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Metal-Free Assembly of Polysubstituted Pyridines from Oximes and Acroleins

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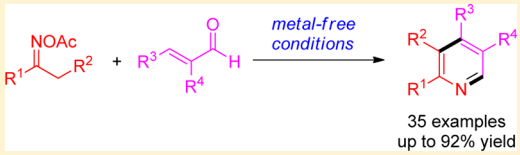
Supporting Information

ABSTRACT: Transition-metal-catalyzed synthesis of N-heterocycles from oximes has been previously well established. In this paper, for the first time a metal-free protocol with the combinational employment of iodine and triethylamine has been demonstrated to be effective to trigger the oxime-based synthesis of pyridines with high chemo-selectivity and wide functional group tolerance. A broad range of functional pyridines were prepared in moderate to excellent yields. While neither iodine nor triethylamine could trigger this transformation, mechanistic experiments indicated a radical pathway for the reaction. The resultant 2-aryl-substituted pyridines have been proved to be versatile building blocks in a range of transition-metal-catalyzed C−H functionalization reactions.

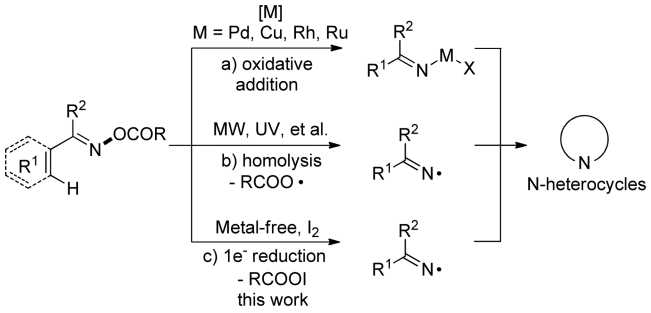


INTRODUCTION

Functionalized pyridines represent privileged heterocycles, which are widely found in natural products, functional materials, and medicinal chemicals.[1] Due to their high significance in industrial applications, the synthesis of polysubstituted pyridines from acyclic precursors has been attracting great interest in synthetic chemistry.[2]

Oxime chemistry is well-known for the classic Beckmann rearrangement and Semmler−Wolff reaction as well as for the synthetic manifold in organic preparation and industrial application.[3] In the past decade, oxime derivatives have proved to be versatile building blocks with a range of transition-metal catalysts, such as of Pd, Cu, Rh, and Ru, especially for the construction of nitrogen-containing heterocycles (Scheme 1a).[4]

Scheme 1. N-Containing Heterocycle Synthesis from Oxime Esters



Besides, the homolysis of the oxime N−O bond under microwave or UV irradiation followed by radical cyclization was also utilized to generate several heterocycles (Scheme 1b).[5] Very recently, Yu and Zhang reported a visible-light-triggered imino radical generation for the efficient preparation of pyridines, quinolines, and phenanthridines from *O*-acyl oximes,[5f] in which the reaction conditions are quite mild by employing electron-deficient benzoates as the leaving groups.

Particularly, oximes bearing α-methylene have a structural advantage to provide, formally, the vinyl amine (C=C−N) moiety in the assembly of pyridines.[6] In previous works, Cu catalysts were well demonstrated to play key roles in the N−O bond activation of oximes, generally leading to imino radicals or otherwise imino-[Cu^{III}] species as the highly active intermediates.[4c] In view of sustainable development, chemical procedures under metal-free conditions are always of significance especially in the pharmaceutical industry, and that could also bring reduced environmental disruption to water and soil.[7] Given the state of iodine-catalyzed transformation[8] and our previous work, we questioned whether a metal-free and mild protocol could be devised for the oxime-based heterocycle synthesis. Herein we disclose for the first time a metal-free system for the synthesis of substituted pyridines by the intermolecular assembly of ketoximes and α,β-unsaturated aldehydes. In such a transformation, iodine was demonstrated to be highly effective for the 1e$^-$ reduction of oximes (Scheme 1c), generating an imino radical which reacts with cinnamaldehyde with high efficiency to give functionalized pyridines.

RESULTS AND DISCUSSION

We commenced our investigation using *O*-acetyl ketoxime **1a** and α,β-unsaturated aldehyde **2a** as the model system (Table 1). Initially, a mixture of two isomers of pyridines (**3a** and **3a′**) was observed when adding iodine to the system (Table 1, entry 1), while the sole treatment with triethylamine gave the pyridines with a chemoselectivity of 1:1, albeit in a low yield (Table 1, entry 2). Delightedly, when we combined I_2 with triethylamine in the reaction system, pyridine **3a** was exclusively

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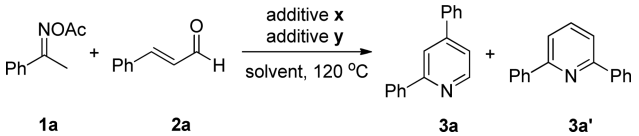
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a 3a'

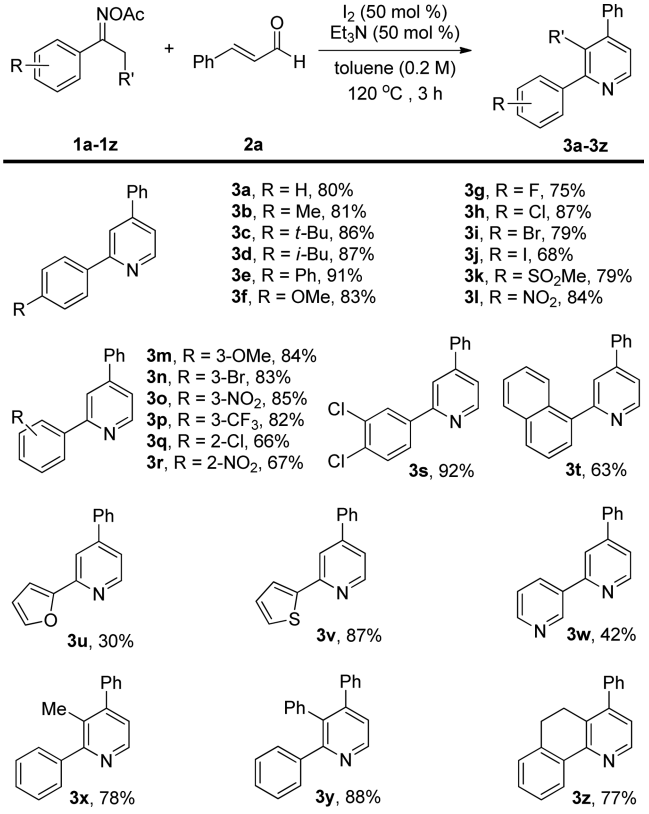
entry	add. x	add. y	solvent	yield[b]	3a/3a′
1	I_2	none	toluene	16	8:1
2	none	Et_3N	toluene	9	1:1
3	I_2	Et_3N	toluene	86	>99:1
4	I_2	Et_2NH	toluene	50	>99:1
5	I_2	$^iPr_2NH$	toluene	54	>99:1
6	NIS	Et_3N	toluene	70	>99:1
7	$PhI(OAc)_2$	Et_3N	toluene	trace	–
8[c]	KI	Et_3N	toluene	trace	–
9[d]	I_2	Et_3N	toluene	78	>99:1
10[e]	I_2	Et_3N	toluene	35	>99:1
11[f]	I_2	Et_3N	toluene	80	>99:1
12[g]	I_2	Et_3N	toluene	78	>99:1
13[h]	I_2	Et_3N	toluene	50	>99:1
14[i]	I_2	Et_3N	toluene	84	>99:1
15	I_2	Et_3N	DMSO	43	>99:1
16	I_2	Et_3N	DMF	40	>99:1
17	I_2	Et_3N	PhCl	36	>99:1
18	I_2	Et_3N	PhOMe	45	>99:1
19	I_2	Et_3N	CH_3CN	65	>99:1
20[j]	I_2	Et_3N	toluene	76	>99:1

