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Decarboxylative Arylation of Pyridine 1-Oxides and Anilides with Benzoic Acid *via* Palladium-Catalyzed C-H Functionalization

Minoo Dabiri*, Seyed Iman Alavioon and Siyavash Kazemi Movahed

Abstract: A novel method for the palladium-catalyzed decarboxylative *ortho* C-H bond arylation of pyridine 1-oxides and anilides with benzoic acids as aryl sources is described. The established methodology provides a direct approach for the synthesis of 2-arylpyridine 1-oxides and 2-ayl anilides in good isolated yields.

Introduction

During the early decades, the inert C-H bonds activation to prepare compounds with various properties was a great challenge for organic chemists.[1] But nowadays, there are many reports in the literatures about transition metals-catalyzed C-H or C-heteroatom activation to replace hydrogen or heteroatom with different functional groups.[2] Transition metal catalyzed C-H activation is a powerful tool for the selective C-H functionalization using various active directing groups such as imines, amides, carbonyls, heterocycles, etc.[3,4] Directing groups mainly are used for trigger C-H bond cleavage and regioselective functionalization.

Transition metal catalyzed C-C bond formation reaction is one of the most important procedure in organic synthesis for the synthesis of complex molecules from simple precursors via the one-step proceeding.[5] Carboxylic acids as aryl source for C-C bond formation have unique advantages.[6] They are cheap, non-toxic, stable, widely commercially available, and ease of handling relative to expensive and/or sensitive organometallic reagents.[7] Since the first report by Nilsson regarding the copper-mediated decarboxylative biaryl coupling,[8] the exciting breakthroughs have been achieved by Myers,[9–11] Gooßen,[12,13,13,14] and others in the development of transition-metal-catalyzed decarboxylative cross-coupling reactions. Tan reported the Pd-catalyzed decarboxylative coupling of thiazoles and benzoxazole with various substituted benzoic acids.[15] Su reported the direct arylation of a wide range of indoles with benzoic acids using $Pd(TFA)_2/Ag_2CO_3$/propionic acid catalyst system through a decarboxylation/C-H bond activation.[16]

2-Arylpyridin 1-oxide and 2-aryl anilide derivatives are the main building blocks of compounds with diverse medicinal properties such as PDE4 inhibitors for the treatment and prevention of stroke, myocardial infarct and cardiovascular inflammatory diseases (**A**),[17] P38 Kinase inhibitors (**B**[18] and **C**[19]), C-FMS kinase inhibitors (**D**)[20], treatment of kidney disorders (**E**)[21], and anti-cancer (**F**)[22] (Figure 1).

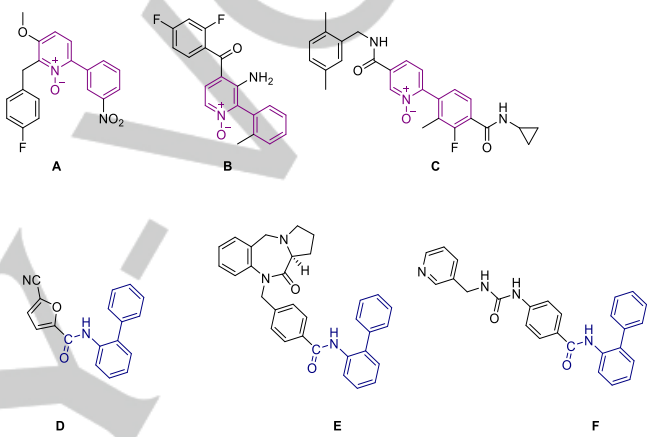

Figure 1. Examples of bioactive 2-arylpyridin 1-oxide and 2-aryl anilide derivatives

Moreover, pyridine 1-oxides frequently are used as protecting groups, auxiliary agents in asymmetric substances synthesis and oxidants in heterocycle materials synthesis.[23,24] *N*-O bond in pyridine 1-oxides and carbonyl in aniliids as instrumental directing groups for the transition metal catalyzed *ortho*-C-H functionalization has previously been widely studied to obtain one *regio*- and *chemo*-selective product[25] (Scheme 1). Fagnou reported a new approach for the synthesis of 2-aryl pyridine by using the inexpensive, commercially available, and bench-stable pyridine 1-oxides as replacements of unstable 2-pyridyl organometallic.[26] Toward anilides, Shi reported an efficient method for the generation of $C(sp^2)$ -$C(sp^2)$ bonds via palladium catalyzed C-H activation of *N*-alkylacetanilides with arylboronic acid.[27] Pd-catalyzed decarboxylative *ortho*-arylation of anilides with aryl acylperoxides was developed by Wang.[28]

Very recently, we reported the arylation of pyridine 1-oxides with phenyl hydrazines using palladium supported on mesoporous silica/graphene nanohybrid as the powerful heterogeneous catalyst.[29] Based on above introduction and also as part of our ongoing studies on the C-H activation reactions and organic synthesis,[29–35] herein, we report the successful palladium-catalyzed decarboxylative C-H arylation of pyridine 1-oxides and anilides with benzoic acids (Scheme 1).

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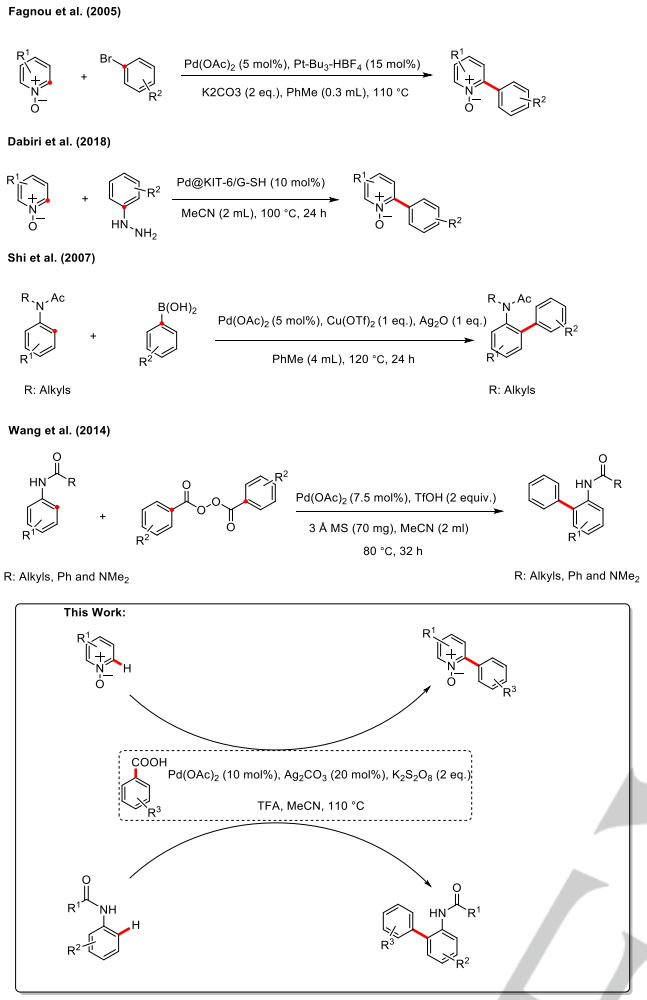
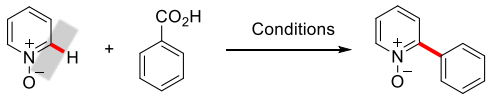


