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Palladium-Catalyzed Aryl C(sp^2)−H Bond Hydroxylation of 2-Arylpyridine Using TBHP as Oxidant

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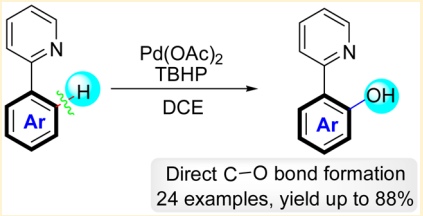
Supporting Information

ABSTRACT: An efficient synthesis of phenols via Pd-catalyzed, pyridyl-directed homogeneous hydroxylation of the aryl C−H bond was developed, in which *tert*-butyl hydroperoxide was used as the sole oxidant. The method had a broad group tolerance and was available for both electron-rich and electron-deficient substrates. The reaction of a series of 2-arylpyridine derivatives gave the *ortho*-hydroxylation products in moderate to good yields.



As a class of important compounds, phenols are naturally abundant. Besides their application in organic synthesis, phenols are major constituents of many biological and natural compounds and almost ubiquitously exist in the structural organization of plants and animals.[1] Phenolic compounds were generally industrially synthesized by multistep procedures as represented by the cumene process.[1b] In view of green and sustainable chemistry as well as in economic terms, a direct C(sp^2)−H bond hydroxylation for phenol synthesis with an inexpensive oxidant and without any sacrificial reactant is desired. Transition-metal-catalyzed C(sp^2)−H bond functionalization provided the possibility for this transformation.[1a,2] Though the transition-metal-catalyzed C−O bond formation is considered to be more difficult compared with C−C and some other C−heteroatom bonds,[3] there have been many successful examples in this regard. A range of palladium-catalyzed alkoxylations of the C(sp^2)−H bond were developed.[4] Moreover, a series of encouraging progress on the direct oxidation of aryl C(sp^2)−H bonds catalyzed by transition metals to form phenols have also been achieved in recent years. These hydroxylations regioselectively took place at the *ortho*-position of aromatic rings directed by the carbonyl,[5] ester,[6] carbamyl,[7] carbamate,[8] carboxyl,[9] acylamino,[10] phosphate,[11] and some azacyclic groups.[12] After the *ortho*-hydroxylation of the aryl moiety of 2-arylpyridines using Pd(OAc)$_2$/oxone in PEG-3400/*t*-BuOH reported by Kim et al.,[12a] Jiao et al.[12b] developed a novel $PdCl_2$ and NHPI (*N*-hydroxyphthalimide)-cocatalyzed aromatic C(sp^2)−H bond hydroxylation of 2-phenylpyridines, in which molecular oxygen was used as a heterogeneous oxidant for this transformation. Patel et al.[12e] also obtained a hydroxylation product of 2-phenylpyridine by using *tert*-butyl hydroperoxide (TBHP) as the oxidant in their study on the palladium-catalyzed acylation of 2-phenylpyridines, but further study was not done. In our continuous study on the palladium-catalyzed oxidative coupling reaction, we found that the peroxide could be an effective homogeneous oxidant for C−H bond functionalization.[13] We herein present an efficient method for the synthesis of phenols via Pd-catalyzed, pyridyl-directed homogeneous hydroxylation of the aryl C−H bond using TBHP as the sole oxidant.

We initiated our study by employing 2-phenylpyridine (**1a**) as the reactant in the presence of catalyst and TBHP (Table 1). Without the palladium catalyst, the reaction could not take place at all (entry 1). Thus, Pd(OAc)$_2$, $PdCl_2$, Pd(PPh$_3$)$_2$Cl$_2$, and Pd(CH$_3$CN)$_2$Cl$_2$ were tested for this transformation, in which Pd(OAc)$_2$ was proven to be the most effective (entries 5 and 14−16). The oxidation reaction could be catalyzed by 5 mol % of Pd(OAc)$_2$ to give the hydroxylation product 2-(pyridin-2-yl)phenol (**2a**) in 58% yield using 4.0 equiv of TBHP as the oxidant in DCE (1,2-dichloroethane) (entry 3). The amount of the oxidant had an evident effect on this oxidation. In the absence of TBHP, no desired product was detected (entry 2). Increasing TBHP to 6.0 equiv led to a higher yield of 82% (entry 5); further increasing it to 7.0 equiv did not improve the yield (entry 6). Another influencing factor of this reaction was the solvent. In DCE, the reaction proceeded smoothly and gave the highest yield; in TCE (1,1,2,2-tetrachloroethane), the hydroxylation product with a lower yield of 79% was obtained (entry 8). In CH$_3$CN, dioxane, or DMF, however, only trace desired product was found (entries 9−11). The reaction temperature was also crucial. The appropriate temperature was proven to be 115 °C. Increasing the temperature to 125 °C failed to further increase the yield (entry 13), but at 100 °C, only 43% yield was obtained (entry 12). It is noticeable that, when the reaction proceeded in nitrogen atmosphere, a result similar to that in air was obtained (entry 17).

