JOC The Journal of Organic Chemistry

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Synthesis of 3-Substituted 2-Arylpyridines via Cu/Pd-Catalyzed Decarboxylative Cross-Coupling of Picolinic Acids with (Hetero)Aryl Halides

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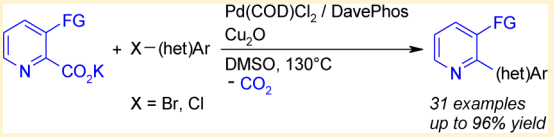
Supporting Information

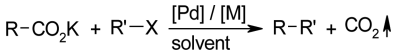
ABSTRACT: A decarboxylative cross-coupling of 3-substituted picolinic acids with (hetero)aryl halides is presented. In the presence of catalytic Cu_2O and Pd(1,5-cyclooctadiene)Cl_2 with 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl as the ligand, both electron-rich and electron-deficient aryl bromides and chlorides as well as heteroaryl bromides were successfully coupled with various picolinate salts under mild conditions in yields up to 96%. This protocol provides an efficient entry to 2-(hetero)arylpyridines, an attractive substance class in drug discovery.



Within the last decades, decarboxylative cross-coupling reactions have emerged as a powerful methodology for the regioselective formation of C−C and C−heteroatom bonds.[1−3] The key advantage of this reaction type is that it draws on stable and readily available carboxylic acids as the coupling partners. As a result, a steadily growing number of atom-economic and waste-minimized protocols including decarboxylative Heck-type reactions,[4−7] redox-neutral cross-couplings,[8−11] allylations,[12,13] oxidative couplings,[14,15] C−H arylations,[16−19] Chan−Evans−Lam-type reactions,[20] and photoredox-induced couplings have recently been disclosed.[21,22]

In redox-neutral decarboxylative cross-couplings, carboxylic acids are used as the source of carbon nucleophiles in place of sensitive and costly organometallic reagents. In this reaction variant, a Cu^I or Ag^I catalyst mediates the extrusion of CO_2 to form the carbon nucleophile, which is then transmetalated to a Pd complex, where the coupling with the carbon electrophile takes place (Scheme 1). Bimetallic Cu/Pd systems proved to have a particularly broad scope with regard to both coupling partners.[8,23,24] Various aromatic carboxylates have successfully been coupled with a broad range of (hetero)aryl halides and pseudohalides, and key limitations such as the restriction to benzoates bearing electron-withdrawing *ortho*-substituents have recently been overcome with customized catalyst systems.[25]

Scheme 1. Redox-Neutral Decarboxylative Cross-Couplings[a]



[a]M = Cu, Ag; R = (hetero)aryl, vinyl, acyl; R′ = (hetero)aryl, alkenyl; X = I, Br, Cl, OTf, OTs, OMs.

Among the heterocyclic carboxylates, five-membered ring heteroarenes such as oxazole-, thiazole-, pyrrole-, thiophene-, and furancarboxylic acids react with particular ease and can be coupled even with monometallic catalyst systems.[26,27] In contrast, pyridinecarboxylic acids belong to the most challenging substrates in decarboxylative couplings. 3-Pyridinecarboxylic acids can be converted under standard conditions but tend to give low yields,[28] whereas 4-pyridinecarboxylic acids require customized catalyst systems.[29] Arguably, the coupling of 2-pyridinecarboxylic acids poses the greatest challenge due to the instability of the 2-metallapyridines[30] and their tendency toward protodecarboxylation even in the absence of a metal catalyst (see the Supporting Information, Table S1).[31−36] In order to allow a regiospecific cross-coupling step, the unwanted protodecarboxylation, which starts at 120 °C, needs to be suppressed, and the high activation barrier of the metal-mediated decarboxylation pathway has to be lowered (Scheme 2).

Several dedicated catalyst systems have been designed specifically for decarboxylative couplings of 2-pyridinecarboxylates. Wu and Stoltz disclosed bimetallic Cu/Pd catalyst systems that allow decarboxylative cross-couplings of picolinic acid with (hetero)aryl bromides, albeit in only moderate yields at temperatures as high as 190 °C or with high catalyst loadings (Scheme 3, (1)).[35,36] Hoarau et al. used an indirect strategy for their coupling that involves the protection/activation of the picolinic acids by upfront conversion into the *N*-oxides (Scheme 3, (2)).[38] Stoichiometric amounts of a silver or copper salt along with the palladium catalyst were still required to obtain reasonable yields. This protocol follows a mechanism that is related to the direct arylation of pyridine *N*-oxides.[39−42]

To date, the importance of the 2-arylpyridine structural unit remains in stark contrast to the lack of effective and flexible tools for its preparation. 2-Aryl-3-fluoropyridines, in particular,

Received: January 9, 2017

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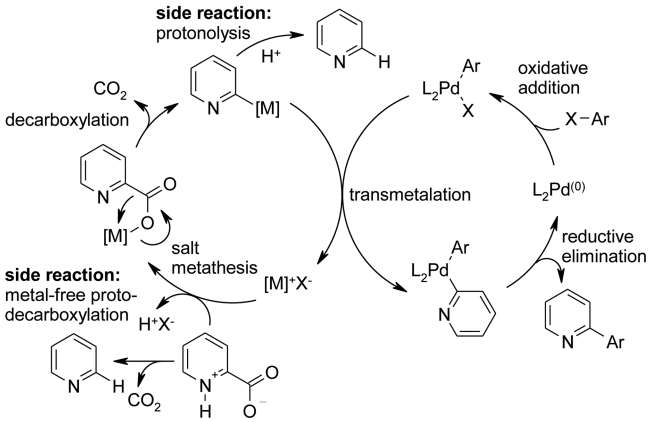
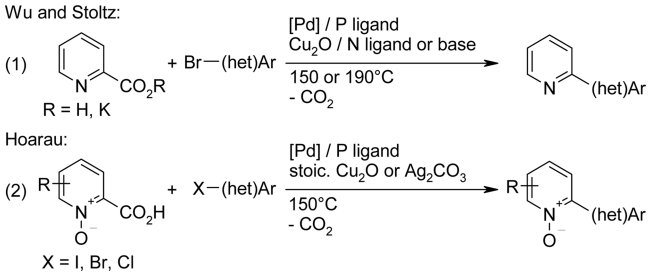
DOI: 10.1021/acs.joc.7b00046
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. Competing Reaction Pathways in the Coupling of 2-Pyridinecarboxylic Acids[36,37]



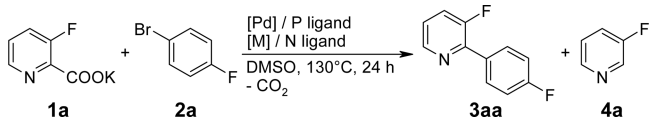
Scheme 3. Decarboxylative Cross-Coupling of Picolinic Acid Derivatives



would be interesting pharmacophores and, in addition, could be used as synthetic hubs for further derivatization via nucleophilic aromatic fluorine substitution.[43−50] The C−H arylation of *N*-oxides would likely give mixtures of regioisomers and require subsequent reduction.[40,51] Suzuki−Miyaura couplings are challenging for this substrate class because of the instability of some heterocyclic boronates, particularly the 2-pyridyl derivatives.[30,52] Data from the Pfizer internal electronic laboratory notebook shows that of 358 reactions attempted using pyridine-2-boronates, only 28 experiments, corresponding to <8% of examples, achieved a yield of at least 20%.[53] A decarboxylative cross-coupling of 3-fluoropicolinic acid appeared to be the most promising and versatile approach to directing the formation of the new bond between the nitrogen atom and the fluorine substituent.

In search of an efficient and generally applicable protocol for the synthesis of 3-fluoro-2-arylpyridines, the utility of various literature protocols was investigated in the coupling of potassium 3-fluoropicolinate (**1a**) with 1-bromo-4-fluorobenzene (**2a**). ^{19}F NMR was employed to determine yields and selectivity for cross-coupling versus protodecarboxylation. When restricting the catalyst loading to a maximum of 10 mol % of copper/5 mol % of palladium and the temperature to 130 °C, the desired product was obtained in low yields. The best result was obtained using a catalyst system consisting of Cu_2O/1,10-phenanthroline and $PdCl_2/PPh_3$, which had previously been optimized for similar transformations (Table 1, entry 1).[35,36] A decisive increase in yield was observed when switching the solvent from NMP to DMSO (entry 2). Only a 1:1 mixture of NMP/mesitylene gave comparable results, whereas other solvents such as DMF, DMAc, or mesitylene were inferior for this substrate combination (see the Supporting Information, Table S2). Systematic variation of the palladium source showed $Pd(COD)Cl_2$ to be the most effective, with a yield increased to 74% yield (entries 3−5). In investigations of

