

# Straightforward Synthesis of Various 2,3-Diarylimidazo[1,2-*a*]pyridines in PEG<sub>400</sub> Medium through One-Pot Condensation and C–H Arylation

Marie-Aude Hiebel,<sup>[a]</sup> Yacoub Fall,<sup>[a]</sup> Marie-Christine Scherrmann,<sup>[b]</sup> and Sabine Berteina-Raboin<sup>\*[a]</sup>

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PEG<sub>400</sub> is described herein as a suitable medium for the condensation of various 2-amino pyridines with  $\alpha$ -bromo ketones. 2-Arylimidazo[1,2-*a*]pyridines were synthesized in a short time through microwave irradiation in moderate to excellent yields. After optimization, a convenient one-pot

process enabled access to 2,3-diarylimidazo[1,2-*a*]pyridines by using a reduced amount of palladium catalyst without ligand for the C–H arylation step in the same environmentally-sound medium.

## Introduction

Imidazo[1,2-*a*]pyridines exhibit a broad range of biological activities.<sup>[1]</sup> Some synthetic drugs that contain this pyridine core have been commercialized such as the sedative Zolpidem, the anxiolytic Alpidem or Saridipem, and the heart-failure drug Olprinone (Figure 1).

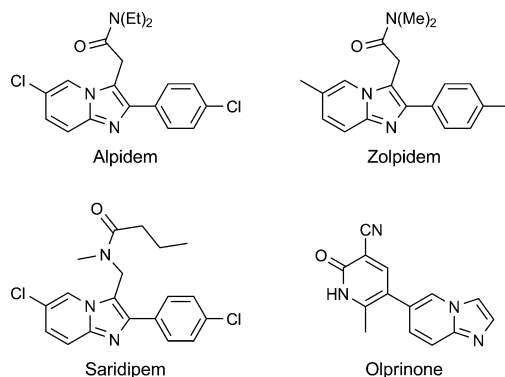


Figure 1. Examples of imidazoheterocyclic-containing therapeutics.

More specifically, the 2,3-diarylimidazo[1,2-*a*]pyridine family has shown antiprotozoal,<sup>[2]</sup> antiherpes,<sup>[3]</sup> and antiapoptotic activities,<sup>[4]</sup> and also acts as a kinase inhibitor<sup>[5]</sup> and antileishmanial agent.<sup>[6]</sup> Its value in the pharmaceutical and agrochemical area has therefore prompted continued effort to obtain efficiently this key structural unit.<sup>[1–6]</sup> Imid-

azo[1,2-*a*]pyridines are generally synthesized through a condensation between 2-aminopyridines and  $\alpha$ -haloketones in polar organic solvents.<sup>[1–7]</sup> To introduce further diversity our group, among others, reported metal-catalyzed cross-coupling reactions. However, these methods such as Suzuki,<sup>[8]</sup> Stille,<sup>[9]</sup> Heck,<sup>[10]</sup> Sonogashira,<sup>[11]</sup> or Negishi-type<sup>[12]</sup> reactions require a halogenated precursor, which makes the sequence longer and increases waste production. Recently, direct C–H bond functionalization became an elegant and requisite method to introduce various substitutions in an environmentally improved route.<sup>[6,13]</sup> In our effort to develop environmentally benign tools, we have continuously tried to promote the use of non-toxic media.<sup>[14]</sup> Recently, some polymer media have been used as new solvents in organic synthesis, in particular polyethylene glycol (PEG).<sup>[15]</sup> By convention, PEG usually represents polymers with a molecular weight that does not exceed 20000 and the notation PEG<sub>400</sub> means poly(ethylene glycol) with an average molecular weight of 400. PEG<sub>400</sub> is a viscous sustainable liquid soluble in water and many organic solvents. This medium has the advantage of being non-toxic, odorless, neutral, non-volatile, and non-irritating and is used in a variety of pharmaceuticals and medications. Herein we report the use of PEG<sub>400</sub> as an efficient medium to synthesize and functionalize the imidazo[1,2-*a*]pyridine moiety in a one-pot condensation and C–H-activation process.

## Results and Discussion

We first focused on the condensation of 2-aminopyridine (1 equiv.) and 2-bromoacetophenone (1 equiv.) and decided to optimize the conditions by using benign solvents. In the presence of sodium hydrogen carbonate (2 equiv.) at room temperature in PEG<sub>400</sub>, 2-phenylimidazo[1,2-*a*]pyridine (**1a**) was obtained in moderate yield after 22 h

[a] Institut de Chimie Organique et Analytique (ICOA), Université d'Orléans, UMR-CNRS 7311, BP 6759, rue de Chartres, 45067 Orléans cedex 2, France  
E-mail: sabine.berteina-raboin@univ-orleans.fr  
www.icoa.fr

[b] Institut de Chimie Moléculaire et des Matériaux d'Orsay, UMR CNRS 8182, Université Paris-Sud, Bâtiment 410, 91400 Orsay, France

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(Table 1, Entry 1). A decrease in the yield was noticed in water, perhaps owing to the poor solubility of the reagents in this medium. To shorten the reaction time, microwave irradiation was used, and completion of the reaction was obtained after 10 min. With its permanent dipole and its high boiling point, PEG is an excellent solvent for microwave irradiation.<sup>[16]</sup> However, some degradation was observed when the temperature rose above 120 °C (Table 1, Entries 2–4). Then, the amount of base was studied, and even if **1a** was obtained in 78% with 3 equiv. of NaHCO<sub>3</sub>, the improvement was not sufficient to justify the use of excess base (Table 1, Entries 3 and 5–6).

Dilution of the mixture appeared to have no influence on the reaction, nor did the use of potassium carbonate, whereas cesium carbonate induced a drastic drop in yield (Table 1, Entries 9 and 10). Finally, the optimal reaction conditions chosen were irradiation of a stoichiometric amount of 2-aminopyridine and 2-bromoacetophenone, and NaHCO<sub>3</sub> at 120 °C for 10 min in PEG<sub>400</sub> (8 mL/mmol).

