JOC The Journal of Organic Chemistry

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Cu(I)-Catalyzed Synthesis of Imidazo[1,2-*a*]pyridines from Aminopyridines and Nitroolefins Using Air as the Oxidant

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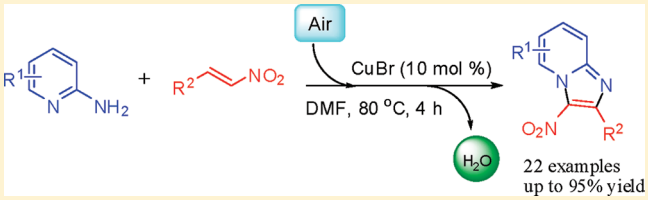
Supporting Information

ABSTRACT: A copper-catalyzed method for the synthesis of imidazo[1,2-*a*]pyridines with aminopyridines and nitroolefins using air as oxidation agent in a one-pot procedure has been developed. In this process, the reaction appears to be very general and suitable for construction of a variety of imidazo[1,2-*a*]pyridines.



The imidazo[1,2-*a*]pyridine core is one of the most important heterocycles since it has not only found widespread applications in medicinal chemistry and drug synthesis[1] but because it is also broadly used in material science.[2] Consequently, it has attracted considerable interest for synthetic chemists and stimulated the development of numerous methods for their preparation.[3] Recently, several new approaches based on dehydrogenation through C−H activation catalyzed by transition metals[4] and tetrabutylammonium iodide (TBAI)-catalyzed oxidative coupling[5] have been developed for the construction of imidazo[1,2-*a*]pyridines. However, there are very few general methods that convert commercially available or readily accessible materials in one step to polysubstituted imidazo[1,2-*a*]pyridines. Thus, there is still a need for direct and efficient methods to afford functionalized imidazo[1,2-*a*]pyridines.

In accordance with the ideology of green chemistry,[6] air is the ideal oxidant because of its abundance, low cost, and lack of toxic byproduct.[7] With the development of C−H activation, air has attracted much attention because it is safe and cheap in industrial applications.[8] Therefore, using air as the oxidant to construct heterocycles with simple and readily accessible substrates is a challenging area. As part of our continuing study on the utilization of oxygen in organic chemistry,[9] we report here a facile and efficient method to synthesize polysubstituted imidazo[1,2-*a*]pyridines using air as the oxidant.

At the beginning of our study, pyridin-2-amine (**1a**) and (*E*)-(2-nitrovinyl)benzene (**2a**) were chosen as test substrates for this cyclization using CuI in DMF under air at 80 °C to achieve the transformation. Gratifyingly, the desired 3-nitro-2-phenylimidazo[1,2-*a*]pyridine (**3aa**) was obtained in 88% yield after 4 h (Table 1, entry 1). It is worth mentioning that we confirmed the structure of **3ba** unambiguously through an X-ray crystal analysis.[10] When O_2 was employed as the oxidant, only 84% of **3aa** was isolated (Table 1, entry 2). Thus, air was chosen as oxidant for its abundance, low cost, and convenience. The yield decreased when the temperature changed to 110 or 60 °C (Table 1, entries 3 and 4). Furthermore, when the copper salts were changed to CuBr, CuCl, CuOTf, $Cu(OAc)_2$, and $Cu(OTf)_2$, CuBr showed the highest activity for this reaction and resulted in 90% yield (Table 1, entries 5−9). Other solvents such as DMSO, NMP, CH_3CN, and CH_3OH were also evaluated, and no better result was obtained (Table 1, entries 11−14). In addition, in a control reaction with no metal salts as catalyst, no target product was obtained (Table 1, entry 10).

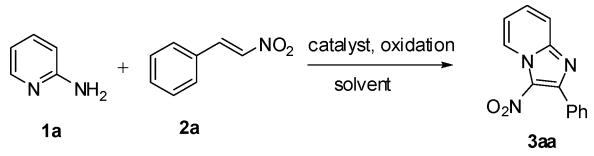
Under the optimized reaction conditions, we examined a series of aminopyridines and nitroolefins to establish the scope and limitations of this process. Generally, the reaction of aminopyridines and nitroolefins proceeded smoothly and afforded the corresponding imidazo[1,2-*a*] **3** with great efficiency (Table 2). To our delight, a wide range substituted groups of nitroolefins or aminopyridines all gave the desired products in good yields, which include methyl, methoxyl, ester, naphthyl, piperonyl, bromo, or chloro groups. For the electronic effects of these reactions, we found the electron-rich nitroolefins or aminopyridines show better reactivity and gave higher yields than electron-deficient ones. Further investigations demonstrated that the steric hindrance of the substitutes on the pyridine rings can affect the yields, the substrates **1a** and **1d** reacted with **2e** and **2a** to form the products **3ae** and **3da** in 68% and 49%, respectively (Table 2, entries 5 and 20). Moreover, heteroaryl species such as furanyl also underwent the desired reaction to give the corresponding product in 38% yield (Table 2, entry 14).

