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Article

Palladium(II)-Catalyzed *Ortho* Arylation of 2-Phenoxypyridines with Potassium Aryltrifluoroborates via C−H Functionalization

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An efficient synthesis of *ortho*-arylated 2-phenoxypyridines catalyzed by palladium acetate is described. Treatment of 2-phenoxypyridines with two and a half equivalents of potassium aryltrifluoroborate and 10 mol % of $Pd(OAc)_2$ in the presence of two equivalents of Ag_2CO_3, one equivalent of *p*-benzoquinone (BQ), and four equivalents of DMSO with (or without) H_2O at 130−140 °C for 48 h in dried CH_2Cl_2 gave the *ortho*-arylated 2-phenoxypyridines in modest to excellent yields. *p*-Benzoquinone is found to be an important ligand and co-oxidant for the transmetalation reductive elimination step in the catalytic reaction. The investigation of kinetic isotope effect (k_H/k_D) is determined to be 5.25, which indicates that C−H bond cleavage occurs in the rate-determining step. One of the arylated compounds, 2-(4′-nitrobiphenyl-2-yloxy)pyridine, was treated with methyl trifluoromethanesulfonate and subsequently sodium methoxide to give the 2-(4-nitrophenyl)phenol in 79% yield, demonstrating that pyridine is a removable directing group.

Introduction

Recently, transition metal-catalyzed direct functionalization of organic molecules via carbon−hydrogen (C−H) bond activation has received great attention.[1] Selective C−H bond activation/functionalization emerged as an efficient strategy for the synthesis of natural products and pharmaceutical compounds.[2] Traditional methods of carbon−carbon (C−C) bond formation usually require two prefunctionalized arenes (Ar−X/Ar−M) as starting materials to generate a new C−C bond (e.g., Suzuki−Miyaura cross-coupling reaction).[3] Nevertheless, direct C−H functionalization needs only one or no pre-existing functional groups of starting reagents instead of the conventional protocol. Concurrently, the methodology can also improve the synthetic efficiency and atom economy. To date, many papers have demonstrated that arenes containing so-called directing group (such as pyridine,[4] pyridine *N*-oxide,[5] oxazoline,[6] isoxazole,[7] oxime,[8] imine,[9] amide,[10] urea,[11] carboxylic

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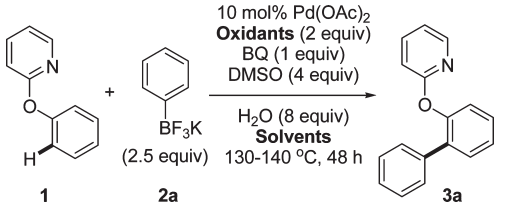
acid,[12] hydroxy,[13] ester,[14] ketone,[15] and *O*-carbamate[16]) can be regioselectively functionalized by a variety of coupling reagents in the presence of transition metal catalysts. In the literature, rare examples utilizing C−H bond activation/functionalization were investigated toward 2-aryloxypyridine compounds.[17] On the other hand, herbicidal and antimycobacterial activities of aryloxypyridine derivatives have been systematically investigated,[18] whereas the structure−activity relationship of phenoxypyridine and its analogues in the investigation of thyroid hormone was also studied.[19] We herein present palladium(II)-catalyzed direct *ortho* arylation of 2-phenoxypyridine and its derivatives with potassium aryltrifluoroborates via C−H bond activation and demonstrated that the pyridines can be further removed to produce *ortho*-arylated phenols.

Results and Discussion

Screens of Oxidants and Solvents for the Reaction of 2-Phenoxypyridine with Potassium Phenyltrifluoroborate. Our investigation on the *ortho* arylation of 2-phenoxypyridine with potassium phenyltrifluoroborate was initiated by screening of the oxidants and solvents. Thus, a variety of oxidants and solvents were used in this study, and the results are shown in Table 1. In our previous study,[4a] copper acetate and silver acetate are the optimal oxidants and 1,4-dioxane is the best solvent in the *ortho* arylation of 2-phenylpyridines. However, on the basis of experimental results, silver(I) carbonate and dichloromethane appear to be the optimal oxidant and solvent for the reaction of 2-phenoxypyridine (**1**) with potassium phenyltrifluoroborate (**2a**), respectively.

Table 1. Oxidant and Solvent Effect on the Reaction of 2-Phenoxypyridine (1) with Potassium Phenyltrifluoroborate (2a)



entry	oxidant	solvent[b]	product	yield (%)[a]
1	absence		**3a**	0
2	Ag_2CO_3		**3a**	63 (39)[c]
3	AgOAc		**3a**	46
4	Ag_2O		**3a**	27
5	$K_2S_2O_8$	DCM	**3a**	22
6	Oxone		**3a**	0
7	$Cu(OAc)_2$		**3a**	0
8	$Cu(OTf)_2$		**3a**	0
9	$Hg(OAc)_2$		**3a**	0
10		DCE	**3a**	60
11		TCE	**3a**	58
12		benzene	**3a**	56
13		toluene	**3a**	40
14	Ag_2CO_3	xylene	**3a**	27
15		acetonitrile	**3a**	14
16		*tert*-butanol	**3a**	13
17		1,4-dioxane	**3a**	11
18		DMF	**3a**	8
19		THF	**3a**	0

[a] Product yield was determined by ^{1}H NMR spectroscopy. [b] DCM = dichloromethane; DCE = 1,2-dichloroethane; TCE = 1,1,2,2-tetrachloroethane; DMF = *N*,*N*-dimethylformamide; THF = tetrahydrofuran. [c] Yield in parentheses was obtained by using 1 equiv of Ph-BF_3K (**2a**).

Catalytic Reaction of 2-Phenoxypyridine and Its Derivatives with Various Potassium Aryltrifluoroborates. On the basis of optimal reaction conditions (2.5 equiv of Ar-BF_3K, 10 mol % $Pd(OAc)_2$, 2 equiv of Ag_2CO_3, 1 equiv of *p*-benzoquinone (BQ),[20] and 4 equiv of DMSO[21] with (or without) 8 equiv of H_2O[22] at 130−140 °C for 48 h in dry CH_2Cl_2), we carried out the reaction of 2-phenoxypyridine (**1**) with various potassium aryltrifluoroborates, **2a**−**m**. A series of *ortho*-arylated 2-phenoxypyridines, **3a**−**m**, were obtained in 0−95% yields (Table 2).