Table 1. Optimization of the condensation step in PEG<sub>400</sub> media.

| Entry | Base [equiv.]                       | V [mL] | T [°C] <sup>[a]</sup> | t [min]           | Yield <sup>[b]</sup> [%] |
|-------|-------------------------------------|--------|-----------------------|-------------------|--------------------------|
| 1     | NaHCO <sub>3</sub> (2)              | 8      | r.t.                  | 22 <sup>[c]</sup> | 61 (49) <sup>[d]</sup>   |
| 2     | NaHCO <sub>3</sub> (2)              | 8      | 100                   | 10                | 73                       |
| 3     | NaHCO <sub>3</sub> (2)              | 8      | 120                   | 10                | 73 (72) <sup>[e]</sup>   |
| 4     | NaHCO <sub>3</sub> (2)              | 8      | 160                   | 10                | 61                       |
| 5     | NaHCO <sub>3</sub> (1)              | 8      | 120                   | 10                | 73 (55) <sup>[f]</sup>   |
| 6     | NaHCO <sub>3</sub> (3)              | 8      | 120                   | 10                | 78                       |
| 7     | NaHCO <sub>3</sub> (1)              | 16     | 120                   | 10                | 68                       |
| 8     | NaHCO <sub>3</sub> (1)              | 4      | 120                   | 10                | 70                       |
| 9     | Cs <sub>2</sub> CO <sub>3</sub> (1) | 8      | 120                   | 10                | 38                       |
| 10    | K <sub>2</sub> CO <sub>3</sub> (1)  | 8      | 120                   | 10                | 68                       |

[a] Microwave irradiation. [b] Isolated yields. [c] Hours. [d] Reaction in water. [e] 20 min of irradiation. [f] Reaction performed at 100 °C.

Table 2. Condensation of various 2-aminopyridine with  $\alpha$ -bromo ketones in PEG<sub>400</sub> media.

|                                  |                                  |                                  |
|----------------------------------|----------------------------------|----------------------------------|
|                                  |                                  |                                  |
| <b>1a</b> <sup>[18]</sup> (73 %) | <b>1b</b> <sup>[19]</sup> (80 %) | <b>1c</b> <sup>[20]</sup> (80 %) |
|                                  |                                  |                                  |
| <b>1d</b> <sup>[7c]</sup> (71 %) | <b>1e</b> <sup>[7c]</sup> (72 %) | <b>1f</b> <sup>[21]</sup> (71 %) |
|                                  |                                  |                                  |
| <b>1g</b> <sup>[22]</sup> (90 %) | <b>1h</b> <sup>[23]</sup> (79 %) | <b>1i</b> <sup>[24]</sup> (85 %) |
|                                  |                                  |                                  |
| <b>1j</b> <sup>[19]</sup> (70 %) | <b>1k</b> <sup>[25]</sup> (52 %) | <b>1l</b> <sup>[26]</sup> (63 %) |
|                                  |                                  |                                  |
| <b>1m</b> (65 %)                 | <b>1n</b> <sup>[27]</sup> (43 %) | <b>1o</b> <sup>[7c]</sup> (30 %) |
|                                  |                                  |                                  |
| <b>1p</b> <sup>[28]</sup> (50 %) |                                  |                                  |

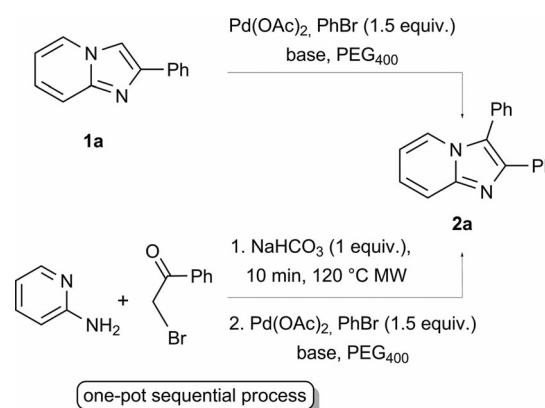
With optimized conditions in hand, the scope and limitation of the reaction were examined (Table 2). Initially, condensation with different  $\alpha$ -bromo ketones with 2-aminopyridine was attempted. Electron-withdrawing or donating groups on various positions on the aromatic ring exhibited no influence and the expected product was obtained in excellent yield (**1a–1g**).

Different 2-aminopyridines were then used for the reaction. 2-Phenylimidazo[1,2-*a*]pyridines substituted in position 6, 7 and 8 were isolated in good yield with electron-donating substituents (**1h–1j** and **1l**). However, mild or moderate electron-attracting groups in 6 and 7, such as halogen, trifluoromethyl or ester groups reduced the nucleophilic activity of the primary amine or of the endocyclic nitrogen, moderating the yield of the reaction (**1k** and **1m–1p**). Finally, this reaction tolerated alkyl, ether, ester, nitroso, trifluoromethyl, and halogen-containing moieties.

We studied C–H activation at C3 position (Table 3). The experimental conditions described by Doucet<sup>[13g]</sup> were attempted, but only traces of the desired product were obtained. Fortunately, a higher amount of  $\text{Pd}(\text{OAc})_2$  (1 mol-%) enabled formation of **2a** in excellent yield without extra addition of ligand (Table 3, Entry 2), and the reaction was almost quantitative when 2.5 mol-% of catalyst was used. However we decided to promote a lower catalyst loading. We then examined the influence of the nature of the base on conversion. Surprisingly, conversion of the reaction was incomplete with  $\text{CsOAc}$  and  $\text{NaOAc}$ , (26 and 64%, respectively). On the other hand, carbonated bases gave poorer results (Table 3, Entries 6–8) and despite the possible crown effect of  $\text{PEG}_{400}$ , only starting material was recovered with potassium carbonate and potassium hydroxide.<sup>[17]</sup> Microwave irradiation significantly reduced the reaction time from 24 to 1 h. The resulting optimal reaction conditions were irradiation of **1a** with bromobenzene (1.5 equiv.), KOAc (2 equiv.), and  $\text{Pd}(\text{OAc})_2$  (1 mol-%) in  $\text{PEG}_{400}$  (8 mL/mmol) at 180 °C for 1 h. With these optimized conditions for C–H arylation, we decided to apply them in the sequential one-pot condensation and C–H arylation procedure (Table 3, Entries 12–16). Disappointingly, in this case the conversion was incomplete because 34% of **1a** was isolated after the second microwave irradiation. A longer reaction time and an increase in the amount of catalyst resulted in no significant change. However a larger amount of base combined with a higher temperature led to completion of the reaction (Table 3, Entry 16) and **2a** was isolated in 69% yield, which was consistent with the result of the two-step procedure (66%). In an endeavor to expand the scope of the methodology, the one-pot procedure was applied to different  $\alpha$ -bromo ketones, aryl bromides, and 2-aminopyridines (Table 4). To our delight, the expected products were exclusively afforded in moderate to excellent yields. Significant steric and/or electronic effects of the substituents on the reactivity were observed. The result revealed that varying the aryl group at C2 induced moderate changes in reactivity on C3. Electron-rich and electron-withdrawing groups in the *para* position were well tolerated (**2d–2f**). However, partial conversion or a lower yield for

substrates with substitutions in *ortho* and *meta* positions indicated that steric hindrance had an influence on the C–H arylation step (**2b** and **2c**). An unusual solubility issue with intermediate **1g** in  $\text{PEG}_{400}$  could explain the moderate yield of **2g**. In addition, various aryl bromides were used. Unfortunately, failure in the introduction of 2-bromotoluene confirmed that bulky substituents disturbed the reaction even if the reaction time was increased (**2h**).