On the basis of the results obtained above, a plausible mechanism of this reaction is illustrated in Scheme 1.The reaction may undergo the following steps. The first step involves a coupling of the substrates **1** and **2** to produce the Michael addition intermediate **4**. A one-electron oxidation of intermediate **4** with copper catalyst generates radical cation **5**, which is followed by hydrogen abstraction with oxidation

Received: December 1, 2011
Published: January 12, 2012

dx.doi.org/10.1021/jo202447p | *J. Org. Chem.* 2012, 77, 2024−2028

Table 1. Optimization of the Reaction Conditions[a]

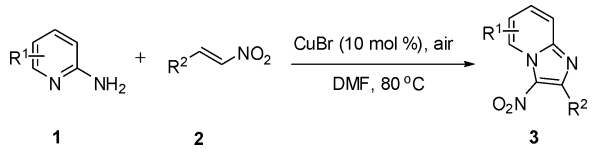


1a 2a 3aa

entry	catalyst	oxidant	solvent	temp (°C)	yield (%)
1	CuI	air	DMF	80	88
2[b]	CuI	O_2	DMF	80	84
3	CuI	air	DMF	110	85
4	CuI	air	DMF	60	73
5	CuBr	air	DMF	80	90
6	CuCl	air	DMF	80	81
7	$Cu(OTf)_2$	air	DMF	80	72
8	$Cu(OAc)_2$	air	DMF	80	79
9	CuOTf	air	DMF	80	86
10		air	DMF	80	0
11	CuBr	air	DMSO	80	87
12	CuBr	air	NMP	80	83
13	CuBr	air	CH_3CN	80	48
14	CuBr	air	CH_3OH	80	53

[a]Reaction conditions: **1a** (0.30 mmol), **2a** (0.36 mmol), catalysts (0.03 mmol), 2 mL of solvent, in an open tube, 4 h. [b]O_2 (1 atm).

Table 2. Synthesis of Imidazo[1,2-*a*]pyridines from Aminopyridines and Nitroolefins[a]



1 2 3

entry		R^1		R^2	product	yield (%)
1	**1a**	H	**2a**	Ph	**3aa**	90
2	**1a**	H	**2b**	3-Me-Ph	**3ab**	95
3	**1a**	H	**2c**	4-Me-Ph	**3ac**	84
4	**1a**	H	**2d**	3,4-diMe-Ph	**3ad**	81
5	**1a**	H	**2e**	2-MeO-Ph	**3ae**	68
6	**1a**	H	**2f**	4-MeO-Ph	**3af**	86
7	**1a**	H	**2g**	2-Cl-Ph	**3ag**	80
8	**1a**	H	**2h**	3-Cl-Ph	**3ah**	86
9	**1a**	H	**2i**	4-Cl-Ph	**3ai**	70
10	**1a**	H	**2j**	3-Br-Ph	**3aj**	88
11	**1a**	H	**2k**	4-Br-Ph	**3ak**	66
12	**1a**	H	**2l**	1-naphthyl	**3al**	92
13	**1a**	H	**2m**	piperonyl	**3am**	65
14	**1a**	H	**2n**	2-furyl	**3an**	38
15	**1b**	3-Me	**2a**	Ph	**3ba**	94
16	**1b**	3-Me	**2b**	3-Me-Ph	**3bb**	70
17	**1b**	3-Me	**2j**	3-Br-Ph	**3bj**	72
18	**1b**	3-Me	**2c**	4-Me-Ph	**3bc**	76
19	**1c**	5-Me	**2a**	Ph	**3ca**	86
20	**1d**	6-Me	**2a**	Ph	**3da**	49
21	**1e**	5-Cl	**2a**	Ph	**3ea**	61
22	**1f**	4-COOEt	**2a**	Ph	**3fa**	56