[a]Unless otherwise noted, the reaction was performed in a sealed tube with oxime ester (0.2 mmol, 1.0 equiv), aldehyde (0.3 mmol, 1.5 equiv), additive **x** (0.1 mmol, 50 mol %), additive **y** (0.1 mmol, 50 mol %) in toluene (1.0 mL) at 120 °C for 3 h. [b]Determined by GC analysis with dodecane as an internal standard. [c]Under an O_2 atmosphere. [d]Using 40 mol % of I_2. [e]Using 20 mol % of I_2. [f]Under oxygen. [g]Under argon. [h]At 110 °C. [i]At 130 °C. [j]Gram-scale reaction was conducted (oxime 10 mmol, 1 equiv).

generated and the yield was enhanced to 86% (Table 1, entry 3). Secondary aliphatic amines such as Et_2NH and $^iPr_2NH$ led to reduced yields of the desired product (Table 1, entries 4 and 5), which indicates a distinct reaction pathway from the previously reported copper-catalyzed system.[6b] Other iodine reagents did not improve the yield. While NIS, being also able to serve as a radical initiator, gave a slightly decreased yield (Table 1, entry 6), $PhI(OAc)_2$ and KI quenched the desired transformation completely (Table 1, entries 7 and 8). For the loading of I_2, the employment of 0.4 equiv and 0.2 equiv of I_2 afforded **3a** in 78% and 35% yield, respectively (Table 1, entries 9 and 10). Then we found that the reaction received slight collapse in the yield when treated under oxygen or argon atmosphere (Table 1, entries 11 and 12). Then the reaction temperature was tested, which revealed that the reaction performed at 120 °C gave the highest yield of the pyridine product, and a dramatic decrease in yield was observed when the reaction temperature was reduced to 110 °C (Table 1, entries 13 and 14). The screening of a series of solvents indicated that polar solvents such as DMSO and DMF disfavored the desired transformation (entries 15–19) and that toluene was the best reaction media. Finally, gram-scale reaction using 10 mmol of **1a** was then conducted, which gave a good yield of **3a** (entry 20).

With the optimized conditions established, the scope and generality of the cyclization were probed. Various substituted acetophenone oxime acetates were first tested in the I_2/Et_3N-mediated system (Scheme 2). Generally, aromatic methyloximes employed reacted smoothly to give the corresponding

Scheme 2. Scope of Oximes for the Metal-Free Cyclization[a]



[a]Reaction conditions: Oxime derivatives (0.5 mmol), enal derivatives (0.75 mmol), I_2 (0.25 mmol), and Et_3N (0.25 mmol) in 2.5 mL of toluene at 120 °C for 3 h. Products **3a–w** formed from the oximes derived from methyl ketones, i.e., R′ = H.

pyridines in good to excellent yields (Scheme 2, **3a–t**, 63–92%), regardless of the functional groups at the para-, meta-, or ortho-position. A large range of functional groups on the benzene ring such as alkyl (**3b–d**), phenyl (**3e**), methoxyl (**3f**), fluoro (**3g**), chloro (**3h**, **3m**, **3q**, and **3s**), bromo (**3i** and **3n**), iodo (**3j**), nitro (**3l**, **3o**, and **3r**), and trifluoromethyl (**3p**) were all tolerated well. The electronic effects of the substituents on the yield are elusive with the fact that methoxyl and nitro groups showed the same efficiency (**3f** and **3l**). However, the steric effects of the substituents are apparent (*p*-Cl 87% vs *o*-Cl 66% and *p*-NO_2 84% vs *o*-NO_2 67%), and the oximes with an iodo group afforded relatively low yield (**3j**). Naphthyl oxime furnished the corresponding product **3t** in moderate yield. Heteroaromatic oximes produced furyl, thienyl, and pyridyl products (**3u–w**) with a big gap in the yield, and only the thienyl substrate among them gave an excellent yield of the corresponding pyridine. While non-methyl oximes could also transfer into the desired products in good yields (**3x–z**), very low yield of the products could be observed when using aliphatic methyl oximes derived from, for example, cyclohexanone and cyclopropylmethylketone in the present system.

Subsequently, a range of substituted α,β-unsaturated aldehydes were evaluated (Scheme 3). All the cinnamaldehydes screened performed very well when the substitution group was located at the benzene ring (Scheme 3, **4a–d**). Analogously,

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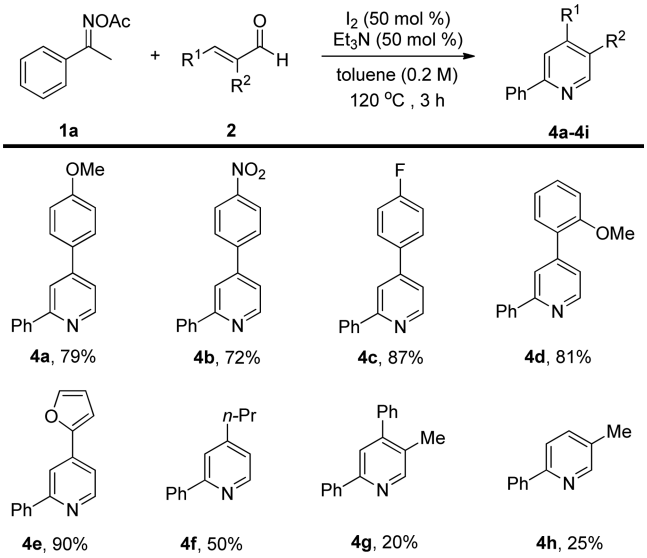
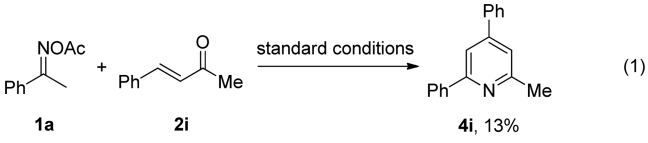
Scheme 3. Scope of Acroleins for the Metal-Free Cyclization[a]



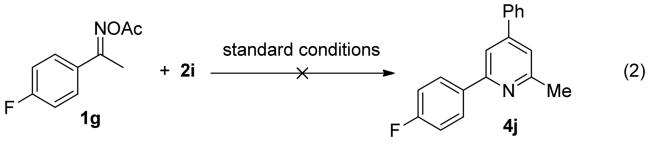
[a]Reaction conditions: oxime derivatives (0.5 mmol), enal derivatives (0.75 mmol), I_2 (0.25 mmol), Et_3N (0.25 mmol) in 2.5 mL toluene at 120 °C for 3 h.

there seems to be no steric effect among those substituents (**4a** vs **4d**), which, in connection of the previous observation, indicates that the reaction probably proceeds via a radical procedure. Notably, when we tested the 3-furylacrolein, the corresponding adduct **4e** was obtained in 90% yield. Then we found that (*E*)-2-hexenal was also accommodated by the system, which furnished the pyridine **4f** in moderate yield. Unfortunately, when the *α*-hydrogen of the carbonyl was substituted by even a methyl, the reactions were dramatically blocked, giving highly reduced yields of the products (**4g**,**h**).