Table 1. Optimization of the Reaction Conditions[a]



entry	[M]	N ligand	[Pd]	P ligand	**3aa** (%)	**4a** (%)
1[b]	Cu_2O	phen	$PdCl_2$	PPh_3	19	trace
2	Cu_2O	phen	$PdCl_2$	PPh_3	60	7
3	Cu_2O	phen	$Pd(COD)Cl_2$	PPh_3	74	8
4	Cu_2O	phen	PdI_2	PPh_3	54	11
5	Cu_2O	phen	$Pd(acac)_2$	PPh_3	67	9
6[c]	CuCl	phen	$Pd(COD)Cl_2$	PPh_3	66	nd
7	Ag_2CO_3	phen	$Pd(COD)Cl_2$	PPh_3	66	10
8	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	PPh_3	83	nd
9	Cu_2O	NO_2-phen	$Pd(COD)Cl_2$	PPh_3	49	17
10	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	P(*p*-Tol)$_3$	84	trace
11	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	BINAP	75	nd
12	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	PCy_3	28	trace
13	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	CyJohnPhos	82	10
14	Cu_2O	Me_4-phen	$Pd(COD)Cl_2$	DavePhos	92	7
15	Cu_2O	–	$Pd(COD)Cl_2$	DavePhos	93	trace
16	–	–	$Pd(COD)Cl_2$	DavePhos	7	32
17	Cu_2O	–	–	–	nd	nd

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), [M] (5 mol %), N ligand (10 mol %), [Pd] (5 mol %), P ligand (15 mol %), DMSO (2 mL), 130 °C, 24 h; ^{19}F NMR yield with 1,4-difluorobenzene as internal standard; NO_2-phen = 5-nitro-1,10-phenanthroline, Tol = tolyl, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, CyJohnPhos = (2-biphenyl)dicyclohexylphosphine, DavePhos = 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl; nd = not detected. [b]In NMP (2 mL). [c]10 mol % of [M] was used.

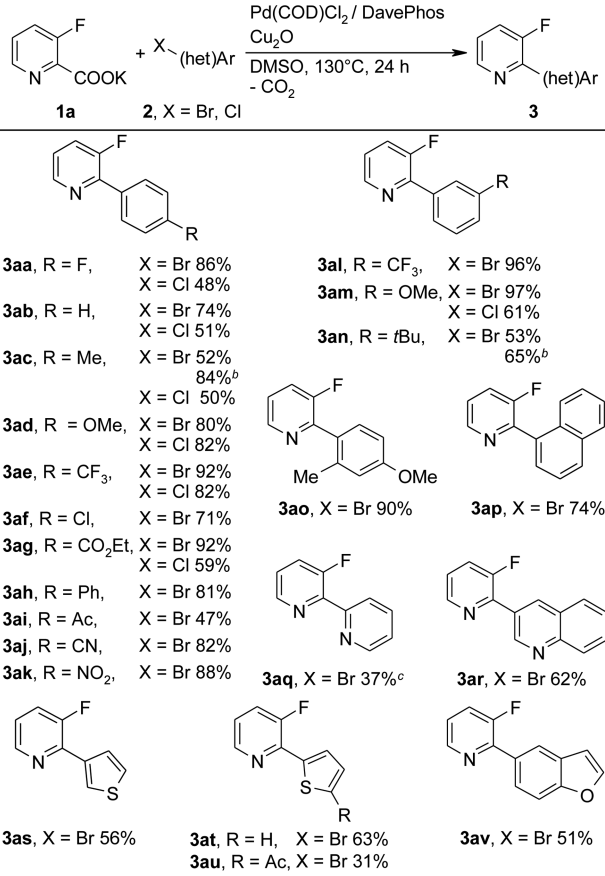
DOI: 10.1021/acs.joc.7b00046
J. Org. Chem. XXXX, XXX, XXX−XXX

silver- and copper-based decarboxylation catalysts, Cu_2O was identified as the most efficient in combination with 3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4-phen) (entries 6–9). The choice of the phosphine ligand was similarly critical (entries 10–14). Not only did the phosphine affect the yields, but in addition, undesired P–C bond cleavage resulted in aryl group transfer to the pyridine with formation of hard-to-separate 2-arylpyridine byproducts. Because the quality of pharmacological structure–activity relationships is strongly affected by such structurally related impurities, a key criterion for the choice of the phosphine ligand was its stability under the reactions conditions. In this respect, DavePhos turned out to be most effective. Notably, with this ligand, the optimal yield and selectivity was obtained in the absence of Me_4-phen (entry 15). Control experiments confirmed that both Pd and Cu are essential components of the catalyst system (entries 16 and 17).

In the presence of 5 mol % of $Pd(COD)Cl_2$, 15 mol % of DavePhos, and 5 mol % of Cu_2O, the desired product was formed in 93% yield within 24 h at 130 °C in DMSO. This optimized protocol is applicable to the coupling of **1a** with a broad range of aryl bromides substituted in the *ortho*-, *meta*-, or *para*-position (Table 2). Common functionalities including ether, ester, carbonyl, trifluoromethyl, cyano, and nitro groups are tolerated. Heteroaryl bromides were also found to be suitable coupling partners. We were pleased to find that aryl chlorides, which are available in greater structural diversity and are less expensive, but less reactive, were smoothly converted without further adjustments to the catalyst or conditions. As the main side reactions, homocoupling of the excess aryl halide and protodecarboxylation of the picolinic acid were observed.

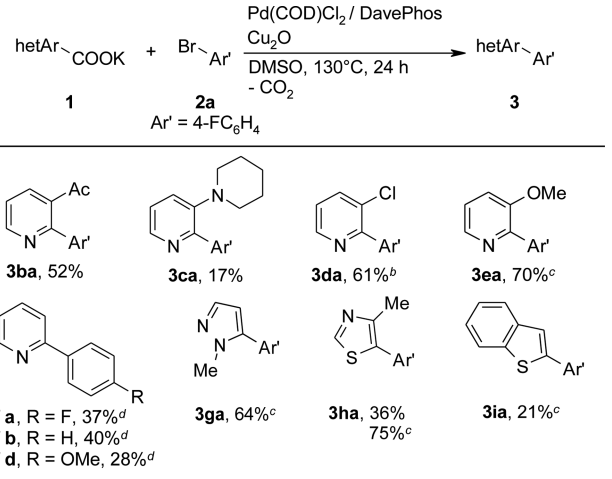
Having thus established a versatile protocol for our synthetic needs, we briefly investigated whether this catalyst system is advantageous also for other heteroaromatic carboxylates (Table 3). 3-Acetylpicolinate was also converted in moderate yield, whereas the yield was low for 3-piperidylpicolinate. 3-Chloropicolinate (**1d**) was converted most effectively using a silver-based decarboxylation catalyst, which is in line with observations made for *ortho*-chloro-substituted benzoates.[24] Slightly modified reaction conditions (5 mol % of $PdCl_2$, 15 mol % of CyJohnPhos, 5 mol % of Cu_2O, and 10 mol % of phen in 2 mL of NMP/mesitylene (1:1) at 150 °C) were necessary to efficiently convert 3-methoxypicolinate (**1e**). Remarkably, picolinic acids devoid of substituents in the 3-position could only be converted at 190 °C. This indicates that a substituent *ortho* to the carboxylate facilitates decarboxylation not only for benzoates but also for picolinates. Picolinic acids substituted in another position of the heteroaromatic ring (4-Cl, 5-F, 6-F/Cl/OMe) did not react under our reaction conditions, again underlining the unique reactivity of pyridines substituted in the 3-position. Further studies revealed that five-membered heteroaromatic carboxylates, including *N*-methylpyrazole, thiazole, or benzothiophene derivatives, can also be converted in reasonable yields using the new catalyst system. As side products, homocoupling products of the aryl halides were detected along with unreacted starting materials.

Table 2. Scope with Regard to the Electrophilic Coupling Partner[a]



[a]Reaction conditions: **1a** (0.5 mmol), **2** (1.0 mmol), Cu_2O (5 mol %), $Pd(COD)Cl_2$ (5 mol %), DavePhos (15 mol %), DMSO (2 mL), 130 °C, 24 h. Yields of isolated products. [b]**1a** (0.5 mmol), **2** (1.0 mmol), Cu_2O (5 mol %), phen (10 mol %), $PdCl_2$ (5 mol %), CyJohnPhos (15 mol %), NMP/mesitylene (1:1, 2 mL), 150 °C, 24 h. Yield of isolated products. [c]**1a** (0.75 mmol), **2** (0.5 mmol).

Table 3. Scope with Regard to the Carboxylate[a]

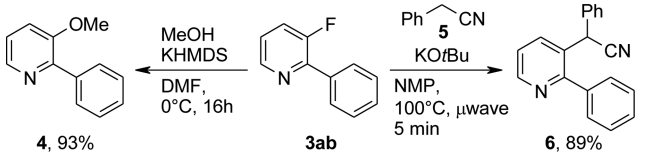


[a]Reaction conditions: **1** (0.5 mmol), **2a** (1.0 mmol), Cu_2O (5 mol %), $Pd(COD)Cl_2$ (5 mol %), DavePhos (15 mol %), DMSO (2 mL), 130 °C, 24 h. Yields of isolated products. [b]Ag_2CO_3 (5 mol %) was used instead of Cu_2O. [c]**1** (0.5 mmol), **2** (1.0 mmol), Cu_2O (5 mol %), phen (10 mol %), $PdCl_2$ (5 mol %), CyJohnPhos (15 mol %), NMP/mesitylene (1:1, 2 mL), 150 °C, 24 h. Yields of isolated products. [d]**1f** (0.5 mmol), **2** (1.0 mmol), Cu_2O (5 mol %), $Pd(COD)Cl_2$ (5 mol %), DavePhos (15 mol %), NMP/mesitylene (1:1, 2 mL), 190 °C, 24 h. Yields of isolated products.