Scheme 1. Some examples of the Palladium-catalyzed arylation of pyridine 1-oxides and anilides. TFA= trifluoroacetic acid, TfOH= Triflic acid, MS= molecular sieve

Results and Discussion

Our initial investigation began with the C-H arylation of pyridine1-oxide (**1a**) with benzoic acid (**2a**) as a model reaction in different conditions. Different solvents, catalysts, oxidants, co-oxidants, and temperatures were tested to optimize the reaction conditions (Table 1). Various palladium and copper-based catalysts were first screened (Table 1, entries 1-7). The results showed that the $Pd(OAc)_2$ is the best catalyze for the reaction (Table 1, entry 1). In the absence of the catalyst, the reaction did not proceed (Table 1, entry 8). In the next step, the different loading of $Pd(OAc)_2$ were tested and the results showed that the 10 mol% catalyst loading was most effective and gave the higher yield than 5 mol% of $Pd(OAc)_2$ (Table 1, entries 1 and 9). The effect of oxidant was also investigated and no improvement in yields were observed in the presence of Ag_2OAc and AgBr (Table 1, entries 10 and 11). Additionally, in the absence of the oxidant, the reaction did not proceed (Table 1, entry 12). The different types of co-oxidants such as $(NH_4)_2S_2O_8$, *tert*-butyl hydroperoxide (TBHP), and di-*tert*-butyl peroxide (DTBP) were tested and they showed low efficiency and yields (Table 1, entries 12–15). The yield was decreased to 36% when the reaction was done in the absence of the co-oxidant (Table 1, entry 16). These results indicated that the oxidant and co-oxidants were necessary for the decarboxylative arylation. Additionally, the various solvents such as chlorobenzene, dimethyl sulfoxide (DMSO), 1,2-dichloroethane (DCE), 1,2-dimethoxyethane (DME), and dichloromethane (DCM) were tested which afforded moderate to poor yields of product (Table 1, entries 17-21). Also, no improvement in the product yield was observed even when the reaction temperature was increased from 110 °C to 120 °C; however, the yield decreased when the reaction temperature was increased to 100 °C (Table 1, entries 22 and 23).

Table 1. Optimization of the reaction condition for the decarboxylative *ortho* C-H bond arylation of pyridine 1-oxide (**1a**) with benzoic acid (**1b**) [a]



1a **2a** **3a**

Entry	Catalyst (mol%)	Additive	Solvent	Yield [%][b]
1	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	69
2	$PdCl_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	61
3	$PdCl_2$(COD) (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	42
4	$Pd(dba)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	27
5	$Cu(OAc)_2.H_2O$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	66
6	$CuBr_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	Trace
7	$CuCl_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	Trace
8	-	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	Trace
9	$Pd(OAc)_2$ (5)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	54
10	$Pd(OAc)_2$ (10)	$AgOAc/K_2S_2O_8$/TFA	MeCN	62
11	$Pd(OAc)_2$ (10)	$AgBr/K_2S_2O_8$/TFA	MeCN	Trace
12	$Pd(OAc)_2$ (10)	$K_2S_2O_8$/TFA	MeCN	Trace
13	$Pd(OAc)_2$ (10)	$Ag_2CO_3/(NH_4)_2S_2O_8$/TFA	MeCN	58
14	$Pd(OAc)_2$ (10)	Ag_2CO_3/TBHP/TFA	MeCN	Trace
15	$Pd(OAc)_2$ (10)	Ag_2CO_3/DTBP/TFA	MeCN	Trace
16	$Pd(OAc)_2$ (10)	Ag_2CO_3/TFA	MeCN	36
17	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	PhCl	Trace
18	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	DCE	38
19	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	DCM	34

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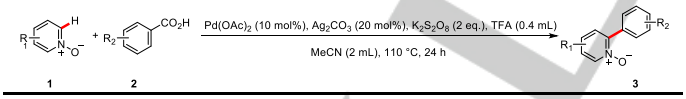
20	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	DME	45
21	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	DMSO	Trace
22[c]	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	43
23[d]	$Pd(OAc)_2$ (10)	$Ag_2CO_3/K_2S_2O_8$/TFA	MeCN	69

[a] pyridine 1-oxides (0.5 mmol), benzoic acid (1 mmol), catalyst (mol%), oxidant (20 mol%), co-oxidant (2 eq.), TFA (0.4 mL), Time = 24 h, temp. = 110 °C. [b] isolated yield. [c] Temp. = 100 °C. [d] Temp. = 120 °C

After optimizing the reaction condition, the reaction scope and substituent effect were examined in the Pd-catalyzed decarboxylative *ortho* C-H bond arylation of various pyridine 1-oxides with benzoic acids under optimal condition (Table 2). The derivatives bearing electron-donating and electron-withdrawing substituents on both aromatic rings in starting materials reacted and gave moderate to good yields. The presence of electron-donating substituents on benzoic acids such as *p*-OMe and *p*-Me resulted in slightly higher yield than electron-withdrawing substituents such as *p*-F, *p*-Br and *p*-CF_3 (Table 2, **3b**, **3c**, **3d**, **3e**, and **3f**). The hindered benzoic acids such as *o*-NO_2 and *o*-Br reacted well and gave the desired products in moderate yields (Table 2, **3g** and **3h**). The substituted effect on pyridine 1-oxides was evaluated in the decarboxylative *ortho* C-H bond arylation. The electron-donating substituents such as *m*-Me and 3,5-diMe and electron-withdrawing substituents such as *m*-CO_2Et, *m*-Cl, *p*-CN on pyridine 1-oxides gave the arylated products (Table 2, **3i**, **3j**, **3k**, **3l**, and **3m**). The electron-donating substituents on pyridine 1-oxides provided higher arylated products yield than electron-withdrawing substituents which could be attributed to the electrophilic acyloxylation C–H activation to form a C–Pd bond.[30] Additionally, the *meta*- substituted (-Cl) benzoic acid reacted and good yield of the product (**3n**) was obtained.

Table 2. Pd-catalyzed decarboxylative *ortho* C-H bond arylation of various pyridine 1-oxides with benzoic acids



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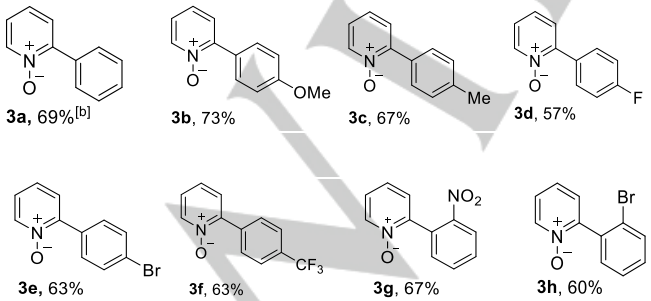
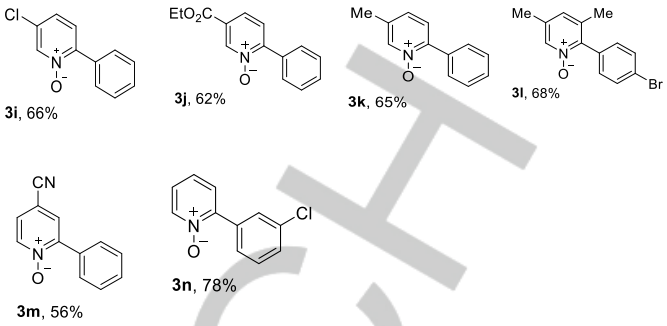


3a, 69%[b] **3b**, 73% **3c**, 67% **3d**, 57%

3e, 63% **3f**, 63% **3g**, 67% **3h**, 60%



3i, 66% **3j**, 62% **3k**, 65% **3l**, 68%

3m, 56% **3n**, 78%

[a] pyridine 1-oxide (0.5 mmol), benzoic acid (0.7 mmol), $Pd(OAc)_2$ (10 mol-%), Ag_2CO_3 (20 mol%) $K_2S_2O_8$ (2.0 equiv.), TFA (0.4 mL), MeCN (2.0 mL), temp. = 110 °C, time = 24 h. [b] isolated yield.