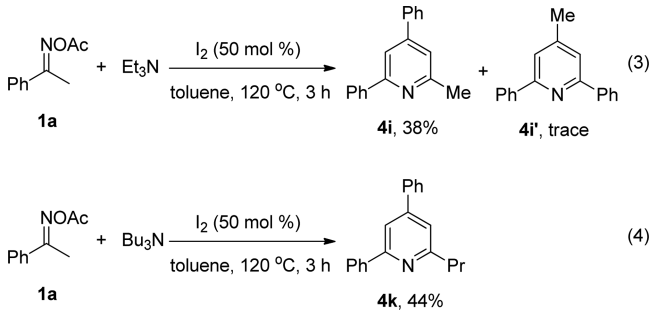
Interestingly, we obtained the desired product 2-methyl-4,6-diphenylpyridine **4i** when enone **2i** was used as the substrate, albeit in a very low yield [eq 1]. However, a **4i** analogue, i.e.,



2,4-bis(4-fluorophenyl)-6-methylpyridine, was also detected with the treatment of substituted acetophenone oximes while the desired corresponding **4j** was not observed [eq 2], which



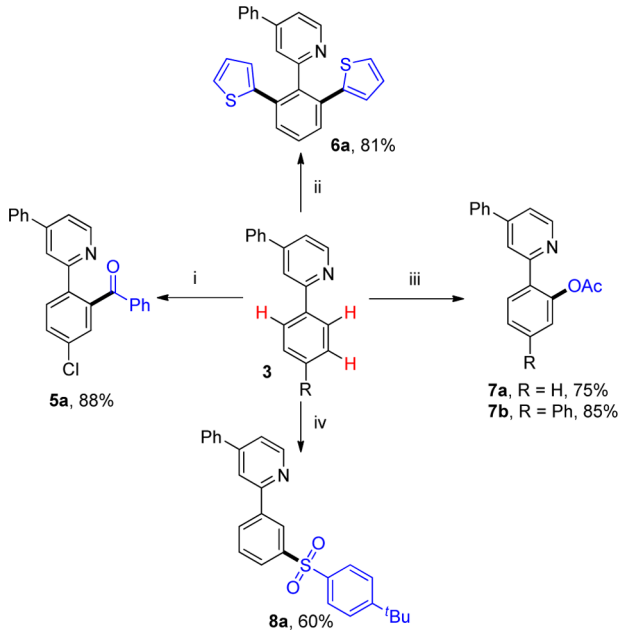
indicated that the enone **2i** was not involved in the cyclization. Indeed, **4i** was isolated in 38% yield in the absence of enals or enones in the present system, in which the two-carbon moiety of the Et_3N was assembled into the pyridine **4i** [eq 3]. To further demonstrate this reasoning, Bu_3N was used as the substrate, which, as expected, gave 2-Pr-substituted pyridine **4k** in 44% GC yield [eq 4]. This observation is really interesting while, in previous work, oximes such as **1a** reacted with



aldehydes likewise via reductive condensation, affording exclusively pyridines of symmetry such as **4i**′.[6a,d]

The resultant 2-arylpyridines were often used in the directed C−H activation, and a large range of functional groups can be embedded in the aryl ortho-position and meta-position.[10] Our further manipulations for the resultant pyridines started with the palladium-catalyzed acylation of **3h** (Scheme 4, i), and the

Scheme 4. Derivation of the Resultant 2-Arylpyridines[a]



[a]Reaction conditions: (i) **3** (0.2 mmol), benzil (1.5 equiv), $Pd(OAc)_2$ (3 mol %), TBHP (3 equiv), THF (0.8 mL), 100 °C, 12 h; (ii) **3a** (0.2 mmol), 2-bromothiophene (2.5 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (2.5 mol %), KOAc (3 equiv), NMP (0.6 mL), 120 °C, 24 h; (iii) **3** (0.2 mmol), $Pd(OAc)_2$ (6 mol %), $PhI(OAc)_2$ (2.5 equiv), CH_3CN (1.25 mL), 100 °C, 12 h; (iv) **3a** (0.2 mmol), sulfonyl chloride (3 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %), K_2CO_3 (2 equiv), CH_3CN (0.6 mL), 115 °C, 15 h.

acylation product **5a** was delivered in 88% yield. The arylation of **3a** was demonstrated by Ru-catalyzed ortho-dithienylation using 2-bromothiophene, which gave the corresponding product **6a** in 81% yield (Scheme 4, ii). Moreover, Pd-catalyzed ortho-acetoxylation of **3a** and **3e** furnished the expected pyridines **7a** and **7b**, respectively, in good yields (Scheme 4, iii). Finally, meta-functionalion of the pyridine **3a** was exemplified by Ru-catalyzed sulfurylation using 4-(*tert*-butyl)benzene-1-sulfonyl chloride, which afforded the desired product **8a** in moderate yield (Scheme 4, iv).

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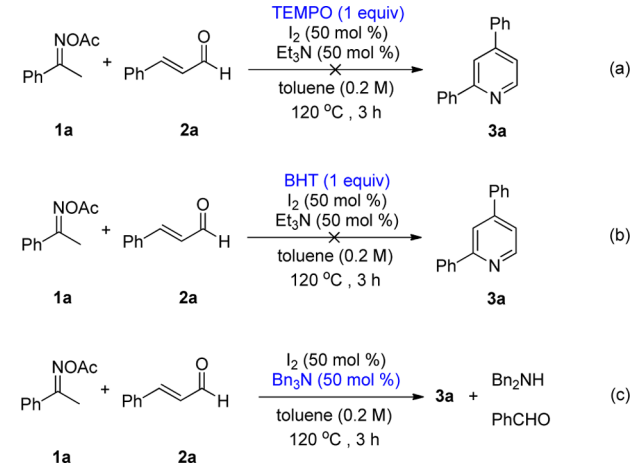
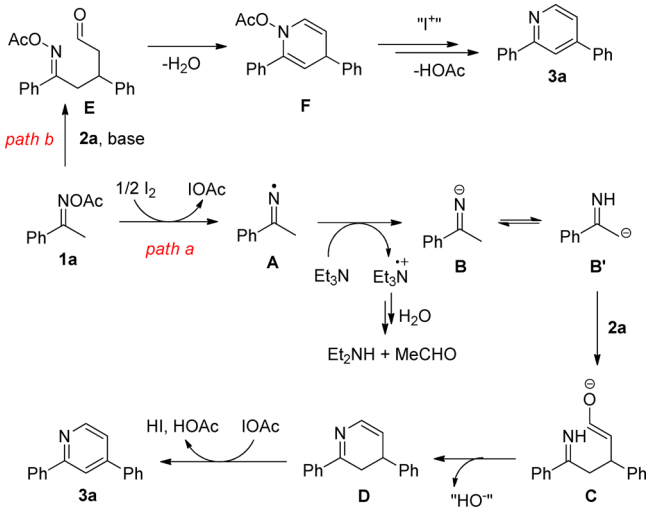
To get information about the reaction mechanism, some control experiments were conducted. The addition of a radical scavenger, such as TEMPO and BHT, to the reaction system prevented the desired transformation completely (Scheme 5a,b). Furthermore, when we used Bn_3N instead of Et_3N in the reaction system, Bn_2NH and benzaldehyde were detected as the main byproducts derived from the base (Scheme 5c).

