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Direct *ortho*-Arylation of *N*-Phenacylpyridinium Bromide by Palladium-Catalyzed C–H-Bond Activation

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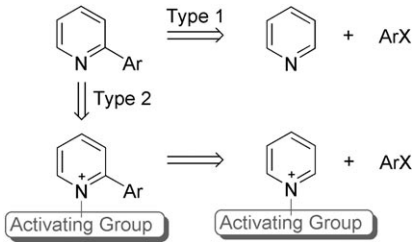
Abstract: A novel palladium catalyzed direct *ortho*-arylation of *N*-phenacylpyridinium bromide was developed. The amazing *N*-phenacyl group regioselectively activates the C–H bond of pyridine and automatically departs from the arylated products. A kinetic isotope effect study proved that the reaction went through a C–H-bond activation pathway and 2,6-diphenylpyridine was produced stepwise from 2-phenylpyridine.

Keywords: arylation · catalysis · C–H activation · palladium · pyridine

Introduction

Ortho-arylated pyridines have found important applications in medicinal[1] and material researches.[2] Although transition-metal-catalyzed cross-coupling reactions between organometallic electron-rich heterocycles and arylhalides have been widely used, their application has been limited to pyridine derivatives.[3,4] The reason for this is that the pyridine ring is electron deficient and the highly effective and relatively stable *ortho*-pyridyl organometallics have only been presented recently.[5] However, direct arylation of heterocycles has emerged as an alternative to the traditional cross-coupling reaction in past years[6] and pioneering work on the direct *ortho*-arylation of pyridine has made significant achievements.[7,8] These reactions have great attraction as pyridine derivatives are used as substrates rather than the stoichiometric *ortho*-pyridyl organometallics.

As shown in Scheme 1, two types of procedure were reported based on the substrates used with either pyridines[7] or *N*-substituted pyridiniums[8] (*N*-oxides and *N*-iminopyridiniums). The latter is more practical when using relatively mild conditions and low-cost catalysts because the *N*-substituent may act as an activating group for the C–H-bond activation at the *ortho*-position of pyridine. But, one drawback of those otherwise efficient procedures is that one additional step is needed to remove the activating groups from the target products.



Scheme 1. Two types of *ortho*-arylation of pyridine.

Therefore, the development of desirable *N*-substituents as the activating groups for highly efficient direct *ortho*-arylations of pyridine is greatly needed. Herein, we report the use of *N*-phenacylpyridinium bromide (**1a**) as a substrate to smoothly achieve a novel direct *ortho*-arylation of pyridine. The amazing *N*-phenacyl group not only has a high ability to activate the C–H bond at the *ortho*-position of pyridine, but also automatically departs from the arylated pyridines after the reaction.

Results and Discussion

It is well known that *N*-phenacylpyridinium halide (**1**) is an essential substrate in Kröhnke pyridine synthesis, in which the *N*-phenacyl group is a real reactant and the pyridine ring plays a crucial role as an activating group (Scheme 2).[9]

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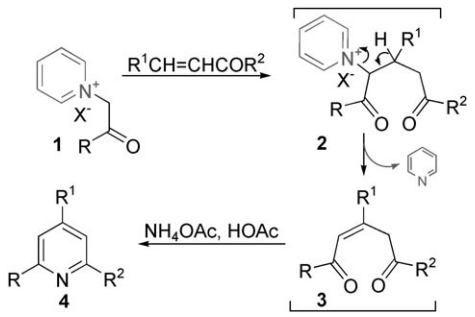
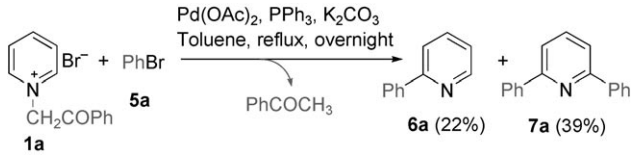


Scheme 2. The Kröhnke pyridine synthesis.

The key reason for its success is that the pyridine ring can automatically depart from the intermediate **2** by an *N*-alkenylpyridinium mechanism.