With the optimal conditions in hand, a series of 2-arylpyridines were tested, and the results are summarized in

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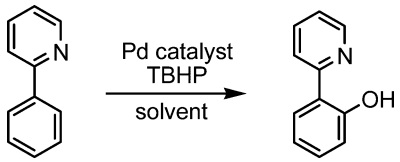
Table 1. Optimization of Reaction Conditions[a]



1a 2a

entry	catalyst (mol %)	TBHP (equiv)	solvent	yield (%)
1		6.0	DCE	0
2	$Pd(OAc)_2$ (5)		DCE	0
3	$Pd(OAc)_2$ (5)	4.0	DCE	58
4	$Pd(OAc)_2$ (5)	5.0	DCE	77
5	$Pd(OAc)_2$ (5)	6.0	DCE	82
6	$Pd(OAc)_2$ (5)	7.0	DCE	83
7	$Pd(OAc)_2$ (10)	6.0	DCE	86
8	$Pd(OAc)_2$ (5)	6.0	TCE	79
9	$Pd(OAc)_2$ (5)	6.0	CH_3CN	trace
10	$Pd(OAc)_2$ (5)	6.0	dioxane	trace
11	$Pd(OAc)_2$ (5)	6.0	DMF	trace
12[b]	$Pd(OAc)_2$ (5)	6.0	DCE	43
13[c]	$Pd(OAc)_2$ (5)	6.0	DCE	80
14	$PdCl_2$ (5)	6.0	DCE	62
15	$Pd(PPh_3)_2Cl_2$ (5)	6.0	DCE	45
16	$Pd(CH_3CN)_2Cl_2$ (5)	6.0	DCE	53
17[d]	$Pd(OAc)_2$ (5)	6.0	DCE	85

[a]Unless otherwise specified, the reactions were carried out in a sealed tube in the presence of 2-phenypyridine (**1a**, 0.3 mmol), solvent (1 mL), catalyst, and TBHP under air atmosphere at 115 °C for 20 h. [b]At 100 °C. [c]At 125 °C. [d]In N_2 atmosphere.

Table 2. The *meta*- or *para*-halogenated substrates were compatible with the process and afforded corresponding hydroxylated products in good yields (**2c**–**2h**). However, 2-(2-fluorophenyl)pyridine gave the desired product in a relatively lower yield of 55% (**2b**), which might be because of the steric effect. Arenes containing other electron-withdrawing groups also afforded the expected product with good yields, except in the case of carbonyl or ester-containing compounds, which only gave moderate yields (**2n**, **2o**). Interestingly, the reaction of 2-(naphthalen-2-yl)pyridine gave a *β*-hydroxylation product (**2w**), which might also be attributed to the less steric hindrance of its *β*-position. The large conjugated reactant benzo[*h*]quinolone also gave a 10-hydroxylated product in 79% yield (**2x**). Some substrates with electron-donating groups seemed to be disadvantageous to the reaction. For example, moderate yields were obtained from methoxy-, ethyl-, or *n*-pentyl-substituted 2-phenylpyridines (**2p**, **2s**, **2t**), and the exact reason is not clear. In general, formation of the dihydroxylation product was not observed, and for *meta*-substituted substrates, the hydroxylation proceeded at the less sterically hindered position with high regioselectivity. It must be pointed out that, when 7 mmol (1.09 g) **1a** was used, product **2a** was still achieved with a yield of 79%, which demonstrated the practical utility of the present method.

A control experiment was also carried out (Scheme 1). A radical-trapping reagent 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added in the reaction mixture of **1a** under the established reaction conditions. The results showed that, in the presence of 2 equiv of TEMPO, the yield of **2a** was reduced to 30%, and when the amount of TEMPO was increased to 4 equiv, a yield lower than 10% was obtained (Scheme 1). The obvious inhibitory effect of TEMPO indicated that the radicals maybe existed in this transformation.

