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# Synthesis of Imidazo[1,5-*a*]pyridines *via* $I_2$-Mediated $sp^3$ C–H Amination†

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A transition-metal-free $sp^3$ C–H amination reaction has been established for imidazo[1,5-*a*]pyridine synthesis employing molecular iodine from 2-pyridyl ketones and alkylamines. In the presence of sodium acetate (NaOAc), $I_2$-mediated oxidative annulations of readily available substrates produced a variety of imidazo[1,5-*a*]pyridine derivatives efficiently in a one-pot manner. The present synthetic approach is operationally simple and can be conveniently carried out on a gram scale. Moreover, under the optimal reaction conditions a series of 1-(2-pyridyl)imidazo[1,5-*a*]pyridine cysteine protease inhibitors were easily prepared from corresponding di-2-pyridyl ketones and substituted benzylamines in satisfactory yields.

## Introduction

In the past decade, interest in direct C–H amination has increased significantly[1] owing to its high atom- and step-economy in C–N bond formation. In particular, more challenging $sp^3$ C–H amination reactions were also successfully achieved in the presence of Cu or Pd catalysts.[1d, 2] However, such transformations under transition-metal-free conditions only rarely investigated. In 2009, Fan *et al.*[3] reported $PhI(OAc)_2/I_2$-mediated intermolecular amination of $sp^3$ C–H bonds with sulfonamides. Later, Wang[4] and Li[5] groups described imidazo[1,5-*a*]pyridine and quinazolinone synthesis using *tert*-butyl peroxide reagents, respectively. In 2015, Park and co-workers[6] developed an NIS-promoted imidazo[1,2-*a*]pyridine synthesis from 2-phenylacetaldehydes. We recently discovered a $KI/I_2$-mediated $sp^3$ C–H amination reaction of alkyl ketone hydrazones to produce 1*H*-pyrazoles.[7]

Imidazo[1,5-*a*]pyridines are prevalent in many biologically active compounds[8] and fluorescence probes,[9] and also have applications in organic synthesis as substrates or ligands.[10] Therefore, considerable efforts have been dedicated to the synthesis of this compound class.[11] Classical synthetic methods include dehydrative,[12] desulfurative[13] and oxidative[14] cyclization of 2-pyridinylmethylamine derivatives (with carbonyl compounds) in the intra-/intermolecular manners. Imidazo[1,5-*a*]pyridine derivatives can also be prepared via decarboxylative cyclization of α-amino acids with 2-pyridyl ketones/aldehydes or their variants.[15] Moreover, annulations of readily accessible alkylamines with 2-pyridyl carbonyl compounds are one of most straightforward strategies for the construction of this heterocyclic system. Such reactions were previously accomplished by NIS/TBHP-mediated[4] and Cu-catalyzed aerobic[16] oxidative $sp^3$ C–H amination. As a continuation of our research interest in $I_2$-mediated C–H functionalization,[7, 17] herein we describe a facile and one-pot synthetic approach via this strategy under transition-metal-free conditions.

## Results and discussion

Initial solvent screening (Table 1, entries 1–7) demonstrated that both toluene and 1,2-dichloroethane (DCE) are ideal media for this transformation. In the presence of NaOAc as base, $I_2$-mediated oxidative annulation of 2-benzoylpyridine (**2a**) and benzylamine (**3a**) produced the desired product **1a** in excellent yields in both solvents. The structure of imidazo[1,5-*a*]pyridine **1a** was further confirmed by X-ray crystallography.[18] Considering the broader substrate scope in DCE (cf. Scheme 1), it was chosen for further optimization of the reaction conditions. The complete consumption of ketone **2a** requires 1.1 equiv of benzylamine (entries 7–9) and 1.2 equiv of iodine (entries 7, 10–11). The yield was significantly decreased when using oxidants such as NBS, TBHP, $H_2O_2$, DDQ, CAN and $O_2$ in the presence of a catalytic amount of iodine (entries 12–17). Base screening suggested that NaOAc is the optimal one for this reaction. Utilizing $NaHCO_3$ as the base slightly affected the formation of **1a** (entry 18); while with stronger base (e.g. $K_2CO_3$), the yield of the product was dramatically decreased (entry 19). In the presence of DBU, only a trace amount of the product was formed, which could be due the interaction between iodine with the nitrogen atoms of this amidine base.[19] In addition, the synthesis of product **1a** was successfully conducted on a gram scale under the optimum oxidative annulation conditions (entry 7).

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†Electronic Supplementary Information (ESI) available: Copies of $^1H$ and $^{13}C$ NMR spectra of products **1**. See DOI: 10.1039/x0xx00000x

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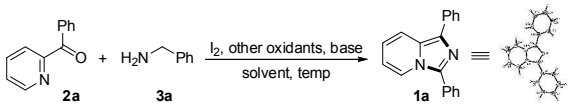
**Table 1.** Optimization of the Reaction Conditions for the Synthesis of Imidazo[1,5-*a*]pyridine **1a**[a]




