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Palladium-catalyzed C–H arylation using aryltrifluoroborates in conjunction with a Mn^{III} oxidant under mild conditions

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ABSTRACT

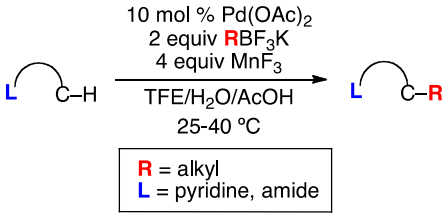
This paper describes the development of a mild Pd-catalyzed C–H arylation reaction using potassium aryltrifluoroborates in conjunction with $Mn(OAc)_3$ as the oxidant. The scope of this transformation is explored with a variety of different aryltrifluoroborates and arylpyridine substrates. Preliminary mechanistic studies suggest that the reaction proceeds via a high-valent Pd mechanism with C–H activation occurring at or before the rate determining step.

1. Introduction

Palladium-catalyzed C–C bond-forming reactions serve as valuable synthetic methods for the formation of aryl–aryl linkages in a wide variety of synthetic contexts.[1] Traditional Pd-catalyzed cross-coupling sequences suffer from the disadvantage that they require two pre-functionalized starting materials. This necessitates the independent preparation of the two coupling partners, which can increase the cost and the number of steps required for the overall target synthesis. In contrast, Pd-catalyzed C–H arylation reactions eliminate the need for at least one prefunctionalization step, and thus can serve as a more expedient strategy for aryl–aryl bond construction.[2]

Over the past 10 years, numerous Pd-catalyzed C–H arylation reactions have been developed.[3] Many different aryl coupling partners have been utilized in these transformations, including diaryliodonium salts,[4] aryl halides,[5] aryl C–H bonds,[6] and organometallic reagents.[7] Among these, arylboron compounds are particularly attractive for reasons that include their low toxicity, low cost, and high stability.[8] As such, a number of reports have explored the use of arylboronic acids,[9] arylboronate esters,[10] and aryltrifluoroborates[11] as coupling partners for the C–H arylation of substrates bearing directing groups such as pyridines, anilides, benzoic acids, and oximes. However, the vast majority of these reactions are limited by the requirement for relatively high temperatures (usually ≥90 °C).[12] Furthermore, additives and promoters such as stoichiometric bases, silver salts, and/or benzoquinone (BQ) are generally required in all of these transformations. These features can limit functional group tolerance and also render the reactions operationally complex. For example, in reactions where insoluble additives are present, stir rate can be a major factor that impacts reaction yield and scalability.[13] Finally, the identification of oxidants that are competent and compatible with these transformations can also be a challenge. To date, the vast majority of reported examples of Pd-catalyzed C–H arylation with arylboron reagents involve Cu^{II}- or Ag^{I}-based oxidants and proceed via $Pd^{II/0}$ catalytic manifolds.

In response to these challenges, we sought to develop an operationally simple and mild method for C–H arylation using readily available arylboron reagents. Our efforts in this area were inspired by our recent development of a related room temperature Pd-catalyzed C–H alkylation reaction using alkyltrifluoroborate salts. This transformation utilizes MnF_3 as a stoichiometric oxidant and proceeds at unprecedentedly low reaction temperatures (Scheme 1).[14] Unlike rare prior examples of Pd-catalyzed C–H alkylation with alkylboron reagents, the MnF_3-mediated transformation is believed to involve C–C bond-forming reductive elimination from a high-valent Pd center. Notably, this alkylation does not require the use of additives like benzoquinone, and it proceeds readily at low temperatures (3–6 h at 25–40 °C) under only mildly acidic conditions. The current paper describes the development, optimization, and scope of a related Pd-catalyzed C–H arylation reaction involving aryltrifluoroborate salts in conjunction



Scheme 1. Pd-catalyzed C–H alkylation with alkyltrifluoroborates in conjunction with MnF_3.[14]

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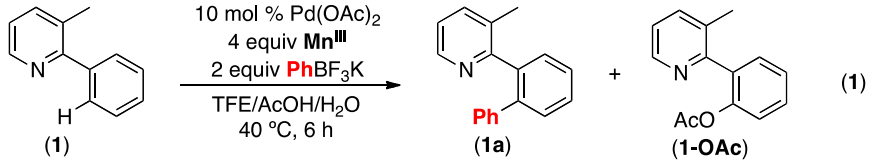
with a Mn^{III} oxidant. Preliminary investigations of the mechanism of this transformation are also presented.

2. Results and discussion

2.1. Reaction optimization

We first tested the $Pd(OAc)_2$-catalyzed C–H arylation of 3-methyl-2-phenylpyridine (**1**) with $PhBF_3K$ under the conditions that had proven optimal for C–H alkylation with CH_3BF_3K [0.10 equiv $Pd(OAc)_2$, 4 equiv MnF_3, 2 equiv RBF_3K, 8:1:1 TFE/AcOH/H_2O (TFE=2,2,2-trifluoroethanol), 40 °C, 6 h]. As shown in Eq. 1, this reaction provided the *ortho*-phenylated product **1a** in moderate yield (46%), along with a substantial quantity (14%) of the *ortho*-acetoxylated product **1**-OAc. Interestingly, however, the use of a different Mn^{III} oxidant [$Mn(OAc)_3$] in place of MnF_3 provided a comparable yield of **1a** (34%) without formation of the undesired acetoxylated product **1**-OAc. Consequently, all subsequent optimization studies were conducted with $Mn(OAc)_3$ as the oxidant.