As mentioned in our optimization of reaction conditions, when the reaction proceeded in nitrogen atmosphere, a result similar to that in air was obtained (Table 1, entry 17), which revealed that TBHP was the sole hydroxyl source. On the basis of our experimental results and related reports,[14] we proposed a possible mechanism for this direct hydroxylation of the aryl C–H bond (Scheme 2). Initially, the chelation-assisted C–H activation at the *ortho*-position of the directing group with $Pd(OAc)_2$ formed a Pd(II) intermediate **A**. Homolysis of TBHP gave HO• and *t*-BuO•,[13] which could abstract a hydrogen radical from HOAc, then release AcO•, followed by oxidative addition of HO• and AcO• to form Pd(IV) intermediate **B**. Finally, reductive elimination of **B** gave the product **2a** and regenerated the Pd(II) species.

In summary, a simple method for the synthesis of phenols by $Pd(OAc)_2$-catalyzed, pyridyl-directed aryl sp^2 C–H bond activation using TBHP as the sole oxidant and without any ligand has been explored. Various substituents on the aryl ring, including some coupling-reaction-sensitive groups (Cl, Br), tolerated the reaction and gave the hydroxylation products in moderate to good yields.

EXPERIMENTAL SECTION

General. All reactions were run in air. All reagents were commercially available and were used without further purification. NMR spectra were recorded at 400 MHz (^1H) and 100 MHz ($^{13}C\{^1H\}$) using TMS as an internal standard. Chemical shifts are given relative to $CDCl_3$ (7.28 ppm for ^1H NMR, 77.16 ppm for $^{13}C\{^1H\}$ NMR). The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, td = triplet of doublets, br s = broad singlet. Melting points are uncorrected. For the HRMS measurements, a Q-TOF analyzer was used.

General Experimental Procedures for Palladium-Catalyzed *ortho*-Hydroxylation of 2-Arylpyridines and Characterizations. A mixture of 2-arylpyridines **1** (0.3 mmol), $Pd(OAc)_2$ (3.4 mg, 5 mol %), and TBHP (0.25 mL, 6.0 equiv, 70% aqueous solution) combined in DCE (1 mL) was sealed in a 25 mL tube with a Teflon-lined cap. The tube was then placed in an oil bath, stirred, and heated at 115 °C for 20 h. After being cooled to room temperature, the reaction mixture was quenched with brine and extracted with dichloromethane (30 mL × 3). The combined organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed under vacuum. The crude product was purified over a column of silica gel (eluant: hexane/ethyl acetate) to afford the desired product **2**.

*2-(Pyridin-2-yl)phenol (**2a**):*[12b] Yellow oil (42.1 mg, 82% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.34 (br s, 1H), 8.52 (d, J = 4.5 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.89–7.76 (m, 2H), 7.35–7.28 (m, 1H), 7.28–7.23 (m, 1H), 7.04 (dd, J = 8.2, 1.0 Hz, 1H), 6.95–6.87 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 157.8, 145.8, 137.8, 131.5, 126.2, 121.5, 119.1, 118.8, 118.6.

*3-Fluoro-2-(pyridin-2-yl)phenol (**2b**):* Yellow solid (31.2 mg, 55% yield); mp 55–57 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.86 (br s, 1H), 8.61–8.53 (m, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.93–7.85 (m, 1H), 7.32 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H), 7.24 (td, J = 8.3, 6.4 Hz, 1H), 6.86 (dt, J = 8.3, 1.0 Hz, 1H), 6.67 (ddd, J = 12.7, 8.2, 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.0 (d, J = 251.2 Hz), 161.3 (d, J = 5.6 Hz), 154.5, 145.4, 138.1, 130.9 (d, J = 12.7 Hz), 124.7 (d, J = 21.1 Hz), 122.0, 114.2 (d, J = 2.8 Hz), 108.7 (d, J = 11.4 Hz), 106.2 (d, J = 25.0 Hz); HRMS-ESI (m/z) calcd for $C_{11}H_8FNONa$ $[M + Na]^+$ 212.0482, found 212.0484.

