4 Hz), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 158.9, 158.7, 143.5, 143.4, 132.1, 130.2, 122.9, 119.9, 117.3, 115.0, 101.5, 64.4, 64.3, 41.4, 12.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_4$: 301.1188; found 301.1176.

(*E*)-5-Methyl-*N*-(3-(3-nitrophenyl)allyl)isoxazole-3-carboxamide (10f): The compound **10f** ((*E*) major isomer) was obtained after purification by column chromatography on neutral alumina (EtOAc:Hexanes = 35:65) as a colourless liquid; R_f = 0.50 (EtOAc/Hexanes = 1:4); Yield: 64% (46 mg, *E:Z* = 98:2); IR (DCM): 3325, 1674, 1529, 1457 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ 8.22 (s, 1H), 8.10 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.7 Hz), 7.68 (d, 1H, *J* = 7.7 Hz), 7.50 (t, 1H, *J* = 8.0 Hz), 7.11 (br. s, 1H), 6.66 (d, 1H, *J* = 15.9 Hz), 6.49 (s, 1H), 6.42 (dt, 1H, J_1 = 15.9 Hz, J_2 = 5.9 Hz), 4.29-4.27 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 159.1, 158.6, 148.6, 138.2, 132.2, 129.9, 129.5, 128.3, 122.4, 121.1, 101.5, 41.0, 12.4; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}N_3O_4$: 288.0984; found 288.0971.

ASSOCIATED CONTENT

Supporting Information

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

X-ray structure of compound **10e** (Figures S1 and S2) and brief X-ray structure data of compound **10e** (Table S1), copies of $^1H/^{13}C$ NMR charts and copies of the crude NMR spectra of reactions revealing the observed *E*/*Z* ratios (PDF)

X-ray structure data of compound **10e** (cif)

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected reviews on the cross-coupling reactions, see: (a) Colacot, T. *New trends in cross-coupling: theory and Applications*; 1st ed.; The Royal Society of Chemistry: 2015. (b) de Meijere, A.; Bräse, S.; Oestreich, M. *Metal-catalyzed cross-coupling reactions and more*; 1st ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2014. (c) de Meijere, A.; Diederich, F. *Metal-catalyzed cross-coupling reactions*; 1st ed.; Wiley-VCH: Weinheim, 2004. (d) Diederich, F.; Stang, P. J. *Metal-catalyzed cross-coupling reactions*; 1st ed.; Wiley-VCH: New York, 1998. (e) Molnár, A. *Palladium-catalyzed coupling reactions*; 1st ed.; Wiley-VCH: Weinheim, Germany, 2013. (f) Burke, A. J.; Marques, C. S. *Catalytic arylation methods*; 1st ed; Wiley-VCH: Weinheim, 2014.

(2) For selected reviews on the cross-coupling reactions, see: (a) Farina, V.; Krishnamurthy, V.; Scott, W. *The Stille reaction*; 1st ed.; Wiley: New York, 1998. (b) Oestreich, M. *The Mizoroki-Heck reaction*; 1st ed.; Wiley: Hoboken, N. J., 2009. (c) Molander, G. A.; Wolfe, J.; Larhed, M. *Cross coupling and Heck-type reactions*; 1st ed.; Thieme: Stuttgart, 2013. (d) Miyaura, N. *Cross-coupling reactions*; 1st ed.; Springer: Berlin, 2002.

(3) For selected reviews on the cross-coupling reactions, see: (a) Negishi, E.-i. *Angew. Chem. Int. Ed.* **2011**, *50*, 6738. (b) Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6722. (c) Johansson S., C.; Kitching, M.; Colacot, T.; Snieckus, V. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062. (d) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442. (e) Maluenda, I.; Navarro, O. *Molecules* **2015**, *20*, 7528. (f) Ruiz-Castillo, P.; Buchwald, S. L. *Chem. Rev.* **2016**, *116*, 12564. (g) Nielsen, M. B. *Synthesis* **2016**, *48*, 2732. (h) Bolm, C. *J. Org. Chem.* **2012**, *77*, 5221.

(4) For selected reviews on the C-H activation/functionalization reactions, see: (a) For a themed issue on C-H activation reactions, see: C–H Functionalisation in organic synthesis, *Chem. Soc. Rev.* **2011**, *40*, 1845. (b) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826. (c) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879. (d) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010,** *110,* 1147. (e) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. *Chem. Rev.* DOI: 10.1021/acs.chemrev.6b00622. (f) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960. (g) McMurray, L.; OHara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (h) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936.