| entry | 3a (equiv) | $I_2$ (equiv) | other oxidants[b] | base | solvent | temp. | time (h) | yield (%)[c] |
|---|---|---|---|---|---|---|---|---|
| **1** | 1.1 | 1.2 | – | NaOAc | EtOH | reflux | 20 | 30 |
| **2** | 1.1 | 1.2 | — | NaOAc | DMF | 110 °C | 20 | 29 |
| **3** | 1.1 | 1.2 | — | NaOAc | toluene | reflux | 6 | 99 |
| **4** | 1.1 | 1.2 | — | NaOAc | MeCN | reflux | 12 | 51 |
| **5** | 1.1 | 1.2 | — | NaOAc | 1,4-dioxane | reflux | 12 | 11 |
| **6** | 1.1 | 1.2 | — | NaOAc | DMSO | 110 °C | 12 | 8 |
| **7** | **1.1** | **1.2** | — | **NaOAc** | **DCE** | **reflux** | **6** | **99 (98)**[d] |
| **8** | 1.0 | 1.2 | — | NaOAc | DCE | reflux | 10 | 91 |
| **9** | 1.2 | 1.2 | — | NaOAc | DCE | reflux | 6 | 99 |
| **10** | 1.1 | 1.0 | — | NaOAc | DCE | reflux | 10 | 89 |
| **11** | 1.1 | 1.4 | — | NaOAc | DCE | reflux | 7 | 98 |
| **12** | 1.1 | 0.2 | NBS | NaOAc | DCE | reflux | 12 | 21 |
| **13** | 1.1 | 0.2 | TBHP | NaOAc | DCE | reflux | 12 | 0 |
| **14** | 1.1 | 0.2 | $H_2O_2$ | NaOAc | DCE | reflux | 12 | 11 |
| **15** | 1.1 | 0.2 | DDQ | NaOAc | DCE | reflux | 12 | trace |
| **16** | 1.1 | 0.2 | CAN | NaOAc | DCE | reflux | 12 | 0 |
| **17** | 1.1 | 0.2 | O2 | NaOAc | DCE | reflux | 12 | 27 |
| **18** | 1.1 | 1.2 | — | $NaHCO_3$ | DCE | reflux | 7 | 95 |
| **19** | 1.1 | 1.2 | — | $K_2CO_3$ | DCE | reflux | 20 | 13 |
| **20** | 1.1 | 1.2 | — | DBU | DCE | reflux | 24 | trace |

[a]Optimal reaction conditions (entry 7): **2a** (0.5 mmol), **3a** (0.55 mmol), $I_2$ (0.6 mmol), NaOAc (1.5 mmol), DCE (5 mL), reflux. [b]Isolated yields. [c]The yield of gram-scale synthesis.

With the optimal reaction conditions (Table 1, entry 7) in hand, we set out to investigate the substrate scope and generality of this synthetic method. As shown in Scheme 1, this reaction tolerates a range of *ortho*-, *meta*-, *para*- and di-substituents on the aromatic ring of benzylamines 3. All these substrates were all smoothly transformed into the expected imidazo[1,5-*a*]pyridines (**1a**–**j**) though the $I_2$-mediated annulations with 2-benzoylpyridine (**2a**) efficiently. α-Naphthyl, 2-pyridyl, and 2-furyl substituted products (**1k**–**m**) were also synthesized from the corresponding amines in high yields. *n*-Butylamine and 2-phenylethylamine failed to produce the desired products (**1n**–**o**). This could be due to the presence of β-hydrogens at the $R^3$ group which may cause β-elimination of the iodide intermediate.[20] On the other hand, 2,2,2-trifluoroethylamine was successfully converted into the expected 3-trifluoromethyl imidazo[1,5-*a*]pyridine **1p** in a satisfactory yield.

To further explore the reaction scope, a variety of 2-pyridyl ketone derivatives (**2**) were subjected to the above annulations conditions (Scheme 2). To our delight, the present synthetic approach is compatible with both electron-donating groups (EDGs) and electron-withdrawing groups (EWGs) on either the pyridine or the benzene rings of the diaryl ketones (**1q**–**r** and **1t**–**z**). Besides, this protocol is also amenable to the 2-benzoylquinoline substrate (**1s**). Replacement of aromatic ring at $R^2$ position with aliphatic groups led to 1-alkyl imidazo[1,5-*a*]pyridines (**1aa**–**ac**). Decreased stability of the corresponding imine intermediates[20] could be responsible for the lower yields of 1-alkyl substituted products **1ab**–**ac**. No desired product **1ad** was obtained from the reaction of pyridyl isopropyl ketone with benzylamine under the standard cyclization conditions possibly attributed to the steric hindrance effect of the isopropyl group. Furthermore, the annulations of di-2-pyridyl ketones with substituted benzylamines produced a series of 1-(2-pyridyl)imidazo[1,5-

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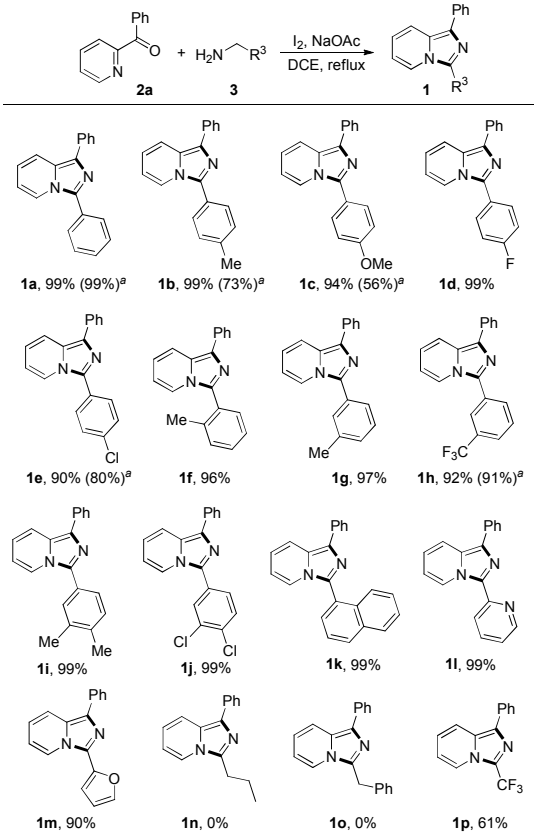
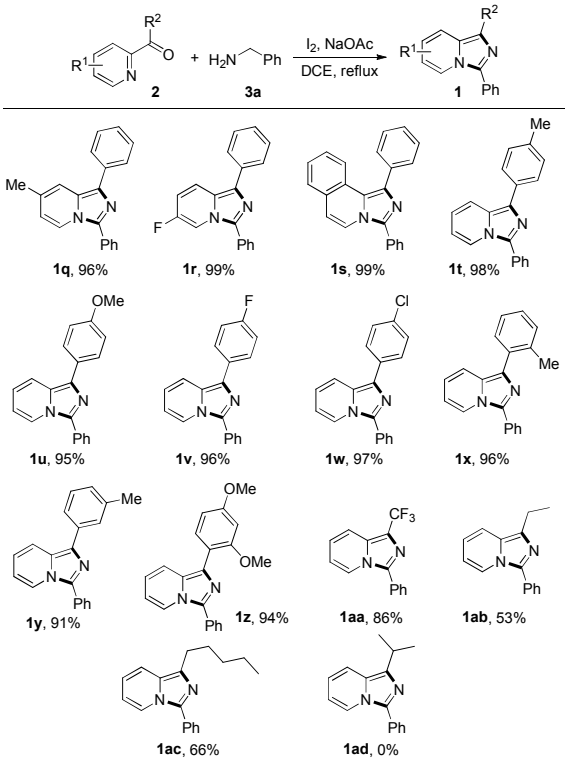
*a*]pyridine cysteine protease inhibitors[8b] (**1ae**–**ah**) (Scheme 3). It is worth to mention that good functional group tolerance allows the preparation of the product containing a phenolic hydroxyl group (**1ag**).