Following our investigation of Pd-catalyzed decarboxylative *ortho* C-H bond arylation, the arylation of *N*-phenylpivalamide derivatives with benzoic acids was evaluated. The C-H arylation between *N*-phenylpivalamide (**4a**) and benzoic acid (**2a**) was chosen as the model reaction. The reaction conditions was optimized and the different conditions such as solvent, catalyst, oxidant, co-oxidant, and temperature were tested (Table S1). The various metal salts catalysts such as $Pd(OAc)_2$, $PdCl_2$, $PdCl_2$(COD) (COD = 1,5-cyclooctadiene), $Pd(dba)_2$ (dba = dibenzylideneacetone), $Cu(OAc)_2.H_2O$, and $CuCl_2$ were tested and $Pd(OAc)_2$ showed the best result (Table S1, entries 1-6). In the absence of the catalyst, the reaction did not proceed (Table S1, entry 7). The decrease of the Pd loading to 5 mol % afforded a lower yield (47%) (Table S1, entry 8). The effect of oxidant was also investigated and no improvement in yields was observed in the presence of AgOAc and AgBr (Table S1, entries 9 and 10). The reaction did not proceed in the absence of the oxidant (Table S1, entry 11). The different types of co-oxidants were tested and they showed low efficiency and afforded low yields (Table S1, entries 12 and 13). The reaction was carried out in the absence of the co-oxidant and yield was decreased to 9% (Table S1, entry 14). Additionally, the various solvents were tested which afforded moderate to poor yields of product (Table S1, entries 15-17). Also, no improvement in the product yield was observed even when the reaction temperature was increased from 110 °C to 130 °C; however, the yield decreased when the reaction temperature was increased to 90 °C (Table S1, entries 18 and 19).

The substituted anilides and benzoic acids were reacted under the optimized conditions to afford the corresponding *ortho*-arylated anilides in good yields. The results are summarized in Table 3. Anilides with both electron-donating and electron-withdrawing substituents reacted good and resulted in the corresponding 2-aryl anilides in moderate to good yields. Anilides bearing electron-donating substituents such as *p*-Me and *p*-OMe (Table 3, **5f** and **5j**) gave higher yields than electron-withdrawing substituents *p*-Cl and *p*-CF_3 (Table 3, **5i** and **5h**). The electron-donating and electron-withdrawing substituents on benzoic acids reacted slightly and gave *ortho*-arylated anilides in moderate to good yields (Table 3, **5c**, **5d**, **5e**, and **5f**).

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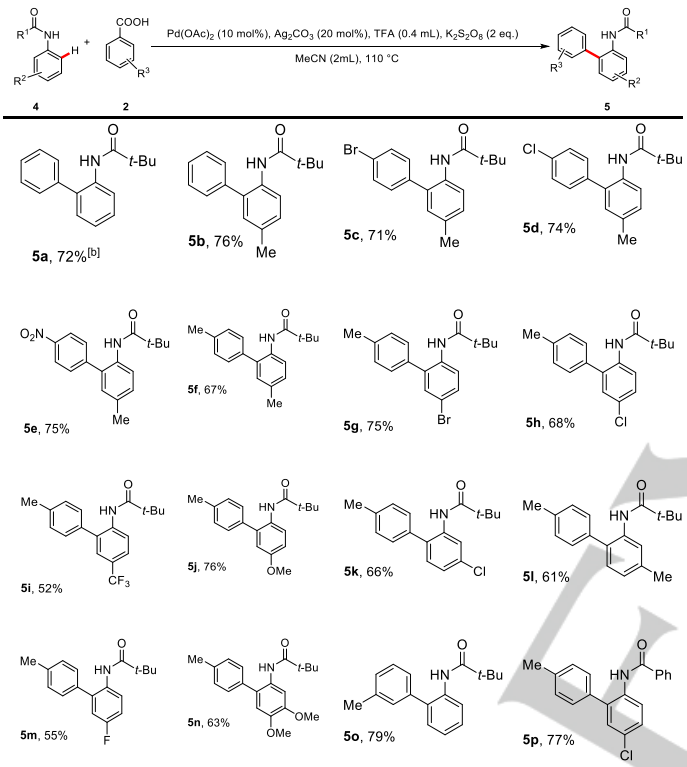
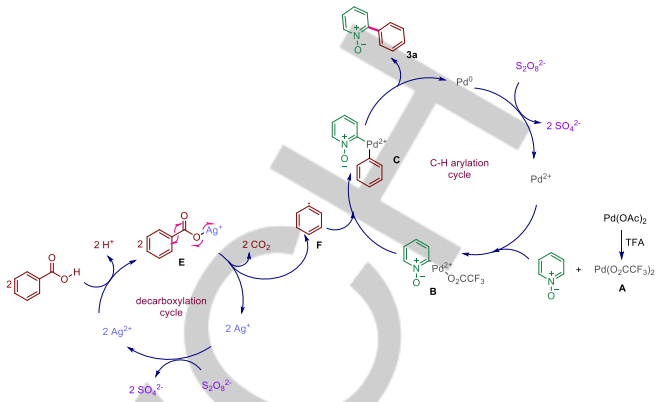
Additionally, the *meta*- substituted (-Me) benzoic acid reacted and good yield of the product (**5o**) was obtained. In addition to the acetamido group, phenyl moieties were tested in this *ortho*-C-H bond arylation and the product (**5p**) was isolated in good yield.

Table 3. Pd-catalyzed decarboxylative *ortho* C-H bond arylation of various anilides with benzoic acids



[a] anilide derivative (0.5 mmol), benzoic acid derivative (0.7 mmol), $Pd(OAc)_2$ (10 mol-%), Ag_2CO_3 (20 mol%) $K_2S_2O_8$ (2.0 equiv.), TFA (0.4 mL), MeCN (2.0 mL), temp. = 110 °C, time = 24 h. [b] isolated yield.

On the achieved results and based on the well-documented literatures for the Pd-catalyzed the decarboxylative C-H bond functionalization of various types of compounds *via* Pd^0/Pd^{II} mechanisms (Scheme 2).[16,36–38] In two intertwined catalytic cycles, palladium acetate in the presence of TFA turns into palladium trifluoroacetate (**A**). The palladium species performs an electrophilic palladation (**A** to **B**) and the biaryl formation through reductive elimination (**C** to **3a**), whereas an Ag^I cation is oxidized to an Ag^{II} cation by peroxodisulfate. Then, carboxylic acid reacts with the Ag^{II} cation to form cation salt (**E**) by losing a proton. The cation salt (**E**) further loses one molecule of CO_2 and the Ag^I cation to form aryl radical (**F**). Finally, oxidation of Pd^0 to Pd^{II} (**A**), also performed by the $K_2S_2O_8$, completes the arylation cycle.