MnF_3:	46%	14%
$Mn(OAc)_3$:	34%	<1%

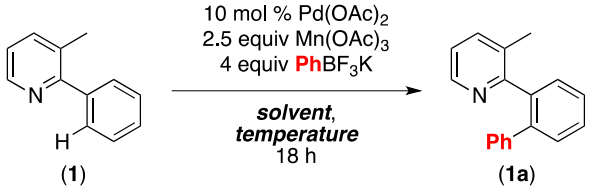
Increasing the reaction time to 18 h and the reaction temperature to 50 °C using 2.5 equiv $Mn(OAc)_3$ and 4 equiv $PhBF_3K$ provided a modest improvement in reaction yield (Table 1, entry 2 vs entry 1). Evaluation of a number of solvent systems under these conditions (entries 3–7) showed that a 1:1 mixture of TFE and AcOH provided the highest yield of **1a** at 50 °C (77%, entry 7). Lowering the temperature to 40 or 25 °C resulted in a decrease in yield and conversion (entries 8 and 9). The addition of 1 equiv of NaOAc, an additive that is sometimes used to modulate alkene oxidation reactions using $Mn(OAc)_3$,[15] had a negligible impact on the yield and conversion with substrate **1** (compare entry 7 with entry 10). Nevertheless, this additive was subsequently found to provide an improvement in yield with some other substrates and aryltrifluoroborates; consequently it was routinely added to the scale-up reactions shown in Tables 2 and 3. The addition of 1 equiv of benzoquinone, which is known to promote the reductive elimination step of $Pd^{II/0}$-catalyzed C–H arylation reactions, resulted in a significant reduction in both yield and conversion (compare entry 7 with entry 11). Under the optimized reaction conditions, phenylboronic acid, phenylboronic acid pinacol ester, and triphenylboroxine were less effective arylating reagents than $PhBF_3K$ (compare entry 7 with entries 12–14). Finally, as expected, no product was formed in the absence of Pd (entry 15), and only trace quantities of **1a** could be detected when Mn^{III} was excluded from the reaction mixture (entry 16).

2.2. Substrate scope

C–H arylation of **1** proceeded smoothly using diverse aryltrifluoroborates (Table 2). Both electron-withdrawing and electron-donating substituents on the $ArBF_3K$ reagent were well tolerated in this transformation. In general, electron-neutral and electron-rich aryltrifluoroborates provided the highest yields (between 52 and 80% for mono-arylation products **1a**–**1f** and **1n**). Potentially sensitive iodide and aldehyde substituents were compatible with the reaction conditions (**1j**, **1k**, and **1m**). Interestingly *ortho*-substituted 2-methoxyphenyltrifluoroborate provided the C–H arylation product **1e** in 71% yield, compared to a more modest 52% yield using the electronically similar *para*-substituted analogue (**1f**).

A range of substituted 2-arylpyridine derivatives could also be arylated using this methodology. As shown in Table 3, good to excellent yields were obtained for arylpyridine substrates bearing electron-donating substituents at the 2′- or 4′-position (**2a**–**4a**, **10a**). More modest conversions and yields were attained with substrates bearing electron-withdrawing groups on either the arene or the pyridine ring. In some cases where significant starting material remained at the end of the reaction, difficulty in separating phenylated product from starting material led to low isolated yields relative to the calibrated GC yields of the crude reaction mixture (**6a**, **7a**, and **13a**). However, the low isolated yields of **11a** and **12a** are comparable to the GC yields observed for the crude reaction mixtures, and reflect inherently low reactivity/conversion of these substrates under the standard conditions.

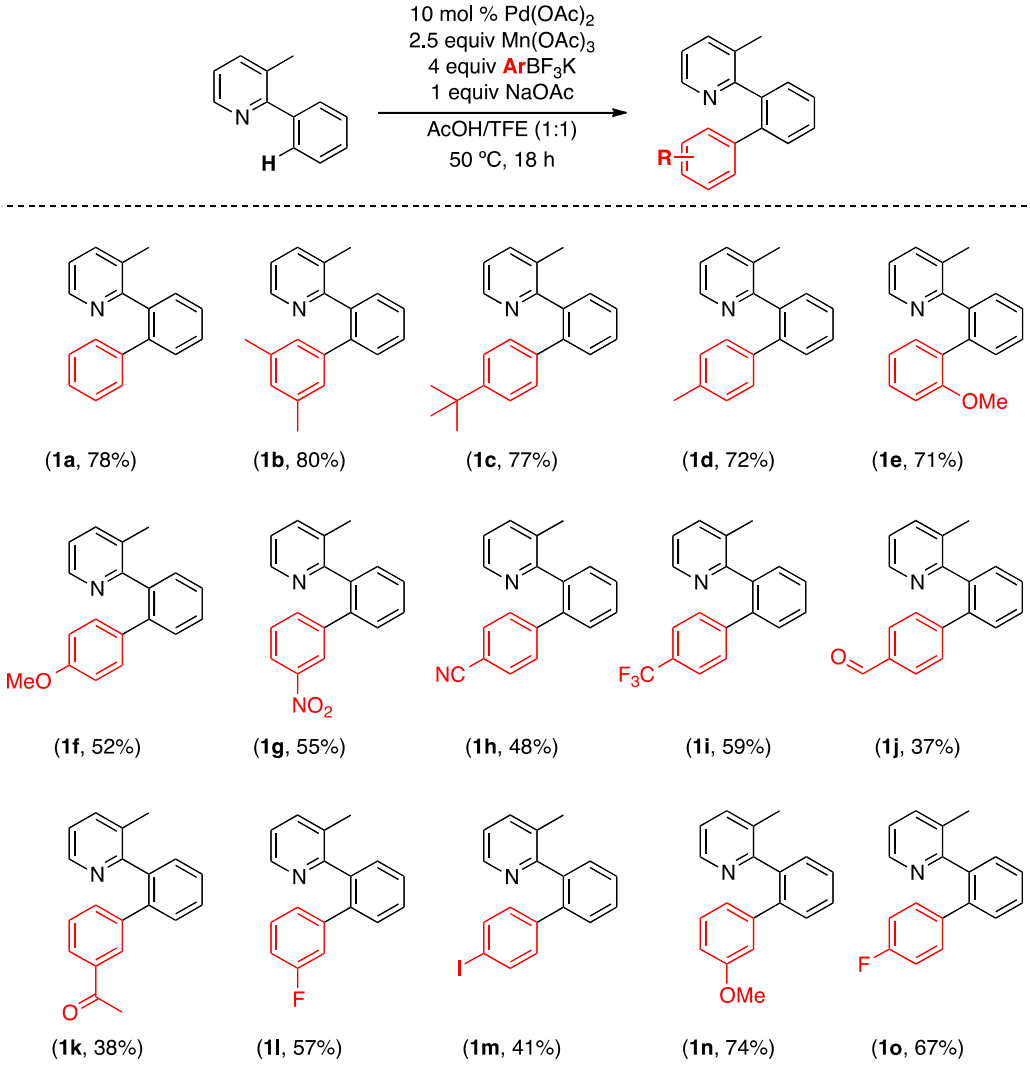
Table 1
Optimization of the $Pd(OAc)_2$-catalyzed C–H phenylation of **1**[a]