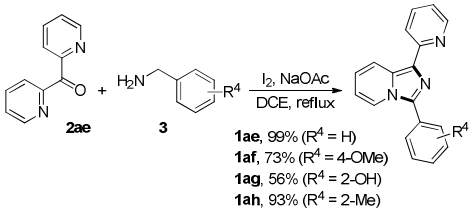
On the basis of the experimental results along with the previous work,[7, 16a, 16b] a tentative mechanism for the formation of imidazo[1,5-*a*]pyridines via iodine-mediated $sp^3$ C–H amination is proposed (Scheme 4). Firstly, the condensation of substrates **2** and **3** generates an imine intermediate **A**. Then, the base-promoted iodination of imine **A** produces a plausible iodio species **B**. Subsequently, the C–I bond in iodide **B** is cleaved with intramolecular rearrangement to give intermediate **C**. Finally, base-promoted deprotonation yields the imidazo[1,5-*a*]pyridine framework **1**.



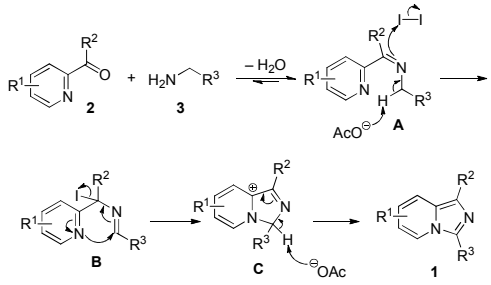

**Scheme 1.** Scope of amines **3**. Reaction conditions: **2a** (0.5 mmol), **3** (0.55 mmol), $I_2$ (0.6 mmol), NaOAc (1.5 mmol), DCE (5 mL), reflux (isolated yields are given). [a]The yields of the reactions performed in toluene.




**Scheme 2.** Scope of ketones **2**. Reaction conditions: **2** (0.5 mmol), **3a** (0.55 mmol), $I_2$ (0.6 mmol), NaOAc (1.5 mmol), DCE (5 mL), reflux (isolated yields are given).




**Scheme 3.** Synthesis of 1-(2-pyridyl)imidazo[1,5-*a*]pyridine cysteine protease inhibitors (**1ae**–**1af**).




**Scheme 4.** Proposed reaction mechanism.

## Experimental section

**General Information.** $^1$H and $^{13}$C NMR spectra were recorded on a 400 MHz (100 MHz for $^{13}$CNMR) spectrometer. Chemical shift values are given in ppm (parts per million) with reference to tetramethylsilane (TMS) as an internal standard. The peak

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patterns are as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined on a micromelting point apparatus and are uncorrected. High-resolution mass spectra (HRMS) were obtained on a Q-TOF Mass Spectrometer equipped with an electrospray ion source (ESI), operated in the positive mode. Flash column chromatography was performed over silica gel 200–300 mesh, and the eluent was a mixture of ethyl acetate (EtOAc) and petroleum ether (PE). 1,2-Dichloromethane (DCE) was analytical reagent grade and used without any pretreatment.

**General Procedure for Synthesis of Imidazo[1,5-*a*]pyridines 1.** A mixture of ketone **2** (0.5 mmol) and amine **3** (0.55 mmol) in DCE (5 mL) was treated with molecular iodine (153 mg, 0.6 mmol) and NaOAc (123 mg, 1.5 mmol) in sequence, and then stirred at the reflux temperature for the time indicated below. Upon complete consumption of the ketone **2** (monitored by TLC), the reaction was allowed to cool room temperature, quenched with 5% $Na_2S_2O_3$ (5 mL) and $H_2O$ (15 mL), and extracted with $CH_2Cl_2$ (10 mL x 3). The combined organic layer was dried over anhydrous $Na_2SO_4$, concentrated, and purified through silica gel column chromatography using a mixture of EtOAc and PE as eluent to afford the corresponding product **1**.

**1,3-Diphenylimidazo[1,5-*a*]pyridine (1a).** 5.5 h; eluent: EtOAc/PE 15:85; yield: 134 mg, 99%; yellow solid, mp 114-116 ºC (lit.[16b] mp 110-111 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.24 (dt, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.95-7.93 (m, 2H), 7.85-7.83 (m, 3H), 7.56-7.52 (m, 2H), 7.49-7.43 (m, 3H), 7.32-7.28 (m, 1H), 6.80-6.76 (m, 1H), 6.59-6.55 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 138.1, 134.9, 132.0, 130.2, 129.0, 128.9, 128.7, 128.4, 127.7, 126.8, 126.6, 121.8, 119.7, 119.2, 113.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{15}N_2$, 271.1230, found 271.1231.