Table 3. C–H arylation and one-pot optimization in  $\text{PEG}_{400}$  media.

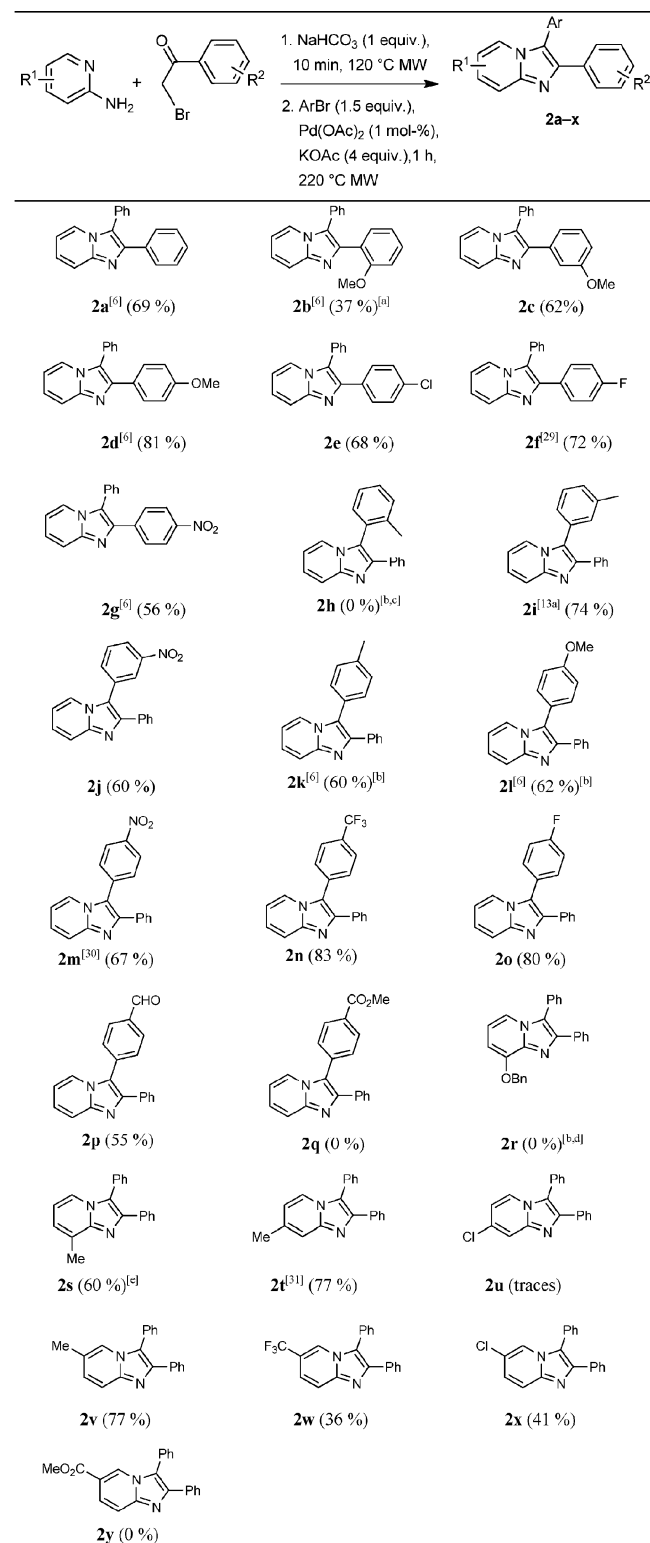


| Entry | $\text{Pd}(\text{OAc})_2$ [a] | Base                     | <i>t</i> [h] | <i>T</i> [°C] | Yield [b]        |
|-------|-------------------------------|--------------------------|--------------|---------------|------------------|
| 1     | 0.1                           | KOAc                     | 16           | 150           | traces [c]       |
| 2     | 1                             | KOAc                     | 24           | 150           | 93               |
| 3     | 2.5                           | KOAc                     | 24           | 150           | 96               |
| 4     | 1                             | $\text{CsOAc}$           | 24           | 150           | 26 [d]           |
| 5     | 1                             | $\text{NaOAc}$           | 24           | 150           | 64 [d]           |
| 6     | 1                             | $\text{NaHCO}_3$         | 24           | 150           | 17 [d]           |
| 7     | 1                             | $\text{Cs}_2\text{CO}_3$ | 24           | 150           | — [e]            |
| 8     | 1                             | $\text{K}_2\text{CO}_3$  | 24           | 150           | — [f]            |
| 9     | 1                             | KOH                      | 24           | 150           | — [f]            |
| 10    | 1                             | KOAc                     | 2            | 180 (MW)      | 93               |
| 11    | 1                             | KOAc                     | 1            | 180 (MW)      | 90               |
| 12    | 1                             | KOAc                     | 1            | 180 (MW)      | 48 [g]           |
| 13    | 1                             | KOAc                     | 2            | 180 (MW)      | 75 [d]           |
| 14    | 2                             | KOAc                     | 1            | 180 (MW)      | 72 [d]           |
| 15    | 1                             | $\text{KOAc}^{[h]}$      | 1            | 180 (MW)      | 49 [d]           |
| 16    | 1                             | $\text{KOAc}^{[h]}$      | 1            | 220 (MW)      | 100 [d] (69) [g] |

[a] In mol-%. [b] Isolated yields. [c] 1 equiv. of PhBr and 1.5 equiv. of **1a** were used. [d] Yield as calculated by  $^1\text{H}$  NMR spectroscopy. [e] **1a** recovered. [f] Degradation. [g] Isolated yield from the sequential one-pot procedure; 34% of **1a** was recovered. [h] Introduction of 4 equiv. of KOAc.

However functional groups including electron-rich and electron-withdrawing groups in the *para* and *meta* positions were well tolerated. 4-Bromoanisole and 4-bromotoluene required only a longer reaction time for the C–H arylation step. Modification of the imidazo core was then attempted. Mild electron-donating and -withdrawing groups gave the expected products in moderate to good yields over the two-step process (**2s–2w**), but no coupling product was observed

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Table 4. Synthesis of various 2,3-diarylimidazo[1,2-*a*]pyridines in a sequential one-pot process in PEG<sub>400</sub> medium.