According to the experimental results, we found the reaction of **1** with potassium aryltrifluoroborates **2a**−**g** (Table 2, entries 1−7) resulted in modest to excellent yields (50−95%). In addition, the reaction of **1** with potassium 4-iodophenyl trifluoroborate (**2h**) gave compound **3h** in only 7% yield (Table 2, entry 8). The low yield might be due to the side reactions, including possible self-polymerization of **2h** by Suzuki coupling reaction, although we did not isolate the corresponding polymers. In the above entries, we found that adding a small amount of water could increase the reaction rate and produce better chemical yields. After tuning the amount of water, adding eight equivalents of water into the reaction mixture turned out to yield the best result. On the other hand, low yields (34−48%, Table 2, entries 9−11)

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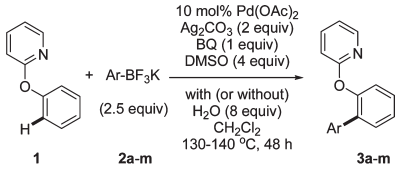
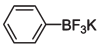
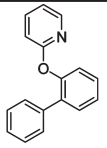
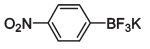
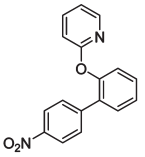
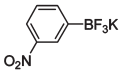
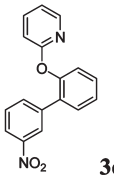
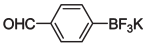
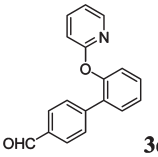
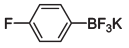
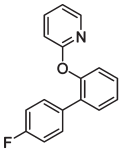
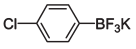
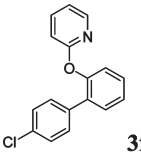
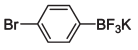
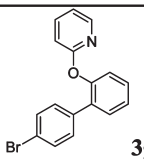
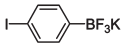
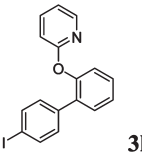
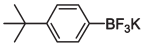
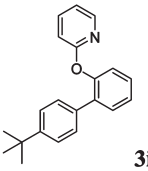
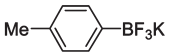
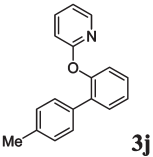
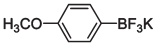
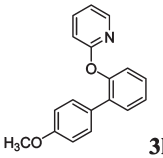
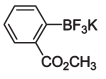
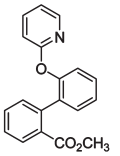
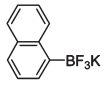
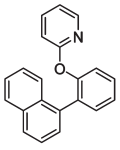
(20) Fresh *p*-benzoquinone through sublimation was used.
(21) Catalytic system of Pd(II)/DMSO, see: (a) Steinhoff, B. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 4348–4355, and references therein. DMSO might slow catalyst decomposition and Pd(0) aggregation and further increase the product yield; see: (b) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 11904–11905. (c) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 9651–9653. (d) Zierkiewicz, W.; Privalov, T. *Organometallics* **2005**, *24*, 6019–6028.
(22) The yield of 2-(biphenyl-2-yloxy)pyridine (**3a**) in the reaction of 2-phenoxypyridine (**1**) with potassium phenyltrifluoroborate (**2a**) was determined to be 21%, 63%, 62%, and 12% in the presence of 0, 8, 16, and 32 equivalents of water, respectively. Trifluoroborate salts might undergo hydrolysis to afford boronic acids and further participate in the transmetalation−reductive elimination with palladacycle **I**. See: Bulters, M.; Harvey, J. M.; Jover, J.; Lennox, A, J. J.; Lloyd-Jones, G. C.; Murray, P. M. *Angew. Chem., Int. Ed.* DOI: 10.1002/anie.201001522.

Table 2. *Ortho* Arylation of 2-Phenoxypyridine (1) with Potassium Aryltrifluoroborate 2a−m[a]



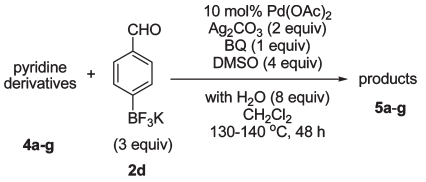
Entry	Ar-BF$_3$K	Product	Yield (%)[b]
1	 **2a**	 **3a**	63 (60)[c]
2	 **2b**	 **3b**	95
3	 **2c**	 **3c**	90
4	 **2d**	 **3d**	75
5	 **2e**	 **3e**	80
6	 **2f**	 **3f**	50
7	 **2g**	 **3g**	65
8	 **2h**	 **3h**	7
9	 **2i**	 **3i**	48
10	 **2j**	 **3j**	40
11	 **2k**	 **3k**	34
12	 **2l**	 **3l**	18
13	 **2m**	 **3m**	0

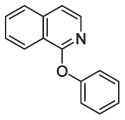
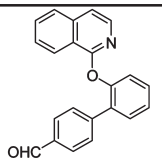
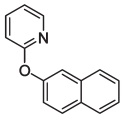
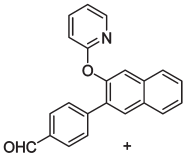
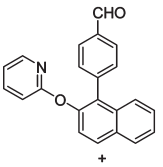
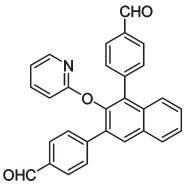
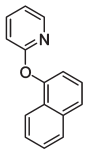
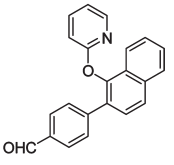
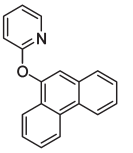
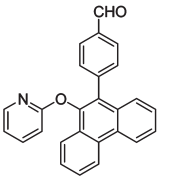
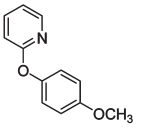
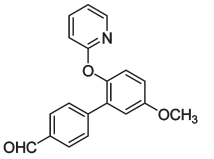
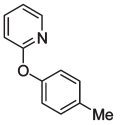
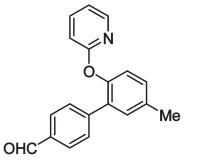
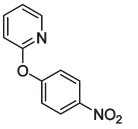
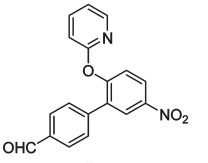
[a] 8 equiv of H_2O was added in entries 1−8, 12, and 13, and no water was added in entries 9−11. [b] All yields were determined by ^{1}H NMR spectroscopy. [c] Yield in parentheses was obtained by using 1.0 mmol scale of 2-phenoxypyridine (**1**).

were observed by using potassium aryltrifluoroborates **2i**−**k**, bearing electron-donating groups (^{t}Bu, Me, and OMe). No water was added in these three cases because we found that the self-coupling reactions of aryltrifluoroborates took place faster than the *ortho* arylation reactions by adding water into the reaction mixture. The reaction of potassium *o*-methoxycarbonylphenyltrifluoroborate (**2l**) (Table 2, entry 12) and potassium 1-naphthyltrifluoroborate (**2m**) (Table 2, entry 13) with 2-phenoxypyridine (**1**) led to compounds **3l** and **3m** in 18% and 0% yields, respectively. The poor yields could be due to the steric hindrance interfering with the C−C bond formation.

In addition to 2-phenoxypyridine (**1**), we also carried out the reactions of pyridine derivatives **4a**−**g** with potassium 4-formylphenyl trifluoroborate (**2d**). The *ortho*-arylated products **5a**−**g** were obtained in 0 to 84% yields (Table 3). The isoquinoline group of 1-phenoxyisoquinoline (**4a**) can also be utilized as a directing group. Reaction of **4a** with **2d** under the optimal reaction conditions gave compound **5a** in 73% yield (Table 3, entry 1). On the other hand, reaction of **4a** with **2d** led to the formation of three products, **5b**, **5b′**, and **5b″**, in a ratio of 60:25:15, and the total yield is 72% (Table 3, entry 2). When the reaction of 2-(naphthalen-1-yloxy)-pyridine (**4c**) and 2-(phenanthren-9-yloxy)pyridine (**4d**) was

Table 3. *Ortho* Arylation of Pyridine Derivatives 4a−g with Potassium 4-Formylphenyl Trifluoroborate (2d)



Entry	Pyridine derivatives	Product	Yield (%)[a]
1	 **4a**	 **5a**	73
2	 **4b**	 +  +  **5b + 5b' +5b"** (60:25:15)[b]	72
3	 **4c**	 **5c**	84
4	 **4d**	 **5d**	61
5	 **4e**	 **5e**	33
6	 **4f**	 **5f**	34
7	 **4g**	 **5g**	0

[a,b] Yields and product ratio were all determined by ^{1}H NMR spectroscopy.