DOI: 10.1021/acs.joc.7b00046
J. Org. Chem. XXXX, XXX, XXX–XXX

In order to demonstrate the utility of the 2-aryl-3-fluoropyridines as synthetic hubs for further derivatization via nucleophilic aromatic fluorine substitution, **3ab** was applied in a C−O and a C−C bond formation (Scheme 4). Reaction of **3ab**

Scheme 4. Derivatization of 3ab



with methanol, which can also be replaced by more complex alcohols, in the presence of potassium bis(trimethylsilyl)amide (KHMDS)[45] gave the desired product **4**, and treatment of **3ab** in the presence of nitrile **5** and potassium *tert*-butoxide under microwave conditions furnished compound **6**,[44] both in good yield.

In conclusion, an efficient protocol for the Cu/Pd-catalyzed decarboxylative cross-coupling of picolinic acid derivatives with (hetero)aryl bromides and chlorides has been developed, which gives convenient access to otherwise hard to synthesize 3-substituted arylpyridines. It draws on stable picolinate salts as the source of the nucleophile, proceeds at reasonable temperatures, and requires only catalytic amounts of transition metals.

EXPERIMENTAL SECTION

General Remarks. Chemicals and solvents were either purchased (puriss. p.A.) from commercial suppliers or purified by standard procedures prior to use.[54] All reactions were performed in oven-dried glassware under an argon atmosphere containing a Teflon-coated stirrer bar and dry septum. Microwave-assisted reactions were performed in sealed microwave vessels using the Biotage Initiator 2.5 EXP microwave system (external IR sensor) with the Initiator Remote Viewer reaction monitoring software. Solvents and liquid reactants were degassed with argon. Reactions were monitored by ^{19}F NMR using 1,4-difluorobenzene as an internal standard or by GC using dodecane as an internal standard. Response factors of the products with regard to dodecane were obtained experimentally by analyzing known quantities of the substances. GC analyses were carried out using a capillary column (phenyl methyl siloxane, 30 m × 320 × 0.25, 100/2.3−30−300/3, 2 min at 60 °C, heating rate 30 °C min^{-1}, 3 min at 300 °C). Column chromatography was performed on a flash chromatography machine. NMR spectra were recorded at ambient temperature using $CDCl_3$ or DMSO-d_6 as solvent, with proton, carbon, and fluorine resonances at 400/300/200/250, 151/101/75/63/50, and 377/235/41 MHz, respectively. Mass spectral data were acquired on a GC-MS and on a GC-HRMS with a TOF mass analyzer. The ionization was achieved by EI. Infrared spectra were recorded on a FT-IR spectrometer with an ATR sampling accessory. Melting points were measured on a melting point apparatus.

General Procedure for the Synthesis of Potassium Carboxylate Salts. A 250 mL round-bottomed flask was charged with the carboxylic acid (20.0 mmol) and ethanol (20 mL). A solution of potassium *tert*-butoxide (2.24 g, 20.0 mmol) in ethanol (20 mL) was added dropwise over 1 h. After complete addition, the reaction mixture was stirred for another 1 h at rt. A gradual formation of a precipitate was observed. The resulting solid was collected by filtration, washed sequentially with ethanol (2 × 10 mL) and diethyl ether (10 mL), and dried in vacuum to provide the corresponding potassium carboxylate. If after the addition of the potassium *tert*-butoxide solution a formation of a precipitate was not observed, the solution was concentrated in vacuum. The resulting solid was collected by filtration, washed with diethyl ether (10 mL), and dried in vacuum to provide the corresponding potassium carboxylate.

General Procedure for the Biaryl Synthesis. *Method A.* An oven-dried 20 mL vessel was charged with copper(I) oxide (3.61 mg, 25.0 μmol, 5 mol %), dichloro(1,5-dicyclooctadien)palladium(II) (7.13 mg, 25.0 μmol, 5 mol %), DavePhos (29.5 mg, 75 μmol, 15 mol %), and the potassium carboxylate **1** (0.50 mmol). DMSO (2 mL) and the aryl halide **2** (1 mmol) were added, and the resulting mixture was stirred at 130 °C under a dry atmosphere of argon. After 24 h, the mixture was allowed to cool to rt, washed with distilled water (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the volatiles were removed under reduced pressure. The residue was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate gradient) yielding the corresponding biaryl **3**.

Method B. An oven-dried 20 mL vessel was charged with copper(I) oxide (3.61 mg, 25.0 μmol, 5 mol %), palladium(II) chloride (4.44 mg, 25.0 μmol, 5 mol %), 1,10-phenanthroline (9.01 mg, 50 μmol, 10 mol %), CyJohnPhos (26.3 mg, 75 μmol, 15 mol %), and the potassium carboxylate **1** (0.50 mmol). NMP/mesitylene (2 mL, 1/1) and the aryl bromide **2** (1 mmol) were added, and the resulting mixture was stirred at 150 °C under a dry atmosphere of argon. After 24 h, the mixture was allowed to cool to rt, washed with distilled water (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the volatiles were removed under reduced pressure. The residue was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate gradient) yielding the corresponding biaryl **3**.

*3-Fluoro-2-(4-fluorophenyl)pyridine (**3aa**) [CAS: 511522-74-0].* Compound **3aa** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3aa** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless solid (82 mg, 86%). Compound **3aa** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-4-fluorobenzene **2a′** (133 mg, 108 μL, 1.0 mmol). **3aa** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless solid (45 mg, 48%): mp 63−64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49−8.54 (m, 1H), 7.96−8.03 (m, 2H), 7.50 (ddd, 1H, *J* = 11.0, 8.3, 1.5 Hz), 7.25−7.31 (m, 1H), 7.14−7.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.4 (d, J_{C-F} = 249.3 Hz), 157.4 (d, J_{C-F} = 259.8 Hz), 145.4 (d, J_{C-F} = 5.5 Hz), 145.2 (d, J_{C-F} = 10.5 Hz), 131.4 (dd, J_{C-F} = 5.5, 3.3 Hz), 130.7 (dd, J_{C-F} = 8.6, 6.4 Hz), 124.2 (d, J_{C-F} = 19.9 Hz), 128.4 (d, J_{C-F} = 4.4 Hz), 115.4 (d, J_{C-F} = 21.6 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −112.1,−123.0; IR ν 3048, 3021, 1603, 1516, 1447, 1227, 833, 756 cm^{-1}; MS *m*/*z* (%) 191.0 (100) [M]$^+$, 190 (58), 172 (16), 170 (10), 74 (12), 50 (16); HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{11}H_7F_2N$ 191.0547; found 191.0548.

*3-Fluoro-2-phenylpyridine (**3ab**) [CAS: 1214342-78-5].* Compound **3ab** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and bromobenzene **2b** (159 mg, 106 μL, 1.0 mmol). **3ab** was isolated (SiO_2, cyclohexane/ethyl acetate =9/1) as a colorless solid (64 mg, 74%). Compound **3ab** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and chlorobenzene **2b′** (113 mg, 102 μL, 1.0 mmol). **3ab** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (44 mg, 71%): mp 48−49 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50−8.58 (m, 1H), 7.93−8.04 (m, 2H), 7.42−7.55 (m, 4H), 7.25−7.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 157.5 (d, J_{C-F} = 258.9 Hz), 146.2 (d, J_{C-F} = 10.9 Hz), 145.4 (d, J_{C-F} = 5.5 Hz), 135.3 (d, J_{C-F} = 5.4 Hz), 129.2, 128.8 (d, J_{C-F} = 5.4 Hz), 128.4, 124.1 (d, J_{C-F} = 20.0 Hz), 123.4 (d, J_{C-F} = 3.6 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −123.0; IR ν 3064, 1596, 1431, 1250, 1188, 798 cm^{-1}; MS, *m*/*z* (%) 173 (100) [M]$^+$, 172 (78), 145 (11), 125 (11), 51 (13), 50 (23); HRMS (EI) *m*/*z* [M]$^+$ calcd for $C_{11}H_8FN$ 173.0641; found 173.0639.