[a] 35% of **1b** was recovered. [b] 2 h of irradiation at 220 °C with ArBr. [c] Synthesis of **1a** only. [d] 37% of **1i** was isolated. [e] 35% of **1h** was recovered.

for **2r**. In this case, the reactivity of the C3 position dropped completely. It is worth noting that during the reaction, ex-

cept for the synthesis of **2u** in which significant degradation was observed, no cleavage of the C–Cl bond was noticed, allowing further transformations (**2e** and **2x**). A series of functional groups such as alkyl, ether, halogen, nitro, trifluoromethyl, and aldehyde were compatible under these experimental conditions. But unlike previously, ester groups were not tolerated (**2q** and **2y**).

## Conclusions

We have developed an efficient method to obtain various 2,3-diarylimidazo[1,2-*a*]pyridines in PEG<sub>400</sub>. The salient features of our method are the facile introduction of miscellaneous aryl substituents in a one-pot manner from commercially available starting materials in an environmentally-friendly alternative solvent. The first step is the formation of the 2-arylimidazo[1,2-*a*]pyridine core by condensation between different 2-aminopyridines and  $\alpha$ -bromo ketones, followed directly by C–H activation at C3. Various 2,3-diarylimidazo[1,2-*a*]pyridines have been synthesized in moderate to excellent yields that demonstrates the generality of this method.

## Experimental Section

**General:** All reagents were purchased from commercial suppliers and were used without further purification. Microwave assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured with an IR sensor. The reactions were monitored by thin-layer chromatography (TLC) analysis with silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed with silica gel 60 (230–400 mesh, 0.040–0.063 mm). Melting points were recorded with samples in open capillary tubes. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with a Bruker spectrometer at 250 MHz (<sup>13</sup>C, 62.9 MHz). Chemical shift signals are reported relative to tetramethylsilane as internal standard. HRMS were performed on a Maxis Bruker 4G by the “Federation de Recherche” ICOA/CBM (FR2708) platform.

**General Procedure for the Synthesis of 1a–1o:** 2-Aminopyridine (1 mmol),  $\alpha$ -bromo ketone (1 mmol) and NaHCO<sub>3</sub> (1 mmol) were dissolved in PEG<sub>400</sub> (8 mL) in a sealed vial before being irradiated for 10 min at 120 °C. Then AcOEt (10 mL) and a saturated solution of NaHCO<sub>3</sub> (10 mL) were added to the reaction mixture. The resulting aqueous layer was extracted with AcOEt (3 × 5 mL). The combined organic phase was then washed with a saturated solution of NaHCO<sub>3</sub> (5 × 5 mL) and dried with MgSO<sub>4</sub>. After filtration and concentration under reduced pressure the crude product was purified either by recrystallization when specified or by flash chromatography with a mixture of ethyl acetate and petroleum ether (10–40%) as eluent to provide the expected product.

**2-Phenylimidazo[1,2-*a*]pyridine (**1a**):**<sup>[18]</sup> White solid, m.p. 131.6–132.3 °C (lit. m.p. 131–133 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.10 (dt, *J* = 6.8, 1.1 Hz, 1 H), 8.00–7.91 (m, 2 H), 7.85 (s, 1 H), 7.63 (dq, *J* = 9.1, 1.0 Hz, 1 H), 7.50–7.39 (m, 2 H), 7.38–7.28 (m, 1 H), 7.16 (ddd, *J* = 9.1, 6.8, 1.3 Hz, 1 H), 6.76 (td, *J* = 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>):  $\delta$  = 146.0, 145.8, 133.9, 128.8, 128.1, 126.2, 125.7, 124.7, 117.7, 112.5, 108.2 ppm.

**2-(2-Methoxyphenyl)imidazo[1,2-*a*]pyridine (1b):**<sup>[19]</sup> Brown solid, m.p. 91.0–93.9 °C (lit. m.p. 94–96 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.41 (dd, *J* = 7.7, 1.8 Hz, 1 H), 8.18 (s, 1 H), 8.09 (br. d, *J* = 6.8 Hz, 1 H), 7.61 (br. d, *J* = 9.1 Hz, 1 H), 7.30 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1 H), 7.19–7.05 (m, 2 H), 6.99 (dd, *J* = 8.2, 1.2 Hz, 1 H), 6.71 (ddd, *J* = 6.8, 6.7, 1.2 Hz, 1 H), 3.98 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 156.8, 144.5, 141.3, 128.9, 128.7, 125.7, 124.5, 122.5, 121.1, 117.4, 112.6, 112.0, 110.5, 55.5 ppm.

**2-(3-Methoxyphenyl)imidazo[1,2-*a*]pyridine (1c):**<sup>[20]</sup> Orange solid, m.p. 62.4–63.5 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.07 (br. d, *J* = 6.6 Hz, 1 H), 7.82 (s, 1 H), 7.63 (d, *J* = 9.1 Hz, 1 H), 7.58–7.54 (m, 1 H), 7.50 (br. d, *J* = 7.6 Hz, 1 H), 7.33 (dd, *J* = 7.7, 7.7 Hz, 1 H), 7.14 (br. dd, *J* = 7.8, 6.7 Hz, 1 H), 6.88 (br. dd, *J* = 8.2, 2.6 Hz, 1 H), 6.74 (dd, *J* = 7.1, 6.1 Hz, 1 H), 3.88 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 160.1, 145.7, 145.7, 135.3, 129.8, 125.7, 124.8, 118.6, 117.6, 114.3, 112.6, 111.1, 108.5, 55.5 ppm.

**2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine (1d):**<sup>[7c]</sup> Recrystallized from EtOH. Beige solid, m.p. 136.8–137.4 °C (lit. m.p. 135–136 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.06 (br. d, *J* = 6.7 Hz, 1 H), 7.88 (br. d, *J* = 8.9 Hz, 2 H), 7.74 (s, 1 H), 7.60 (d, *J* = 9.1 Hz, 1 H), 7.13 (ddd, *J* = 9.0, 6.8, 1.3 Hz, 1 H), 7.96 (br. d, *J* = 8.8 Hz, 2 H), 6.73 (ddd, *J* = 6.8, 6.6, 1.1 Hz, 1 H), 3.84 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 159.7, 145.8, 145.7, 127.4, 126.6, 125.6, 124.6, 117.4, 114.2, 112.3, 107.3, 55.4 ppm.

