ORGANOMETALLICS

Article

pubs.acs.org/Organometallics

Palladium(II)-Catalyzed Direct Ortho Arylation of 4-Methyl-*N*-phenylpyridin-2-amines via C−H Activation/C−C Coupling and Synthetic Applications

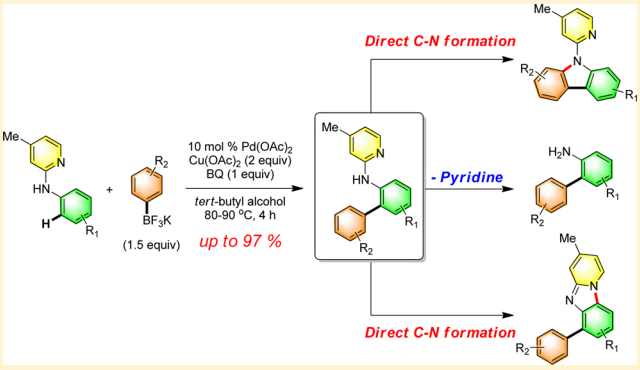
Jean-Ho Chu,*[,†] Hao-Ping Huang,[†] Wen-Ting Hsu,[†] Shih-Tien Chen,[†] and Ming-Jung Wu*[,†,‡]

[†]Department of Chemistry, National Sun Yat-sen University, Kaohsiung, Taiwan 804

[‡]Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, Taiwan 807

Supporting Information

ABSTRACT: The direct ortho arylation of 4-methyl-*N*-phenylpyridin-2-amines via palladium(II)-catalyzed C−H activation is described. Treatment of 4-methyl-*N*-phenylpyridin-2-amine with potassium aryltrifluoroborate using 10 mol % of palladium(II) acetate as the catalyst, 2 equiv of copper(II) acetate as the oxidant, and 1 equiv of *p*-benzoquinone in *tert*-butyl alcohol gave ortho-arylated products in modest to excellent yields. This reaction shows good functional group compatibility. A series of ^{1}H NMR titration experiments and controlled experiments elucidating the reaction mechanism were carried out. The key intermediate, 4-methyl-*N*-phenylpyridin-2-amine palladacycle, was isolated and characterized by X-ray crystallography. The advanced transformations of ortho-phenylated 4-methyl-*N*-phenylpyridin-2-amine to *N*-(4-methylpyridin-2-yl)-9*H*-carbazole, biphenyl-2-amine, and 3-methyl-6-phenylpyrido[1,2-*a*]benzimidazole were successfully demonstrated as potential synthetic applications.



INTRODUCTION

The utility of transition metals to catalyze direct C−H activation and functionalization has received great attention and has been increasingly explored in the past decade.[1] It has been widely recognized as an efficient strategy, both in synthetic steps and atom-economy aspects, for the construction of various organic molecules. To date, many practical syntheses based on the idea have been reported.[2,3] Especially in the case of biaryl, it is an important scaffold found in natural products,[4] pharmaceuticals,[5] and optoelectronic materials.[6] Therefore, the development of simpler and more efficient protocols regarding the synthesis of biaryl is still highly desirable. Transition-metal-catalyzed C−H activation and subsequent C−C coupling has been recognized as a powerful method to synthesize various biaryls, and the regioselectivity (e.g., ortho C−H arylation) can be efficiently controlled by the directing group.

In 2006, Yu and co-workers successfully demonstrated a pioneering work on the direct ortho alkylation of 2-oxazolines and 2-aryl(and/or alkyl)pyridines by the employment of the directing group to assist the transition-metal-catalyzed C−H activation and C−C coupling.[7] To date, they have already developed numerous efficient synthetic methods to obtain versatile organic molecules on the basis of this synthetic strategy. However, the direct arylation of secondary *N*-arylamines via C−H activation has still rarely been studied in the literature,[3b,8] especially at the ortho position of the aniline moiety.[3b,8e,f] In 2011, we applied the directing group (pyridinyl) methodology on *N*-phenylpyridin-2-amines via C−H activation to generate a variety of 9-(pyridin-2-yl)-9*H*-carbazoles. In those reactions, we also found the ortho-monoarylated *N*-phenylpyridin-2-amines as minor products.[3b] Meanwhile, Schnüch and co-workers reported the direct ortho arylation of *N*-phenylpyridin-2-amines using similar palladium-(II)-catalyzed C−H activation with arylboronic acids in 2012.[8f] In their work, a large amount of boronic acid (3 equiv) and a longer reaction time (24 h) are required.

To further improve these synthetic conditions[3b,8f] and most importantly to understand the electronic factors on the directing group governing the direct ortho arylation of *N*-phenylpyridin-2-amines via C−H activation, we carried out multiple experiments by the variation of electron-donating/-withdrawing substituents on the directing group. Furthermore, in order to illustrate the synthetic applications, transformations of ortho-phenylated 4-methyl-*N*-phenylpyridin-2-amine to *N*-(4-methylpyridin-2-yl)-9*H*-carbazole, biphenyl-2-amine, and 3-methyl-6-phenylpyrido[1,2-*a*]benzimi-dazole were demonstrated.

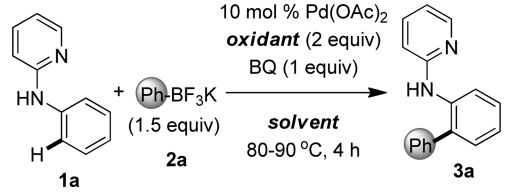
Received: December 10, 2013
Published: February 21, 2014

   dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

RESULTS AND DISCUSSION

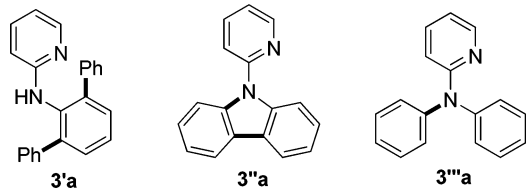
Screening of Oxidants and Solvents for the Direct Ortho Arylation of *N*-Phenylpyridin-2-amine and Reactivity Investigation of the Substituent Electronic Effect on the Directing Group. We commenced our studies with the direct ortho coupling of *N*-phenylpyridin-2-amine (**1a**) and potassium phenyltrifluoroborate (**2a**) to afford *N*-([1,1′-biphenyl]-2-yl)pyridin-2-amine (**3a**) in the presence of palladium(II) acetate. Various oxidants and solvents were screened, as shown in Table 1, for this reaction that was carried out at 80−90 °C for 4 h in the presence of *p*-benzoquinone (BQ).[3,9] Copper(II) acetate, silver(I) nitrate, and silver(I) acetate were found to be comparable oxidants, and *tert*-butyl alcohol was the best solvent for the reaction (see Table 1). Copper(II) acetate was eventually chosen as the best oxidant because of its lower cost and good starting substrate compatibility.[10] Trace amounts of the side products *N*-(pyridin-2-yl)-9*H*-carbazole (**3″a**) and *N*,*N*-diphenylpyridin-2-amine (**3‴a**) were isolated during these processes. After finalizing the optimized reaction conditions, we subsequently carried out the catalytic reaction of **1** with **2a** to study the reactivity changes influenced by the substituent electronic effect on the directing group (pyridinyl). These results are summarized in Table 2.

Table 1. Screening of Oxidants and Solvents for the Direct Ortho Phenylation of 1a



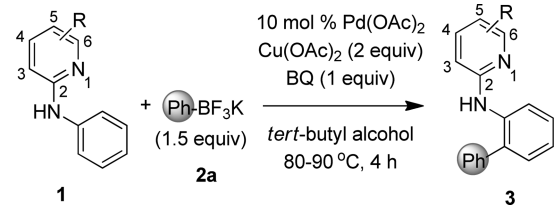
entry	oxidant	solvent	product ratio (**3a**:**3′a**:**3″a**:**3‴a**)[a]	total yield (%)[b]
1	none	*tert*-butyl alcohol	100:0:0:0	15 (10)[c]
2	$Cu(OAc)_2$	*tert*-butyl alcohol	**89:0:11:0**	**69 (57)**
3	$Cu(OTf)_2$	*tert*-butyl alcohol		0
4	$AgNO_3$	*tert*-butyl alcohol	**92:0:8:0**	**70 (65)**
5	AgOAc	*tert*-butyl alcohol	**94:0:6:0**	**68 (60)**
6	Ag_2CO_3	*tert*-butyl alcohol	100:0:0:0	50
7	Ag_2O	*tert*-butyl alcohol	59:0:0:41	13
8	$K_2S_2O_8$[11]	*tert*-butyl alcohol	100:0:0:0	53
9	oxone[11]	*tert*-butyl alcohol	100:0:0:0	52
10	$Cu(OAc)_2$	DMF	27:0:23:50	56
11	$Cu(OAc)_2$	acetonitrile	100:0:0:0	46
12	$Cu(OAc)_2$	THF	60:0:40:0	31
13	$Cu(OAc)_2$	1,2-dichloroethane	89:0:11:0	31
14	$Cu(OAc)_2$	1,4-dioxane	55:0:45:0	30
15	$Cu(OAc)_2$	dichloromethane	70:0:30:0	21
16	$Cu(OAc)_2$	benzene	100:0:0:0	15
17	$Cu(OAc)_2$	toluene	100:0:0:0	8

[a]The product ratio **3a**:**3′a**:**3″a**:**3‴a** was determined by GC-MS for three runs, where **3′a** = diphenylated *N*-phenylpyridin-2-amine, **3″a** = *N*-(pyridin-2-yl)-9*H*-carbazole, and **3‴a** = *N*,*N*-diphenylpyridin-2-amine.



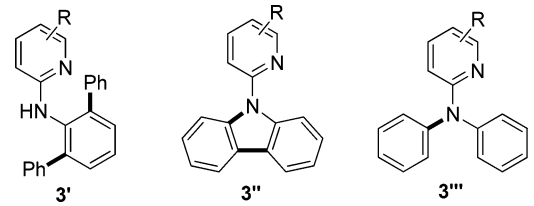
[b]The total yield was obtained as an average by GC-MS for three runs (using *n*-octadecane as the internal standard). [c]Values in parentheses are isolated yields.

Table 2. Reactivity Investigation of the Substituent Electronic Effect on the Directing Group (Pyridinyl) of 1



entry	substrate (R)	product ratio (**3**:**3′**:**3″**:**3‴**)[a]	total yield (%)[b]
1	H (**1a**)	89:0:11:0	69 (57)[c]
2	3-OMe (**1b**)	35:65:0:0	85
3	3-Me (**1c**)	40:60:0:0	80
4	3-NO_2 (**1d**)	75:0:25:0	55
5	4-OMe (**1e**)	**100:0:0:0**	**90 (82)**
6	4-Me (**1f**)	**100:0:0:0**	**87 (80)**
7	4-NO_2 (**1g**)	95:0:5:0	47 (37)
8	5-OMe (**1h**)	100:0:0:0	85 (80)
9	5-Me (**1i**)	100:0:0:0	75 (70)
10	5-NO_2 (**1j**)		0
11	6-OMe (**1k**)	100:0:0:0	20
12	6-Me (**1l**)	20:0:0:80	25
13	6-NO_2 (**1m**)		0

[a]The product ratio **3**:**3′**:**3″**:**3‴** was determined by GC-MS for three runs, where **3′** = diphenylated products, **3″** =*N*-(pyridin-2-yl)-9*H*-carbazoles, and **3‴** = *N*,*N*-diphenylpyridin-2-amines.

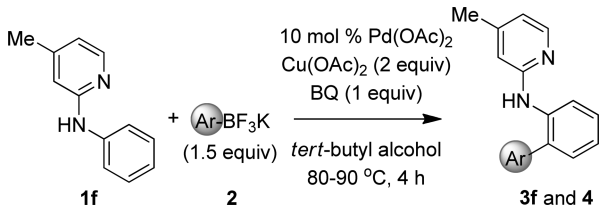


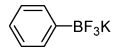
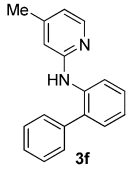
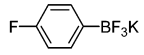
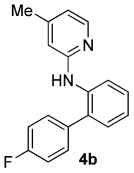
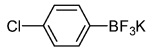
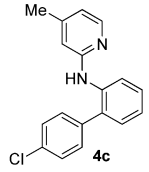
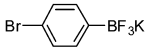
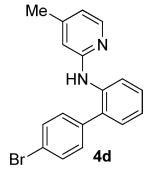
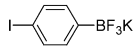
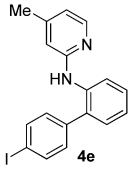
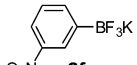
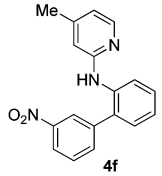
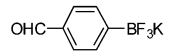
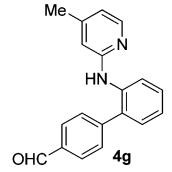
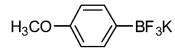
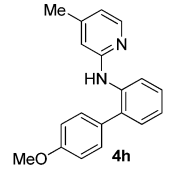
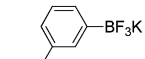
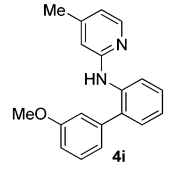
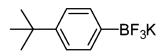
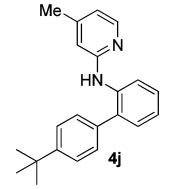
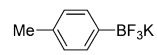
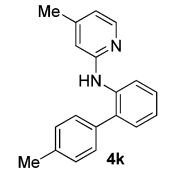
[b]The total yield was obtained as an average by GC-MS for three runs (using *n*-octadecane as the internal standard). [c]Values in parentheses are isolated yields.

In the case of **1a** (R = H) bearing a neutral substituent, only a 69% total yield of products **3a** and **3″a** was given, and the product ratio was determined by GC-MS to be 89:11 (entry 1, Table 2). When an electron-donating or -withdrawing group such as OMe, Me, or NO_2 was tagged on each position (3, 4, 5, and 6) of the pyridinyl group, a dramatic change in the reactivity was observed (vide infra). In the cases of **1b−d** (R = 3-OMe, 3-Me, 3-NO_2, entries 2−4, Table 2), a mixture of **3b,c** (monophenylated products) and **3′b,c** (diphenylated products) was generated in the following product ratios: **3b**:**3′b** = 35:65 (85% total yield) and **3c**:**3′c** = 40:60 (80% total yield), whereas **3d** and **3″d** (product ratio 75:25) were isolated in 55% total yield. Furthermore, the cases of **1e−g** (R = 4-OMe, 4-Me, 3-NO_2, entries 5−7, Table 2) showed that single products **3e,f** were generated in 90% and 87% yields, respectively, and only a 47% product yield of **3g** and **3″g** was obtained in the product ratio 95:5. Single products **3h,i** were isolated in 85% and 75%

dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

Table 3. Direct Ortho Arylation of 1f with 2



entry	Ar-BF_3K	product	total yield (%)[a]
1	 **2a**	 **3f**	87
2	 **2b**	 **4b**	83
3	 **2c**	 **4c**	85(77)[b]
4	 **2d**	 **4d**	81(75)[b]
5	 **2e**	 **4e**	37, 65[c]
6	 **2f**	 **4f**	56, 91[c]
7	 **2g**	 **4g**	59, 85[c]
8	 **2h**	 **4h**	43
9	 **2i**	 **4i**	85(75)[b]
10	 **2j**	 **4j**	76(70)[b]
11	 **2k**	 **4k**	79(70)[b]

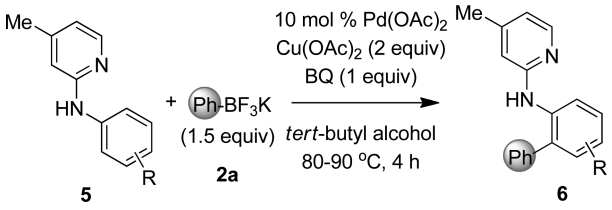
[a]The product yield was obtained as an average by GC-MS for three runs (using *n*-octadecane as the internal standard). [b]Values in parentheses are isolated yields. [c]The product yield after the comma was obtained by using $AgNO_3$ as the oxidant.