Scheme 5. Mechanistic Study



Based on the experimental observation, a plausible reaction mechanism is proposed for the metal-free heterocyclization of oximes and enals (Scheme 6). In path a as shown, I_2-mediated

Scheme 6. Plausible Reaction Mechanism for the Metal-Free Pyridine Formation



reduction of oxime **1a** gives a $[I^+]$ species and imino-radical **A**, which traps an electron to form the corresponding anion **B**. Then Michael-type addition of the carbon-centered anion **B′**, generated by 1,3-H-shift of **B**, would take place to the unsaturated aldehydes to generate intermediate **C**, which eliminates hydroxyl anion to furnish the dihydropyridine **D**. Finally, the desired pyridine **3a** is afforded through aromatization of **D** with the $[I^+]$ species as the main oxidant. Additionally, one molecule of Et_3N as the base could provide two electrons and decays into $Et_2N^+{=}CHCH_3$, which would be further hydrolyzed into secondary amine and aldehyde. It is therefore reasonable to utilize 0.5 equiv of Et_3N as the electron donor.[9] For the fact that NIS could promote the reaction and afford the pyridine product in good yield (Table 1, entry 6), alternatively a condensation-based reaction pathway (path b) was set out. 1,4-Dihydropyridine **F** may be the key intermediate, which, on the assistance from iodine reagent, eliminates a molecule of AcOH to afford the final pyridine.

CONCLUSION

In summary, we have developed a metal-free protocol for the synthesis of polysubstituted pyridines from the *O*-acetyl ketoximes and *α,β*-unsaturated aldehydes. The present strategy features high chemoselectivity and excellent tolerance for a broad range of functional groups. Moreover, the combinational use of iodine and triethylamine has been demonstrated to be robust to activate the N−O bond of oximes and enable the assembly of pyridines, which also opens a new entry to oxime-based N-heterocycle synthesis based on metal-free systems. Further studies on the detailed mechanism and application in the preparation of complex N-containing compounds are currently in progress.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under standard conditions unless otherwise noted. Column chromatography was performed using silica gel (200−300 mesh). ^1H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer, and the chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Generally, chloroform was used as the solvent with TMS as the internal standard. GC−MS data were obtained using electron ionization. HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed using commercially available 100−400 mesh silica gel plates (GF254). The structure of known compounds was further corroborated by comparing their ^1H NMR, ^{13}C NMR, and MS data with those in the literature. Melting points were measured with a melting point instrument without correction. Oximes were prepared using a previous method.[6b] All other reagents were obtained from commercial suppliers and used without further purification.

General Procedure for the Synthesis of Pyridines. To a mixture of acetophenone *O*-acetyl oxime derivative (0.5 mmol) and enal derivative (0.75 mmol) were added successively I_2 (0.25 mmol), Et_3N (0.25 mmol), and 2.5 mL of toluene. The reaction mixture was stirred at 120 °C for 3 h and then cooled to room temperature. Subsequently, the reaction mixture was diluted with ethyl acetate and concentrated under reduced pressure, and the residue was separated by column chromatography (petroleum ether/EtOAc 20:1 to 30:1) to give the pure product.

*2,4-Diphenylpyridine (**3a**, CAS: 26274-35-1).*[6b] Yellow oil (92.4 mg, 80% yield); ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 4.8 Hz, 1H), 8.06 (d, J = 6.8 Hz, 2H), 7.94 (s, 1H), 7.70 (d, J = 6.8 Hz, 2H), 7.54−7.40 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.1, 150.1, 149.3, 139.5, 138.5, 129.1, 129.00, 128.99, 128.7, 127.1, 127.0, 120.2, 118.7; MS (EI) m/z (%) 231 (100), 202, 154, 102, 77.

*4-Phenyl-2-(p-tolyl)pyridine (**3b**).*[11] Yellow oil (99.2 mg, 81% yield); ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.72 (d, J = 4.8 Hz, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.91 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.51−7.42 (m, 4H), 7.31 (d, J = 7.6 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.1, 150.0, 149.3, 139.0, 138.7, 136.7, 129.5, 129.1, 129.0, 127.1, 126.9, 120.0, 118.5, 21.3; HRMS calcd for: $C_{18}H_{16}N$ $[M + H]^+$ 246.1277, found 246.1276.

*2-(4-(tert-Butyl)phenyl)-4-phenylpyridine (**3c**, CAS: 1188087-46-8).*[12] Yellow oil (123.4 mg, 86% yield); ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.73 (d, J = 4.8 Hz, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.92 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.54−7.43 (m, 6H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.9, 152.1, 149.9, 149.0, 138.5,

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136.6, 129.0, 128.8, 126.9, 126.6, 125.6, 119.8, 118. 3, 34.6, 31.2; MS (EI) *m*/*z* (%) 211 (100), 196, 181, 154, 57.

2-(4-Isobutylphenyl)-4-phenylpyridine (**3d**). Yellow oil (124.8 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.71 (d, J = 4.8 Hz, 1H), 7.96 (d, J = 7.2 Hz, 2H), 7.91 (s, 1H), 7.68 (d, J = 7.2 Hz, 2H), 7.52−7.41 (m, 4H), 7.27 (d, J = 7.6 Hz, 2H), 2.54 (d, J = 6.8 Hz, 2H), 1.97−1.85 (m, 1H), 0.93 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.1, 150.0, 149.2, 142.8, 138.6, 136.9, 129.5, 129.0, 128.9, 127.0, 126.7, 119.9, 118.4, 45.2, 30.2, 22.3; HRMS calcd for: $C_{21}H_{22}N$ $[M + H]^+$ 288.1743, found 288.1747.

2-([1,1′-Biphenyl]-4-yl)-4-phenylpyridine (**3e**). White solid (139.7 mg, 91% yield); mp = 101−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.76 (d, J = 5.2 Hz, 1H), 8.15 (d, J = 8.4 Hz, 2H), 7.99 (s, 1H), 7.76−7.67 (m, 6H), 7.55−7.34 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.6, 150.1, 149.4, 141.8, 140.6, 138.5, 138.3, 129.13, 129.06, 128.8, 127.5, 127.4, 127.1, 126.4, 120.3, 118.7, 110.0; HRMS calcd for: $C_{23}H_{18}N$ $[M + H]^+$ 308.1434, found 308.1431.