**2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridine (1e):**<sup>[7c]</sup> Recrystallized from MeOH. White solid, m.p. 206.5–207.0 °C (lit. m.p. 207–209 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.06 (br. d, *J* = 6.7 Hz, 1 H), 7.86 (br. d, *J* = 8.5 Hz, 2 H), 7.79 (s, 1 H), 7.60 (d, *J* = 9.1 Hz, 1 H), 7.38 (br. d, *J* = 8.5 Hz, 2 H), 7.15 (br. dd, *J* = 9.1, 6.7 Hz, 1 H), 6.75 (br. dd, *J* = 6.8, 6.7 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 145.8, 144.7, 133.8, 132.4, 129.0, 127.3, 125.7, 125.0, 117.6, 112.7, 108.3 ppm.

**2-(4-Fluorophenyl)imidazo[1,2-*a*]pyridine (1f):**<sup>[21]</sup> Recrystallized from MeOH. White solid, m.p. 163.1–163.4 °C (lit. m.p. 165–166 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.10 (dt, *J* = 6.8, 1.2 Hz, 1 H), 7.96–7.84 (m, 2 H), 7.79 (br. s, 1 H), 7.61 (ddd, *J* = 9.1, 1.1, 1.0 Hz, 1 H), 7.21–7.05 (m, 3 H), 6.77 (ddd, *J* = 6.8, 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 164.8, 160.9, 145.5 (d, *J* = 45.5 Hz), 130.2 (d, *J* = 3.1 Hz), 127.8 (d, *J* = 8.1 Hz), 125.7, 124.9, 117.7, 155.8 (d, *J* = 21.6 Hz), 112.6, 107.9 ppm.

**2-(4-Nitrophenyl)imidazo[1,2-*a*]pyridine (1g):**<sup>[22]</sup> Recrystallized from EtOH. Yellow solid, m.p. > 260 °C (lit. m.p. 266–267 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.30 (br. d, *J* = 9.0 Hz, 2 H), 8.18–8.08 (m, 3 H), 8.00 (d, *J* = 0.8 Hz, 1 H), 7.66 (ddd, *J* = 9.2, 1.0, 1.0 Hz, 1 H), 7.29–7.19 (m, 1 H), 6.85 (ddd, *J* = 6.9, 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, [D<sub>6</sub>]DMSO): δ = 146.5, 145.2, 142.0, 140.5, 127.3, 126.3, 125.9, 124.2, 117.0, 112.9, 111.7 ppm.

**8-Methyl-2-phenylimidazo[1,2-*a*]pyridine (1h):**<sup>[23]</sup> Recrystallized from EtOH. Beige solid, m.p. 104.9–105.2 °C (lit. m.p. 105–106 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.02–7.90 (m, 3 H), 7.81 (s, 1 H), 7.49–7.39 (m, 2 H), 7.37–7.27 (m, 1 H), 6.93 (d, *J* = 6.8 Hz, 1 H), 6.65 (dd, *J* = 6.8, 6.7 Hz, 1 H), 2.70 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.3, 145.3, 134.2, 128.8, 127.8, 128.7, 126.2, 123.5, 123.3, 112.4, 108.7, 17.2 ppm.

**8-(Benzyloxy)-2-phenylimidazo[1,2-*a*]pyridine (1i):**<sup>[24]</sup> Yellow solid, m.p. 130.9–133.6 °C (lit. m.p. 132–135 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.06–7.98 (m, 2 H), 7.84 (s, 1 H), 7.75 (dd, *J* = 6.7, 1.0 Hz, 1 H), 7.52 (d, *J* = 6.8 Hz, 2 H), 7.46–7.29 (m, 6 H), 6.59 (dd, *J* = 7.7, 6.7 Hz, 1 H), 6.43 (d, *J* = 7.5 Hz, 1 H), 5.43 (s, 2 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 147.9, 145.0, 140.3,

136.4, 133.8, 128.6, 128.6, 127.8, 127.2, 126.3, 118.8, 112.1, 109.2, 103.2, 70.8 ppm.

**7-Methyl-2-phenylimidazo[1,2-*a*]pyridine (1j):**<sup>[19]</sup> Recrystallized from EtOH. White solid, m.p. 164.3–164.7 °C (lit. m.p. 165–167 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.93 (br. d, *J* = 7.1 Hz, 3 H), 7.73 (s, 1 H), 7.46–7.26 (m, 4 H), 6.56 (br. d, *J* = 7.0 Hz, 1 H), 2.37 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.2, 145.6, 135.6, 134.0, 128.7, 127.9, 126.0, 124.9, 116.0, 115.1, 107.6, 21.5 ppm.

**7-Chloro-2-phenylimidazo[1,2-*a*]pyridine (1k):**<sup>[25]</sup> Beige solid, m.p. 181.5–183.0 °C (lit. m.p. 180–181 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.98 (dd, *J* = 7.2, 0.9 Hz, 1 H), 7.95–7.88 (m, 2 H), 7.78 (d, *J* = 0.7 Hz, 1 H), 7.61 (dd, *J* = 1.9, 0.9 Hz, 1 H), 7.47–7.38 (m, 3 H), 7.37–7.29 (m, 1 H), 6.74 (dd, *J* = 7.2, 2.1 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.9, 145.5, 133.4, 131.1, 128.9, 128.4, 126.2, 125.9, 116.4, 114.2, 108.3 ppm.

**6-Methyl-2-phenylimidazo[1,2-*a*]pyridine (1l):**<sup>[26]</sup> Beige solid, m.p. 172.0–172.5 °C (lit. m.p. 171–173 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.99–7.98 (m, 2 H), 7.86–7.78 (m, 1 H), 7.75–7.69 (m, 1 H), 7.51 (d, *J* = 9.2 Hz, 1 H), 7.46–7.37 (m, 2 H), 7.35–7.26 (m, 1 H), 6.97 (dd, *J* = 9.2, 1.9 Hz, 1 H), 2.27 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 145.6, 144.8, 134.1, 128.8, 127.9, 126.0, 123.4, 122.0, 116.9, 107.9, 18.2 ppm.

**2-Phenyl-6-(trifluoromethyl)imidazo[1,2-*a*]pyridine (1m):** Yellow solid, m.p. 191.5–192.7 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.49 (br. s, 1 H), 8.00–7.97 (m, 1 H), 7.94 (br. s, 2 H), 7.72 (br. d, *J* = 9.5 Hz, 1 H), 7.51–7.41 (m, 2 H), 7.41–7.35 (m, 1 H), 7.32 (dd, *J* = 9.5, 1.8 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 148.0, 145.5, 133.1, 129.0, 128.8, 126.4, 125.8, 124.7 (q, *J* = 5.8 Hz), 121.5, 120.7 (q, *J* = 2.7 Hz), 118.3, 117.0 (q, *J* = 33.9 Hz), 109.3 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>14</sub>H<sub>10</sub>F<sub>3</sub>N<sub>2</sub> 263.079059; found 263.079503.