*4-Fluoro-2-(pyridin-2-yl)phenol (**2c**):*[12b] Yellow solid (40.9 mg, 72% yield); mp 76–77 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 13.98 (br s, 1H), 8.61–8.50 (m, 1H), 7.87 (ddd, J = 13.4, 10.0, 4.9 Hz, 2H), 7.47

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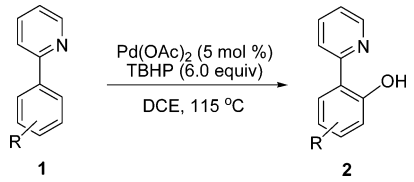
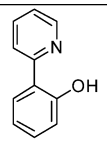
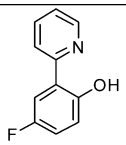
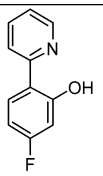
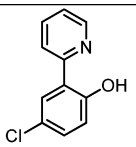
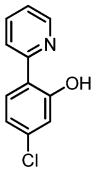
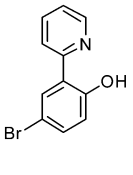
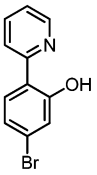
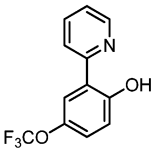
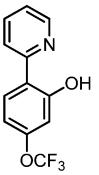
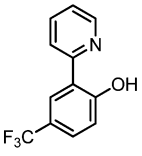
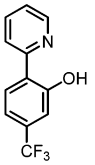
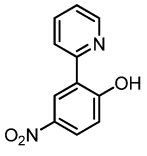
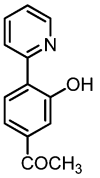
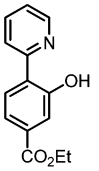
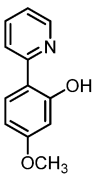
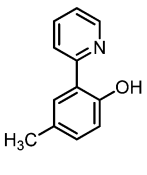
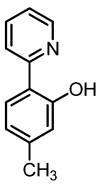
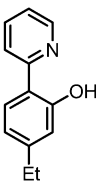
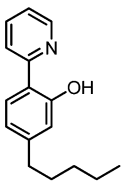
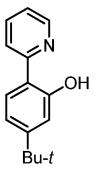
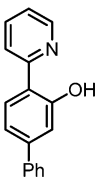
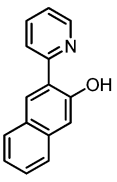
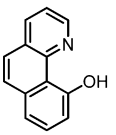
Table 2. Palladium-Catalyzed Hydroxylation of 2-Arylpyridines with TBHP[a]



 **2a**, 82%, (79%)[b]	 **2b**, 55%	 **2c**, 72%	 **2d**, 70%	 **2e**, 68%
 **2f**, 84%	 **2g**, 76%	 **2h**, 73%	 **2i**, 84%	 **2j**, 88%
 **2k**, 85%	 **2l**, 85%	 **2m**, 87%	 **2n**, 64%	 **2o**, 69%
 **2p**, 51%	 **2q**, 80%	 **2r**, 73%	 **2s**, 59%	 **2t**, 62%
 **2u**, 83%	 **2v**, 65%	 **2w**, 61%	 **2x**, 79%	

[a]Reaction conditions: 2-arylpyridine (**1**, 0.3 mmol), $Pd(OAc)_2$ (5 mol %), and TBHP (6.0 equiv) in DCE (1 mL) under air atmosphere at 115 °C for 20 h. [b]The reaction of **1a** (7 mmol, 1.09 g) under the standard reaction conditions.

(dd, J = 9.9, 2.9 Hz, 1H), 7.30 (ddd, J = 6.7, 5.0, 1.5 Hz, 1H), 7.11−6.93 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.7 (d, J = 2.8 Hz), 156.0 (d, J = 1.6 Hz), 155.7 (d, J = 236.3 Hz), 146.0, 138.1, 122.1, 119.5 (d, J = 7.9 Hz), 119.3, 118.8 (d, J = 7.2 Hz), 118.4 (d, J = 23.2 Hz), 111.8 (d, J = 24.3 Hz).