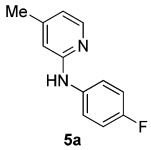
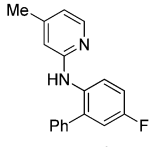
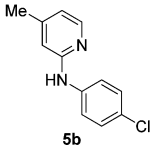
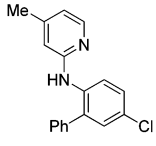
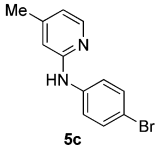
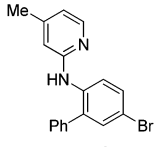
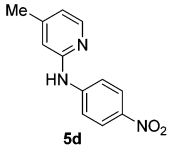
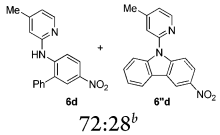
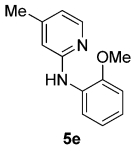
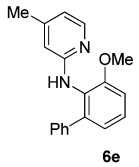
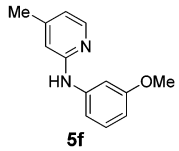
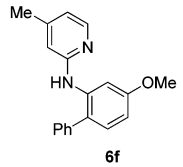
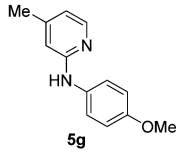
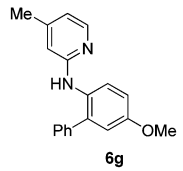
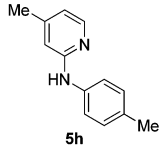
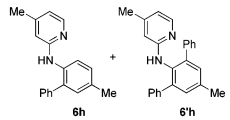
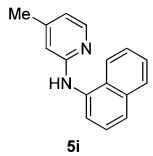
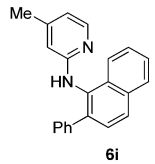
yields, respectively, in the cases of **1h,i** (R = 5-OMe, 5-Me, entries 8 and 9, Table 2), but none of the anticipated product **3j** was observed with only the recovery of the starting substrate in the case of **1j** (R = 5-NO_2, entry 10, Table 2). Finally, **1k−m** (R = 6-OMe, 6-Me, 6-NO_2, entries 11−13, Table 2) showed poor results in which only a 20% yield of single product **3k** was obtained and a mixture of **3l** and **3‴l** (product ratio 20:80) was generated in 25% total yield. None of the desired product **3m** was obtained, and we only recovered the starting substrate **1m**.

On the basis of these experimental results in Table 2, the electron-donating substituent (e.g., OMe or Me) on the pyridinyl group can obviously increase the reactivity while the electron-withdrawing substituent (e.g., NO_2) decreases it. This implies the electron-donating effect on the directing group might promote the binding affinity of the pyridinyl nitrogen with the palladium(II) ion and raise the probability of ortho C−H activation, and that eventually causes the efficient conversion of **1** to **3**. In the study, substitution at the 3-

dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

Table 4. Direct Ortho Phenylation of 5 with 2a



entry	substrate **5**	product	total yield (%)[a]
1	 **5a**	 **6a**	73
2	 **5b**	 **6b**	88(77)[c]
3	 **5c**	 **6c**	77(70)[c]
4	 **5d**	 **6d** **6"d** 72:28[b]	65
5	 **5e**	 **6e**	61(52)[c]
6	 **5f**	 **6f**	65(53)[c]
7	 **5g**	 **6g**	97(87)[c]
8	 **5h**	 **6h** **6'h** 80:20[b]	90(78)[c]
9	 **5i**	 **6i**	0

[a]The product yield was obtained as an average by GC-MS for three runs (using n-octadecane as the internal standard). [b]The product ratio was determined by GC-MS for three runs. [c]Values in parentheses are isolated yields.

position of the pyridinyl group (i.e., 3-OMe, 3-Me, and 3-NO_2) shows product yields similar to that with the 4-position; however, the product selectivity is not good while the diphenylated product (**3′b** and **3′c**) was formed as a major product with a minor monophenylated product (**3b** and **3c**). Regarding the diphenylation in these two cases, it might be due to the steric repulsion between the 3-MeO (or 3-Me) group and another ortho C−H bond[12] and eventually facilitates the second ortho C−H activation and phenylation. Additionally, MeO- and Me-substitution at the 5-position led to relatively lower product yields in comparison to that at the 4-position and this result might indicate that the electron-donating influence of MeO (or Me) substituted at the 5-position is slightly poorer than that at the 4-position in terms of the electron density of the pyridinyl nitrogen. For the formation of carbazole **3″d** in the reaction of **1d** with **2a**, it might result from the better binding affinity of the amine nitrogen with the palladium(II) ion,[13] which then facilitates the second C−H activation and C−N formation of **3d**. Finally, the MeO and/or Me substituent next to the nitrogen of pyridine (i.e., 6-position) is believed to offer steric hindrance and prohibit the binding of the pyridinyl nitrogen with the palladium(II) ion that results in the poor reactivity. Moreover, the electron-withdrawing effect of the 6-NO_2 substituent is still believed to play as a key factor for the reactivity in addition to the steric hindrance. In the reaction of **1l** with **2a**, *N*,*N*-diphenylpyridin-2-amine **3‴l** was generated as a predominant product that might be due to the C−N coupling of the amine group and borane reagent mediated or catalyzed by copper catalysts.[14]

Catalytic Reaction of 1f with 2. On the basis of the investigation of substituent electronic effects on the directing group, we chose 4-methyl-*N*-phenylpyridin-2-amine (**1f**) as the modeling substrate for the direct arylation.[15] With the optimized conditions in hand, we subsequently carried out

dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

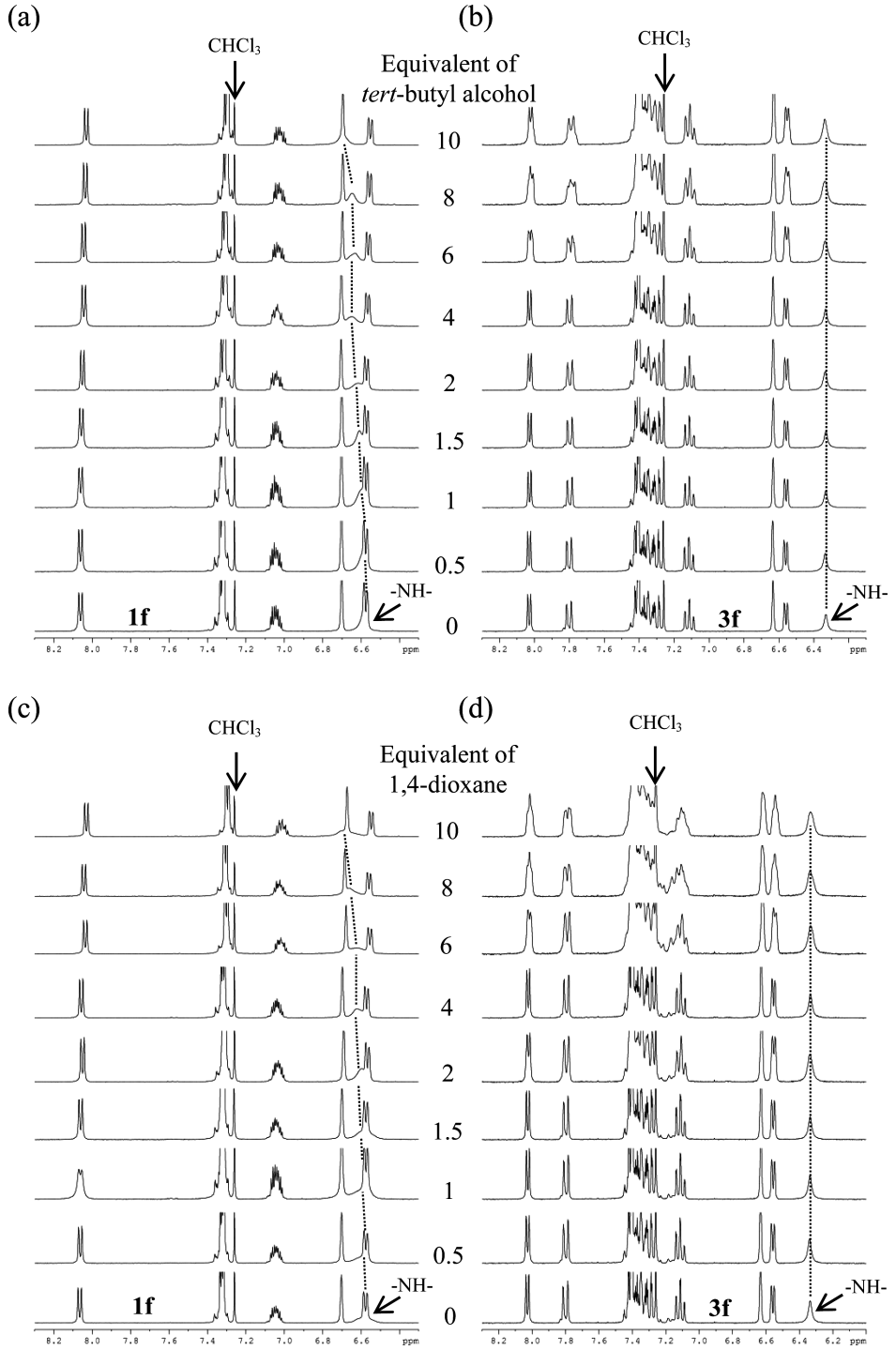
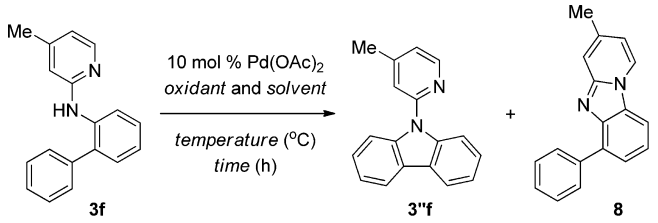


Figure 1. ^{1}H NMR titration experiments of (a) **1f** and (b) **3f** with *tert*-butyl alcohol and of (c) **1f** and (d) **3f** with 1,4-dioxane in *d*-chloroform. The concentrations of **1f** and **3f** are 2.2×10^{-2} and 1.5×10^{-2} M, respectively, and the amounts of *tert*-butyl alcohol or 1,4-dioxane are 0, 0.5, 1, 1.5, 2, 4, 6, 8, and 10 equiv (from bottom to top), respectively. Chloroform ($CHCl_3$) was employed as the internal standard.

the palladium(II)-catalyzed direct ortho arylation of **1f** with **2**. These experimental results are summarized in Table 3. According to these experimental results, the expected products **3f** and **4** were successfully synthesized in modest to excellent yields (37−91%). In these reactions, no obvious substituent electronic effect for the coupling partner **2** was observed and it gave anticipated products in similar yields for most cases. Concurrently, the reaction showed good functional group compatibility. Among this, we found that only a 37% yield of **4e** with the concomitant product **4‴e** (9% yield) was obtained in the case of **2e** (entry 5, Table 3). Furthermore, a 56% yield of **4f** and a 19% yield of **4‴f** were isolated from the reaction of **1f** with **2f** (entry 6, Table 3), and **4g** was obtained in modest yield (59%, entry 7, Table 3) under the optimized reaction conditions. Herein, the generation of **4‴e** and **4‴f** should be also due to copper(II) ion mediated or catalyzed intermolecular C−N coupling of the amine and borane reagents.[14b] Interestingly, the yields of **4e−g** can be improved to 65%,

dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

Table 5. Intramolecular C−N Cyclization of 3f via C−H Activation



3f 3″f 8

entry	oxidant	solvent	temp (°C)	time (h)	product (3″f:8)[a]	yield (%)[b]
1	AgOAc	1,4-dioxane	130−140	2	100:0	>99
2	AgOAc	*tert*-butyl alcohol	130−140	24	100:0	>99
3	$Cu(OAc)_2$	1,4-dioxane	130−140	24	100:0	>99
4	$Cu(OAc)_2$	*tert*-butyl alcohol	130−140	24	44:56	71
5	AgOAc	1,4-dioxane	80−90	2 (24)	100:0	15 (>99)
6	AgOAc	*tert*-butyl alcohol	80−90	24	100:0	21
7	$Cu(OAc)_2$	1,4-dioxane	80−90	24	100:0	50
8	$Cu(OAc)_2$	*tert*-butyl alcohol	80−90	24	20:80	14

[a]The product ratio was determined by GC-MS for three runs. [b]The product yield was obtained as an average by GC-MS for three runs (using *n*-octadecane as the internal standard).

91%, and 85%, respectively, by using $AgNO_3$ instead of $Cu(OAc)_2$ (entries 5−7, Table 3).

Next substrate **5**, the modified derivative of **1f**, was subjected to direct ortho phenylation. These experimental results are summarized in Table 4. The expected product **6** was obtained in modest to excellent yields (60−97%) by the reaction of **5** with **2a**, and none of the anticipated product **6i** was detected or isolated in the reaction of **5i** with **2a** (entry 9, Table 4). A minor product, *N*-(4-methylpyridin-2-yl)-3-nitro-9*H*-carbazole (**6″d**), was isolated in the reaction of **5d** with **2a**, and the product ratio of **6d** and **6″d** was determined to be 72:28 (entry 4, Table 4). A possible reason for the formation of **6″d** is that the nitro group of **6d** deactivates its aryl ring, and this promotes the palladium(II)-catalyzed intramolecular C−N coupling of the amine and another phenyl ring to generate carbazole **6″d**. Moreover, a mixture of **6h** and **6′h** (90% total yield) was isolated in the reaction of **5h** with **2a**, and the product ratio of **6h** and **6′h** was 80:20 (entry 8, Table 4). Regarding the formation of diphenylated product **6′h**, the para methyl group of **5h** might properly activate its aryl ring, and this resulted in the occurrence of double C−H activation and diphenylation. However, we did not detect or isolate the diphenylated product **6′g** from the reaction of **5g** (R = *p*-MeO) with **2a** (entry 7, Table 4).

^{1}H NMR Titration Experiments of 1f and 3f and Controlled Experiments for the Transformation of 3f to 3″f. In our previous work,[3b] *N*-(pyridin-2-yl)-9*H*-carbazole (**3″a**) was easily generated as a major product by the reaction of **1a** with **2a**, where AgOAc and 1,4-dioxane were used as the oxidant and solvent, respectively. However, some carbazole **3″a** (14% yield) was detected when the solvent (1,4-dioxane) was changed to *tert*-butyl alcohol, whereas monophenylated product **3a** (85% yield) remained as the predominant product. Similar results were also observed in the reaction of **1f** with **2a**, especially in the use of $Cu(OAc)_2$ and *tert*-butyl alcohol, which gave the single product **3f** in 87% yield. Therefore, we are interested in finding out why the reagent system of AgOAc and 1,4-dioxane favors production of a carbazole via a tandem C−H activation process, while $Cu(OAc)_2$ with *tert*-butyl alcohol preferentially leads to monoarylated products in this study. We first carried out these studies of solvent effects by ^{1}H NMR titration experiments of **1f** and **3f** with *tert*-butyl alcohol and 1,4-dioxane, respectively, as shown in Figure 1. According to the experimental analysis, we found that the amine proton of **1f** was gradually shifted downfield in the presence of an increasing amount of *tert*-butyl alcohol (6.58 to 6.70 ppm) and 1,4-dioxane (6.58 to 6.72 ppm), as shown in Figure 1a,c, but no obvious changes for chemical shifts of **3f** was observed when either *tert*-butyl alcohol or 1,4-dioxane was added, as shown in Figure 1b,d. On the basis of ^{1}H NMR titration studies, both *tert*-butyl alcohol and 1,4-dioxane are suggested to have a potential influence on the solution state of **1f**. Although no obvious chemical shift changes are observed in the ^{1}H NMR titration of **3f**, the possibility of steric hindrance for 1,4-dioxane and hydrogen bonding for *tert*-butyl alcohol in the solution state of **3f** are not completely excluded.