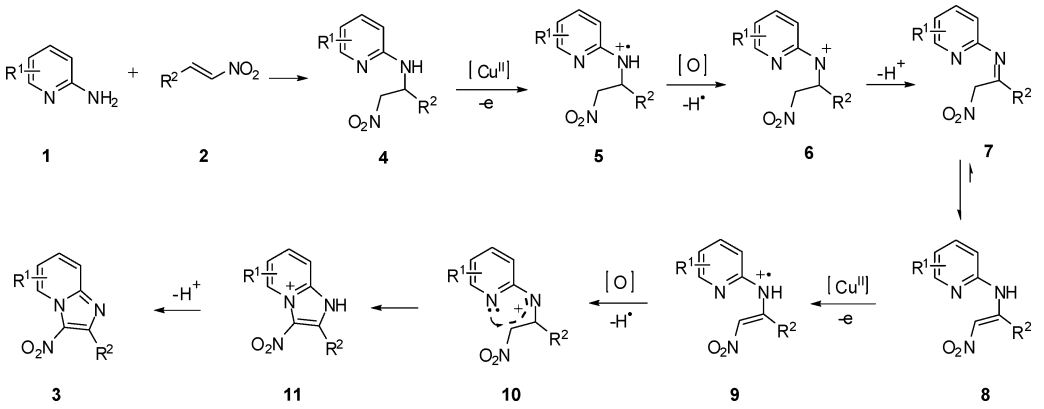
[a]Reaction conditions: 1 (0.3 mmol), 2 (0.36 mmol), CuBr (0.03 mmol), 2 mL DMF, in an open tube, 80 °C, 4 h.

resulting in the formation of nitrenium ion **6**.[11] The imine **7** is then formed by proton elimination and equilibrates to enamine **8**. Similarly, intermediate **9**, produced by one-electron oxidation with copper catalyst from enamine **8**, generates the nitrenium ion **10** by hydride abstraction with oxidation. Finally, intermediate **10** undergoes intramolecular nucleophilic addition to give intermediate **11** and the subsequent proton elimination to afford product **3**.

In conclusion, we have developed a direct Cu(I)-catalyzed method for the synthesis of imidazo[1,2-*a*]pyridines with aminopyridines and nitroolefins in a one-pot manner under air. Various substitutes are tolerated in this reaction, which proceeds smoothly in moderate to good yields. The procedure,

dx.doi.org/10.1021/jo202447p | J. Org. Chem. 2012, 77, 2024−2028

Scheme 1. Plausible Reaction Mechanism



using air as oxidative agent, is a simple, economical, and environmentally friendly protocol for the synthesis of imidazo-[1,2-*a*]pyridines.

EXPERIMENTAL SECTION

Typical Procedure for the Preparation of Imidazo[1,2-*a*]pyridines 3. A tube was charged with **1** (0.30 mmol), **2** (0.36 mmol), and CuBr (4.3 mg, 0.03 mmol). Then 2 mL of DMF was added to the reaction system. The reaction mixture was stirred at 80 °C under air for 4 h. After the mixture was cooled to room temperature, the solvent was diluted with 10 mL of ethyl acetate, washed with 5 mL of brine, and dried over anhydrous Na_2SO_4. After the solvent was evaporated in vacuo, the residues were purified by column chromatography, eluting with petroleum ether/EtOAc to afford pure **3**.

3-Nitro-2-phenylimidazo[1,2-*a*]pyridine 3aa: yellow solid; mp 172−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52−9.50 (d, J = 7.2 Hz, 1 H), 7.92−7.89 (m, 2 H),7.85 −7.83 (d, J = 9.2 Hz, 1 H),7.67−7.63 (m, 1 H), 7.51−7.50 (t, J = 3.2 Hz, 3 H), 7.29−7.26 (q, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 145.1, 131.8, 130.8, 130.1, 130.0, 128.16, 128.12, 118.3, 116.4; IR (neat, cm^{-1}) 3061, 3034, 1630, 1531, 1367, 923, 759, 693; HRMS calcd for $C_{13}H_{10}N_3O_2$ [M + H] $^+$ 240.0768, found 240.0761.