*3-Fluoro-2-(4-methylphenyl)pyridine (**3ac**).* Compound **3ac** was prepared following methods A and B, respectively, from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-methylbenzene **2c** (175 mg, 126 μL, 1.0 mmol). **3ac** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (48 mg, 52% (method A); 79 mg, 84% (method B)). Compound **3ac** was

DOI: 10.1021/acs.joc.7b00046
J. Org. Chem. XXXX, XXX, XXX−XXX

prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-4-methylbenzene **2c′** (129 mg, 121 μL, 1.0 mmol). **3ac** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (47 mg, 50%): mp 51−52 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.45−8.58 (m, 1H), 7.90 (dd, 2H, *J* = 8.3, 1.5 Hz), 7.47 (ddd, 1H, *J* = 11.0, 8.3, 1.0 Hz), 7.31 (d, 2H, *J* = 8.3 Hz), 7.20−7.27 (m, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 157.4 (d, J_{C-F} = 259.8 Hz), 146.2 (d, J_{C-F} = 10.9 Hz), 145.2 (d, J_{C-F} = 5.4 Hz), 139.2, 132.5 (d, J_{C-F} = 5.4 Hz), 129.1, 128.6 (d, J_{C-F} = 6.4 Hz), 123.9 (d, J_{C-F} = 20.9 Hz), 123.0 (d, J_{C-F} = 3.6 Hz), 21.3; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −123.0; IR ν 3050, 3027, 2921, 1596, 1444, 1405, 1251, 1187, 1106 cm^{-1}; MS, *m*/*z* (%) 187 (100) $[M]^+$, 186 (60), 185 (17), 91 (12), 63 (10), 50 (11); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{12}H_{10}FN$ 187.0797; found 187.0796.

*3-Fluoro-2-(4-methoxyphenyl)pyridine (**3ad**) [CAS: 847226-10-2].* Compound **3ad** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-methoxybenzene **2d** (187 mg, 126 μL, 1.0 mmol). **3ad** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow oil (82 mg, 80%). Compound **3ad** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-4-methoxybenzene **2d′** (145 mg, 125 μL, 1.0 mmol). **3ad** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow oil (83 mg, 82%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.45−8.53 (m, 1H), 7.97 (dd, 2H, *J* = 8.8, 1.5 Hz), 7.46 (ddd, 1H, *J* = 11.3, 8.3, 1.3 Hz), 7.18−7.25 (m, 1H), 6.97−7.07 (m, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 160.4, 157.3 (d, J_{C-F} = 259.8 Hz) 145.8 (d, J_{C-F} = 10.0 Hz) 145.2 (d, J_{C-F} = 5.5 Hz) 130.1 (d, J_{C-F} = 5.5 Hz) 127.9 (d, J_{C-F} = 5.4 Hz) 123.9 (d, J_{C-F} = 20.9 Hz) 122.7 (d, J_{C-F} = 4.5 Hz), 113.8, 55.3; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −123.2; IR ν 3064, 3006, 2838, 1611, 1513, 1436, 1307, 1245, 1175, 1023 cm^{-1}; MS, *m*/*z* (%) 203 (100) $[M]^+$, 188 (54), 160 (35), 159 (22); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{12}H_{10}FNO$ 203.0746; found 203.0745.

*3-Fluoro-2-[4-(trifluoromethyl)phenyl]pyridine (**3ae**) [CAS: 1261805-54-2].* Compound **3ae** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-(trifluoromethyl)benzene **2e** (227 mg, 142 μL, 1.0 mmol). **3ae** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless oil (111 mg, 92%). Compound **3ae** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-4-(trifluoromethyl)benzene **2e′** (184 mg, 136 μL, 1.0 mmol). **3ae** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless oil (99 mg, 82%): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.51−8.61 (m, 1H), 8.13 (d, 2H, *J* = 8.1 Hz), 7.75 (d, 2H, *J* = 8.4 Hz), 7.46−7.60 (m, 1H), 7.30−7.38 (m, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 157.8 (d, J_{C-F} = 260.8 Hz), 145.6, 144.5 (d, J_{C-F} = 9.7 Hz), 138.6, 131.0 (q, J_{C-F} = 33.3 Hz), 129.1 (d, J_{C-F} = 6.9 Hz), 125.4 (q, J_{C-F} = 4.2 Hz), 124.6, 124.43, 124.37 (q, J_{C-F} = 273.3 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.7, −122.5; IR ν 3067, 1619, 1597, 1446, 1406, 1323, 1252, 1163, 1114, 1068, 1016 cm^{-1}; MS, *m*/*z* (%) 241 (100) $[M]^+$, 222 (19), 221 (17), 172 (27), 68 (15), 50 (12); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{12}H_7F_4N$ 241.0515; found 241.0519.

*2-(4-Chlorophenyl)-3-fluoropyridine (**3af**) [CAS: 1233702-02-7].* Compound **3af** was prepared following method A from 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-4-bromobenzene **2f** (191 mg, 1.0 mmol). **3af** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (73 mg, 71 mmol): mp 74−75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.52 (d, 1H, *J* = 4.5 Hz), 7.95 (dd, 2H, *J* = 8.5, 1.3 Hz), 7.41−7.55 (m, 3H), 7.24−7.33 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 157.5 (d, J_{C-F} = 260.7 Hz), 145.3, 144.9 (d, J_{C-F} = 10.0 Hz), 135.4, 133.6, 130.1 (d, J_{C-F} = 5.5 Hz), 128.7, 124.3 (d, J_{C-F} = 20.9 Hz), 123.8; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −123.0; IR ν 3048, 3016, 1599, 1497, 1445, 1398, 1254, 1190, 1092 cm^{-1}; MS, *m*/*z* (%) 209 (33) $[M]^+$, 208 (16), 207 (100) $[M]^+$, 172 (55), 145 (10), 75 (7), 50 (9); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{11}H_7{}^{35}ClFN$ 207.0251; found 207.0249.

*4-(3-Fluoro-2-pyridinyl)benzoic Acid Ethyl Ester (**3ag**) [CAS: 1246461-83-5].* Compound **3ag** was prepared following method A from 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 4-bromobenzoic acid ethyl ester **2g** (231 mg, 162 μL, 1.0 mmol). **3ag** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow oil (113 mg, 92%). Compound **3ag** was prepared following method A from 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 4-chlorobenzoic acid ethyl ester **2g′** (188 mg, 158 μL, 1.0 mmol). **3ag** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow oil (72 mg, 59%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.51−8.59 (m, 1H), 8.11−8.21 (m, 2H), 8.01−8.10 (m, 2H), 7.52 (ddd, 1H, *J* = 10.9, 8.4, 1.0 Hz), 7.30−7.35 (m, 1H), 4.42 (q, 2H, *J* = 7.1 Hz), 1.43 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.3, 157.8 (d, J_{C-F} = 261.6 Hz), 145.6 (d, J_{C-F} = 5.4 Hz), 145.0 (d, J_{C-F} = 10.9 Hz), 139.4 (d, J_{C-F} = 5.5 Hz), 130.8, 129.6, 128.7 (d, J_{C-F} = 6.4 Hz), 124.3 (d, J_{C-F} = 25.4 Hz), 124.2, 61.1, 14.3; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.1; IR ν 3064, 2984, 1711, 1443, 1402, 1367, 1267, 1186, 1095, 1016 cm^{-1}; MS, *m*/*z* (%) 245 (59) $[M]^+$, 217 (47), 201 (16), 200 (100), 172 (27), 125 (10); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{14}H_{12}FNO_2$ 245.0852; found 245.0847.

*2-[1,1′-Biphenyl]-4-yl-3-fluoropyridine (**3ah**).* Compound **3ah** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 4-bromo-1,1′-biphenyl **2h** (259 mg, 1.0 mmol). **3ah** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (100 mg, 81%): mp 97−98 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.52−8.59 (m, 1H), 8.09 (dd, 2H, *J* = 8.4, 1.6 Hz), 7.72−7.77 (m, 2H), 7.64−7.71 (m, 2H), 7.45−7.56 (m, 3H), 7.36−7.42 (m, 1H), 7.28−7.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 156.3 (d, J_{C-F} = 259.8 Hz), 145.7 (d, J_{C-F} = 10.1 Hz), 145.2 (d, J_{C-F} = 5.5 Hz), 142.0, 140.5, 134.0 (d, J_{C-F} = 5.5 Hz), 129.2 (d, J_{C-F} = 6.4 Hz), 128.8, 127.6, 127.17, 127.15, 124.3 (d, J_{C-F} = 20.9 Hz), 123.4 (d, J_{C-F} = 3.6 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.7; IR ν 3062, 3024, 1594, 1485, 1440, 1397, 1246 cm^{-1}; MS, *m*/*z* (%) 249 (100) $[M]^+$, 248 (23), 51 (8), 50 (10), 44 (8); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{17}H_{12}FN$ 249.0954; found 249.0938.