**1-Phenyl-3-(*p*-tolyl)imidazo[1,5-*a*]pyridine (1b).** 2 h; eluent: EtOAc/PE 15:85; yield: 141 mg, 99%; yellow solid, mp 136-138 ºC (lit.[16b] mp 137-138 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.20 (d, *J* = 7.2 Hz, 1H), 7.95-7.93 (m, 2H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 6.77-6.73 (m, 1H), 6.56-6.52 (m, 1H), 2.43 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 138.9, 138.3, 135.0, 131.8, 129.7, 128.7, 128.3, 127.5, 127.3, 126.8, 126.5, 121.9, 119.6, 119.1, 113.1, 21.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1381.

**3-(4-Methoxyphenyl)-1-phenylimidazo[1,5-*a*]pyridine (1c).** 7 h; eluent: EtOAc/PE 15:85; yield: 141 mg, 94%; yellow solid, mp 161-162 ºC (lit.[16b] mp 161-162 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.16 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.83 (d, *J* = 9.2 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.78-6.75 (m, 1H), 6.55 (t, *J* = 6.8 Hz, 1H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 160.1, 138.1, 135.1, 131.7, 129.8, 128.7, 127.4, 126.8, 126.4, 122.7, 121.8, 119.4, 119.1, 114.5, 113.0, 55.4; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2O$, 301.1335, found 301.1335.

**3-(4-Fluorophenyl)-1-phenylimidazo[1,5-*a*]pyridine (1d).** 4h; eluent: EtOAc/PE 15:85; yield: 143 mg, 99%; yellow solid, mp 166-167 ºC (lit.[16b] mp 167-168 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.15 (d, *J* = 7.2 Hz, 1H), 7.94-7.91 (m, 2H), 7.85-7.79 (m, 3H), 7.49-7.45 (m, 2H), 7.32-7.28 (m, 1H), 7.25-7.21 (m, 2H, overlapped with the peak of chloroform), 6.81-6.77 (m, 1H), 6.60-6.57 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 162.9 (d, $J_{C-F}$ = 247.5 Hz), 137.2, 134.9, 132.0, 130.3, 130.2, 128.8, 127.6, 126.8, 126.6, 126.4 (d, $J_{C-F}$ = 3.3 Hz), 121.5, 119.7, 119.2, 116.2 (d, $J_{C-F}$ = 21.6 Hz), 113.4. HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{14}FN_2$, 289.1136, found 289.1133.

**3-(4-Chlorophenyl)-1-phenylimidazo[1,5-*a*]pyridine (1e).**[16b] 6 h; eluent: EtOAc/PE 15:85; yield: 137 mg, 90%; yellow solid, mp 180-181 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.18 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.84 (d, *J* = 9.2 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.52-7.45 (m, 4H), 7.31 (t, *J* = 7.2 Hz, 1H), 6.82-6.78 (m, 1H), 6.60 (t, *J* = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 136.9, 134.8, 134.7, 132.3, 129.5, 129.3, 128.8, 128.7, 127.9, 126.8, 126.7, 121.6, 119.9, 119.3, 113.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{14}ClN_2$, 305.0840, found 305.0841.

**1-Phenyl-3-(*o*-tolyl)imidazo[1,5-*a*]pyridine (1f).**[16b] 4.5 h; eluent: EtOAc/PE 15:85; yield: 136 mg, 96%; yellow solid, mp 104-105 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98-7.96 (m, 2H), 7.87 (d, *J* = 9.2 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.51-7.44 (m, 3H), 7.41-7.27 (m, 4H), 6.82-6.78 (m, 1H), 6.55-6.51 (m, 1H), 2.26 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 138.6, 137.8, 135.2, 131.1, 130.8, 130.7, 129.6, 129.3, 128.7, 126.7, 126.6, 126.4, 126.1, 122.0, 119.6, 119.0, 112.8, 19.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1383.

**1-Phenyl-3-(*m*-tolyl)imidazo[1,5-*a*]pyridine (1g).**[16b] 5 h; eluent: EtOAc/PE 10:90; yield: 138 mg, 97%; yellow solid, mp 84-86 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.24 (d, *J* = 7.2 Hz, 1H), 7.95-7.93 (m, 2H), 7.83 (d, *J* = 9.2 Hz, 1H), 7.68 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.49-7.40 (m, 3H), 7.32-7.25 (m, 2H, overlapped with the peak of chloroform), 6.80-6.76 (m, 1H), 6.58-6.55 (m, 1H), 2.45 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 138.9, 138.3, 135.0, 131.9, 130.0, 129.7, 129.3, 128.8, 128.7, 127.6, 126.9, 126.5, 125.1, 121.9, 119.7, 119.2, 113.2, 21.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$ 285.1386, found 285.1384.

**1-Phenyl-3-(3-(trifluoromethyl) phenyl) imidazo[1,5-*a*]pyridine (1h).** 5.5 h; eluent: EtOAc/PE 15:85; yield: 155 mg, 92%; yellow solid, mp 98-99 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.22 (d, *J* = 7.2 Hz, 1H), 8.14 (s, 1H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.94-7.92 (m, 2H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.71-7.64 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 6.86-6.82 (m, 1H), 6.67-6.64 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 136.4, 134.6, 132.7, 131.6 (q, $J_{C-F}$ = 32.4 Hz), 131.2, 131.1, 129.6, 128.8, 128.1, 126.9, 126.8, 125.3 (q, $J_{C-F}$ = 3.8 Hz), 125.1 (q, $J_{C-F}$ = 3.8 Hz), 123.91 (q, $J_{C-F}$ = 271.0 Hz, partially overlapped with other peaks), 121.3, 120.1, 119.4, 113.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{14}F_3N_2$, 339.1104, found 339.1096.