3-Nitro-2-*m*-tolylimidazo[1,2-*a*]pyridine 3ab: yellow solid; mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49−9.47 (t, 1 H), 7.83−7.80 (q, 1 H), 7.70−7.69 (d, J = 6.8 Hz, 2 H), 7.65−7.61 (t, 1 H), 7.40−7.36 (t, J = 8 Hz, 1 H), 7.32−7.30 (d, J = 7.6 Hz, 1 H), 7.27−7.23 (t, 1 H), 2.44 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.0, 137.7, 131.7, 130.9, 130.7, 130.3, 128.0, 127.9, 127.1, 118.1, 116.3, 21.3; IR (neat, cm^{-1}) 3061, 3030, 2920, 1632, 1528, 1432, 1369, 751, 689; HRMS calcd for $C_{14}H_{12}N_3O_2$ [M + H]$^+$ 254.0924, found 254.0932.

3-Nitro-2-*p*-tolylimidazo[1,2-*a*]pyridine 3ac: yellow solid; mp 204−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 7.2 Hz, 1 H), 7.95−7.93 (d, J = 8.8 Hz, 2 H), 7.81−7.79 (d, J = 8.8 Hz, 1 H), 7.65−7.62 (t, 1 H), 7.25−7.23 (d, J = 6.8 Hz, 1 H), 7.03−7.01 (d, J = 8.8 Hz, 2 H), 3.89 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 145.1, 140.4, 130.7, 129.9, 128.9, 128.8, 128.1, 118.1, 116.2, 21.5; IR (neat, cm^{-1}) 3058, 3026, 2917, 1674, 1537, 1475, 1362, 1362, 750; HRMS calcd for $C_{14}H_{12}N_3O_2$ [M + H]$^+$ 254.0924, found 254.0921.

2-(3,4-Dimethylphenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ad: yellow solid; mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 6.8 Hz, 1 H), 7.84−7.81 (d, J = 9.2 Hz, 1 H), 7.69−7.62 (m, 3 H), 7.28−7.24 (d, 2 H), 2.35 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 145.1, 139.2, 136.5, 130.9, 130.7, 129.4, 129.2, 128.2, 127.5, 118.2, 116.2, 19.8, 19.7; IR (neat, cm^{-1}) 3064, 3031, 2916, 1628, 1534, 1478, 1374, 883; HRMS calcd for $C_{15}H_{14}N_3O_2$ [M + H]$^+$ 268.1081, found 268.1084.

2-(2-Methoxyphenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ae: yellow solid; mp 200−202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48−9.47 (d, J = 6.8 Hz, 1 H), 7.84−7.82 (d, J = 8.8 Hz, 1 H), 7.64−7.57 (m, 2 H), 7.50−7.46 (m, 1 H), 7.27−7.24 (m, 1 H), 7.12−7.08 (t, J = 7.6 Hz, 1 H), 7.03−7.01 (d, J = 8.4, 1 H), 3.82 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 146.9, 145.0, 131.3, 130.5, 130.1, 127.5, 121.8, 120.5, 118.1, 116.1, 110.8, 55.5; IR (neat, cm^{-1}) 3068, 3037, 2926, 1631, 1537, 1438, 1368, 1216, 758; HRMS calcd for $C_{14}H_{12}N_3O_3$ [M + H]$^+$ 270.0873, found 270.0878.

2-(4-Methoxyphenyl)-3-nitroimidazo[1,2-*a*]pyridine 3af: yellow solid; mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 7.2 Hz, 1 H), 7.95−7.93 (d, J = 8.8 Hz, 2 H), 7.81−7.79 (d, J = 8.8 Hz, 1 H), 7.65−7.62 (t, 1 H), 7.25−7.23 (d, J = 6.8 Hz, 1 H), 7.03−7.01 (d, J = 8.8 Hz, 2 H), 3.89 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3,150.2, 145.2, 131.8, 130.8, 128.3, 124.0, 118.0, 116.1, 113.6, 55.3; IR (neat, cm^{-1}) 3090, 3016, 2940, 1633, 1540, 1444, 1368, 1210, 961, 760, 705; HRMS calcd for $C_{14}H_{12}N_3O_3$ [M + H]$^+$ 270.0873, found 270.0874.

