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Lewis Acid-Catalyzed Denitrogenative Transannulation of Pyridotriazoles with Nitriles: Synthesis of Imidazopyridines

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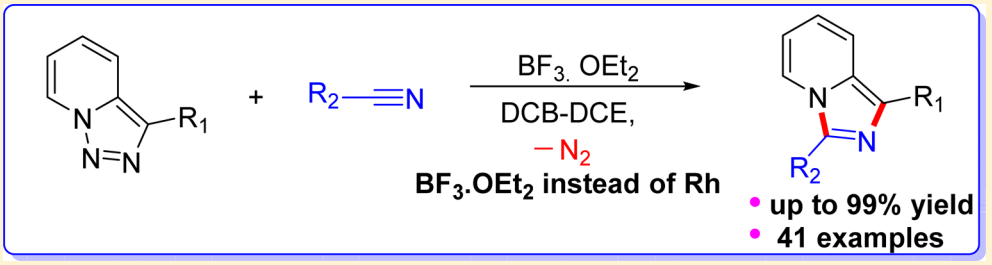
Supporting Information



ABSTRACT: The synthesis of imidazo[1,5-*a*]pyridines through denitrogenative transannulation of pyridotriazoles with nitriles using $BF_3{\cdot}Et_2O$ as catalyst has been described. The combination of solvents (dichlorobenzene-dichloroethane) plays a crucial role in achieving quantitative yields of desired products under metal-free conditions.

Triazoles are important heterocyclic units and exhibit a wide range of biological activities.[1] Recently, transition metal-catalyzed ring opening of 1,2,3-triazoles are well-known for the generation of metallocarbene intermediates, and they undergo a wide range of synthetically useful transformations like cycloadditions, ring expansions, ylide formation, and so forth.[2,3] However, such a reaction requires precious metal salts like Rh and Ni catalysts. Hence, the development of alternative catalysts for such reactions is desirable. Imidazo[1,5-*a*]pyridines are an important class of bridged head nitrogen heterocyclic compounds; these scaffolds are found in many pharmacologically important compounds and included in material chemistry like those actively probed in the context of organic light-emitting diodes (OLED) and organic thin layer field effect transistors (FET).[4−6] However, few synthetic methods are available for synthesizing imidazo[1,5-*a*]pyridines, and the reported methods mainly rely on traditional Vilsmeier-type cyclizations.[7] Transannulation reactions have become an indispensable tool for the synthesis of many natural products by making or breaking of C−C and C−hetero bonds.[8] Recently, Gevorgyan et al. reported the Rh(II) metal-catalyzed denitrogenative transannulation of pyridotriazoles, which is an efficient method for the synthesis of imidazo[1,5-*a*]pyridines with nitriles. For such transformation, it is essential to have substituents at the C-7 position (activating group (AG)) and an electron-withdrawing group (EWG) at the C-3 position of pyridotriazoles.[9] As an alternate to rhodium, we recently reported a copper-catalyzed transannulation of pyridotriazoles with benzyl amines and amino acids;[10] however, this method has some drawbacks such as not being suitable for aliphatic and heterocyclic amines. Moreover, the separation of metal catalyst and its residual toxicity in the target compound is a central issue to consider. Furthermore, transition metal-catalyzed reactions generate hazardous waste that is environmentally problematic; hence, it should be avoided whenever possible. Further, the use of benzylamines generates corresponding imines as side products under aerobic conditions.[11] In this connection, performing the reactions under metal-free conditions is an attractive target. Rare reports exist in the literature describing metal-free systems for denitrogenative transannulation of pyridotriazoles.[12] Within our program on the synthesis of fused heterocycles[13] and C−H activation under metal-free conditions,[14] we have now devised a protocol for the denitrogenative transannulation of pyridotriazoles with nitriles using $BF_3{\cdot}Et_2O$ as catalyst, which we report herein (Scheme 1). We initiated our studies by probing the reaction conditions for the denitrogenative transannulation of pyridotriazoles with nitriles using Lewis acid catalysts and solvents (see Table S1). Preliminary experiments revealed that $BF_3{\cdot}Et_2O$ as the catalyst and dichlorobenzene (DCB) as solvent were most effective.

The denitrogenative transannulation of pyridotriazole occurred under metal-free reaction conditions (see Table S1) in which a higher ratio of benzonitrile **2a** was used with respect to 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine **1a** to ensure a satisfactory performance of the reaction at 150 °C in DCB as solvent (Table 1, entries 1 and 2). Marginal improvement in yield was observed when catalyst loading was increased to 25 mol % while decreasing the quantities of **2a** and solvent (Table 1, entries 3−5). There was no advantage when dichloroethane (DCE) was used as solvent (entry 6). Gratifyingly, a significant enhancement in yield was observed by conducting the reaction

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Scheme 1. Transannulation Reactions of Pyridotriazoles

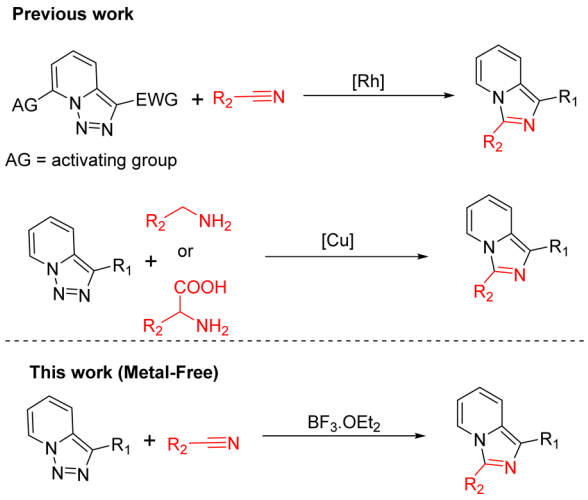
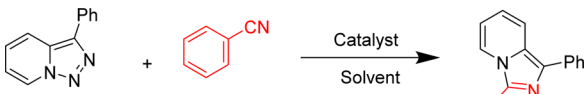


Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

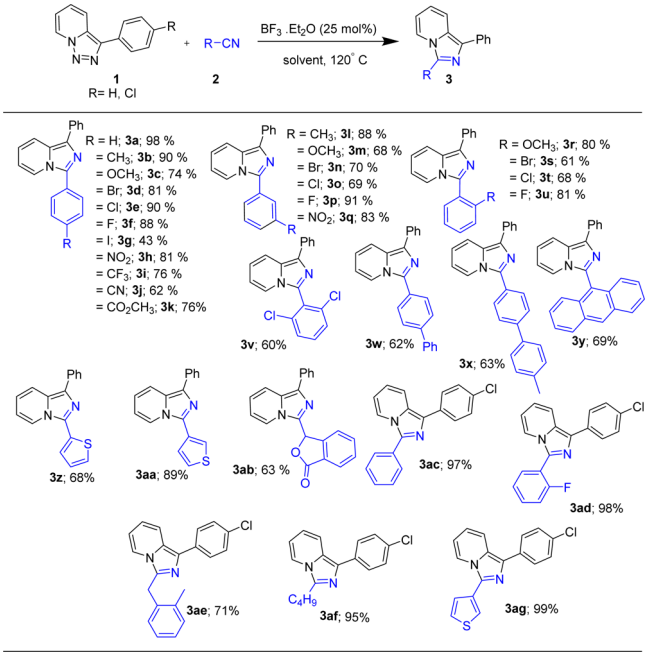
entry	2a (eq)	catalyst (mol %)	solvent (mL)	T (°C)	t (h)	yield (%)
1	10	$BF_3(OEt_2)$ (10)	DCB (1)	150	4	30
2	10	$BF_3(OEt_2)$ (20)	DCB (1)	150	4	52
3	3	$BF_3(OEt_2)$ (25)	DCB (0.5)	150	4	65
4	3	$BF_3(OEt_2)$ (25)	DCB (0.25)	140	4	64
5	3	$BF_3(OEt_2)$ (25)	DCB (0.25)	140	4	63
6	3	$BF_3(OEt_2)$ (25)	DCE (1)	120	12	50
7	3	$BF_3(OEt_2)$ (25)	DCB (0.2) + DCE (0.25)	120	10	98
8	3	$BF_3(OEt_2)$ (10)	DCB (0.2) + DCE (0.25)	120	12	15
9	1.2	$BF_3(OEt_2)$ (20)	DCB (0.2) + DCE (0.25)	120	12	45
10	**1.2**	**$BF_3(OEt_2)$ (25)**	**DCB (0.2) + DCE (0.25)**	**120**	**10**	**98**

[a]Conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst, solvent in an oil bath, closed tube, isolated yield.

with the combination of DCB and DCE as solvent (entry 7). With this solvent combination, decreasing the catalyst loading to 10 and 20 mol % did not result in any improvement of yield (Table 1, entries 8 and 9). Further optimization allowed us to reduce the amount of **2a** to 1.2 equiv without any loss of yield (entry 10).

With this set of optimized conditions (Table 1, entry 10), the denitrogenative transannulation of pyridotriazole with different nitriles was examined (Scheme 2). The results in Scheme 2 demonstrate the versatility of the reaction with a high degree of functional group tolerance and with a broad substrate scope. Initially, benzonitrile bearing electron-donating and -withdrawing groups (Me, OMe, halogens, NO_2, CF_3, CN, and CO_2Me) at the para position could react with 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine (**1a**) smoothly to afford the

Scheme 2. Substrate Scope of Denitrogenative Transannulation Reactions[a]



[a]Conditions: **1** (0.2 mmol), **2** (0.24 mmol), $BF_3{\cdot}Et_2O$ (25 mol %), solvent {DCB (0.2 mL) + DCE (0.25 mL)} in an oil bath in a closed tube, 120 °C, 16 h, isolated yield.

corresponding transannulated products **3a–k** in moderate to excellent yields (43–98%). Similarly, the presence of electron-donating and -withdrawing groups at either the ortho or meta position of benzonitriles provided the corresponding transannulated products (**3l–u**) in good yields (61–91%). The presence of 2,6-dichloro-*ortho* substituents also gave desired product **3v** in 60% yield. As evident from the yields of products **3b–v**, the electronic effects associated with electron-donating or -withdrawing substituents on the benzonitrile do not affect the efficiency of the transformation.

The versatile metal-free denitrogenative transannulation was not limited to the benzonitrile substrates. Indeed, the benzonitriles bearing extended aromatics, such as [1,1′-biphenyl]-4-carbonitrile, 4′-methyl-[1,1′-biphenyl]-4-carbonitrile, and anthracene-9-carbonitrile, proved to be amenable to this procedure and afford the differently decorated products **3w–y** in good yields. The scope with regard to the benzonitrile coupling partner was also extended toward heterocycles. The reactions of **1a** with thiophene-2-carbonitrile, thiophene-3-carbonitrile, and 3-oxo-1,3-dihydroisobenzofuran-1-carbonitrile were also tolerated and gave desired products **3z**, **3aa**, and **3ab** in 68, 89, and 63% yields, respectively. Thus, this demonstrates the potential utility of this methodology for the synthesis of medicinally relevant scaffolds.

To further expand the scope of the methodology, we evaluated the denitrogenative transannulation reaction of chloro-substituents in the pyridotriazole derivatives with representative nitriles under the optimized conditions. The 3-(4-chlorophenyl)-[1,2,3]triazolo[1,5-*a*]pyridine reacts with aromatic, aliphatic, and heteroaromatic nitriles to produce the corresponding imidazo[1,5-*a*]pyridines **3ac–ag** in good to quantitative yields.

The successful transformation of denitrogenative transannulation of pyridotriazole under metal-free conditions

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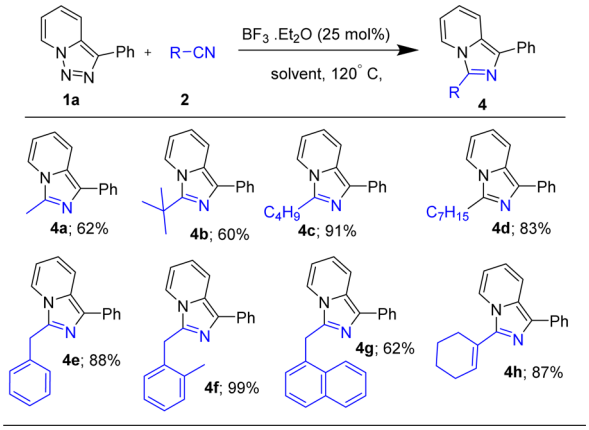
prompted us to investigate the generality of this method toward aliphatic nitrile substrates. Thus, syntheses of alkyl-aryl imidazo[1,5-*a*]pyridines **4** were carried out by reacting **1a** with different alkyl nitriles **2** (Scheme 3). It is remarkable to

Scheme 3. Denitrogenative Transannulation of 1a with Alkyl Nitriles[a]

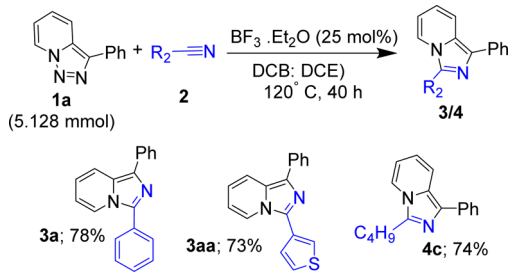


[a]Conditions: **1a** (0.2 mmol), **2** (0.24 mmol), solvent {DCB (0.2 mL) + DCE (0.25 mL)} in an oil bath in a closed tube, 16 h, isolated yield.

note that the simple aliphatic nitriles, such as acetonitrile and branched pivalonitrile, and long chain nitriles, such as pentane nitrile and octane nitrile, were also competent reactants under the optimized conditions and produced the corresponding imidazo[1,5-*a*]pyridines **4a−d** in good to excellent yields. To our delight, we found this transformation to be very general for a wide range of nitriles, such as 2-phenylacetonitrile, 2-(*o*-tolyl)acetonitrile, 2-(naphthalen-1-yl)acetonitrile), and 2-(cyclohex-1-en-1-yl)acetonitrile, and produced corresponding products **4e−h** in good yields.