*1-[4-(3-Fluoro-2-pyridinyl)phenyl]ethanone (**3ai**).* Compound **3ai** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-(4-bromophenyl)-ethanone **2i** (203 mg, 1.0 mmol). **3ai** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless solid (50 mg, 47%): mp 88−89 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.57 (dt, 1H, J_d = 4.5, J_t = 1.5 Hz), 8.03−8.15 (m, 4H), 7.47−7.60 (m, 1H), 7.28−7.38 (m, 1H), 2.66 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 197.8, 157.8 (d, J_{C-F} = 261.6 Hz), 145.6 (d, J_{C-F} = 5.1 Hz), 144.8 (d, J_{C-F} = 10.2 Hz), 139.6 (d, J_{C-F} = 5.9 Hz), 137.2, 128.9 (d, J_{C-F} = 6.2 Hz), 128.4, 124.34 (d, J_{C-F} = 20.9 Hz), 124.30 (d, J_{C-F} = 4.0 Hz), 26.7; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.1; IR ν 3078, 3009, 1674, 1603, 1443, 1400, 1246 cm^{-1}; MS, *m*/*z* (%) 215 (17) $[M]^+$, 201 (14), 200 (100), 172 (30); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{13}H_{10}FNO$ 215.0746; found 215.0741.

*4-(3-Fluoro-2-pyridinyl)benzonitrile (**3aj**) [CAS: 1352794-83-2].* Compound **3aj** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 4-bromobenzonitrile **2j** (184 mg, 1.0 mmol). **3aj** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless solid (81 mg, 82%): mp 124−125 °C; ^{1}H NMR ($CDCl_3$, 75 MHz) δ 8.57 (dt, 1H, J_d = 4.4, J_t = 1.6 Hz), 8.10−8.17 (m, 2H), 7.74−7.81 (m, 2H), 7.55 (ddd, 1H, *J* = 11.1, 8.3, 1.3 Hz), 7.32−7.40 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.8 (d, J_{C-F} = 262.0 Hz), 145.7 (d, J_{C-F} = 5.5 Hz), 143.9 (d, J_{C-F} = 9.9 Hz), 139.5 (d, J_{C-F} = 5.5 Hz), 132.2 (d, J_{C-F} = 0.7 Hz), 129.3 (d, J_{C-F} = 6.6 Hz), 124.8 (d, J_{C-F} = 4.0 Hz), 124.6 (d, J_{C-F} = 20.9 Hz), 118.7, 112.7 (d, J_{C-F} = 1,1 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −121.9; IR ν 3061, 2226, 1605, 1595, 1441, 1402, 1248, 1099 cm^{-1}; MS *m*/*z* (%) 198 (100) $[M]^+$, 197 (56), 50 (8); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{12}H_7FN_2$ 198.0593; found 198.0585.

*3-Fluoro-2-(4-nitrophenyl)pyridine (**3ak**).* Compound **3ak** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-nitrobenzene **2k** (204 mg, 1.0 mmol). **3ak** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (96 mg, 88%): mp 140−141 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.59 (dt, 1H, J_d = 4.5 Hz, J_t = 1.5 Hz), 8.30−8.40 (m, 2H), 8.16−8.26 (m, 2H), 7.51−7.63 (m, 1H), 7.34−7.45 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 157.9 (d, J_{C-F} = 262.0), 148.0, 145.8 (d, J_{C-F} = 5.5 Hz), 143.4 (d, J_{C-F} = 9.9 Hz), 141.3 (d, J_{C-F} = 5.9 Hz), 129.6 (d, J_{C-F} = 6.6 Hz), 125.0 (d, J_{C-F} = 4.4 Hz),

DOI: 10.1021/acs.joc.7b00046
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124.6 (d, J_{C-F} = 20.5 Hz), 123.5; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −121.6; IR ν 3076, 1593, 1514, 1440, 1342, 1188, 1103 cm^{-1}; MS m/z (%) 218 (100) [M]$^+$, 188 (38), 172 (35), 160 (19), 145 (20), 125 (17), 44 (15); HRMS (EI) m/z [M]$^+$ calcd for $C_{11}H_7FN_2O_2$ 218.0492; found 218.0486.

*3-Fluoro-2-[3-(trifluoromethyl)phenyl]pyridine (**3al**) [CAS: 1261634-22-3].* Compound **3al** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-3-(trifluoromethyl)benzene **2l** (227 mg, 141 μL, 1.0 mmol). **3al** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless oil (116 mg, 96%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49−8.61 (m, 1H), 8.30 (s, 1H), 8.19 (d, 1H, J = 7.8 Hz), 7.71 (d, 1H, J = 8.0 Hz), 7.62 (t, 1H, J = 7.8 Hz), 7.54 (ddd, J = 11.0, 8.3, 1.3 Hz), 7.29−7.39 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): 157.6 (d, J_{C-F} = 261.6 Hz), 145.6 (d, J_{C-F} = 5.4 Hz), 144.5 (d, J_{C-F} = 10.9 Hz), 136.0 (d, J_{C-F} = 5.5 Hz), 131.8−132.1 (m), 130.9 (q, J_{C-F} = 31.8 Hz), 128.9, 125.7−125.9 (m), 125.5−125.7 (m), 124.4 (d, J_{C-F} = 20.9 Hz), 124.2 (d, J_{C-F} = 4.5 Hz), 123.9 (q, J_{C-F} = 273.4 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.6, −122.8; IR ν 3071, 1597, 1444, 1421, 1334, 1303, 1252, 1163, 1119, 1074 cm^{-1}; MS, m/z (%) 241 (100) [M]$^+$, 222 (20), 221 (19), 172 (25), 69 (16), 50 (12); HRMS (EI) m/z [M]$^+$ calcd for $C_{12}H_7F_4N$ 241.0515; found 241.0503.

*3-Fluoro-2-(3-methoxyphenyl)pyridine (**3am**) [CAS: 1269225-56-0].* Compound **3am** was prepared following method A from 3-fluoropyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-3-methoxybenzene **2m** (191 mg, 129 μL, 1.0 mmol). **3am** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as an orange oil (99 mg, 97%). Compound **3am** was prepared following method A from 3-fluoropyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-chloro-3-methoxybenzene **2m′** (145 mg, 125 μL, 1.0 mmol). **3am** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as an orange oil (62 mg, 61%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.52−8.54 (m, 1H), 7.54−7.60 (m, 2H), 7.50 (ddd, 1H, J = 11.0, 8.3, 1.5 Hz), 7.41 (t, 1H, J = 7.9 Hz), 7.26−7.30 (m, 1H), 6.98−7.03 (m, 1H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 159.7, 157.5 (d, J_{C-F} = 260.4 Hz), 146.0 (d, J_{C-F} = 10.3 Hz), 145.3 (d, J_{C-F} = 5.1 Hz), 136.6 (d, J_{C-F} = 5.1 Hz), 129.4, 124.1 (d, J_{C-F} = 21.3 Hz), 123.5 (d, J_{C-F} = 3.7 Hz), 121.3 (d, J_{C-F} = 7.3 Hz), 115.4, 113.8 (d, J_{C-F} = 5.1 Hz), 55.3; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.4; IR ν 3068, 2935, 2836, 1585, 1463, 1439, 1417, 1288, 1253, 1229 cm^{-1}; MS, m/z (%) 203 (97) [M]$^+$, 202 (100), 174 (39), 173 (27), 172 (46), 159 (14); HRMS (EI) m/z [M]$^+$ calcd for $C_{12}H_{10}FNO$ 203.0746; found 203.0744.

*2-[3-(tert-Butyl)phenyl]-3-fluoropyridine (**3an**).* Compound **3an** was prepared following method A from 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-3-(1,1-dimethylethyl)benzene **2n** (213 mg, 170 μL, 1.0 mmol). **3an** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless liquid (61 mg, 53%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.54 (dt, 1H, J_d = 4.5 Hz, J_t = 1.5 Hz), 8.00 (d, 1H, J = 1.5 Hz), 7.76 (dq, 1H, J_d = 7.5 Hz, J_q = 1.6 Hz), 7.40−7.53 (m, 3H), 7.23−7.30 (m, 1H), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 157.5 (d, J_{C-F} = 262.5 Hz), 151.3, 146.8 (d, J_{C-F} = 10.9 Hz), 145.1 (d, J_{C-F} = 5.4 Hz), 134.7 (d, J_{C-F} = 4.5 Hz), 128.1, 126.4, 126.0 (d, J_{C-F} = 5.4 Hz), 125.8 (d, J_{C-F} = 4.5 Hz), 124.1 (d, J_{C-F} = 20.9 Hz), 123.3 (d, J_{C-F} = 3.6 Hz), 34.8, 31.3; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.9; IR ν 3064, 2963, 2868, 1596, 1438, 1409, 1364, 1249 cm^{-1}; MS, m/z (%) 229 (28) [M]$^+$, 215 (15), 214 (100), 199 (11), 185 (10), 43 (15); HRMS (EI) m/z [M]$^+$ calcd for $C_{15}H_{16}FN$ 229.1267; found 229.1285.