Entry	Solvent	Temp (°C)	Conv[b] (%)	Yield[b] (%)
1[c]	TFE/AcOH/H_2O (8:1:1)	40	73	34
2	TFE/AcOH/H_2O (8:1:1)	50	68	56[d]
3	TFE	50	34	26
4	AcOH	50	76	50[d]
5	AcOH/H_2O (9:1)	50	81	55[d]
6	TFE/AcOH (9:1)	50	77	58[d]
7	TFE/AcOH (1:1)	50	84	77
8	TFE/AcOH (1:1)	40	73	70
9	TFE/AcOH (1:1)	25	35	30
10[e]	TFE/AcOH (1:1)	50	86	77
11[f]	TFE/AcOH (1:1)	50	56	34
12[g]	TFE/AcOH (1:1)	50	60	50
13[h]	TFE/AcOH (1:1)	50	82	60
14[i]	TFE/AcOH (1:1)	50	51	38
15[e,j]	TFE/AcOH (1:1)	50	6	0
16[k]	TFE/AcOH (1:1)	50	≤2	2

[a] General conditions: **1** (1 equiv), $Pd(OAc)_2$ (0.10 equiv), $PhBF_3K$ (4 equiv), $Mn(OAc)_3$ (2.5 equiv), solvent (0.067 M in **1**), 18 h.
[b] Determined by gas chromatographic analysis of the crude reaction mixture using neopentylbenzene as a standard.
[c] Reaction run for 6 h using 4 equiv $Mn(OAc)_3$ and 2 equiv $PhBF_3K$.
[d] C–H acetoxylation product (~3%) formed.
[e] NaOAc (1 equiv) added.
[f] Benzoquinone (1 equiv) added.
[g] $PhB(OH)_2$ (4 equiv) was used instead of $PhBF_3K$.
[h] Phenylboronic acid pinacol ester (4 equiv) was used instead of $PhBF_3K$.
[i] 1,3,5-Triphenylboroxine (4 equiv) was used instead of $PhBF_3K$.
[j] Control reaction without Pd.
[k] Control reaction without Mn^{III}.

Table 2
Palladium-catalyzed C–H arylation of **1** with diverse aryltrifluoroborate salts[a]



[a] Isolated yields.

2.3. Mechanistic studies

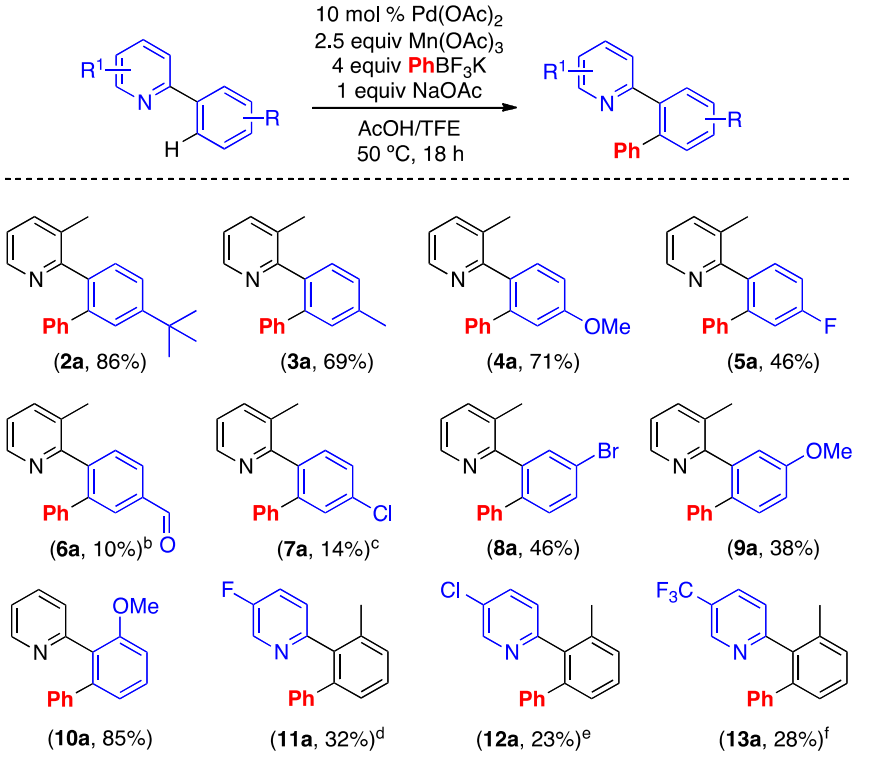
A key mechanistic question in this arylation system concerns the role of $Mn(OAc)_3$. Mn^{III} reagents have been previously utilized as oxidants for C–H bond functionalization reactions proposed to involve high-valent Pd-catalysis.[14,16] Furthermore, our group has recently reported a Pd-catalyzed C–H alkylation reaction employing alkyltrifluoroborates and MnF_3 as a stoichiometric oxidant (Eq. 1, vide supra).[14] Preliminary mechanistic evidence in that system suggests that MnF_3 serves as an oxidant for Pd^{II}. Based on this precedent, we hypothesize that $Mn(OAc)_3$ likely serves an analogous role in the current arylation system.

To preliminarily probe this possibility, we examined the effect of substituting $Mn(OAc)_3$ with other oxidants under the optimized reaction conditions. A number of oxidants commonly used to promote $Pd^{II/0}$-catalyzed C–H arylation with organoboron compounds were tested. As shown in Table 4, Cu^{II} and Ag^{I}-based oxidants provided <10% conversion of **1** and <2% yield of the arylation product **1a** (entries 3–5). Low conversion was similarly observed when benzoquinone was used in place of $Mn(OAc)_3$ (entry 6, 17% conversion, 7% yield). Notably, this reagent may effect C–C bond formation, albeit in low yields, by promoting reductive elimination from Pd^{II} (rather than serving to oxidize Pd^{II}).

In marked contrast, a number of oxidants that are known to be competent for the oxidation of Pd^{II} to Pd^{IV} were capable of promoting this transformation.[17] In particular, the hypervalent iodine reagents $PhI(OAc)_2$ and $PhI(TFA)_2$ were highly effective oxidants, providing near quantitative conversion and >80% yield of **1a** (Table 4, entries 11 and 12). These results are consistent with a reaction mechanism involving oxidation of a Pd^{II} intermediate by the bystanding stoichiometric oxidant. Arylation using other known oxidants for Pd^{II}, including *N*-chlorosuccinimide (NCS),[18] *N*-fluoro-2,4,6-trimethylpyridinium triflate (NFTPT),[19] $K_2S_2O_8$,[20] and *t*-BuOOH[20] could also be achieved, albeit in modest yield (2–11%). Notably, the use of these oxidants resulted in extensive side reactions of the starting material (32–100% conversion) to form an *ortho*-chlorinated product (using NCS, entry 9, ~22% yield) and/or mixtures of other unidentified side products.