In addition to ^{1}H NMR titration, we also carried out studies of the influence of oxidants, solvents, and reaction temperatures on the palladium(II)-catalyzed C−H activation and intramolecular C−N formation of **3f**. These experimental results were summarized in Table 5. In this study, AgOAc and 1,4-dioxane again act as an excellent oxidant and solvent, respectively, for the transformation of **3f** to carbazole **3″f**. However, the use of $Cu(OAc)_2$ and *tert*-butyl alcohol will disfavor the reaction, while an additional compound, pyrido-[1,2-*a*]benzimidazole **8**, was generated (see Table 5). The product ratio of **3″f** and **8** was determined to be 44:55 (130−140 °C) and 20:80 (80−90 °C), respectively (entries 4 and 8, Table 5).[16b,c] Moreover, a higher reaction temperature (130−140 °C) was found to be critical for the conversion of **3f** to **3″f**, in which the consumption of **3f** can be completed within 2 h by using the reagent system of AgOAc and 1,4-dioxane (entry 1, Table 5). Finally, a longer reaction time (24 h) was required when the reaction temperature was reduced to 80−90 °C (entry 5, Table 5). On the basis of these controlled experiments, we suggested that the good affinity of the copper(II) oxidant and amine nitrogen[16a] might prevent the coordination of the palladium(II) ion with the amine nitrogen, eventually leading to the failure of the palladium(II)-catalyzed second C−H activation and C−N coupling of **3f**, especially in *tert*-butyl alcohol.

Preparation of 4-Methyl-*N*-phenylpyridin-2-amine Palladacycle. In order to isolate the key intermediate for the catalytic reaction,[17] we independently synthesized palladacycle **I** by the reaction of **1f** with a stoichiometric amount of $Pd(OAc)_2$ (the synthetic procedure is referenced from ref 3b) and the solid-state structure of **I** was secured by X-ray crystallography, which showed a head-to-tail U-shaped overall structure (Figure 2).[18] The coordinated orientation of **I** is found to be opposite to that of the *N*-phenylpyridin-2-amine palladacycle (a head-to-head U-shaped structure).[3b]

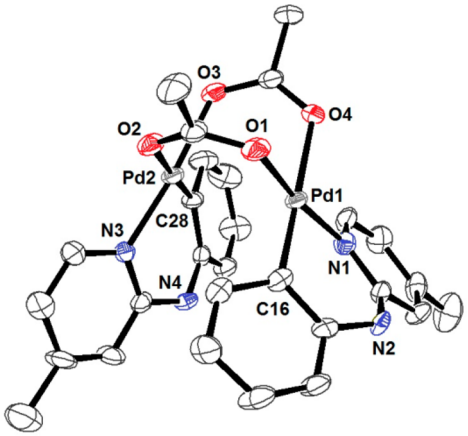


Figure 2. ORTEP drawing of 4-methyl-*N*-phenylpyridin-2-amine palladacycle (**I**).[18] Ellipsoids are shown at the 40% probability level. Selected bond lengths (Å): Pd1−Pd2 = 2.905(1); Pd1−N1 = 1.998(7); Pd1−C16 = 1.962(9); Pd1−O1 = 2.059(6); Pd1−O4 = 2.156(6); Pd2−N3 = 2.006(7); Pd2−C28 = 1.967(9); Pd2−O2 = 2.176(6); Pd2−O3 = 2.082(6). All hydrogen atoms are omitted for clarity.

Synthetic Applications. To demonstrate the potential of ortho-arylated 4-methyl-*N*-phenylpyridin-2-amines in synthetic applications, compound **3f** was selected as an example. The treatment of **3f** with a series of reaction conditions can easily give *N*-(4-methylmethylpyridin-2-yl)-9*H*-carbazole (**3″f**),[19a] biphenyl-2-amine (**7**),[19b] and 3-methyl-6-phenylbenzo[4,5]-imidazo-[1,2-*a*]pyridine (**8**)[19c] in 70−99% yields, respectively (Scheme 1). Interestingly, the acetoxylated product **9** was isolated and the product ratio of **8** and **9** was determined to be 77:23 by GC-MS using $PhI(OAc)_2$ as the reaction reagent at ambient temperature.

In contrast with the case of $PhI(OAc)_2$, only compound **8** was isolated in 75% yield by the use of $PhI(OTFA)_2$ (even when the reaction temperature was raised to 60 °C).

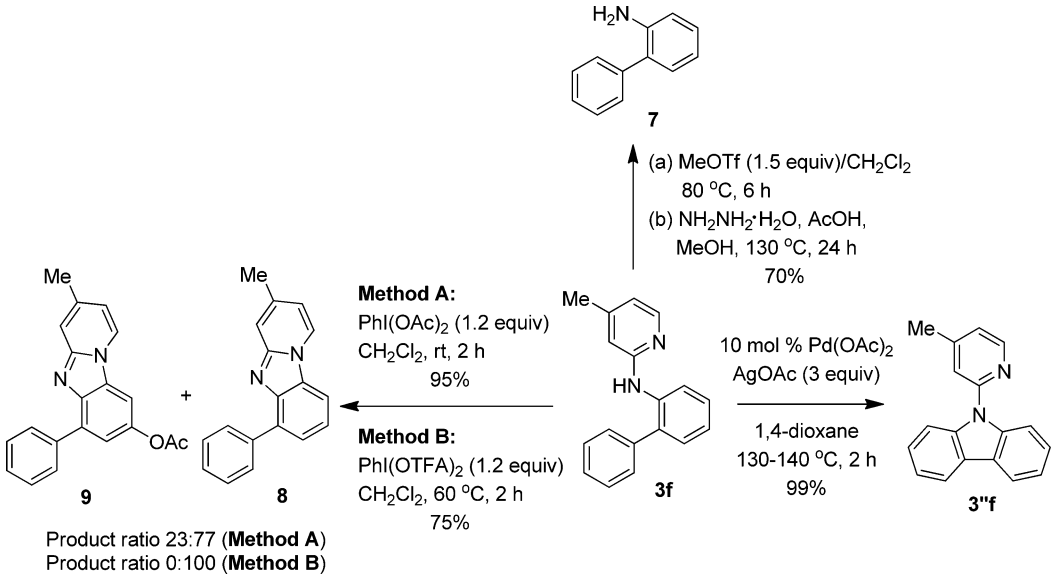
CONCLUSION

We have successfully developed a simple, practical, and efficient protocol for the synthesis of ortho-monoarylated 4-methyl-*N*-phenylpyridin-2-amines catalyzed by palladium(II) acetate via C−H activation. The substituent electronic effect on the directing group has been systematically investigated, and we found that the high reactivity is correlated to the electron-donating effect. The palladium(II)-catalyzed intramolecular C−N cyclization of ortho-monophenylated 4-methyl-*N*-phenylpyridin-2-amine via C−H activation to construct the carbazole skeleton has been investigated, and a possible explanation is presented. The key intermediate palladacycle has been isolated and characterized by X-ray crystallography. The synthetic application to approach the *N*-(4-methylpyridin-2-yl)-9*H*-carbazole, biphenyl-2-amine, and 3-methyl-6-phenylpyrido-[1,2-*a*]benzimidazole from ortho-monoarylated 4-methyl-*N*-phenylpyridin-2-amine is demonstrated. Finally, we believe that the developed methodology can be provided as a useful synthetic tool in the fields of pharmaceuticals and optoelectronic materials.

EXPERIMENTAL SECTION

General. Solvents and reagents were purchased from commercial suppliers and used without purification. ^1H NMR spectra were measured on 300 and 500 MHz NMR spectrometers. Natural-abundance ^{13}C NMR spectra were measured by using 300 and 500 MHz NMR spectrometers operating at 75 and 125 MHz, respectively. Chemical shifts are given in parts per million (ppm) and coupling constants *J* in hertz (Hz) for both nuclei, with the solvent (usually $CDCl_3$) peak as an internal standard. The reference peak for ^1H is δ 7.26 of chloroform, and for ^{13}C it is the central peak at δ 77.0. Low- and high-resolution mass spectrometry was obtained by the following

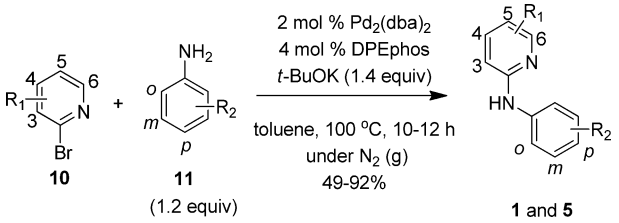
Scheme 1. Synthetic Applications of 3f



dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

ionization method and mass analyzer type: EI-magnetic sector. Melting points were measured by using open capillary tubes and uncorrected.

General Procedure for the Synthesis of Starting Substrates 1 and 5.[20]



A well-stirred solution of 2-bromopyridines **10** (1 equiv) and anilines **11** (1.2 equiv) in toluene (10 mL) was followed by the addition of potassium *tert*-butoxide (1.4 equiv). Subsequently, to the solution were added tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$) (0.02 equiv) and bis(2-diphenylphosphinophenyl)ether (DPEphos) (0.04 equiv) under nitrogen gas, and the mixture was heated to 100 °C for 10−12 h. After it was cooled to room temperature, the solution was washed with water (20 mL) and extracted with ethyl acetate (15 mL × 3). The organic layers were combined, dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by silica gel chromatography using *n*-hexane/ethyl acetate (40/1 to 20/1) as the eluent to give a series of compounds **1** and **5**. The amounts used of **10** and **11** are shown as follows. (a) For **10**: **10a** (R_1 = H), 474 mg, 3.00 mmol for **1a**; **10b** (R_1 = 3-OMe), 564 mg, 3.00 mmol for **1b**; **10c** (R_1 = 3-Me), 516 mg, 3.00 mmol for **1c**; **10d** (R_1 = 3-NO_2), 609 mg, 3.00 mmol for **1d**; **10e** (R_1 = 4-OMe), 564 mg, 3.00 mmol for **1e**; **10f** (R_1 = 4-Me), 516 mg, 3.00 mmol for **1f**; **10g** (R_1 = 4-NO_2), 609 mg, 3.00 mmol for **1g**; **10h** (R_1 = 5-OMe), 564 mg, 3.00 mmol for **1h**; **10i** (R_1 = 5-Me), 516 mg, 3.00 mmol for **1i**; **10j** (R_1 = 5-NO_2), 609 mg, 3.00 mmol for **1j**; **10k** (R_1 = 6-OMe), 564 mg, 3.00 mmol for **1k**; **10l** (R_1 = 6-Me), 516 mg, 3.00 mmol for **1l**; **10m** (R_1 = 6-NO_2), 609 mg, 3.00 mmol for **1m**. (b) For **11**: **11a** (R_2 = H), 335 mg, 3.60 mmol for **1a**−**m**; **11b** (R_2 = *p*-F), 400 mg, 3.6 mmol for **5a**; **11c** (R_2 = *p*-Cl), 459 mg, 3.60 mmol for **5b**; **11d** (R_2 = *p*-Br), 619 mg, 3.60 mmol for **5c**; **11e** (R_2 = *p*-NO_2), 497 mg, 3.60 mmol for **5d**; **11f** (R_2 = *o*-OMe), 443 mg, 3.60 mmol for **5e**; **11g** (R_2 = *m*-OMe), 443 mg, 3.60 mmol for **5f**; **11h** (R_2 = *p*-OMe), 443 mg, 3.60 mmol for **5g**; **11i** (R_2 = *p*-Me), 385 mg, 3.60 mmol for **5h**; **11j** (−C_6H_4-R_2 = 1-naphthyl), 515 mg, 3.60 mmol for **5i**.

All isolated product yields are shown as follows: **1a**, 75% (383 mg, 2.25 mmol); **1b**, 89% (534 mg, 2.67 mmol); **1c**, 80% (442 mg, 2.40 mmol); **1d**, 55% (355 mg, 1.65 mmol); **1e**, 84% (504 mg, 2.52 mmol); **1f**, 90% (497 mg, 2.70 mmol); **1g**, 49% (316 mg, 1.47 mmol); **1h**, 84% (504 mg, 2.52 mmol), **1i**, 91% (503 mg, 2.73 mmol); **1j**, 51% (329 mg, 1.53 mmol); **1k**, 89% (534 mg, 2.67 mmol); **1l**, 79% (437 mg, 2.37 mmol); **1m**, 52% (335 mg, 1.56 mmol); **5a**, 81% (491 mg, 2.43 mmol), **5b**, 77% (505 mg, 2.31 mmol); **5c**, 78% (615 mg, 2.34 mmol); **5d**, 42% (288 mg, 1.26 mmol); **5e**, 83% (533 mg, 2.49 mmol), **5f**, 80% (514 mg, 2.40 mmol); **5g**, 88% (565 mg, 2.64 mmol); **5h**, 92% (547 mg, 2.76 mmol); **5i**, 68% (478 mg, 2.04 mmol).

General Procedure for the Synthesis of Compound 3 (Reactivity Investigation on the Directing Group). A well-stirred solution of *N*-phenylpyridin-2-amines **1** (**1a**, 68 mg, 0.40 mmol; **1b**, 80 mg, 0.4 mmol; **1c**, 74 mg, 0.40 mmol; **1d**, 86 mg, 0.40 mmol; **1e**, 80 mg, 0.40 mmol; **1f**, 74 mg, 0.40 mmol; **1g**, 86 mg, 0.40 mmol; **1h**, 80 mg, 0.40 mmol; **1i**, 74 mg, 0.40 mmol; **1j**, 86 mg, 0.40 mmol; **1k**, 80 mg, 0.40 mmol; **1l**, 74 mg, 0.40 mmol; **1m**, 86 mg, 0.40 mmol) with potassium phenyltrifluoroborate (**2a**; 10 mg, 0.60 mmol), 10 mol % $Pd(OAc)_2$ (9 mg, 0.04 mmol), $Cu(OAc)_2$ (145 mg, 0.800 mmol), and BQ (43 mg, 0.40 mmol) in *tert*-butyl alcohol (7 mL) was heated to 80−90 °C and stirred at this temperature for 4 h. After it was cooled to room temperature, the solution was filtered through a pad of Celite and washed with water (15 mL). The solution was then extracted with ethyl acetate (10 mL × 2). Finally, the organic layers were combined, dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by silica gel chromatography using *n*-hexane/ethyl acetate (60/1 to 10/1) as the eluent to give a series of compounds **3**. All product yields were determined by GC-MS using *n*-octadecane as the internal standard and shown as follows: **3a**, 61% (62 mg, 0.25 mmol); **3″a**, 8% (9.7 mg, 0.030 mmol); **3b**, 30% (33 mg, 0.12 mmol), **3′b**, 55% (78 mg, 0.22 mmol); **3c**, 32% (34 mg, 0.13 mmol), **3′c**, 48% (64 mg, 0.19 mmol); **3d**, 41% (48 mg, 0.17 mmol); **3″d**, 14% (17 mg, 0.060 mmol); **3e**, 90% (99.5 mg, 0.360 mmol), **3f**, 87% (91 mg, 0.35 mmol); **3g**, 45% (52 mg, 0.18 mmol); **3″g**, 2% (2.6 mg, 0.010 mmol); **3h**, 85% (94 mg, 0.34 mmol), **3i**, 75% (78 mg, 0.30 mmol), **3j**, 0% (0 mg, 0 mmol); **3k**, 20% (22 mg, 0.080 mmol), **3l**, 5% (5.2 mg, 0.020 mmol); **3‴l**, 20% (21 mg, 0.080 mmol); **3m**, 0% (0 mg, 0 mmol).