(5) For selected reviews on the C-H activation/functionalization reactions, see: (a) Castro, L. C. M.; Chatani, N. *Chem. Lett.* **2015**, *44*, 410. (b) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281. (c) Hirano, K.; Miura, M. *Chem. Lett.* **2015**, *44*, 868. (d) Zhu, R.-Y.; Farmer, M. E.; Chen, Y.-Q.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2016**, *55*, 10578. (e) Zhang, Q.; Chen, K.; Shi, B.-F. *Synlett* **2014**, *25*, 1941. (f) Dey, A.; Agasti, S.; Maiti, D. *Org. Biomol. Chem.* **2016**, *14*, 5440. (g) Li, H.; Li, B.-J.; Shi, Z.-J. *Catal. Sci. Technol.* **2011**, *1*, 191.

(6) For selected reviews on the C-H activation/functionalization reactions, see: (a) Wencel-Delord, J.; Colobert, F. *Synlett* **2015**, *26*, 2644. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (c) Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902. (d) Yan, G.; Borah,

A. J.; Yang, M. *Adv. Synth. Catal.* **2014**, *356*, 2375. (e) Ros, A.; Fernández, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229. (f) Zhang, X.-S.; Chen, K.; Shi, Z-J. *Chem. Soc. Rev.* **2014**, *5*, 2146. (g) Wu, X.-F. *Chem. Eur. J.* **2015**, *21*, 12252.

(7) For selected reviews on the C-H activation/functionalization reactions, see: (a) I. B. Krylov, V. A. Vil', A. O. Terent'ev, *Beilstein J. Org. Chem.* **2015**, *11*, 92. (b) Moghimi, S.; Mahdavi, M.; Shafiee, A.; Foroumadi, A. *Eur. J. Org. Chem.* **2016**, 3282. (c) Gensch, T.; Hopkinson, M. N.; Glorius, F. Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900. (d) Gulías, M.; Mascareñas, J. L. *Angew. Chem. Int. Ed.* **2016**, *55*, 11000. (e) Fairlamb, I. J. S. *Angew. Chem. Int. Ed.* **2015**, *54*, 10415. (f) Shaikh, T. M.; Hong, F.-E. *J. Organomet. Chem.* **2016**, *801*, 139. (g) Subramanian, P.; Rudolf, G. C.; Kaliappan, K. P. *Chem. Asian J.* **2016**, *11*, 168.

(8) For selected reviews on the C-H activation/functionalization reactions, see: (a) Dastbaravardeh, N.; Christakakou, M.; Haider, M.; Schnürch, M. *Synthesis* **2014**, *46*, 1421. (b) Hartwig, J. F.; Larsen, M. A. *ACS Cent. Sci.* **2016**, *2*, 281. (c) Bheeter, C.B.; Chen, L.; Soulé, J.-F.; Doucet, H. *Catal. Sci. Technol.* **2016**, *6*, 2005. (d) Banerjee, A.; Sarkar, S.; Patel, B. K. *Org. Biomol. Chem.* **2017**, *15*, 505. (e) Cheng, C.; Hartwig, J. F. *Chem. Rev.* **2015**, *115*, 8946. (f) Su, B.; Cao, Z.-C.; Shi, Z.-J. *Acc. Chem. Res.* **2015**, *48*, 886. (g) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236.

(9) For selected reviews on the bidentate directing group-directed C-H functionalization, see: (a) Daugulis, O.; Roane, J.; Tran, L. D. *Acc. Chem. Res.* **2015**, *48*, 1053. (b) Wang, C.; Huang, Y. *Synlett* **2013**, *24*, 145. (c) Hui, C.; Xu, J. *Tetrahedron Lett.* **2016**, *57*, 2692. (d) Corbet, M.; De Campo, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 9896. (e) Yang, X.; Shan, G.; Wang, L.; Rao, Y. *Tetrahedron Lett.* **2016**, *57*, 819.

(10) For selected reviews on the bidentate directing group-directed C-H functionalization, see: (a) Rouquet, G.; Chatani, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 11726. (b) Liu, J. Chen, G.; Tan, Z. *Adv. Synth. Catal.* **2016**, *358*, 1174. (c) Zhang, B.; Guan, H.; Shi, B.-F. *Chin. J. Org. Chem.* **2014**, *34*, 1487. (d) Yadav, M. R.; Rit, R. K.; Shankar, M.; Sahoo, A. K. *Asian J. Org. Chem.* **2015**, *4*, 846. (e) He, G.; Wang, B.; Nack, W. A.; Chen, G. *Acc. Chem. Res.* **2016**, *49*, 635. (f) Noisier, A. F. M.; Brimble, M. A. *Chem. Rev.* **2014**, *114*, 8775. (g) Rit, R. K.; Yadav, M. R.; Ghosh, K.; Sahoo, A. K. *Tetrahedron* **2015**, *71*, 4450.

(11) (a) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, 127, 13154. (b) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965.