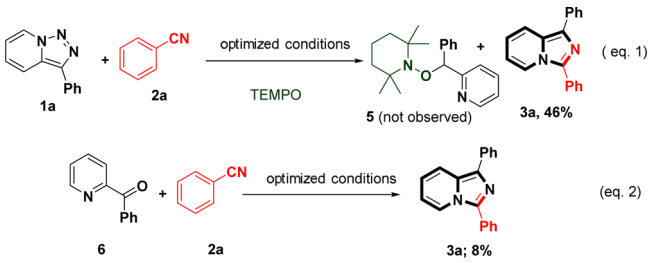
To validate the process for scale up studies, we performed the reaction of **1a** with benzonitrile, thiophene-3-carbonitrile, and pentane nitrile and obtained corresponding products **3a**, **3aa**, and **4c** in 78% (1.079 g), 73% (0.950 g), and 74% (1.03 g) yields, respectively, under the optimized conditions. This study indicates the feasibility of the method for industrial/commercial production (Scheme 4).

Scheme 4. Scale Up Studies



To gain insight into the reaction mechanism, we performed some control experiments (Scheme 5). Initially, the reaction was conducted by the addition of radical scavenger TEMPO under optimized conditions to know whether the reaction proceeds via radical or ionic path (Scheme 5, eq 1). Under these conditions, no TEMPO adduct **5** formation was observed. It indicates that the reaction does not proceed via the radical

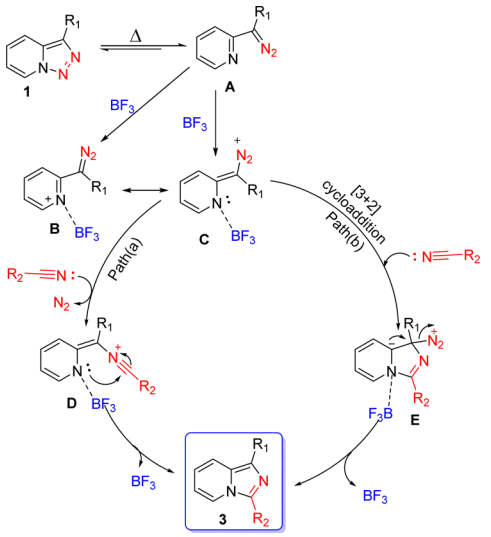
Scheme 5. Control Experiments



pathway. Another reaction was performed with 2-benzoylpyridine **6** instead of pyridotriazole **1a** under the optimized conditions to know whether the reaction proceeds through intermediate **6** by the hydrolysis of pyridotriazole (Scheme 5, eq 2). Interestingly, a trace amount of product **3a** formation was observed. This experiment clearly suggests that the reaction may proceed via *α*-imino diazo compound formation followed by cyclization to give the desired product.

On the basis of these observations and our previous results on imidazo[1,5-*a*]pyridines,[10] a plausible reaction mechanism has been proposed for this transformation (Scheme 6). Initially,

Scheme 6. Plausible Mechanism



triazolo[1,5-*a*]pyridine at high temperature will be in equilibrium with *α*-imino diazo compound **A**; its reaction with BF_3 would generate the intermediates **B**/**C**.[15] Product **3** may be obtained by either path (a) or path (b) from intermediate **C**. In path (a), nucleophilic substitution at the sp^2 carbon of **C** with nitrile derivative may generate intermediate **D**, and its cyclization will give desired product **3** by the elimination of BF_3. On the other hand, [3 + 2] cycloaddition of **C** with nitrile generates another intermediate **E** [path (b)]. Denitrogenation and simultaneous elimination of BF_3 from **E** afford desired product **3**.

CONCLUSIONS

In summary, we have developed an efficient method for the synthesis of imidazo[1,5-*a*]pyridines denitrogenative transannulation of pyridotriazoles with nitriles using $BF_3{\cdot}Et_2O$ as catalyst. The combination of solvents (dichlorobenzene-dichloroethane) is essential to achieve quantitative yields of

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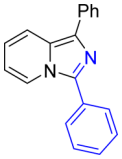
desired products under metal-free conditions. The commercially available nitriles with a wide range of substituted benzonitriles, aliphatic, branched aliphatic, cyclic, biphenyl, anthracene, and thiophene nitriles, including acetonitrile and 3-oxo-1,3-dihydroisobenzofuran-1-carbonitrile, were amenable to this procedure.

EXPERIMENTAL SECTION

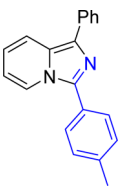
General. All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively. The spectra were recorded in $CDCl_3$ and DMSO-d_6 as solvent. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), and so forth, and coupling constants (J) are given in Hz. Chemical shifts are reported in ppm relative to TMS as an internal standard. The peaks around delta values of ^{1}H NMR (7.2) and ^{13}C NMR (77.0) correspond to the deuterated solvent chloroform and ^{1}H NMR (2.50) and ^{13}C NMR (39.43) correspond to the deuterated solvent DMSO, respectively. Mass spectra were obtained using the electron impact (EI) ionization method. Progress of the reactions was monitored by thin layer chromatography (TLC). All products were purified through column chromatography using silica gel with 100−200 mesh size using hexane/ethyl acetate as eluent unless otherwise indicated.

General Procedure for the Synthesis of Imidazo[1,5-*a*]pyridine (3a). To a reaction tube equipped with a magnetic stir bar were added DCE (0.25 mL), $BF_3{\cdot}OEt_2$ (40−50% purity, 25 mol %), 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine **1a** (39.0 mg, 0.2 mmol), benzonitrile **2a** (25.68 mg, 0.24 mmol), and 0.2 mL of 1,2-dichlorobenzene. The mixture was heated in an oil bath at 120 °C in a closed tube. The reaction was monitored by TLC; after completion, the solution was allowed to cool to room temperature. Then, the mixture was poured into 30 mL of sodium chloride solution. The product was extracted with EtOAc (15 mL × 3) and dried with anhydrous Na_2SO_4. Removal of the solvent under reduced pressure left the residue, which was purified by column chromatography using silica gel (4% EtOAc/hexane) to afford **3a** (53.0 mg, 98% yield).

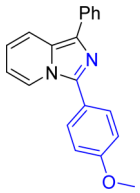
Characterization Data. *1,3-Diphenylimidazo[1,5-a]pyridine (**3a**).*[10] Eluent, 4% EtOAc/hexane; 98% yield (53.0 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 7.0 Hz, 1H), 7.94 (d, J = 7.5 Hz, 2H), 7.84−7.83 (m, 3H), 7.55 (t, J = 7.5 Hz, 2H), 7.48−7.43 (m, 3H), 7.31 (t, J = 7.5 Hz, 1H), 6.79 (dd, J = 9.0 Hz, J = 6.5, 1H), 6.58 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 134.9, 131.9, 130.1, 128.9, 128.7, 128.6, 128.3, 127.6, 126.7, 126.5, 121.7, 119.6, 119.1, 113.2; mp 115−117 °C.