Thus, pyridinium **1** may be expected to be used as a substrate in the direct *ortho*-arylation of pyridine. In contrast with Kröhnke pyridine synthesis, the pyridine ring could be used as a real reactant and the *N*-phenacyl group as an activating group. Therefore, in the presence of Pd catalyst, the carbonyl group of **1** may coordinate with Pd to activate the C–H bond at the *ortho*-position of pyridine. Once the arylation is finished, the carbonyl group will be enolized to form an *N*-alkenylpyridinium under the basic conditions, by which the *N*-phenacyl group will depart from the arylated pyridines.

To prove our hypothesis, the direct *ortho*-arylation of *N*-phenacylpyridinium bromide (**1a**, it is a commercially available and easily prepared crystal product.) was tested. As shown in Scheme 3, after the mixture of **1a** (1.5 equiv), bromobenzene (**5a**, 1 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.15 equiv), and K_2CO_3 (3 equiv) in toluene was refluxed overnight, two products, 2-phenylpyridine (**6a**) and 2,6-diphenylpyridine (**7a**), were obtained in 22 and 39% yields, respectively. In this approach, the *N*-phenacyl group produces two unique results: 1) it had a high ability to activate the C–H bond at the *ortho*-position of pyridine and 2) it departed from the arylated pyridines automatically as acetophenone in 47% yield (since acetophenone was not chemically stable under our conditions, some part of it may be converted to other products).



Scheme 3. A novel direct *ortho*-arylation.

Further control experiments proved that iodobenzene can replace **5a** to give the exact same result, but not chlorobenzene. As shown in Table 1, many Pd sources can be used as catalysts and the low-cost $Pd(OAc)_2$ gave the best yield (entry 1).

Table 1. Effects of Pd sources on the direct *ortho*-arylation of **1a**.[a]

Entry	Pd Sources	**6a** [%][b]	**7a** [%][b]	Total yield [%][b]
1	$Pd(OAc)_2+PPh_3$	22	39	61
2	$Pd(TFA)_2+PPh_3$	32	20	52
3	$PdCl_2+PPh_3$	17	33	50
4	$[Pd(PPh_3)_2Cl_2]$	15	29	44
5	$[Pd(PPh_3)_4]$	14	21	35
6	$[Pd_2(dba)_3]+PPh_3$[c]	14	20	34
7	$Pd/C+PPh_3$	11	19	30

[a] The mixture of **1a** (1.5 mmol), **5a** (1.0 mmol), Pd catalyst (0.05 mmol), PPh_3 (0.15 mmol), and K_2CO_3 (3 mmol) in toluene (5 mL) was refluxed for 12 h. [b] The isolated yield was used. [c] dba: dibenzylideneacetone.

In the presence of $Pd(OAc)_2$ and with PPh_3 as the ligand, the best yield of the products was produced (Table 2, entry 1) and PCy_3 gave nothing (entry 2). No catalytic activity was observed when Pd was coordinated by strong chelating ligands, such as DPPE and DPPP (entries 3 and 4), whereas weak chelating ligand DPPF gave the desired products in 40% yield (entry 5).

Table 2. Effects of ligands on the direct *ortho*-arylation of **1a**.[a]

Entry	Ligands ([mol%])	**6a** [%][b]	**7a** [%][b]	Total yield [%][b]
1	PPh_3 (15)	22	39	61
2	PCy_3 (15)	0	0	0
3	DPPE (7.5)[c]	0	0	0
4	DPPP (7.5)[c]	0	0	0
5	DPPF (7.5)[c]	16	24	40

[a] The mixture of **1a** (1.5 mmol), **5a** (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), and K_2CO_3 (3 mmol) in toluene (5 mL) was refluxed for 12 h. [b] The isolated yield was used. [c] DPPE: 1,2-bis(diphenylphosphino)ethane; DPPP: 1,3-bis(diphenylphosphino)propane; DPPF: 1,1′-bis(diphenylphosphino)ferrocene.