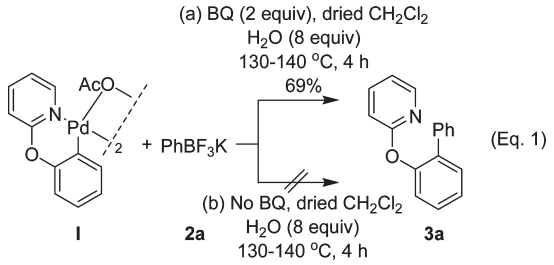
carried out to react with **2d** under the described reaction conditions, both reactions produced a single product, **5c** and **5d**, respectively. No other regioisomer was found in these two reactions (Table 3, entries 3 and 4). The high regioselectivity for both reactions could be explained by the formation of the six-membered palladacycles, which are more stable than the seven-membered palladacycles. The structure of **5c** was unambiguously determined by X-ray crystallography analysis, as shown in Figure 1. In addition to substrates **4a**−**d**, we also carried out the reaction of 2-phenoxypyridines **4e**−**g**, bearing either an electron-donating or withdrawing group on the phenyl ring, with **2d**, which led to **5e**−**g** in 33%, 34%, and 0% yields, respectively. The result shows that when 2-phenoxypyridine bears a strong electron-withdrawing group, such as a nitro group, the reaction took place very slowly and led to no coupling product. The low yields obtained by the reaction of **4e** and **4f** may be due to the steric effect that destabilizes the palladacycles, which would not be efficiently transformed into the desired products.

In order to understand the detailed information on the reaction mechanism, we independently synthesized the important intermediate 2-phenoxypyridine palladacycle **I** (which was first reported by Steel and co-workers in 1999, but they did not obtain its X-ray crystal structure[23]) by treatment of 2-phenoxypyridine (**1**) with a stoichiometric amount of Pd(OAc)$_2$ in dichloromethane. The structure of intermediate **I** (a head-to-tail geometric structure) was confirmed by X-ray crystallographic analysis, as shown in Figure 2.

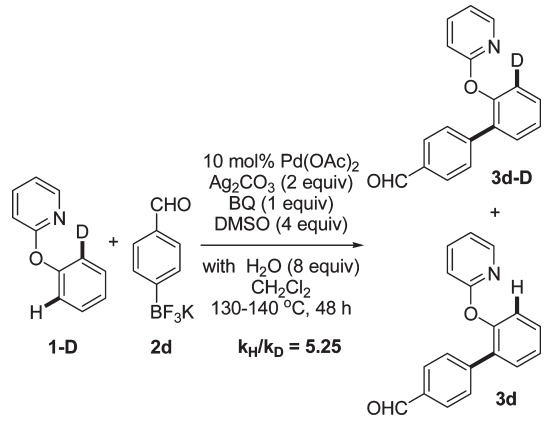
With this intermediate in hand, we carried out the reaction of **I** with potassium phenyltrifluoroborate (**2a**) with or

(23) de Geest, D. J.; O'Keefe, B. J.; Steel, P. J. *J. Organomet. Chem.* **1999**, *579*, 97–105.

without two equivalents of BQ (eq 1). These controlled experiments indicated that 2-(biphenyl-2-yloxy)pyridine (**3a**) was obtained in 69% yield only in the presence of BQ. In the absence of BQ, no **3a** was observed. According to these results, we believe that BQ is an important ligand and co-oxidant in the reductive elimination step of the catalytic reaction.[24]



Investigation of Kinetic Isotope Effect. The kinetic isotope effect (k_H/k_D) of the catalytic reaction was carried out by the reaction of *ortho* monodeutero-2-phenoxypyridine (**1-D**) with potassium 4-formylphenyl trifluoroborate (**2d**) to give the products **3d-D** and **3d**, respectively (eq 2). The kinetic isotope effect (k_H/k_D) was determined to be 5.25 (compared with the standard ^{1}H NMR spectrum of compound **3d**). This indicates that *ortho* C−H bond cleavage occurs in the rate-determining step.



Proposed Mechanism for the Reaction of 2-Phenoxypyridine with Potassium Aryltrifluoroborates. A possible mechanism for the present palladium(II)-catalyzed *ortho* arylation of 2-phenoxypyridine (**1**) via C−H bond activation is proposed as shown in Figure 3. First of all, coordination of 2-phenoxypyridine (**1**) to $Pd(OAc)_2$ following an *ortho* C−H bond activation would form a pyridine palladacycle **I**. Subsequently, the aryl group of aryldifluoroborane **2-BF$_2$** (generated from potassium aryltrifluoroborate **2** by a release

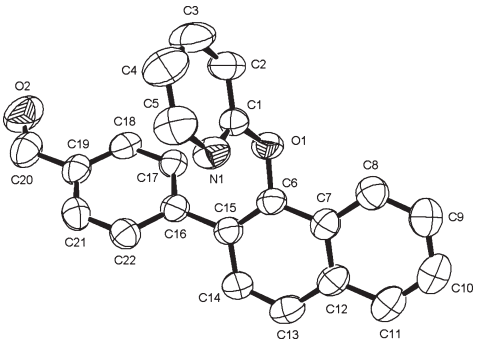
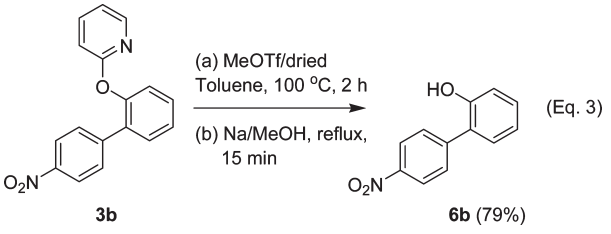


Figure 1. ORTEP drawing of compound **5c** (where all hydrogen atoms are omitted for clarity).

of KF) is bound to the Pd center of **I** via ligand exchange with release of F_2BOAc.[25] *p*-Benzoquinone (BQ) herein is an important ligand and co-oxidant to coordinate with Pd to form intermediate **II**. Eventually, intermediate **II** is further transformed to *ortho*-arylated product **3**. The released Pd(0) is reoxidized by Ag_2CO_3 and *p*-benzoquinone to regenerate Pd(II), which would continue the catalytic cycle.

Synthesis of 4′-Nitrobiphenyl-2-ol (6b) through Depyridinylation of Compound 3b. To demonstrate the utility of pyridine as a removable directing group that would direct the C−H bond activation/functionalization and could be removed to form a variety of biphenyl alcohols from *ortho*-arylated 2-phenoxypyridines, herein compound **3b** was treated with methyl trifluoromethanesulfonate (MeOTf) to form 1-methyl-2-(4′-nitrobiphenyl-2-yloxy)pyridinium in toluene. Subsequently, crude 1-methyl-2-(4′-nitrobiphenyl-2-yloxy)-pyridinium was added into a refluxing Na/MeOH solution to generate 4′-nitrobiphenyl-2-ol (**6b**) in 79% yield in two steps (eq 3).



Conclusion

We have developed the reaction conditions for the synthesis of *ortho*-arylated 2-phenoxypyridines with potassium aryltrifluoroborates via C−H bond activation using palladium(II) acetate as a catalyst. The products can further be converted to biphenyl alcohols in good yield by the treatment of methyl trifluoromethanesulfonate then sodium methoxide in methanol solution. The presented methodology provides a useful tool in organic synthesis.