(12) For selected articles, see: (a) Ye, S.; Yang, W.; Coon, T.; Fanning, D.; Neubert, T.; Stamos, D.; Yu, J.-Q. *Chem. Eur. J.* **2016**, *22*, 4748 and references cited therein.

(13) For selected articles dealing with the bidentate directing group-directed C-H functionalization, see: (a) Shang, R.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2015**, *137*, 7660. (b) Gutekunst, W. R.; Gianatassio, R.; Baran, P. S. *Angew. Chem. Int. Ed.* **2012**, *51*, 7507. (c) Chen, K.; Zhang, S.-Q.; Xu, J.-W.; Hu, F.; Shi, B.-F. *Chem. Commun.* **2014**, *50*, 13924. (d) Roman, D. S.; Charette, A. B. *Org. Lett.* **2013**, *15*, 4394. (e) Zhang, Y.-F.; Zhao, H.-W.; Wang, H.; Wei, J.-B.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2015**, *54*, 13686.

(14) For selected articles dealing with the bidentate directing group-directed C-H functionalization, see: (a) Wang, B.; Nack, W. A.; He, G.; Zhang, S.-Y.; Chen, G. *Chem. Sci.* **2014**, *5*, 3952 and references cited therein. (b) Kanyiva, K. S.; Kuninobu, Y.; Kanai, M. *Org. Lett.* **2014**, *16*, 1968. (c) Hoshiya, N.; Takenaka, K.; Shuto, S.; Uenishi, J. *Org. Lett.* **2016**, *18*, 48. (d) Tang, H.; Huang, X.-R.; Yao, J.; Chen, H. *J. Org. Chem.* **2015**, *80*, 4672. (e) Reddy, V. P.; Qiu, R.; Iwasaki, T.; Kambe, N. *Org. Biomol. Chem.* **2015**, *13*, 6803. (f) Affron, D. P.; Davis, O.

A.; Bull, J. A. *Org. Lett.* **2014**, *16*, 4956. (g) Parella, R.; Babu, S. A. *J. Org. Chem.* **2015**, *80*, 2339 and references cited therein.

(15) For selected articles dealing with the bidentate directing group-directed C-H functionalization, see: (a) Berger, M.; Chauhan, R.; Rodrigues, C. A. B.; Maulide, N. *Chem. Eur. J.* **2016**, *22*, 16805. (b) Aihhara, Y.; Chatani, N. *ACS Catal.* **2016**, *6*, 4323 and references cited therein. (c) Deb, A.; Bag, S.; Kancherla, R.; Maiti, D. *J. Am. Chem. Soc.* **2014**, *136,* 13602. (d) Dey, A.; Pimparkar, S.; Deb, A.; Guin, S.; Maiti, D. *Adv. Synth. Catal.* **2017**, *359*, 1301. (e) Reddy, B. V. S.; Reddy, L. R.; Corey, E. J. *Org. Lett.* **2006**, *8*, 3391. (f) Gopalakrishnan, B.; Mohan, S.; Parella, R. Babu, S. A. *J. Org. Chem.* **2016**, *81*, 8988 and references cited therein.

(16) For selected articles dealing with the bidentate directing group-directed C-H functionalization, see: (a) Reddy, M. D.; Watkins, E. B. *J. Org. Chem.* **2015**, *80*, 11447. (b) Feng, R.; Wang, B.; Liu, Y.; Liu, Z.; Zhang, Y. *Eur. J. Org. Chem.* **2015**, 142. (c) Liu, J.; Xie, Y.; Zeng, W.; Lin, D.; Deng, Y.; Lu, X. *J. Org. Chem.* **2015**, *80*, 4618. (d) Zhang, S.-K.; Yang, X.-Y.; Zhao, X.-M.; Li, P.-X. Niu, J.-L.; Song, M.-P. *Organometallics.* **2015**, *34*, 4331 and references cited therein. (e) Jerhaoui, S.; Chahdoura, F.; Rose, C.; Djukic, J.-P.; Wencel-Delord, J.; Colobert, F. *Chem. Eur. J.* **2016**, *22*, 17397. (f) Naveen, Rajkumar, V.; Babu, S.A.; Gopalakrishnan, B. *J. Org. Chem.* **2016**, *81*, 12197 and references cited therein