Scheme 2. The possible mechanism for Pd-catalyzed decarboxylative *ortho* C-H bond arylation of pyridine 1-oxide

Conclusions

In conclusion, an efficient method for the *ortho* C–H bond arylation of pyridine 1-oxides and anilides with benzoic acids as aryl sources has been disclosed. The synthetic method allows the synthesis of a broad range of 2-arylpyridine 1-oxides and 2-aryl anilides with inexpensive and accessible starting materials. A wide substrates tolerance with both electron-donating and electron-withdrawing substituents on both coupling participants is an advantage of the method. Moreover, the N-O bond in pyridine 1-oxide and carbonyl in anilde as directing groups, in the final product can easily remove to become pyridine and aniline derivative.

Experimental Section

General Information. All solvents, pyridine aniline and benzoic acid derivatives were purchased from Merck and Sigma. Other reagents were purchased from commercial distributors and used without further purification. Pyridine *N*-oxide and anilide derivatives were synthesized according to the literatures.[39,40] Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F254 plates. The products were purified by preparative column chromatography on silica gel (0.063-0.200 mm; Merck). ^1H and ^{13}C-NMR Spectra: were recorded on Bruker DRX 300 and INOVA 500 MHz advance instruments in $CDCl_3$; δ in ppm, *J* in Hz. Mass spectra were recorded on an Agilent Technology (HP) 5973 Network Mass Selective Detector operating at an ionization potential of 70 eV. IR spectra were recorded on a Bomem MB-Series FT-IR spectrophotometer.

General Procedure for Synthesis of 2-phenylpyridine-1-oxides

Pyridine-1-oxides (0.5 mmol) and benzoic acid (0.7 mmol), MeCN (2 mL) as solvent Ag_2CO_3 (20 mol%), $K_2S_2O_8$ (2.0 equiv.), TFA (0.4 ml) and $Pd(OAc)_2$(10 mol % of Pd) were added to the tube and stirred at 110 °C for 24 h. After this time, the mixture was cooled to room temperature, diluted with CH_2Cl_2 and filtered. The residue was purified by column chromatography to yield the optimal product.

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2-phenylpyridine 1-oxide (3a): Yellow solid, m.p.: 142–144 °C (lit.[41] m.p.: 141-142 °C); IR (KBr, υ/cm^{-1}): 3076, 3013, 1490, 1397, 1229, 863, 760, 744, 671; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.40 (d, J = 6 Hz, 1H) , 7.84 – 7.81 (m, 2H), 7.62 (t, J = 6 Hz, 1H), 7.49-7.46 (m, 2H), 7.43-7.38 (m, 3 H), ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 139.43, 133.35, 129.65, 129.57, 128.22, 127.46, 126.53, 126.25, 124.52. MS (EI): *m/z* (relative intensity %) = 172 (28) [M]$^+$,170 (100), 154 (21), 142 (49), 127 (11), 117 (58), 51 (31).

2-(4-methoxyphenyl)pyridine 1-oxide (3b): Yellow solid, m.p.: 125–127 °C (lit.[41] m.p.: 121-123 °C); IR (KBr, υ/cm^{-1}): 3050, 2989, 1573, 1466, 1456, 1351, 1268, 1211, 1180, 829, 749; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.37 (d, J = 5.5 Hz, 1H), 8.24 – 8.21 (m, 1H), 7.84 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 7.0 Hz, 1H), 7.37 (t, J = 2.8 Hz, 1H), 7.13 (d, J = 8.6 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) = 160.57, 153.96, 142.53, 130.76, 126.88, 125.48, 123.81, 121.61, 113.71, 55.34. MS (EI): *m/z* (relative intensity %) = 201 (89) [M]$^+$, 200 (100), 185 (31), 172 (26), 158 (40), 130 (51), 117 (21), 102 (10), 78 (24).

2-(p-tolyl)pyridine 1-oxide (3c): Yellow solid, m.p.: 127–129 °C (lit.[41] m.p.: 129-131 °C); IR (KBr, υ/cm^{-1}): 3046, 3081, 2929, 1630, 1427, 1251, 999, 827, 774; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm)= 8.33 (d, J = 6.5 Hz, 1H), 7.73 (d, J = 7.8 Hz, 2H), 7.55 – 7.50 (m, 1H), 7.44 (d, J = 7.9 Hz, 2H), 7.28 – 7.22 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm)= 140.38, 137.81, 133.05, 131.05, 129.06, 125.17, 123.26, 121.90, 22.21. MS (EI): *m/z* (relative intensity %) = 185 (71) [M]$^+$, 184 (100), 156 (57), 149 (38), 117 (28), 95 (58), 69 (36), 57 (42).

2-(4-fluorophenyl)pyridine 1-oxide (3d): Yellow solid, m.p.: 163–165 °C (lit.[41] m.p.: 161-163 °C); IR (KBr, υ/cm^{-1}): 3066, 3041, 2464, 1916, 1594, 1247, 1019, 759, 572; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.38 (d, J = 6.4 Hz, 1H), 7.90 – 7.85 (m, 2H), 7.46 – 7.42 (m, 1H), 7.34 – 7.28 (m, 1H), 7.19 (t, J = 8.5 Hz, 2H), ^{13}C NMR (126 MHz, Chloroform-*d*) δ (ppm): 163.32 (d, J = 250.2 Hz), 140.18, 136.14, 131.41 (d, J = 8.6 Hz), 128.60, 127.16, 125.66, 124.51, 116.39 (d, J = 21.7 Hz). MS (EI): *m/z* (relative intensity %) = 189 (63) [M]$^+$, 188 (100), 160 (31), 133 (35), 117 (28), 95 (15), 57 (42).

2-(4-bromophenyl)pyridine 1-oxide (3e): Brown oil. IR (KBr, υ/cm^{-1}): 3051, 1623, 1439, 1336, 1250, 1104, 840, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.01 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.37 (d, J = 8.2 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 143.15, 139.17, 136.66, 130.66, 129.63, 127.41, 122.62, 118.90, 115.77. MS (IE) m/z (relative intensity %) 251 (50) [M+1]$^+$, 250 (50) [M]$^+$, 200 (39), 183 (54), 155 (17), 141 (33), 115 (52), 95 (30), 59 (100).

2-(4-(trifluoromethyl)phenyl)pyridine (3f): Yellow solid, m.p.: 125–127 °C (lit.[26] m.p.: 127-129 °C); IR (KBr, υ/cm^{-1}): 2949, 1703, 1593, 1517, 1353, 1265, 1238, 1127, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.48 – 8.45 (m, 2H), 8.06 – 8.02 (m, 2H), 7.73 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.52 – 7.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 150.75, 144.06, 138.51, 135.01 (*q, J* = 32 Hz), 129.74, 127.94, 125.91, 125.10, 124.93, 123.9 (*q, J* = 272 Hz), 119.78. MS (IE) m/z (relative intensity %) 239 (7) [M]$^+$, 211 (7), 183 (12), 140 (100), 125 (11), 111 (21), 97 (38), 85 (43), 71 (48), 57 (62).

