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Catalytic Electrochemical C−H Iodination and One-Pot Arylation by ON/OFF Switching of Electric Current

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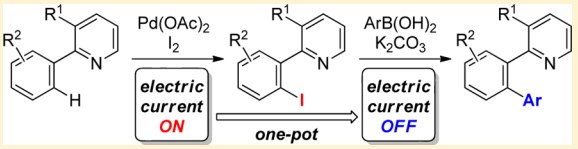
Supporting Information

ABSTRACT: Palladium-catalyzed electrochemical iodination and one-pot arylation of arylpyridines are described. Ortho-selective C−H iodination proceeded via dual activation of each substrate by a palladium catalyst and an electrode. Various aryl groups were introduced at the ortho positions of arylpyridines by ON/OFF switching of two different catalytic cycles using the same palladium catalyst in a one-pot fashion.



Metal-catalyzed cross-coupling between aryl halides and organometallic reagents is one of the most important methods for efficient synthesis of functionalized aromatic compounds.[1] However, these methods require preinstallation of reactive carbon−halogen bonds precisely at the bond-forming sites, which may become cumbersome depending on the substrate structure. In this context, catalytic regioselective halogenation of arenes via chelation-assisted C−H bond cleavage has attracted much attention in recent years.[2−5] Our group has reported that ortho-selective chlorination and bromination of arenes proceeds using a combination of palladium-catalyzed C−H bond cleavage and electrochemical oxidation.[6,7] Because halonium ions can be generated in situ as active halogenating agents from inexpensive, stable aqueous HCl and HBr solutions, the reaction does not require the addition of more than 1 equiv of halogenating agents with strong oxidizing ability. This method offers relatively clean environments in the reaction vessels because generation of the halogenating agent can be halted by simply turning off the electricity.

The controllability of generation of halogenating agents led us to investigate one-pot halogenation/cross-coupling reaction (Figure 1). The palladium-catalyzed electrochemical C−H halogenation is considered to proceed via a Pd(II)/Pd(IV) or Pd(II)/Pd(III) catalytic cycle (Cycle A).[2a,4,8,9] A palladacycle formed after chelation-assisted C−H bond cleavage reacts with an electrochemically generated halonium ion to provide aryl halides. After the halogenation, if the electricity is turned off, the formation of unstable halonium ions would stop, allowing the reaction system to be free of strong oxidants. Therefore, we speculated that it would become possible to generate Pd(0) species,[10] which can cleave the newly formed carbon−halogen bonds and may be further used for cross-coupling reactions such as widely applicable Suzuki−Miyaura coupling (Cycle B). In this way, ON/OFF switching of electricity may be used to employ a palladium catalyst for two different catalytic cycles, a Pd(II)/Pd(IV) or Pd(II)/Pd(III) cycle[9] and a Pd(0)/Pd(II) cycle, in an one-pot fashion.

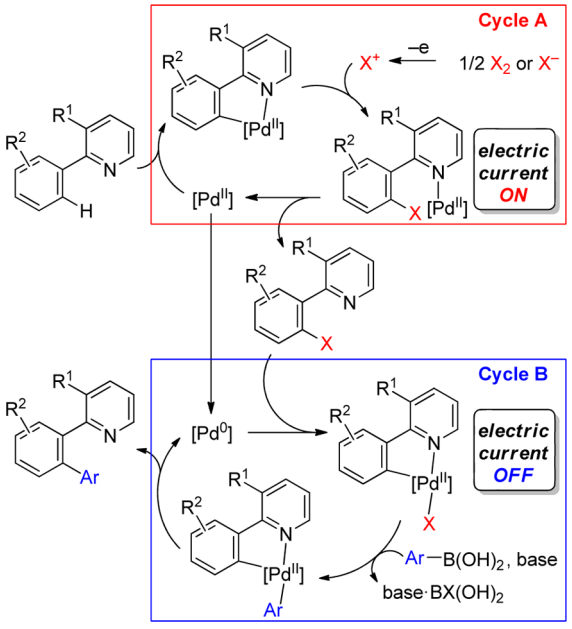


Figure 1. One-pot C−H halogenation/Suzuki−Miyaura coupling by ON/OFF switching of electric current.

To achieve this goal, we first developed a palladium-catalyzed electrochemical *ortho*-selective iodination of arenes, because carbon−iodine bonds are regarded as the most reactive carbon−halogen bonds in cross-coupling. By applying this iodination method, we succeeded in one-pot Suzuki−Miyaura

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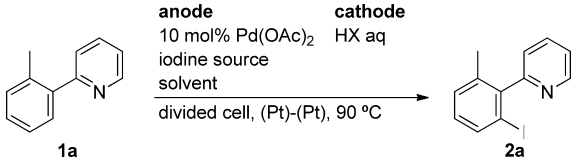
coupling, which enables the introduction of various aryl groups at ortho-positions.

We initiated our efforts to develop catalytic electrochemical C−H iodination by screening reaction conditions using 2-(*o*-tolyl)pyridine (**1a**) as a substrate. As an initial attempt, aqueous HI solution, instead of an HCl or HBr solution, was used under the previously reported electrochemical C−H halogenation conditions,[6] but the desired iodination product **2a** was not observed (Table 1, entry 1). Next, separate addition of iodine source and electrolyte was considered. When potassium iodide and sulfuric acid, both stable, inexpensive reagents, were used as an iodine source and an electrolyte, the iodination reaction proceeded and aryl iodide **2a** was obtained. When 2 equiv of potassium iodide was used with a 10 mA electric current, **2a** was obtained in 71% yield, but 5.5 h and 8.2 F/mol of electricity were necessary to complete the reaction (entry 2). Although increase of the amount of potassium iodide led to improvement in yield, it did not reduce the reaction time nor the amount of electricity (entry 3). Decrease of the electric current to 5 mA further elongated the reaction time (entry 4).