*3-Fluoro-2-(5-methoxy-2-methylphenyl)pyridine (**3ao**).* Compound **3ao** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-bromo-4-methoxy-2-methylbenzene **2o** (207 mg, 228 μL, 1.0 mmol). **3ao** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow oil (98 mg, 90%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.41−8.47 (m, 1H), 7.36−7.45 (m, 1H), 7.19−7.29 (m, 2H), 6.74−6.81 (m, 2H), 3.78 (s, 3H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 159.9, 157.0 (d, J_{C-F} = 256.1 Hz), 148.1 (d, J_{C-F} = 14.5 Hz), 145.1 (d, J_{C-F} = 5.4 Hz), 138.3, 131.1 (d, J_{C-F} = 1.8 Hz), 127.6 (d, J_{C-F} = 3.6 Hz), 123.3 (d, J_{C-F} = 2.7 Hz), 123.2 (d, J_{C-F} = 14.5 Hz), 115.7, 111.2, 55.2, 19.9; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −121.2; IR ν 3061, 3002, 2930, 2835, 1608, 1575, 1507, 1436, 1283, 1240, 1185 cm^{-1}; MS, m/z (%) 217 (67) [M]$^+$, 216 (28), 198 (77), 197 (100), 183 (25), 182 (24), 154 (23); HRMS (EI) m/z [M]$^+$ calcd for $C_{13}H_{12}FNO$ 217.0903; found 217.0901.

*3-Fluoro-2-(1-naphthalenyl)pyridine (**3ap**).* Compound **3ap** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 2-bromonaphthalene **2p** (213 mg, 1.0 mmol). **3ap** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (82 mg, 74%): mp 93−94 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59−8.68 (m, 1H), 7.89−8.03 (m, 2H), 7.76 (d, 1H, J = 8.0 Hz), 7.56−7.69 (m, 3H), 7.46−7.56 (m, 2H), 7.37−7.45 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 157.5 (d, J_{C-F} = 257.9 Hz), 147.4 (d, J_{C-F} = 14.5 Hz), 145.4 (d, J_{C-F} = 5.4 Hz), 133.7, 132.8 (d, J_{C-F} = 3.6 Hz), 131.2, 129.5, 128.4, 127.9 (d, J_{C-F} = 1.0 Hz), 126.5, 125.9, 125.2 (d, J_{C-F} = 1.8 Hz), 125.1, 123.9 (d, J_{C-F} = 3.6 Hz), 123.6 (d, J_{C-F} = 20.0 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −120.3; IR ν 3047, 3010, 1592, 1561, 1447, 1395, 1341, 1253, 1201 cm^{-1}; MS, m/z (%) 223 (34) [M]$^+$, 222 (100), 221 (7), 111 (8), 50 (9); HRMS (EI) m/z [M]$^+$ calcd for $C_{15}H_{10}FN$ 223.0797; found 223.0785.

*3-Fluoro-2,2′-bipyridine (**3aq**) [CAS: 1863378-49-7].* Compound **3aq** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (136 mg, 0.75 mmol) and 2-bromopyridine **2q** (80 mg, 48 μL, 0.5 mmol). **3aq** was isolated (SiO_2, cyclohexane/ethyl acetate = 1/1) as a colorless oil (32 mg, 37%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.81 (d, 1H, J = 4.8 Hz), 8.59 (dt, 1H, J_d = 4.5 Hz, J_t = 1.5 Hz), 7.94−8.04 (m, 1H), 7.77−7.89 (m, 1H), 7.48−7.62 (m, 1H), 7.31−7.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 158.0 (d, J_{C-F} = 264.3 Hz), 153.5 (d, J_{C-F} = 6.4 Hz), 149.6, 145.5 (d, J_{C-F} = 5.5 Hz), 144.8 (d, J_{C-F} = 9.1 Hz), 136.7, 124.9 (d, J_{C-F} = 3.6 Hz), 124.7 (d, J_{C-F} = 20.9 Hz), 124.2 (d, J_{C-F} = 5.4 Hz), 123.6; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.5; IR ν 3059, 3011, 1585, 1454, 1422, 1256, 1196, 802 cm^{-1}; MS, m/z (%) 174 (100) [M]$^+$, 173 (33), 147 (20), 146 (20), 76 (15), 51 (26), 50 (25); HRMS (EI) m/z [M]$^+$ calcd for $C_{10}H_7FN_2$ 174.0593; found 174.0597.

*3-(3-Fluoro-2-pyridinyl)quinoline (**3ar**).* Compound **3ar** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 3-bromoquinoline **2r** (104 mg, 68 μL, 0.50 mmol). **3ar** was isolated (SiO_2, cyclohexane/ethyl acetate = 4/1) as a colorless solid (70 mg, 62%): mp 138−139 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 9.57 (s, 1H), 8.77−8.82 (m, 1H), 8.59−8.65 (m, 1H), 8.18 (d, 1H, J = 8.3 Hz), 7.95 (dd, 1H, J = 8.1, 1.5 Hz), 7.72−7.84 (m, 1H), 7.52−7.66 (m, 2H), 7.31−7.43 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 158.0 (d, J_{C-F} = 261.3 Hz), 150.3 (d, J_{C-F} = 6.6 Hz), 148.0, 145.8 (d, J_{C-F} = 5.1 Hz), 143.6 (d, J_{C-F} = 11.0 Hz), 136.0 (d, J_{C-F} = 7.0 Hz), 130.2, 129.3, 128.6, 128.2 (d, J_{C-F} = 5.9 Hz), 127.5, 126.9, 124.3 (d, J_{C-F} = 16.8 Hz), 124.1 (d, J_{C-F} = 4.0 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −122.3; IR ν 3061, 3038, 1595, 1410, 1344, 1113 cm^{-1}; MS, m/z (%) 224 (100) [M]$^+$, 223 (45), 205 (10), 122 (10), 76 (10), 50 (14); HRMS (EI) m/z [M]$^+$ calcd for $C_{14}H_9FN_2$ 224.0750; found 224.0739.

*3-Fluoro-2-(3-thienyl)pyridine (**3as**).* Compound **3as** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 3-bromothiophene **2s** (168 mg, 97 μL, 1.0 mmol). **3as** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless oil (50 mg, 56%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.46 (dt, 1H, J_d = 4.5 Hz, J_t = 1.6 Hz), 8.04−8.12 (m, 1H), 7.86 (dt, 1H, J_d = 5.1 Hz, J_t = 1.3 Hz), 7.36−7.53 (m, 2H), 7.14−7.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 156.8 (d, J_{C-F} = 260.5 Hz), 145.1 (d, J_{C-F} = 4.8 Hz), 142.1 (d, J_{C-F} = 11.0 Hz), 136.9 (d, J_{C-F} = 6.2 Hz), 127.6 (d, J_{C-F} = 4.8 Hz), 126.2 (d, J_{C-F} = 11.0 Hz), 125.3 (d, J_{C-F} = 1.5 Hz), 123.7 (d, J_{C-F} = 20.5 Hz), 122.7 (d, J_{C-F} = 4.0 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −121.4; IR ν 3113, 3065, 3021, 1597, 1454, 1440, 1206, 1099 cm^{-1}; MS, m/z (%) 179 (100) [M]$^+$, 178 (26), 160 (37), 135 (10), 107 (10), 45 (11); HRMS (EI) m/z [M]$^+$ calcd for C_9H_6FNS 179.0205; found 179.0208.

*3-Fluoro-2-(2-thienyl)pyridine (**3at**).* Compound **3at** was prepared following method A from potassium 3-fluoropyridinecrboxylate **1a** (90.5 mg, 0.50 mmol) and 2-bromothiophene **2t** (166 mg, 99 μL, 1.0 mmol). **3at** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (56 mg, 63%): mp 43−44 °C; ^{1}H NMR ($CDCl_3$, 200

DOI: 10.1021/acs.joc.7b00046
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MHz) δ 8.41 (dt, 1H, J_d = 4.9 Hz, J_t = 1.6 Hz), 7.80−7.86 (m, 1H), 7.38−7.53 (m, 2H), 7.12−7.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 155.7 (d, J_{C-F} = 263.1 Hz), 145.0 (d, J_{C-F} = 4.8 Hz), 141.3 (d, J_{C-F} = 11.3 Hz), 139.8 (d, J_{C-F} = 7.7 Hz), 128.2 (d, J_{C-F} = 2.2 Hz), 128.1 (d, J_{C-F} = 5.5 Hz), 127.9 (d, J_{C-F} = 7.3 Hz), 123.6 (d, J_{C-F} = 19.4 Hz), 122.6 (d, J_{C-F} = 4.0 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz) δ −120.7; IR ν 3123, 3082, 1597, 1449, 1362, 1260, 1204, 1101 cm^{-1}; MS, m/z (%) 179 (100) [M]$^+$, 178 (13), 135 (17), 134 (8), 107 (10), 45 (14); HRMS (EI) m/z [M]$^+$ calcd for C_9H_6FNS 179.0205; found 179.0200.