2-(2-nitrophenyl)pyridine 1-oxide (3g): Yellow solid, m.p.: 157–159 °C (lit.[42] m.p.: 160-161 °C); IR (KBr, υ/cm^{-1}): 3070, 3051, 1587, 1434, 1369, 1238, 1102, 926, 751; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 8.44 (d, J = 6.4 Hz, 1H), 8.24 – 8.22 (m, 3H), 8.02 (d, J = 8.5 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.63 – 7.55 (m, 1H), 7.51 – 7.46 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 139.39, 135.53, 133.73, 132.42, 131.33, 130.06, 126.91, 126.25, 125.92, 123.42, 119.94. MS (IE) m/z (relative intensity %) 216 (5) [M]$^+$, 169 (10), 158 (10), 155 (15), 140 (17), 113 (21), 97 (34), 71 (63), 43 (100).

2-(2-bromophenyl)pyridine 1-oxide (3h): Yellow solid, m.p.: 110–112 °C (lit.[43] m.p.: 113 °C); IR (KBr, υ/cm^{-1}): IR (KBr, ν/cm^{-1}): 3049, 1637, 1432, 1325, 1243, 1109, 852, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm)= 7.87 (d, J = 7.8 Hz, 1H), 7.69 – 7.62 (m, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.35 -7.28 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 134.24, 133.68, 132.89, 132.30, 131.54, 131.02, 130.92, 128.10, 127.51, 127.10, 127.01. MS (IE) m/z (relative intensity %) 251 (48) [M+1]$^+$, 250 (48) [M]$^+$, 200 (37), 183 (49), 155 (21), 141 (41), 115 (58), 95 (23), 59 (100).

5-chloro-2-phenylpyridine 1-oxide (3i): Yellow solid, m.p.: 156–158 °C IR (KBr, υ/cm^{-1}): 3036, 1612, 1509, 1489, 1321, 1275, 1214, 1098, 745, 673; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm)= 7.62 (s, 1H), 7.29 – 7.24 (m, 2H), 6.97- 6.92 (m, 2H), 6.90 – 6.83 (m, 2H), 6.78 (d, J = 8.0 Hz, 1H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 143.12, 137.14, 133.33, 129.35, 129.19, 128.34, 127.19, 122.98, 121.31. MS (EI): *m/z* (relative intensity %) = 205 (18) [M]$^+$, 203 (8), 150 (64), 108 (100), 92 (35), 77 (56), 65 (23).

5-(ethoxycarbonyl)-2-phenylpyridine 1-oxide (3j): Brown oil, IR (KBr, υ/cm^{-1}): 3046, 1609, 1550, 1477, 1428, 1314, 1271, 1233, 1130, 1100, 965, 855, 804; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 8.37 (s, 1H), 8.11 (d, J = 6.4 Hz, 1H), 7.43 (dd, J = 8.2, 1.7 Hz, 2H), 7.40 – 7.38 (m, 3H), 7.28 – 7.26 (m, 1H), 4.26 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm)= 163.29, 138.96, 138.27, 136.82, 129.25, 128.58, 127.65, 124.16, 119.05, 116.81, 112.53, 39.14, 14.11. MS (IE) m/z (relative intensity %) 244 (47) [M+1]$^+$, 243 (47) [M]$^+$, 171 (100), 155 (57), 79 (46), 57 (66).

5-methyl-2-phenylpyridine 1-oxide (3k): Yellow solid, m.p.: 162–164 °C (lit.[41] m.p.: 168-169 °C); IR (KBr, υ/cm^{-1}): 3058, 2965, 1609, 1532, 1478, 1377, 1325, 1254, 1103, 833, 737, 684; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 8.24 (s, 1H), 7.96 (d, J = 6.4 Hz, 2H), 7.49 – 7.28 (m, 3H), 7.16 (d, J = 8.3 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm)= 145.90, 142.09, 138.72, 134.20, 130.26, 129.07, 127.82, 127.12, 124.82, 22.72. MS (EI): *m/z* (relative intensity %) = 185 (21) [M]$^+$, 184 (32), 167 (16), 149 (72), 106 (68), 97 (49), 85 (57), 71 (73), 57 (100).

2-(4-bromophenyl)-3,5-dimethylpyridine 1-oxide (3l): Brown oil, IR (KBr, υ/cm^{-1}): 3055, 2965, 1619, 1556, 1460, 1388, 1331, 1254, 1116, 827, 740, 682; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm)= 8.42 (s, 1H), 8.24 (s, 1H), 7.38 – 7.28 (m, 5H), 7.06 (s, 1H), 2.52 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)=136.12, 131.13, 131.07, 128.73, 127.11, 126.93, 126.19, 123.55, 23.75, 20.63. MS (IE) m/z (relative intensity %) 279 (49) [M+1]$^+$, 278 (49) [M]$^+$, 264 (70), 262, (58), 250 (34), 199 (61), 123 (42), 79 (64), 58 (100).

4-cyano-2-phenylpyridine 1-oxide (3m): Brown oil, IR (KBr, υ/cm^{-1}): 3050, 3017, 2994, 2226, 1555, 1475, 1452, 1368, 1259, 1247, 984, 857, 786; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 8.42 - 8.23 (m, 3H), 7.52 – 7.27 (m, 3H), 7.10 (d, J = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 151.78, 146.93, 142.38, 133.62, 131.89, 128.36, 125.14, 122.78, 121.08, 114.63. MS (EI): *m/z* (relative intensity %) = 196 (8) [M]$^+$, 180 (26), 167 (42), 152(36), 105 (52), 93 (31), 77 (100), 51 (35).

2-(3-chlorophenyl)pyridine 1-oxide (3n): White solid, m.p. 81–83 °C; IR (KBr, υ/cm^{-1}): 3046, 1613, 1511, 1483, 1325, 1266, 1220, 1086, 746, 667; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 8.48 (d, J = 8.3 Hz, 1H), 8.08 (d, J = 7.9 Hz, 1H), 7.84 - 7.79 (m, 4H), 7.56 – 7.52 (m, 2H); ^{13}C NMR

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(126 MHz, $CDCl_3$): δ (ppm)= 137.7, 133.0, 131.9, 130.9, 129.8, 128.9, 128.6, 124.4, 120.0. MS (EI): *m*/*z* (relative intensity %) = 205 (15), 149 (91), 121 (20), 93 (100), 77 (31), 57 (91), 41 (40).

General Procedure for Synthesis of 2-aryl anilides

Anilide derivatives (0.5 mmol) and benzoic acid (0.7 mmol), MeCN (2 mL) as solvent, Ag_2CO_3 (20 mol%) $K_2S_2O_8$ (2.0 equiv.), TFA (0.4 ml) and $Pd(OAc)_2$(10 mol % of Pd) were added to the tube and stirred at 110 °C for 24 h. After this time, the mixture was cooled to room temperature, diluted with CH_2Cl_2 and filtered. The residue was purified by column chromatography to yield the desired product.