Table 1. Optimization of Palladium-Catalyzed Electrochemical Ortho C−H Iodination of Arylpyridine 1a[a]



entry	iodine source	HX	*I* (mA)	time (h)	F/mol	yield (%)
1	-	HI[b]	20	9.0	27	nd[c]
2	2 equiv KI	H_2SO_4	10	5.5	8.2	71
3	4 equiv KI	H_2SO_4	10	7.0	10	85
4	4 equiv KI	H_2SO_4	5	10.5	7.8	83
5	2 equiv I_2	H_2SO_4	5	3.5	2.6	88
6	2 equiv I_2	H_2SO_4	5	4.5	3.4	89
7	1 equiv I_2	H_2SO_4	5	4.5	3.4	79
8	2 equiv I_2	H_2SO_4	2.5	5.5	2.1	88

[a]Reaction conditions: **1a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), iodine source, acetonitrile (10 mL) [anode], and 0.2 M H_2SO_4 aq [cathode] in an H-type divided cell with two platinum electrodes and an anion-exchange membrane, 90 °C. [b]A 2 M aqueous solution of HI was used. [c]Not detected.

Electrochemical C−H iodination using potassium iodide was taken under close examination by GC, and it revealed that there were induction periods prior to the initiation of the iodination reaction (Figure 2). When the reaction was carried out with 2 equiv of potassium iodide and a 10 mA electric current, the desired product was not observed until the electricity was passed for 1.5 h, which means that more than 2 F/mol of electricity was consumed (ca. 2.2 F/mol). When 4 equiv of potassium iodide was used with a 10 or 5 mA electric current, the observed induction periods were 2.5 or 5 h, respectively, which corresponds to ca. 4 F/mol of electricity in each case. These results show that there is a strong correlation between the amounts of potassium iodide and the electricity consumed during the induction period, which essentially matches the time required to convert all the iodide ion to I_2 (1 F/mol is necessary for the conversion of 1 equiv of iodide ion to 0.5 equiv of I_2).

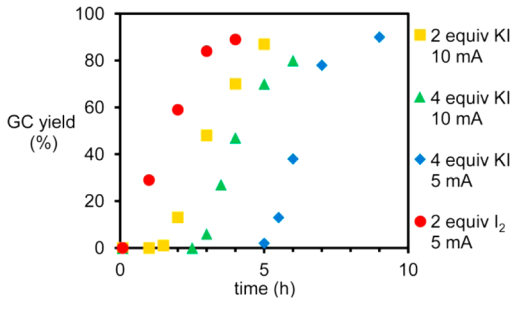
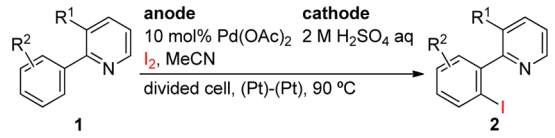


Figure 2. Plot of yield of **2a** versus time.

The results of the GC monitoring led us to examine the electrochemical C−H iodination using I_2 as an iodine source (Table 1, entries 5−8). As expected, when the reaction was performed with 2 equiv of I_2 and a 5 mA electric current, no induction period was observed and **2a** was obtained in 88% yield using only 2.6 F/mol of electricity (entry 5).[11] The result suggests that iodonium ion, generated from I_2 by electrochemical oxidation, is the active iodinating agent in the C−H iodination. Yoshida and co-workers have reported the electrochemical generation of iodonium ion in acetonitrile, and applied it for electrophilic iodination of arenes.[12,13] Extension of the reaction time to 4.5 h slightly improved the product yield to 89% (entry 6). The electrochemical C−H iodination can also be performed with 1 equiv of I_2 to afford 79% yield of **2a** (entry 7). When the reaction was conducted with a 2.5 mA electric current, the reaction became slower (see the Supporting Information) but 88% yield of **2a** was obtained using only 2.1 F/mol of electricity (entry 8). As a result, the reaction conditions using 2 equiv of I_2 with a 5 mA electric current were chosen as standard conditions for the screening of substrates.

The electrochemical C−H iodination was then investigated using various arylpyridines (Table 2). The reaction of arylpyridine **1b** bearing an electron-withdrawing trifluoromethyl group at an ortho position for 11 h at a 10 mA provided iodination product **2b** in 79% yield (entry 1). The C−H iodination is also applicable to substrates with a 3-methyl-2-

Table 2. Palladium-Catalyzed Electrochemical Ortho C−H Iodination of Arylpyridines[a]



entry	1	R^1	R^2	*I* (mA)	time (h)	F/mol	2	yield (%)
1[b]	**1b**	H	*o*-CF_3	10	11	16	**2b**	79
2	**1c**	Me	H	5	4	3.0	**2c**	70
3	**1d**	Me	*p*-Me	5	5	3.7	**2d**	85
4	**1e**	Me	*m*-Me	5	3.5	2.6	**2e**	75
5[c]	**1f**	Me	*p*-F	5	10.5	7.8	**2f**	61
6[b]	**1g**	Me	*p*-CF_3	10	11	16	**2g**	70
7[d]	**1h**	Me	*m*-CF_3	5	9.5	7.1	**2h**	64

[a]Reaction conditions: **1** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), I_2 (2 equiv), acetonitrile (10 mL) [anode], and 0.2 M H_2SO_4 aq [cathode] in an H-type divided cell with two platinum electrodes and an anion-exchange membrane, 90 °C, 5 mA. [b]Performed with 8 equiv of I_2 at 10 mA. [c]Performed with 4 equiv of I_2. [d]Performed with 20 mol % of $Pd(OAc)_2$ and 10 equiv of I_2.