DMF, DMSO, MeCN, and PhMe were all desirable solvents and gave comparable results. However, the use of PhMe made the workup procedure more convenient. Attempts to improve the selectivity between **6a** and **7a** by using different *N*-phenacyl groups, such as *N*-(2-methylphenacyl)pyridinium bromide and *N*-(4-nitrophenacyl)pyridinium bromide, failed. However, this selectivity could be improved conveniently by changing the ratio of **1a** and **5a** (Table 3). When 10:1 (by molar amount) of **1a**/**5a** was used, the total yield was as high as 95% with monoarylated **6a** as

Table 3. Effects of the ratio of **1a**/**5a** on the direct *ortho*-arylation of **1a**.[a]

Entry	**1a**/**5a** (by mole)	**6a** [%][b]	**7a** [%][b]	Total yield [%][b]
1	1.5:1	22	39	61
2	3:1	46	40	86
3	6:1	53	37	90
4	10:1	64	31	95
5	1:4	12	50	62

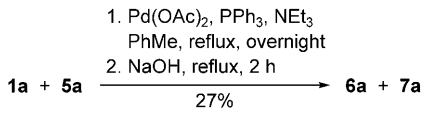
[a] The mixture of **1a**, **5a**, $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.15 mmol), and K_2CO_3 (3 mmol) in toluene (5 mL) was refluxed for 12 h. [b] The isolated yield was used.

a major product (entry 4). Whereas, by using a larger proportion of **5a**, diarylated compound **7a** was produced as a major product (entry 5).

Experiments indicated that the base was necessary for the reaction. The scanning of different bases revealed that tertiary amines (NEt_3, iPr_2NEt) or strong bases (NaO*t*Bu, NaOH, Cs_2CO_3) could not offer any desired product **6a** or **7a**. However, when NaOAc, K_3PO_4, and K_2CO_3 were used as a base, mixtures of **6a** and **7a** were obtained in 10, 47, and 61% yields, respectively. Based on the conditions of the entry 2 in Table 3, control experiments further showed that four equivalents (the summation of the amounts of **1a** and **5a**) of K_2CO_3 gave the best total yield (86%). However, both total yields and selectivity were decreased upon reducing the amounts of K_2CO_3. For example, the total yields were obtained in 71 (38:33 for **6a**/**7a**) and 59% (29:30 for **6a**/**7a**) by using three and two equivalents of K_2CO_3, respectively.

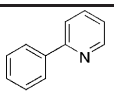
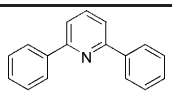
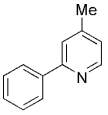
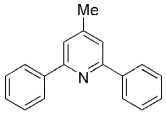
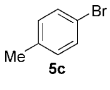
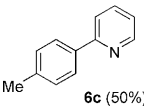
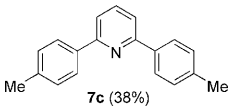
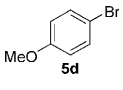
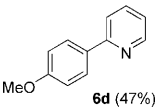
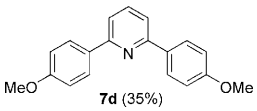
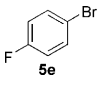
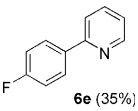
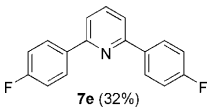
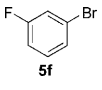
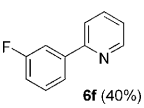
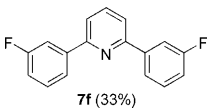
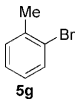
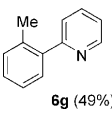
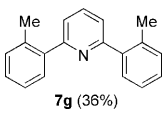
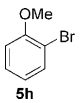
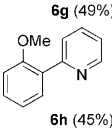
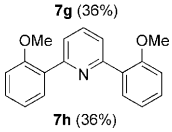
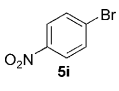
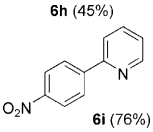
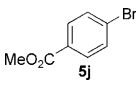
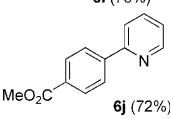
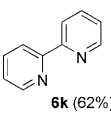
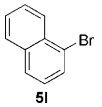
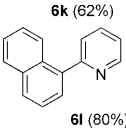
We interestingly observed that, when the reaction mixture was treated sequentially with NEt_3 for 12 h, followed by NaOH for 2 h, the desired products were obtained in 27% yield (Scheme 4). Thus, the behavior of these bases can be well explained by this result: 1) the tertiary amines may be not be strong enough to enolize the ketone to remove the *N*-phenacyl group from the target products and 2) the strong bases probably attack **1a** quickly to replace the pyridine by a nucleophilic substitution reaction before the arylation.