***N*-([1,1'-biphenyl]-2-yl)pivalamide (5a):** White crystal, m.p.: 68-70 °C (lit.[28] m.p.: 65-67 °C); IR (KBr, υ/cm^{-1}) 3266, 1639, 1571, 940, 647; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.38 (d, *J* = 8.3 Hz, 1H), 7.53 – 7.48 (m, 4H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.25 (br, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 1.11 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.32, 138.06, 135.13, 132.20, 129.74, 129.35, 129.07, 128.49, 128.09, 123.93, 120.91, 39.81, 27.39. MS (EI): *m*/*z* (relative intensity %) = 253 (52) $[M]^+$, 169 (61), 57(100), 41 (16).

***N*-(5-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5b):** Colorless crystal, m.p.: 97-99 °C (lit.[44] m.p.: 94-96 °C); IR (KBr, υ/cm^{-1}) 3285, 2960, 1653, 1558, 1268, 798, 688; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.29 (d, *J* = 8.7 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.31 – 7.20 (m, 3H), 7.08 (d, *J* = 2.1 Hz, 1H), 2.37 (s, 3H), 1.12 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.29, 137.86, 135.24, 135.06, 132.08, 129.86, 129.74, 129.22, 128.29, 123.85, 120.78, 39.73, 27.45, 21.38. MS (EI): *m*/*z* (relative intensity %) = 267 (67) $[M]^+$, 210 (16), 183 (78), 182 (36), 167 (12), 57 (100), 41 (29).

***N*-(4'-bromo-5-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5c):** Colorless crystal, m.p.: 121-123 °C (lit.[44] m.p.: 122-124 °C); IR (KBr, υ/cm^{-1}) 3268, 2967, 1647, 1525, 1192, 912, 726, 663; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.10 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.33 (br, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.04 (d, *J* = 2.5 Hz, 1H), 2.36 (s, 3H), 1.15 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.31, 137.37, 134.09, 132.28, 132.03, 131.71, 130.99, 130.30, 129.32, 122.24, 122.09, 39.67, 27.49, 20.89. MS (EI): *m*/*z* (relative intensity %) = 347 (61) $[M+2]^+$, 345 (62) $[M]^+$, 263 (37), 261 (44),180 (34),167 (27),149 (331), 57 (100), 41 (23).

***N*-(4'-chloro-5-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5d):** Colorless crystal, m.p.: 108-109 °C (lit.[44] m.p.: 105-107 °C); IR (KBr, υ/cm^{-1}) 3278, 2969, 1649, 1505, 1225, 821, 763; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.11 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.33 – 7.31 (m, 3H), 7.21 – 7.18 (m, 1H), 7.05 (d, *J* = 2.1 Hz, 1H), 2.37 (s, 3H), 1.15 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.31, 136.90, 134.06, 132.36, 131.73, 130.68, 130.36, 129.36, 129.28, 129.08, 122.21, 39.67, 27.47, 20.86. MS (EI): *m*/*z* (relative intensity %) = 303 (10) $[M+2]^+$, 301 (8) $[M]^+$, 225 (29), 190 (85), 141 (65), 106 (30), 77 (22), 57 (100), 41 (24).

***N*-(5-methyl-4'-nitro-[1,1'-biphenyl]-2-yl)pivalamide (5e):** Yellow precipitate, m.p.: 132-134 °C (lit.[44] m.p.: 133-135 °C); IR (KBr, υ/cm^{-1}) 3267, 3001, 1559, 1546, 1375, 786. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.34 (d, *J* = 8.7 Hz, 2H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.30 – 7.25 (m, 1H), 7.19 (br, 1H), 7.10 (d, *J* = 2.3 Hz, 1H), 2.40 (s, 3H), 1.15 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.50, 147.29, 145.69, 135.04, 131.96, 131.84, 130.28, 130.24, 130.20, 123.95, 123.72, 39.60, 27.46, 20.89. MS (EI): *m*/*z* (relative intensity %) = 312 (100) $[M]^+$, 262 (28), 228 (73), 211 (36), 180 (43), 57 (81).

***N*-(4',5-dimethyl-[1,1'-biphenyl]-2-yl)pivalamide (5f):** White crystal, m.p.: 102-104 °C (lit.[44] m.p.: 101-103 °C); IR (KBr, υ/cm^{-1}) 3248, 3027, 1652, 1524, 1291, 857, 701; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.24 (d, *J* = 8.1 Hz, 1H), 7.45 (br, 1H), 7.29 – 7.24 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.06 (s, 1H), 2.44 (s, 3H), 2.36 (s, 3H), 1.13 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.09, 137.65, 135.28, 133.36, 132.68, 132.17, 130.37, 129.60, 129.14, 128.72, 120.98, 39.69, 27.43, 21.19, 20.80. MS (IE) m/z (relative intensity %) 281 (26) $[M]^+$, 233 (60), 197 (32), 119 (14), 105 (100), 57 (41).

***N*-(5-bromo-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5g):** Yellow crystal, m.p.: 99-101 °C (lit.[44] m.p.: 98-100 °C); IR (KBr, υ/cm^{-1}) 3274, 2952, 1630, 1564, 1206, 939, 754, 676; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.31 (d, *J* = 8.8 Hz, 1H), 7.51 – 7.42 (m, 2H), 7.37 (br, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 2.44 (s, 3H), 1.11 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.31, 138.49, 134.44, 133.88, 133.63, 132.43, 131.05, 129.91, 129.01, 122.22, 116.39, 39.87, 27.37, 21.29. MS (IE) m/z (relative intensity %) 347 (61) $[M+2]^+$, 345 (63) $[M]^+$, 263 (34), 261 (47),180 (36),167 (27),149 (35), 57 (100), 41 (19).

***N*-(5-chloro-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5h):** Colorless crystal, m.p.: 100-102 °C (lit.[44] m.p.: 102-104 °C); IR (KBr, υ/cm^{-1}) 3261, 2988, 1633, 1518, 1201, 826, 749; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.36 (d, *J* = 8.8 Hz, 1H), 7.53 (br, 1H), 7.35 – 7.30 (m, 3H), 7.26 (s, 1H), 7.24 – 7.22 (m, 2H), 2.45 (s, 3H), 1.13 (s, 9H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm)= 176.55, 143.60, 137.62, 135.15, 135.12, 128.78, 128.66, 128.48, 128.28, 123.85, 120.28, 39.88, 27.82, 21.18. MS (IE) m/z (relative intensity %) 303 (41) $[M+2]^+$, 301 (100) $[M]^+$, 217 (84), 180 (26), 57 (71).

***N*-(4'-methyl-5-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)pivalamide (5i):** Colorless crystal, m.p.: 87-89 °C (lit.[44] m.p.: 83-85 °C); IR (KBr, υ/cm^{-1}) 3278, 2973, 1653, 1525, 1317, 883, 784; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.61 (d, *J* = 8.7 Hz, 1H), 7.71 (br, 1H), 7.65 – 7.62 (m, 1H), 7.51 (d, *J* = 2.2 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.32 – 7.17 (m, 2H), 2.48 (s, 3H), 1.14 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.60, 138.75, 138.43, 133.60, 131.85, 130,08, 126.77 (*q*, *J* = 5.0 Hz),125.40 (*q*, *J* = 84.4 Hz), 125.40 (*q*, *J* = 5.0 Hz), 123.40 (*q*, *J* = 269.5 Hz), 120.10, 40.02, 27.34, 21.29. MS (IE) m/z (relative intensity %) 335 (67) $[M]^+$, 278 (14), 251 (81), 250 (33), 248 (29), 235 (19), 18 (17), 85 (19), 57 (100), 41 (29).