*5-Fluoro-2-(pyridin-2-yl)phenol (**2d**):*[12b] Yellow solid (39.7 mg, 70% yield); mp 109−111 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.81 (br s, 1H), 8.56−8.44 (m, 1H), 7.89−7.81 (m, 2H), 7.77 (dd, J = 8.9, 6.5 Hz, 1H), 7.32−7.20 (m, 1H), 6.74 (dd, J = 10.6, 2.6 Hz, 1H), 6.64 (ddd, J = 8.9, 8.0, 2.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.6 (d, J = 250.3 Hz), 162.0 (d, J = 12.9 Hz), 157.2, 145.6, 137.9, 127.5 (d, J = 10.8 Hz), 121.5, 118.8, 115.4 (d, J = 2.8 Hz), 106.3 (d, J = 22.4 Hz), 105.2 (d, J = 23.3 Hz).

*4-Chloro-2-(pyridin-2-yl)phenol (**2e**):* Yellow solid (41.9 mg, 68% yield); mp 95−96 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.34 (br s, 1H), 8.54 (dt, J = 5.0, 1.5 Hz, 1H), 7.92−7.81 (m, 2H), 7.77 (d, J = 2.5

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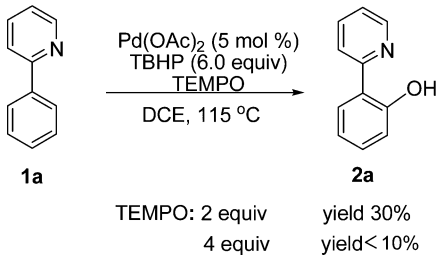
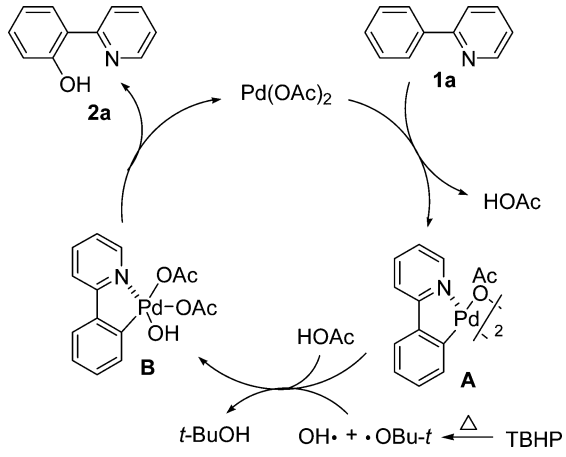
Scheme 1. Effect of TEMPO on the Reaction



Scheme 2. Plausible Reaction Mechanism



Hz, 1H), 7.34−7.18 (m, 2H), 6.99 (d, J = 8.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 156.6, 146.0, 138.1, 131.2, 125.7, 123.5, 122.1, 120.0, 119.8, 119.2; HRMS-ESI (m/z) calcd for $C_{11}H_9ClNO$ $[M + H]^+$ 206.0367, found 206.0365.

5-Chloro-2-(pyridin-2-yl)phenol (**2f**):[12b] Yellow solid (51.8 mg, 84% yield); mp 82−83 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.70 (br s, 1H), 8.52 (dt, J = 5.0, 1.4 Hz, 1H), 7.91−7.80 (m, 2H), 7.72 (d, J = 8.6 Hz, 1H), 7.33−7.21 (m, 1H), 7.05 (d, J = 2.2 Hz, 1H), 6.90 (dd, J = 8.6, 2.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8, 157.0, 145.8, 138.0, 136.7, 127.0, 121.8, 119.1, 119.0, 118.6, 117.4.

4-Bromo-2-(pyridin-2-yl)phenol (**2g**): Yellow solid (57.0 mg, 76% yield); mp 111−114 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.22 (br s, 1H), 8.54 (dt, J = 5.0, 1.4 Hz, 1H), 7.92−7.86 (m, 3H), 7.39 (dd, J = 8.8, 2.4 Hz, 1H), 7.34−7.29 (m, 1H), 6.94 (d, J = 8.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 156.4, 145.9, 138.1, 134.1, 128.7, 122.2, 120.5, 120.4, 119.2, 110.6; HRMS-ESI (m/z) calcd for $C_{11}H_8BrNONa$ $[M + Na]^+$ 271.9681, found 271.9694.

5-Bromo-2-(pyridin-2-yl)phenol (**2h**): Yellow solid (54.8 mg, 73% yield); mp 67−68 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.64 (br s, 1H), 8.51 (dt, J = 5.0, 1.4 Hz, 1H), 7.91−7.81 (m, 2H), 7.65 (d, J = 8.5 Hz, 1H), 7.32−7.25 (m, 1H), 7.22 (d, J = 2.0 Hz, 1H), 7.04 (dd, J = 8.5, 2.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8, 157.0, 145.8, 138.0, 127.1, 124.9, 122.0, 121.9, 121.6, 119.0, 117.7; HRMS-ESI (m/z) calcd for $C_{11}H_8BrNONa$ $[M + Na]^+$ 271.9681, found 271.9691.