To generalize this novel method, different substrates **1a–b** and bromobenzenes **5a–l** were tested. As shown in Table 4, they all gave the desired products in satisfactory yields under our optimized conditions (see note of Table 4). It is noteworthy that the chemoselectivity of the arylation was also strongly influenced by bromobenzenes. Normally, a mixture was obtained with 2-arylpyridines as the major products (they were separated easily) (entries 1–8). By using the bromobenzenes with strong elec-



Scheme 4. Effects of bases on the direct *ortho*-arylation of **1a**.

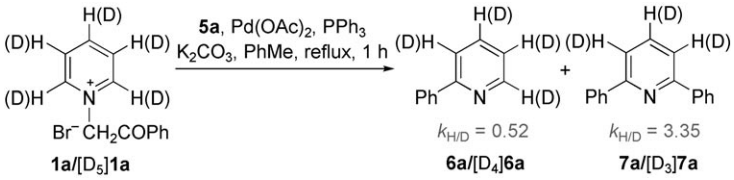
Table 4. The direct *ortho*-arylation between **1a–b** and **5a–l**.[a]

Entry	1	5	6	7	Yield [%][b]
1	**1a**	 **5a**	 **6a** (46%)	 **7a** (40%)	86
2	**1b**[c]	 **5b**	 **6b** (47%)	 **7b** (38%)	85
3	**1a**	 **5c**	 **6c** (50%)	 **7c** (38%)	88
4	**1a**	 **5d**	 **6d** (47%)	 **7d** (35%)	82
5	**1a**	 **5e**	 **6e** (35%)	 **7e** (32%)	67
6	**1a**	 **5f**	 **6f** (40%)	 **7f** (33%)	73
7	**1a**	 **5g**	 **6g** (49%)	 **7g** (36%)	85
8	**1a**	 **5h**	 **6h** (45%)	 **7h** (36%)	81
9	**1a**	 **5i**	 **6i** (76%)	–	76
10	**1a**	 **5j**	 **6j** (72%)	–	72
11	**1a**	 **5k**	 **6k** (62%)	–	62
12	**1a**	 **5l**	 **6l** (80%)	–	80

[a] The optimized conditions: a mixture of **1** (3 mmol), **5** (1 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.15 mmol), and K_2CO_3 (3 mmol) in toluene (5 mL) was refluxed for 12–15 h. [b] The isolated yield was used. [c] **1b** is 4-methylpyridinium bromide.

tron-withdrawing or large sterically sized substituents, 2-aryl-pyridines were obtained as single products (entries 9–12).

Theoretically, Pd-catalyzed direct *ortho*-arylation of pyridine may proceed through three possible pathways: C–H activation, a Heck reaction, or electrophilic substitution.[10] To clarify the pathway for our method, a kinetic isotope effect study was performed.[11] As shown in Scheme 5, by using the reaction of **1a**/[D_5]**1a** and **5a**, values of $k_{H/D}=0.52$ for **6a**/[D_4]**6a** and 3.35 for **7a**/[D_3]**7a** were obtained, respectively, from their ^{1}H NMR spectra. These data proved that the isotopic effect occurred in this reaction and a C–H-activation pathway was suggested.



Scheme 5. The kinetic isotope effect study results of **1a**/[D_5]**1a**.

To help to understand the abnormal phenomenon of $k_{H/D}<1.0$ for **6a**/[D_4]**6a**, the kinetic isotope effect of the mono-arylated product 2-(4-nitrophenyl)pyridine (**6i**) was studied. As shown in Scheme 6, by the reaction of **1a**/[D_5]**1a** and **5i**, the normal result ($k_{H/D}=2.0$) was obtained for **6i**/[D_4]**6i**.

Thus, $k_{H/D}=0.52$ for **6a**/[D_4]**6a** can be well explained as shown in Scheme 7. In the first step, the reaction of **1a** proceeded faster than the reaction of [D_5]**1a** because of the kinetic isotope effect, which led to the faster formation of **6a** than of [D_4]**6a**. Since both **6a** and [D_4]**6a** are intermediates for the secondary step, they continuously reacted with **5i**. Again, as a result of the kinetic isotope effect, the conversion of **6a** into **7a** was faster than the conversion of [D_4]**6a** into [D_3]**7a**. Therefore, $k_{H/D}=0.53$ for **6a**/[D_4]**6a** and 3.35 for **7a**/[D_3]**7a** are the final results for a two-step reaction. This result also indicated that the C–H cleavage was the initial step and 2,6-diphenylpyridine (**7a**) was produced stepwise from 2-phenylpyridine (**6a**).