**3-(3,4-Dimethylphenyl)-1-phenylimidazo[1,5-*a*]pyridine (1i).** 2 h; eluent: EtOAc/PE 15:85; yield: 156 mg, 80%; yellow solid, mp 106-107 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.22 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 2H), 7.82 (d, *J* = 9.2 Hz, 1H),7.63 (s, 1H), 7.55-7.53 (m, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.31-7.28 (m, 2H), 6.78-6.74 (m, 1H), 6.55 (t, *J* = 6.8 Hz, 1H), 2.35 (d, *J* = 4.0 Hz, 6H ); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 138.5, 137.6, 137.5, 135.1, 131.8, 130.1, 129.7, 128.7, 127.7, 127.5, 126.8, 126.4, 125.4,

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122.0, 119.5, 119.1, 113.0, 19.9, 19.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{21}H_{19}N_2$, 299.1543, found 299.1543.

**3-(3,4-Dichlorophenyl)-1-phenylimidazo[1,5-*a*]pyridine (1j).** 1 h; eluent: $CH_2Cl_2$/PE 70:30; yield: 185 mg, 94%; yellow solid, mp 168-169 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.20 (d, $J$ = 7.2 Hz, 1H), 7.98 (d, $J$ = 1.6 Hz, 1H), 7.91 (d, $J$ = 7.6 Hz, 2H), 7.86 (d, $J$ = 9.6 Hz, 1H), 7.71-7.69 (m, 1H), 7.61-7.59 (m, 1H), 7.48 (t, $J$ = 7.6 Hz, 2H), 7.32 (t, $J$ = 7.6 Hz, 1H), 6.86-6.82 (m, 1H), 6.66 (t, $J$ = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 135.6, 134.6, 133.4, 132.74, 132.69, 131.0, 130.2, 129.9, 128.8, 128.2, 127.0, 126.9, 121.4, 120.1, 119.4, 114.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{13}Cl_2N_2$, 339.0450, found 339.0454.

**3-(Naphthalen-1-yl)-1-phenylimidazo[1,5-*a*]pyridine (1k).** 6 h; eluent: EtOAc/PE 15:85; yield: 159 mg, 99%; yellow solid, mp 119-120 ºC (lit.[16b] mp 123-124 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03-8.00 (m, 3H), 7.96-7.91 (m, 2H), 7.80 (dd, $J$ = 8.0, 0.8 Hz, 1H), 7.75 (d, $J$ = 8.0 Hz, 1H), 7.65-7.60 (m, 2H), 7.55-7.45 (m, 4H), 7.31 (t, $J$ = 7.6 Hz, 1H), 6.84-6.80 (m, 1H), 6.50-6.47 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 136.9, 135.1, 134.0, 132.0, 131.7, 130.1, 129.0, 128.8, 128.6, 127.23, 127.20, 127.1, 126.8, 126.5, 126.4, 125.6, 125.5, 122.3, 119.9, 119.0, 112.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{23}H_{17}N_2$, 321.1386, found 321.1385.

**1-Phenyl-3-(pyridin-2-yl)imidazo[1,5-*a*]pyridine (1l).** 2 h; eluent: EtOAc/PE 25:75; yield: 135 mg, 99%; yellow solid, mp 96-98 ºC (lit.[16b] mp 100-101 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 10.01 (d, $J$ = 7.6 Hz, 1H), 8.64 (d, $J$ = 4.8 Hz, 1H), 8.50 (d, $J$ = 8.0 Hz, 1H), 7.97 (d, $J$ = 8.0 Hz, 2H), 7.89 (d, $J$ = 9.2 Hz, 1H), 7.81-7.76 (m, 1H), 7.49 (t, $J$ = 7.6 Hz, 2H), 7.32 (t, $J$ = 7.6 Hz, 1H), 7.21-7.18 (m, 1H), 6.94-6.90 (m, 1H), 6.75 (t, $J$ = 7.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 151.0, 148.1, 136.5, 134.9, 134.8, 132.2, 129.2, 128.8, 127.0, 126.8, 126.4, 122.3, 121.7, 121.1, 118.4, 113.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{14}N_3$, 272.1182, found 272.1184.

**3-(Furan-2-yl)-1-phenylimidazo[1,5-*a*]pyridine (1m).** 2 h; eluent: $CH_2Cl_2$/PE 50:50; yield: 112 mg, 86%; yellow solid, mp 124-126 ºC (lit.[16b] mp 123-124 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.66 (d, $J$ = 7.2 Hz, 1H), 7.91 (d, $J$ = 7.6 Hz, 2H), 7.83 (d, $J$ = 9.2 Hz, 1H), 7.60 (m, 1H), 7.47 (t, $J$ = 7.6 Hz, 2H), 7.31 (t, $J$ = 7.6 Hz, 1H), 7.10 (d, $J$ = 2.8 Hz, 1H), 6.84-6.80 (m, 1H), 6.68 (t, $J$ = 6.8 Hz, 1H), 6.61-6.60 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 146.1, 142.2, 134.5, 132.3, 130.1, 128.8, 127.4, 127.0, 126.8, 123.3, 120.0, 119.0, 113.9, 111.8, 108.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{17}H_{13}N_2O$, 261.1022, found 261.1026.