General Procedure for the Synthesis of Compounds 4 and 6 by Direct Ortho Arylation of 1f and 5 with 2. The synthetic procedure for **4** and **6** is the same as that for **3**. (a) Reaction conditions for the synthesis of **4** are shown as follows: 4-methyl-*N*-phenylpyridin-2-amines **1f** (74 mg, 0.40 mmol), potassium aryltrifluoroborates **2** (**2b**, 24 mg, 0.12 mmol; **2c**, 26 mg, 0.12 mmol; **2d**, 32 mg, 0.12 mmol; **2e**, 37 mg, 0.12 mmol; **2f**, 28 mg, 0.12 mmol; **2g**, 25 mg, 0.12 mmol; **2h**, 26 mg, 0.12 mmol; **2i**, 26 mg, 0.12 mmol; **2j**, 29 mg, 0.12 mmol; **2k**, 24 mg, 0.12 mmol), 10 mol % $Pd(OAc)_2$ (9 mg, 0.04 mmol), $Cu(OAc)_2$ (145 mg, 0.800 mmol), BQ (43 mg, 0.40 mmol). All product yields were determined by GC-MS using *n*-octadecane as the internal standard and are shown as follows: **4b**, 83% (92 mg, 0.33 mmol); **4c**, 85% (100 mg, 0.34 mmol); **4d**, 81% (110 mg, 0.32 mmol); **4e**, 37% (58 mg, 0.15 mmol); **4‴e**, 9% (15 mg, 0.040 mmol); **4f**, 56% (67 mg, 0.22 mmol); **4‴f**, 19% (24 mg, 0.080 mmol); **4g**, 59% (69 mg, 0.24 mmol); **4h**, 43% (49 mg, 0.17 mmol); **4i**, 85% (20.0 mg, 0.069 mmol); **4j**, 76% (95 mg, 0.30 mmol), **4k**, 79% (88 mg, 0.32 mmol). (b) Reaction conditions for the synthesis of **6** are shown as follows: **5a**, 81 mg, 0.40 mmol; **5b**, 88 mg, 0.40 mmol; **5c**, 105 mg, 0.40 mmol; **5d**, 92 mg, 0.40 mmol; **5e**, 86 mg, 0.40 mmol; **5f**, 86 mg, 0.40 mmol; **5g**, 86 mg, 0.40 mmol; **5h**, 79 mg, 0.40 mmol; **5i**, 94 mg, 0.40 mmol; potassium phenyltrifluoroborate (**2a**), 110 mg, 0.60 mmol. All product yields were determined by GC-MS using *n*-octadecane as the internal standard and shown as follows: **6a**, 73% (81 mg, 0.29 mmol); **6b**, 88% (103 mg, 0.35 mmol); **6c**, 77% (105 mg, 0.310 mmol); **6d**: ,47% (58 mg, 0.19 mmol); **6″d**, 18% (21 mg, 0.070 mmol); **6e**, 61% (70 mg, 0.24 mmol); **6f**, 65% (76 mg, 0.26 mmol); **6g**, 97% (113 mg, 0.39 mmol); **6h**, 72% (80 mg, 0.29 mmol); **6′h**, 18% (25 mg, 0.070 mmol); **6i**, 0% (0 mg, 0 mmol).

Synthesis of Palladacycle I. To a well-stirred solution of **1f** (100 mg, 0.54 mmol) was added a stoichiometric amount of palladium(II) acetate (120 mg, 0.54 mmol) in dichloromethane (20 mL), and the mixture was then heated to 60−70 °C for 2 h. After the mixture was cooled to room temperature, the precipitate was collected and the filtrate was treated with a pad of Celite. The precipitate was dissolved in dichloromethane again and combined with the previous filtrate. The organic layer was dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by silica gel chromatography using *n*-hexane/ethyl acetate (5/1 to 100% ethyl acetate) as the eluent to give palladacycle **I** (169 mg, 0.240 mmol) in 90% isolated yield.

Synthesis of Compound 3″f. The synthetic procedure of **3″f** followed the literature report,[3b] and 99% yield (20 mg, 0.076 mmol) was obtained. Reagent conditions are as follows: **3f** (20 mg, 0.08 mmol), $Pd(OAc)_2$ (2 mg, 0.008 mmol), AgOAc (39 mg, 0.23 mmol), 1,4-dioxane (4 mL), water (5 mL), ethyl acetate (5 mL × 2), eluent (*n*-hexane/ethyl acetate 40/1).

Synthesis of Compound 7. A well-stirred solution of **3f** (30 mg, 0.1 mmol) and methyl trifluoromethanesulfonate (MeOTf) (28 mg, 0.17 mmol) in dichloromethane (4 mL) was heated to 80 °C for 6 h. After it was cooled to room temperature, the solution was evaporated under vacuum. The residue was then dissolved in a small amount of methanol (1 mL), followed by the addition of the mixed solution hydrazine/acetic acid (2.5 mL/0.7 mL). The solution was heated to 130 °C and stirred for 24 h. After it was cooled to room temperature, the solution was added to water (10 mL) and extracted with dichloromethane (5 mL × 2). The organic layers were combined, dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by silica gel chromatography using *n*-hexane/ethyl acetate

dx.doi.org/10.1021/om401195w | *Organometallics* 2014, 33, 1190−1204

(40/1) as the eluent to give **7** (14 mg, 0.081 mmol) in 70% isolated yield.

Synthesis of Compounds 8 and 9. A well-stirred solution of **3f** (20 mg, 0.08 mmol) and $PhI(OAc)_2$ (38 mg, 0.12 mmol) or $PhI(OTFA)_2$ (50 mg, 0.1 mmol) in dichloromethane (4 mL) was kept at room temperature or 60 °C for 2 h. After that, the solution was washed with water (10 mL) and the organic layer was dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by silica gel chromatography using *n*-hexane/ethyl acetate (5/1 to 1/2) as the eluent to give **8** (15 mg, 0.056 mmol) and **9** (5.3 mg, 0.017 mmol) in 95% total yield for the case of $PhI(OAc)_2$, whereas **8** (15 mg, 0.058 mmol) was obtained in 75% yield for the case of $PhI(OTFA)_2$.

Characterization Data of Compounds 1 and 3−9. *N-Phenylpyridin-2-amine (**1a**):* white solid; mp 105−106 °C; R_f = 0.45 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (bs, 1 H), 6.74 (dd, J = 7.0, 5.0 Hz, 1 H), 6.88 (d, J = 8.5 Hz, 1 H), 7.05−7.08 (m, 1 H), 7.32−7.36 (m, 4 H), 7.51 (ddd, J = 7.5, 7.5, 2.0 Hz, 1 H), 8.19 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.4 (CH), 115.0 (CH), 120.5 (CH × 2), 123.0 (CH), 129.3 (CH × 2), 138.0 (CH), 140.2 (Cq), 147.8 (CH), 155.8 (Cq); MS (EI, *m*/*z*) 170 (M^+, 26), 169 (M^+ − 1, 100).

*3-Methoxy-N-phenylpyridin-2-amine (**1b**):* pale yellow viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90 (s, 3 H), 6.69 (dd, J = 8.0, 5.0 Hz, 1 H), 6.95−6.99 (m, 2 H), 7.04 (bs,1 H), 7.32 (dd, J = 7.0, 7.0 Hz, 2 H), 7.70 (d, J = 8.5 Hz, 2 H), 7.83 (dd, J = 5.0, 1.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4 (CH_3), 113.9 (CH), 114.6 (CH), 118.8 (CH × 2), 121.5 (CH), 128.9 (CH × 2), 138.2 (CH), 140.5 (Cq), 142.3 (Cq), 146.5 (Cq); MS (EI, *m*/*z*) 200 (M^+, 100), 199 (M^+ − 1, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2O$ 200.0950, found 200.0953.

*3-Methyl-N-phenylpyridin-2-amine (**1c**):* colorless solid; mp 115−116 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.13 (bs, 1 H), 6.71 (dd, J = 7.5, 5.0 Hz, 1 H), 7.00 (dd, J = 7.5, 7.5 Hz, 1 H), 7.32 (dd, J = 8.5, 8.5 Hz, 2 H), 7.36 (dd, J = 7.5, 1.0 Hz, 1 H), 7.55 (d, J = 8.5 Hz, 2 H), 8.11 (d, J = 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.4 (CH_3), 115.3 (CH), 118.0 (Cq), 119.5 (CH × 2), 121.9 (CH), 128.9 (CH × 2), 137.9 (CH), 140.8 (Cq), 145.4 (CH), 153.9 (Cq); MS (EI, *m*/*z*) 184 (M^+, 54), 183 (M^+ − 1, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2$ 184.1000, found 184.0997.

*3-Nitro-N-phenylpyridin-2-amine (**1d**):* orange-red solid; mp 60−61 °C; R_f = 0.60 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (dd, J = 8.0, 4.5 Hz, 1 H), 7.19 (dd, J = 7.5, 7.5 Hz, 1 H), 7.40 (dd, J = 8.0, 8.0 Hz, 2 H), 7.65 (d, J = 8.0 Hz, 2 H), 8.49 (dd, J = 4.5, 1.5 Hz, 1 H), 8.53 (dd, J = 8.0, 1.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 113.9 (CH), 122.6 (CH × 2), 124.9 (CH), 129.0 (CH × 2), 135.5 (CH), 137.8 (Cq), 150.3 (Cq), 155.3 (Cq); MS (EI, *m*/*z*) 215 (M^+, 91), 214 (M^+ − 1, 100), 168 (86); HRMS (EI-magnetic sector) calcd for $C_{11}H_9N_3O_2$ 215.0695, found 215.0695.

*4-Methoxy-N-phenylpyridin-2-amine (**1e**):* colorless solid; mp 83−84 °C; R_f = 0.49 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.79 (s, 3 H), 6.35 (dd, J = 6.0, 2.0 Hz, 1 H), 6.39 (d, J = 2.0 Hz, 1 H), 6.62 (bs, 1 H), 7.06 (dd, J = 7.5, 7.5 Hz, 1 H), 7.29−7.35 (m, 4 H), 8.03 (d, J = 6.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.0 (CH_3), 92.4 (CH), 103.0 (CH), 120.7 (CH × 2), 123.0 (CH), 129.3 (CH × 2), 140.4 (Cq), 149.5 (CH), 157.7 (Cq), 167.3 (Cq); MS (EI, *m*/*z*) 200 (M^+, 58), 199 (M^+ − 1, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2O$ 200.0950, found 200.0953.

*4-Methyl-N-phenylpyridin-2-amine (**1f**):* colorless solid; mp 113−114 °C; R_f = 0.55 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (s, 3 H), 6.58 (d, J = 5.0 Hz, 1 H), 6.61 (bs, 1 H), 6.70 (s, 1 H), 7.04−7.07 (m, 1 H), 7.30−7.35 (m, 4 H), 8.05 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (CH_3), 108.5 (CH), 116.6 (CH), 120.5 (CH × 2), 122.8 (CH), 129.3 (CH × 2), 140.4 (Cq), 147.7 (CH), 149.1 (Cq), 156.0 (Cq); MS (EI, *m*/*z*) 184 (M^+, 34), 183 (M^+ − 1, 100), 88 (27), 70 (40), 61 (64); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2$ 184.1000, found 184.1002.

*4-Nitro-N-phenylpyridin-2-amine (**1g**):* orange solid; mp 105−106 °C; R_f = 0.43 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (bs, 1 H), 7.19 (dd, J = 7.5, 7.5 Hz, 1 H), 7.35−7.43 (m, 5 H), 7.49 (d, J = 1.0 Hz, 1 H), 8.41 (d, J = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 100.6 (CH), 107.0 (CH), 121.6 (CH × 2), 124.7 (CH), 129.7 (CH × 2), 138.7 (Cq), 150.8 (CH), 155.6 (Cq), 158.0 (Cq); MS (EI, *m*/*z*) 215 (M^+, 87), 214 (M^+ − 1, 100), 168 (51); HRMS (EI-magnetic sector) calcd for $C_{11}H_9N_3O_2$ 215.0695, found 215.0692.

*5-Methoxy-N-phenylpyridin-2-amine (**1h**):* pale yellow viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3 H), 6.47 (bs, 1 H), 6.89 (d, J = 9.0 Hz, 1 H), 6.99 (d, J = 7.5, 7.5 Hz, 1 H), 7.16 (dd, J = 9.0, 2.5 Hz, 1 H), 7.25−7.32 (m, 4 H), 7.92 (d, J = 3.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.2 (CH_3), 109.7 (CH), 118.9 (CH × 2), 121.9 (CH), 125.1 (CH), 129.3 (CH × 2), 133.6 (CH), 141.4 (Cq), 150.1 (Cq × 2); MS (EI, *m*/*z*) 200 (M^+, 97), 199 (M^+ − 1, 100), 88 (27), 70 (42), 61 (71); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2O$ 200.0950, found 200.0949.

*5-Methyl-N-phenylpyridin-2-amine (**1i**):* colorless solid; mp 101−102 °C; R_f = 0.60 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 6.48 (bs, 1 H), 6.84 (d, J = 9.0 Hz, 1 H), 7.01 (dddd, J = 8.5, 8.5, 1.5, 1.5 Hz, 1 H), 7.27−7.34 (m, 5 H), 8.04 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.5 (CH_3), 108.2 (CH), 119.6 (CH × 2), 122.3 (CH), 124.2 (Cq), 129.3 (CH × 2), 138.6 (CH), 140.9 (Cq), 148.0 (CH), 153.8 (Cq); MS (EI, *m*/*z*) 184 (M^+, 45), 183 (M^+ − 1, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2$ 184.1000, found 184.1001.

*5-Nitro-N-phenylpyridin-2-amine (**1j**):* yellow solid; mp 120−121 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, J = 9.0 Hz, 1 H), 7.24 (dd, J = 7.5, 7.5 Hz, 1 H), 7.37−7.45 (m, 5 H), 8.25 (dd, J = 9.5, 3.0 Hz, 1 H), 9.09 (d, J = 3.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 106.3 (CH), 122.6 (CH × 2), 125.7 (CH), 129.7 (CH × 2), 133.4 (CH), 137.1 (Cq), 137.9 (Cq), 146.7 (CH), 159.6 (Cq); MS (EI, *m*/*z*) 215 (M^+, 85), 214 (M^+ − 1, 100), 168 (44); HRMS (EI-magnetic sector) calcd for $C_{11}H_9N_3O_2$ 215.0695, found 215.0696.

*6-Methoxy-N-phenylpyridin-2-amine (**1k**):* pale yellow viscous liquid; R_f = 0.60 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.91 (s, 3 H), 6.20 (d, J = 8.0 Hz, 1 H), 6.38 (bs, 1 H), 6.39 (d, J = 8.0 Hz, 1 H), 7.02 (dd, J = 7.5 Hz, 1 H), 7.30−7.33 (m, 2 H), 7.36−7.42 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.4 (CH_3), 99.7 (CH), 100.1 (CH), 119.8 (CH × 2), 122.3 (CH), 129.1 (CH × 2), 140.1 (CH), 140.6 (Cq), 154.3 (Cq), 163.6 (Cq); MS (EI, *m*/*z*) 200 (M^+, 100), 199 (M^+ − 1, 100), 184 (34); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2O$ 200.0950, found 200.0949.

*6-Methyl-N-phenylpyridin-2-amine (**1l**):* pale yellow viscous liquid; R_f = 0.53 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.45 (s, 3 H), 6.61 (d, J = 7.5 Hz, 1 H), 6.65 (bs, 1 H), 6.73 (d, J = 8.0 Hz, 1 H), 7.04 (dddd, J = 7.5, 7.5, 1.5, 1.5 Hz, 1 H), 7.28−7.34 (m, 4 H), 7.40 (dd, J = 8.0, 8.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 104.8 (CH), 114.4 (CH), 120.3 (CH × 2), 122.8 (CH), 129.3 (CH × 2), 138.2 (CH), 140.5 (Cq), 155.3 (Cq), 157.1 (Cq); MS (EI, *m*/*z*) 184 (M^+, 100), 183 (M^+ − 1, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{12}N_2$ 184.1000, found 184.1002

*6-Nitro-N-phenylpyridin-2-amine (**1m**):* orange solid; mp 83−84 °C; R_f = 0.45 (*n*-hexane/ethyl acetate 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (bs, 1 H), 7.13 (d, J = 8.0 Hz, 1 H), 7.15−7.19 (m, 1 H), 7.38−7.42 (m, 4 H), 7.62 (d, J = 8.0 Hz, 1 H), 7.36 (d, J = 8.0, 8.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 107.9 (CH), 113.3 (CH), 121.4 (CH × 2), 124.6 (CH), 129.6 (CH × 2), 138.7 (Cq), 140.5 (CH), 155.5 (Cq), 155.9 (Cq); MS (ESI+, *m*/*z*) 215 (M^+, 100), 169 (92), 77 (32); HRMS (EI-magnetic sector) calcd for $C_{11}H_9N_3O_2$ 215.0695, found 215.0696.