Experimental Section

General Procedure for Synthesis of Starting Materials 1 and 4a−g.[26] A well-stirred solution of 2-iodopyridine (500 mg, 2.44 mmol) or 1-bromoisoquinoline (208 mg, 1.00 mmol) with a

(24) Similar phenomena were observed by using the *p*-benzoquinone or olefin to promote transmetalation reductive elimination in the literature; see: (a) References 4g and 6c. (b) Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tasumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333–6340. (c) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619–4631. (d) Bäckvall, J. E.; Gogoll, A. *Tetrahedron Lett.* **1988**, *29*, 2243–2246. (e) Kálmán, K. J. *Organometallics* **1998**, *17*, 1677–1686.

(25) (a) Molander, G. A.; Cavalcanti, L. N.; Canturk, B.; Pan, P.-S.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 7364–7369. (b) Ting, R.; Harwing, C. W.; Lo, J.; Li, Y.; Adam, M. J.; Ruth, T. J.; Perrin, D. M. *J. Org. Chem.* **2008**, *73*, 4662–4670.

(26) Starting materials **1** and **4a−g** can be synthesized by following the literature procedure: D'Angelo, N. D.; Peterson, J. J.; Booker, S. K.; Fellows, I.; Dominguez, C.; Hungate, R.; Reider, P. J.; Kim, T.-S. *Tetrahedron Lett.* **2006**, *47*, 5045–5048.

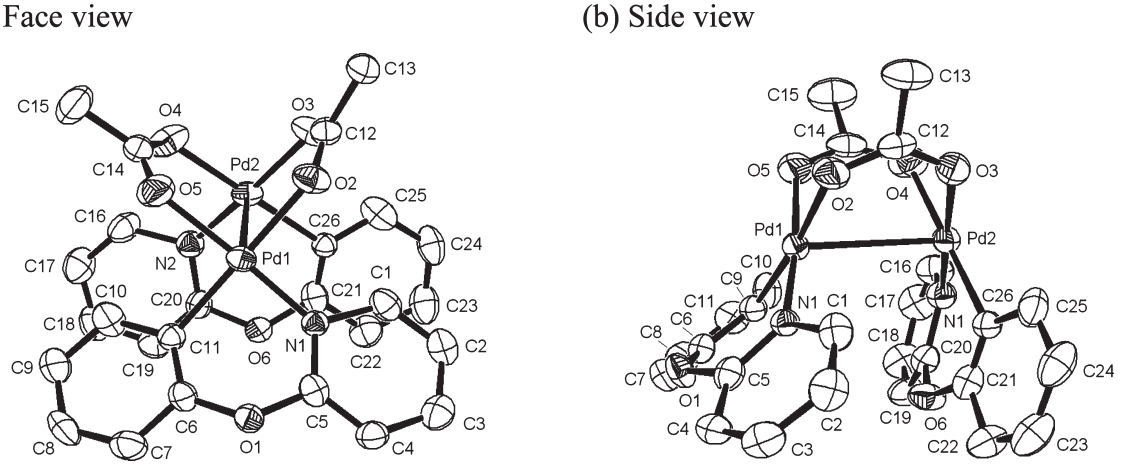


Figure 2. (a) Face view and (b) side view of ORTEP drawing of 2-phenoxypyridine palladacycle **I**. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Pd1−Pd2 = 2.9122(13); Pd1−N1 = 1.896(14); Pd1−C11 = 2.08(3); Pd1−O2 = 2.099(4); Pd1−O5 = 2.097(4); Pd2−N2 = 1.907(17); Pd2−C26 = 2.138(17); Pd2−O3 = 2.110(4); Pd2−O4 = 2.090(4).

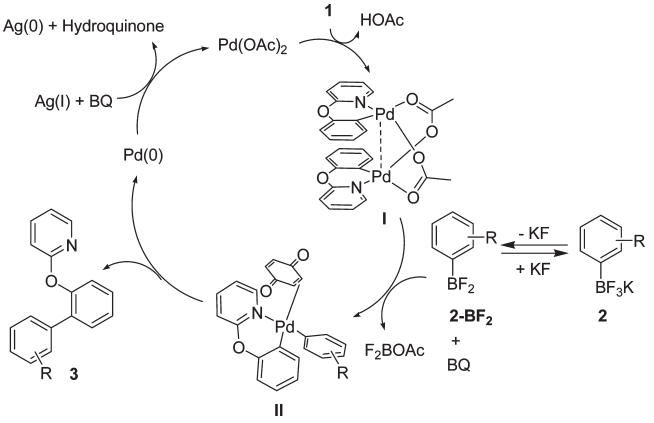


Figure 3. Proposed mechanism of palladium(II)-catalyzed 2-phenoxypyridine (**1**) with potassium aryltrifluoroborates **2**.

variety of phenols (344 mg, 3.66 mmol for **1**; 141 mg, 1.50 mmol for **4a**; 527 mg, 3.66 mmol for **4b**,**c**; 710 mg, 3.66 mmol for **4d**; 454 mg, 3.66 mmol for **4e**; 395 mg, 3.66 mmol for **4f**; 501 mg, 3.66 mmol for **4g**), copper powder (16 mg, 0.24 mmol for **1** and **4b**−**g**; 6.4 mg, 0.1 mmol for **4a**), and cesium carbonate (2.39 g, 7.32 mmol for **1** and **4b**−**g**; 978 mg, 3.00 mmol for **4a**) in *N*,*N*-dimethylformamide (5 mL) was heated at 100 °C for 18 h. After cooling to room temperature, water (20 mL) was added into the solution, and the solution was further extracted by dichloromethane (15 mL × 3). The organic layer was dried over MgSO4, filtered, and evaporated under vacuum. The residue was further purified by silica gel chromatography using *n*-hexane/ethyl acetate (35/1 to 20/1) as eluent to give **1** and **4a**−**g**. All yields are as follows: **1**, 91% (380 mg, 2.22 mmol); **4a**, 85% (188 mg, 0.850 mmol); **4b**, 70% (377 mg, 1.71 mmol); **4c**, 88% (475 mg, 2.15 mmol); **4d**, 40% (264 mg, 0.970 mmol); **4e**, 85% (427 mg, 2.13 mmol); **4f**, 85% (384 mg, 2.10 mmol); **4g**, 15% (78.8 mg, 0.365 mmol).