**6-Bromo-2-phenylimidazo[1,2-*a*]pyridine (1n):**<sup>[27]</sup> Recrystallized from EtOH. Beige solid, m.p. 200.0–201.0 °C (lit. m.p. 201–202 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.24 (dd, *J* = 1.9, 0.8 Hz, 1 H), 7.96–7.88 (m, 2 H), 7.80 (s, 1 H), 7.53 (d, *J* = 9.5 Hz, 1 H), 7.48–7.39 (m, 2 H), 7.38–7.29 (m, 1 H), 7.22 (dd, *J* = 9.5, 1.8 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.7, 144.2, 133.3, 128.9, 128.5, 128.3, 126.2, 125.7, 118.2, 108.4, 107.1 ppm.

**6-Chloro-2-phenylimidazo[1,2-*a*]pyridine (1o):**<sup>[7c]</sup> White solid, m.p. 199.7–202.4 °C (lit. m.p. 204–206 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.12 (dd, *J* = 2.0, 0.9 Hz, 1 H), 7.95–7.88 (m, 2 H), 7.78 (br. s, 1 H), 7.58 (br. d, *J* = 9.6 Hz, 1 H), 7.47–7.39 (m, 2 H), 7.38–7.29 (m, 1 H), 7.12 (dd, *J* = 9.6, 2.0 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.8, 144.1, 133.2, 128.9, 128.4, 126.3, 126.2, 123.5, 120.7, 117.9, 108.6 ppm.

**Methyl 2-Phenylimidazo[1,2-*a*]pyridine-6-carboxylate (1p):**<sup>[28]</sup> Beige solid, m.p. 180.5–181.4 °C (lit. m.p. 180–181 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.92 (br. s, 1 H), 8.01–7.95 (m, 2 H), 7.94 (s, 1 H), 7.73 (dd, *J* = 9.5, 1.6 Hz, 1 H), 7.63 (d, *J* = 9.6 Hz, 1 H), 7.51–7.32 (m, 3 H), 3.97 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 165.5, 147.8, 146.3, 133.2, 129.9, 129.0, 128.6, 126.4, 124.5, 116.9, 116.6, 109.6, 52.6 ppm.

**General Procedure for the Synthesis of 2a–2w:** 2-Aminopyridine (1 mmol), α-bromo ketone (1 mmol) and NaHCO<sub>3</sub> (1 mmol) were dissolved in PEG400 (8 mL) in a sealed vial before being irradiated for 10 min at 120 °C. Then ArBr (1.5 mmol), KOAc (4 mmol) and Pd(OAc)<sub>2</sub> (1 mol-%) were added and the reaction mixture was irradiated for 1 or 2 h at 220 °C. AcOEt (10 mL) and a saturated solution of NaHCO<sub>3</sub> (10 mL) were added to the reaction mixture. The

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resulting aqueous layer was extracted with AcOEt (3 × 5 mL). The combined organic phase was then washed with a saturated solution of NaHCO<sub>3</sub> (5 × 5 mL) and dried with MgSO<sub>4</sub>. After filtration and concentration under reduced pressure the crude product was purified by flash chromatography with a mixture of ethyl acetate and petroleum ether (10–40%) as eluent or recrystallization when specified to provide the expected product.

**2,3-Diphenylimidazo[1,2-*a*]pyridine (2a):**<sup>[6]</sup> White solid, m.p. 145.3–148.1 °C (lit. m.p. 149–150 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.99 (d, *J* = 6.9 Hz, 1 H), 7.77–7.65 (m, 3 H), 7.60–7.42 (m, 5 H), 7.37–7.17 (m, 4 H), 6.77 (ddd, *J* = 6.8, 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.8, 142.4, 134.2, 130.7, 129.9, 129.6, 128.9, 128.3, 128.1, 128.0, 127.5, 124.7, 123.3, 121.1, 117.5, 112.9 ppm.

**2-(2-Methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyridine (2b):**<sup>[6]</sup> Beige solid, m.p. 121.8–123.0 °C (lit. m.p. 124–125 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.24 (ddd, *J* = 7.0, 1.2, 1.1 Hz, 1 H), 7.72 (ddd, *J* = 9.1, 1.2, 1.1 Hz, 1 H), 7.63 (dd, *J* = 7.5, 1.8 Hz, 1 H), 7.48–7.31 (m, 5 H), 7.21 (ddd, *J* = 9.1, 6.7, 1.3 Hz, 1 H), 7.02 (ddd, *J* = 7.5, 7.4, 1.1 Hz, 1 H), 6.84 (dd, *J* = 8.3, 1.0 Hz, 1 H), 6.78 (ddd, *J* = 6.9, 6.8, 1.2 Hz, 1 H), 3.37 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 156.8, 144.9, 140.8, 132.2, 130.9, 129.3, 129.2, 128.9, 127.9, 124.2, 123.8, 123.2, 122.8, 120.7, 118.0, 112.3, 111.0, 54.8 ppm.

**2-(3-Methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyridine (2c):** Beige solid, m.p. 99.0–100.8 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.94 (d, *J* = 6.9 Hz, 1 H), 7.68 (d, *J* = 9.0 Hz, 1 H), 7.60–7.40 (m, 5 H), 7.29–7.22 (dq, *J* = 4.0, 1.4 Hz, 2 H), 7.22–7.12 (m, 1 H), 6.80 (ddd, *J* = 8.0, 2.6, 1.3 Hz, 1 H), 6.76–6.68 (m, 1 H), 3.68 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 159.6, 144.8, 142.4, 135.6, 130.9, 130.1, 129.6, 129.4, 129.0, 124.8, 123.4, 121.3, 120.7, 117.7, 114.3, 112.7, 112.4, 55.2 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>17</sub>N<sub>2</sub>O 301.133893; found 301.133540.

**2-(4-Methoxyphenyl)-3-phenylimidazo[1,2-*a*]pyridine (2d):**<sup>[6]</sup> Beige solid, m.p. 102.0–105.7 °C (lit. m.p. 101–102 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.92 (br. d, *J* = 6.6 Hz, 1 H), 7.70–7.56 (m, 3 H), 7.55–7.36 (m, 5 H), 7.22–7.10 (m, 1 H), 6.81 (br. d, *J* = 8.7 Hz, 2 H), 6.73–6.62 (m, 1 H), 3.77 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 159.2, 144.8, 142.4, 130.8, 130.1, 129.6, 126.4, 128.8, 126.9, 124.5, 123.2, 120.3, 117.4, 113.8, 112.1, 55.3 ppm.