*N-([1,1′-Biphenyl]-2-yl)pyridin-2-amine (**3a**):* See ref 3b.

*9-(Pyridin-2-yl)-9H-carbazole (**3″a**):* See ref 3b.

*N,N-Diphenylpyridin-2-amine (**3‴a**):* white solid; mp 89−90 °C; R_f = 0.54 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73−6.79 (m, 2 H), 7.10−7.19 (m, 6 H), 7.29−7.34 (m, 4 H), 7.44 (dd, J = 7.7, 7.7 Hz, 1 H), 8.23 (d, J = 7.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 113.8 (CH), 116.1 (CH), 124.5 (CH × 2), 126.3 (CH × 4), 129.3 (CH × 4), 137.3 (CH), 146.1 (Cq), 148.3 (CH),

159.0 (Cq); MS (EI, *m*/*z*) 246 (M^+, 16), 245 ($M^+ - 1$, 100); HRMS (EI-magnetic sector) calcd for $C_{17}H_{14}N_2$ 246.1157, found 246.1158.

*N-([1,1′-Biphenyl]-2-yl)-3-methoxypyridin-2-amine (**3b**):* colorless solid; mp 59−60 °C; R_f = 0.60 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3 H), 6.67 (dd, *J* = 7.5, 5.0 Hz, 1 H), 6.88 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.04 (ddd, *J* = 7.5, 7.5, 0.5 Hz, 1 H), 7.24 (dd, *J* = 8.3, 1.5 Hz, 1 H), 7.36−7.40 (m, 2 H), 7.45−7.46 (m, 4 H), 7.83 (dd, *J* = 5.0, 1.0 Hz, 1 H), 8.64 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4 (CH_3), 113.9 (CH), 114.7 (CH), 119.2 (CH), 121.4 (CH), 127.4 (CH), 128.3 (CH), 128.7 (CH × 2), 129.5 (CH × 2), 130.0 (CH), 131.3 (Cq), 137.6 (Cq), 138.3 (CH), 139.1 (Cq), 142.7 (Cq), 146.7 (Cq); MS (EI, *m*/*z*) 276 (M^+, 100), 275 ($M^+ - 1$, 57), 199 (30); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1260.

*N-([1,1′:3′,1″-Terphenyl]-2′-yl)-3-methoxypyridin-2-amine (**3′b**):* colorless solid; mp 87−88 °C; R_f = 0.53 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 (s, 3 H), 6.21 (bs, 1 H), 6.35 (dd, *J* = 7.8, 5.5 Hz, 1 H), 6.64 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.16−7.25 (m, 6 H), 7.33−7.43 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2 (CH_3), 113.0 (CH), 114.4 (CH), 125.9 (CH), 126.6 (CH × 2), 127.7 (CH × 4), 128.8 (CH × 4), 130.1 (CH × 2), 134.4 (Cq), 138.6 (CH), 139.6 (Cq × 2), 140.5 (Cq × 2), 142.4 (Cq), 148.0 (Cq); MS (EI, *m*/*z*) 352 (M^+, 49), 275 (100); HRMS (EI-magnetic sector) calcd for $C_{24}H_{20}N_2O$ 352.1576, found 352.1573.

*N-([1,1′-Biphenyl]-2-yl)-3-methylpyridin-2-amine (**3c**):* pale yellow viscous liquid; R_f = 0.60 (*n*-hexane/ethyl acetate 12/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.85 (s, 3 H), 6.31 (bs, 1 H), 6.67 (dd, *J* = 7.0, 5.0 Hz, 1 H), 7.05 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.24−7.27 (m, 2 H), 7.36−7.40 (m, 2 H), 7.44−7.48 (m, 4 H), 8.11 (d, *J* = 5.0 Hz, 1 H), 8.42 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.9 (CH_3), 115.1 (CH), 118.4 (Cq), 119.6 (CH), 121.6 (CH), 127.6 (CH), 128.3 (CH), 128.9 (CH × 2), 129.4 (CH × 2), 129.9 (CH), 131.5 (Cq), 137.6 (CH), 137.9 (Cq), 139.0 (Cq), 145.3 (CH), 153.9 (Cq); MS (EI, *m*/*z*) 260 (M^+, 31), 259 ($M^+ - 1$, 47), 85 (90), 71 (100), 57 (95); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1312.

*N-([1,1′-Biphenyl]-2-yl)-3-methylpyridin-2-amine (**3′c**):* white solid; mp 71−72 °C; R_f = 0.55 (*n*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (s, 3 H), 5.52 (bs, 1 H), 6.39 (dd, *J* = 7.0, 5.0 Hz, 1 H), 7.02 (d, *J* = 7.0 Hz, 1 H), 7.17−7.26 (m, 6 H), 7.32−7.41 (m, 7 H), 7.73 (d, *J* = 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.0 (CH_3), 114.3 (CH), 117.8 (Cq), 125.5 (CH), 126.7 (CH × 2), 127.9 (CH × 4), 128.8 (CH × 4), 130.1 (CH × 2), 135.2 (Cq), 136.8 (CH), 138.5 (Cq × 2), 140.5 (Cq × 2), 145.4 (CH), 154.8 (Cq); MS (EI, *m*/*z*) 336 (M^+, 17), 259 (100); HRMS (EI-magnetic sector) calcd for $C_{24}H_{20}N_2$ 336.1626, found 336.1629.

*N-([1,1′-Biphenyl]-2-yl)-3-nitropyridin-2-amine (**3d**):* orange-red solid; mp 61−62 °C; R_f = 0.58 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (dd, *J* = 8.0, 4.5 Hz, 1 H), 7.26 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.36−7.45 (m, 7 H), 8.16 (d, *J* = 8.0 Hz, 1 H), 8.42−8.44 (m, 2 H), 9.96 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 113.7 (CH), 123.8 (CH), 125.0 (CH), 127.9 (CH), 128.0 (CH), 128.8 (CH × 2), 129.1 (CH × 2), 130.5 (CH), 135.3 (Cq), 135.4 (CH), 135.5 (Cq), 138.5 (CH), 150.3 (Cq), 155.1 (CH); MS (EI, *m*/*z*) 291 (M^+, 100), 290 ($M^+ - 1$, 56), 244 (44), 214 (38); HRMS (EI-magnetic sector) calcd for $C_{17}H_{13}N_3O_2$ 291.1008, found 291.1006.

*9-(3-Nitropyridin-2-yl)-9H-carbazole (**3″d**):* yellow solid; mp 95−96 °C; R_f = 0.60 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.43 (m, 6 H), 7.58 (dd, *J* = 8.0, 4.5 Hz, 1 H), 8.11 (d, *J* = 7.5 Hz, 2 H), 8.54 (dd, *J* = 8.0, 1.5 Hz, 1 H), 8.94 (dd, *J* = 4.5, 1.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.9 (CH × 2), 120.6 (CH × 2), 121.8 (CH × 2), 122.4 (CH), 124.8 (Cq × 2), 126.5 (CH × 2), 135.1 (CH), 139.2 (Cq × 2), 144.2 (Cq), 153.2 (CH); MS (EI, *m*/*z*) 289 (M^+, 100), 258 (35), 242 (66); HRMS (EI-magnetic sector) calcd for $C_{17}H_{11}N_3O_2$ 289.0851, found 289.0851.

*N-([1,1′-Biphenyl]-2-yl)-4-methoxypyridin-2-amine (**3e**):* pale yellow viscous liquid; R_f = 0.53 (*n*-hexane/ethyl acetate 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3 H), 6.30 (s, 1 H), 6.32 (dd, *J* = 6.0, 2.0 Hz, 1 H), 6.55 (bs, 1 H), 7.14 (ddd, *J* = 8.0, 8.0, 1.0 Hz, 1 H), 7.31−7.36 (m, 3 H), 7.39−7.43 (m, 4 H), 7.71 (d, *J* = 8.0 Hz, 1 H), 7.97 (d, *J* = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1 (CH_3), 92.7 (CH), 103.1 (CH), 121.5 (CH), 123.4 (CH), 127.6 (CH), 128.3 (CH), 128.8 (CH × 2), 129.2 (CH × 2), 130.9 (CH), 133.9 (Cq), 137.3 (Cq), 138.8 (Cq), 149.1 (Cq), 157.7 (Cq), 167.3 (Cq); MS (EI, *m*/*z*) 276 (M^+, 92), 275 ($M^+ - 1$, 100), 260 (25), 199 (50); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1261.

*N-([1,1′-Biphenyl]-2-yl)-4-methylpyridin-2-amine (**3f**):* pale yellow viscous liquid; R_f = 0.44 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.34 (bs, 1 H), 6.56 (d, *J* = 5.1 Hz, 1 H), 6.32 (s, 1 H), 7.11 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1 H), 7.28−7.42 (m, 7 H), 7.80 (d, *J* = 8.4 Hz, 1 H), 8.03 (d, *J* = 5.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2 (CH_3), 109.0 (CH), 116.6 (CH), 120.8 (CH), 122.8 (CH), 127.5 (CH), 128.2 (CH), 128.8 (CH × 2), 129.3 (CH × 2), 130.8 (CH), 133.4 (Cq), 137.6 (Cq), 138.9 (Cq), 147.9 (CH), 148.8 (Cq), 156.1 (Cq); MS (EI, *m*/*z*) 260 (M^+, 100), 259 ($M^+ - 1$, 100), 244 (72), 183 (96); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2$, 260.1313 found 260.1315.

*9-(4-Methylpyridin-2-yl)-9H-carbazole (**3″f**):* pale yellow viscous liquid; R_f = 0.60 (*n*-hexane/ethyl acetate 7/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3 H), 7.13 (d, *J* = 5.0 Hz, 1 H), 7.31 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 2 H), 7.42−7.45 (m, 3 H), 7.81 (d, *J* = 8.0 Hz, 2 H), 8.11 (d, *J* = 8.0 Hz, 2 H), 8.58 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 111.1 (CH × 2), 119.7 (CH), 120.2 (CH × 2), 120.7 (CH × 2), 122.5 (CH), 124.2 (Cq × 2), 126.1 (CH × 2), 139.6 (Cq × 2), 149.2 (CH), 150.0 (Cq), 151.8 (Cq); MS (EI, *m*/*z*) 258 (M^+, 100), 257 ($M^+ - 1$, 57); HRMS (EI-magnetic sector) calcd for $C_{18}H_{14}N_2$ 258.1157, found 258.1154.

*N-([1,1′-Biphenyl]-2-yl)-4-nitropyridin-2-amine (**3g**):* orange solid; mp 81−82 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (bs, 1 H), 7.26 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.33−7.44 (m, 9 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 8.34 (d, *J* = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 100.8 (CH), 106.9 (CH), 122.3 (CH), 125.0 (CH), 127.8 (CH), 128.6 (CH), 128.9 (CH × 2), 129.1 (CH × 2), 131.1 (CH), 134.8 (Cq), 135.8 (Cq), 138.3 (Cq), 150.7 (CH), 155.4 (Cq), 157.9 (Cq); MS (EI, *m*/*z*) 291 (M^+, 100), 290 ($M^+ - 1$, 42), 244 (33); HRMS (EI-magnetic sector) calcd for $C_{17}H_{13}N_3O_2$ 291.1008, found 291.1010.

*9-(4-Nitropyridin-2-yl)-9H-carbazole (**3″g**):* yellow solid; mp 175−176 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 6/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 7.5, 7.5 Hz, 2 H), 7.49 (ddd, *J* = 8.0, 8.0, 1.0 Hz, 2 H), 7.94−7.97 (m, 3 H), 8.13 (d, *J* = 8.0 Hz, 2 H), 8.42 (d, *J* = 1.5 Hz, 1 H), 8.98 (d, *J* = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.9 (CH), 111.3 (CH × 2), 112.8 (CH), 120.4 (CH × 2), 122.2 (CH × 2), 125.0 (Cq × 2), 126.7 (CH × 2), 138.9 (Cq × 2), 151.6 (CH), 154.1 (Cq), 155.6 (Cq); MS (EI, *m*/*z*) 289 (M^+, 29), 177 (100), 161 (69); HRMS (EI-magnetic sector) calcd for $C_{17}H_{11}N_3O_2$ 289.0851, found 289.0852.

*N-([1,1′-Biphenyl]-2-yl)-5-methoxypyridin-2-amine (**3h**):* pale yellow viscous liquid; R_f = 0.43 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 3 H), 6.38 (bs, 1 H), 6.81 (d, *J* = 9.0 Hz, 1 H), 7.06 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.13 (dd, *J* = 9.0, 3.0 Hz, 1 H), 7.26−7.36 (m, 3 H), 7.40−7.44 (m, 4 H), 7.72 (d, *J* = 8.0 Hz, 1 H), 7.87 (d, *J* = 3.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.2 (CH_3), 110.2 (CH), 119.1 (CH), 122.1 (CH), 125.3 (CH), 127.5 (CH), 128.2 (CH), 128.8 (CH × 2), 129.3 (CH × 2), 130.7 (CH), 132.4 (Cq), 133.2 (Cq), 138.3 (CH), 138.9 (Cq), 150.0 (Cq), 150.1 (Cq); MS (EI, *m*/*z*) 276 (M^+, 100), 275 ($M^+ - 1$, 59), 199 (30); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1265.

*N-([1,1′-Biphenyl]-2-yl)-5-methylpyridin-2-amine (**3i**):* pale yellow viscous liquid; R_f = 0.53 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3 H), 6.31 (bs, 1 H), 6.78 (d, *J* = 8.0 Hz, 1H), 7.08 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.27−7.36 (m, 4 H), 7.39−7.43 (m, 4 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 8.00 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.5 (CH_3), 108.5 (CH), 119.8 (CH), 122.4 (CH), 124.2 (Cq), 127.5 (CH), 128.2 (CH), 128.8 (CH × 2), 129.3 (CH × 2), 130.7 (CH), 132.8 (Cq), 137.9 (Cq), 138.5 (CH), 138.9 (Cq), 148.1 (CH), 153.8 (Cq); MS (EI, *m*/*z*) 260 (M^+, 85), 259 ($M^+ - 1$, 100),

244 (28), 183 (66); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1313.

*N-([1,1′-Biphenyl]-2-yl)-6-methoxypyridin-2-amine (**3k**):* pale yellow viscous liquid; R_f = 0.53 (*n*-hexane/ethyl acetate 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 3 H), 6.18 (d, *J* = 8.0 Hz, 1 H), 6.27 (bs, 1 H), 6.30 (d, *J* = 8.0 Hz, 1 H), 7.09 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.27−7.46 (m, 8 H), 7.96 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.4 (CH_3), 100.0 (CH), 100.1 (CH), 120.8 (CH), 122.5 (CH), 127.6 (CH), 128.1 (CH), 128.9 (CH × 2), 129.4 (CH × 2), 130.6 (CH), 132.7 (Cq), 137.6 (Cq), 138.8 (Cq), 140.0 (CH), 154.5 (Cq), 163.5 (Cq); MS (EI, *m*/*z*) 276 (M^+, 100), 217 (38); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1261.

*N-([1,1′-Biphenyl]-2-yl)-6-methylpyridin-2-amine (**3l**):* pale yellow viscous liquid; R_f = 0.55 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 6.37 (bs, 1 H), 6.77 (d, *J* = 8.5 Hz, 1 H), 7.08 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.27−7.36 (m, 4 H), 7.39−7.43 (m, 4 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 7.99 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.5 (CH_3), 108.5 (CH), 119.9 (CH), 122.4 (CH), 124.1 (Cq), 127.5 (CH), 128.2 (CH), 128.8 (CH × 2), 129.3 (CH × 2), 130.7 (CH), 132.9 (Cq), 137.9 (Cq), 138.5 (CH), 138.8 (Cq), 147.9 (CH), 153.8 (Cq); MS (EI, *m*/*z*) 260 (M^+, 100), 259 ($M^+ - 1$, 100), 244 (43), 183 (89); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1316.