***N*-(5-methoxy-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5j):** Colorless crystal, m.p.: 105-107 °C (lit.[44] m.p.: 109-111 °C); IR (KBr, υ/cm^{-1}) 3286, 2997, 1662, 1547, 1271, 766, 699; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.17 (d, *J* = 2.7 Hz, 1H), 7.61 (br, 1H), 7.32 – 7.22 (m, 4H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.74 - 6.70 (m, 1H), 3.88 (s, 3H), 2.43 (s, 3H), 1.13 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.40, 159.58, 137.54, 136.26, 134.87, 130.46, 129.77, 129.44, 214.17, 110.56, 105.08, 55.42, 39.95, 27.43, 21.23. MS (IE) m/z (relative intensity %) 297 (100) $[M]^+$, 240 (15), 213 (562), 198 (59), 168 (16), 57 (33).

***N*-(4-chloro-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5k):** White crystal, m.p.: 80-82 °C lit.[45] m.p.: 78-81 °C); IR (KBr, υ/cm^{-1}) 3281, 2952, 1661, 1519, 1218, 856, 767; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm)= 8.31 (d, *J* = 1.9 Hz, 1H), 7.55 (br, 1H), 7.32 – 7.25 (m, 4H), 7.17 (d, *J* = 7.7 Hz, 1H), 7.03 – 7.00 (m, 1H), 2.44 (s, 3H), 1.14 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.25, 144.65, 137.60, 135.15, 135.12, 129.70, 129.66, 129.46, 129.28, 123.35, 120.20.39.81, 27.42, 21.19. MS (IE) m/z (relative intensity %) 303 (45) $[M+2]^+$, 301 (100) $[M]^+$, 213 (53), 180 (18), 57 (37).

***N*-(4,4'-dimethyl-[1,1'-biphenyl]-2-yl)pivalamide (5l):** Yellow oil, IR (KBr, υ/cm^{-1}) 3275, 2942, 1676, 1570, 1248 , 764, 668; ^{1}H NMR (300

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MHz, $CDCl_3$), δ (ppm)= 8.24 (s, 1H), 7.72 (br, 1H), 7.32 – 7.21 (m, 4H), 7.13 (d, J = 7.7 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H), 1.13 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.35, 138.27, 137.65, 135.08, 134.98, 129.72, 129.68, 129.31, 124.66, 121.32, 39.84, 27.45, 21.53, 21.28. MS (IE) m/z (relative intensity %) 281 (52) $[M]^+$, 224 (16), 197 (43), 180 (19), 167 (13), 149 (25), 57 (100), 41 (54).

***N*-(5-fluoro-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5m):** Colorless crystal, m.p.: 76-78 °C (lit.[44] m.p.: 75-77 °C); IR (KBr, υ/cm^{-1}) 3285, 2944, 1643, 1590, 1345, 1237, 759, 720, 649; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.32 – 8.29 (m, 1H), 7.44 (br, 1H), 7.35 – 7.30 (m, 2H), 7.28 – 7.26 (m, 2H), 7.10 – 7.05 (m, 1H), 6.99 – 6.96 (m, 1H), 2.46 (s, 3H), 1.14 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.29, 158.93 (d, J = 304.9 Hz), 138.37 (d, J = 8.8 Hz), 134.25 , 134.08, 131.27 (d, J = 3.8 Hz), 129.82, 128.97, 122.87 (d, J = 10.1 Hz), 116.45 (d, J = 27.7 Hz), 114.61 (d, J = 27.7 Hz), 39.71, 27.41, 21.27. MS (IE) m/z (relative intensity %) 285 (24) $[M]^+$, 201 (27), 167 (33), 149 (68), 71 (26), 57 (100), 43 (31), 41 (56).

***N*-(4,5-dimethoxy-4'-methyl-[1,1'-biphenyl]-2-yl)pivalamide (5n):** Brown oil, IR (KBr, υ/cm^{-1}) 3426, 2978, 1677, 1603, 1563, 1414, 1272, 765, 635; ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm)= 8.12 (s, 1H), 7.48 (br, 1H), 7.33 – 7.26 (m, 4H), 6.77 (s, 1H), 3.97 (s, 3H), 3.88 (s, 3H), 2.45 (s, 3H), 1.15 (s, 9H), ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 176.27, 148.34, 145.15, 137.67, 129.74, 129.37, 128.72, 124.01, 112.81, 105.06, 56.16, 56.04, 39.78, 27.46, 21.24. MS (IE) m/z (relative intensity %) 327 (100) $[M]^+$, 228 (31), 211 (23), 196 (17), 57 (51).

***N*-(3'-methyl-[1,1'-biphenyl]-2-yl)pivalamide(5o):** White crystal, m.p. 85–87 °C (lit.[46] m.p.: 85-87 °C); IR (KBr, υ/cm^{-1}) 3268, 2978, 1671, 1580, 1247 , 776, 656; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= δ 8.36 (d, J = 8.2 Hz, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.57 (s, 1H), 7.47 (s, 1H), 7.42 - 7.34 (m, 2H), 7.24 – 7.17 (m, 3H), 2.43 (s, 3H), 1.13 (s, 9H).; ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm)= δ 176.5, 138.7, 137.9, 130, 129.7, 129.1, 129.0, 128.7, 128.3, 126.3, 125.2, 124.0, 39.8, 31.9, 27.3. MS (EI): *m/z* (relative intensity %) = 267 (49), 210 (14), 183 (43), 152 (21), 115 (11), 85 (13), 57 (100).

***N*-(5-chloro-4'-methyl-[1,1'-biphenyl]-2-yl)benzamide (5p):** Light yellow crystal, m.p:101-103 °C; IR (KBr, υ/cm^{-1}) 3260, 2989, 1656, 1531, 1229, 822, 766; ^{1}H NMR (300 MHz $CDCl_3$), ^{1}H NMR (300 MHz) δ (ppm)= 8.57 – 8.52 (m, 1H), 8.04 (d, J = 9.0 Hz, 1H), 7.61 (s, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.44 - 7.37 (m, 4H), 7.34 – 7.23 (m, 5H), 2.46 (s, 3H)., ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)= 163.7, 150.8, 148.3, 143.0, 141.9, 141.5, 134.9, 131.4, 129.7, 127.9, 123.8, 123.4, 122.8, 121.0, 118.0, 21.5. MS (IE) m/z (relative intensity %) 323(29) $[M+2]^+$, 321 (100) $[M]^+$.