(17) For selected articles dealing with the bidentate directing group-directed C-H functionalization, see: (a) Liu, Y.-J.; Xu, H.; Kong, W.-J.; Shang, M.; Dai, H.-X.; Yu, J.-Q. *Nature* **2014**, *515*, 389. (b) Fan, M.-Y.; Ma, D.-W. *Angew. Chem. Int. Ed.* **2013**, *52*, 12152. (c) Poveda, A.; Alonso, I.; Fernández-Ibáñez, M. Á. *Chem. Sci.* **2014**, *5*, 3873. (d) Seki, A.; Takahashi, Y.; Miyake, T. *Tetrahedron Lett.* **2014**, *55,* 2838. (e) He, G.; Zhao, Y.; Zhang, S.; Lu, C.; Chen, G. *J. Am. Chem. Soc.* **2012**, *134*, 3. (f) For a recent paper dealing with the Pd-catalyzed

picolinamide-directed hydroarylation of alkynes affording homoallyl amines, see: Liu, Z.; Derosa, J.; Engle, K. M. *J. Am. Chem. Soc.* **2016**, *138*, 13076. (g) Takamatsu, K.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2015**, *80*, 3242. (h) Liu, M.; Niu, Y.; Wu, Y.-F.; Ye, X.-S. *Org. Lett.* **2016**, *18*, 1836.

(18) For selected articles dealing with the bidentate directing group-directed remote C-H functionalization, see: (a) Pearson, R.; Zhang, S.; He, G.; Edwards, N.; Chen, G. *Beilstein J. Org. Chem.* **2013**, *9*, 891. (b) Calvert, M. B.; Sperry, J. *Org. Biomol. Chem.* **2016**, *14*, 5728. (c) Wang, C.; Zhang, L.; Chen, C.; Han, J.; Yao, Y.; Zhao, Y. *Chem. Sci.* **2015**, *6*, 4610. (d) Chen, C.; Guan, M.; Zhang, J.; Wen, Z.; Zhao, Y. *Org. Lett.* **2015**, *17*, 3646.

(19) For selected reviews dealing with the functionalization of remote C-H bonds, see: (a) Dey, A.; Maity, S.; Maiti, D. *Chem. Commun.* **2016**, *52*, 12398. (b) Schranck, J.; Tlili, A.; Beller, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 9426. (c) Qiu, G.; Wu, J. *Org. Chem. Front.* **2015**, *2*, 169. (d) Yizhi, Y.; Song, S.; Ning, J. *Acta. Chim. Sinica* **2015**, *73*, 1231.

(20) For selected articles dealing with the functionalization of remote C-H bonds, see: (a) Tang, R-Y.; Li, G.; Yu, J.-Q. *Nature* **2014**, *507*, 215. (b) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* **2015**, *137*, 11888. (c) Aspin, S.; Goutierre, A.-S.; Larini, P.; Jassar, R.; Baudoin, O. *Angew. Chem. Int. Ed.* **2012**, *51*, 10808. (d) Li, S.; Ji, H.; Cai, L.; Li, G. *Chem. Sci.* **2015**, *6*, 5595. (e) Paterson, A. J.; John-Campbell, S. S.; Mahon, M. F.; Press, N. J.; Frost, C. G. *Chem. Commun.* **2015**, *51*, 12807.

(21) For selected articles dealing with the functionalization of remote C-H bonds, see: (a) Legarda, P. D.; García-Rubia, A.; Gómez-Arrayás, R.; Carretero, J. C. *Adv. Synth. Catal.* **2016**,

358, 1065. (b) Topczewski, J. J.; Cabrera, P. J.; Saper, N. I.; Sanford, M. S. *Nature* **2016**, *531*, 220. (c) Juliá-Hernández, F.; Simonetti, M.; Larrosa, *Angew. Chem. Int. Ed.* **2013**, *52*, 11458.

(22) For selected articles dealing with the biologically active compounds and drugs-based on allylamine derivatives, see: (a) Kitahata, N.; Han, S.-Y.; Noji, N.; Saito, T.; Kobayashi, M.; Nakano, T.; Kuchitsu, K.; Shinozaki, K.; Yoshida, S.; Matsumoto, S.; Tsujimoto, M.; Asami, T. *Bioorg. Med. Chem.* **2006**, *14*, 5555. (b) Ganança, M. M.; Caovilla, H. H.; Munhoz, M. S. L.; Ganança, F. G.; da Silva, M. L. G.; Serafini, F.; Ganança, F. F. *Rev. Bras. Otorrinolaringol.* **2007**, *73*, 12. (c) Stütz, A.; Georgopoulos, A.; Granitzer, W.; Petranyi, G.; Berney, D. *J. Med. Chem.* **1986**, *29*, 112. (d) Poignet, H.; Beaughard, M.; Lecoin, G.; Massingham, R. *J. Cereb. Blood Flow Metab.* **1989**, *9*, 646. (e) Taghdiri, F.; Togha, M.; Razeghi J., S.; Refaeian, F. *Springer Puls* **2014**, *3*, 231. (f) Galaffu, N.; Man, S. P.; Wilkes, R. D.; Wilson, J. R. H. *Org. Process Res. Dev.* **2007**, *11*, 406 and references cited therein.