**1-Phenyl-3-(trifluoromethyl)imidazo[1,5-*a*]pyridine (1p).** 5 h; eluent: EtOAc/PE 15:85; yield: 80 mg, 61%; yellow solid, mp 89-90 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.15 (d, $J$ = 7.2 Hz, 1H), 7.91 (d, $J$ = 9.2 Hz, 1H), 7.86 (d, $J$ = 7.6 Hz, 2H), 7.48 (t, $J$ = 7.6 Hz, 2H), 7.35 (t, $J$ = 7.2 Hz, 1H), 7.01-6.97 (m, 1H), 6.82 (t, $J$ = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 133.7, 132.2, 129.0, 128.9, 127.4, 127.1, 125.4, 122.3 (d, $J_{C-F}$ = 3.3 Hz), 121.6, 119.9 (d, $J_{C-F}$ = 266.7 Hz), 119.1, 115.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{14}H_{10}F_3N_2$, 263.0791, found 263.0792.

**7-Methyl-1,3-diphenylimidazo[1,5-*a*]pyridine (1q).** 3.5 h; eluent: EtOAc/PE 15:85; yield: 137 mg, 96%; yellow solid, mp 125-127 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.15 (d, $J$ = 7.2 Hz, 1H), 7.99 (d, $J$ = 8.0 Hz, 2H), 7.82 (d, $J$ = 7.6 Hz, 2H), 7.59 (s, 1H), 7.52 (t, $J$ = 7.6 Hz, 2H), 7.48-7.41 (m, 3H), 7.30-7.25 (m, 1H, overlapped with the peak of chloroform), 6.41 (d, $J$ = 7.2 Hz, 1H) , 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 137.6, 135.3, 130.4, 130.35, 130.2, 129.0, 128.7, 128.6, 128.2, 128.1, 126.7, 126.2, 121.3, 116.7, 116.1, 21.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1386.

**7-Fluoro-1,3-diphenylimidazo[1,5-*a*]pyridine (1r).** 3 h; eluent: EtOAc/PE 15:85; yield: 143 mg, 99%; yellow solid, mp 98-100 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.15 (d, $J$ = 3.6 Hz, 1H), 7.90 (d, $J$ = 7.6 Hz, 2H), 7.83-7.80 (m, 3H), 7.55 (t, $J$ = 7.6 Hz, 2H), 7.47 (t, $J$ = 7.6 Hz, 3H), 7.33 (t, $J$ = 7.6 Hz, 1H), 6.76-6.71 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 154.3 (d, $J_{C-F}$ = 238.2 Hz), 139.0 (d, $J_{C-F}$ = 2.8 Hz), 134.5, 133.7, 129.8, 129.2, 129.1, 128.8, 128.1, 127.0, 126.9, 126.0, 120.3 (d, $J_{C-F}$ = 9.8 Hz), 112.7 (d, $J_{C-F}$ = 27.3 Hz), 107.6 (d, $J_{C-F}$ = 41.4 Hz); HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{14}FN_2$, 289.1136, found 289.1136.

**1,3-Diphenylimidazo[5,1-*a*]isoquinoline (1s).** 3 h; eluent: EtOAc/PE 15:85; yield: 159 mg, 99%; yellow solid, mp 156-159 ºC; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.07 (d, $J$ = 8.0 Hz, 1H), 7.99 (d, $J$ = 7.2 Hz, 1H), 7.82 (d, $J$ = 7.6 Hz, 2H), 7.79 (d, $J$ = 7.2 Hz, 2H), 7.55-7.41 (m, 7H), 7.36 (t, $J$ = 7.6 Hz, 1H), 7.29 (t, $J$ = 8.0 Hz, 1H), 6.77 (d, $J$ = 7.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 140.4, 136.4, 135,6, 129.9, 129.8, 129.1, 129.0, 128.9, 128.6, 128.0, 127.8, 127.7, 127.1, 126.8, 125.8, 124.1, 122.7, 120.8, 114.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{23}H_{17}N_2$, 321.1386, found 321.1380.

**3-Phenyl-1-(*p*-tolyl)imidazo[1,5-*a*]pyridine (1t).** 2 h; eluent: EtOAc/PE 15:85; yield: 139 mg, 98%; yellow solid, mp 126-127 ºC (lit.[16b] mp 123-124 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.21 (d, $J$ = 7.2 Hz, 1H), 7.84-7.80 (m, 5H), 7.53 (t, $J$ = 7.6 Hz, 2H), 7.44 (t, $J$ = 7.2 Hz, 1H), 7.28 (d, $J$ = 7.6 Hz, 2H), 6.77-6.73 (m, 1H), 6.54 (t, $J$ = 6.8 Hz, 1H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 137.9, 136.3, 132.13, 132.07, 130.2, 129.5, 129.0, 128.8, 128.4, 127.4, 126.8, 121.7, 119.4, 119.3, 113.2, 21.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1385.

**1-(4-Methoxyphenyl)-3-phenylimidazo[1,5-*a*]pyridine (1u).**[16b] 2 h; eluent: EtOAc/PE 15:85; yield: 143 mg, 95%; yellow solid, mp 86-87 ºC; $^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 8.21 (d, $J$ = 7.2 Hz, 1H), 7.88-7.82 (m, 4H), 7.78 (d, $J$ = 9.2 Hz, 1H), 7.53 (t, $J$ = 7.6 Hz, 2H), 7.44 (t, $J$ = 7.2 Hz, 1H), 7.04-7.00 (m, 2H), 6.76-6.72 (m, 1H), 6.54 (t, $J$ = 7.2 Hz, 1H), 3.86 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 158.6, 137.8, 132.0, 130.2, 129.0, 128.8, 128.3, 128.1, 127.7, 127.1, 121.6, 119.2, 114.2, 113.2, 55.4; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2O$, 301.1335, found 301.1337.