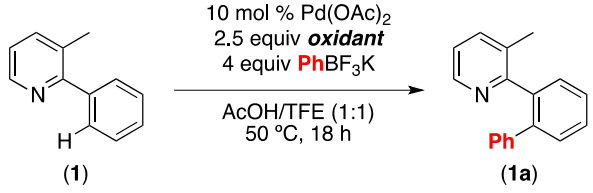
We also conducted experiments to determine the kinetic isotope effect associated with this transformation. The intermolecular

Table 3
Palladium-catalyzed C–H phenylation of diverse arylpyridine substrates[a]



[a] Isolated yields.
[b] GC yield (from crude reaction mixture) was 24%.
[c] GC yield (from crude reaction mixture) was 38%.
[d] GC yield (from crude reaction mixture) was 32%.
[e] GC yield (from crude reaction mixture) was 20%.
[f] GC yield (from crude reaction mixture) was 56%.

Table 4
Evaluation of different oxidants for Pd-Catalyzed C–H phenylation of **1**[a]



Entry	Oxidant	Conv[b] (%)	Yield[b] (%)
1	$Mn(OAc)_3$	84	77
2	MnF_3	95	57
3	$AgCO_3$	≤2	≤2
4	Ag_2O	≤2	nd
5	$Cu(OAc)_2$	16	nd
6	BQ	17	7
7	$K_2S_2O_8$	100	2
8	*t*-BuOOH	32	6
9	NCS	64	6[c]
10	NFTPT	100	11
11	$PhI(OAc)_2$	98	83
12	$PhI(OTFA)_2$	99	91

[a] Conditions: **1** (1 equiv), $Pd(OAc)_2$ (0.10 equiv), $PhBF_3K$ (4 equiv), oxidant (2.5 equiv), AcOH/TFE (1:1, 0.067 M in **1**), 50 °C, 18 h.
[b] Determined by gas chromatographic analysis of the crude reaction mixture using neopentylbenzene or hexadecane as an internal standard.
[c] C–H chlorination product (~22%) formed.

kinetic isotope effect was established by comparing the initial rates of phenylation of 3-methyl-2-phenylpyridine (**1**) and 3-methyl-2-phenylpyridine-d_5 (**1**-d_5) (Eq. 2). The optimized reaction conditions were employed, although the reactions were run at a lower temperature (36 °C) in order to more conveniently monitor reaction progress. As shown in Fig. 1, the initial reaction rates were significantly different for **1** versus **1**-d_5, with k_H/k_D=8.3. This large KIE is markedly different than that observed for a related Pd-catalyzed C–H arylation of arylpyridines using diaryliodonium reagents (k_H/k_D=1).[21] In the latter system, the rate-limiting step was shown to be oxidation of Pd^{II} to Pd^{IV} by Ph_2I^+, with C–H activation taking place after the turnover-limiting step (i.e., the resting state of the catalyst is a palladacycle). In contrast, the large KIE observed for C–H arylation using $ArBF_3K$ and $Mn(OAc)_3$ indicates that the

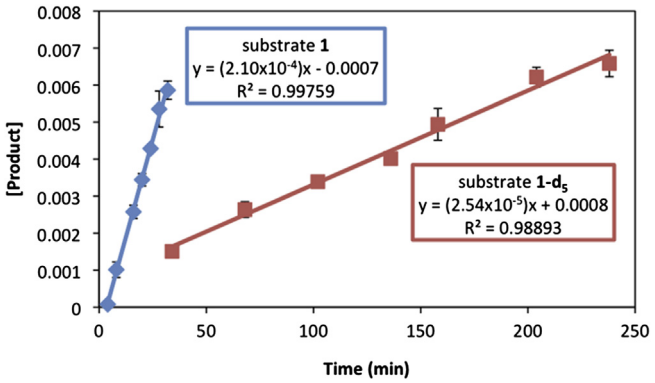
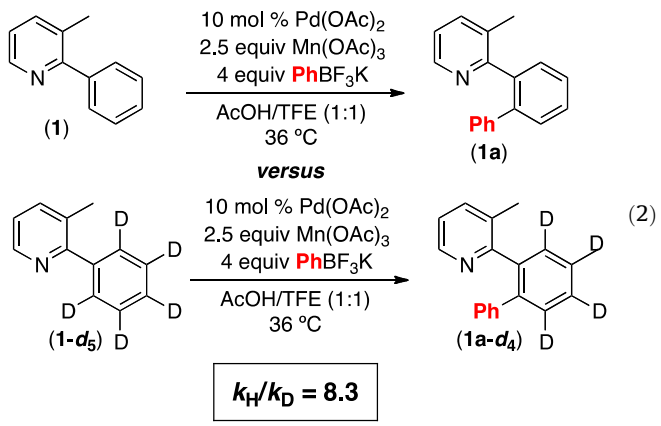


Fig. 1. Initial rates of C–H arylation with **1** versus **1**-d_5.

catalyst resting state under these conditions is not cyclometalated and that C–H bond cleavage occurs before or during the turnover-limiting step.



(2)

3. Conclusion

In summary, this paper describes the development of a mild Pd-catalyzed C–H arylation reaction using aryltrifluoroborates in conjunction with $Mn(OAc)_3$. This transformation proceeds in good yield for arylpyridine substrates bearing electron-donating substituents at the 2′- and 4′-positions, and moderate yields for substrates bearing electron-withdrawing substituents. A variety of substituted aryl groups can be installed using the corresponding $ArBF_3K$ reagents. Preliminary mechanistic studies suggest that the reaction likely involves high-valent Pd-catalysis and that C–H activation occurs at or before the rate-determining step. Ongoing work aims to elucidate the mechanistic details of this C–H arylation, as well as of the analogous C–H alkylation reactions.