2-(2-Chlorophenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ag: yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 7.2 Hz, 1 H), 7.88−7.86 (d, J = 8.8 Hz, 1 H), 7.70−7.66 (m, 1 H), 7.55−7.52 (m, 2 H), 7.47−7.31 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 144.9, 133.9, 131.9, 130.8, 130.7, 130.6, 129.5, 127.7, 126.7, 118.5, 116.7; IR (neat, cm^{-1}) 3053, 1672, 1632, 1539, 1369, 763, 732; HRMS calcd for $C_{13}H_9ClN_3O_2$ [M + H]$^+$ 274.0378, found 274.0383.

2-(3-Chlorophenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ah: yellow solid; mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 7.2 Hz, 1 H), 7.91−7.79 (m, 3 H), 7.70−7.66 (m, 1 H), 7.50−7.42 (m, 2 H), 7.33−7.29 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 145.0, 134.0, 133.5, 131.0, 130.1, 130.0, 129.3, 128.2, 128.0, 118.3, 116.7; IR (neat, cm^{-1}) 3030, 1631, 1529, 1477, 1366, 787, 746; HRMS calcd for $C_{13}H_9ClN_3O_2$ [M + H]$^+$ 274.0378, found 274.0382.

2-(4-Chlorophenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ai: yellow solid; mp 184−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52−9.50 (d, J = 6.8 Hz, 1H),7.89−7.83 (m, 3 H), 7.69−7.65 (m, 1 H), 7.49−7.47 (d, J = 8.8 Hz, 2 H), 7.31−7.28 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 145.1, 136.4, 131.4, 131.0, 130.2, 128.4, 128.1, 118.3, 116.6; IR (neat, cm^{-1}) 3059, 3026, 1632, 1530, 1336, 861, 828; HRMS calcd for $C_{13}H_9ClN_3O_2$ [M + H]$^+$ 274.0378, found 274.0380 .

2-(3-Bromophenyl)-3-nitroimidazo[1,2-*a*]pyridine 3aj: yellow solid; mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51−9.50 (d, J = 6.8 Hz, 1 H), 8.06−8.05 (t, 1 H), 7.86−7.84 (d, J = 8.4 Hz, 2 H), 7.70−7.62 (m, 2 H), 7.39−7.35 (t, J = 8 Hz, 1 H), 7.33−7.29 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 145.0, 133.8, 133.1, 132.8, 131.0, 129.6, 128.7, 128.1, 122.1, 118.4, 116.7; IR (neat, cm^{-1}) 3031, 1630, 1529, 1371, 747, 723; HRMS calcd for $C_{13}H_9BrN_3O_2$ [M + H]$^+$ 317.9873, found 317.9876.

2-(4-Bromophenyl)-3-nitroimidazo[1,2-*a*]pyridine 3ak: yellow solid; mp 186−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52−9.50 (d, J = 6.8 Hz, 1 H), 7.85−7.79 (m, 3 H), 7.69−7.63 (m, 3 H), 7.32−7.28 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 145.1, 131.6, 131.3, 131.0, 130.7, 128.1, 124.8, 118.3, 116.6; IR (neat, cm^{-1})

dx.doi.org/10.1021/jo202447p | J. Org. Chem. 2012, 77, 2024−2028

3029, 1630, 1594, 1530, 1370, 861, 827; HRMS calcd for $C_{13}H_9BrN_3O_2$ $[M + H]^+$ 317.9873, found 317.9876.

2-(Naphthalen-2-yl)-3-nitroimidazo[1,2-*a*]pyridine 3al: yellow solid; mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57−9.55 (d, J = 7.2 Hz, 1 H), 8.01−7.99 (d, J = 8 Hz, 1 H), 7.94−7.92 (d, J = 8 Hz, 1 H), 7.89−7.87 (d, J = 9.2 Hz, 1 H), 7.71−7.65 (m, 3 H), 7.61−7.57 (t, 1 H), 7.53−7.49 (m,1 H), 7.46−7.42 (m,1 H), 7.33−7.29 (m,1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 145.2, 133.3, 131.1, 130.8, 130.2, 129.9, 128.5, 128.2, 127.9, 126.8, 126.0, 124.9, 124.8, 118.4, 116.6; IR (neat, cm^{-1}) 3052, 1630, 1532, 1481, 1364, 775, 743; HRMS calcd for $C_{17}H_{12}N_3O_2$ $[M + H]^+$ 290.0924, found 290.0925.