**1-(4-Fluorophenyl)-3-phenylimidazo[1,5-*a*]pyridine (1v).** 3 h; eluent: EtOAc/PE 15:85; yield: 139 mg, 96%; yellow solid, mp 134-135 ºC (lit.[10a] mp 134.5-135 ºC); $^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 8.24 (d, $J$ = 7.2 Hz, 1H), 7.91-7.87 (m, 2H), 7.84-7.82 (m, 2H), 7.77 (d, $J$ = 9.2 Hz, 1H), 7.54 (t, $J$ = 7.6 Hz, 2H), 7.47-7.44 (m, 1H), 7.18-7.14 (m, 2H), 6.81-6.77 (m, 1H), 6.59-6.56 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 161.8 (d, $J_{C-F}$ = 243.9 Hz), 138.1, 131.14, 131.12 130.1, 129.1, 128.9, 128.4, 128.3, 127.4, 121.8, 119.8, 118.9, 115.7 (d, $J_{C-F}$ = 21.3 Hz), 113.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{14}FN_2$, 289.1136, found 289.1132.

**1-(4-Chlorophenyl)-3-phenylimidazo[1,5-*a*]pyridine (1w).** 4.5 h; eluent: EtOAc/PE 15:85; yield: 148 mg, 97%; yellow solid, mp 177-179 ºC (lit.[11e] mp 177-179 ºC); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.24 (d, $J$ = 7.2 Hz, 1H), 7.89-7.86 (m, 2H), 7.83-7.78

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(m, 3H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.48-7.45 (m, 1H), 7.44-7.41 (m, 2H), 6.84-6.80 (m, 1H), 6.61-6.57 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 138.3, 133.5, 132.1, 130.7, 130.0, 129.1, 129.0, 128.9, 128.4, 127.9, 127.8, 121.9, 120.2, 118.9, 113.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{14}ClN_2$, 305.0840, found 305.0840.

**3-Phenyl-1-(*o*-tolyl)imidazo[1,5-*a*]pyridine (1x).** 3 h; eluent: EtOAc/PE 15:85; yield: 137 mg, 96%; yellow solid, mp 121-123 ºC (lit.[16b] mp 121-122 ºC); $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.28 (d, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.54-7.49 (m, 3H), 7.45-7.41 (m, 2H), 7.34-7.32 (m, 1H), 7.29-7.25 (m, 2H, overlapped with the peak of chloroform), 6.73-6.69 (m, 1H), 6.57 (t, *J* = 6.8 Hz, 1H), 2.46 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 137.42, 137.40, 133.6, 132.8, 130.8, 130.43, 130.38, 129.0, 128.6, 128.5, 128.1, 127.4, 125.6, 121.5, 119.2, 118.9, 113.2, 20.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1385.

**3-Phenyl-1-(*m*-tolyl)imidazo[1,5-*a*]pyridine (1y).**[16b] 3.5 h; eluent: EtOAc/PE 15:85; yield: 129 mg, 91%; yellow solid, mp 119-121 ºC; $^1$HNMR (400 MHz, $CDCl_3$): *δ* 8.22 (d, *J* = 7.2 Hz, 1H), 7.85-7.79 (m, 4H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 6.79-6.75 (m, 1H), 6.56 (t, *J* = 7.2 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 138.4, 138.1, 134.9, 132.2, 130.2, 129.0, 128.8, 128.6, 128.4, 127.7, 127.6, 127.4, 123.8, 121.8, 119.6, 119.3, 113.2, 21.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{17}N_2$, 285.1386, found 285.1384.

**1-(2,4-Dimethoxyphenyl)-3-phenylimidazo[1,5-*a*]pyridine (1z).** 1.5 h; eluent: EtOAc/PE 15:85; yield: 155 mg, 94%; yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.20 (d, *J* = 7.2 Hz, 1H), 7.84-7.82 (m, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.53-7.48 (m, 3H), 7.43-7.39 (m, 1H), 6.69-6.60 (m, 3H), 6.54-6.50 (m, 1H), 3.86-3.85 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 160.3, 157.5, 137.9, 132.2, 130.5, 129.2, 128.9, 128.5, 128.4, 128.3, 121.3, 120.7, 118.1, 116.9, 113.0, 105.0, 98.9, 55.51, 55.50; HRMS (m/z) $[M + H]^+$ calcd for $C_{21}H_{19}N_2O$, 331.1441, found 331.1446.

**3-Phenyl-1-(trifluoromethyl)imidazo[1,5-*a*]pyridine (1aa).**[12d] 5 h; eluent: $CH_2Cl_2$/PE 40:60; yield: 113 mg, 86%; yellow solid, mp 70-72 ºC; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.27 (d, *J* = 8.0 Hz, 1H), 7.79-7.77 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.57-7.47 (m, 3H), 7.02-6.98 (m, 1H), 6.71 (t, *J* = 8.0 Hz ,1H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 138.8, 129.9 (d, $J_{C-F}$ = 2.2 Hz), 129.6, 129.1, 129.0, 128.5, 122.9 (q, $J_{C-F}$ = 26.5 Hz), 122.3 ($J_{C-F}$ = 40.7 Hz), 120.5 (d, $J_{C-F}$ = 38.9 Hz), 117.8, 117.7, 113.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{14}H_9F_3N_2Na$, 285.0610, found 285.0613.

**1-Ethyl-3-phenylimidazo[1,5-*a*]pyridine (1ab).** 2.5 h; eluent: EtOAc/PE 15:85; yield: 59 mg, 53%; yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.16 (d, *J* = 7.2 Hz, 1H), 7.79-7.77 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 2H), 6.62-6.58 (m, 1H), 6.49-6.45 (m, 1H), 2.95 (q, *J* = 7.6 Hz, 2H), 1.38 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 136.6, 135.1, 130.6, 128.9, 128.3, 127.9, 127.3, 121.2, 118.3, 117.0, 112.8, 20.7, 14.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{15}H_{15}N_2$, 223.1230, found 223.1230.