**2-(4-Chlorophenyl)-3-phenylimidazo[1,2-*a*]pyridine (2e):** Beige solid, m.p. 138.5–139.5 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.93 (dd, *J* = 6.7, 1.5 Hz, 1 H), 7.66 (br. d, *J* = 9.3 Hz, 1 H), 7.60 (br. d, *J* = 8.7 Hz, 2 H), 7.55–7.35 (m, 5 H), 7.24 (br. d, *J* = 8.7 Hz, 2 H), 7.21–7.13 (m, 1 H), 6.72 (dd, *J* = 7.3, 6.9 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.9, 141.4, 133.4, 132.9, 130.7, 129.8, 129.7, 129.4, 129.2, 128.6, 124.6, 125.0, 123.4, 121.3, 117.6, 112.5 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>14</sub>ClN<sub>2</sub> 305.084003; found 305.084365.

**2-(4-Fluorophenyl)-3-phenylimidazo[1,2-*a*]pyridine (2f):**<sup>[29]</sup> Yellow solid, m.p. 93.0–95.5 °C (lit. m.p. 104 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.89 (ddd, *J* = 6.9, 1.2, 1.2 Hz, 1 H), 7.67–7.57 (m, 3 H), 7.53–7.35 (m, 5 H), 7.14 (ddd, *J* = 9.1, 6.7, 1.3 Hz, 1 H), 6.99–6.88 (m, 2 H), 6.67 (ddd, *J* = 6.8, 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 164.3, 160.4, 144.8, 141.5, 130.4 (*J* = 33 Hz), 129.7 (*J* = 8.1 Hz), 129.6, 129.6, 129.0, 124.8, 123.3, 120.8, 117.4, 115.2 (*J* = 21.4 Hz), 112.3 ppm.

**2-(4-Nitrophenyl)-3-phenylimidazo[1,2-*a*]pyridine (2g):**<sup>[6]</sup> Recrystallized from EtOH. Yellow solid, m.p. 164.8–166.8 °C (lit. m.p. 157–158 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.16–8.08 (m, 2 H),

7.96–7.90 (m, 1 H), 7.87–7.79 (m, 2 H), 7.69 (br. d, *J* = 9.1 Hz, 1 H), 7.64–7.53 (m, 3 H), 7.49–7.41 (m, 2 H), 7.30–7.21 (m, 1 H), 6.79 (br. dd, *J* = 6.9, 6.9 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 146.9, 145.2, 141.0, 140.0, 130.7, 130.0, 129.7, 129.1, 128.4, 125.7, 123.7, 123.7, 123.1, 117.9, 113.0 ppm.

**2-Phenyl-3-(*m*-tolyl)imidazo[1,2-*a*]pyridine (2i):**<sup>[13a]</sup> Beige solid, m.p. 163.1–163.4 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.93 (ddd, *J* = 6.9, 1.2, 1.2 Hz, 1 H), 7.73–7.63 (m, 3 H), 7.41 (ddd, *J* = 7.3, 7.2, 1.2 Hz, 1 H), 7.35–7.12 (m, 7 H), 6.71 (ddd, *J* = 6.9, 6.8, 1.2 Hz, 1 H), 2.40 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.8, 142.3, 139.4, 134.4, 131.3, 129.9, 129.8, 129.6, 128.4, 128.1, 128.0, 128.0, 127.5, 124.7, 123.5, 121.4, 117.6, 112.3, 21.6 ppm.

**3-(3-Nitrophenyl)-2-phenylimidazo[1,2-*a*]pyridine (2j):** Recrystallized from EtOH. Yellow solid, m.p. 165.8–167.5 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.38 (br. s, 1 H), 8.32 (d, *J* = 8.1 Hz, 1 H), 7.99 (d, *J* = 6.9 Hz, 1 H), 7.80–7.64 (m, 3 H), 7.59 (dd, *J* = 6.7, 3.0 Hz, 2 H), 7.39–7.21 (m, 5 H), 6.83 (dd, *J* = 6.9, 6.7 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 149.1, 145.5, 144.0, 137.1, 133.6, 131.9, 130.8, 128.6, 128.4, 128.2, 125.5, 125.2, 123.6, 122.8, 118.5, 118.1, 113.2 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>14</sub>N<sub>3</sub>O<sub>2</sub> 316.108053; found 316.108243.

**2-Phenyl-3-(*p*-tolyl)imidazo[1,2-*a*]pyridine (2k):**<sup>[6]</sup> Beige solid, m.p. 133.2–135.6 °C (lit. m.p. 136–137 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.92 (br. d, *J* = 7.0 Hz, 1 H), 7.74–7.62 (m, 3 H), 7.32 (s, 4 H), 7.29–7.21 (m, 3 H), 7.21–7.12 (m, 1 H), 6.69 (br. dd, *J* = 6.9, 6.8 Hz, 1 H), 2.45 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.8, 142.3, 138.9, 132.2, 130.7, 130.4, 128.3, 128.1, 127.5, 126.9, 124.6, 123.4, 121.2, 117.6, 112.2, 21.6 ppm.

**3-(4-Methoxyphenyl)-2-phenylimidazo[1,2-*a*]pyridine (2l):**<sup>[6]</sup> White solid, m.p. 125.0–126.1 °C (lit. m.p. 129–130 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.91 (ddd, *J* = 6.9, 1.2, 1.2 Hz, 1 H), 7.73–7.63 (m, 3 H), 7.37 (br. d, *J* = 8.8 Hz, 2 H), 7.33–7.24 (m, 3 H), 7.24–7.14 (m, 1 H), 7.06 (br. d, *J* = 8.8 Hz, 2 H), 6.72 (ddd, *J* = 6.8, 1.2, 1.2 Hz, 1 H), 3.90 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 160.1, 144.8, 142.3, 134.5, 134.5, 132.2, 128.4, 128.1, 127.5, 124.6, 123.5, 122.0, 117.6, 115.2, 112.3, 55.5 ppm.

**3-(4-Nitrophenyl)-2-phenylimidazo[1,2-*a*]pyridine (2m):**<sup>[30]</sup> Yellow solid, m.p. 157.5–159.0 °C (lit. m.p. 150–152 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.34 (d, *J* = 8.8 Hz, 2 H), 8.08 (d, *J* = 7.3 Hz, 1 H), 7.72 (d, *J* = 8.8 Hz, 1 H), 7.64 (br. d, *J* = 8.8 Hz, 2 H), 7.61–7.57 (m, 2 H), 7.37–7.21 (m, 4 H), 6.81 (ddd, *J* = 6.9, 6.9, 1.1 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 147.5, 145.7, 144.5, 136.7, 133.5, 131.1, 128.6, 128.6, 128.2, 125.7, 124.8, 122.9, 118.8, 118.1, 113.2 ppm.