*6-Methyl-N,N-diphenylpyridin-2-amine (**3‴l**):* pale yellow viscous liquid; R_f = 0.60 (*n*-hexane/ethyl acetate 6/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.40 (s, 3 H), 6.52 (d, *J* = 8.0 Hz, 1 H), 6.68 (d, *J* = 7.5 Hz, 1 H), 7.10 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.17−7.19 (m, 4 H), 7.28−7.31 (m, 4 H), 7.35 (dd, *J* = 8.0, 8.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4 (CH_3), 111.4 (CH), 115.9 (CH), 123.9 (CH × 2), 125.9 (CH × 4), 129.1 (CH × 4), 137.5 (CH), 146.3 (Cq × 2), 157.2 (Cq), 158.5 (Cq); MS (EI, *m*/*z*) 260 (M^+, 45), 259 ($M^+ - 1$, 100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1312.

*N-(4′-Fluoro-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**4b**):* pale yellow viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 6.30 (bs, 1 H), 6.57−6.62 (m, 2 H), 7.08−7.14 (m, 3 H), 7.27 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.34−7.38 (m, 3 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 8.02 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.8 (CH), 115.8 (d, J_{C-F} = 21.0 Hz, CH × 2), 116.7 (CH), 121.2 (CH), 123.1 (CH), 128.4 (CH), 130.8 (CH), 131.0 (d, J_{C-F} = 8.3 Hz, CH × 2), 132.6 (Cq), 134.8 (d, J_{C-F} = 3.3 Hz, Cq), 137.5 (Cq), 147.8 (CH), 148.9 (Cq), 155.9 (Cq), 162.3 (d, J_{C-F} = 245.6 Hz, Cq); MS (EI, *m*/*z*) 278 (M^+, 71), 277 ($M^+ - 1$, 100), 262 (18), 183 (44); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}FN_2$ 278.1219, found 278.1222.

*N-(4′-Chloro-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**4c**):* pale yellow viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 6.31 (bs, 1 H), 6.57 (d, *J* = 5.0 Hz, 1 H), 6.60 (s, 1 H), 7.13 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.27 (dd, *J* = 9.0, 1.0 Hz, 1 H), 7.31−7.39 (m, 5 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 8.02 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.8 (CH), 116.7 (CH), 121.4 (CH), 123.2 (CH), 128.6 (CH), 129.0 (CH × 2), 130.6 (CH × 2), 132.4 (Cq), 133.6 (Cq), 137.3 (Cq), 137.5 (Cq), 147.8 (CH), 149.0 (Cq), 155.9 (Cq); MS (EI, *m*/*z*) 296 (M^+ + 2, 34), 294 (M^+, 100), 293 ($M^+ - 1$, 100), 278 (39), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}{}^{35}ClN_2$ 294.0924, found 294.0921.

*N-(4′-Bromo-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**4d**):* pale yellow viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.24 (bs, 1 H), 6.57 (d, *J* = 5.0 Hz, 1 H), 6.61 (s, 1 H), 7.12 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.26−7.28 (m, 3 H), 7.36 (ddd, *J* = 8.5, 8.5, 1.5 Hz, 1 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 8.02 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.8 (CH), 116.7 (CH), 121.3 (CH), 121.8 (Cq), 123.2 (CH), 128.6 (CH), 130.6 (CH), 131.0 (CH × 2), 132.0 (CH × 2), 132.3 (Cq), 137.5 (Cq), 137.8 (Cq), 148.0 (CH), 148.9 (Cq), 155.9 (Cq); MS (EI, *m*/*z*) 340 (M^+ + 2, 75), 338 (M^+, 76), 324 (28), 257 (29), 183 (96); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}{}^{79}BrN_2$ 338.0419, found 338.0422.

*N-(4′-Iodo-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**4e**):* pale yellow viscous liquid; R_f = 0.48 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.23 (bs, 1 H), 6.57 (d, *J* = 5.0 Hz, 1 H), 6.61 (s, 1 H), 7.11−7.15 (m, 3 H), 7.25−7.27 (m, 1 H), 7.36 (ddd, *J* = 7.6, 7.6, 1.5 Hz, 1 H), 7.73−7.77 (m, 3 H), 8.03 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 93.3 (Cq), 108.8 (CH), 116.8 (CH), 121.3 (CH), 123.2 (CH), 128.6 (CH), 130.5 (CH), 131.2 (CH × 2), 132.4 (Cq), 137.4 (Cq), 137.9 (CH × 2), 138.4 (Cq), 148.0 (CH), 148.9 (Cq), 155.9 (Cq); MS (EI, *m*/*z*) 386 (M^+, 88), 385 ($M^+ - 1$, 74), 370 (29), 258 (33), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}IN_2$ 386.0280, found 386.0277.

*N-(4-Iodophenyl)-4-methyl-N-phenylpyridin-2-amine (**4‴e**):* pale yellow viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate 6/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 6.58 (s, 1 H), 6.67 (d, *J* = 5.0 Hz, 1 H), 6.90 (d, *J* = 9.0 Hz, 2 H), 7.14−7.18 (m, 3 H), 7.32−7.35 (m, 2 H), 7.58 (d, *J* = 9.0 Hz, 2 H), 8.11 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 87.6 (Cq), 114.8 (CH), 118.3 (CH), 125.0 (CH), 126.5 (CH × 2), 127.5 (CH × 2), 129.6 (CH × 2), 138.2 (CH × 2), 145.6 (Cq), 146.0 (Cq), 147.7 (CH), 149.0 (Cq), 158.6 (Cq); MS (EI, *m*/*z*) 386 (M^+, 56), 385 (M^+ −1, 100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}N_2I$ 386.0280, found 386.0277.

*4-Methyl-N-(3′-nitro-[1,1′-biphenyl]-2-yl)pyridin-2-amine (**4f**):* yellow viscous liquid; R_f = 0.46 (*n*-hexane/ethyl acetate 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 6.35 (bs, 1 H), 6.57 (s, 2 H), 7.22 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.34 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.41 (ddd, *J* = 8.5, 8.5, 1.5 Hz, 1 H), 7.56 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.69 (d, *J* = 8.5 Hz, 1 H), 7.76 (d, *J* = 7.5 Hz, 1 H), 7.98 (d, *J* = 5.0 Hz, 1 H), 8.18 (d, *J* = 8.5 Hz, 1 H), 8.28 (dd, *J* = 3.5, 3.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.8 (CH), 116.9 (CH), 122.4 (CH), 122.6 (CH), 124.1 (CH), 124.2 (CH), 129.5 (CH), 129.6 (CH), 130.8 (CH), 132.1 (Cq), 135.4 (CH), 137.4 (Cq), 140.8 (Cq), 147.5 (CH), 148.6 (Cq), 149.3 (Cq), 155.7 (Cq); MS (EI, *m*/*z*) 305 (M^+, 93), 304 ($M^+ - 1$, 84), 257 (53), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}N_3O_2$ 305.1164, found 305.1167.

*4-Methyl-N-(3-nitrophenyl)-N-phenylpyridin-2-amine (**4‴f**):* yellow viscous liquid; R_f = 0.43 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 6.58 (s, 1 H), 6.75 (d, *J* = 5.0 Hz, 1 H), 7.18−7.26 (m, 3 H), 7.37−7.42 (m, 4 H), 7.86 (ddd, *J* = 7.5, 2.0, 2.0 Hz, 1 H), 7.97 (dd, *J* = 2.0, 2.0 Hz, 1 H), 8.13 (d, *J* = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 115.5 (CH), 117.8 (CH), 119.1 (CH), 119.2 (CH), 125.9 (CH), 127.1 (CH), 129.5 (CH), 130.1 (CH × 2), 130.2 (CH), 145.1 (Cq), 147.4 (Cq), 148.0 (CH), 148.9 (Cq), 149.2 (Cq), 158.4 (Cq); MS (EI, *m*/*z*) 305 (M^+, 51), 304 ($M^+ - 1$, 100), 258 (42), 88 (65), 70 (91), 61 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}N_3O_2$ 305.1164, found 305.1167.

*2′-((4-Methylpyridin-2-yl)amino)-[1,1′-biphenyl]-4-carbaldehyde (**4g**):* pale yellow viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate 3/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.31 (bs, 1 H), 6.57 (d, *J* = 5.0 Hz, 1 H), 6.60 (s, 1 H), 7.18 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.33 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.40 (ddd, *J* = 8.3, 8.3, 1.5 Hz, 1 H), 7.59 (d, *J* = 8.5 Hz, 2 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 7.92 (d, *J* = 8.5 Hz, 2 H), 8.01 (d, *J* = 5.0 Hz, 1 H), 10.03 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.8 (CH), 116.8 (CH), 121.9 (CH), 123.5 (CH), 129.2 (CH), 129.9 (CH × 2), 130.2 (CH × 2), 130.6 (CH), 132.6 (Cq), 135.3 (Cq), 137.4 (Cq), 145.4 (Cq), 147.9 (CH), 149.0 (Cq), 155.9 (Cq), 191.8 (CH); MS (EI, *m*/*z*) 288 (M^+, 29), 287 ($M^+ - 1$, 30), 88 (45), 70 (66), 61 (100); HRMS (EI-magnetic sector) calcd for $C_{19}H_{16}N_2O$ 288.1263, found 288.1260.

*N-(4′-Methoxy-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**4h**):* pale yellow viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 3.83 (s, 3 H), 6.57 (bs, 1 H), 6.14−6.71 (m, 2 H), 6.94 (d, *J* = 8.5 Hz, 2 H), 7.11 (d, *J* = 7.5, 7.5 Hz, 1 H), 7.28−7.33 (m, 4 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 8.01 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.3 (CH_3), 108.9 (CH), 114.2 (CH × 2), 116.5 (CH), 121.2 (CH), 123.1 (CH), 127.9 (CH), 130.4 (CH × 2), 130.8 (CH), 131.1 (Cq), 133.4 (Cq), 137.5 (Cq), 149.0 (Cq), 156.0 (Cq), 159.0 (Cq); MS (EI, *m*/*z*) 290

(M^+, 41), 289 ($M^+ - 1$, 39), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1419.

N-(3′-Methoxy-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine ***(4i):*** colorless solid; mp 57−58 °C; R_f = 0.44 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 3.78 (s, 3 H), 6.41 (bs, 1 H), 6.56 (d, J = 5.0 Hz, 1 H), 6.62 (s, 1 H), 6.88−6.92 (m, 2 H), 6.98 (d, J = 7.5 Hz, 1 H), 7.11 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H), 7.29−7.37 (m, 3 H), 7.81 (d, J = 8.5 Hz, 1 H), 8.03 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.2 (CH_3), 109.0 (CH), 113.3 (CH), 114.7 (CH), 116.6 (CH), 120.7 (CH), 121.6 (CH), 122.7 (CH), 128.3 (CH), 129.8 (CH), 130.6 (CH), 133.1 (Cq), 137.6 (Cq), 140.2 (Cq), 147.9 (CH), 148.8 (Cq), 156.0 (Cq), 159.9 (Cq); MS (EI, m/z) 290 (M^+, 64), 289 ($M^+ - 1$, 66), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1422.

N-(4′-(tert-Butyl)-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine ***(4j):*** pale yellow viscous liquid; R_f = 0.54 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 9 H), 2.24 (s, 3 H), 6.48 (bs, 1 H), 6.56 (d, J = 5.0 Hz, 1 H), 6.68 (s, 1 H), 7.10 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H), 7.29−7.34 (m, 4 H), 7.43 (d, J = 8.5 Hz, 2 H), 7.76 (d, J = 8.0 Hz, 1 H), 8.02 (d, J = 3.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 31.3 (CH_3), 34.6 (Cq), 109.0 (CH), 116.5 (CH), 120.5 (CH), 122.8 (CH), 125.8 (CH × 2), 128.0 (CH), 128.9 (CH × 2), 130.8 (CH), 133.2 (Cq), 135.7 (Cq), 137.6 (Cq), 147.8 (CH), 148.9 (Cq), 150.4 (Cq), 156.0 (Cq); MS (EI, m/z) 316 (M^+, 74), 315 ($M^+ - 1$, 65), 300 (43), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{22}H_{24}N_2$ 316.1939, found 316.1942.

4-Methyl-N-(4′-methyl-[1,1′-biphenyl]-2-yl)pyridin-2-amine ***(4k):*** pale yellow viscous liquid; R_f = 0.49 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 2.38 (s, 3 H), 6.44 (bs, 1 H), 6.55 (d, J = 5.0 Hz, 1 H), 6.64 (s, 1 H), 7.10 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H), 7.22 (d, J = 8.0 Hz, 2 H), 7.28−7.29 (m, 3 H), 7.33 (ddd, J = 8.3, 8.3, 1.5 Hz, 1 H), 7.78 (d, J = 8.0 Hz, 1 H), 8.02 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3 × 2), 108.9 (CH), 116.5 (CH), 120.7 (CH), 122.8 (CH), 128.0 (CH), 129.1 (CH × 2), 129.5 (CH × 2), 130.7 (CH), 133.3 (CH), 135.8 (Cq), 137.3 (Cq), 137.5 (Cq), 147.7 (Cq), 148.9 (Cq), 156.0 (Cq); MS (EI, m/z) 274 (M^+, 76), 273 ($M^+ - 1$, 100), 258 (29), 183 (40); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2$ 274.1470, found 274.1467.

N-(4-Fluorophenyl)-4-methylpyridin-2-amine ***(5a):*** colorless solid; mp 93−94 °C; R_f = 0.45 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3 H), 6.44 (bs, 1 H), 6.55 (s, 1 H), 6.57 (d, J = 5.0 Hz, 1 H), 7.03 (dd, J = 8.5, 8.5 Hz, 2 H), 7.28 (dd, J = 9.0, 4.5 Hz, 2 H), 8.04 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.1 (CH), 115.9 (d, J_{C-F} = 22.4 Hz, CH), 116.5 (CH), 122.9 (d, J_{C-F} = 8.3 Hz, CH), 136.5 (d, J_{C-F} = 2.8 Hz, Cq), 147.9 (CH), 148.9 (Cq), 156.5 (Cq), 158.9 (d, J_{C-F} = 240.5 Hz, Cq); MS (EI, m/z) 202 (M^+, 46), 201 ($M^+ - 1$, 100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{11}FN_2$ 202.0906, found 202.0909.

N-(4-Chlorophenyl)-4-methylpyridin-2-amine ***(5b):*** colorless solid; mp 97−98 °C; R_f = 0.56 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (s, 3 H), 6.56 (bs, 1 H), 6.60 (d, J = 5.0 Hz, 1 H), 6.62 (s, 1 H), 7.26−7.31 (m, 4 H), 8.07 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.9 (CH), 116.9 (CH), 121.3 (CH), 127.2 (Cq), 129.2 (CH), 139.3 (Cq), 148.0 (CH), 149.0 (Cq), 155.7 (Cq); MS (EI, m/z) 220 ($M^+ + 2$, 34), 218 (M^+, 100), 217 ($M^+ - 1$, 100), 182 (41), 91 (45), 80 (53), 65 (39); HRMS (EI-magnetic sector) calcd for $C_{12}H_{11}{}^{35}ClN_2$ 218.0611, found 218.0608.