2-(4-Methoxyphenyl)-4-phenylpyridine (**3f**, *CAS: 1426022094*).[6b] Yellow solid (108.3 mg, 83% yield); mp = 65−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.70 (d, J = 4.8 Hz, 1H), 8.02 (d, J = 8.4 Hz, 2H), 7.88 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.53−7.40 (m, 4H), 7.02 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.5, 157.7, 149.9, 149.2, 138.7, 132.1, 129.1, 128.9, 128.3, 127.0, 119.6, 118.0, 114.1, 55.3; MS (EI) *m*/*z* (%) 261 (100), 246, 218, 96, 77.

2-(4-Fluorophenyl)-4-phenylpyridine (**3g**, *CAS: 1188022-73-2*). Yellow oil (93.4 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.72 (d, J = 4.8 Hz, 1H), 8.05 (q, J = 4.5 Hz, 2H), 7.88 (s, 1H), 7.69 (d, J = 6.8 Hz, 2H), 7.54−7.42 (m, 4H), 7.18 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.5 (d, J = 246.9 Hz), 156.9, 150.0, 149.3, 138.3, 135.5 (d, J = 3.1 Hz), 129.1, 129.0, 128.8 (d, J = 8.3 Hz), 127.0, 120.1, 118.3, 115.6 (d, J = 21.5 Hz); HRMS calcd for: $C_{17}H_{13}FN$ $[M + H]^+$ 250.1027, found 250.1029.

2-(4-Chlorophenyl)-4-phenylpyridine (**3h**).[11] Yellow oil (115.3 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.73 (d, J = 5.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.90 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.54−7.46 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.8, 150.1, 149.5, 138.3, 137.9, 135.2, 129.1, 128.9, 128.3, 127.1, 120.5, 118.5; HRMS calcd for: $C_{17}H_{13}NCl$ $[M + H]^+$ 266.0731, found 266.0730.

2-(4-Bromophenyl)-4-phenylpyridine (**3i**, *CAS: 504413-43-8*).[6b] Yellow solid (122.1 mg, 79% yield); mp = 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 4.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 7.91 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.54−7.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.8, 150.1, 149.6, 138.33, 138.27, 131.9, 129.18, 129.16, 128.6, 127.1, 123.6, 120.6, 118.5; MS (EI) *m*/*z* (%) 309 (100), 229, 205, 154, 77.

2-(4-Iodophenyl)-4-phenylpyridine (**3j**, *CAS: 1426022-12-9*).[6b] Yellow solid (121.4 mg, 68% yield); mp = 94−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.73 (d, J = 4.8 Hz, 1H), 7.90 (s, 1H), 7.86−7.70 (m, 4H), 7.69 (d, J = 7.2 Hz, 2H), 7.54−7.49 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.0, 150.2, 149.5, 138.9, 138.3, 137.9, 129.1, 128.7, 127.1, 120.6, 118.4, 95.4; MS (EI) *m*/*z* (%) 357 (100), 230, 152, 115, 77.

2-(4-(Methylsulfonyl)phenyl)-4-phenylpyridine (**3k**). Light yellow solid (122.1 mg, 79% yield); mp = 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.79 (d, J = 4.8 Hz, 1H), 8.27 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.99 (s, 1H), 7.70 (d, J = 6.8 Hz, 2H), 7.56−7.47 (m, 4H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.8, 150.4, 149.8, 144.6, 140.6, 138.0, 129.3, 129.2, 127.9, 127.8, 127.0, 121.4, 119.3, 44.5; HRMS calcd for: $C_{18}H_{16}NO_2S$ $[M + H]^+$ 310.0896, found 310.0895.

2-(4-Nitrophenyl)-4-phenylpyridine (**3l**). Yellow solid (115.9 mg, 84% yield); mp = 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.80 (d, J = 4.8 Hz, 1H), 8.36 (d, J = 8.8 Hz, 2H), 8.25 (d, J = 8.8 Hz, 2H), 8.01 (s, 1H), 7.71 (d, J = 6.8 Hz, 2H), 7.58−7.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.5, 150.5, 149.8, 148.2, 145.4, 138.0, 129.4, 129.3, 127.8, 127.1, 124.0, 121.6, 119.4; HRMS calcd for: $C_{17}H_{13}O_2N_2$ $[M + H]^+$ 277.0972, found 277.0970.

2-(3-Methoxyphenyl)-4-phenylpyridine (**3m**). Yellow oil (109.6 mg, 84% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 4.8 Hz, 1H), 7.93 (s, 1H), 7.72−7.57 (m, 4H), 7.55−7.35 (m, 5H), 6.99 (d, J = 7.6 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.0, 157.7, 149.9, 149.1, 140.8, 138.3, 129.6, 129.0, 128.9, 126.9, 120.2, 119.3, 118.7, 115.0, 112.2, 55.2; HRMS calcd for: $C_{18}H_{16}ON$ $[M + H]^+$ 262.1224, found 262.1226.

2-(3-Bromophenyl)-4-phenylpyridine (**3n**). Yellow solid (123.6 mg, 80% yield); mp = 57−59 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 5.2 Hz, 1H), 8.22 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.60−7.43 (m, 5H), 7.37 (t, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.5, 150.2, 149.5, 141.5, 138.2, 131.9, 130.2, 130.1, 129.1, 128.5, 127.1, 125.5, 123.0, 120.8, 118.8; HRMS calcd for: $C_{17}H_{13}BrN$ $[M + H]^+$ 310.0220, found 310.0226.

2-(3-Nitrophenyl)-4-phenylpyridine (**3o**, *CAS: 1426022-18-5*).[6b] White solid (117.3 mg, 85% yield); mp = 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.92 (s, 1H), 8.78 (d, J = 4.8 Hz, 1H), 8.45 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.00 (s, 1H), 7.70 (q, J = 8.4 Hz, 3H), 7.56−7.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.4, 150.4, 149.9, 148.8, 141.1, 138.0, 132.8, 129.7, 129.4, 129.2, 127.1, 123.6, 121.9, 121.4, 118.8; MS (EI) *m*/*z* (%) 276 (100), 246, 202, 115, 77.

4-Phenyl-2-(3-(trifluoromethyl)phenyl)pyridine (**3p**). Yellow oil (122.6 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (d, J = 4.8 Hz, 1H), 8.34 (s, 1H), 8.25 (d, J = 7.2 Hz, 1H), 7.95 (s, 1H), 7.71 (d, J = 6.8 Hz, 3H), 7.62 (t, J = 7.5 Hz, 1H), 7.56−7.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.3, 150.2, 149.6, 140.1, 138.1, 131.1 (q, J = 32 Hz), 130.1, 129.17, 129.15, 129.1, 127.0, 125.5 (q, J = 3.8 Hz), 124.2 (q, J = 270.7 Hz), 123.8 (q, J = 3.9 Hz), 120.8, 118.6; HRMS calcd for: $C_{18}H_{13}F_3N$ $[M + H]^+$ 300.0990, found 300.0995.