4. Experimental section

4.1. General

All reactions were performed with magnetic stirring in scintillation vials. Flash chromatography was performed on EM Science silica gel 60 (0.040–0.063 mm particle size, 230–400 mesh) and thin layer chromatography was performed on Merck TLC plates pre-coated with silica gel 60 F_{254}.

4.2. Materials

Pyridine substrates **7** and **8** were prepared according to literature procedures.[22,23] Substrates **1**–**6** and **9** were synthesized via Suzuki coupling of 2-bromo-3-methylpyridine with the corresponding arylboronic acids.[24] Pyridine substrates **11**–**13** were also prepared Suzuki couplings of 2-bromopyridine derivatives with *o*-tolylphenylboronic acid.[24] Substrate **10** was prepared by Suzuki coupling of 2-methoxyphenylboronic acid with 2-chloropyridine.[25] Potassium 2,6-dimethylphenyltrifluoroborate and potassium 3-acetylphenyltrifluoroborate were synthesized from the corresponding boronic acids and KHF_2.[26] The rest of the aryltrifluoroborates were obtained from commercial sources (Alfa Aesar, Aldrich, and Frontier Scientific). $Pd(OAc)_2$, MnF_3, and $Mn(OAc)_3\cdot 2H_2O$ were obtained from Pressure Chemical, Alfa Aesar, and Strem, respectively. 2,2,2-Trifluoroethanol was obtained from TCI America, and all other solvents were obtained from Fisher Chemical. All commercial substrates, reagents, and solvents were used as received and without further purification.

4.3. Instrumentation

NMR spectra were obtained on a Varian vnmrs 700 (699.76 MHz for ^1H; 175.95 MHz for ^{13}C) and a Varian MR400 (376.87 MHz for ^{19}F). ^1H and ^{13}C chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), quartet (q), and multiplet (m). IR spectra were obtained on a Perkin–Elmer Spectrum BX FT-IR spectrometer. Melting points were determined with a Mel-Temp 3.0, a Laboratory Devices Inc, USA instrument, and are uncorrected. HRMS data were obtained on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer. Gas chromatography was performed on a Shimadzu GC-17A equipped with a Restek Rtx©-5 column (15 m, 0.25 mm ID, 0.25 μm df) and an FID detector. GC yields are reported relative to neopentylbenzene or hexadecane as an internal standard.

4.4. General procedures

4.4.1. General procedure A for isolated products. Substrate, solvent, NaOAc, $Pd(OAc)_2$, and $Mn(OAc)_3\cdot 2H_2O$ were combined in a 20 mL scintillation vial. The vial was sealed with a Teflon-lined cap and heated at 50 °C for 18 h with vigorous stirring. After cooling to room temperature, the reaction mixture was diluted with EtOAc (50 mL) and washed with 10 wt % aqueous Na_2SO_3 (1×15 mL), saturated aqueous $NaHCO_3$ (2×25 mL), and brine (1×10 mL). The combined aqueous layers were extracted with EtOAc (2×25 mL). The organic layers were then combined, dried over $MgSO_4$, filtered, and concentrated to afford the crude product, which was purified by column chromatography on silica gel. The characterization data (^1H and ^{13}C NMR spectra, IR, and melting points, where appropriate) for previously reported products matched that reported in the literature.

4.4.2. General procedure B for kinetic experiments. Kinetics experiments were run in 4 mL scintillation vials sealed with Teflon-lined caps. Each data point within a kinetics run represents a reaction in an individual vial, with each vial containing a constant concentration of oxidant, catalyst, and substrate. The reported value of initial rate at each time point is the average of three trials, and error is reported as standard deviation. To $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol, 0.1 equiv) and $PhBF_3K$ (36.8 mg, 0.20 mmol, 4 equiv) in a 4 mL vial was added 0.75 mL of a 0.067 M stock solution of substrate (0.050 mmol, 1 equiv) in AcOH/TFE (1:1), followed by $Mn(OAc)_3\cdot H_2O$ (33.5 mg, 0.125 mmol, 2.5 equiv). The reaction mixtures were heated to 36 °C under vigorous stirring on an aluminum heating-block. The reaction mixtures were quenched after the indicated time by adding 0.5 mL of 10 wt % aqueous Na_2SO_3 and shaking vigorously. The crude reaction mixtures were then diluted with EtOAc (3 mL), and neopentylbenzene was added as an internal standard. The reactions were analyzed by gas chromatography, and the calibrated GC yields of products were determined relative to neopentylbenzene.

4.5. Characterization data for new compounds

*4.5.1. 2-(3′,5′-Dimethyl-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1b**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 3,5-dimethyl phenyltrifluoroborate (424 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1b** was obtained as a clear viscous liquid (110.0 mg, 81% yield, R_f=0.12 in 80% hexanes/20% Et_2O). ^1H NMR (700 MHz, C_6D_6): δ 8.53 (d, J=4.7 Hz, 1H), 7.52 (dd, J=7.2, 1.5 Hz, 1H), 7.43 (dd, J=7.4, 1.5 Hz, 1H), 7.27–7.21 (multiple

peaks, 2H), 6.93 (s, 2H), 6.78 (d, J=7.7 Hz, 1H), 6.65 (dd, J=7.7, 4.7 Hz, 1H), 6.62 (s, 1H), 2.02 (s, 6H), 1.67 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.9, 146.5, 141.0, 140.9, 139.6, 137.5, 137.2, 131.8, 129.9, 129.8, 129.7, 128.4, 127.3, 122.0, 121.3, 21.3, 19.0. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{20}H_{20}N$: 274.1590; found: 274.1593.

*4.5.2. 2-(4′-(tert-Butyl)-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1c**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 4-*tert*-butylphenyltrifluoroborate (480 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1c** was obtained as a clear oil (115.8 mg, 77% yield, R_f=0.16 in 80% hexanes/20% Et_2O). ^1H NMR (700 MHz, acetone-d_6): δ 8.43 (dd, J=4.8, 1.1 Hz, 1H), 7.57–7.44 (multiple peaks, 2H), 7.43 (td, J=7.5, 1.8 Hz, 1H), 7.38 (dd, J=7.6, 1.1 Hz, 1H), 7.32 (dd, J=7.6, 1.1 Hz, 1H), 7.22 (d, J=8.6 Hz, 2H), 7.15 (dd, J=7.7, 4.8 Hz, 1H), 7.06 (d, J=8.6 Hz, 2H), 1.74 (s, 3H), 1.24 (s, 9H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.8, 149.6, 146.7, 140.6, 139.5, 138.2, 137.5, 131.8, 130.1, 129.8, 128.9, 128.4, 127.3, 124.8, 122.2, 34.5, 31.4, 18.9. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{22}H_{24}N$: 302.1903; found: 302.1907.