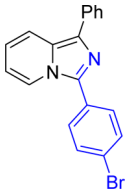
*1-Phenyl-3-(p-tolyl)imidazo[1,5-a]pyridine (**3b**).*[10] Eluent, 4% EtOAc/hexane; 90% yield (52.2 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 7.0 Hz, 1H), 7.94 (dd, J = 8.5 Hz, J = 1.0 Hz, 2H), 7.83 (d, J = 9.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 7.5 Hz, 1H), 6.77−6.74 (m, 1H), 6.55 (dd, J = 10.0 Hz, J = 3.5 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.2, 135.0, 131.7, 129.6, 128.6, 128.2, 127.4, 127.2, 126.7, 126.4, 121.8, 119.4, 119.0, 113.0, 21.3; mp 137−139 °C.



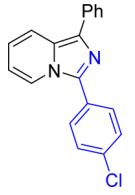
*3-(4-Methoxyphenyl)-1-phenylimidazo[1,5-a]pyridine (**3c**).*[10] Eluent, 5% EtOAc/hexane; 74% yield (44.1 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.0 Hz, 1H), 7.84 (d, J = 7.5 Hz, 2H), 7.70 (d, J = 9.0 Hz, 1H) 7.64 (d, J = 8.5 Hz, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 9.0 Hz, 2H), 6.63 (dd, J = 9.0 Hz, J = 6.0 Hz, 1H), 6.41 (t, J = 6.5 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 138.0, 135.0, 131.5, 130.9, 129.6, 128.6, 127.2, 126.6, 126.3, 122.5, 121.6, 119.3, 118.9, 114.3, 112.9, 55.3; mp 159−161 °C.



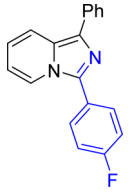
*3-(4-Bromophenyl)-1-phenylimidazo[1,5-a]pyridine (**3d**).* Eluent, 5% EtOAc/hexane; 81% yield (56.5 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 7.0 Hz, 1H), 7.83−7.82 (m, 2H), 7.75 (d, J = 9.0 Hz, 1H), 7.63−7.61 (m, 2H), 7.57−7.55 (m, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.23 (dd, J = 14.0 Hz, J = 0.5 Hz, 1H), 6.71 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.51 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 134.6, 132.3, 132.1, 129.6, 129.0, 128.7, 127.8, 126.7, 126.4, 122.7, 121.4, 119.8, 119.1, 113.5; HRMS calcd for $C_{19}H_{14}N_2Br$ [M + H^+] 349.0340, found 349.0331; mp 179−181 °C.



*3-(4-Chlorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3e**).*[10] Eluent, 4% EtOAc/hexane; 90% yield (55.1 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 9.0 Hz, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.40 (dd, J = 18.0 Hz, J = 7.5 Hz, 4H), 7.22 (t, J = 7.0 Hz, 1H), 6.70 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.49 (t, J = 6.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 134.7, 134.5, 132.2, 129.3, 129.2, 128.7, 128.6, 127.8, 126.7, 126.6, 121.4, 119.7, 119.1, 113.5; mp 181−183 °C.



*3-(4-Fluorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3f**).*[10] Eluent, 4% EtOAc/hexane; 88% yield (50.4 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.0 Hz, J = 0.5 Hz, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.75−7.70 (m, 3H), 7.39 (t, J = 7.5 Hz, 2H), 7.22−7.19 (m, 1H), 7.16−7.11 (m, 2H), 6.70−6.67 (m, 1H), 6.49 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8 (d, J = 247.6 Hz), 137.0, 134.8, 131.9, 130.2 (d, J = 7.8 Hz,), 128.6, 127.5, 126.7, 126.5, 126.3, 121.4, 119.6, 119.1, 116.1 (d, J = 21.6 Hz), 113.3; mp 159−161 °C.



*3-(4-Iodophenyl)-1-phenylimidazo[1,5-a]pyridine (**3g**).* Eluent, 4% EtOAc/hexane; 43% yield (34.3 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 7.5 Hz, 1H), 7.92−7.90 (m, 2H), 7.87 (t, J = 8.5 Hz, 3H), 7.60 (d, J = 8.5 Hz, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.32 (t, J = 7.5 Hz, 1H), 6.82−6.79 (m, 1H), 6.61 (dd, J = 7.5 Hz, J = 1.0

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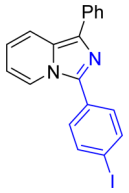
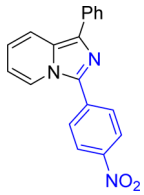
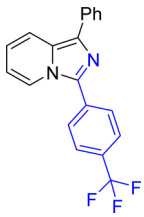
Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.9, 134.7, 132.4, 129.7, 128.7, 127.9, 126.8, 126.6, 121.5, 119.8, 119.2, 113.6, 94.3; HRMS calcd for $C_{19}H_{14}N_2I$ [M + H$^+$] 397.0202, found 397.0193; mp 181−183 °C.



3-(4-Nitrophenyl)-1-phenylimidazo[1,5-a]pyridine (**3h**).[16] Eluent, 15% EtOAc/hexane; 81% yield (51.1 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (dd, J = 14.0 Hz, J = 7.0 Hz, 3H), 8.08 (d, J = 8.5 Hz, 2H), 7.92 (t, J = 7.0 Hz, 3H), 7.50 (t, J = 7.5 Hz, 2H), 7.35 (t, J = 7.5 Hz, 1H), 6.92 (dd, J = 8.5 Hz, J = 7.0 Hz, 1H), 6.74 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 136.3, 135.5, 134.2, 133.7, 133.4, 129.0, 128.8, 128.0, 127.1, 126.8, 124.3, 121.5, 120.7, 119.5, 114.5; mp 189−191 °C.

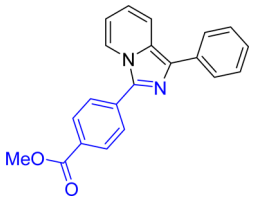


1-Phenyl-3-(4-(trifluoromethyl)phenyl)imidazo[1,5-a]pyridine (**3i**).[10] Eluent, 4% EtOAc/hexane; 76% yield (51.2 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 7.0 Hz, 1H), 7.98 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 9.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.33 (t, J = 7.5 Hz, 1H), 6.84 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.64 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.4, 134.5, 133.6, 132.7, 130.4, 130.1, 128.7, 128.2, 128.1, 126.8, 125.9, 125.0, 122.8, 121.4, 120.1, 119.3, 113.8; mp 140−142 °C.

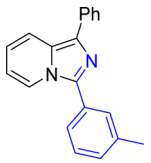


4-(1-Phenylimidazo[1,5-a]pyridin-3-yl)benzonitrile (**3j**). Eluent, 15% EtOAc/hexane; 62% yield (36.9 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 7.5 Hz, 1H), 8.02 (d, J = 8.5 Hz, 2H), 7.92 (t, J = 8.0 Hz, 3H), 7.81 (d, J = 8.5 Hz, 2H), 7.50 (t, J = 8.0 Hz, 2H), 7.35 (t, J = 7.5 Hz, 1H), 6.90 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.71 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 134.4, 133.3, 132.7, 128.8, 128.7, 128.0, 127.0, 126.8, 121.4, 120.5, 119.4, 118.6, 114.3, 111.6; HRMS calcd for $C_{20}H_{14}N_3$ [M + H$^+$] 296.1188, found 296.1187.