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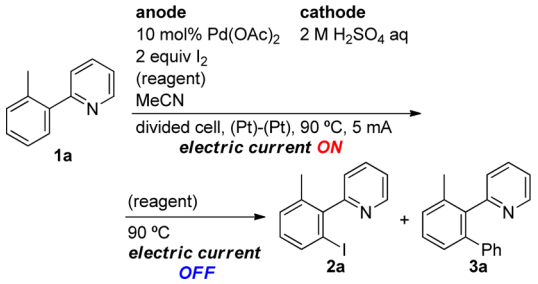
pyridyl directing group. 3-Methyl-2-phenylpyridine (**1c**) possesses two ortho hydrogens, but only the less hindered one was iodinated to give **2c** in 70% yield (entry 2). Substrates with *p*- and *m*-tolyl groups (**1d**,**e**) also gave monoiodination product **2d** and **2e** in 85 and 75% yields, respectively (entries 3 and 4). Arylpyridines with fluoro and trifluoromethyl groups (**1f**–**h**) required more forcing conditions, but the corresponding monoiodination products **2f**–**h** were obtained in 61–70% yields (entries 5–7). Further investigation on the substrates showed that a substituent at the 3-position of the pyridine ring or the ortho position on the benzene ring was necessary to achieve high yield of the iodination product by our catalytic electrochemical C–H iodination.

Next, we examined the one-pot electrochemical C–H iodination/Suzuki–Miyaura coupling (Table 3). As an initial attempt, electrochemical C–H iodination was performed in the presence of phenylboronic acid, but only iodination proceeded to give **2a** in 85% yield, and no arylation product was observed (entry 1). With the former result in hand, electrochemical C–H iodination was performed in the same manner with phenylboronic acid, and then the generation of iodonium ion was stopped by turning off the electricity, and the mixture was heated for an additional 2 h, only to give **2a** in a similar yield (entry 2). An experiment following the same protocol except that phenylboronic acid was added after the electric current was halted also gave a similar result (entry 3). Addition of a base was then investigated because bases are generally necessary for Suzuki–Miyaura coupling to proceed.[1a,b,14] Finally, electrochemical C–H iodination, followed by addition of phenyl boronic acid and potassium carbonate and heating without supplying additional electric current, provided phenylation product **3a** in 84% yield (entry 4).[15,16] No remaining **2a** was observed in this case. Phenylboronic acid can also be present in the reaction system from the start of the one-pot process (entry 5). The C–H iodination in the presence of phenylboronic acid, followed by addition of potassium carbonate, also gave **3a** in 78% yield.

This one-pot electrochemical C–H iodination/arylation process can be performed with various substrates (Table 4).

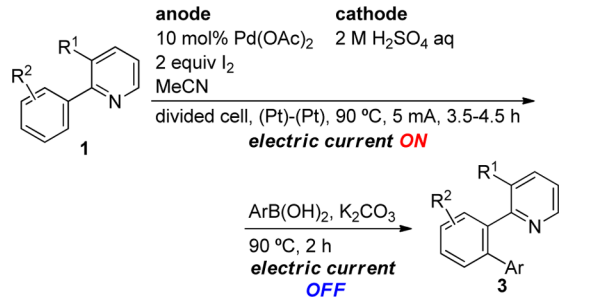
Table 3. Optimization of Palladium-Catalyzed Electrochemical Ortho C–H Iodination of Arylpyridine 1a[a]



	electric current ON		electric current OFF		yields (%)	
entry	reagent	time (h)	reagent	time (h)	**2a**	**3a**
1	$PhB(OH)_2$	4.5	-	-	85	nd[b]
2	$PhB(OH)_2$	4.5	-	2	84	nd[b]
3	-	4.5	$PhB(OH)_2$	2	86	nd[b]
4	-	4.5	$PhB(OH)_2$, K_2CO_3	2	nd[b]	84[c]
5	$PhB(OH)_2$	4.5	K_2CO_3	2	nd[b]	78[c]

[a]Reaction conditions: **1a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), I_2 (0.5 mmol), acetonitrile (10 mL), $PhB(OH)_2$ (0.75 mmol, if added) [anode], and 0.2 M H_2SO_4 aq [cathode] in an H-type divided cell with two platinum electrodes and an anion-exchange membrane, 90 °C, 5 mA, 4.5 h, and then $PhB(OH)_2$ (0.75 mmol, if added) and K_2CO_3 (0.75 mmol, if added) [anode], and K_2CO_3 (2.5 mmol, if added) [cathode], 90 °C, 2 h without electric current. [b]Not detected. [c]Yield determined by the ^1H NMR integral ratio of the purified material.

Table 4. One-Pot Ortho C–H Iodination/Arylation of Arylpyridines[a]



entry	**1**	R^1	R^2	Ar	**3**	yield (%)
1	**1c**	Me	H	Ph	**3b**	70
2	**1d**	Me	*p*-Me	Ph	**3c**	84
3	**1e**	Me	*m*-Me	Ph	**3d**	73
4	**1a**	H	*o*-Me	*o*-MeC_6H_4	**3e**	67
5	**1a**	H	*o*-Me	*m*-MeC_6H_4	**3f**	81
6	**1a**	H	*o*-Me	*p*-MeC_6H_4	**3g**	76
7	**1a**	H	*o*-Me	*p*-^{n}PentC_6H_4	**3h**	74
8	**1a**	H	*o*-Me	*p*-^{i}PrC_6H_4	**3i**	69
9	**1a**	H	*o*-Me	*p*-^{t}BuC_6H_4	**3j**	82
10	**1a**	H	*o*-Me	*p*-$MeOC_6H_4$	**3k**	63
11	**1d**	Me	*p*-Me	*p*-$MeOC_6H_4$	**3l**	66
12	**1a**	H	*o*-Me	*p*-FC_6H_4	**3m**	63
13	**1a**	H	*o*-Me	*p*-$CF_3C_6H_4$	**3n**	53
14	**1a**	H	*o*-Me	*p*-BrC_6H_4	**3o**	58