As shown in Figure 1, DFT (B3LYP/6-31G(d)) treatment of **1a** indicated that the HOMO is almost completely located on the benzene ring (Figure 1a). However, when the ylid of **1a** was produced, the pyridine ring had an extended HOMO on its C2, C4, and C6 atoms (Figure 1b and c). This result is in full agreement with the *N*-iminopyridinium ylid (Figure 1d) and strongly implies that the ylids (Figure 1b and c) may be the real reactants. Since no arylated product on C4 is produced, it is suggested that the *N*-phenacyl group may be involved in the C–H-activation steps by coordination with Pd.

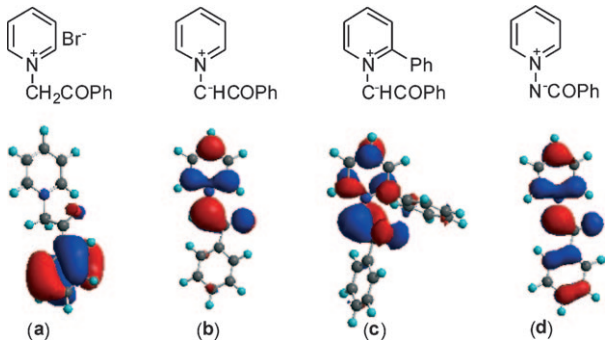
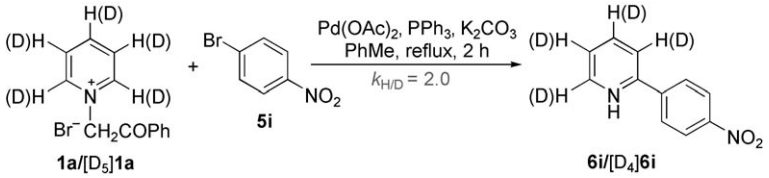
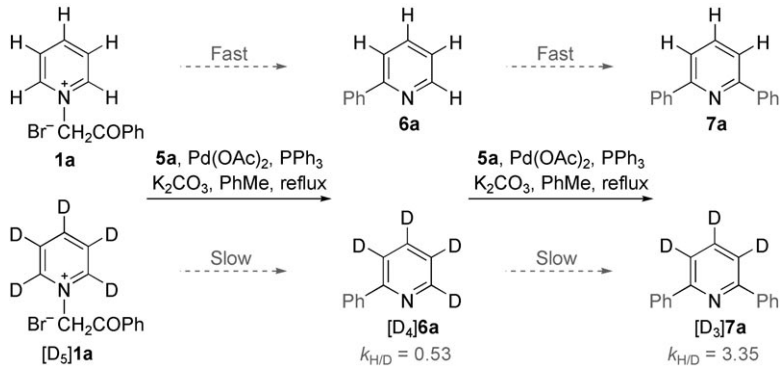


Figure 1. DFT calculated HOMO densities at **1a** and its ylids.



Scheme 6. The kinetic isotope effect of **6i**/[D_4]**6i**.



Scheme 7. A stepwise mechanism for the formation of **7a**.

Conclusion

A novel Pd-catalyzed direct *ortho*-arylation of *N*-phenacylpyridinium bromide was developed. Its unique feature is that the activating group can depart from the arylated pyridines automatically. A kinetic isotope effect study proved that the reaction went through a C–H-bond activation pathway. The results from experiments and DFT calculations indicated that the *N*-phenacyl group played two crucial roles: 1) activation of the pyridine ring by forming

an ylid and 2) regioselective control of the arylation by coordination with Pd at the *ortho*-position of pyridine. Further mechanistic studies and investigations into the applications of this methodology in organic synthesis are underway.

Experimental Section

Procedure for the test of the isotopic effect of the reaction of 1a/[D_5]1a and 5a: A mixture of *N*-phenacylpyridinium bromide (**1a**, 278 mg, 1 mmol), [D_5]-*N*-phenacylpyridinium bromide ([D_5]**1a**, 283 mg, 1 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PPh_3 (39.3 mg, 0.15 mmol), and K_2CO_3 (552 mg, 4 mmol) in toluene (5 mL) was stirred for 5 min at room temperature under nitrogen. Then, PhBr (**5a**, 157 mg, 1.0 mmol, 1.0 equiv) was added and the resultant mixture was heated to reflux for 1 h. The reaction system was then cooled to room temperature and the solid was filtered off. After removal of the solvent, the crude product was purified by chromatography (silica gel, EtOAc/PE 1:25) to give a mixture of products **6a**/[D_4]**6a** and **7a**/[D_3]**7a** (total 15% yield). The ^{1}H NMR spectrum of the mixture was determined and the value of k_H/k_D was calculated.