General Procedure for Synthesis of *ortho*-Arylated 2-Phenoxypyridine Derivatives 3a−m. A well-stirred solution of 2-phenoxypyridine (15 mg, 0.088 mmol) with potassium aryltrifluoroborates (2.5 equiv), Ag_2CO_3 (2 equiv), BQ (1 equiv), DMSO (4 equiv), and H_2O (8 or 0 equiv) using 10 mol % $Pd(OAc)_2$ as a catalyst in dry CH_2Cl_2 (5 mL) was heated at 130−140 °C for 48 h (note: a Teflon container sealed with a steel cylinder is used). After cooling to room temperature, the crude solution was filtered through a pad of Celite and washed by water (5 mL × 2). The aqueous layer was then extracted by dichloromethane (5 mL × 2), and 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 (20/1 to 5/1) as the eluent to give a series of *ortho*-arylated 2-phenoxypyridines, **3a**−**m**. All yields are as follows: **3a**, 63% (14 mg, 0.055 mmol); **3b**, 95% (25 mg, 0.084 mmol); **3c**, 90% (23 mg, 0.079 mmol); **3d**, 75% (18 mg, 0.066 mmol); **3e**, 80% (19 mg, 0.070 mmol); **3f**, 50% (13 mg, 0.044 mmol); **3g**, 65% (19 mg, 0.057 mmol); **3h**, 41% (14 mg, 0.036 mmol); **3i**, 48% (13 mg, 0.042 mmol); **3j**, 40% (9.2 mg, 0.035 mmol); **3k**, 34% (8.3 mg, 0.030 mmol); **3l**, 18% (4.8 mg, 0.016 mmol); **3m**, 0% (0 mg, 0 mmol). The general procedure for the synthesis of pyridine derivatives **5a**−**g** was the same as that of *ortho*-arylated pyridine derivatives **3a**−**m**. The amounts used of pyridine derivatives **4a**−**g** are as follows: **4a**, 15 mg, 0.068 mmol; **4b**, 15 mg, 0.068 mmol; **4c**, 15 mg, 0.068 mmol; **4d**, 15 mg, 0.055 mmol; **4e**, 15 mg, 0.075 mmol; **4f**, 15 mg, 0.081 mmol; **4g**, 15 mg, 0.069 mmol. All yields are as follows (note: three equivalents of potassium 4-formylphenyl trifluoroborate **2d** was used): **5a**, 73% (16 mg, 0.050 mmol); **5b**, 43% (9.4 mg, 0.029 mmol); **5b′**, 18% (4.2 mg, 0.012 mmol); **5b″**, 11% (3 mg, 0.007 mmol); **5c**, 84% (19 mg, 0.057 mmol); **5d**, 61% (13 mg, 0.034 mmol); **5e**, 29% (6.9 mg, 0.023 mmol); **5f**, 34% (8.0 mg, 0.027 mmol); **5g**, 0% (0 mg, 0 mmol).

General Procedure for Synthesis of 2-(4′-Nitrophenyl) Phenol (6b). To a well-stirred solution of compound **3b** (36 mg, 0.13 mmol) in dry toluene (5 mL) was added MeOTf (21 μL, 0.19 mmol) at 100 °C for 2 h under nitrogen gas. After cooling to room temperature, the solution was evaporated under vacuum. Without purification, the crude product was subsequently added into a Na (73.9 mg, 3.21 mmol)/MeOH (5 mL) solution, heated to reflux, and stirred for a further 15 min. After cooling to room temperature, the solvent was evaporated under vacuum and water (15 mL) was added to the residue. The aqueous solution was extracted by ethyl acetate (10 mL × 3), and the organic layers were combined, dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was further purified by silica gel chromatography using *n*-hexane/ethyl acetate (20/1 to 5/1) as the eluent to give 2-(4′-nitrophenyl) phenol (**6b**) (22.1 mg, 0.103 mmol) in 79% yield.

2-(Biphenyl-2-yloxy)pyridine (3a): colorless, viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74 (d, J = 9.0 Hz, 1 H), 6.88 (dd, J = 7.2, 5.4 Hz, 1 H), 7.18 (dd, J = 8.1, 1.1 Hz, 1 H), 7.26−7.42 (m, 5 H), 7.45−7.49 (m, 3 H), 7.56 (td, J = 7.2, 2.1 Hz, 1 H), 8.11 (dd, J = 4.8, 1.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.3 (CH), 118.0 (CH), 122.6 (CH), 125.3 (CH), 127.1 (CH), 128.0 (CH × 2), 128.6 (CH), 129.1 (CH × 2), 131.2 (CH), 134.7 (Cq), 137.8 (Cq), 139.2

(CH), 147.6 (CH), 150.9 (Cq), 163.8 (Cq); MS (EI, *m*/*z*) 247 (M^+, 9), 246 ($M^+ - H^+$, 17), 230 (13), 84 (100), 47 (17); HRMS *m*/*z* calcd for $C_{17}H_{13}NO$ 247.0997, found 247.1001.

2-(4′-Nitrobiphenyl-2-yloxy)pyridine (3b): pale yellow solid; mp 76−77 °C; R_f = 0.43 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (d, J = 8.1 Hz, 1 H), 6.92 (dd, J = 8.1, 4.5 Hz, 1 H), 7.21 (d, J = 8.1 Hz, 1 H), 7.31−7.36 (m, 1 H), 7.44−7.50 (m, 2 H), 7.60 (td, J = 8.4, 2.1 Hz, 1 H), 7.65 (d, J = 8.7 Hz, 2 H), 8.09 (dd, J = 4.8, 1.8 Hz, 1 H), 8.16 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.4 (CH), 118.5 (CH), 122.9 (CH), 123.3 (CH × 2), 125.6 (CH), 129.9 (CH × 2), 130.1 (CH), 130.8 (CH), 132.5 (Cq), 139.5 (CH), 144.7 (Cq), 146.9 (Cq), 147.6 (CH), 151.0 (Cq), 163.3 (Cq); MS (EI, *m*/*z*) 292 (M^+, 71), 291 ($M^+ - H^+$, 100), 275 (63), 217 (46), 139 (32), 84 (78), 78 (32); HRMS *m*/*z* calcd for $C_{17}H_{12}N_2O_3$ 292.0848, found 292.0840.

2-(5′-Nitrobiphenyl-2-yloxy)pyridine (3c): pale yellow solid; mp 84−85 °C; R_f = 0.33 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (d, J = 8.7 Hz, 1 H), 6.91 (dd, J = 6.9, 5.4 Hz, 1 H), 7.23 (d, J = 7.8 Hz, 1 H), 7.32−7.37 (m, 1 H), 7.44−7.50 (m, 3 H), 7.60 (td, J = 6.6, 1.8 Hz, 1 H), 7.83 (d, J = 7.8 Hz, 1 H), 8.08−8.12 (m, 2 H), 8.37−8.38 (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 111.4 (CH), 118.5 (CH), 122.0 (CH), 122.9 (CH), 124.1 (CH), 125.6 (CH), 128.9 (CH), 129.9 (CH), 130.8 (CH), 132.3 (Cq), 135.2 (CH), 139.5 (CH + Cq), 147.6 (CH), 148.1 (Cq), 151.0 (Cq), 163.3 (Cq); MS (EI, *m*/*z*) 292 (M^+, 15), 291 ($M^+ - H^+$, 14), 88 (29), 70 (89), 61 (100); HRMS *m*/*z* calcd for $C_{17}H_{12}N_2O_3$ 292.0848, found 292.0855.

2′-(Pyridin-2-yloxy)biphenyl-4-carbaldehyde (3d): pale orange solid; mp 72−73 °C; R_f = 0.43 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (d, J = 8.1 Hz, 1 H), 6.89 (dd, J = 6.6, 5.7 Hz, 1 H), 7.20 (d, J = 8.1 Hz, 1 H), 7.30−7.35 (m, 1 H), 7.42−7.49 (m, 2 H), 7.57 (td, J = 8.1, 1.5 Hz, 1 H), 7.65 (d, J = 8.1 Hz, 2 H), 7.82 (d, J = 8.1 Hz, 2 H), 8.09 (d, J = 4.2 Hz, 1 H), 9.98 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 111.3 (CH), 118.3 (CH), 122.8 (CH), 125.4 (CH), 129.4 (CH × 2), 129.6 (CH), 129.7 (CH × 2), 130.9 (CH), 133.4 (Cq), 135.0 (Cq), 139.3 (CH), 144.2 (Cq), 147.6 (CH), 151.0 (Cq), 163.4 (Cq), 192.0 (CH); MS (EI, *m*/*z*) 275 (M^+, 61), 274 ($M^+ - H^+$, 100), 258 (81), 170 (27), 78 (19); HRMS *m*/*z* calcd for $C_{18}H_{13}NO_2$ 275.0946, found 275.0938.