2-(Pyridin-2-yl)-4-(trifluoromethoxy)phenol (**2i**): Yellow solid (64.3 mg, 84% yield); mp 62−64 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.26 (br s, 1H), 8.55 (dt, J = 5.0, 1.4 Hz, 1H), 7.94−7.82 (m, 2H), 7.65 (d, J = 2.7 Hz, 1H), 7.35−7.29 (m, 1H), 7.22−7.17 (m, 1H), 7.04 (d, J = 9.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 156.5, 145.9, 141.0 (d, J = 2.0 Hz), 138.1, 122.3, 120.7 (q, J = 257.0 Hz), 119.6, 119.3, 119.0, 119.0; HRMS-ESI (m/z) calcd for $C_{12}H_9F_3NO_2$ $[M + H]^+$ 256.0580, found 256.0584.

2-(Pyridin-2-yl)-5-(trifluoromethoxy)phenol (**2j**): Yellow solid (67.4 mg, 88% yield); mp 68−70 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.69 (br s, 1H), 8.51 (dt, J = 5.1, 1.4 Hz, 1H), 7.89−7.83 (m, 2H), 7.80 (d, J = 8.8 Hz, 1H), 7.32−7.25 (m, 1H), 6.90 (dd, J = 2.4, 1.1 Hz, 1H), 6.77 (ddd, J = 8.8, 2.4, 1.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 156.8, 151.2 (d, J = 1.7 Hz), 145.8, 138.0, 127.2, 121.9, 120.4 (q, J = 257.7 Hz), 119.1, 117.3, 110.8, 110.4; HRMS-ESI (m/z) calcd for $C_{12}H_9F_3NO_2$ $[M + H]^+$ 256.0580, found 256.0584.

2-(Pyridin-2-yl)-4-(trifluoromethyl)phenol (**2k**): Yellow solid (60.1 mg, 85% yield); mp 88−89 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.77 (br s, 1H), 8.56 (d, J = 4.7 Hz, 1H), 8.07 (d, J = 1.4 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.95−7.88 (m, 1H), 7.56 (dd, J = 8.6, 1.9 Hz, 1H), 7.35 (ddd, J = 7.2, 5.1, 0.9 Hz, 1H), 7.12 (d, J = 8.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 156.5, 145.8, 138.3, 128.2 (q, J = 3.5 Hz), 124.5 (q, J = 272.1 Hz), 123.6 (q, J = 3.9 Hz), 122.4, 120.9 (q, J = 32.7 Hz), 119.3, 119.1, 118.4; HRMS-ESI (m/z) calcd for $C_{12}H_9F_3NO$ $[M + H]^+$ 240.0631, found 240.0627.

2-(Pyridin-2-yl)-5-(trifluoromethyl)phenol (**2l**):[12b] Yellow solid (60.1 mg, 85% yield); mp 107−108 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.51 (br s, 1H), 8.57 (d, J = 4.8 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.94−7.87 (m, 2H), 7.39−7.32 (m, 1H), 7.29 (s, 1H), 7.17−7.09 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.1, 156.5, 146.0, 138.2, 132.9 (q, J = 32.6 Hz), 126.6, 123.8 (q, J = 272.4 Hz), 122.6, 121.5, 119.6, 115.8 (q, J = 3.9 Hz), 115.0 (q, J = 3.8 Hz).

4-Nitro-2-(pyridin-2-yl)phenol (**2m**): Yellow solid (56.4 mg, 87% yield); mp 212−213 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 15.65 (br s, 1H), 8.82 (d, J = 2.7 Hz, 1H), 8.59 (ddd, J = 5.0, 1.7, 0.9 Hz, 1H), 8.22 (dd, J = 9.1, 2.7 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.00 (ddd, J = 8.3, 7.6, 1.8 Hz, 1H), 7.42 (ddd, J = 7.5, 5.1, 1.1 Hz, 1H), 7.10 (d, J = 9.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.1, 155.8, 145.7, 139.8, 138.7, 126.9, 123.0, 122.7, 119.5, 119.3, 118.1; HRMS-ESI (m/z) calcd for $C_{11}H_8N_2O_3Na$ $[M + Na]^+$ 239.0427, found 239.0429.