By using a similar procedure, the isotopic effect of the reaction of **1a**/[D_5]**1a** and **5i** was tested.

A typical procedure for the preparation of 2-phenylpyridine (6a) and 2,6-diphenylpyridine (7a): A mixture of *N*-phenacylpyridinium bromide (**1a**, 834 mg, 3 mmol, 3.0 equiv), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.05 equiv), PPh_3 (39.3 mg, 0.15 mmol, 0.15 equiv), and K_2CO_3 (552 mg, 4 mmol, 4.0 equiv) in toluene (5 mL) was stirred for 5 min at room temperature under nitrogen. Then, PhBr (**5a**, 157 mg 1.0 mmol, 1.0 equiv) was added and the resulting mixture was heated to reflux for 12 h. The reaction system was then cooled to room temperature and the solid was filtered off. After removal of the solvent, the crude product was purified by chromatography (silica gel, EtOAc/PE 1:25) to give products **6a** (71.3 mg, 46%) and **7a** (46.2 mg, 40%).

By using a similar procedure, products **6b–l** and **7b–h** were prepared (Table 4).[12]

2-Phenylpyridine (6a): Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.66–8.64 (m, 1H), 7.99–7.97 (m, 2H), 7.64–7.60 (m, 2H), 7.45–7.36 (m, 3H), 7.14–7.09 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 157.1, 149.4, 139.2, 136.4, 128.7, 128.5, 126.7, 121.8, 120.2 ppm.

2,6-Diphenylpyridine (7a): White solid; m.p. 79–80 °C (EtOAc/PE) (lit.[12] 80–81 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.12 (d, J = 7.5 Hz, 4H), 7.68–7.63 (m, 1H), 7.57 (d, J = 7.2, 2H), 7.47–7.35 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 156.6, 139.4, 137.4, 128.9, 128.6, 126.9, 118.5 ppm.

4-Methyl-2-phenylpyridine (6b): Yellow solid; m.p. 47–48 °C (EtOAc/PE) (lit.[12] < 50 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.54 (d, J = 5.1 Hz, 1H), 7.97 (d, J = 7.2 Hz, 2H), 7.52 (s, 1H), 7.48–7.38 (m, 3H), 7.03 ppm (d, J = 4.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 157.2, 149.3, 147.6, 139.4, 128.7, 128.6, 126.8, 123.0, 121.4, 21.1 ppm.

4-Methyl-2,6-diphenylpyridine (7b): Yellow solid; m.p. 71–72 °C (EtOAc/PE) (lit.[12] 72–73 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.11 (d, J = 7.2 Hz, 4H), 7.47–7.42 (m, 6H), 7.39–7.35 (m, 2H), 2.36 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 156.6, 148.2, 139.5, 128.7, 128.5, 126.9, 119.6, 21.3 ppm.

2-(4-Methylphenyl)pyridine (6c): Colorless oil; ^{1}H NMR: δ = 8.63 (d, J = 1.4 Hz, 1H), 7.88 (d, J = 8.3 Hz, 2H), 7.60–7.56 (m, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.08–7.04 (m, 1H), 2.33 ppm (s, 3H); ^{13}C NMR: δ = 157.0, 149.2, 138.5, 136.3, 129.1, 126.4, 121.4, 119.8, 20.9 ppm.

2,6-Di(4-methylphenyl)pyridine (7c): White solid; m.p. 163–165 °C (EtOAc/PE) (lit.[12] 165–166 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.04 (d, J = 8.3 Hz, 4H), 7.76–7.71 (m, 1H), 7.61 (d, J = 7.2 Hz, 2H), 7.28 (d, J = 7.9 Hz, 4H), 2.41 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 156.7, 138.8, 137.3, 136.8, 129.3, 126.8, 118.0, 21.3 ppm.