[a]Reaction conditions: **1a** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), I_2 (0.5 mmol), acetonitrile (10 mL) [anode], and 0.2 M H_2SO_4 aq [cathode] in an H-type divided cell with two platinum electrodes and an anion-exchange membrane, 90 °C, 5 mA, 3.5–4.5 h, and then $ArB(OH)_2$ (0.75 mmol) and K_2CO_3 (0.75 mmol) [anode], and K_2CO_3 (2.5 mmol) [cathode], 90 °C, 2 h without electric current.

Arylpyridines **1c**–**e** were phenylated to give **3b**–**d** in high yields (entries 1–3). Introduction of *o*-, *m*-, and *p*-tolyl groups to **1a** can be conducted to provide arylation products **3e**–**g** in high yields (entries 4–6). Particularly, *o*-tolylboronic acid has not been reported to be used for the direct C–H arylation of arylpyridines.[17] In addition to methyl group, arylboronic acids bearing *n*-pentyl, isopropyl, and *tert*-butyl substituents were also used for the one-pot arylation, and the corresponding products **3h**–**j** were obtained in 69–82% yields (entries 7–9). Both electron-donating and -withdrawing groups such as methoxy, trifluoromethyl, and fluoro groups were tolerated to give the arylation products **3k**–**n** (entries 10–13). The one-pot arylation using *p*-bromophenylboronic acid was also possible, and the corresponding arylation product **3o** bearing a bromo group was obtained in 58% yield (entry 14).

In summary, palladium-catalyzed electrochemical iodination and one-pot arylation of arylpyridines were achieved. Using I_2 as an iodine source, ortho-selective C–H iodination proceeded via dual activation of each substrate by a palladium catalyst and an electrode. Various aryl groups were introduced at the ortho-

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positions of arylpyridines by the one-pot arylation process, taking advantage of the wide generality of Suzuki−Miyaura coupling. The ON/OFF switching of two different catalytic cycles, a Pd(II)/Pd(IV) or Pd(II)/Pd(III) cycle and a Pd(0)/Pd(II) cycle, was also accomplished using the same palladium catalyst in a one-pot fashion. This one-pot arylation method employs only simple, easily accessible reagents and may be regarded as a convenient way to obtain arylation products.

EXPERIMENTAL SECTION

General Procedure A for Electrochemical Iodination using I_2. The electrochemical oxidation was carried out in an H-type divided cell (anion-exchange membrane) equipped with two platinum electrodes (1.7 × 1.7 cm^2). The anodic chamber was charged with a solution of arylpyridine (0.25 mmol), I_2 (0.50 mmol), and palladium acetate (0.025 mmol) in acetonitrile (10 mL). A 0.2 M aqueous solution (10 mL) of sulfuric acid was introduced into the cathodic chamber. An electric field was applied at 90 °C under a 5 or 10 mA constant current condition, and the mixture in the anodic chamber was stirred. After the reaction, the mixture was quenched with an aqueous solution of K_2CO_3 and was extracted with EtOAc or Et_2O. The obtained organic portions were washed with saturated $Na_2S_2O_3$ and then with brine. The resulting solution was dried over anhydride Na_2SO_4 or $MgSO_4$ and concentrated. The iodination product was isolated by flash column chromatography.

2-(2-Iodo-6-methylphenyl)pyridine (2a). General procedure A was followed with 42.3 mg (0.250 mmol) of 2-(*o*-tolyl)pyridine (**1a**), prepared according to the procedure reported by Kumada and co-workers,[18] and the reaction was carried out under a 5 mA constant current condition for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 65.4 mg of **2a** (0.222 mmol, 89% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 6.98 (t, J = 7.8 Hz, 1H), 7.19−7.26 (m, 2H), 7.26−7.33 (m, 1H), 7.27−7.83 (m, 2H), 8.73 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 98.6, 122.4, 124.5, 129.6, 129.9, 136.4, 136.5, 137.7 144.8, 149.5, 161.7; IR (neat) 3048 w, 1589 s, 1563 s, 1476 m, 1443 s, 1279 w, 1174 m, 1146 w, 1085 w, 1025 m, 990 m, 829 w, 769 s, 748 s, 655 m, 620 m, 526 w cm^{-1}; MS m/z (% relative intensity) 296 (4, M^+), 295 (33), 294 (100), 168 (13), 167 (51), 166 (11), 139 (10), 84 (21); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{12}H_{11}IN$) m/z 295.9936, found 295.9937.