2-(2-Chlorophenyl)-4-phenylpyridine (**3q**). Yellow solid (87.5 mg, 66% yield); mp = 60−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 5.2 Hz, 1H), 7.88 (s, 1H), 7.72−7.62 (m, 3H), 7.56−7.42 (m, 5H), 7.41−7.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 149.9, 148.4, 139.2, 138.1, 132.2, 131.5, 130.1, 129.6, 129.12, 129.10, 127.1, 127.0, 122.9, 120.4; HRMS calcd for: $C_{17}H_{13}ClN$ $[M + H]^+$ 266.0729, found 266.0731.

2-(2-Nitrophenyl)-4-phenylpyridine (**3r**). Yellow solid (113.2 mg, 82% yield); mp = 98−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.70 (d, J = 4.8 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 5.2 Hz, 5H), 7.59−7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.0, 150.0, 149.42, 149.36, 137.8, 135.4, 132.4, 131.3, 129.3, 129.23, 129.16, 127.1, 124.4, 120.9, 120.7; HRMS calcd for: $C_{17}H_{13}O_2N_2$ $[M + H]^+$ 277.0967, found 277.0972.

2-(3,4-Dichlorophenyl)-4-phenylpyridine (**3s**, *CAS: 1426022-20-9*).[6b] White solid (137.5 mg, 92% yield); mp = 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 4.8 Hz, 1H), 8.19 (s, 1H), 7.91 (d, J = 10.0 Hz, 2H), 7.69 (d, J = 7.2 Hz, 2H), 7.58−7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.5, 150.2, 149.7, 139.3, 138.1, 133.2, 133.1, 130.7, 129.3, 129.2, 128.9, 127.1, 126.1, 121.0, 118.5; MS (EI) *m*/*z* (%) 299 (100), 264, 228, 154, 77.

2-(Naphthalen-1-yl)-4-phenylpyridine (**3t**). Yellow solid (88.52 mg, 63% yield); mp = 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.85 (d, J = 5.2 Hz, 1H), 8.14 (d, J = 7.6 Hz, 1H), 7.94 (d, J = 8.0 Hz, 2H), 7.83 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 6.8 Hz, 1H), 7.58 (t, J = 7.5 Hz, 2H), 7.53−7.44 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 159.7, 149.9, 148.9, 138.5, 138.2, 133.9, 131.2, 129.14, 129.12, 128.9, 128.4, 127.5, 127.1, 126.5, 125.9, 125.6, 125.3, 123.0, 120.0; HRMS calcd for: $C_{21}H_{16}N$ $[M + H]^+$ 282.1274, found 282.1277.

2-(Furan-2-yl)-4-phenylpyridine (**3u**).[6b] Yellow oil (33.2 mg, 30% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.64 (d, J = 5.2 Hz, 1H), 7.93 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.56−7.48 (m, 4H), 7.39 (d, J = 4.0 Hz, 1H), 7.14 (d, J = 2.8 Hz, 1H), 6.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 153.5, 149.9, 149.7, 149.3, 143.4, 138.2, 129.2, 129.1, 127.0, 120.0, 116.6, 112.1, 109.0; MS (EI) *m*/*z* (%) 221 (100), 192, 165, 154, 125.

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J. Org. Chem. 2016, 81, 1499−1505

*4-Phenyl-2-(thiophen-2-yl)pyridine (**3v**).*[13] Yellow oil (103.1 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.61 (d, J = 5.2 Hz, 1H), 7.86 (s, 1H), 7.67 (d, J = 4.8 Hz, 3H), 7.52−7.40 (m, 4H), 7.36 (d, J = 5.2 Hz, 1H), 7.14 (t, J = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 152.9, 149.8, 149.1, 144.7, 138.1, 128.98, 128.96, 127.9, 127.5, 126.9, 124.6, 119.9, 116.7; MS (EI) m/z (%) 237 (100), 204, 165, 127, 77.

*4-Phenyl-2,3′-bipyridine (**3w**).* Yellow oil (48.7 mg, 42% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 9.26 (s, 1H), 8.77 (d, J = 5.2 Hz, 1H), 8.67 (s, 1H), 8.39 (d, J = 8.0 Hz, 1H), 7.95 (s, 1H), 7.70 (d, J = 6.8 Hz, 2H), 7.53−7.41 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.4, 150.4, 149.9, 149.6, 148.2, 138.1, 135.0, 134.5, 129.3, 129.2, 127.0, 123.6, 120.9, 118.8; HRMS calcd for: $C_{16}H_{13}N_2$ $[M + H]^+$ 233.1071, found 233.1073.

*3-Methyl-2,4-diphenylpyridine (**3x**, CAS: 875228-76-5).*[6b] Yellow oil (95.6 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.56 (d, J = 4.8 Hz, 1H), 7.56 (d, J = 7.2 Hz, 2H), 7.49−7.37 (m, 8H), 7.15 (d, J = 4.8 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 159.7, 150.8, 146.3, 141.0, 139.8, 129.0, 128.6, 128.4, 128.3, 128.1, 127.8, 123.1, 17.9; MS (EI) m/z (%) 245 (100), 166, 139, 115, 77.

*2,3,4-Triphenylpyridine (**3y**, CAS: 130318-01-3).*[6b] White solid (135.1 mg, 88% yield); mp = 178−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 4.8 Hz, 1H), 7.35 (d, J = 4.8 Hz, 1H), 7.27 (d, J = 6.0 Hz, 3H), 7.21−7.18 (m, 5H), 7.12−7.02 (m, 5H), 6.88 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.4, 149.9, 148.2, 140.7, 139.4, 137.7, 134.4, 131.4, 129.9, 129.3, 127.9, 127.7, 127.6, 127.34, 127.32, 126.6, 123.6; MS (EI) m/z (%) 307 (100), 202, 176, 152, 77.

*4-Phenyl-5,6-dihydrobenzo[h]quinoline (**3z**, CAS: 95545-95-2).*[6b] White solid (98.95 mg, 77% yield); mp = 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.8 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 7.53−7.30 (m, 7H), 7.22 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 4.8 Hz, 1H), 2.93 (t, J = 6.6 Hz, 2H), 2.83 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 148.6, 147.1, 138.9, 138.1, 134.8, 129.5, 129.1, 128.7, 128.4, 128.0, 127.5, 127.2, 125.5, 123.3, 28.1, 25.5; MS (EI) m/z (%) 257 (100), 226, 151, 127, 77.

*4-(4-Methoxyphenyl)-2-phenylpyridine (**4a**, CAS: 1350737-69-7).*[6b] Yellow solid (103.1 mg, 79% yield); mp = 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.70 (d, J = 4.8 Hz, 1H), 8.04 (d, J = 7.2 Hz, 2H), 7.90 (s, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.58−7.35 (m, 4H), 7.04 (d, J = 8.4 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.5, 157.9, 149.9, 148.7, 139.5, 130.6, 128.9, 128.7, 128.2, 127.0, 119.7, 118.2, 114.5, 55.3; MS (EI) m/z (%) 261 (100), 246, 230, 189, 77.