**1-Pentyl-3-phenylimidazo[1,5-*a*]pyridine (1ac).** 4.5 h; eluent: EtOAc/PE 10:90; yield: 87 mg, 66%; yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.16 (d, *J* = 7.2 Hz, 1H), 7.78-7.76 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42-7.37 (m, 2H), 6.62-6.58 (m, 1H), 6.49-6.45 (m, 1H), 2.90 (t, *J* = 8.0 Hz, 2H), 1.83-1.75 (m, 2H), 1.40-1.34 (m, 4H), 0.92-0.88 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 136.7, 133.9, 130.6, 128.9, 128.3, 127.9, 127.7, 121.2, 118.4, 117.0, 112.8, 31.8, 30.2, 27.5, 22.6, 14.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{21}N_2$, 265.1699, found 265.1701.

**3-Phenyl-1-(pyridin-2-yl)imidazo[1,5-*a*]pyridine (1ae).**[8b] 1 h; eluent: EtOAc/PE 15:85; yield: 134 mg, 99%; yellow solid, mp 111-113 ºC; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.71 (dt, *J* = 9.2, 1.2 Hz, 1H), 8.64-8.62 (m, 1H), 8.27-8.24 (m, 2H), 7.85-7.83 (m, 2H), 7.71 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.48-7.44 (m, 1H), 7.11-7.07 (m, 1H), 6.94-6.89 (m, 1H), 6.66-6.62 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 155.1, 149.0, 138.1, 136.2, 130.6, 130.2, 130.16, 129.1. 128.9, 128.4, 121.9, 121.6, 121.0, 120.4, 119.9, 113.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{14}N_3$, 272.1182, found 272.1182.

**3-(4-Methoxyphenyl)-1-(pyridin-2-yl)imidazo[1,5-*a*]pyridine (1af).**[8b] 1.5 h; eluent: EtOAc/PE 15:85; yield: 110 mg, 73%; yellow solid, mp 105-107 ºC; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.68 (d, *J* = 9.2 Hz, 1H), 8.62 (d, *J* = 4.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 7.2 Hz, 1H), 7.77-7.68 (m, 3H), 7.10-7.05 (m, 3H), 6.91-6.87 (m, 1H), 6.64-6.60 (m, 1H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 160.1, 155.1, 149.0, 138.1, 136.2, 130.2, 139.94, 129.87, 122.6, 121.8, 121.6, 120.8, 120.3, 119.9, 114.5, 113.7, 55.5 ; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{16}N_3O$, 302.1288, found 302.1294.

**2-(1-(Pyridin-2-yl)imidazo[1,5-*a*]pyridin-3-yl)phenol (1ag).**[8b] 2 h; eluent: EtOAc/PE 20:80; yield: 81 mg, 56%; yellow solid, mp 180-182 ºC; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 11.78 (s, 1H), 8.80 (d, *J* = 9.2 Hz, 1H), 8.64 (d, *J* = 4.8 Hz, 1H), 8.55 (d, *J* = 7.2 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.80-7.72 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.20-7.12 (m, 2H), 7.05-6.97 (m, 2H), 6.77 (t, *J* = 7.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 156.4, 153.9, 149.1, 136.4, 135.5, 130.1, 129.6, 128.6, 124.6, 122.32, 122.28, 121.7, 120.9, 119.8, 119.2, 117.8, 114.9, 114.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{14}N_3O$, 288.1131, found 288.1144.

**1-(Pyridin-2-yl)-3-(*o*-tolyl)imidazo[1,5-*a*]pyridine (1ah).**[8b] 1 h; eluent: EtOAc/PE 15:85; yield: 133 mg, 93%; yellow solid, mp 108-112 ºC; $^1$H NMR (400 MHz, $CDCl_3$): *δ* 8.73 (dt, *J* = 9.2, 1.2 Hz, 1H), 8.67-8.65 (m, 1H), 8.27-8.24 (m, 1H), 7.75-7.70 (m, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.47-7.35 (m, 3H), 7.13-7.09 (m, 1H), 6.97-6.93 (m, 1H), 6.64-6.61 (m, 1H), 2.28 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 155.2, 149.0, 138.6, 137.7, 136.2, 130.9, 130.7, 130.0, 129.7, 129.3, 129.2, 126.2, 121.7, 121.6, 120.9, 120.3, 119.9, 113.6, 19.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{19}H_{15}N_3Na$, 308.1158, found 308.1161.

## Conclusions

In summary, we have developed a facile and efficient one-pot approach for the synthesis of imidazo[1,5-*a*]pyridines from readily available 2-pyridyl ketones and alkylamines via $I_2$-mediated $sp^3$ C–H amination under transition-metal-free conditions. This operationally simple synthetic process can be safely conducted on a gram scale. In addition, cyclization of di-2-pyridyl ketones with substituted benzylamines produced a series of biologically interesting pyridylimidazo[1,5-*a*]pyridine in satisfactory yields. Further application of this synthetic



 

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strategy to the contruction of other heterocyclic frameworks is currently in progress in our laboratory.

## Conflicts of interest

There are no conflicts to declare.

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# Synthesis of Imidazo[1,5-*a*]pyridines *via* $I_2$-Mediated $sp^3$ C−H Amination

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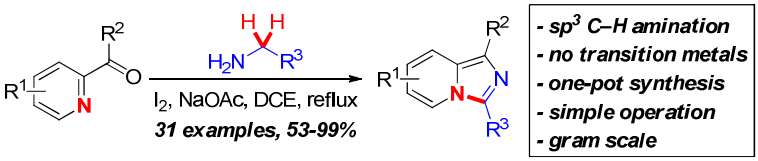


A transition-metal-free $sp^3$ C−H amination reaction has been developed employing molecular iodine for imidazo[1,5-*a*]pyridine synthesis.