2-(4-Methoxyphenyl)pyridine (6d): White solid; m.p. 53–54 °C (EtOAc/PE) (lit.[12] 54–55 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.63 (d, J = 4.8 Hz, 1H), 7.96–7.93 (m, 2H), 7.69–7.61 (m, 2H), 7.16–7.10 (m, 1H), 6.99–6.96 ppm (m, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 160.3, 156.9, 149.4, 136.5, 131.9, 128.0, 121.3, 119.6, 114.0, 55.2 ppm.

2,6-Di(4-methoxylphenyl)pyridine (7d): Yellowish solid; m.p. 185–188 °C (EtOAc/PE) (lit.[12[185–186 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.10 (d, J = 8.2 Hz, 4H), 7.74–7.69 (m, 1H), 7.55 (d, J = 7.5 Hz, 2H), 7.01 (d, J = 8.2 Hz, 4H), 3.86 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 160.4, 156.3, 137.3, 132.3, 128.2, 117.1, 114.0, 55.3 ppm.

2-(4-Fluorophenyl)pyridine (6e): White solid; m.p. 36–38 °C (EtOAc/PE) (lit.[12] 39–40.5 °C); IR (KBr): $\tilde{\nu}$ = 3454, 1599, 1511, 1466, 1163, 846, 779, 737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.66 (d, J = 4.5 Hz, 1H), 7.99–7.94 (m, 2H), 7.73–7.62 (m, 2H), 7.21–7.11 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 163.4 (d, J = 246.7 Hz), 156.3, 149.6, 136.7, 135.5, 128.6 (d, J = 8.6 Hz), 121.9, 120.1, 115.5 ppm (d, J = 21.5 Hz); MS (EI): m/z (%): 173 (100) $[M]^+$, 172 (68.0); elemental analysis calcd (%) for $C_{11}H_8FN$: C 76.29, H 4.66, N 8.09; found: C 76.32; H 4.64; N 8.07.

2,6-Di(4-fluorophenyl)pyridine (7e): White solid; m.p. 93–94 °C (EtOAc/PE) (lit.[12] 94–95 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.12–8.07 (m, 4H), 7.78–7.72 (m, 1H), 7.58 (d, J = 7.5 Hz, 2H), 7.18–7.12 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 163.5 (d, J = 245.9 Hz), 155.7, 137.6, 135.4 (d, J = 2.87 Hz), 128.7 (d, J = 7.9 Hz), 118.1, 115.5 ppm (d, J = 21.5 Hz).

2-(3-Fluorophenyl)pyridine (6f): Yellowish oil; IR: $\tilde{\nu}$ = 3071, 1583, 1567, 1472, 1454, 1423, 1285, 1190, 883, 770 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.64 (d, J = 3.8 Hz, 1H), 7.76–7.71 (m, 2H), 7.62–7.58 (m, 2H), 7.39–7.32 (m, 1H), 7.16–7.12 (m, 1H), 7.09–7.02 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 163.0 (d, J = 243.8 Hz), 155.5, 149.4, 141.4 (d, J = 7.2 Hz), 136.5, 129.9 (d, J = 8.6 Hz), 122.3, 122.1 (d, J = 19.4 Hz), 120.2, 115.4 (d, J = 29.8 Hz), 113.5 ppm (d, J = 23.0 Hz); MS (70 eV): m/z (%): 173 (100) $[M]^+$, 172 (55.4); elemental analysis calcd (%) for $C_{11}H_8FN$: C 76.29, H 4.66, N 8.09; found: C 76.27, H 4.64, N 8.13.

2,6-Di(3-fluorophenyl)pyridine (7f): White solid; m.p. 71–72 °C (EtOAc/PE); IR: $\tilde{\nu}$ = 3418, 1579, 1567, 1459, 1264, 1192, 784, 691 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.79 (d, J = 10.3 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H), 7.62–7.56 (m, 1H), 7.40–7.37 (m, 2H), 7.32–7.24 (m, 2H), 7.04–6.98 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 163.1 (d, J = 243.1 Hz), 154.8, 141.2 (d, J = 7.2 Hz), 137.4, 129.9 (d, J = 7.9 Hz), 122.1 (d, J = 8.6 Hz), 118.7, 115.6 (d, J = 20.8 Hz), 113.5 ppm (d, J = 22.9 Hz); MS (70 eV): m/z (%): 267 (100) $[M]^+$, 266 (41); elemental analysis calcd (%) for $C_{17}H_{11}F_2N$: C 76.39, H 4.15, N 5.24; found: C 76.41, H 4.17, N 5.22.