(23) For selected articles dealing with the biologically active compounds and drugs-based on allylamine derivatives, see: (a) Ripin, D. H. B.; Bourassa, D. E.; Brandt, T.; Castaldi, M. J.; Frost, H. N.; Hawkins, J.; Johnson, P. J.; Massett, S. S.; Neumann, K.; Phillips, J.; Raggon, J. W.; Rose, P. R.; Rutherford, J. L.; Sitter, B.; Stewart, III, M.; Vetelino, M. G.; Wei, L. *Org. Process Res. Dev.* **2005**, *9*, 440 and references cited therein. (b) Serrano, A.; Menéndez, J.; Casarejos, M. J.; Solano, R. M.; Gallaego, E.; Sánchez, M.; Mena, M. A.; de Yebenes, J. G. *Neuropharmacology* **2005**, *49*, 208. (c) Thompson, A.J.; Tyring, S.K. *Curr. Derm. Rep.* **2013**, *2*, 191 and references cited therein. (d) McDonald, I. A.; Lacoste, J. M.; Bey, P.; Palfreyman, M. G.; Zreika, M. *J. Med. Chem.* **1985**, *28*, 186.

(24) For selected papers dealing with the use of allylamines in organic synthesis, see: (a) Kröger, D.; Schlüter, T.; Fischer, M.; Geibel, I.; Martens, J. *ACS Comb. Sci.* **2015**, *17*, 202. (b)

García-González, M. C.; Hernández-Vázquez, E.; Gordillo-Cruz, R. E.; Miranda, L. D. *Chem. Commun.* **2015**, *51*, 11669. (c) Wu, X.-S.; Chen, Y.; Li, M.-B.; Zhou, M.-G.; Tian, S.-K. *J. Am. Chem. Soc.* **2012**, *134*, 14694. (d) Yan, F.; Liang, H.; Song, J.; Cui, J.; Liu, Q.; Liu, S.; Wang, P.; Dong, Y.; Liu, H. *Org. Lett.* **2017**, *19*, 86. (e) Tsui, G. C.; Menard, F.; Lautens, M. *Org. Lett.* **2010**, *12*, 2456. (f) Cai, Q.; Liang, X.-W.; Wang, S.-G.; You, S.-L. *Org. Biomol. Chem.* **2013**, *11*, 1602.

(25) For selected papers dealing with the use of allylamines in organic synthesis, see: (a) Yu, H.; Zhang, G.; Huang, H. *Angew. Chem. Int. Ed.* **2015**, *54*, 10912. (b) Shi, Z.; Suri, M.; Glorius, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 4892. (c) Wang, H.; Wang, Y.; Liang, D.; Liu, L.; Zhang, J.; Zhu, Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 5678. (d) Jensen, T.; Pedersen, H.; Bang-Andersen, B.; Madsen, R.; Jørgensen, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 888. (e) Klein, J. E. M. N.; Geoghegan, K.; Méral, N.; Evans, P. *Chem. Commun.* **2009**, *46*, 937. (f) DeLuca, R. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 11454.

(26) For selected papers dealing with the use of allylamines in organic synthesis, see: (a) Zheng, J.; Huang, L.; Huang, C.; Wu, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 1235. (b) Ma, X.-T.; Wang, Y.; Dai, R.-H.; Liu, C. -R.; Tian, S.-K. *J. Org. Chem.* **2013**, *78*, 11071 and references cited therein. (c) Tian, Y.; Qi, J.; Sun, C.; Yin, D.; Wang, X.; Xiao, Q. *Org. Biomol. Chem.* **2013**, *11*, 7262. (d) Baxter, C. A.; Cleator, E.; Alam, M.; Davies, A. J.; Goodyear, A.; O'Hagan, M. *Org. Lett.* **2010**, *12*, 668. (e) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Masciocchi, N.; Sottocornola, S. *Org. Lett.* **2006**, *8*, 4521.

(27) For selected reviews dealing with the synthesis of allylamines by other than the Heck-type reactions, see: (a) Lu, Z.; Ma, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 258. (b) Trost, B. M.; Zhang, T.; Sieber, J. D. *Chem. Sci.* **2010**, *1*, 427. (c) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**,

98, 1689. (d) Trost, B. M.; Vranken, D. L. V. *Chem. Rev.* **1996**, *96*, 395. (e) Miyabe, H.; Takemoto, Y. *Synlett* **2005**, 1641.