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Keywords: Palladium • C-H functionalization • Arylation • Synthetic methods • Carboxylic acids

[1] R. Sharma, K. Thakur, R. Kumar, I. Kumar, U. Sharma, *Catal. Rev.* **2015**, *57*, 345–405.
[2] J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740–4761.
[3] Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, *Org. Chem. Front.* **2015**, *2*, 1107–1295.
[4] T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169.
[5] J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960–9009.
[6] R. Shang, Q. Xu, Y.-Y. Jiang, Y. Wang, L. Liu, *Org. Lett.* **2010**, *12*, 1000–1003.
[7] J. Lindh, P. J. R. Sjöberg, M. Larhed, *Angew. Chem. Int. Ed.* **2010**, *49*, 7733–7737.
[8] M. Nilsson, *Acta Chem Scand* **1966**, *20*, 423–426.
[9] D. Tanaka, S. P. Romeril, A. G. Myers, *J. Am. Chem. Soc.* **2005**, *127*, 10323–10333.
[10] A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250–11251.
[11] D. Tanaka, A. G. Myers, *Org. Lett.* **2004**, *6*, 433–436.
[12] L. J. Gooßen, G. Deng, L. M. Levy, *Science* **2006**, *313*, 662.
[13] L. J. Goossen, B. Melzer, *J. Org. Chem.* **2007**, *72*, 7473–7476.
[14] L. J. Goossen, N. Rodríguez, C. Linder, *J. Am. Chem. Soc.* **2008**, *130*, 15248–15249.
[15] K. Xie, Z. Yang, X. Zhou, X. Li, S. Wang, Z. Tan, X. An, C.-C. Guo, *Org. Lett.* **2010**, *12*, 1564–1567.
[16] J. Zhou, P. Hu, M. Zhang, S. Huang, M. Wang, W. Su, *Chem. – Eur. J.* **2010**, *16*, 5876–5881.
[17] J. Singh, M. Gurney, A. Burgin, A. Kiselyov, M. Rao, T. Hagen, *Biaryl Pde4 Inhibitors for Treating Pulmonary and Cardiovascular Disorders*, **2009**, WO2009067621A1.
[18] W. Lumeras, F. Caturla, L. Vidal, C. Esteve, C. Balagué, A. Orellana, M. Domínguez, R. Roca, J. M. Huerta, N. Godessart, B. Vidal, *J. Med. Chem.* **2009**, *52*, 5531–5545.
[19] A. L. Walker, *3-Aminocarbonyl, 6-Phenyl Substituted Pyridine-1-Oxides as P38 Kinase Inhibitors*, **2010**, US7838540B2.
[20] M. R. Player, N. Baindur, B. Brandt, N. Chadha, R. J. Patch, D. Asgari, T. Georgiadis, *Inhibitors of C-FMS Kinase*, **2005**, US2005113566 (A1).
[21] J. P. Snyder, D. C. Liotta, H. Venkatesan, M. Wang, M. C. Davis, *Nonpeptide Agonists and Antagonists of Vasopressin Receptors*, **2002**, US2002128208 (A1).
[22] T. C. Fleischer, D. M. Cimbora, J. S. Flick, A. D. Gassman, V. R. Baichwal, D. I. Papac, *Therapeutic and Diagnostic Methods*, **2014**, US8912184 (B1).
[23] A. Albini, *Heterocyclic N-Oxides*, CRC Press, **1991**.
[24] A. Albini, *Synthesis* **1993**, *1993*, 263–277.
[25] B.-J. Li, S.-D. Yang, Z.-J. Shi, *Synlett* **2008**, *2008*, 949–957.
[26] L.-C. Campeau, S. Rousseaux, K. Fagnou, *J. Am. Chem. Soc.* **2005**, *127*, 18020–18021.
[27] Z. Shi, B. Li, X. Wan, J. Cheng, Z. Fang, B. Cao, C. Qin, Y. Wang, *Angew. Chem.* **2007**, *119*, 5650–5654.
[28] D. Li, N. Xu, Y. Zhang, L. Wang, *Chem. Commun.* **2014**, *50*, 14862–14865.
[29] M. Dabiri, S. I. Alavioon, S. K. Movahed, *ChemistrySelect* **2018**, *3*, 3487–3494.
[30] M. Dabiri, N. F. Lehi, S. K. Movahed, H. R. Khavasi, *Org. Biomol. Chem.* **2017**, *15*, 6264–6268.
[31] M. Dabiri, P. Salehi, M. Bahramnejad, F. Sherafat, *J. Comb. Chem.* **2010**, *12*, 638–642.
[32] M. Dabiri, S. C. Azimi, H. Arvin-Nezhad, A. Bazgir, *Heterocycles* **2008**, *75*, 87–94.
[33] M. Dabiri, P. Salehi, M. S. Khajavi, A. Mohammadi, *Heterocycles* **2004**, *63*, 1417–1421.
[34] M. Dabiri, P. Salehi, M. Baghbanzadeh, M. S. Nikcheh, *Tetrahedron Lett.* **2008**, *49*, 5366–5368.
[35] Z. N. Tisseh, F. Ahmadi, M. Dabiri, H. R. Khavasi, A. Bazgir, *Tetrahedron Lett.* **2012**, *53*, 3603–3606.
[36] J. Cornella, P. Lu, I. Larrosa, *Org. Lett.* **2009**, *11*, 5506–5509.
[37] H. Li, P. Li, Q. Zhao, L. Wang, *Chem. Commun.* **2013**, *49*, 9170–9172.
[38] W.-M. Zhao, X.-L. Chen, J.-W. Yuan, L.-B. Qu, L.-K. Duan, Y.-F. Zhao, *Chem. Commun.* **2014**, *50*, 2018–2020.
[39] S. Duric, C. C. Tzschucke, *Org. Lett.* **2011**, *13*, 2310–2313.
[40] T. Xiong, Y. Li, Y. Lv, Q. Zhang, *Chem. Commun.* **2010**, *46*, 6831–6833.
[41] M. Li, X. Li, H. Chang, W. Gao, W. Wei, *Org. Biomol. Chem.* **2016**, *14*, 2421–2426.
[42] D. E. Butler, P. Bass, I. C. Nordin, F. P. Hauck, Y. J. L'Italien, *J. Med. Chem.* **1971**, *14*, 575–579.
[43] S. P. Zucker, F. Wossidlo, M. Weber, D. Lentz, C. C. Tzschucke, *J. Org. Chem.* **2017**, *82*, 5616–5635.
[44] E. Kianmehr, A. Tanbakouchian, *Tetrahedron* **2017**, *73*, 5337–5343.
[45] H. Xu, M. Shang, H.-X. Dai, J.-Q. Yu, *Org. Lett.* **2015**, *17*, 3830–3833.
[46] R. Haridharan, K. Muralirajan, C.-H. Cheng, *Adv. Synth. Catal.* **2015**, *357*, 366–370.

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Layout 1:

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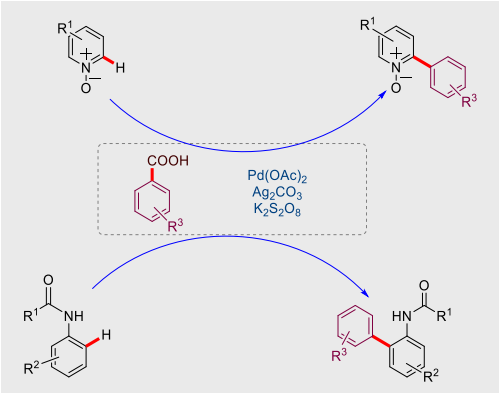
A novel method for palladium-catalyzed decarboxylative *ortho* C-H bond arylation of pyridine 1-oxides and anilides with benzoic acids as aryl sources are described.



Decarboxylative arylation

*Seyed Iman Alavioon, Siyavash Kazemi Movahed and Minoo Dabiri**

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Decarboxylative Arylation of Pyridine 1-Oxides and Anilides with Benzoic Acid *via* Palladium-Catalyzed C-H Functionalization

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