2-(2-Methylphenyl)pyridine (6g): Yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.68–8.66 (m, 1H), 7.71–7.64 (m, 1H), 7.40–7.34 (m, 2H), 7.26–7.23 (m, 3H), 7.20–7.15 (m, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 160.0, 149.1, 140.4, 136.0, 135.7, 130.7, 129.5, 128.2, 125.8, 124.0, 121.5, 20.2 ppm.

2,6-Di(2-methylphenyl)pyridine (7g): White solid; m.p. 66–68 °C (EtOAc/PE) (lit.[12] 68–70 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.76 (t, J = 7.8 Hz, 1H), 7.45–7.42 (m, 2H), 7.33 (d, J = 7.9 Hz, 2H), 7.27–7.22 (m, 6H), 2.42 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 159.4, 140.6, 136.2, 135.7, 130.6, 129.8, 128.1, 125.7, 121.9, 20.5 ppm.

2-(2-Methoxylphenyl)pyridine (6h): Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.65 (dd, J = 4.8, 1.0 Hz, 1H), 7.82–7.75 (m, 2H), 7.55 (dt, J = 7.5, 1.5 Hz, 1H), 7.31–7.25 (m, 1H), 7.06–7.01 (m, 2H), 6.88 (d, J = 8.3 Hz, 1H), 3.68 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 156.3, 155.4, 148.7, 135.0, 130.5, 129.4, 128.4, 124.5, 121.0, 120.3, 110.7, 54.8 ppm.

2,6-Di(2-methoxylphenyl)pyridine (7h): Yellowish solid; m.p. 118–120 °C (EtOAc/PE) (lit.[12] 117 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS):

δ = 7.93 (dd, J = 7.7, 1.4 Hz, 2H), 7.79–7.67 (m, 3H), 7.38–7.31 (m, 2H), 7.07 (t, J = 7.5 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H), 3.84 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 157.0, 155.3, 135.1, 131.4, 129.6, 129.5, 123.0, 121.0, 111.3, 55.6 ppm.

2-(4-Nitrophenyl)pyridine (6i): Yellowish solid; m.p. 129–130 °C (EtOAc/PE) (lit.[12] 130–131 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.75 (d, J = 4.8 Hz, 1H), 8.33–8.30 (m, 2H), 8.19–8.16 (m, 2H), 7.84–7.81 (m, 2H), 7.37–7.32 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 154.7, 150.1, 148.1, 145.2, 137.1, 127.6, 123.9, 123.5, 121.2 ppm.

Methyl 4-(2-pyridyl)benzoate (6j): Yellowish solid; m.p. 98–99 °C (EtOAc/PE) (lit.[3] 99–100 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.68 (d, J = 4.5 Hz, 1H), 8.11 (d, J = 8.6 Hz, 2H), 8.04 (d, J = 8.3 Hz, 2H), 7.70–7.66 (m, 2H), 7.24–7.18 (m, 1H), 3.89 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 166.5, 155.7, 149.5, 143.2, 136.6, 130.0, 129.7, 126.5, 122.6, 120.6, 51.8 ppm.

2,2′-Bipyridine (6k): White solid; m.p. 68–70 °C (EtOAc/PE) (lit.[12] 72 °C); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.69 (d, J = 4.1 Hz, 2H), 8.40 (dd, J = 7.2, 1.0 Hz, 2H), 7.81 (dt, J = 7.6, 1.7 Hz, 2H), 7.33–7.28 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 155.9, 149.0, 136.7, 123.5, 120.9 ppm.

2-(1-Naphathyl)pyridine (3l): Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.79 (d, J = 4.1 Hz, 1H), 8.10–8.07 (m, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.80 (dt, J = 7.5, 1.0 Hz, 1H), 7.61–7.36 (m, 3H), 7.51–7.46 (m, 2H), 7.33–7.29 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 159.2, 149.5, 138.4, 136.3, 133.9, 131.1, 128.8, 128.3, 127.4, 126.4, 125.8, 125.5, 125.2, 125.0, 122.0 ppm.

Acknowledgements

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[12] With the exception of **6f** and **7f**, all other products are known compounds and the cited references for their physical data can be found in the Supporting Information.

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