(28) For selected papers dealing with the synthesis of allylamines by other than the Heck-type reactions, see: (a) Ohshima, T.; Ipposhi, J.; Nakahara, Y.; Shibuya, R.; Mashima, K. *Adv. Synth. Catal.* **2012**, *354*, 2447. (b) Nishikata, T.; Lipshutz, B. H. *Org. Lett.* **2009**, *11*, 2377. (c) Chen, K.; Li, Y.; Pullarkat, S. A.; Leung, P.-H. *Adv. Synth. Catal.* **2012**, *354*, 83. (d) Fischer, D. F.; Xin, Z.-q.; Peters, R. *Angew. Chem. Int. Ed.* **2007**, *46*, 7704. (e) Banerjee, D.; Junge, K.; Beller, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 13049. (f) Hopkins, B. A.; Wolfe, J. P. *Angew. Chem. Int. Ed.* **2012**, *51*, 9886. (g) Liu, G.; Yin, G.; Wu, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 4733. (h) Ghosh, R.; Sarkar, A. *J. Org. Chem.* **2011**, *76*, 8508.

(29) For selected papers dealing with the synthesis of allylamines by other than the Heck-type reactions, see: (a) Xiong, T.; Li, Y.; Mao, L.; Zhang, Q.; Zhang, Q. *Chem. Commun.* **2012**, *48*, 2246. (b) Bennasar, M.-L.; Zulaica, E.; Solé, D.; Alonso, S. *Chem. Commun.* **2009**, 3372. (c) Hirakawa, T.; Kawatsura, M.; Itoh, T. *J. Fluorine. Chem.* **2013**, *152*, 62. (d) Strambeanu, I. I.; White, M. C. *J. Am. Chem. Soc.* **2013**, *135*, 12032. (e) Ye, K.-Y.; He, H.; Liu, W.-B.; Dai, L.-X.; Helmchen, G.; you, S.-L. *J. Am. Chem. Soc.* **2011**, *133*, 19006. (f) Harvey, M. E.; Musaev, D. G.; Bois, J. D. *J. Am. Chem. Soc.* **2011**, *133*, 17207. (g) Nagano, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2009**, *131*, 4200.

(30) For selected papers dealing with the synthesis of allylamines by other than the Heck-type reactions, see: (a) Hikawa, H.; Yokoyama, Y. *J. Org. Chem.* **2011**, *76*, 8433. (b) Kawatsura, M.; Terasaki, S.; Minakawa, M.; Hirakawa, T.; Ikeda, K.; Itoh, T. *Org. Lett.* **2014**, *16*, 2442. (c) Wei, Y.; Liang, F.; Zhang, X. *Org. Lett.* **2013**, *15*, 5186. (d) Chen, Z.; Lu, B.; Ding, Z.; Gao, K.; Yoshikai, N. *Org. Lett.* **2013**, *15*, 1966. (e) Kinder, R. E.; Zhang, Z.; Widenhoefer, R. A. *Org.*

Lett. **2008**, *10*, 3157. (f) Ribelin, T. P.; Judd, A. S.; Akritopoulou-Zanze, I.; Henry, R. F.; Cross, J. L.; Whittern, D. N.; Djuric, S. W. *Org. Lett.* **2007**, *9*, 5119. (g) Utsunomiya, M.; Miyamoto, Y.; Ipposhi, J.; Ohshima, T.; Mashima, K. *Org. Lett.* **2007**, *9*, 3371.

(31) For reviews dealing with applications of the C-C coupling and Mizoroki-Heck reactions in organic synthesis/medicinal chemistry, see: (a) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. (b) Phan, N. T. S.; Sluys, M. V. D.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609. (c) Blaser, H.-U.; Indolese, A.; Naud, F.; Nettekoven, U.; Schnyder, A. *Adv. Synth. Catal.* **2004**, *346*, 1583. (d) Farina, V. *Adv. Synth. Catal.* **2004**, *346*, 1553. (e) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (f) Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027. (g) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442. (h) de Vries, J. G. *Can. J. Chem.* **2001**, *79*, 1086.

(32) For reviews dealing with applications of the C-C coupling and Mizoroki-Heck reactions in organic synthesis/medicinal chemistry, see: (a) Cartney, D. M.; Guiry, P. J. *Chem. Soc. Rev.* **2011**, *40*, 5122. (b) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (c) Oestreich, M. *Eur. J. Org. Chem.* **2005**, 783. (d) Daves, Jr., G. D.; Hallberg, A.; *Chem. Rev.* **1989**, *89*, 1433. (e) Knowles, J. P.; Whiting, A. *Org. Biomol.Chem.* **2007**, *5*, 31. (f) Felpin, F.-X.; Hardy, L. N.; Callonnec, F. L.; Fouquet, E. *Tetrahedron* **2011**, *67*, 2815. (g) Alonso, F.; Beletskaya, I. P.; Yus, M. *Tetrahedron* **2005**, *61*, 11771.