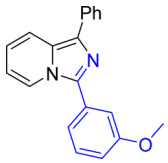
Methyl 4-(1-phenylimidazo[1,5-a]pyridin-3-yl)benzoate (**3k**). Eluent, 10% EtOAc/hexane; 76% yield (50.1 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 7.0 Hz, 1H), 8.09 (d, J = 8.5 Hz, 2H), 7.85 (t, J = 8.5 Hz, 4H), 7.75 (d, J = 9.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.23 (t, J = 7.5 Hz, 1H), 6.73 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.53 (t, J = 6.5 Hz, 1H), 3.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 136.7, 134.5, 134.3, 132.7, 130.1, 129.6, 128.6, 128.2, 127.6, 126.77, 126.71, 121.6, 120.1, 119.1, 113.8, 25.1; HRMS calcd for $C_{21}H_{17}N_2O_2$ [M + H$^+$] 329.1290, found 329.1297; mp 189−191 °C.



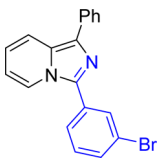
1-Phenyl-3-(m-tolyl)imidazo[1,5-a]pyridine (**3l**).[10] Eluent, 4% EtOAc/hexane; 88% yield (50.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, J = 7.0 Hz, J = 0.5 Hz, 1H), 7.94 (dd, J = 8.0 Hz, J = 1.0 Hz, 2H), 7.81−7.79 (m, 1H), 7.66 (s, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.30−7.23 (m, 2H), 6.75−6.72 (m, 1H), 6.54 (t, J = 6.5 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 138.2, 134.9, 131.8 129.9, 129.1, 128.7, 128.6, 127.5, 126.7, 126.4, 125.0, 121.7 119.5, 119.0, 113.0, 21.4.



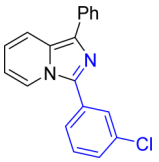
3-(3-Methoxyphenyl)-1-phenylimidazo[1,5-a]pyridine (**3m**).[10] Eluent, 5% EtOAc/hexane; 68% yield (40.7 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 7.5 Hz, 1H), 7.84 (d, J = 7.5 Hz, 2H), 7.72 (d, J = 9.0 Hz, 1H), 7.36 (dd, J = 15.5 Hz, J = 4.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.29−7.28 (m, 2H), 7.21 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.67 (dd, J = 9.0 Hz, J = 6.5 Hz, 2H), 6.45 (t, J = 6.5 Hz, 1H), 3,37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 137.8, 134.8, 131.8, 131.2, 129.8, 128.6, 127.6, 126.7, 126.4, 121.8, 120.2, 119.6, 118.9, 114.7, 113.6, 113.1, 55.3.



3-(3-Bromophenyl)-1-phenylimidazo[1,5-a]pyridine (**3n**). Eluent, 4% EtOAc/hexane; 70% yield (48.6 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 7.5 Hz, 1H), 8.0 (s, 1H), 7.92 (d, J = 7.5 Hz, 2H), 7.83 (d, J = 9.0 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 8.0 Hz, 1H), 7.31 (t, J = 7.0 Hz, 1H), 6.80 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.61 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.3, 134.6, 132.3, 132.1, 131.6, 131.0, 128.7, 127.9, 126.7, 126.6, 126.4, 123.0, 121.4, 119.9, 119.1, 113.6; HRMS calcd for $C_{19}H_{14}N_2Br$ [M + H$^+$] 349.0340, found 349.0337.



3-(3-Chlorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3o**).[10] Eluent, 4% EtOAc/hexane; 69% yield (41.2 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 7.0 Hz, 1H), 7.92 (dd, J = 7.5 Hz, J = 1.0 Hz, 2H), 7.85−7.82 (m, 2H), 7.72 (dd, J = 7.5 Hz, J = 1.5 Hz, 1H), 7.48−7.43 (m, 3H), 7.41−7.39 (m, 1H), 7.32−7.28 (m, 1H), 6.81−6.78 (m, 1H), 6.61−6.58 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.4, 134.9, 134.6, 132.3, 131.8, 130.2, 128.7, 128.2, 127.9, 126.7, 126.6, 126.0, 121.5, 119.9, 119.1, 113.6.



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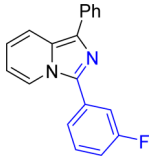
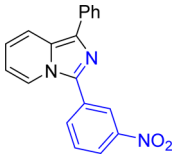
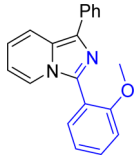
3-(3-Fluorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3p**).[10] Eluent, 4% EtOAc/hexane; 91% yield (52.3 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 7.5 Hz, 1H), 7.93−7.91 (m, 2H), 7.85 (d, J = 9.5 Hz, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.58−7.55 (m, 1H), 7.51−7.45 (m, 3H), 7.32 (t, J = 7.0 Hz, 1H), 8.15 (td, J = 8.5 Hz, J = 2.0 Hz, 1H), 6.82 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.62 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0 (d, J = 245.3 Hz), 136.6, 134.6, 132.3, 132.2, 132.1, 130.6 (d, J = 8.2 Hz), 128.7, 127.9, 126.7, 126.6, 123.6, 121.5, 119.9, 119.2, 115.7 (d, J = 21.0 Hz), 115.3 (d, J = 22.6 Hz), 113.6; mp 93−95 °C.



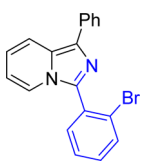
3-(3-Nitrophenyl)-1-phenylimidazo[1,5-a]pyridine (**3q**).[16] Eluent, 10% EtOAc/hexane; 83% yield (51.9 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71(s, 1H), 8.26 (dd, J = 7.0 Hz, J = 5.0 Hz, 2H), 8.22 (d, J = 8.0 Hz, 1H), 7.92 (t, J = 7.5 Hz, 2H), 7.88 (d, J = 9.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 1H), 6.88 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.70 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 135.2, 134.3, 133.7, 132.9, 131.8, 130.0, 128.7, 128.4, 126.9, 126.3, 123.0, 122.3, 121.1, 120.3, 119.3, 114.3; mp 169−171 °C.



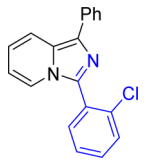
3-(2-Methoxyphenyl)-1-phenylimidazo[1,5-a]pyridine (**3r**).[10] Eluent, 4% EtOAc/hexane; 80% yield (48.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 2H), 7.85 (d, J = 9.5 Hz, 1H), 7.68 (dd, J = 7.5 Hz, J = 1.5 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.47−7.43 (m, 3H), 7.28 (dd, J = 15.0 Hz, J = 5.5 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 6.80 (dd, J = 9.5 Hz, J = 6.5 Hz, 1H), 6.53 (t, J = 6.5 Hz, 1H), 3.79(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 136.1, 135.1, 132.7, 131.3, 130.0, 128.5, 127.3, 126.6, 126.1, 123.4, 121.1, 119.4, 119.0, 118.5, 118.3, 118.2, 111.9, 111.1, 55.4.