2-(Benzo[*d*][1,3]dioxol-5-yl)-3-nitroimidazo[1,2-*a*]pyridine 3am: yellow solid; mp 198−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50−9.48 (d, J = 6.8 Hz, 1 H), 7.81−7.79 (d, J = 8.8 Hz, 1 H), 7.66−7.62 (m, 1 H), 7.53−7.50 (q, 1 H), 7.429−7.425 (d, 1 H), 7.27−7.24 (m, 1 H), 6.94−6.92 (d, J = 8 Hz, 1 H), 6.05 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 149.4, 147.4, 145.0, 130.9, 128.2, 125.4, 125.0, 118.1, 116.3, 110.4, 108.1, 101.4; IR (neat, cm^{-1}) 3032, 2917, 1628, 1536, 1478, 1213, 1037, 762, 747; HRMS calcd for $C_{14}H_{10}N_3O_4$ $[M + H]^+$ 284.0666, found 284.0673.

2-(Furan-2-yl)-3-nitroimidazo[1,2-*a*]pyridine 3an: yellow solid; mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55−9.54 (d, J = 7.2 Hz, 1 H), 7.94−7.93(d, J = 3.6 Hz, 1 H), 7.87−7.85 (d, J = 8.8 Hz, 1 H),7.748−7.746 (d, 1 H), 7.69−7.64 (m, 1 H), 7.28−7.24 (m, 1 H), 6.68−6.66 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 145.69, 145.64, 139.8, 131.4, 128.1, 118.4, 118.1, 116.3, 112.5; IR (neat, cm^{-1}) 3033, 1633, 1589, 1480, 1351, 1215, 1021, 747; HRMS calcd for $C_{11}H_8N_3O_3$ $[M + H]^+$ 230.0560, found 230.0564.

8-Methyl-3-nitro-2-phenylimidazo[1,2-*a*]pyridine 3ba: yellow solid; mp 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36−9.34 (d, J = 6.8 Hz, 1 H), 7.91−7.89 (q, 2 H), 7.51−7.48 (m, 3 H), 7.44−7.42 (d, J = 7.2 Hz, 1 H), 7.17−7.14 (t, 1 H), 2.71 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 145.1, 132.1, 130.0, 129.9, 129.8, 128.5, 128.0, 125.8, 116.3, 16.5; IR (neat, cm^{-1}) 3059, 2923, 1623, 1533, 1474, 1364, 1237, 1154, 749, 695; HRMS calcd for $C_{14}H_{12}N_3O_2$ $[M + H]^+$ 254.0924, found 254.0916.

8-Methyl-3-nitro-2-*m*-tolylimidazo[1,2-*a*]pyridine 3bb: yellow solid; mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33−9.32 (d, J = 6.8 Hz, 1 H), 7.69−7.67 (d, J = 7.2 Hz, 2 H), 7.42−7.35 (m, 2 H), 7.30−7.28 (d, J = 7.6 Hz, 1 H), 7.15−7.12 (t, 1 H), 2.70 (s, 3 H), 2.43 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 145.0, 137.7, 132.0, 130.7, 130.4, 129.7, 128.4, 127.9, 127.1, 125.7, 116.3, 21.3, 16.5; IR (neat, cm^{-1}) 3036, 2922, 1621, 1529, 1476, 1363, 1235, 1149, 755, 709; HRMS calcd for $C_{15}H_{14}N_3O_2$ $[M + H]^+$ 268.1081, found 268.1089.

2-(3-Bromophenyl)-8-methyl-3-nitroimidazo[1,2-*a*]pyridine 3bj: yellow solid; mp 188−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35−9.34 (d, J = 6.8 Hz, 1 H), 8.05−8.04 (t, J = 1.6 Hz, 1 H), 7.85−7.83 (d, J = 8 Hz, 1 H), 7.62−7.60 (q, 1 H), 7.47−7.45 (d, J = 7.2 Hz, 1 H), 7.38−7.34 (t, J = 8 Hz, 1 H), 7.21−7.18 (t, 1 H), 2.72 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 145.0, 134.1, 132.8, 130.0, 129.5, 128.77, 128.74, 125.7, 122.0, 116.7, 16.5; IR (neat, cm^{-1}) 3064, 2924, 1622, 1529, 1473, 1448, 1360, 1233, 1155, 751, 723; HRMS calcd for $C_{14}H_{11}BrN_3O_2$ $[M + H]^+$ 332.0029, found 332.0028.