(33) For selected papers dealing with the intermolecular/intramolecular Mizoroki-Heck reactions, see: (a) Quin, L.; Ren, X.; Lu, Y.; Li, Y.; Zhou, J. S. *Angew. Chem. Int. Ed.* **2012**, *51*, 5915. (b) Werner, E. W.; Sigman, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 9692. (c) Ruan, J.; Iggo, J. A.; Berry, N. G.; Xiao, J. *J. Am. Chem. Soc.* **2010**, *132*, 16689. (d) Mo, J.; Xu, L.; Xiao, J. *J. Am. Chem. Soc.* **2005**, *127*, 751. (e) Netz, N.; Opatz, T. *J. Org. Chem.* **2016**, *81*, 1723. (f) Kashinath,

K.; Dhara, S.; Reddy, D. S. *Org. Lett.* **2015**, *17*, 2090. (g) Quin, L.; Ren, X.; Lu, Y.; Li, Y.; Zhou, J. S. *Angew. Chem. Int. Ed.* **2012**, *51*, 5915.

(34) For papers dealing with the Pd-catalyzed synthesis of *β*-arylated allylamine, see: (a) Olofsson, K.; Sahlin, H.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2001**, *66*, 544 and references cited therein. (b) Olofsson, K. Larhed, M.; Hallberg, A. *J. Org. Chem.* **2000**, *65*, 7235. (c) Wu, J.; Marcoux, J.-F.; Davies, I. W.; Reider, P. J. *Tetrahedron Lett.* **2001**, *42*, 159.

(35) Deng, Y.; Jiang, Z.; Yao, M.; Xu, D.; Zhang, L.; Li, H.; Tang, W.; Xu, L. *Adv. Synth. Catal.* **2012**, *354*, 899.

(36) Zhang, L.; Jiang, Z.; Dong, C.; Xue, X.; Qui, R.; Tang, W.; Li, H.; Xiao, J.; Xu, L. *ChemCatChem* **2014**, *6*, 311.

(37) Jiang, Z.; Zhang, L.; Dong, C.; Ma, B.; Tang, W.; Xu, L.; Fan, Q.; Xiao, J. *Tetrahedron* **2012**, *68*, 4919.

(38) (a) Busacca, C. A.; Dong, Y. *Tetrahedron Lett.* **1996**, *37*, 3947. (b) Leikoski, T.; Wrigstedt, P.; Helminen, J.; Matikainen, J.; Sipilä, J.; Yli-Kauhaluoma, J. *Tetrahedron* **2013**, *69*, 839. (c) Reddington, M. V.; Cunninghan-Bryant, D. *Tetrahedron Lett.* **2011**, *52*, 181. For a paper dealing with double arylation of allylamine system, see: (d) Guo, H.-M.; Rao, W.-H.; Niu, H.-Y.; Jiang, L.-L.; Zhang, Y.; Qu, G.-R. *RSC Adv.* **2011**, *1*, 961.

(39) Zhang, L.; Dong, C.; Ding, C.; Chen, J.; Tang, W.; Li, H.; Xu, L.; Xiao, J. *Adv. Synth. Catal.* **2013**, *355*, 1570.

(40) He, Z.; Wibbelling, B.; Studer, A. *Adv. Synth. Catal.* **2013**, *355*, 3639.

(41) (a) Prediger, P.; Barbosa, L. F.; Génisson, Y.; Correia, C. R. D. *J. Org. Chem.* **2011**, *76*, 7737. (b) Ye, Z.; Brust, T. F.; Watts, V. J.; Dai, M. *Org. Lett.* **2015**, *17*, 892. (c) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Sferrazza, A. *Org. Biomol. Chem.* **2011**, *9*, 1727.

(42) (a) Xue, X.; Xu, J.; Zhang, L.; Xu, C.; Pan, Y.; Xu, L.; Li, H.; Zhang, W. *Adv. Synth. Catal.* **2016**, *358*, 573. (b) Jiang, Z.; Zhang, L.; Dong, C.; Cai, Z.; Tang, W.; Li, H.; Xu, L.; Xiao, J. *Adv. Synth. Catal.* **2012**, *354*, 3225. (c) Gigant, N.; Bäckvall, J.-E. *Org. Lett.* **2014**, *16*, 4432.

(43) Lei, Y.; Qiu, R.; Zhang, L.; Xu, C.; Pan, Y.; Qin, X.; Li, H.; Xu, L.; Deng, Y. *ChemCatChem.* **2015**, *7*, 1275.

(44) (a) Sun, R.; Liu, J.; Yang, S.; Chen, M.; Sun, N.; Chen, H.; Xie, X.; You, X.; Li, S.; Liu, Y. *Chem. Commun.* **2015**, *51*, 6426. (b) The Pd(II)-catalyzed reactions involving substrates **1h-m** were unsuccessful (See the SI).