1-(3-Hydroxy-4-(pyridin-2-yl)phenyl)ethanone (**2n**): Yellow solid (40.9 mg, 64% yield); mp 116−117 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.48 (br s, 1H), 8.56 (ddd, J = 5.0, 1.7, 0.9 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.94−7.84 (m, 2H), 7.58 (d, J = 1.8 Hz, 1H), 7.50 (dd, J = 8.3, 1.8 Hz, 1H), 7.34 (ddd, J = 7.4, 5.0, 1.1 Hz, 1H), 2.62 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.8, 160.0, 156.7, 146.1, 139.2, 138.1, 126.3, 122.6, 122.5, 119.8, 119.0, 118.0, 26.8; HRMS-ESI (m/z) calcd for $C_{13}H_{11}NO_2Na$ $[M + Na]^+$ 236.0682, found 236.0687.

Ethyl 3-Hydroxy-4-(pyridin-2-yl)benzoate (**2o**): Yellow solid (50.4 mg, 69% yield); mp 94−95 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.41 (br s, 1H), 8.55 (d, J = 4.9 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.92−7.83 (m, 2H), 7.70 (d, J = 1.7 Hz, 1H), 7.57 (dd, J = 8.3, 1.7 Hz, 1H), 7.32 (ddd, J = 7.4, 5.0, 0.9 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.2, 159.7, 156.9, 146.0, 138.0, 132.9, 126.1, 122.4, 119.8, 119.8, 119.5, 61.1, 14.3; HRMS-ESI (m/z) calcd for $C_{14}H_{13}NO_3Na$ $[M + Na]^+$ 266.0788, found 266.0793.

5-Methoxy-2-(pyridin-2-yl)phenol (**2p**): Yellow oil (30.8 mg, 51% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.66 (br s, 1H), 8.45 (d, J = 5.0 Hz, 1H), 7.83−7.76 (m, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.21−7.13 (m, 1H), 6.56 (d, J = 2.6 Hz, 1H), 6.49 (dd, J = 8.8, 2.6 Hz, 1H), 3.84 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4, 161.9, 157.8, 145.5, 137.6, 127.2, 120.5, 118.3, 112.1, 106.6, 102.2, 55.3; HRMS-ESI (m/z) calcd for $C_{12}H_{12}NO_2$ $[M + H]^+$ 202.0863, found 202.0860.

4-Methyl-2-(pyridin-2-yl)phenol (**2q**): Yellow oil (44.4 mg, 80% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.01 (br s, 1H), 8.55−8.48 (m, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.88−7.79 (m, 1H), 7.61 (d, J = 1.7 Hz, 1H), 7.25 (ddd, J = 7.4, 5.0, 1.0 Hz, 1H), 7.14 (dd, J = 8.2, 1.9 Hz, 1H), 6.96 (d, J = 8.3 Hz, 1H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 157.7, 145.9, 137.7, 132.4, 127.7, 126.3, 121.4, 119.0, 118.4, 20.8; HRMS-ESI (m/z) calcd for $C_{12}H_{11}NONa$ $[M + Na]^+$ 208.0733, found 208.0735.

5-Methyl-2-(pyridin-2-yl)phenol (**2r**):[12b] Yellow oil (40.6 mg, 73% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.19 (br s, 1H), 8.50 (d, J = 4.8 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.86−7.79 (m, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.25−7.19 (m, 1H), 6.87 (s, 1H), 6.73 (d, J = 8.1 Hz, 1H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 158.0, 145.8, 142.1, 137.7, 125.9, 121.1, 119.9, 118.9, 118.7, 116.2, 21.4.

5-Ethyl-2-(pyridin-2-yl)phenol (**2s**): Yellow oil (35.3 mg, 59% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.24 (br s, 1H), 8.52 (ddd, J = 5.1, 1.8, 0.9 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.84 (ddd, J = 8.3, 7.4, 1.8 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.24 (ddd, J = 7.3, 5.1, 1.1 Hz,

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1H), 6.95−6.88 (m, 1H), 6.78 (dd, J = 8.1, 1.8 Hz, 1H), 2.66 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 157.9, 148.5, 145.7, 137.8, 126.1, 121.1, 118.9, 118.8, 117.6, 116.4, 28.8, 15.1; HRMS-ESI (m/z) calcd for $C_{13}H_{14}NO$ $[M + H]^+$ 200.1070, found 200.1068.