*4.5.3. 2-(2′-Methoxy-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1e**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 2-methoxy phenyltrifluoroborate (428 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1e** was obtained as a pale yellow liquid (98.2 mg, 71% yield, R_f=0.17 in 60% hexanes/40% Et_2O). ^1H NMR (700 MHz, C_6D_6): δ 8.40 (dd, J=4.8, 1.1 Hz, 1H), 7.53 (dd, J=7.7, 1.1 Hz, 1H), 7.50 (dd, J=7.5, 1.1 Hz, 1H), 7.27–7.20 (multiple peaks, 3H), 6.95 (td, J=8.0, 1.8 Hz, 1H), 6.83 (dd, J=7.7, 1.1 Hz, 1H), 6.67 (t, J=7.5 Hz, 1H), 6.57 (dd, J=7.8, 4.8 Hz, 1H), 6.43 (d, J=8.0 Hz, 1H), 3.12 (s, 3H), 1.87 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.6, 156.1, 146.1, 140.4, 137.6, 137.2, 132.2, 131.6, 131.1, 130.0, 129.7, 128.4, 127.7, 127.3, 121.7, 120.1, 110.4, 55.0, 18.9. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{19}H_{18}NO$: 276.1383; found: 276.1384.

*4.5.4. 2-(3′-Nitro-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1g**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 3-nitrophenyltrifluoroborate (458 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1g** was obtained as a pale yellow solid (79.3 mg, 55% yield, R_f=0.13 in 60% hexanes/40% Et_2O, mp=75.7–76.5 °C). ^1H NMR (700 MHz, acetone-d_6): δ 8.43 (dd, J=4.8, 1.1 Hz, 1H), 8.06 (ddd, J=8.2, 2.4, 1.0 Hz, 1H), 7.97 (t, J=2.0 Hz, 1H), 7.62–7.55 (multiple peaks, 4H), 7.51 (t, J=8.0 Hz, 1H), 7.47 (d, J=7.7 Hz, 1H), 7.44 (d, J=7.4 Hz, 1H), 7.18 (dd, J=7.7, 4.8 Hz, 1H), 1.85 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 158.6, 148.0, 147.0, 142.8, 139.7, 138.3, 138.0, 135.4, 131.6, 130.2, 129.7, 128.9, 128.8, 128.7, 124.1, 122.7, 121.7, 19.0. IR (thin film): 1527.2, 1349.5 cm^{-1}. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}N_2O_2$: 291.1128; found: 291.1133.

*4.5.5. 2-(4′-Cyano-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1h**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 4-cyanophenyltrifluoroborate (418 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1h** was obtained as a pale yellow solid (65.2 mg, 48% yield, R_f=0.10 in 60% hexanes/40% Et_2O, mp=153.6–157.4 °C). ^1H NMR (700 MHz, $CDCl_3$): δ 8.46 (d, J=4.7 Hz, 1H), 7.53–7.49 (multiple peaks, 2H), 7.47–7.41 (multiple peaks, 4H), 7.36 (d, J=7.7 Hz, 1H), 7.22 (d, J=7.9 Hz, 2H), 7.13 (dd, J=7.6, 4.7 Hz, 1H), 1.80 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 232.3, 158.7, 147.0, 146.1, 139.6, 139.0, 138.0, 131.8, 131.6, 130.3, 130.0, 129.7, 128.8, 122.7, 119.0, 110.6, 19.0. IR (thin film): 2226.5 cm^{-1}. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{19}H_{15}N_2$: 271.1235; found: 271.1234.

*4.5.6. 2′-(3-Methylpyridin-2-yl)-[1,1′-biphenyl]-4-carbaldehyde (**1j**).* General procedure A was followed using substrate **1** (42 mg, 0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.10 equiv), NaOAc (21 mg, 0.25 mmol, 1.0 equiv), potassium 4-formylphenyl trifluoroborate (212 mg, 1.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (168 mg, 0.625 mmol, 2.5 equiv) in TFE/AcOH (1:1; 3.8 mL total) at 50 °C for 18 h. Product **1j** was obtained as a white solid (25.6 mg, 37% yield, R_f=0.07 in 60% hexanes/40% Et_2O, mp=126.1–127.8 °C). ^1H NMR (700 MHz, $CDCl_3$): δ 9.94 (s, 1H), 8.49 (d, J=4.8 Hz, 1H), 7.68 (d, J=8.4 Hz, 2H), 7.53–7.47 (multiple peaks, 3H), 7.44 (m, 1H), 7.33 (d, J=7.6 Hz, 1H), 7.29 (d, J=8.2 Hz, 2H), 7.12 (dd, J=7.6, 4.8 Hz, 1H), 1.80 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 192.2, 158.9, 147.7, 146.9, 139.7, 139.5, 137.9, 134.7, 131.7, 130.3, 130.0, 129.8, 129.4, 128.7, 128.6, 122.6, 19.0. IR (thin film): 1701.6, 1604.9 cm^{-1}. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{19}H_{16}NO$: 274.1226; found: 274.1225.

*4.5.7. 2-(3′-Fluoro-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1l**).* General procedure A was followed using substrate **1** (94 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 3-fluorophenyltrifluoroborate (404 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1l** was obtained as a greasy yellow solid (75.3 mg, 57% yield, R_f=0.13 in 80% hexanes/20% Et_2O). ^1H NMR (700 MHz, $CDCl_3$): δ 8.49 (d, J=4.6 Hz, 1H), 7.50–7.43 (multiple peaks, 3H), 7.40 (d, J=7.0 Hz, 1H), 7.34 (d, J=7.7 Hz, 1H), 7.41–7.09 (multiple peaks, 2H), 6.90–6.82 (multiple peaks, 3H), 1.80 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 162.4 (d, $^1J_{C-F}$=245.3 Hz), 159.2, 146.8, 143.5 (d, $^3J_{C-F}$=7.5 Hz), 139.6, 139.5 (d, $^4J_{C-F}$=2.0 Hz), 137.7, 131.7, 130.1, 129.7, 129.3 (d, $^3J_{C-F}$=8.6 Hz), 128.6, 128.1, 125.2 (d, $^4J_{C-F}$=2.9 Hz), 122.4, 116.2 (d, $^2J_{C-F}$=21.4 Hz), 113.7 (d, $^2J_{C-F}$=21.0 Hz), 19.0 $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$): δ −113.7 (m, 1F). HRMS EI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}FN$: 264.1183; found: 264.1186.