(45) For a selected papers dealing with the chelation-based functionalization of alkenyl C-H bond, see: (a) Parella, R.; Babu, S. A. *J. Org. Chem.* **2015**, *80*, 12379 and references cited therein. (b) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *135*, 5308. (c) Xu, Y.-H.; Wang, M.; Lu, P.; Loh, T. P. *Tetrahedron* **2013**, *69*, 4403. (d) Gu, Q.; Al Mamari, H. H.; Graczyk, K.; Diers, E.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, *53*, 3868. (e) Ilies, L.; Matsubara, T.; Ichikawa, S.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 13126. (f) Shang, R.; Ilies, L.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 14349.

(46) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley Jr., J. P. *J. Org. Chem.* **1972**, *37*, 2320. (c) de Meijere, A.; Meyer, F. E. *Angew. Chem. Int. Ed. Engl.* **1995**, *33*, 2379. (d) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (e) Botella, L.; Nájera, C. *J. Org. Chem.* **2005**, *70*, 4360. (f) Bernini, R.; Cacchi, S.; Salve, I. D. Fabrizi, G. *Synlett* **2006**, 2947. (g) Chaudhary, A. R.; Bedekar, A. V. *Tetrahedron Lett.* **2012**, *53*, 6100. (h) McMahon, C. M.; Alexanian, E. J. *Angew. Chem. Int. Ed.* **2014**, *53*, 5974.

(47) (a) For a selected review dealing with the ligand-free Mizoroki–Heck reaction, see: de Vries, J. G.; Reetz, M. T. *Chem. Commun.* **2004**, 1559. For selected articles dealing with the

ligand-free Mizoroki–Heck reaction using the $Pd(OAc)_2/K_2CO_3$ catalytic system, see: (b) Qu, X.; Sun, P.; Li, T.; Mao, J. *Adv. Synth. Catal.* **2011**, *353*, 1061. (c) Sun, P.; Qu, X.; Li, T.; Zhu, Y.; Yang, H.; Xing, Z.; Mao, J. *Synlett* **2012**, *23*, 150. (d) Kanagaraj, K.; Pitchumani, K. *Chem. Eur. J.* **2013**, *19*, 14425. (e) Du, Z.; Zhou, W.; Bai, L.; Wang, F.; Wang, J.-X. *Synlett* **2011**, *22*, 369.

(48) For selected articles dealing with the Mizoroki–Heck reaction using the $Pd(OAc)_2/K_2CO_3$ catalytic system and other ligands instead of phosphine ligands, see: (a) Cui, X.; Li, Z.; Tao, C.-Z.; Xu, Y.; Li, J.; Guo, Q.-X. *Org. Lett.* **2006**, *8*, 2467. (b) Cui, X.; Li, J.; Liu, L.; Guo, Q. X. *Chin. Chem. Lett.* **2007**, *18*, 625. (c) Cui, X.; Li, J.; Zhang, Z.-P.; Fu, Y.; Liu, L.; Guo, Q.-X. *J. Org. Chem.* **2007**, *72*, 9342 and references cited therein. For selected articles revealing $Pd(OAc)_2$ (without any added ligand) as an active catalyst for the Mizoroki–Heck reaction, see: (d) Yao, Q.; Kinney, E. P.; Yang, Z. *J. Org. Chem.* **2003**, *68*, 7528 and references cited therein. (e) Amini, M.; Bagherzadeh, M.; Moradi-Shoeili, Z.; Boghaei, D. M. *RSC Adv.* **2012**, *2*, 12091.

(49) The observed *E*-selective *γ*-C-H arylations of **1e-g** could also be demonstrated *via* the plausible ligand free Heck-type reaction mechanism as suggested by Yao et al. (ref. 48d) in concurrence with the literature reports (see refs. 47,48) and also based on the discussions and control experiments reported in our previous work, see ref. 45a.

(50) (a) Moon, N. G.; Harned, A. M. *Tetrahedron Lett.* **2013**, *54*, 2960. (b) Anchoori, R. K.; Kortenhorst, M. S. Q.; Hidalgo, M.; Sarkar, T.; Hallur, G.; Bai, R.; Diest, P. J. V.; Hamel, E.; Khan, S. R. *J. Med. Chem.* **2008**, *51*, 5953. (c) Papadopoulos, G. N.; Kokotos, C. G. *J. Org. Chem.* **2016**, *81*, 7023. (d) Sergeyev, S.; Hesse. M. *Synlett* **2002**, 1313. (e) Saikia, U. P.; Baruah, D.; Pahari, P.; Borah, M. J.; Goswami, A.; Konwar, D. *Tetrahedron Lett.* **2014**, *55*, 4328.