8-Methyl-3-nitro-2-*p*-tolylimidazo[1,2-*a*]pyridine 3bc: yellow solid; mp 102−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34−9.32 (d, J = 6.8 Hz, 1 H), 7.83−7.81 (d, J = 8 Hz, 2 H), 7.41−7.39 (d, J = 7.2 Hz, 1 H), 7.30−7.28 (d, J = 8.0 Hz, 2 H), 7.14−7.11 (t, J = 7.2 Hz, 1 H), 2.69 (s, 3 H), 2.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 145.1, 140.1, 129.9, 129.7, 129.2, 128.7, 128.3, 125.8, 116.2, 21.4, 16.5; IR (neat, cm^{-1}) 3028, 2922, 2854, 1651, 1543, 1476, 1363, 1237, 817, 752; HRMS calcd for $C_{15}H_{14}N_3O_2$ $[M + H]^+$ 268.1081, found 268.1087.

6-Methyl-3-nitro-2-phenylimidazo[1,2-*a*]pyridine 3ca: yellow solid; mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1 H), 7.90−7.87 (m, 2 H), 7.74−7.71 (d, J = 8.8 Hz, 1 H), 7.50−7.48 (q, 4 H), 2.50 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 144.1, 133.6, 132.0, 130.0, 129.9, 128.1, 126.8, 126.1, 117.5, 18.6; IR (neat, cm^{-1}) 3054, 3025, 2919, 1651, 1527, 1481, 1353, 1218, 1199, 739, 693; HRMS calcd for $C_{14}H_{12}N_3O_2$ $[M + H]^+$ 254.0924, found 254.0920.

5-Methyl-3-nitro-2-phenylimidazo[1,2-*a*]pyridine 3da: yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.98 (t, 2 H), 7.74 (s, 1 H), 7.56−7.54 (d, J = 8.8 Hz, 1 H), 7.46−7.42 (t, 2 H), 7.34−7.31 (t, J = 7.2 Hz, 1 H), 7.16−7.12 (q, 1 H), 6.62−6.60 (d, J = 6.8 Hz, 1 H), 2.61 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 145.7, 134.3, 133.9, 128.6, 127.8, 126.0, 124.8, 114.9, 111.5, 18.7; IR (neat, cm^{-1}) 3064, 3033, 2921, 1679, 1547, 1479, 1273, 1154, 776, 742; HRMS calcd for $C_{14}H_{12}N_3O_2$ $[M + H]^+$ 254.0924, found 254.0928.

6-Chloro-3-nitro-2-phenylimidazo[1,2-*a*]pyridine 3ea: yellow solid; mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56−9.55 (q, 1 H), 7.89−7.86 (m, 2 H), 7.77−7.75 (q, 1 H), 7.62−7.59 (d d, J = 9.2, 2 Hz, 1 H), 7.51−7.49 (q, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 143.3, 131.9, 131.4, 130.3, 129.9, 128.1, 126.0, 124.9,118.5; IR (neat, cm^{-1}) 3052, 3019, 1654, 1529, 1480, 1365, 738, 697; HRMS calcd for $C_{13}H_9ClN_3O_2$ $[M + H]^+$ 274.0378, found 274.0373.

Ethyl 3-nitro-2-phenylimidazo[1,2-*a*]pyridine-7-carboxylate 3fa: yellow solid; mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51−9.49 (d, J = 7.2 Hz, 1 H), 8.48 (s, 1 H), 7.92−7.89 (q, 2 H), 7.83−7.81 (q, 1 H), 7.52−7.51 (q, 3 H), 4.51−4.45 (q, J = 7.2 Hz, 2 H), 1.48−1.44 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 150.8, 144.2, 132.1, 131.4, 130.4, 130.0, 128.2, 127.7, 119.9, 115.4, 62.3, 14.1; IR (neat, cm^{-1}) 3092, 3066, 2922, 2852, 1718, 1530, 1498, 1473, 1362, 1309, 1211, 759, 742, 699; HRMS calcd for $C_{16}H_{14}N_3O_4$ $[M + H]^+$ 312.0979, found 312.0972.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral data for all new compounds and X-ray data for **3ba** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENTS

We thank the National Science Foundation (NSF-20732002, NSF-20090443, and NSF-20872052) for financial support.

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