*4.5.8. 2-(4′-Iodo-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1m**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 4-iodophenyltrifluoroborate (608 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1m** was obtained as a white solid (87.5 mg, 41% yield, R_f=0.11 in 80% hexanes/20% Et_2O, mp=108.6–113.9 °C). ^1H NMR (700 MHz, C_6D_6): δ 8.55 (d, J=4.6 Hz, 1H), 7.52 (m, 1H), 7.36 (d, J=8.4 Hz, 2H), 7.30–7.27 (multiple peaks, 3H), 6.87 (d, J=8.4 Hz, 2H), 6.82 (d, J=7.8 Hz, 1H), 6.71 (dd, J=7.7, 4.6 Hz, 1H), 1.65 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.2, 146.8, 140.8, 139.6, 139.5, 137.8, 137.1, 131.7, 131.3, 130.1, 129.6, 128.6, 128.0, 122.4, 92.8, 19.0. HRMS EI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}IN$: 372.0244; found: 372.0245.

*4.5.9. 2-(3′-Methoxy-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**1n**).* General procedure A was followed using substrate **1** (85 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium 3-methoxyphenyl trifluoroborate (428 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3\cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **1n** was obtained as a pale yellow liquid (102.0 mg, 74% yield, R_f=0.18 in 60% hexanes/40% Et_2O). ^1H NMR (700 MHz, C_6D_6): δ 8.51 (d, J=4.7 Hz, 1H), 7.59–7.43 (multiple peaks, 3H), 7.40 (d, J=7.4 Hz, 1H), 7.31 (d, J=7.8 Hz, 1H), 7.13–7.09 (multiple peaks, 2H), 6.80 (d, J=7.6 Hz, 1H), 6.72 (dd, J=8.2, 2.5 Hz, 1H), 6.59 (s, 1H), 3.55 (s,

3H), 1.77 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.8, 159.0, 146.6, 142.6, 140.6, 139.6, 137.6, 132.0, 130.0, 129.7, 129.0, 128.5, 127.7, 122.3, 121.7, 114.4, 113.4, 55.1, 19.0. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{18}NO$: 276.1388; found: 276.1389.

*4.5.10. 2-(5-(tert-Butyl)-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**2a**).* General procedure A was followed using substrate **2** (113 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **2a** was obtained as a pale yellow solid (130.0 mg, 86% yield, R_f=0.15 in 80% hexanes/20% Et_2O, mp=129.6–133.0 °C). ^1H NMR (700 MHz, C_6D_6): δ 8.53 (d, *J*=4.8 Hz, 1H), 7.59 (d, *J*=2.0 Hz, 1H), 7.53 (d, *J*=8.0 Hz, 1H), 7.37–7.32 (multiple peaks, 3H), 7.03–6.99 (multiple peaks, 2H), 6.95 (dd, *J*=7.1, 1.0 Hz, 1H), 6.78 (dd, *J*=7.7, 1.0 Hz, 1H), 6.64 (dd, *J*=7.7, 4.8 Hz, 1H), 1.67 (s, 3H), 1.26 (s, 9H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.7, 151.3, 146.7, 141.9, 140.3, 137.5, 136.7, 131.8, 129.7, 129.4, 127.9, 126.8, 126.5, 124.6, 122.0, 34.8, 31.5, 19.1. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{22}H_{24}N$: 302.1909; found: 302.1903.

*4.5.11. 2-(5-Methoxy-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**4a**).* General procedure A was followed using substrate **4** (100 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **4a** was obtained as a clear oil (102.1 mg, 71% yield, R_f=0.14 in 60% hexanes/40% Et_2O). ^1H NMR (700 MHz, C_6D_6): δ 8.53 (d, *J*=4.7 Hz, 1H), 7.44 (d, *J*=8.4 Hz, 1H), 7.28 (multiple peaks, 2H), 7.06 (d, *J*=2.7, 1H), 6.99–6.90 (multiple peaks, 3H), 6.84 (dd, *J*=8.3, 2.7 Hz, 1H), 6.78 (d, *J*=7.5 Hz, 1H), 6.64 (dd, *J*=7.5, 4.8 Hz, 1H), 3.34 (s, 3H), 1.68 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.6, 159.4, 146.7, 142.1, 141.2, 137.5, 132.3, 132.0, 131.3, 129.3, 127.9, 126.9, 122.0, 115.1, 113.1, 55.5, 19.0. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{18}NO$: 276.1383; found: 276.1385.

*4.5.12. 2-(5-Fluoro-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**5a**).* General procedure A was followed using substrate **5** (94 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **5a** was obtained as a white powder (60.5 mg, 46% yield, R_f=0.13 in 80% hexanes/20% Et_2O, mp=97.2–99.4 °C). ^1H NMR (700 MHz, C_6D_6): δ 8.47 (d, *J*=4.8 Hz, 1H), 7.25 (dd, *J*=8.2, 6.0 Hz, 1H), 7.08 (d, *J*=7.5 Hz, 2H), 7.07 (dd, *J*=9.9, 2.3 Hz, 1H), 6.94–6.87 (multiple peaks, 3H), 6.85 (td, *J*=8.4, 2.6 Hz, 1H), 6.74 (d, *J*=7.6 Hz, 1H), 6.62 (dd, *J*=7.6, 4.8 Hz, 1H), 1.54 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 162.7 (d, $^1J_{C-F}$=246.8 Hz), 158.7, 146.8, 142.9 (d, $^3J_{C-F}$=7.5 Hz), 140.1 (d, $^4J_{C-F}$=2.1 Hz), 137.7, 135.7 (d, $^4J_{C-F}$=3.2 Hz), 131.9, 131.8 (d, $^3J_{C-F}$=8.5 Hz), 129.2, 128.1, 127.3, 122.4, 116.5 (d, $^2J_{C-F}$=21.8 Hz), 114.4 (d, $^2J_{C-F}$=21.5 Hz), 18.9. $^{19}F\{^1H\}$ NMR (377 MHz, C_6D_6): δ −114.3 (m, 1F). HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{15}FN$: 264.1183; found: 264.1189.