2-(4′-Fluorobiphenyl-2-yloxy)pyridine (3e): colorless, viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74 (d, J = 8.4 Hz, 1 H), 6.89 (dd, J = 6.9, 5.4 Hz, 1 H), 6.95−7.01 (m, 2 H), 7.17 (dd, J = 8.1, 0.9 Hz, 1 H), 7.29−7.46 (m, 5 H), 7.57 (td, J = 8.6, 2.0 Hz, 1 H), 8.11 (dd, J = 5.0, 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.2 (CH), 114.9 (d, J_{C-F} = 21.2 Hz, CH x 2), 118.1 (CH), 122.7 (CH), 125.4 (CH), 128.8 (CH), 130.7 (d, J_{C-F} = 8.3 Hz, CH × 2), 131.1 (CH), 133.8 (Cq), 139.2 (CH), 147.6 (CH), 150.9 (Cq), 162.1 (d, J_{C-F} = 244.8 Hz, Cq), 163.6 (Cq); MS (EI, *m*/*z*) 265 (M^+, 11), 264 ($M^+ - H^+$, 19), 84 (100), 47 (17); HRMS *m*/*z* calcd for $C_{17}H_{12}NFO$ 265.0903, found 265.0901.

2-(4′-Chlorobiphenyl-2-yloxy)pyridine (3f): colorless, viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.75 (d, J = 8.4 Hz, 1 H), 6.90 (dd, J = 7.1, 5.4 Hz, 1 H), 7.17 (dd, J = 7.8, 0.9 Hz, 1 H), 7.26−7.37 (m, 3 H), 7.40−7.44 (m, 4 H), 7.58 (td, J = 7.5, 1.8 Hz, 1 H), 8.11 (dd, J = 5.0, 1.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 111.3 (CH), 118.2 (CH), 122.7 (CH), 125.4 (CH), 128.2 (CH × 2), 129.0 (CH), 130.4 (CH × 2), 131.0 (CH), 133.2 (Cq), 133.5 (Cq), 136.3 (Cq), 139.3 (CH), 147.6 (CH), 150.9 (Cq), 163.6 (Cq); MS (EI, *m*/*z*) 282 ($M^+ + 1$, 1), 291 ($M^+ - 2$, 3), 84 (100), 47 (23); HRMS *m*/*z* calcd for $C_{17}H_{12}{}^{35}ClNO$ 281.0607, found 281.0600.

2-(4′-Bromobiphenyl-2-yloxy)pyridine (3g): pale brown, viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (d, J = 8.7 Hz, 1 H), 6.90 (dd, J = 7.0, 5.4 Hz, 1 H), 7.17 (d, J = 8.1 Hz, 1 H), 7.29−7.44 (m, 7 H), 7.59 (td, J = 7.5, 1.8 Hz, 1 H), 8.11 (dd, J = 5.3, 1.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.3 (CH), 118.2 (CH), 121.4 (Cq), 122.8 (CH), 125.4 (CH), 129.0 (CH), 130.7 (CH × 2), 130.9 (CH), 131.2 (CH), 133.6 (Cq), 136.7 (Cq), 139.3 (CH), 147.6 (CH), 150.8 (Cq), 163.6 (Cq); MS (EI, *m*/*z*) 326 ($M^+ + 1$, 1), 324 ($M^+ - 1$, 1), 84 (100), 47 (20); HRMS *m*/*z* calcd for $C_{17}H_{12}{}^{79}BrNO$ 325.0102, found 325.0108.

2-(4′-Iodobiphenyl-2-yloxy)pyridine (3h): pale brown, viscous liquid; R_f = 0.40 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (d, J = 8.4 Hz, 1 H), 6.91 (dd, J = 6.6, 5.1 Hz, 1 H), 7.17 (d, J = 7.8 Hz, 1 H), 7.22 (d, J = 8.4 Hz, 2 H), 7.30 (d, J = 8.0 Hz, 1 H), 7.37−7.43 (m, 2 H), 7.59 (td, J = 7.8, 2.1 Hz, 1 H), 7.63 (d, J = 8.4 Hz, 2 H), 8.11 (dd, J = 5.4, 1.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 93.1 (Cq), 111.3 (CH), 118.3 (CH), 122.8 (CH), 125.4 (CH), 129.0 (CH), 130.9 (CH), 131.0 (CH x 2), 133.6 (Cq), 137.2 (CH × 2), 137.4 (Cq), 139.3 (CH), 147.6 (CH), 150.8 (Cq), 163.6 (Cq); MS (EI, *m*/*z*) 373 (M^+, 1), 84 (100), 47 (17); HRMS *m*/*z* calcd for $C_{17}H_{12}INO$ 372.9964, found 372.9967.

2-(4′-*tert*-Butylbiphenyl-2-yloxy)pyridine (3i): colorless, viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 9 H), 6.77 (d, J = 8.1 Hz, 1 H), 6.89 (dd, J = 7.1, 5.4 Hz, 1 H), 7.15 (dd, J = 8.1, 0.9 Hz, 1 H), 7.26−7.36 (m, 4 H), 7.41 (d, J = 8.4 Hz, 2 H), 7.47 (dd, J = 7.5, 1.8 Hz, 1 H), 7.57 (td, J = 7.4, 1.8 Hz, 1 H), 8.14 (dd, J = 5.1, 1.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.3 (CH_3 × 3), 34.5 (Cq), 111.5 (CH), 118.0 (CH), 122.5 (CH), 125.0 (CH × 2), 125.2 (CH), 128.3 (CH), 128.7 (CH × 2), 131.2 (CH), 134.4 (Cq), 134.7 (Cq), 139.1 (CH), 147.7 (CH), 149.9 (Cq), 151.1 (Cq), 163.9 (Cq); MS (EI, *m*/*z*) 303 (M^+, 10), 302 ($M^+ - H^+$, 12), 84 (100), 47 (24); HRMS *m*/*z* calcd for $C_{21}H_{21}NO$ 303.1623, found 303.1629.

2-(4′-Methylbiphenyl-2-yloxy)pyridine (3j): colorless, viscous liquid; R_f = 0.45 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 6.75 (d, J = 8.7 Hz, 1 H), 6.89 (dd, J = 7.1, 4.8 Hz, 1 H), 7.12 (d, J = 7.8 Hz, 2 H), 7.16 (dd, J = 7.8, 0.9 Hz, 1 H), 7.29 (dd, J = 7.7, 1.4 Hz, 1 H), 7.34−7.39 (m, 3 H), 7.46 (dd, J = 7.5, 1.8 Hz, 1 H), 7.56 (td, J = 7.2, 1.8 Hz, 1 H), 8.13 (dd, J = 4.8, 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 111.3 (CH), 118.0 (CH), 122.6 (CH), 125.3 (CH), 128.4 (CH), 128.8 (CH × 2), 128.9 (CH × 2), 131.2 (CH), 134.7 (Cq), 134.8 (Cq), 136.8 (Cq), 139.1 (CH), 147.6 (CH), 150.9 (Cq), 163.9 (Cq); MS (EI, *m*/*z*) 261 (M^+, 8), 260 ($M^+ - H^+$, 13), 244 (11), 84 (100), 47 (21); HRMS *m*/*z* calcd for $C_{18}H_{15}NO$ 261.1154, found 261.1148.