*4-(4-Nitrophenyl)-2-phenylpyridine (**4b**, CAS: 1062144-59-5).*[14] White solid (99.4 mg, 72% yield); mp = 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.82 (d, J = 4.8 Hz, 1H), 8.38 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 7.2 Hz, 2H), 7.94 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.60−7.42 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.5, 150.4, 148.2, 146.9, 144.9, 138.9, 129.4, 128.9, 128.0, 127.0, 124.3, 120.2, 118.7; MS (EI) m/z (%) 276 (100), 230, 202, 101, 77.

*4-(4-Fluorophenyl)-2-phenylpyridine (**4c**).*[11] Yellow oil (108.3 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (d, J = 5.2 Hz, 1H), 8.05 (d, J = 7.2 Hz, 2H), 7.88 (s, 1H), 7.67 (q, J = 4.5 Hz, 2H), 7.54−7.39 (m, 4H), 7.20 (t, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.3 (d, J = 247.6 Hz), 158.0, 150.0, 148.0, 139.2, 134.4 (d, J = 2.8 Hz), 129.0, 128.7 (d, J = 7.9 Hz), 128.6, 126.9, 119.9, 118.3, 116.0 (d, J = 21.5 Hz); MS (EI) m/z (%) 249 (100), 220, 172, 154, 125.

*4-(2-Methoxyphenyl)-2-phenylpyridine (**4d**, CAS: 1426022-44-7).*[6b] Yellow oil (105.7 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.72 (d, J = 4.8 Hz, 1H), 8.03 (d, J = 7.2 Hz, 2H), 7.91 (s, 1H), 7.51−7.35 (m, 6H), 7.12−6.97 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.2, 156.5, 149.2, 147.1, 139.6, 130.4, 130.0, 128.7, 128.6, 127.9, 127.0, 122.8, 121.3, 121.0, 111.4, 55.5; MS (EI) m/z (%) 261 (100), 230, 189, 154, 77.

*4-(Furan-2-yl)-2-phenylpyridine (**4e**).*[6b] Yellow oil (99.5 mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.69 (d, J = 5.2 Hz, 1H), 8.04 (d, J = 7.2 Hz, 2H), 7.98 (s, 1H), 7.58 (s, 1H), 7.52−7.42 (m, 4H), 6.95 (d, J = 3.2 Hz, 1H), 6.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.0, 151.5, 150.0, 143.8, 139.3, 138.3, 129.1, 128.7, 127.0, 116.3, 114.7, 112.1, 108.7; MS (EI) m/z (%) 221 (100), 192, 165, 96, 77.

*2-Phenyl-4-propylpyridine (**4f**, CAS: 53911-34-5).*[15] Yellow oil (49.3 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.59 (d, J = 4.8 Hz, 1H), 7.99 (d, J = 7.6 Hz, 2H), 7.56 (s, 1H), 7.50−7.37(m, 3H), 7.09 (d, J = 4.4 Hz, 1H), 2.67 (t, J = 7.4 Hz, 2H), 1.78−1.66 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.3, 152.5, 149.3, 139.4, 128.8, 128.7, 127.0, 122.5, 121.0, 37.5, 23.5, 13.7; MS (EI) m/z (%) 197 (100), 182, 169, 154, 77.

*5-Methyl-2,4-diphenylpyridine (**4g**, CAS: 83575-92-2).*[16] Yellow oil (24.5 mg, 20% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.03 (d, J = 7.2 Hz, 2H), 7.73 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.54−7.40 (m, 6H), 7.34 (s, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.8, 157.6, 149.7, 138.8, 129.0, 128.9, 128.8, 128.7, 127.2, 127.1, 119.9, 116.2, 110.0, 24.7; MS (EI) m/z (%) 245 (100), 230, 202, 168, 77.

*5-Methyl-2-phenylpyridine (**4h**, CAS: 27012-22-2).*[17] Yellow oil (21.1 mg, 25% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.53 (s, 1H), 7.97 (d, J = 7.2 Hz, 2H), 7.64 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 154.8, 150.0, 139.4, 137.3, 131.6, 128.7, 128.6, 126.7, 120.0, 18.1; MS (EI) m/z (%) 169 (100), 154, 141, 115, 77.

*2-Methyl-4,6-diphenylpyridine (**4i**, CAS: 1912-16-9).*[6b] Yellow oil (46.6 mg, 38% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.04 (d, J = 7.2 Hz, 2H), 7.74 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.53−7.40 (m, 6H), 7.35 (s, 1H), 2.73 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.8, 157.6, 149.7, 139.7, 138.8, 129.0, 128.9, 128.8, 128.7, 127.2, 127.1, 119.9, 116.2, 24.7; MS (EI) m/z (%) 245 (100), 230, 202, 168, 77.

*(5-Chloro-2-(4-phenylpyridin-2-yl)phenyl)(phenyl)methanone (**5a**).* Yellow oil (64.9 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.40 (d, J = 5.2 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.2 Hz, 3H), 7.62−7.53(m, 4H), 7.49−7.38 (m, 4H), 7.29 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 196.4, 156.1, 149.5, 148.9, 141.1, 138.0, 137.9, 137.3, 134.9, 132.7, 130.2, 130.0, 129.4, 129.13, 129.07, 128.9, 128.2, 126.9, 120.7, 120.2; HRMS calcd for: $C_{24}H_{17}ClNO$ $[M + H]^+$ 370.0993, found 370.0993.

*2-(2,6-Di(thiophen-2-yl)phenyl)-4-phenylpyridine (**6a**).* Yellow oil (64 mg, 81% yield);^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.59 (d, J = 5.2 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 7.8 Hz, 1H), 7.44−7.35 (m, 7H), 7.15 (d, J = 4.8 Hz, 2H), 6.83 (t, J = 4.2 Hz, 2H), 6.74 (d, J = 3.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.8, 149.1, 148.2, 142.6, 138.4, 138.1, 134.8, 130.1, 128.97, 128.96, 128.4, 127.3, 127.0, 126.8, 125.9, 124.4, 120.2; HRMS calcd for: $C_{25}H_{18}NS_2$ $[M + H]^+$396.0875, found 396.0870.

*2-(4-Phenylpyridin-2-yl)phenyl acetate (**7a**).* Yellow oil (43.4 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.61 (d, J = 5.2 Hz, 1H), 8.23 (s, 1H), 7.66 (d, J = 7.2 Hz, 2H), 7.54−7.46 (m, 4H), 7.28 (t, J = 8.2 Hz, 2H), 6.97 (d, J = 8.4 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 168.7, 160.1, 155.2, 150.1, 149.0, 146.7, 137.9, 130.6, 129.5, 129.3, 126.9, 122.3, 120.2, 116.1, 114.4, 113.8, 21.3; HRMS calcd for: $C_{19}H_{16}NO_2$ $[M + H]^+$ 290.1176, found 290.1175.