*1-[5-(3-Fluoro-2-pyridinyl)-2-thienyl]ethanone (**3au**).* Compound **3au** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 1-(5-bromo-2-thienyl)ethanone **2u** (207 mg, 1.0 mmol). **3au** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a yellow solid (34 mg, 31%): mp 146−147 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.44 (dt, 1H, J_d = 4.5 Hz, J_t = 1.6 Hz), 7.76−7.82 (m, 1H), 7.69−7.74 (m, 1H), 7.43−7.55 (m, 1H), 7.22−7.32 (m, 1H), 2.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 190.7, 156.4 (d, J_{C-F} = 262.6 Hz), 147.0 (d, J_{C-F} = 7.7 Hz), 145.4 (d, J_{C-F} = 5.0 Hz), 144.9 (d, J_{C-F} = 3.3 Hz), 140.1 (d, J_{C-F} = 11.1 Hz), 133.0 (d, J_{C-F} = 2.2 Hz), 128.3 (d, J_{C-F} = 12.2 Hz), 124.3 (d, J_{C-F} = 3.3 Hz), 124.1 (d, J_{C-F} = 18.2 Hz), 26.9; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −119.4; IR ν 3121, 3063, 2920, 2850, 1646, 1425, 1273, 1259 cm^{-1}; MS, m/z (%) 221 (42) [M]$^+$, 207 (14), 206 (100), 178 (23), 134 (17), 107 (9); HRMS (EI) m/z [M]$^+$ calcd for $C_{11}H_8FNOS$ 221.0311; found 221.0304.

*3-Fuoro-2-(5-benzofuranyl)pyridine (**3av**).* Compound **3av** was prepared following method A from potassium 3-fluoro-2-pyridinecarboxylate **1a** (90.5 mg, 0.50 mmol) and 5-bromobenzofuran **2v** (203 mg, 1.0 mmol). **3av** was isolated (SiO_2, cyclohexane/ethyl acetate =9/1) as a yellow solid (54 mg, 51%): mp 81−82 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.50−8.58 (m, 1H), 8.23 (t, 1H, J = 1.5 Hz), 7.91−8.00 (m, 1H), 7.44−7.70 (m, 3H), 7.21−7.32 (m, 1H), 6.86 (dd, 1H, J = 2.3, 1.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.4 (d, J_{C-F} = 259.8 Hz), 155.4, 146.5 (d, J_{C-F} = 10.5 Hz), 145.6, 145.3 (d, J_{C-F} = 5.5 Hz), 130.3 (d, J_{C-F} = 5.5 Hz), 127.6, 125.3 (d, J_{C-F} = 5.5 Hz), 124.1 (d, J_{C-F} = 20.5 Hz), 123.0 (d, J_{C-F} = 3.9 Hz), 122.0 (d, J_{C-F} = 6.1 Hz), 111.3, 107.0; ^{19}F NMR ($CDCl_3$, 41 MHz) δ −120.7; IR ν 3156, 3125, 3042, 3013, 1597, 1443, 1192, 1024 cm^{-1}; MS, m/z (%) 213 (100) [M]$^+$, 212 (14), 185 (17), 184 (13); HRMS (EI) m/z [M]$^+$ calcd for $C_{13}H_8FNO$ 213.0590; found 213.0585.

*1-[2-(4-Fluorophenyl)-3-pyridinyl]ethanone (**3ba**) [CAS: 280573-47-9].* Compound **3ba** was prepared following method A from potassium 3-acetyl-2-pyridinecarboxylate **1b** (102 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ba** was isolated (SiO_2, cyclohexane/ethyl acetate = 2/1) as an orange oil (56 mg, 52%): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.75 (dd, 1H, J = 4.8, 1.7 Hz), 7.86 (dd, 1H, J = 7.7, 1.7 Hz), 7.51−7.61 (m, 2H), 7.35 (dd, 1H, J = 7.7, 4.9 Hz), 7.11−7.22 (m, 2H), 2.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 203.3, 163.6 (d, J_{C-F} = 250.0 Hz), 156.0, 150.9, 136.2, 136.2, 135.8 (d, J_{C-F} = 3.7 Hz), 131.0 (d, J_{C-F} = 8.3 Hz), 122.0, 115.8 (d, J_{C-F} = 22.1 Hz), 30.2; ^{19}F NMR ($CDCl_3$, 235 MHz) δ −111.7; IR ν 3046, 2922, 2853, 1686, 1510, 1425, 1221, 843 cm^{-1}; MS, m/z (%) 215 (42) [M]$^+$, 214 (26), 200 (100), 172 (45), 145 (20), 43 (43); HRMS (EI) m/z [M]$^+$ calcd for $C_{13}H_{10}FNO$ 215.0746; found 215.0742.

*3-(1-Piperidinyl)-2-(4-fluorophenyl)pyridine (**3ca**).* Compound **3ca** was prepared following method A from potassium 3-(1-piperidinyl)-2-pyridinecarboxylate **1c** (122 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ca** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a brown oil (22 mg, 17%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.30 (dd, 1H, J = 4.5, 1.5 Hz), 7.95−8.08 (m, 2H), 7.34 (dd, 1H, J = 8.3, 1.5 Hz), 7.04−7.21 (m, 3H), 2.78 (m, 4H), 1.44−1.64 (m, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 162.5 (d, J_{C-F} = 246.6 Hz), 151.3, 147.9, 142.7, 136.6 (d, J_{C-F} = 3.7 Hz), 130.3 (d, J_{C-F} = 8.1 Hz), 126.0, 122.5, 114.9 (d, J_{C-F} = 21.2 Hz), 52.3, 25.9, 23.9; ^{19}F NMR ($CDCl_3$, 41 MHz) δ −114.4 IR ν 3060, 2935, 2854, 1602, 1573, 1507, 1432, 1219 cm^{-1}; MS, m/z (%) 256 (100) [M]$^+$, 255 (39), 199 (15), 160 (17), 159 (7), 145 (8); HRMS (EI) m/z [M]$^+$ calcd for $C_{16}H_{17}FN_2$ 256.1376; found 256.1365.

*3-Chloro-2-(4-fluorophenyl)pyridine (**3da**) [CAS: 847226-00-0].* Compound **3da** was prepared following method A from potassium 3-chloro-2-pyridinecarboxylate **1d** (97.8 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol) in the presence of Ag_2CO_3 (6.96 mg, 25 μmol, 5 mol %) instead of Cu_2O. **3da** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (63 mg, 49%): mp 80−81 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (dd, 1H, J = 4.7, 1.6 Hz), 7.71−7.83 (m, 3H), 7.12−7.26 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 163.1 (d, J_{C-F} = 248.1 Hz), 155.5, 147.6, 138.2, 134.2 (d, J_{C-F} = 3.3 Hz), 131.3 (d, J_{C-F} = 8.4 Hz), 130.1, 123.1, 115.0 (d, J_{C-F} = 22.0 Hz); ^{19}F NMR ($CDCl_3$, 41 MHz) δ −112.6; IR ν 3044, 1599, 1574, 1513, 1432, 1402, 1161, 848 cm^{-1}; MS, m/z (%) 209 (30) [M]$^+$, 208 (12), 207 (73) [M]$^+$, 173 (12), 172 (100), 145 (20), 43 (20); HRMS (EI) m/z [M]$^+$ calcd for $C_{11}H_7{}^{35}ClFN$ 207.0251; found 207.0237; [M]$^+$ calcd for $C_{11}H_7{}^{37}ClFN$ 209.0222; found 209.0211.

*2-(4-Fluorophenyl)-3-methoxypyridine (**3ea**) [CAS: 1214324-71-6].* Compound **3ea** was prepared following method B from potassium 3-methoxy-2-pyridinecarboxylate **1e** (95.6 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ea** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless oil (71 mg, 70%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (dd, 1H, J = 4.6, 1.4 Hz), 7.90−7.97 (m, 2H), 7.28−7.32 (m, 1H), 7.22−7.26 (m, 1H), 7.09−7.17 (m, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 162.8 (d, J_{C-F} = 247.0 Hz), 153.4, 147.0, 141.3, 133.7 (d, J_{C-F} = 2.7 Hz), 131.2 (d, J_{C-F} = 8.2 Hz), 122.9, 118.5, 114.8 (d, J_{C-F} = 20.9 Hz), 55.4; ^{19}F NMR ($CDCl_3$, 377 MHz) δ −113.7; IR ν 3061, 3006, 2942, 2839, 1601, 1508, 1430, 1266, 1220, 1196, 1158, 1125, 1013 cm^{-1}; MS m/z (%) 203 (71) [M]$^+$, 202 (100), 174 (14), 173 (18), 172 (32), 133 (28), 50 (12); HRMS (EI) m/z [M]$^+$ calcd for $C_{12}H_{10}FNO$ 203.0746; found 203.0744.

*2-(4-Fluorophenyl)-pyridine (**3fa**) [CAS: 58861-53-3].* Compound **3fa** was prepared following method A in NMP/mesitylene (2 mL, 1/1) at 190 °C from potassium 2-pyridinecarboxylate **1f** (81.4 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3fa** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless solid (32 mg, 37%): mp 39−40 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.73−8.63 (m, 1H), 8.06−7.94 (m, 2H), 7.81−7.65 (m, 2H), 7.26−7.12 (m, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 163.5 (d, J_{C-F} = 248.5 Hz), 156.5, 149.7, 136.8, 135.6 (d, J_{C-F} = 3.3 Hz), 128.7 (d, J_{C-F} = 8.4 Hz), 122.0, 120.2, 115.6 (d, J_{C-F} = 21.6 Hz); ^{19}F NMR ($CDCl_3$, 41 MHz) δ −112.0; IR ν 3055, 3011, 1600, 1584, 1509, 1464, 1433, 1219, 1099 cm^{-1}; MS m/z (%) 173 (100) [M]$^+$, 146 (9), 51 (11); HRMS (EI) m/z [M]$^+$ calcd for $C_{11}H_8FN$ 173.0641; found 173.0640.