2-(4′-Methoxybiphenyl-2-yloxy)pyridine (3k): colorless, viscous liquid; R_f = 0.33 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3 H), 6.74 (d, J = 8.7 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 2 H), 6.88 (td, J = 8.0, 5.1 Hz, 1 H), 7.15 (dd, J = 7.8, 1.5 Hz, 1 H), 7.26−7.46 (m, 5 H), 7.56 (td, J = 7.5, 1.8 Hz, 1 H), 8.12 (dd, J = 4.8, 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2 (CH_3), 111.2 (CH), 113.5 (CH × 2), 118.0 (CH), 122.7 (CH), 125.4 (CH), 128.2 (CH), 129.9 (Cq), 130.2 (CH × 2), 131.1 (CH), 134.4 (Cq), 139.2 (CH), 147.6 (CH), 155.4 (Cq), 158.8 (Cq), 163.8 (Cq); MS (EI, *m*/*z*) 277 (M^+, 2), 291 ($M^+ - H^+$, 2), 84 (100), 47 (23); HRMS *m*/*z* calcd for $C_{18}H_{15}NO_2$ 277.1103, found 277.1108.

Methyl 2′-(pyridin-2-yloxy)biphenyl-2-carboxylate (3l): colorless, viscous liquid; R_f = 0.43 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (s, 3 H), 6.69 (d, J = 8.1 Hz, 1 H), 6.82 (dd, J = 6.9, 4.8 Hz, 1 H), 7.18 (d, J = 7.8 Hz, 1 H), 7.28−7.43 (m, 6 H), 7.49 (td, J = 8.1, 1.8 Hz, 1 H), 7.81 (d, J = 8.1 Hz, 1 H), 8.02 (dd, J = 4.8, 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.9 (CH_3), 111.4 (CH), 118.0 (CH), 121.6 (CH), 125.0 (CH), 127.2 (CH), 128.8 (CH), 129.6 (CH), 130.4 (CH), 131.0 (Cq), 131.3 (CH), 131.4 (CH), 134.4 (Cq), 138.2 (Cq), 139.0 (CH), 147.2 (CH), 150.7 (Cq), 163.2 (Cq), 168.4 (Cq); MS (EI, *m*/*z*) 305 (M^+, 1), 304 ($M^+ - H^+$, 2), 211 (14), 84 (100), 47 (18); HRMS *m*/*z* calcd for $C_{19}H_{15}NO_3$ 305.1052, found 305.1046.

2′-(Isoquinolin-1-yloxy)biphenyl-4-carbaldehyde (5a): white solid; mp 140−141 °C; R_f = 0.43 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.22 (d, J = 5.7 Hz, 1 H), 7.32−7.39 (m, 2 H), 7.46−7.58 (m, 3 H), 7.64−7.73 (m, 6 H), 7.87 (d, J = 6.0 Hz, 1 H), 8.27 (d, J = 8.4 Hz, 1 H), 9.88 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.4 (CH), 119.5 (Cq), 123.5 (CH), 123.9 (CH), 125.7 (CH), 126.2 (CH), 127.2 (CH), 129.4 (CH × 2), 129.6 (CH × 2), 130.8 (CH), 130.9 (CH), 133.7 (Cq), 134.9 (Cq), 138.3 (Cq), 139.6 (CH), 144.3 (Cq), 150.7 (Cq), 160.3 (Cq), 192.0 (CH); MS (EI, m/z) 325 (M^+, 66), 324 ($M^+ - H^+$, 37), 308 (100), 220 (32), 128 (18), 84 (13); HRMS m/z calcd for $C_{22}H_{15}NO_2$ 325.1103, found 325.1098.

4-(3-(Pyridin-2-yloxy)naphthalen-2-yl)benzaldehyde (5b): pale yellow solid; mp 148−149 °C; R_f = 0.45 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (d, J = 8.4 Hz, 1 H), 6.88 (t, J = 6.6 Hz, 1 H), 7.48−7.60 (m, 3 H), 7.65 (s, 1 H), 7.75 (d, J = 8.1 Hz, 2 H), 7.80−7.91 (m, 4 H), 7.95 (s, 1 H), 8.06 (dd, J = 4.8, 1.5 Hz, 1 H), 10.00 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.4 (CH), 118.4 (CH), 119.4 (CH), 125.9 (CH), 126.9 (CH), 127.2 (CH), 128.0 (CH), 129.5 (CH × 2), 130.0 (CH × 2), 130.6 (CH), 131.2 (Cq), 133.4 (Cq), 133.9 (Cq), 135.0 (Cq), 139.3 (CH), 144.4 (Cq), 147.6 (CH), 149.2 (Cq), 163.6 (Cq), 192.1 (CH); MS (EI, m/z) 325 (M^+, 2), 324 ($M^+ - H^+$, 2), 84 (100), 47 (21); HRMS m/z calcd for $C_{22}H_{15}NO_2$ 325.1103, found 325.1098.

4-(1-(Pyridin-2-yloxy)naphthalen-2-yl)benzaldehyde (5b′): brown, viscous liquid; R_f = 0.50 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (d, J = 8.1 HZ, 1 H), 6.91 (dd, J = 7.1, 5.0 Hz, 1 H), 7.36 (d, J = 9.0 Hz, 1 H), 7.41−7.58 (m, 6 H), 7.89 (d, J = 8.1 Hz, 2 H), 7.88−7.97 (m, 4 H), 8.10 (dd, J = 4.5, 1.8 Hz, 1 H), 10.05 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.3 (CH), 118.3 (CH), 122.0 (CH), 125.4 (CH × 2), 126.7 (CH), 128.3 (CH), 129.2 (Cq), 129.4 (CH × 2), 129.8 (CH), 131.4 (CH × 2), 133.0 (Cq), 135.3 (Cq), 139.3 (CH), 142.4 (Cq), 147.5 (CH), 148.3 (Cq), 163.8 (Cq), 192.1 (CH); MS (EI, m/z) 325 (M^+, 19), 324 ($M^+ - H^+$, 9), 220 (38), 84 (100), 47 (22); HRMS m/z calcd for $C_{22}H_{15}NO_2$ 325.1103, found 325.1099.

4,4′-(2-(Pyridin-2-yloxy)naphthalene-1,3-diyl)dibenzaldehyde (5b″): brown, viscous liquid; R_f = 0.30 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (d, J = 8.4 Hz, 1 H), 6.68 (dd, J = 7.1, 5.1 Hz, 1 H), 7.30 (td, J = 7.5, 1.8 Hz, 1 H), 7.41−7.56 (m, 5 H), 7.76 (d, J = 8.1 Hz, 2 H), 7.82 (d, J = 8.1 Hz, 2 H), 7.85−7.87 (m, 3 H), 7.97 (d, J = 7.8 Hz, 1 H), 8.01 (s, 1 H), 9.95 (s, 1 H), 10.03 (s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 110.8 (CH), 117.8 (CH), 125.5 (CH), 126.1 (CH), 127.2 (CH), 128.5 (CH), 129.3 (CH × 2), 129.4 (CH × 2), 130.0 (CH × 2), 130.7 (CH), 130.9 (Cq), 131.3 (CH × 2), 131.6 (Cq), 132.9 (Cq), 134.0 (Cq), 135.0 (Cq), 135.3 (Cq), 139.0 (CH), 142.4 (Cq), 144.4 (Cq), 145.7 (Cq), 146.9 (CH), 163.1 (Cq), 192.0 (CH), 192.1 (CH); MS (EI, m/z) 429 (M^+, 3), 207 (100), 91 (44); HRMS m/z calcd for $C_{29}H_{19}NO_3$ 429.1365, found 429.1359.