*5-Pentyl-2-(pyridin-2-yl)phenol (**2t**):* Yellow oil (44.9 mg, 62% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.36 (br s, 1H), 8.51 (ddd, J = 5.0, 1.8, 1.0 Hz, 1H), 7.93−7.86 (m, 1H), 7.82 (ddd, J = 8.4, 7.4, 1.8 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.22 (ddd, J = 7.4, 5.0, 1.1 Hz, 1H), 6.89 (d, J = 1.6 Hz, 1H), 6.76 (dd, J = 8.1, 1.7 Hz, 1H), 2.67−2.52 (m, 2H), 1.74−1.61 (m, 2H), 1.41−1.32 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 158.0, 147.2, 145.8, 137.7, 125.9, 121.1, 119.3, 118.8, 118.2, 116.4, 35.8, 31.5, 30.7, 22.6, 14.0; HRMS-ESI (m/z) calcd for $C_{16}H_{20}NO$ $[M + H]^+$ 242.1539, found 242.1535.

*5-(tert-Butyl)-2-(pyridin-2-yl)phenol (**2u**):* Yellow oil (56.6 mg, 83% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 14.30 (br s, 1H), 8.51 (ddd, J = 5.0, 1.8, 0.9 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.82 (ddd, J = 8.3, 7.4, 1.8 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.22 (ddd, J = 7.3, 5.0, 1.1 Hz, 1H), 7.09 (d, J = 2.0 Hz, 1H), 6.98 (dd, J = 8.4, 2.0 Hz, 1H), 1.36 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7, 157.8, 155.4, 145.8, 137.7, 125.8, 121.1, 118.8, 116.3, 116.2, 115.5, 34.8, 31.1; HRMS-ESI (m/z) calcd for $C_{15}H_{17}NONa$ $[M + Na]^+$ 250.1202, found 250.1202.

*4-(Pyridin-2-yl)-[1,1′-biphenyl]-3-ol (**2v**):*[12b] Yellow solid (48.2 mg, 65% yield); mp 156−157 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.45 (br s, 1H), 8.54 (ddd, J = 5.0, 1.8, 0.9 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.91−7.80 (m, 2H), 7.70 (dq, J = 2.8, 1.7 Hz, 2H), 7.52−7.44 (m, 2H), 7.43−7.37 (m, 1H), 7.34 (d, J = 1.9 Hz, 1H), 7.29−7.23 (m, 1H), 7.20 (dd, J = 8.3, 1.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.3, 157.6, 145.9, 144.2, 140.2, 137.8, 128.8, 127.8, 127.0, 126.6, 121.5, 119.1, 117.8, 117.7, 116.8.

*3-(Pyridin-2-yl)naphthalen-2-ol (**2w**):* Yellow solid (40.5 mg, 61% yield); mp 150−151 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.05 (br s, 1H), 8.59 (d, J = 4.4 Hz, 1H), 8.35 (s, 1H), 8.18 (d, J = 8.1 Hz, 1H), 7.94 (t, J = 7.4 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.45 (t, J = 7.2 Hz, 1H), 7.40 (s, 1H), 7.37−7.29 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.3, 156.6, 145.8, 138.4, 135.9, 128.4, 127.5, 127.4, 127.2, 126.0, 123.3, 122.2, 121.3, 120.6, 112.3; HRMS-ESI (m/z) calcd for $C_{15}H_{11}NONa$ $[M + Na]^+$ 244.0733, found 244.0735.

*Benzo[h]quinolin-10-ol (**2x**):*[4a] Yellow solid (46.3 mg, 79% yield); mp 102−104 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 14.96 (s, 1H), 8.85 (dd, J = 4.7, 1.7 Hz, 1H), 8.27 (dd, J = 8.1, 1.7 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.67−7.61 (m, 2H), 7.58 (dd, J = 8.0, 4.7 Hz, 1H), 7.44 (dd, J = 7.9, 0.9 Hz, 1H), 7.30−7.26 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 148.3, 145.0, 136.3, 135.0, 129.9, 129.2, 126.3, 124.6, 120.8, 118.1, 115.9, 114.0.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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