N-(4-Bromophenyl)-4-methylpyridin-2-amine ***(5c):*** white solid; mp 103−104 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (s, 3 H), 6.50 (bs, 1 H), 6.61 (d, J = 5.0 Hz, 1 H), 6.63 (s, 1 H), 7.25 (d, J = 9.0 Hz, 2 H), 7.41 (d, J = 9.0 Hz, 2 H), 8.07 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 109.1 (CH), 114.6 (Cq), 117.0 (CH), 121.5 (CH × 2), 132.1 (CH × 2), 139.8 (Cq), 148.0 (CH), 149.0 (Cq), 155.6 (Cq); MS (EI, m/z) 264 ($M^+ + 2$, 53), 262 (M^+, 54), 183 (78); HRMS (EI-magnetic sector) calcd for $C_{12}H_{11}{}^{79}BrN_2$ 262.0106, found 262.0106.

4-Methyl-N-(4-nitrophenyl)pyridin-2-amine ***(5d):*** yellow solid; mp 133−134 °C; R_f = 0.40 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 6.73 (s, 1 H), 6.77 (d, J = 4.5 Hz, 1 H), 6.90 (bs, 1 H), 7.56 (d, J = 9.5 Hz, 2 H), 8.18−8.20 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 111.7 (CH), 116.6 (CH × 2), 118.8 (CH), 125.6 (CH × 2), 141.0 (Cq), 147.1 (Cq), 147.9 (CH), 149.4 (Cq), 153.8 (Cq); MS (EI, m/z) 229 (M^+, 64), 228 ($M^+ - 1$, 100), 182 (49); HRMS (EI-magnetic sector) calcd for $C_{12}H_{11}N_3O_2$ 229.0851, found 229.0850.

N-(2-Methoxyphenyl)-4-methylpyridin-2-amine ***(5e):*** pale yellow viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.67 (s, 3 H), 389 (s, 3 H), 6.58 (d, J = 5.0 Hz, 1 H), 6.69 (s, 1 H), 6.89−6.99 (m, 4 H), 8.02 (dd, J = 7.0, 2.5 Hz, 1 H), 8.10 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 55.6 (CH_3), 109.7 (CH), 110.3 (CH), 116.5 (CH), 118.2 (CH), 120.8 (CH), 121.3 (CH), 130.4 (Cq), 147.7 (CH), 148.5 (Cq), 148.6 (Cq), 155.8 (Cq); MS (EI, m/z) 214 (M^+, 24), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{13}H_{14}N_2O$ 214.1106, found 214.1107.

N-(3-Methoxyphenyl)-4-methylpyridin-2-amine ***(5f):*** pale yellow viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3 H), 3.80 (s, 3 H), 6.57−6.60 (m, 2 H), 6.74 (s, 1 H), 6.83 (bs, 1 H), 6.87 (dd, J = 3.0, 1.0 Hz, 1 H), 6.94 (s, 1 H), 7.22 (dd, J = 8.0, 8.0 Hz, 1 H), 8.07 (d, J = 4.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.2 (CH_3), 106.1 (CH), 107.8 (CH), 108.8 (CH), 112.6 (CH), 116.6 (CH), 129.9 (CH), 141.9 (Cq), 147.9 (CH), 148.8 (Cq), 156.0 (Cq), 160.5 (Cq); MS (EI, m/z) 214 (M^+, 56), 213 ($M^+ - 1$, 100), 184 (88), 183 (54); HRMS (EI-magnetic sector) calcd for $C_{13}H_{14}N_2O$ 214.1106, found 214.1103.

N-(4-Methoxyphenyl)-4-methylpyridin-2-amine ***(5g):*** colorless solid; mp 69−70 °C; R_f = 0.51 (*n*-hexane/ethyl acetate 3/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 3.81 (s, 3 H), 6.47 (bs, 1 H), 6.49 (s, 1 H), 6.51 (d, J = 5.0 Hz, 1 H), 6.90 (d, J = 7.5 Hz, 2 H), 7.22 (d, J = 7.5 Hz, 2 H), 8.01 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.5 (CH_3), 107.4 (CH), 114.6 (CH × 2), 115.8 (CH), 124.3 (CH × 2), 133.3 (Cq), 147.9 (CH), 148.8 (Cq), 156.2 (CH), 157.4 (Cq); MS (EI, m/z) 214 (M^+, 100), 199 (89), 184 (81), 88 (33), 70 (51), 61 (76); HRMS (EI-magnetic sector) calcd for $C_{13}H_{14}N_2O$ 214.1106, found 214.1107.

4-Methyl-N-(p-tolyl)pyridin-2-amine ***(5h):*** colorless solid; mp 113−114 °C; R_f = 0.51 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 2.33 (s, 3 H), 6.49 (bs, 1 H), 6.54 (d, J = 5.0 Hz, 1 H), 6.34 (s, 1 H), 7.14 (d, J = 8.5 Hz, 2 H), 7.19 (d, J = 8.5 Hz, 2 H), 8.04 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8 (CH_3), 21.2 (CH_3), 107.9 (CH), 116.2 (CH), 121.3 (CH × 2), 129.8 (CH × 2), 132.7 (Cq), 137.8 (Cq), 148.0 (CH), 148.8 (Cq), 156.7 (Cq); MS (EI, m/z) 198 (M^+, 100), 197 ($M^+ - 1$, 100), 182 (53), 98 (56), 91 (37), 80 (38), 65 (52); HRMS (EI-magnetic sector) calcd for $C_{13}H_{14}N_2$ 198.1157, found 198.1158.

4-Methyl-N-(naphthalen-1-yl)pyridin-2-amine ***(5i):*** pale yellow solid; mp 109−110 °C; R_f = 0.44 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (s, 3 H), 6.46 (s, 1 H), 6.57 (d, J = 5.5 Hz, 1 H), 7.06 (bs, 1 H), 7.47−7.57 (m, 4 H), 7.72 (d, J = 8.0 Hz, 1 H), 7.89 (d, J = 8.5 Hz, 1 H), 8.05−8.07 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (CH_3), 108.2 (CH), 116.2 (CH), 120.7 (CH), 122.3 (CH), 125.4 (CH), 125.8 (CH), 126.3 (CH × 2), 128.5 (CH), 129.3 (Cq), 134.7 (Cq), 135.7 (Cq), 147.1 (CH), 149.6 (Cq), 157.5 (Cq); MS (EI, m/z) 234 (M^+, 100), 233 ($M^+ - 1$, 100); HRMS (EI-magnetic sector) calcd for $C_{16}H_{14}N_2$ 234.1157, found 234.1158.

N-(5-Fluoro-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine ***(6a):*** pale yellow viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3 H), 6.31 (bs, 1 H), 6.46 (s, 1 H), 6.54 (d, J = 5.0 Hz, 1 H), 7.03 (m, 2 H), 7.34−7.43 (m, 5 H), 7.72 (dd, J = 8.5, 5.0 Hz, 1 H), 7.99 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 108.6 (CH), 114.8 (d, J_{C-F} = 21.9 Hz, CH), 116.4 (CH), 117.1 (d, J_{C-F} = 22.4 Hz, CH), 123.9 (d, J_{C-F} = 8.3 Hz, CH), 128.0 (CH), 128.9 (CH), 129.0 (CH), 133.3 (d, J_{C-F} = 2.8 Hz, Cq), 135.9 (d, J_{C-F} = 7.8 Hz, Cq), 137.8 (Cq), 147.4 (CH), 149.1 (Cq), 156.3 (Cq), 158.8 (d, J_{C-F} = 241.5 Hz, Cq); MS (EI, m/z) 278 (M^+, 100), 277 ($M^+ - 1$, 100), 262 (47), 201 (72); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}FN_2$ 278.1219, found 278.1221.

N-(5-Chloro-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine ***(6b):*** pale yellow viscous liquid; R_f = 0.49 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.32 (bs, 1 H), 6.52 (s, 1

H), 6.58 (d, J = 5.0 Hz, 1 H), 7.26 (d, J = 4.0 Hz, 1 H), 7.30 (dd, J = 8.5, 6.0 Hz, 1 H), 7.36−7.38 (m, 3 H), 7.42−7.45 (m, 2 H), 7.84 (d, J = 8.5 Hz, 1 H), 8.03 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 109.4 (CH), 116.9 (CH), 121.8 (CH), 127.4 (Cq), 128.1 (CH × 2), 129.0 (CH × 2), 129.1 (CH × 2), 130.3 (CH), 134.4 (Cq), 136.3 (Cq), 137.6 (Cq), 147.7 (CH), 149.0 (Cq), 155.6 (Cq); MS (EI, m/z) 296 (M^+ + 2, 36), 294 (M^+, 100), 293 (M^+ − 1, 100), 278 (47), 217 (75); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}{}^{35}ClN_2$ 294.0924, found 294.0923.

*N-(5-Bromo-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**6c**):* pale yellow viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.30 (bs, 1 H), 6.53 (s, 1 H), 6.58 (d, J = 5.0 Hz, 1 H), 7.34−7.45 (m, 7 H), 7.82 (d, J = 9.0 Hz, 1 H), 8.03 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 109.5 (CH), 114.7 (Cq), 117.0 (CH), 121.8 (CH), 128.1 (CH), 129.0 (CH × 2), 129.1 (CH × 2), 131.0 (CH), 133.1 (CH), 134.5 (Cq), 136.8 (Cq), 137.5 (Cq), 147.9 (CH), 148.9 (Cq), 155.5 (Cq); MS (EI, m/z) 340 (M^+ + 2, 99), 338 (M^+, 100), 324 (33), 322 (33), 263 (52), 261 (54), 71 (62), 57 (71); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}{}^{79}BrN_2$ 338.0419, found 338.0416.

*4-Methyl-N-(5-nitro-[1,1′-biphenyl]-2-yl)pyridin-2-amine (**6d**):* yellow solid; mp 79−80 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.29 (s, 3 H), 6.57 (s, 1 H), 6.75 (d, J = 5.0 Hz, 1 H), 6.80 (bs, 1 H), 7.44−7.55 (m, 5 H), 8.13 (d, J = 3.0 Hz, 1 H), 8.17 (d, J = 5.0 Hz, 1 H), 8.22 (dd, J = 9.0, 3.0 Hz, 1 H), 8.43 (d, J = 9.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 112.3 (CH), 116.3 (CH), 118.9 (CH), 124.6 (CH), 126.2 (CH), 128.8 (CH), 129.3 (CH × 2), 129.6 (CH × 2), 130.2 (Cq), 136.5 (Cq), 140.8 (Cq), 144.3 (Cq), 147.9 (CH), 149.3 (Cq), 153.7 (Cq); MS (EI, m/z) 305 (M^+, 39), 304 (M^+ − 1, 34), 85 (69), 71 (91), 57 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{15}N_3O_2$ 305.1164, found 305.1168.

*9-(4-Methylpyridin-2-yl)-3-nitro-9H-carbazole (**6″d**):* yellow solid; mp 139−140 °C; R_f = 0.42 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.54 (s, 3 H), 7.25 (d, J = 5.0 Hz, 1 H), 7.42 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H), 7.46 (s, 1 H), 7.54 (ddd, J = 8.0, 8.0, 1.0 Hz, 1 H), 7.75 (d, J = 8.5 Hz, 1 H), 7.82 (d, J = 9.0 Hz, 1 H), 8.19 (d, J = 8.0 Hz, 1 H), 8.34 (d, J = 9.5, 2.5 Hz, 1 H), 8.62 (d, J = 5.0 Hz, 1 H), 9.03 (d, J = 2.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (CH_3), 111.1 (CH), 111.6 (CH), 116.9 (CH), 120.2 (CH), 120.9 (CH), 121.9 (CH), 122.1 (CH), 123.6 (Cq), 123.7 (CH), 124.0 (Cq), 127.7 (CH), 140.9 (Cq), 141.9 (Cq), 142.9 (Cq), 149.6 (CH), 150.6 (Cq), 150.7 (Cq); MS (EI, m/z) 303 (M^+, 81), 257 (45), 85 (61), 71 (91), 57 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{13}N_3O_2$ 303.1008, found 303.1005.

*N-(3-Methoxy-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**6e**):* pale yellow viscous liquid; R_f = 0.46 (*n*-hexane/ethyl acetate 1/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07 (s, 3 H), 3.85 (s, 3 H), 6.01 (s, 1 H), 6.36 (bs, 1 H), 6.40 (d, J = 5.5 Hz, 1 H), 6.97 (dd, J = 8.0, 1.0 Hz, 1 H), 7.02 (dd, J = 8.0, 1.0 Hz, 1 H), 7.20 (dd, J = 7.5, 7.5 Hz, 1 H), 7.24−7.28 (m, 3 H), 7.40 (d, J = 8.9 Hz, 2 H), 7.88 (d, J = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (CH_3), 55.8 (CH_3), 108.2 (CH), 110.5 (CH), 115.7 (CH), 122.9 (CH), 125.7 (CH), 126.2 (Cq), 127.1 (CH), 128.3 (CH × 2), 128.6 (CH × 2), 138.3 (Cq), 139.5 (Cq), 147.0 (CH), 148.1 (Cq), 154.3 (Cq), 156.5 (Cq); MS (EI, m/z) 290 (M^+, 2), 258 (100); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1417.

*N-(4-Methoxy-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**6f**):* white solid; mp 67−68 °C; R_f = 0.49 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3 H), 3.85 (s, 3 H), 6.56 (d, J = 4.5 Hz, 1 H), 6.62 (bs + s, 2 H), 6.70 (dd, J = 8.5, 2.5 Hz, 1 H), 7.21 (d, J = 8.5 Hz, 1 H), 7.29−7.33 (m, 1 H), 7.37−7.41 (m, 4 H), 7.46 (d, J = 2.5 Hz, 1 H), 8.02 (d, J = 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.4 (CH_3), 106.3 (CH), 108.2 (CH), 109.5 (CH), 116.6 (CH), 125.9 (Cq), 127.2 (CH), 128.8 (CH × 2), 129.4 (CH × 2), 131.4 (CH), 138.4 (Cq), 138.6 (Cq), 147.3 (CH), 149.1 (Cq), 155.6 (Cq), 159.6 (Cq); MS (EI, m/z) 290 (M^+, 100), 289 (M^+ − 1, 87), 274 (47), 213 (67); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1417.

*N-(5-Methoxy-[1,1′-biphenyl]-2-yl)-4-methylpyridin-2-amine (**6g**):* pale yellow viscous liquid; R_f = 0.48 (*n*-hexane/ethyl acetate 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.19 (s, 3 H), 3.84 (s, 3 H), 6.42 (s, 1 H), 6.47 (d, J = 5.0 Hz, 1 H), 6.50 (bs, 1 H), 6.90 (d, J = 3.0 Hz, 1 H), 6.93 (dd, J = 8.5, 3.0 Hz, 1 H), 7.29−7.39 (m, 5 H), 7.52 (d, J = 8.5 Hz, 1 H), 7.92 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 55.6 (CH_3), 107.8 (CH), 113.9 (CH), 115.6 (CH), 115.8 (CH), 125.5 (CH), 127.5 (CH), 128.6 (CH × 2), 129.0 (CH × 2), 130.1 (Cq), 137.0 (Cq), 138.9 (Cq), 147.0 (CH), 149.1 (Cq), 156.4 (Cq), 157.1 (Cq); MS (EI, m/z) 290 (M^+, 100), 275 (49); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1420.

*4-Methyl-N-(5-methyl-[1,1′-biphenyl]-2-yl)pyridin-2-amine (**6h**):* pale yellow viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate 4/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3 H), 2.37 (s, 3 H), 6.28 (bs, 1 H), 6.52 (d, J = 5.0 Hz, 1 H), 6.58 (s, 1 H), 7.14 (s, 1 H), 7.16 (dd, J = 8.0, 1.5 Hz, 1 H), 7.32−7.41 (m, 5 H), 7.60 (d, J = 8.0 Hz, 1 H), 7.99 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8 (CH_3), 21.2 (CH_3), 108.4 (CH), 116.2 (CH), 122.0 (CH), 127.4 (CH), 128.7 (CH × 2), 128.8 (CH), 129.2 (CH × 2), 131.4 (CH), 132.7 (Cq), 134.1 (Cq), 134.8 (Cq), 139.0 (Cq), 147.8 (Cq), 148.8 (CH), 156.5 (Cq); MS (EI, m/z) 274 (M^+, 100), 273 (M^+ − 1, 99), 258 (32), 197 (57); HRMS (EI-magnetic sector) calcd for $C_{19}H_{18}N_2$ 274.1470, found 274.1468.