4-(2-(Pyridin-2-yloxy)naphthalen-1-yl)benzaldehyde (5c): pale yellow solid; mp 131−132 °C; R_f = 0.45 (*n*-hexane/ethyl acetate, 5/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (d, J = 8.4 Hz, 1 H), 6.82 (dd, J = 6.8, 5.7 Hz, 1 H), 7.47−7.60 (m, 4 H), 7.73 (d, J = 8.4 Hz, 2 H), 7.83 (d, J = 8.4 Hz, 2 H), 7.87 (d, J = 8.4 Hz, 1 H), 7.91−7.98 (m, 3 H), 9.98 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.1 (CH), 118.0 (CH), 122.7 (CH), 126.0 (CH), 126.8 (CH), 127.6 (CH), 128.0 (CH), 128.1 (Cq), 129.5 (CH × 2), 129.7 (Cq), 130.0 (CH × 2), 134.7 (Cq), 134.9 (Cq), 139.3 (CH), 144.6 (Cq), 146.2 (Cq), 147.7 (CH), 163.7 (Cq), 192.0 (CH); MS (EI, m/z) 325 (M^+, 85), 324 ($M^+ - H^+$, 71), 308 (100), 296 (29), 220 (55), 189 (40), 84 (33); HRMS m/z calcd for $C_{22}H_{15}NO_2$ 325.1103, found 325.1107.

4-(10-(Pyridin-2-yloxy)phenanthren-9-yl)benzaldehyde (5d): white solid; mp (dec) 171−172 °C; R_f = 0.33 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 (d, J = 8.1 Hz, 1 H), 6.84 (dd, J = 7.1, 4.7 Hz, 1 H), 7.47−7.41 (m, 8 H), 7.86 (d, J = 8.4 Hz, 2 H), 7.96−7.98 (m, 2 H), 8.78 (d, J = 8.4 Hz, 2 H), 10.03 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.2 (CH), 118.0 (CH), 122.9 (CH × 2), 123.4 (CH), 126.3 (CH), 126.5 (CH), 127.0 (CH), 127.2 (CH), 127.3 (Cq), 127.4 (CH), 128.0 (Cq), 129.1 (Cq), 129.4 (CH × 2), 131.3 (CH × 2), 131.6 (Cq), 131.7 (Cq), 135.3 (Cq), 139.2 (CH), 142.9 (Cq), 144.8 (Cq), 147.5 (CH), 163.9 (Cq), 192.1 (CH); MS (EI, m/z) 375 (M^+, 18), 374 ($M^+ - H^+$, 9), 270 (29), 84 (100); HRMS m/z calcd for $C_{26}H_{17}NO_2$ 375.1259, found 375.1266.

5′-Methoxy-2′-(pyridin-2-yloxy)biphenyl-4-carbaldehyde (5e): colorless, viscous liquid; R_f = 0.18 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3 H), 6.73 (d, J = 8.4 Hz, 1 H), 6.86 (dd, J = 6.9, 5.4 Hz, 1 H), 6.96−7.00 (m, 2 H), 7.14 (d, J = 9.6 Hz, 1 H), 7.54 (td, J = 7.8, 2.0 Hz, 1 H), 7.64 (d, J = 8.1 Hz, 2 H), 7.80 (d, J = 8.1 Hz, 2 H), 8.07 (dd, J = 4.8, 1.8 Hz, 1 H), 9.97 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6 (CH_3), 110.9 (CH), 114.9 (CH), 115.7 (CH), 124.0 (CH), 129.5 (CH × 2), 129.6 (CH × 2), 134.3 (Cq), 135.0 (Cq), 139.2 (CH), 144.1 (Cq), 144.2 (Cq), 147.5 (CH), 156.8 (Cq), 163.8 (Cq), 192.0 (CH); MS (EI, m/z) 305 (M^+, 8), 304 ($M^+ - H^+$, 10), 84 (100), 47 (23); HRMS m/z calcd for $C_{19}H_{15}NO_3$ 305.1052, found 305.1045.

5′-Methyl-2′-(pyridin-2-yloxy)biphenyl-4-carbaldehyde (5f): colorless, viscous liquid; R_f = 0.33 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 6.75 (d, J = 8.4 Hz, 1 H), 6.87 (dd, J = 7.1, 5.4 Hz, 1 H), 7.10 (d, J = 8.1 Hz, 1 H), 7.24−7.28 (m, 2 H), 7.56 (td, J = 7.8, 1.8 Hz, 1 H), 7.64 (d, J = 8.1 Hz, 2 H), 7.81 (d, J = 8.1 Hz, 2 H), 8.09 (dd, J = 5.3, 1.7 Hz, 1 H), 9.97 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9 (CH_3), 111.2 (CH), 118.1 (CH), 122.8 (CH), 129.5 (CH × 2), 129.7 (CH × 2), 130.3 (CH), 131.4 (CH), 133.1 (Cq), 134.9 (Cq), 135.2 (Cq), 139.3 (CH), 144.4 (Cq), 147.6 (CH), 148.6 (Cq), 163.7 (Cq), 192.0 (CH); MS (EI, m/z) 289 (M^+, 17), 288 ($M^+ - H^+$, 29), 272 (23), 84 (100), 47 (24); HRMS m/z calcd for $C_{19}H_{15}NO_2$ 289.1103, found 289.1092.

2-Phenoxypyridine palladacycle I:[23] yellow crystal; mp (dec) > 210 °C (lit. mp 226−228 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 6 H), 6.59−6.68 (m, 6 H), 6.81−6.90 (m, 6 H), 7.54 (td, J = 8.0, 1.5 Hz, 2 H), 8.03 (dd, J = 6.2, 1.7 Hz, 2 H).

2-(2′-Deutero)phenoxypyridine (1-D): colorless, viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92−7.25 (m, 4 H), 7.39−7.45 (m, 2 H), 7.67−7.73 (m, 1 H), 8.22 (dd, J = 5.0, 2.1 Hz, 1 H).

2-(4′-Nitrophenyl)phenol (6b):[27] yellow solid; mp 107−108 °C; R_f = 0.24 (*n*-hexane/ethyl acetate, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (bs, 1 H), 6.95 (dd, J = 8.7, 1.2 Hz, 1 H), 7.05 (td, J = 7.8, 1.2 Hz, 1 H), 7.29−7.34 (m, 2 H), 7.73 (d, J = 8.9 Hz, 2 H), 8.31 (d, J = 8.9 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.5 (CH), 121.5 (CH), 123.8 (CH × 2), 126.2 (Cq), 130.1 (CH × 2), 130.3 (CH), 130.5 (CH), 144.6 (Cq), 147.3 (Cq), 152.5 (Cq); MS (EI, m/z) 215 (M^+, 100), 185 (23), 168 (30), 141 (36), 115 (43); HRMS m/z calcd for $C_{12}H_9NO_3$ 215.0582, found 215.0574.

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Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

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