2-[2-Iodo-6-(trifluoromethyl)phenyl]pyridine (2b). General procedure A was followed with 55.9 mg (0.250 mmol) of 2-[2-(trifluoromethyl)phenyl]pyridine (**1b**), prepared according to the procedure reported by Huff et al.,[19] except that 2.00 mmol of I_2 was used. The reaction was carried out under a 10 mA constant current condition for 11 h. Column chromatography (silica gel 60N, hexane and then 20:1 hex/EtOAc) afforded 68.8 mg of **2b** (0.197 mmol, 79% yield) as a white solid: mp 113.5−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.28 (m, 2H), 7.37 (dd, J = 7.3, 4.9 Hz, 1H), 7.76−7.82 (2H, m), 8.15 (d, J = 7.8 Hz, 1H), 8.73 (d, J = 4.4 Hz, 1H); ^{13}C NMR δ 101.4, 123.0 (q, J = 274.7 Hz), 123.2, 124.6, 125.9 (d, J = 4.7 Hz), 129.6, 129.8 (q, J = 30.7 Hz), 136.1, 142.6, 143.4 149.1, 159.2; IR (KBr) 1578 (m), 1569 (m), 1482 (w), 1442 (w), 1425 (m), 1306 (s), 1204 (m), 1168 (s), 1137 (s) 1057 (m), 995 (m), 802 (m), 795 (m), 784 (m), 747 (m), 683 (s), 668 (m), 626 (w) cm^{-1}; MS m/z (% relative intensity) 350 (6, M^+), 349 (46), 223 (14), 222 (100), 203 (7), 202 (33), 195 (6), 176 (8), 175 (6), 153 (8), 75 (6), 51 (9), 50 (5); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{12}H_8F_3IN$) m/z 349.9654, found 349.9650.

2-(2-Iodophenyl)-3-methylpyridine (2c). General procedure A was followed with 41.8 mg (0.247 mmol) of 3-methyl-2-phenylpyridine (**1c**), prepared according to the procedure reported by Kumada and co-workers,[18] and the reaction was carried out under a 5 mA constant current condition for 4 h. Column chromatography (Chromatorex NH, hexane and then 100:1 hexane/EtOAc) afforded **2c** (75% yield) and **1c** (3% yield) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, 20:1 CH_2Cl_2/EtOAc) gave 51.1 mg of **2c** (0.173 mmol, 70% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[2d]

2-(2-Iodo-4-methylphenyl)-3-methylpyridine (2d). General procedure A was followed with 46.3 mg (0.253 mmol) of 3-methyl-2-(4-methylphenyl)pyridine (**1d**), prepared according to the procedure reported by Queguiner and co-workers,[20] and the reaction was carried out under a 5 mA constant current condition for 3.5 h. Column chromatography (silica gel 60N, 100:1 CH_2Cl_2/EtOAc) afforded 66.6 mg of **2d** (0.215 mmol, 85% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.36 (s, 3H), 7.13 (d, J = 7.8 Hz, 1H), 7.22−7.25 (m, 2H), 7.58 (d, J = 7.3 Hz, 1H), 7.77 (s, 1H), 8.52 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 20.6, 97.5, 122.8, 128.8, 129.0, 131.5, 137.8, 139.3, 139.4, 142.4, 146.5, 160.9; IR (neat) 2361 (w), 1737 (w), 1698 (w), 1655 (w), 1600 (s), 1568 (m), 1490 (m), 1439 (s), 1380 (m), 1256 (w), 1184 (w), 1118 (m), 1072 (m), 1054 (w), 1014 (m), 823 (s), 791 (s), 682 (w), 666 (w), 587 (m), 568 (w) cm^{-1}; MS m/z (% relative intensity), 310 (8, M^+), 309 (55), 183 (14), 182 (100), 181 (24), 180 (19), 168 (10), 167 (75), 166 (12), 152 (9), 140 (7), 139 (8), 91 (19), 90 (15), 89 (12), 84 (23), 77 (12), 76 (7), 65 (8), 64 (6), 63 (14); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{13}H_{13}IN$) m/z 310.0093, found 310.0099.

2-(2-Iodo-5-methylphenyl)-3-methylpyridine (2e). General procedure A was followed with 45.4 mg (0.248 mmol) of 3-methyl-2-(3-methylphenyl)pyridine (**1e**), prepared according to the procedure reported by Queguiner and co-workers,[20] and the reaction was carried out under a 5 mA constant current condition for 3.5 h. Column chromatography (Chromatorex NH, hexane, then 30:1 hexane/EtOAc) afforded 57.6 mg of **2e** (0.186 mmol, 75% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.32 (s, 3H), 6.90 (d, J = 7.9 Hz, 1H), 7.08 (s, 1H), 7.20−7.25 (m, 1H), 7.57 (d, J = 7.4 Hz, 1H), 7.77 (d, J = 7.9 Hz, 1H), 8.51 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 20.9, 93.4, 122.8, 129.9, 130.3, 131.2, 137.7, 138.2, 138.5, 145.0, 146.4, 160.8; IR (neat) 2921 m, 1583 m, 1570 m, 1444 s, 1382 m, 1266 w, 1202 w, 1178 w, 1118 m, 1076 m, 1011 s, 877 m, 805 s, 791 s, 696 w, 632 m, 589 m, 516 w cm^{-1}; MS m/z (% relative intensity) 310 (6, M^+), 309 (39), 206 (17), 183 (14), 182 (100), 181 (18), 180 (16), 167 (63), 91 (18), 90 (12), 84 (12); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{13}H_{13}IN$) m/z 310.0093, found 310.0088.