*2-Phenylpyridine (**3fb**) [CAS: 1008-89-5].*[35,55] Compound **3fb** was prepared following method A in NMP/mesitylene (2 mL, 1/1) at 190 °C from potassium 2-pyridinecarboxylate **1f** (81.4 mg, 0.50 mmol) and bromobenzene **2b** (159 mg, 106 μL, 1.0 mmol). **3fb** was isolated (SiO_2, cyclohexane/ethyl acetate = 9/1) as a colorless liquid (31 mg, 40%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.72 (dt, 1H, J_d = 4.8, J_t = 1.4 Hz), 8.06−7.95 (m, 2H), 7.83−7.70 (m, 2H), 7.55−7.37 (m, 3H), 7.30−7.21 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 157.5, 149.6, 139.4, 136.8, 129.0, 128.7, 126.9, 122.1, 120.6; MS m/z (%) 155 (100) [M]$^+$.

*2-(4-Methoxyphenyl)-pyridine (**3fd**) [CAS: 5957-90-4].*[35,56] Compound **3fd** was prepared following method A in NMP/mesitylene (2 mL, 1/1) at 190 °C from potassium 2-pyridinecarboxylate **1f** (81.4 mg, 0.50 mmol) and bromo-4-methoxybenzene **2d** (187 mg, 126 μL, 1.0 mmol). **3fd** was isolated (SiO_2, cyclohexane/ethyl acetate = 4/1) as a colorless oil (26 mg, 28%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.67 (dt, 1H, J_d = 4.7 Hz, J_t = 1.5 Hz), 8.01−7.92 (m, 2H), 7.78−7.63 (m, 2H), 7.19 (ddd, 1H, J = 6.6, 4.9, 1.9 Hz) 7.06−6.96 (m, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.5, 157.1, 149.4, 136.7, 131.9, 128.2, 121.4 119.8, 114.1, 55.3; MS m/z (%) 185 (100) [M]$^+$.

*5-(4-Fluorophenyl)-1-methyl-1H-pyrazole (**3ga**) [CAS: 689251-78-3].* Compound **3ga** was prepared following method B from potassium 1-methyl-1*H*-pyrazole-5-carboxylate **1g** (82.1 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ga** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a colorless liquid (56 mg, 64%): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.51 (d,

DOI: 10.1021/acs.joc.7b00046
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1H, J = 1.9 Hz), 7.34−7.44 (m, 2H), 7.08−7.21 (m, 2H), 6.28 (d, 1H, J = 1.9 Hz), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 162.8 (d, J_{C-F} = 248.1 Hz), 142.5, 138.5, 130.6 (d, J_{C-F} = 3.7 Hz), 126.9 (d, J_{C-F} = 8.1 Hz), 115.7 (d, J_{C-F} = 22.0 Hz), 106.1, 37.3; ^{19}F NMR ($CDCl_3$, 235 MHz) δ −112.8; IR ν 3103, 3063, 2947, 1605, 1545, 1493, 1223, 839 cm^{-1}; MS, m/z (%) 176 (100) [M]$^+$, 175 (39), 148 (16), 133 (13), 121 (16), 109 (9); HRMS (EI) m/z [M]$^+$ calcd for $C_{10}H_9FN_2$ 176.0750; found 176.0740.

*5-(4-Fluorophenyl)-4-methylthiazole (**3ha**) [CAS: 623577-48-0].* Compound **3ha** was prepared following methods A and B, respectively, from potassium 4-methyl-5-thiazolecarboxylate **1h** (90.6 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ha** was isolated (SiO_2, cyclohexane/ethyl acetate = 6/1) as a yellow solid (35 mg, 36% (method A); 72 mg, 75% (method B)): mp 35−36 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.68 (s, 1H), 7.35−7.46 (m, 2H), 7.05−7.18 (m, 2H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 162.4 (d, J_{C-F} = 248.5 Hz), 150.2, 148.6 (d, J_{C-F} = 0.7 Hz), 131.0 (d, J_{C-F} = 8.0 Hz), 130.8, 127.9 (d, J_{C-F} = 3.3 Hz), 115.7 (d, J_{C-F} = 22.0 Hz), 15.9; ^{19}F NMR ($CDCl_3$, 235 MHz) δ −113.5; IR ν 3096, 3042, 2922, 1603, 1497, 1240, 831 cm^{-1}; MS, m/z (%) 193 (100) [M]$^+$, 192 (9), 166 (24), 165 (24), 133 (19), 122 (11); HRMS (EI) m/z [M]$^+$ calcd for $C_{10}H_8FNS$ 193.0361; found 193.0352.

*2-(4-Fluorophenyl)-benzo[b]thiophene (**3ia**) [CAS: 936734-96-2].* Compound **3ia** was prepared following method B from potassium benzo[b]thiophene-2-carboxylate **1i** (108 mg, 0.50 mmol) and 1-bromo-4-fluorobenzene **2a** (177 mg, 111 μL, 1.0 mmol). **3ia** was isolated (SiO_2, cyclohexane) as a colorless solid (24 mg, 21%): mp 181−182 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.75−7.89 (m, 2H), 7.63−7.75 (m, 2H), 7.48 (s, 1H), 7.28−7.43 (m, 2H), 7.06−7.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 162.8 (d, J_{C-F} = 248.1 Hz), 143.1, 140.7, 139.5, 130.6, 128.2 (d, J_{C-F} = 8.1 Hz), 124.6, 124.4, 123.5, 122.2, 119.4 (d, J_{C-F} = 1.5 Hz), 115.9 (d, J_{C-F} = 21.6 Hz); ^{19}F NMR ($CDCl_3$, 235 MHz) δ −113.4; IR ν 3061, 1593, 1431, 1233, 818 cm^{-1}; MS, m/z (%) 228 (100) [M]$^+$, 196 (8), 183 (12), 40 (9); HRMS (EI) m/z [M]$^+$ calcd for $C_{14}H_9FS$ 228.0409; found 228.0397.

*Synthesis of 3-Methoxy-2-phenylpyridine (**4**) [CAS: 53698-49-0].*[57] To a solution of methanol (17.6 mg, 22 μL, 0.55 mmol) and **3ab** (86.6 mg, 0.5 mmol) in dry DMF (5 mL) at 0 °C was added dropwise dry KHMDS (0.5 M in toluene, 1.1 mL, 0.55 mmol). The reaction was allowed to warm to rt overnight and then quenched with saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the volatiles were removed under reduced pressure. The residue was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate = 6/1), yielding **4** as colorless oil (86 mg, 93%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.33 (dd, 1H, J = 4.3, 1.8 Hz), 7.96−7.86 (m, 2H), 7.51−7.32 (m, 3H), 7.30−7.19 (m, 2H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.6, 148.2, 141.3, 137.7, 129.4, 128.3, 128.0, 122.9, 118.5, 55.5; MS, m/z (%) 185 (61) [M]$^+$, 184 (100), 154 (33).

*Synthesis of 2-Phenyl-2-(3-(2-phenyl)pyridyl)acetonitrile (**6**).* A 20 mL microwave vessel was charged with **3ab** (86.6 mg, 0.5 mmol) and potassium *tert*-butoxide (318 mg, 2.75 mmol). NMP (1 mL) and benzylcyanide **5** (293 mg, 290 μL, 2.5 mmol) were added, and the mixture was heated at 100 °C in the microwave for 5 min. The mixture was allowed to cool to rt, washed with distilled water (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and the volatiles were removed under reduced pressure. The residue was purified by column chromatography (SiO_2, *n*-pentane/diethyl ether = 2/3), yielding compound **6** as colorless oil (120 mg, 89%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.69 (dd, 1H, J = 4.8, 1.5 Hz), 7.85 (dd, 1H, J = 8.0, 1.6 Hz), 7.53−7.42 (m, 5H), 7.41−7.28 (m, 4H), 7.18−7.06 (m, 2 H), 5.44 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 158.5, 149.3, 138.7, 137.3, 135.2, 130.1, 129.2, 128.9, 128.8, 128.7, 128.3, 127.4, 123.1, 119.4, 38.9; IR ν 3051, 2910, 2241, 1564, 1492, 1435 cm^{-1}; MS, m/z (%) 270.15 (89) [M]$^+$, 269.15 (100); HRMS (EI) m/z [M]$^+$ calcd for $C_{19}H_{14}N_2$ 270.1157; found 270.1146.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00046.

Full optimization table and copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra of all products (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Brian T. O'Neill for helpful discussions, the DFG (SFB/TRR-88 "3MET" and EXC/1069 "RESOLV"), and the Stipendienstiftung Rheinland-Pfalz (fellowship to D.H.) for financial support.

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DOI: 10.1021/acs.joc.7b00046
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