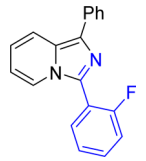
3-(2-Bromophenyl)-1-phenylimidazo[1,5-a]pyridine (**3s**). Eluent, 4% EtOAc/hexane; 61% yield (42.6 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.5 Hz, J = 0.5 Hz, 2H), 7.87 (d, J = 9.5 Hz, 1H), 7.72 (dd, J = 8.0 Hz, J = 0.5 Hz, 1H), 7.62 (dd, J = 7.5 Hz, J = 2.0 Hz, 1H), 7.56 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 8.0 Hz, 3H), 7.37 (td, J = 7.5 Hz, J = 1.5 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 6.83−6.80 (m, 1H), 6.58−6.55 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 134.8, 133.4, 133.0, 131.3, 131.2, 131.0, 128.6, 127.6, 126.9, 126.6, 126.3, 124.2, 122.4, 119.8, 118.7, 112.7; HRMS calcd for $C_{19}H_{14}N_2Br$ [M + H$^+$] 349.0340, found 349.0337.



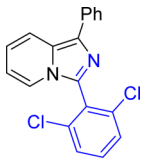
3-(2-Chlorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3t**).[10] Eluent, 4% EtOAc/hexane; 68% yield (40.8 g); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 9.0 Hz, 1H), 7.67 (dd, J = 7.0 Hz, J = 2.0 Hz, 1H), 7.58−7.56 (m, 1H), 7.54 (dd, J = 7.0 Hz, J = 1.0 Hz, 1H), 7.47−7.43 (m, 3H), 7.42−7.39 (m, 1H), 7.29 (t, J = 7.0 Hz, 1H), 6.83 (dd, J = 9.5 Hz, J = 6.5 Hz, 1H), 6.59 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 134.8, 134.2, 133.3, 131.5, 130.7, 129.8, 129.2, 128.6, 127.1, 126.6, 126.4, 122.5, 119.8, 118.7, 112.7; HRMS calcd for $C_{19}H_{14}N_2Cl$ [M + H$^+$] 305.0846, found 305.0834.



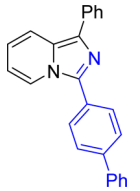
3-(2-Fluorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3u**).[10] Eluent, 4% EtOAc/hexane; 81% yield (46.9 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.5 Hz, J = 1.0 Hz, 2H), 7.87 (d, J = 9.0 Hz, 1H), 7.82 (td, J = 7.5 Hz, J = 1.5 Hz, 1H), 7.77−7.75 (m, 1H), 7.49 (td, J = 7.0 Hz, J = 1.5 Hz, 3H), 7.34−7.28 (m, 2H), 7.26−7.22 (m, 1H), 6.84−6.81 (m, 2H), 6.62−6.59 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0 (d, J = 247.6 Hz), 134.8, 133.3, 132.5, 132.2, 131.0 (d, J = 8.8 Hz), 128.6, 127.8, 126.7, 126.5, 124.9, 122.6 (d, J = 5.8 Hz), 119.9, 118.7, 118.1, 117.9, 116.1 (d, J = 21.0 Hz), 112.9; mp 93−95 °C.



3-(2,6-Dichlorophenyl)-1-phenylimidazo[1,5-a]pyridine (**3v**). Eluent, 4% EtOAc/hexane; 60% yield (40.9 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 9.5 Hz, 1H), 7.48−7.37 (m, 6H), 7.30 (dd, J = 7.5 Hz, J = 7.0 Hz, 1H), 6.88 (dd, J = 8.5 Hz, J = 7.5 Hz, 1H), 6.60 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 134.8, 132.4, 131.6, 128.6, 128.3, 128.2, 126.7, 126.6, 126.4, 121.5, 120.0, 118.9, 113.2; HRMS calcd for $C_{19}H_{13}N_2Cl_2$ [M + H$^+$] 339.0456, found 339.0443.



3-([1,1′-Biphenyl]-4-yl)-1-phenylimidazo[1,5-a]pyridine (**3w**). Eluent, 2% EtOAc/hexane; 62% yield (42.5 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 7.0 Hz, 1H), 7.95 (d, J = 7.5 Hz, 2H), 7.92 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 9.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 7.5 Hz, 2H), 7.48 (t, J = 7.5 Hz, 4H), 7.39 (t, J = 7.5 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 6.79 (dd, J = 9.5 Hz, J = 6.0 Hz, 1H), 6.59 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 140.3, 137.7, 134.8, 132.1, 130.9, 128.8, 128.6, 128.5, 127.7, 127.6, 127.0, 126.7, 126.5, 121.8, 119.7, 119.1, 113.3; HRMS calcd for $C_{25}H_{19}N_2$ [M + H$^+$] 347.1548, found 347.1558.



3-(4′-Methyl-[1,1′-biphenyl]-4-yl)-1-phenylimidazo[1,5-a]-pyridine (**3x**). Eluent, 2% EtOAc/hexane; 63% yield (45.2 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 7.0 Hz, 1H), 7.96−7.94 (m, 2H), 7.91−7.89 (m, 2H), 7.86 (d, J = 9.0 Hz, 1H), 7.75−7.74 (m, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 8.0 Hz, 2H), 7.32 (dd, J = 13.5 Hz, J = 8.0 Hz, 3H), 6.81 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.60−6.57 (m, 1H), 2.41(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 137.5, 129.6, 128.7, 128.5, 127.7, 127.4, 126.88, 126.81, 126.5, 121.8, 119.6, 119.1, 113.2, 21.1; HRMS calcd for $C_{26}H_{21}N_2$ [M + H$^+$] 361.1705, found 361.1703; mp 159−161 °C.

DOI: 10.1021/acs.joc.6b01742
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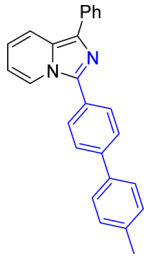
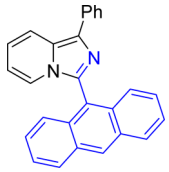
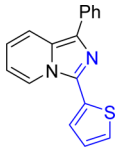


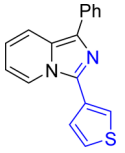
3-(Anthracen-9-yl)-1-phenylimidazo[1,5-a]pyridine (**3y**). Eluent, 10% EtOAc/hexane; 69% yield (50.8 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.09 (dd, J = 7.5 Hz, J = 7.5 Hz, 4H), 8.00 (d, J = 9.5 Hz, 1H), 7.52−7.45 (m, 6H), 7.40−7.37 (m, 2H), 7.32 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 7.0 Hz, 1H), 6.84 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.39 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.1, 131.8, 131.4, 129.4, 128.7, 127.0, 126.9, 126.6, 126.4, 125.6, 125.4, 122.1, 119.9, 118.9, 112.8; HRMS calcd for $C_{27}H_{19}N_2$ [M + H$^+$] 371.1548, found 371.1566; mp 209−211 °C.