2-(4-Fluoro-6-iodophenyl)-3-methylpyridine (2f). General procedure A was followed with 46.9 mg (0.251 mmol) of 2-(4-fluorophenyl)-3-methylpyridine (**1f**), prepared according to the procedure reported by Huff et al.,[19] except that 1.00 mmol of I_2 was used. The reaction was carried out under a 5 mA constant current condition for 10.5 h. Column chromatography (Chromatorex NH, hexane, then 30:1 hexane/EtOAc) afforded **2f** (70% yield) and **1f** (4% yield) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, 20:1 CH_2Cl_2/EtOAc) gave 48.2 mg of **2f** (0.154 mmol, 61% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[2d]

2-[2-Iodo-4-(trifluoromethyl)phenyl]-3-methylpyridine (2g). General procedure A was followed with 59.0 mg (0.249 mmol) of 2-[4-(trifluoromethyl)phenyl]-3-methylpyridine (**1g**), prepared according to the procedure reported by Huff et al.,[19] except that 2.00 mmol of I_2 was used. The reaction was carried out under a 10 mA constant current condition for 11 h. Column chromatography (Chromatorex NH, hexane, then 30:1 hexane/EtOAc) afforded **2g** (82% yield) and **1g** (4% yield) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, CH_2Cl_2) gave 63.3 mg of **2g** (0.174 mmol, 70% yield) as a light yellow oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[2d]

2-[2-Iodo-5-(trifluoromethyl)phenyl]-3-methylpyridine (2h). General procedure A was followed with 59.2 mg (0.250 mmol) of 2-[3-(trifluoromethyl)phenyl]-3-methylpyridine (**1h**), prepared according to the procedure reported by Huff et al.,[19] except that 0.050 mmol of palladium acetate and 2.50 mmol of I_2 were used. The reaction was carried out under a 10 mA constant current condition for 6 h. Column chromatography (Chromatorex NH, hexane, then 30:1 hexane/EtOAc) afforded 57.6 mg of **2h** (0.159 mmol, 64% yield) as a

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colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 7.36−8.28 (m, 2H), 7.52 (s, 1H), 7.63 (d, J = 7.6 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 8.55 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 102.2, 123.5, 123.8 (q, J = 272.6 Hz), 126.0, 130.8, 131.1, 131.3, 138.2, 139.7, 146.2, 146.9, 159.6; IR (neat) 3054 (m), 2927 (m), 2359 (w), 1912 (w), 1603 (s), 1449 (s), 1125 (s), 1171 (s), 1051 (m), 903 (s) 851 (m), 798 (s), 719 (s), 630 (s) cm^{-1}; MS m/z (% relative intensity) 364 (5, M^+), 363 (57), 236 (100), 235 (28), 216 (18), 167 (79), 166 (28), 139 (19), 127 (19), 63 (27); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{13}H_{10}F_3IN$) m/z 363.9810, found 363.9802.

General Procedure B for One-Pot Suzuki−Miyaura Coupling. The electrochemical oxidation was carried out in an H-type divided cell (anion-exchange membrane) equipped with two platinum electrodes (1.7 × 1.7 cm^2). The anodic chamber was charged with a solution of arylpyridine (0.25 mmol), I_2 (0.50 mmol), and palladium acetate (0.025 mmol) in acetonitrile (10 mL). A 0.2 M aqueous solution (10 mL) of sulfuric acid was introduced into the cathodic chamber. An electric field was applied at 90 °C under a 5 mA constant current condition, and the mixture in the anodic chamber was stirred. After the iodination reaction was completed, the electric current was stopped, and arylboronic acid (0.75 mmol) was added to the anodic chamber. K_2CO_3 was added to both anodic (0.75 mmol) and cathodic (2.5 mmol) chambers. The mixture was heated for an additional 2 h at 90 °C. After the completion of the reaction, the resulting materials in both chambers were combined and extracted with EtOAc. The obtained organic portions were washed with brine and dried over anhydrous Na_2SO_4 or $MgSO_4$. The solvent was removed, and the product was isolated by flash column chromatography.

2-(6-Methyl-2-phenylphenyl)pyridine (3a). General procedure B was followed with 42.7 mg (0.252 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded **3a** (84% yield), **1a** (6% yield), and 2-(2-chloro-6-methylphenyl)pyridine (3% yield) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, 5:1 hexane(60 °C)/EtOAc) gave 40.1 mg of **3a** (0.163 mmol, 65% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

3-Methyl-2-(2-phenylphenyl)pyridine (3b). General procedure B was followed with 42.7 mg (0.252 mmol) of 3-methyl-2-phenylpyridine (**1c**). The electrochemical C−H iodination was carried out for 4 h. Column chromatography (silica gel 60N, hexane and then 20:1 hexane/EtOAc) afforded 43.3 mg of **3b** (0.177 mmol, 70% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[21]

3-Methyl-2-(4-methyl-2-phenylphenyl)pyridine (3c). General procedure B was followed with 45.9 mg (0.250 mmol) of 3-methyl-2-(4-methylphenyl)pyridine (**1d**). The electrochemical C−H iodination was carried out for 3.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 54.6 mg of **3c** (0.211 mmol, 84% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 (s, 3H), 2.45 (s, 3H), 7.06−7.16 (m, 6H), 7.24−7.30 (m, 4H), 8.48 (dd, J = 4.7, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 21.3, 121.9, 126.5, 127.7, 128.1, 129.2, 129.8, 130.4, 131.7, 136.6, 137.4, 137.9, 140.5, 141.2, 146.5, 159.5; IR (neat) 3050 (m), 2922 (m), 2860 (w), 1610 (m), 1583 (m), 1489 (m), 1443 (s), 1267 (w), 1022 (w), 1115 (m), 1066 (w), 1022 (m), 887 (w), 826 (s), 792 (s), 773 (s), 742 (m), 701 (s), 792 (s), 773 (s), 742 (m), 701 (s), 594 (m), 573 (w), 511 (w); MS m/z (% relative intensity) 260 (13, M^+), 259 (73), 258 (100), 256 (5), 245 (17), 244 (87), 243 (11), 242 (15), 241 (10), 229 (9), 228 (8), 215 (7), 202 (7), 129 (9), 128 (4), 122 (15), 121 (18), 109 (7); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{19}H_{18}N$) m/z 260.1439, found 260.1434.