*4-(4-Phenylpyridin-2-yl)-[1,1′-biphenyl]-3-yl Acetate (**7b**).* Yellow oil (62.1 mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.62 (d, J = 5.2 Hz, 1H), 8.29 (s, 1H), 7.69−7.64 (m, 5H), 7.56−7.49 (m, 4H), 7.45 (t, J = 7.4 Hz, 2H), 7.37 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 3.6 Hz, 1H), 6.92 (d, J = 3.6 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 168.8, 160.5, 155.2, 150.1, 149.4, 146.7, 143.6, 139.4, 138.0, 129.5, 129.3, 128.8, 128.1, 127.0, 126.9, 122.0, 120.1, 114.4, 112.7, 110.0, 21.4; HRMS calcd for: $C_{25}H_{18}NO_2$ $[M - H]^+$ 364.1343, found 364.1342.

*2-(3-((4-(tert-Butyl)phenyl)sulfonyl)phenyl)-4-phenylpyridine (**8a**).* Yellow oil (51.2 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (d, J = 5.2 Hz, 1H), 8.60 (s, 1H), 8.32 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.8 Hz, 1H), 7.56−7.47 (m, 6H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 157.1, 155.9,

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J. Org. Chem. 2016, 81, 1499−1505

150.2, 149.9, 142.6, 140.7, 138.5, 138.0, 131.6, 129.8, 129.33, 129.27, 128.0, 127.6, 127.1, 126.3, 126.0, 121.1, 118.9, 35.2, 31.0; HRMS calcd for: $C_{27}H_{26}NO_2S$ $[M + H]^+$ 428.1679, found 428.1680.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02624.

Copies of proton and carbon NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451. (b) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337. (c) Su, S.-J.; Chiba, T.; Takeda, T.; Kido, J. *Adv. Mater.* **2008**, *20*, 2125. (d) Sasabe, H.; Kido, J. *Chem. Mater.* **2011**, *23*, 621. (e) Wang, Y.; Daniher, A.; De Klerk, A.; Winkel, C. Pyridine Derivatives with Umami Flavour. US 20120121783, May 17, 2012.

(2) For reviews of pyridine synthesis, see: (a) Bull, J. A.; Mousseau, J. J.; Pelletier, G.; Charette, A. B. *Chem. Rev.* **2012**, *112*, 2642. (b) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084. (c) Allais, C.; Grassot, J.-M.; Rodriguez, J.; Constantieux, T. *Chem. Rev.* **2014**, *114*, 10829.

(3) (a) Tabolin, A. A.; Ioffe, S. L. *Chem. Rev.* **2014**, *114*, 5426. (b) Sukhorukov, A. Y.; Ioffe, S. L. *Chem. Rev.* **2011**, *111*, 5004.

(4) (a) Kitamura, M.; Narasaka, K. *Chem. Rec.* **2002**, *2*, 268. (b) Narasaka, K.; Kitamura, M. *Eur. J. Org. Chem.* **2005**, *2005*, 4505. (c) Huang, H.; Ji, X.; Wu, W.; Jiang, H. *Chem. Soc. Rev.* **2015**, *44*, 1155.

(5) (a) Walton, J. C. *Acc. Chem. Res.* **2014**, *47*, 1406. (b) McBurney, R. T.; Walton, J. C. *J. Am. Chem. Soc.* **2013**, *135*, 7349. (c) Markey, S. J.; Lewis, W.; Moody, C. J. *Org. Lett.* **2013**, *15*, 6306. (d) McBurney, R. T.; Slawin, A. M. Z.; Smart, L. A.; Yu, Y.; Walton, J. C. *Chem. Commun.* **2011**, *47*, 7974. (e) Zard, S. Z. *Chem. Soc. Rev.* **2008**, *37*, 1603. and the references cited therein. (f) Jiang, H.; An, X.; Tong, K.; Zheng, T.; Zhang, Y.; Yu, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 4055.

(6) (a) Ren, Z.-H.; Zhang, Z.-Y.; Yang, B.-Q.; Wang, Y.-Y.; Guan, Z.-H. *Org. Lett.* **2011**, *13*, 5394. (b) Wei, Y.; Yoshikai, N. *J. Am. Chem. Soc.* **2013**, *135*, 3756. (c) Wu, Q.; Zhang, Y.; Cui, S. *Org. Lett.* **2014**, *16*, 1350. (d) Zhao, M.-N.; Hui, R.-R.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *Org. Lett.* **2014**, *16*, 3082. (e) Huang, H.; Ji, X.; Tang, X.; Zhang, M.; Li, X.; Jiang, H. *Org. Lett.* **2013**, *15*, 6254. (f) Jiang, H.; Yang, J.; Tang, X.; Li, J.; Wu, W. *J. Org. Chem.* **2015**, *80*, 8763. (g) Tang, X.; Gao, H.; Yang, J.; Wu, W.; Jiang, H. *Org. Chem. Front.* **2014**, *1*, 1295. (h) Huang, H.; Cai, J.; Ji, X.; Xiao, F.; Chen, Y.; Deng, G.-J. *Angew. Chem., Int. Ed.* **2016**, *55*, 307.

(7) (a) Graham-Rowe, D. *New Sci.* **2012**, *213*, 18. (b) Li, C.-J.; Trost, B. M. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 13197. (c) Dunn, P. J. *Chem. Soc. Rev.* **2012**, *41*, 1452. (d) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219.

(8) (a) Liu, D.; Lei, A. *Chem. - Asian J.* **2015**, *10*, 806. (b) Girard, S.; Huang, H.; Zhou, F.; Deng, G.-J.; Li, C.-J. *Org. Chem. Front.* **2015**, *2*, 279.

(9) Tang, S.; Liu, K.; Liu, C.; Lei, A. *Chem. Soc. Rev.* **2015**, *44*, 1070.

(10) (a) Zhou, W.; Li, H.-J.; Wang, L. *Org. Lett.* **2012**, *14*, 4594. (b) Pozgan, F.; Dixneuf, P. H. *Adv. Synth. Catal.* **2009**, *351*, 1737. (c) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (d) Saidi, O.; Marafie, J.; Ledger, A.; Liu, P.; Mahon, M.; Kociok-Köhn, G.; Whittlesey, M.; Frost, C. *J. Am. Chem. Soc.* **2011**, *133*, 19298.

(11) Wang, S.-W.; Guo, W.-S.; Wen, L.-R.; Li, M. *RSC Adv.* **2014**, *4*, 59218.

(12) Li, C.-X.; Wang, S.-Q.; Huang, Y.-M.; Zheng, B.-Z.; Tian, Q.; Wen, Y.-H.; Li, F. *Dalton Trans.* **2013**, *42*, 4059.

(13) Andersson, H.; Almqvist, F.; Olsson, R. *Org. Lett.* **2007**, *9*, 1335.

(14) Zu, L.-S.; Xie, H.-X.; Li, H.; Wang, J.; Yu, X.-H.; Wang, W. *Chem. - Eur. J.* **2008**, *14*, 6333.

(15) Parish, R. V.; Wright, J. P.; Pritchard, R. G. *J. Organomet. Chem.* **2000**, *596*, 165.

(16) Corriu, R. J. P.; Moreau, J. J. E.; Pataud-Sat, M. *J. Org. Chem.* **1990**, *55*, 2878.

(17) Schinkel, M.; Wallbaum, J.; Kozhushkov, S. I.; Marek, I.; Ackermann, L. *Org. Lett.* **2013**, *15*, 4482.

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