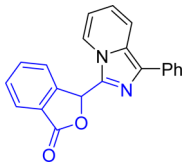
1-Phenyl-3-(thiophen-2-yl)imidazo[1,5-a]pyridine (**3z**). Eluent, 5% EtOAc/hexane; 68% yield (37.8 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 7.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 9.0 Hz, 1H), 7.54 (d, J = 3.5 Hz, 1H), 7.47−7.41 (m, 3H), 7.31 (t, J = 7.5 Hz, 1H), 7.18 (dd, J = 3.5 Hz, J = 3.5 Hz, 1H), 6.79 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.64 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5, 132.5, 132.1, 132.0, 128.6, 127.7, 127.5, 126.8, 126.6, 126.1, 125.2, 121.9, 119.6, 119.0, 113.7; HRMS calcd for $C_{17}H_{13}N_2S$ [M + H$^+$] 277.0799, found 277.0811; mp 87−89 °C.



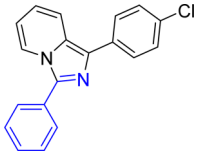
1-Phenyl-3-(thiophen-3-yl)imidazo[1,5-a]pyridine (**3aa**). Eluent, 4% EtOAc/hexane; 89% yield (49.0 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 7.5 Hz, 1H), 7.92 (d, J = 7.0 Hz, 2H), 7.80 (d, J = 9.0 Hz, 1H), 7.72 (d, J = 1.5 Hz, 1H), 7.62 (d, J = 5.0 Hz, 1H), 7.47−7.43 (m, 3H), 7.30 (t, J = 7.0 Hz, 1H), 6.75 (dd, J = 9.5 Hz, J = 6.0 Hz, 1H), 6.57 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 134. 2, 131.5, 130.8, 128.6, 127.4, 127.2, 126.7, 126.4, 126.3, 123.3, 121.7, 119.4, 118.9, 113.3; HRMS calcd for $C_{17}H_{13}N_2S$ [M + H$^+$] 277.0799, found 277.0802; mp 104−106 °C.



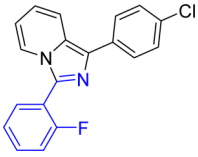
3-(1-Phenylimidazo[1,5-a]pyridin-3-yl)isobenzofuran-1(3H)-one (**3ab**). Eluent, 20% EtOAc/hexane; 63% yield (40.8 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (t, J = 6.5 Hz, 3H), 7.91−7.83 (m, 3H), 7.76 (d, J = 7.5 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 3H), 7.33 (t, J = 7.0 Hz, 1H), 6.90 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.69 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5, 135.0, 130.5, 129.3, 128.5, 128.4, 126.8, 126.5, 126.1, 122.5, 119.0, 118.8, 112.3, 27.9, 25.4, 22.5, 21.8; HRMS calcd for $C_{21}H_{15}N_2O_2$ [M + H$^+$] 327.1134, found 327.1134.



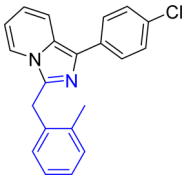
1-(4-Chlorophenyl)-3-phenylimidazo[1,5-a]pyridine (**3ac**). Eluent, 4% EtOAc/hexane; 97% yield (59.5 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 9.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.44−7.38 (m, 3H), 6.77 (dd, J = 9.0 Hz, J = 6.5, 1H), 6.54 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 133.4, 132.4, 131.9, 130.5, 129.8, 128.9, 128.8, 128.7, 128.1, 127.7, 121.7, 120.0, 118.6, 113.2; HRMS calcd for $C_{19}H_{14}N_2Cl$ [M + H$^+$] 305.0846, found 305.0850; mp 177−179 °C.



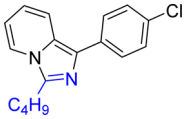
1-(4-Chlorophenyl)-3-(2-fluorophenyl)imidazo[1,5-a]pyridine (**3ad**). Eluent, 4% EtOAc/hexane; 98% yield (64.0 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.5 Hz, 2H), 7.80−7.75 (m, 3H), 7.50−7.45 (m, 1H), 7.42 (d, J = 8.5 Hz, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.26−7.22 (m, 1H), 6.86 (dd, J = 8.5 Hz, J = 7.0, 1H), 6.62 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0 (d, J = 248.1 Hz), 133.5, 133.3, 132.4, 132.0, 131.2 (d, J = 7.8 Hz), 131.0, 128.8, 127.9, 127.7, 124.9, 122.77, 122.73, 120.3, 118.4, 117.9, 117.7, 116.1 (d, J = 21.2 Hz), 113.0; HRMS calcd for $C_{19}H_{13}N_2FCl$ [M + H$^+$] 323.0751, found 323.0739; mp 155−157 °C.



1-(4-Chlorophenyl)-3-(2-methylbenzyl)imidazo[1,5-a]pyridine (**3ae**). Eluent, 4% EtOAc/hexane; 71% yield (47.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 9.5 Hz, 1H), 7.51 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.19 (t, J = 7.5 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 7.5 Hz, 1H), 6.73 (dd, J = 9.5 Hz, J = 6.5 Hz, 1H), 6.46 (t, J = 6.5 Hz, 1H), 4.41 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.6, 136.4, 134.1, 133.6, 131.6, 130.5, 129.0, 128.7, 128.0, 127.5, 126.9, 126.2, 121.3, 119.3, 118.6, 112.6, 31.2, 19.7; HRMS calcd for $C_{21}H_{18}N_2Cl$ [M + H$^+$] 333.1159, found 333.1165.



3-Butyl-1-(4-chlorophenyl)imidazo[1,5-a]pyridine (**3af**). Eluent, 5% EtOAc/hexane; 95% yield (54.0 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79−7.78 (m, 1H), 7.77−7.76 (m, 1H), 7.71 (dd, J = 14.0 Hz, J = 9.5 Hz, 2H), 7.38−7.36 (m, 2H), 6.72 (dd, J = 9.5 Hz, J = 6.0 Hz, 1H), 6.55 (t, J = 6.5 Hz, 1H), 3.01 (t, J = 7.5 Hz, 2H), 1.85−1.79 (m, 2H), 1.50−1.43 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 133.7, 131.5, 128.7, 127.4, 126.4, 121.0, 118.9, 118.6, 112.4, 29.1, 26.3, 22.5, 13.7; HRMS calcd for $C_{17}H_{18}N_2Cl$ [M + H$^+$] 285.1159, found 285.1152; mp 69−71 °C.



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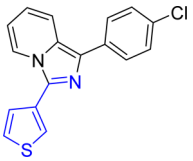
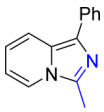
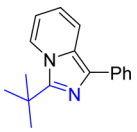
1-(4-Chlorophenyl)-3-(thiophen-3-yl)imidazo[1,5-a]pyridine (***3ag***). Eluent, 4% EtOAc/hexane; 99% yield (61.7 mg); solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 7.5 Hz, 1H), 7.87 (d, J = 8.5 Hz, 2H), 7.78–7.75 (m, 2H), 7.62 (d, J = 5.0 Hz, 1H), 7.51 (dd, J = 4.5 Hz, J = 3.0 Hz, 1H), 7.42 (d, J = 8.5 Hz, 2H), 6.82 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.64 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5, 133.4, 132.0, 130.7, 130.4, 128.8, 127.8, 127.4, 126.5, 123.6, 122.0, 119.9, 118.8, 113.4; HRMS calcd for $C_{17}H_{12}N_2SCl$ [M + H^+] 311.0410, found 311.0401; mp 187–189 °C.