*4.5.13. 6-(3-Methylpyridin-2-yl)-[1,1′-biphenyl]-3-carbaldehyde (**6a**).* General procedure A was followed using substrate **6** (99 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **6a** was obtained as a white solid (13.5 mg, 10% yield, R_f=0.09 in 80% hexanes/20% Et_2O, mp=105.4–106.4 °C). ^1H NMR (700 MHz, $CDCl_3$): δ 10.13 (s, 1H), 8.52 (d, *J*=4.5 Hz, 1H), 7.99 (s, 1H), 7.96 (d, *J*=7.8 Hz, 1H), 7.59 (d, *J*=7.8 Hz, 1H), 7.33 (d, *J*=7.8 Hz, 1H), 7.23–7.17 (multiple peaks, 3H), 7.16–7.12 (multiple peaks, 3H), 1.76 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 192.2, 158.3, 146.9, 145.5, 141.9, 139.8, 137.9, 136.4, 131.6, 131.4, 131.1, 129.3, 128.6, 128.2, 127.5, 122.8, 18.8. IR (thin film): 1697.8 cm^{-1}. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{16}NO$: 274.1226; found: 274.1232.

*4.5.14. 2-(5-Chloro-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**7a**).* General procedure A was followed using substrate **7** (102 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **7a** was obtained as a clear viscous oil (19.5 mg, 14% yield, R_f=0.08 in 88% hexanes/12% Et_2O). ^1H NMR (700 MHz, $CDCl_3$): δ 8.49 (d, *J*=4.5, 1H), 7.46 (d, *J*=2.1 Hz, 1H), 7.42 (dd, *J*=8.2, 2.1 Hz, 1 H), 7.35 (d, *J*=8.1 Hz, 1H), 7.30 (d, *J*=7.3, 1H), 7.20–7.14 (multiple peaks, 3H), 7.13–7.07 (multiple peaks, 3H), 1.74 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 158.5, 146.9, 142.5, 139.9, 138.1, 137.7, 134.2, 131.8, 131.5, 129.7, 129.2, 128.1, 127.6, 127.3, 122.5, 18.9. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{15}ClN$: 280.0888; found: 280.0893.

*4.5.15. 2-(4-Bromo-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**8a**).* General procedure A was followed using substrate **8** (124 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **8a** was obtained as a white solid (74.3 mg, 46% yield, R_f=0.29 in 80% hexanes/20% Et_2O, mp=84.7–88.2 °C). ^1H NMR (700 MHz, C_6D_6): δ 8.42 (d, *J*=4.6 Hz, 1H), 7.65 (d, *J*=2.0 Hz, 1H), 7.32 (dd, *J*=8.3, 2.0 Hz, 1H), 7.10 (d, *J*=7.1 Hz, 2H), 6.97–6.88 (multiple peaks, 4H), 6.69 (d, *J*=7.6, 1H), 6.60 (dd, *J*=7.8, 4.7 Hz, 1H), 1.49 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 157.9, 146.7, 141.2, 139.9, 139.6, 137.7, 132.8, 131.6, 131.4, 131.2, 129.0, 127.9, 127.0, 122.5, 121.4, 18.7. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{18}H_{15}BrN$: 324.0388; found: 324.0384.

*4.5.16. 2-(4-Methoxy-[1,1′-biphenyl]-2-yl)-3-methylpyridine (**9a**).* General procedure A was followed using substrate **9** (100 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **9a** was obtained as a pale yellow oil (51.9 mg, 38% yield, R_f=0.18 in 60% hexanes/40% Et_2O). ^1H NMR (700 MHz, $CDCl_3$): δ 8.51 (d, *J*=4.9 Hz, 1H), 7.38 (d, *J*=8.6 Hz, 1H), 7.29 (d, *J*=7.7 Hz, 1H), 7.15–7.12 (multiple peaks, 3H), 7.10 (dd, *J*=7.7, 4.9 Hz, 1H), 7.09–7.06 (multiple peaks, 2H), 7.03 (dd, *J*=8.6, 2.7 Hz, 1H), 6.94 (d, *J*=2.7 Hz, 1H), 3.37 (s, 3H), 1.75 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 159.5, 159.0, 146.7, 140.9, 140.6, 137.7, 133.6, 131.7, 131.1, 129.3127.9, 126.3, 122.3, 114.8, 114.7, 55.6, 18.9. HRMS EI (*m*/*z*): $[M+H]^+$ calcd for $C_{19}H_{18}NO$: 276.1383; found: 276.1384.

*4.5.17. 2-(3-Methyl-[1,1′-biphenyl]-2-yl)-5-(trifluoromethyl)pyridine (**13a**).* General procedure A was followed using substrate **14** (137 mg, 0.50 mmol, 1.0 equiv), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv), NaOAc (41 mg, 0.50 mmol, 1.0 equiv), potassium phenyltrifluoroborate (368 mg, 2.0 mmol, 4.0 equiv), and $Mn(OAc)_3 \cdot 2H_2O$ (335 mg, 1.25 mmol, 2.5 equiv) in TFE/AcOH (1:1; 7.5 mL total) at 50 °C for 18 h. Product **13a** was obtained as pale yellow needles (45.5 mg, 29% yield, R_f=0.29 in 94% hexanes/6% Et_2O, mp=101.3–104.3 °C). ^1H NMR (700 MHz, acetone-d_6): δ 8.94 (s, 1H), 7.91 (dd, *J*=8.3, 2.2 Hz, 1H), 7.42 (t, *J*=7.6 Hz, 1H), 7.35 (d, *J*=7.7 Hz, 1H), 7.28 (d, *J*=7.7 Hz, 1H), 7.19–7.12 (multiple peaks, 4H), 7.07–7.03 (multiple peaks, 2H), 2.13 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 163.6, 145.9 (q, $^3J_{C-F}$=4.2 Hz), 141.4, 141.2, 138.2, 136.7,

132.9 (q, $^{3}J_{C-F}$=3.4 Hz), 129.8, 129.7, 128.8, 128.0, 127.9, 126.8, 125.6, 124.3 (q, $^{2}J_{C-F}$=34 Hz), 123.8 (q, $^{1}J_{C-F}$=272.8 Hz), 20.6. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$): δ −62.8. (s, 3F). HRMS EI (m/z): $[M+H]^+$ calcd for $C_{19}H_{15}F_3N$: 314.1151; found: 314.1153.

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