*4-Methyl-N-(5′-methyl-[1,1′:3′,1″-terphenyl]-2′-yl)pyridin-2-amine (**6′h**):* white solid; mp 115−116 °C; R_f = 0.40 (*n*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.98 (s, 3 H), 2.44 (s, 3 H), 5.93 (s, 1 H), 6.12 (bs, 1 H), 6.24 (d, J = 5.3 Hz, 1 H), 7.19−7.22 (m, 4 H), 7.26−7.29 (m, 4 H), 7.38−7.40 (m, 4 H), 7.72 (d, J = 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9 (CH_3), 21.0 (CH_3), 107.9 (CH), 115.1 (CH), 127.1 (CH × 2), 128.2 (CH × 4), 128.8 (CH × 4), 131.1 (CH × 2), 131.5 (Cq), 135.4 (Cq), 138.6 (Cq × 2), 139.8 (Cq × 2), 146.9 (CH), 147.9 (Cq), 156.2 (Cq); MS (EI, m/z) 350 (M^+, 6), 273 (13), 183 (100); HRMS (EI-magnetic sector) calcd for $C_{25}H_{22}N_2$ 350.1783, found 350.1784.

*[1,1′-Biphenyl]-2-amine (**7**):* brown viscous liquid; R_f = 0.60 (*n*-hexane/ethyl acetate 7/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (bs, 2 H), 6.77 (d, J = 8.0 Hz, 1 H), 6.82 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H), 7.12−7.17 (m, 2H), 7.33−7.36 (m, 1 H), 7.42−7.46 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.6 (CH), 118.6 (CH), 127.1 (CH), 127.6 (Cq), 128.5 (CH), 128.8 (CH × 2), 129.1 (CH × 2), 130.4 (CH), 139.5 (Cq), 143.5 (Cq); MS (EI, m/z) 169 (M^+, 19), 111 (32), 97 (46), 85 (53), 71 (75), 57 (100); HRMS (EI-magnetic sector) calcd for $C_{12}H_{11}N$ 169.0891, found 169.0891.

*3-Methyl-6-phenylbenzo[4,5]imidazo[1,2-a]pyridine (**8**):* pale yellow solid; mp 97−98 °C; R_f = 0.43 (*n*-hexane/ethyl acetate 1/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3 H), 6.70 (d, J = 7.0 Hz, 1 H), 7.37−7.42 (m, 2 H), 7.51−7.54 (m, 3 H), 7.64 (d, J = 7.5 Hz, 1 H), 7.82 (d, J = 8.0 Hz, 1 H), 8.06 (d, J = 7.5 Hz, 2 H), 8.35 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9 (CH_3), 109.1 (CH), 113.3 (CH), 116.4 (CH), 120.7 (CH), 124.2 (CH + Cq), 124.7 (CH), 127.3 (CH), 128.5 (CH × 2), 129.3 (CH × 2), 132.4 (Cq), 138.6 (Cq), 140.6 (Cq), 142.6 (Cq), 149.0 (Cq); MS (EI, m/z) 258 (M^+, 24), 71 (54), 57 (100); HRMS (EI-magnetic sector) calcd for $C_{18}H_{14}N_2$ 258.1157, found 258.1157.

*3-Methyl-6-phenylbenzo[4,5]imidazo[1,2-a]pyridin-8-yl acetate (**9**):* pale yellow solid; mp 79−80 °C; R_f = 0.53 (*n*-hexane/ethyl acetate 3/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 2.47 (s, 3 H), 6.73 (d, J = 6.5 Hz, 1 H), 7.38 (d, J = 2.0 Hz, 1 H), 7.40 (d, J = 7.0 Hz, 1 H), 7.51−7.54 (m, 2 H), 7.57 (bs, 1 H), 7.64 (d, J = 2.0 Hz, 1 H), 8.04 (d, J = 7.5 Hz, 2 H), 8.26 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (CH_3), 22.0 (CH_3), 102.4 (CH), 113.8 (CH), 116.4 (CH), 118.9 (CH), 124.1 (CH), 127.8 (CH), 128.7 (CH × 2), 128.8 (Cq), 129.2 (CH × 2), 130.2 (Cq), 132.9 (Cq), 134.2 (Cq), 137.5 (Cq), 144.9 (Cq), 149.4 (Cq), 170.0 (Cq); MS (EI, m/z) 316 (M^+, 21), 274 (100), 85 (58), 71 (80), 57 (93); HRMS (EI-magnetic sector) calcd for $C_{20}H_{16}N_2O_2$ 316.1212, found 316.1209.

*4-Methyl-N-phenylpyridin-2-amine palladacycle (**I**):* yellow solid; mp >146 °C dec; ^{1}H NMR (300 MHz, d_8-THF) δ 2.23 (s, 6 H), 2.43 (s, 6 H), 6.48−6.59 (m, 6 H), 6.71 (s, 2 H), 6.81−6.86 (m, 2 H), 7.35

(d, J = 7.8 Hz, 2 H), 8.39 (m, 2 H), 8.77 (s, 2 H); MS (MALDI-TOF, m/z) 697 (M^+). The solubility of the title compound was found to be very poor in most solvents. We only obtained its ^{1}H NMR spectrum in d_8-THF, while the ^{13}C NMR signals were too poor to be reported.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Tables, figures, and a CIF file giving X-ray crystallographic data for **I** and ^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: j_hchu@yahoo.com.tw (J.-H.C.); mijuwu@faculty.nsysu.edu.tw (M.-J.W.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Science Council of the Republic of China (NSC 101-2113-M-110-014-MY3 and NSC-100-2113-M-110-006-MY3) for financial support and Mr. Min-Yuan Hung for his technical support and services for GC-MS at the Center for Research Resources and Development of Kaohsiung Medical University (Taiwan).

■ REFERENCES

(1) Selected reviews of transition-metal-catalyzed C−H functionalization: (a) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236−10254. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802. (c) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814−825. (d) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864−873. (e) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936−946. (f) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464−3484. (g) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651−3678. (h) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215−1292. (i) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293−1314. (j) Ackerman, L. *Chem. Rev.* **2011**, *111*, 1315−1345. (k) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115.

(2) (a) Urones, B.; Arrayás, R. G.; Carretero, J. C. *Org. Lett.* **2013**, *15*, 1120−1123. (b) Rajeshkumar, V.; Lee, T.-H.; Chuang, S.-C. *Org. Lett.* **2013**, *15*, 1468−1471. (c) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518−522. (d) Ackermann, L.; Diers, E.; Manvar, A. *Org. Lett.* **2012**, *14*, 1154−1157. (e) Yadav, M. R.; Rit, R. K.; Sahoo, A. K. *Chem. Eur. J.* **2012**, *18*, 5541−5545. (f) Li, B.-J.; Wang, H.-Y.; Zhu, Q.-L.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 3948−3952. (g) Wencel-Delord, J.; Nimphius, C.; Patureau, F. W.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 2247−2251. (h) Iglesias, A.; Alvarez, R.; de Lera, A. R.; Muñiz, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 2225−2228. (i) Karthikeyan, J.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2012**, *51*, 12343−12347. (j) Jayakumar, J.; Parthasarathy, K.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2012**, *51*, 197−200. (k) Ye, M.; Edmunds, A. J. F.; Morris, J.; Sale, D.; Zhang, Y.; Yu, J.-Q. *Chem. Soc.* **2013**, *4*, 2374−2379. (l) Li, G.; Leow, D.; Wan, L.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2013**, *52*, 1245−1247. (m) Pan, F.; Lei, Z.-Q.; Wang, H.; Li, H.; Sun, J.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2013**, *52*, 2063−2067. (n) Zhang, L.-S.; Chen, K.; Chen, G.-H.; Li, B.-L.; Luo, S.; Guo, Q.-Y.; Wei, J.-B.; Shi, Z.-J. *Org. Lett.* **2013**, *15*, 10−13.

(3) Our work in palladium(II)-catalyzed C−H functionalization: (a) Chu, J.-H.; Wu, C.-C.; Chang, D.-H.; Lee, Y.-M.; Wu, M.-J. *Organometallics* **2013**, *32*, 272−282. (b) Chu, J.-H.; Lin, P.-S.; Lee, Y.-M.; Shen, W.-T.; Wu, M.-J. *Chem. Eur. J.* **2011**, *17*, 13613−13620. (c) Chu, J.-H.; Lin, P.-S.; Wu, M.-J. *Organometallics* **2010**, *29*, 4058−4065. (d) Chu, J.-H.; Tsai, S.-L.; Wu, M.-J. *Synthesis* **2009**, 3757−3764. (e) Chu, J.-H.; Chen, C.-C.; Wu, M.-J. *Organometallics* **2008**, *27*, 5173−5176.

(4) (a) Fürstner, A.; Kennedy, J. W. J. *Chem. Eur. J.* **2006**, *12*, 7398−7410. (b) Kikuchi, H.; Matsuo, Y.; Katou, Y.; Kubohara, Y.; Oshima, Y. *Tetrahedron* **2012**, *68*, 8884−8889. (c) Morales, J. C. C.; Torres, A. G.; González-Zamora, E. *Eur. J. Org. Chem.* **2011**, 3165−3170.

(5) (a) Bright, T. V.; Dalton, F.; Elder, V. L.; Murphy, C. D.; O'Connor, N. K.; Sandford, G. *Org. Biomol. Chem.* **2013**, *11*, 1135−1142. (b) Da, Y.-J.; Yuan, W.-D.; Xin, T.; Nie, Y.-Y.; Ye, Y.; Yan, Y.-J.; Liang, L.-S.; Chen, Z.-L. *Bioorg. Med. Chem.* **2012**, *20*, 7101−7111. (c) Takeuchi, T.; Oishi, S.; Watanabe, T.; Ohno, H.; Sawada, J.; Matsuno, K.; Asai, A.; Asada, A.; Kitaura, K.; Fujii, N. *J. Med. Chem.* **2011**, *54*, 4839−4846.

(6) (a) Manickam, M.; Iqbal, P.; Belloni, M.; Kumar, S.; Preece, J. A. *Isr. J. Chem.* **2012**, *52*, 917−934. (b) An, B.-K.; Gihm, S. H.; Chung, J. W.; Park, J. W.; Park, C. R.; Kwon, S.-K.; Park, S. Y. *J. Am. Chem. Soc.* **2009**, *131*, 3950−3957. (c) Wang, Z. M.; Song, X. H.; Gao, Z.; Yu, D. W.; Zhang, X. J.; Lu, P.; Shen, F. Z.; Ma, Y. G. *RSC Adv.* **2012**, *2*, 9635−9642.

(7) (a) Chen, X.; Li, J.-J.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 78−79. (b) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634−12635.

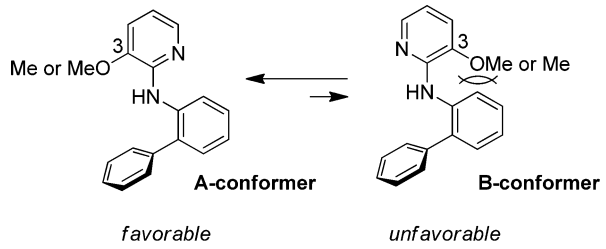
(8) (a) Wang, X.; Leow, D.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 13864−13867. (b) Wasa, M.; Worrell, B. T.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 1275−1277. (c) Wasa, M.; Engle, K. M.; Yu, I.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 9886−9887. (d) Wang, D.-H.; Wasa, M.; Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 7190−7191. (e) Yang, S.; Li, B.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 6066−6067. (f) Koley, M.; Dastbaravardeh, N.; Schnürch, M.; Mihovilovic, M. D. *ChemCatChem.* **2012**, *4*, 1345−1352.

(9) BQ has been demonstrated as an efficient promoter in palladium(II)-catalyzed C−H activation/C−C coupling. See ref 7 and: Giri, R.; Maugel, N.; Li, J.-J.; Wang, D.-H.; Breazzano, S. P.; Saunders, L. B.; Yu, J.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 3510−3511.

(10) In the following exploration of starting substrates, copper(II) acetate generally showed results better than those for silver(I) salts. For example, in the synthesis of **6e−g** (entries 5−7, Table 4), modest to excellent product yields were found, but none of the desired products were isolated by using silver(I) salts. On the other hand, we did not observe the formation of any copper complexes when substrate **1a** and copper(II) acetate were mixed in *tert*-butyl alcohol at 80−90 °C.

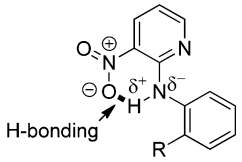
(11) $K_2S_2O_8$ and oxone were demonstrated as good terminal oxidants in palladium-catalyzed C−H functionalization; see: (a) Desai, L. V.; Malik, H. A.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 1141−1144. (b) Gary, J. B.; Cook, A. K.; Sanford, M. S. *ACS Catal.* **2013**, *3*, 700−703. Unfortunately, only moderate yields (53% for $K_2S_2O_8$ and 52% for oxone) of the single product **3a** were obtained by using these peroxide-based oxidants in the reaction.

(12) Two conformers of **3b** and **3c** are shown as follows. Conformer A is believed to be more favorable than conformer B from energetic considerations.



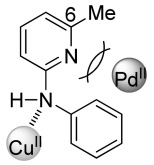
(13) According to the ^{1}H NMR spectroscopic analysis of **1d**, the chemical shift of the amine proton is shifted down to 10.11 ppm which indicates a strong intramolecular hydrogen bond formed between the nitro and amine groups, shown as follows. A similar result is also observed for **3d**, for which the chemical shift of the amine proton

appears at 9.96 ppm. This phenomenon suggests that a more negative charge on the amine nitrogen is formed.



1d, R = H
3d, R = Ph

(14) (a) A possible model of **1l** interacting with the palladium(II) and copper(II) ions is illustrated as follows. (b) For a related paper on



copper(II)-mediated or -catalyzed C–N coupling, see: Wang, X.; Jang, H.-Y. *Bull. Korean Chem. Soc.* **2012**, *33*, 1785–1787 and references cited therein.

(15) Although substrate **1e** (R = 4-OMe) showed a product yield higher than that of **1f** (R = 4-Me), but more synthetic steps for the preparation of **1e** were required, we thus chose **1f** as the model substrate.

(16) (a) Das, S.; Banerjee, P.; Peng, S.-M.; Lee, G.-H.; Kim, J.; Goswami, S. *Inorg. Chem.* **2006**, *45*, 562–570. The formation of pyrido[1,2-*a*]benzimidazole **8** might be due to the copper-catalyzed direct intramolecular C–N coupling of **3f**; see the related report: (b) Wang, H.; Wang, Y.; Peng, C.; Zhang, J.; Zhu, Q. *J. Am. Chem. Soc.* **2010**, *132*, 13217–13219. (c) Masters, K.-S.; Rauws, T. R. M.; Yadav, A. K.; Herrebout, W. A.; Van der Veken, B.; Maes, B. U. W. *Chem. Eur. J.* **2011**, *17*, 6315–6320.

(17) A similar catalytic mechanism was already presented in our previous paper; please refer to ref 3a.

(18) A copy of the deposited crystallographic data CCDC-955701 (**I**) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(19) All reaction conditions were referred to the following. (a) Reference 3b.. References 3a, 8f, and: (b) Pan, S.; Endo, K.; Shibata, T. *Org. Lett.* **2011**, *13*, 4692–4695. (c) Pastine, S. J.; Gribkov, D. V.; Same, D. *J. Am. Chem. Soc.* **2006**, *128*, 14220–14221. (d) Kutsumura, N.; Kunimatsu, S.; Kagawa, K.; Otani, T.; Saito, T. *Synthesis* **2011**, 3235–3240.

(20) The synthetic procedure followed that given in ref 3b and: Sadighi, J. P.; Harris, M. C.; Buckwald, S. L. *Tetrahedron Lett.* **1998**, *39*, 5327–5330.