3-Methyl-2-(5-methyl-2-phenylphenyl)pyridine (3d). General procedure B was followed with 45.4 mg (0.248 mmol) of 3-methyl-2-(3-methylphenyl)pyridine (**1e**). The electrochemical C−H iodination was carried out for 4 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 47.2 mg of **3d** (0.182 mmol, 73% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.73 (s, 3H), 2.43 (s, 3H), 7.07−7.12 (m, 3H), 7.12−7.16 (m, 3H), 7.23 (s, 1H), 7.28 (m, J = 7.8 Hz, 2H), 7.35 (d, J = 7.8 Hz, 1H), 8.51 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7, 21.0, 122.0, 126.4, 127.7, 129.1, 129.2, 129.6, 130.5, 131.7, 137.1, 137.5, 137.8, 139.0, 141.0, 146.4, 159.5; IR (KBr) 3017 (w), 2925 (w), 2360 (w), 2332 (w), 1566 (m), 1480 (m), 1445 (s), 1262 (w), 1113 (m), 1070 (m), 829 (m), 796 (s), 775 (s), 706 (s), 633 (w), 584 (w), 513 (w); MS m/z (% relative intensity) 260 (12, M^+), 259 (71), 258 (96), 245 (21), 244 (100), 243 (11), 242 (17), 241 (13), 129 (10), 122 (21), 121 (21); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{19}H_{18}N_1$) m/z 260.1439, found 260.1453.

2-[6-Methyl-2-(2-methylphenyl)phenyl]pyridine (3e). General procedure B was followed with 42.4 mg (0.251 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 40:1 hexane/EtOAc) afforded **3e** (78% yield), **1a** (4% yield), and 2-(2-chloro-6-methylphenyl)pyridine (4%) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, 200:1 CH_2Cl_2/EtOAc and then 100:1 CH_2Cl_2/EtOAc) gave 43.6 mg of **3e** (0.168 mmol, 67% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 3H), 2.20 (s, 3H), 6.86 (d, J = 7.9 Hz, 1H), 6.94−7.07 (m, 5H), 7.12 (d, J = 7.0 Hz, 1H), 7.28−7.42 (m, 3H), 8.55 (d, J = 4.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 20.5, 121.1, 124.7, 125.1, 126.7, 127.3, 127.6, 129.3, 129.4, 130.4, 135.3, 135.8, 136.5, 139.7, 140.8, 141.0, 148.6, 159.0; MS m/z (% relative intensity) 260 (9, M^+), 259 (57), 258 (100), 245 (13), 244 (61), 243 (8), 242 (13), 241 (11), 215 (8), 165 (9), 129 (12), 128 (7), 122 (18), 121 (17), 80 (18), 79 (20); IR (neat) 3057 (s), 2923 (s), 2736 (w), 1585 (s), 1457 (s), 1276 (m), 1148 (m), 1025 (s), 754 (s) cm^{-1}; HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{19}H_{18}N$) m/z 260.1439, found 260.1447.

2-[6-Methyl-2-(3-methylphenyl)phenyl]pyridine (3f). General procedure B was followed with 42.5 mg (0.251 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 53.0 mg of **3f** (0.204 mmol, 81% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[6-Methyl-2-(4-methylphenyl)phenyl]pyridine (3g). General procedure B was followed with 41.9 mg (0.248 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 3.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 49.0 mg of **3g** (0.189 mmol, 76% yield) as a white solid. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[6-Methyl-2-(4-*n*-pentylphenyl)phenyl]pyridine (3h). General procedure B was followed with 42.6 mg (0.252 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 100:1 hexane/EtOAc) afforded 58.5 mg of **3h** (0.185 mmol, 74% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.1 Hz, 3H), 1.23−1.31 (m, 4H), 1.54 (tt, J = 7.8, 7.3 Hz, 2H), 2.18 (s, 3H), 2.50 (t, J = 7.8 Hz, 2H), 6.87 (ddd, J = 7.8, 1.2, 1.0 Hz, 1H), 6.92−6.98 (m, 4H), 7.09 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 7.26−7.29 (m, 2H), 7.35 (d, J = 8.5, 6.6 Hz, 1H), 7.44 (ddd, J = 1.9, 7.6, 7.8 Hz, 1H), 8.63 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 14.3, 20.6, 23.1, 31.8, 32.1, 35.9, 122.2, 126.3, 128.2, 128.4, 128.6, 129.7, 130.2, 136.3, 137.4, 139.9, 140.7, 141.5, 141.9, 149.6, 160.6; IR (neat) 3127 (w), 3059 (m), 3022 (m), 2957 (s), 2928 (s), 2856 (s), 2733 (w), 1910 (w), 1585 (s), 1562 (s), 1514 (s), 1460 (s), 1423 (s), 1404 (m), 1378 (m), 1283 (w), 1236 (w), 1185 (w), 1147 (m), 1117 (m), 1091 (m), 1053 (w), 1024 (s), 989 (m), 897 (w), 838 (m), 792 (s), 749 (s), 678 (w), 623 (m), 608 (w), 598 (m), 580 (m), 532 (w), 403 (w); MS m/z (% relative intensity) 316 (9, M^+), 315 (46), 314 (100), 258 (16), 257 (12), 256 (10), 244 (6), 242 (8), 241(5); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{23}H_{26}N$) m/z 316.2065, found 316.2085.