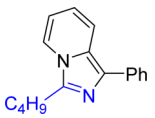
3-Methyl-1-phenylimidazo[1,5-a]pyridine (***4a***).[10] Eluent, 20% EtOAc/hexane; 62% yield (26.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 7.0 Hz, 2H), 7.76 (d, J = 9.0 Hz, 1H), 7.65 (d, J = 7.0 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.27 (t, J = 7.0 Hz, 1H), 6.73 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.58 (t, J = 7.0 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.0, 134.8, 129.8, 128.6, 126.3, 126.1, 120.9, 118.9, 118.6, 112.5, 12.4.



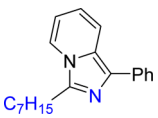
3-(tert-Butyl)-1-phenylimidazo[1,5-a]pyridine (***4b***). Eluent, 5% EtOAc/hexane; 60% yield (30.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 7.0 Hz, 1H), 7.87–7.86 (m, 2H), 7.78 (d, J = 9.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 2H), 7.25 (t, J = 7.0 Hz, 1H), 6.69 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.50 (t, J = 6.5 Hz, 1H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.0, 135.3, 128.6, 126.6, 126.0, 123.1, 119.2, 118.0, 111.6, 33.4, 28.1; HRMS calcd for $C_{17}H_{19}N_2$ [M + H^+] 251.1548, found 251.1539.



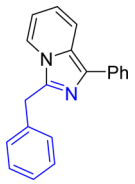
3-Butyl-1-phenylimidazo[1,5-a]pyridine (***4c***).[17] Eluent, 5% EtOAc/hexane; 91% yield (46.1 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86–7.84 (m, 2H), 7.74 (d, J = 9.5 Hz, 1H), 7.69 (d, J = 7.0 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 6.69 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.52 (t, J = 7.5 Hz, 1H), 3.02 (t, J = 7.5 Hz, 2H), 1.85–1.79 (m, 2H), 1.50–1.43 (m, 2H), 0.98 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 135.1, 129.8, 128.5, 126.4, 126.2, 126.0, 120.8, 118.9, 118.4, 112.2, 29.2, 26.4, 22.5, 13.7.



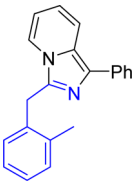
3-Heptyl-1-phenylimidazo[1,5-a]pyridine (***4d***). Eluent, 5% EtOAc/hexane; 83% yield (48.8 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.5 Hz, J = 0.5 Hz, 2H), 7.75 (d, J = 9.0 Hz, 1H), 7.71 (d, J = 7.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 2H), 7.26 (dd, J = 7.5 Hz, J = 7.5 Hz, 1H), 6.70–6.67 (m, 1H), 6.54 (dd, J = 7.5 Hz, J = 7.0 Hz, 1H), 3.02 (t, J = 8.0 Hz, 2H), 1.87 (quin, J = 7.5 Hz, 2H), 1.47–1.41 (m, 2H), 1.38–1.32 (m, 2H), 1.30–1.23 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 135.1, 129.9, 128.6, 126.4, 126.3, 126.0, 120.9, 119.0, 118.5, 112.3, 31.6, 29.4, 28.9, 27.1, 26.7, 22.5, 14.0; HRMS calcd for $C_{20}H_{25}N_2$ [M + H^+] 293.2018, found 293.2021.



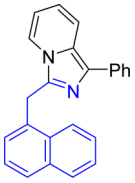
3-Benzyl-1-phenylimidazo[1,5-a]pyridine (***4e***). Eluent, 10% EtOAc/hexane; 88% yield (49.8 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82–7.80 (m, 2H), 7.67 (d, J = 9.5 Hz, 1H), 7.45 (d, J = 7.0 Hz, 1H), 7.37 (dd, J = 8.0 Hz, J = 6.5 Hz, 2H), 7.19–7.16 (m, 3H), 7.12 (d, J = 6.5 Hz, 3H), 6.60–6.56 (m, 1H), 6.36–6.29 (m, 1H), 4.38 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 136.0, 135.0, 132.8, 132.5, 130.9, 130.4, 130.2, 129.8, 128.7, 128.6, 128.2, 126.8, 126.7, 126.4, 126.2, 121.1, 118.96, 118.91, 112.5, 33.5; HRMS calcd for $C_{20}H_{17}N_2$ [M + H^+] 285.1392, found 285.1400.



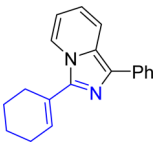
3-(2-Methylbenzyl)-1-phenylimidazo[1,5-a]pyridine (***4f***). Eluent, 8% EtOAc/hexane; 99% yield (58.9 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.5 Hz, 2H), 7.69 (d, J = 9.5 Hz, 1H), 7.39–7.33 (m, 3H), 7.18 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 7.0 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 6.60 (dd, J = 9.5 Hz, J = 6.5 Hz, 1H), 6.33 (t, J = 6.5 Hz, 1H), 4.32 (s, 2H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.4, 136.3, 135.0, 134.2, 130.4, 130.2, 128.6, 128.0, 126.8, 126.7, 126.4, 126.2, 121.1, 118.9, 112.5, 31.2, 19.7; HRMS calcd for $C_{21}H_{19}N_2$ [M + H^+] 299.1548, found 299.1545.



3-(Naphthalen-1-ylmethyl)-1-phenylimidazo[1,5-a]pyridine (***4g***). Eluent, 5% EtOAc/hexane; 62% yield (41.5 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 7.5 Hz, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 9.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.58–7.45 (m, 5H), 7.33–7.27 (m, 2H), 7.02 (d, J = 7.0 Hz, 1H), 6.69 (dd, J = 9.5 Hz, J = 6.0 Hz, 1H), 6.39 (t, J = 6.5 Hz, 1H), 4.93 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.3, 135.0, 133.8, 131.9, 131.7, 130.3, 128.7, 127.7, 126.9, 126.5, 126.4, 126.2, 125.8, 125.7, 125.4, 123.6, 121.4, 119.0, 118.9, 112.6, 31.1; HRMS calcd for $C_{24}H_{19}N_2$ [M + H^+] 335.1548, found 335.1559.



3-(Cyclohex-1-en-1-yl)-1-phenylimidazo[1,5-a]pyridine (***4h***). Eluent, 10% EtOAc/hexane; 87% yield (48.0 mg); semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 7.0 Hz, 1H), 7.87 (d, J = 7.5 Hz, 2H), 7.74 (d, J = 9.0 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.26–7.23 (m, 1H), 6.68 (dd, J = 9.0 Hz, J = 6.5 Hz, 1H), 6.49 (t, J = 7.0 Hz, 1H), 6.27–6.25 (m, 1H), 2.64–2.61 (m, 2H), 2.30–2.27 (m, 2H), 1.86–1.81 (m, 2H), 1.73–1.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 135.0, 130.6, 129.3, 128.5, 126.9, 126.6, 126.1, 122.6, 119.0, 118.8, 112.3, 27.9, 25.4, 22.5, 21.9; HRMS calcd for $C_{19}H_{19}N_2$ [M + H^+] 275.1548, found 275.1559.



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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01742.

Copies of NMR spectra for all compounds and HRMS spectra for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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