2-[2-(4-Isopropylphenyl)-6-methylphenyl]pyridine (3i). General procedure B was followed with 42.3 mg (0.250 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and

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then 30:1 hexane/EtOAc) afforded 49.8 mg of **3i** (0.173 mmol, 69% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (d, J = 6.9 Hz, 6H), 2.17 (s, 3H), 2.80 (sep, J = 6.9 Hz, 1H), 6.87 (ddd, J = 7.8, 1.2, 1.0 Hz, 1H), 6.97−6.99 (m, 4H), 7.08 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 7.25−7.29 (m, 2H), 7.33 (dd, J = 8.1, 7.1 Hz, 1H), 7.43 (ddd, J = 7.8, 7.6, 1.7 Hz, 1H), 8.63 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 23.8, 33.5, 121.2, 125.6, 125.6, 127.6, 127.9, 129.1, 129.5, 135.6, 136.6, 138.9, 139.2, 141.1, 146.7, 148.7, 159.7; IR (neat) 3668 (m), 3128 (m), 3058 (s), 3023 (s), 3001 (s), 2958 (s), 2927 (s), 2869 (s), 2212 (m), 1912 (w), 1733 (m), 1677 (w), 1612 (m), 1586 (s), 1563 (s), 1514 (s), 1459 (s), 1424 (s), 1405 (s), 1382 (m), 1363 (m), 1339 (m), 1265 (m), 1237 (m), 1190 (w), 1171 (m), 1148 (s), 1091 (m), 1053 (s), 1025 (s), 990 (m), 966 (w), 910 (s), 870 (w), 837 (s), 793 (s), 753 (s), 671 (m), 645 (m), 622 (m), 592 (s), 538 (w),525 (w); MS m/z (% relative intensity) 288 (8, M^+), 287 (46), 286 (100), 272 (10), 270 (12), 244 (19), 136 (7), 127 (5); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{21}H_{22}N$) m/z 288.1752, found 288.1748.

2-[2-(4-*tert*-Butylphenyl)-6-methylphenyl]pyridine (3j). General procedure B was followed with 41.9 mg (0.248 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 20:1 CH_2Cl_2/EtOAc) afforded 61.3 mg of **3j** (0.203 mmol, 82% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[2-(4-Methoxyphenyl)-6-methylphenyl]pyridine (3k). General procedure B was followed with 42.3 mg (0.250 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 3.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded 43.3 mg of **3k** (0.157 mmol, 63% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[2-(4-Methoxyphenyl)-4-methylphenyl]-3-methylpyridine (3l). General procedure B was followed with 46.1 mg (0.252 mmol) of 3-methyl-2-(4-methylphenyl)pyridine (**1d**). The electrochemical C−H iodination was carried out for 3.5 h. Column chromatography (Chromatorex NH, hexane and then 1:1 hexane/EtOAc), followed by preparative thin-layer chromatography (3:1 hexane/EtOAc), afforded 48.1 mg of **3l** (0.166 mmol, 66% yield) as an yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74 (s, 3H), 2.44 (s, 3H), 3.74 (s, 3H), 6.69 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 8.7 Hz, 2H), 7.06−7.11 (m, 1H), 7. 20−7.31 (m, 5H), 8.49 (d, J = 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 21.3, 55.1, 113.2, 121.9, 127.7, 129.8, 130.2, 130.2, 131. 7, 133.7, 136.5, 137.4, 137.9, 140.0, 146.5, 158.3, 159.7; IR (neat) 3650 (w), 3374 (w), 3002 (w), 2835 (s), 2735 (w), 2539 (w), 2208 (w), 2039 (w), 1897 (m), 1770 (w), 1721 (w), 1608 (s), 1582 (s), 1517 (s), 1498 (s), 1441 (s), 1381 (s), 1292 (s), 1247 (s), 1178 (s), 1137 (m), 1113 (s), 1067 (s), 1033 (s), 990 (m), 957 (m), 910 (m), 889 (m), 875 (m), 831 (s), 791 (s), 757 (w), 729 (s), 693 (m), 640 (w), 598 (s), 568 (m), 529 (w); MS m/z (% relative intensity) 290 (10, M^+), 289 (48), 288 (28), 275 (20), 274 (100), 246 (6), 245 (8), 231 (15), 230 (8),116 (9); HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{20}H_{20}NO$) m/z 290.1545, found 290.1540.

2-[2-(4-Fluorophenyl)-6-methylphenyl]pyridine (3m). General procedure B was followed with 42.3 mg (0.250 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 3.5 h. Column chromatography (Chromatorex NH, hexane and then 40:1 hexane/EtOAc) afforded 41.6 mg of **3m** (0.158 mmol, 63% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[6-Methyl-2-{4-(trifluoromethyl)phenyl}phenyl]pyridine (3n). General procedure B was followed with 42.3 mg (0.250 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (Chromatorex NH, hexane and then 30:1 hexane/EtOAc) afforded **3n** (70% yield), **1a** (3% yield), and 2-(2-chloro-6-methylphenyl)pyridine (3%) as a mixture. Further purification of the mixture by column chromatography (silica gel 60N, 20:1 CH_2Cl_2/EtOAc) gave 41.2 mg of **3n** (0.131 mmol, 53% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

2-[2-(4-Bromophenyl)-6-methylphenyl]pyridine (3o). General procedure B was followed with 42.2 mg (0.249 mmol) of 2-(*o*-tolyl)pyridine (**1a**). The electrochemical C−H iodination was carried out for 4.5 h. Column chromatography (silica gel 60N, hexane and then 20:1 hexane/EtOAc) afforded **3o** (68%), **1a** (1%), and 2-(2-chloro-6-methylphenyl)pyridine (3%) as a mixture. Further purification by GPC gave 46.8 mg of **3o** (0.144 mmol, 58% yield) as a colorless oil. ^{1}H NMR spectroscopic data are in good agreement with those reported in literature.[15i]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C{^{1}H} NMR spectra of new compounds and Figure S1. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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