**2-Phenyl-3-[4-(trifluoromethyl)phenyl]imidazo[1,2-*a*]pyridine (2n):** Beige solid, m.p. 190.4–191.0 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.00 (d, *J* = 6.9 Hz, 1 H), 7.78 (d, *J* = 8.1 Hz, 2 H), 7.71 (d, *J* = 9.1 Hz, 1 H), 7.66–7.55 (m, 4 H), 7.36–7.18 (m, 4 H), 6.79 (dd, *J* = 6.7, 6.5 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 145.3, 143.6, 133.9, 131.0, 130.8 (q, *J* = 35.4 Hz), 128.5, 128.4, 127.9, 126.5 (d, *J* = 3.7 Hz), 126.2, 125.2, 123.0, 121.9, 119.6, 117.9, 117.5, 112.8 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>14</sub>F<sub>3</sub>N<sub>2</sub> 339.110360; found 339.110713.

**3-(4-Fluorophenyl)-2-phenylimidazo[1,2-*a*]pyridine (2o):** Beige solid, m.p. 146.4–147.4 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.89 (ddd, *J* = 6.9, 1.2, 1.1 Hz, 1 H), 7.73–7.60 (m, 3 H), 7.51–7.37 (m, 2 H), 7.37–7.13 (m, 6 H), 6.73 (ddd, *J* = 6.8, 6.8, 1.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 165.0, 161.1, 145.0, 142.8, 134.1, 132.9, 132.8, 128.4, 128.1, 127.7, 126.0, 129.0, 125.8, 123.2, 120.0, 117.7, 117.1, 113.7, 112.5 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>14</sub>FN<sub>2</sub> 289.113553; found 289.113979.

## Synthesis of Various 2,3-Diarylimidazo[1,2-a]pyridines

**4-(2-Phenylimidazo[1,2-a]pyridin-3-yl)benzaldehyde (2p):** Yellow solid, m.p. 189.7–192.2 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 10.09 (s, 1 H), 8.08 (br. d, *J* = 6.9 Hz, 1 H), 8.02 (br. d, *J* = 8.3 Hz, 2 H), 7.73 (br. d, *J* = 9.0 Hz, 1 H), 7.65 (br. d, *J* = 8.3 Hz, 2 H), 7.62–7.54 (m, 2 H), 7.35–7.21 (m, 4 H), 6.81 (ddd, *J* = 6.9, 6.8, 1.3 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 191.6, 145.6, 144.0, 136.2, 136.1, 133.8, 131.0, 130.8, 128.6, 128.1, 125.5, 123.1, 119.9, 118.0, 113.0 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>15</sub>N<sub>2</sub>O 299.117890; found 299.118222.

**8-Methyl-2,3-diphenylimidazo[1,2-a]pyridine (2s):** Beige solid, m.p. 122.8–123.7 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.83 (d, *J* = 6.9 Hz, 1 H), 7.72–7.64 (m, 2 H), 7.56–7.39 (m, 5 H), 7.33–7.18 (m, 3 H), 6.98 (br. d, *J* = 6.8 Hz, 1 H), 6.63 (td, *J* = 6.9, 6.7, 1.2 Hz, 1 H), 2.70 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 145.4, 142.2, 134.6, 130.8, 130.4, 129.5, 128.8, 128.4, 128.4, 127.6, 127.4, 123.4, 121.6, 121.3, 112.4, 17.3 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>17</sub>N<sub>2</sub> 285.138625; found 285.139121.

**7-Methyl-2,3-diphenylimidazo[1,2-a]pyridine (2t):**<sup>[31]</sup> Beige solid, m.p. 145.9–146.2 °C (lit. m.p. 145.5–146 °C). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.86 (d, *J* = 7.0 Hz, 1 H), 7.69 (d, *J* = 7.6 Hz, 2 H), 7.59–7.39 (m, 6 H), 7.34–7.22 (m, 3 H), 6.57 (d, *J* = 6.8 Hz, 1 H), 2.43 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 145.3, 142.1, 135.7, 134.4, 130.8, 130.1, 129.5, 128.8, 128.3, 128.1, 127.4, 122.6, 120.6, 115.9, 115.0, 21.4 ppm.

**6-Methyl-2,3-diphenylimidazo[1,2-a]pyridine (2v):** Beige solid, m.p. 196.5–197.7 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.75–7.62 (m, 3 H), 7.58 (dd, *J* = 9.2, 1.0 Hz, 1 H), 7.53–7.40 (m, 5 H), 7.31–7.19 (m, 3 H), 7.03 (dd, *J* = 9.2, 1.7 Hz, 1 H), 2.24 (s, 3 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.0, 142.4, 134.5, 130.9, 130.3, 129.6, 128.9, 128.3, 128.1, 127.9, 127.4, 122.0, 121.0, 130.9, 117.0, 18.4 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>17</sub>N<sub>2</sub> 285.138625; found 285.139062.

**2,3-Diphenyl-6-(trifluoromethyl)imidazo[1,2-a]pyridine (2w):** Yellow solid, m.p. 141.9–144.2 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.28 (br. s, 1 H), 7.82–7.73 (m, 1 H), 7.70–7.64 (m, 2 H), 7.59–7.52 (m, 3 H), 7.49–7.43 (m, 2 H), 7.38–7.25 (m, 4 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 144.6, 144.4, 133.5, 130.7, 130.0, 129.7, 128.9, 128.5, 128.2, 128.2, 125.9, 122.4 (q, *J* = 5.8 Hz), 121.7, 120.6 (q, *J* = 2.6 Hz), 118.4, 116.9 (q, *J* = 34.3 Hz) ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>20</sub>H<sub>14</sub>F<sub>3</sub>N<sub>2</sub> 339.110360; found 339.110664.

**6-Chloro-2,3-diphenylimidazo[1,2-a]pyridine (2x):** Beige solid, m.p. 159.9–161.0 °C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.96 (dd, *J* = 2.0, 0.9 Hz, 1 H), 7.69–7.58 (m, 3 H), 7.56–7.49 (m, 3 H), 7.48–7.40 (m, 2 H), 7.32–7.23 (m, 3 H), 7.15 (dd, *J* = 9.5, 2.0 Hz, 1 H) ppm. <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 143.5, 143.2, 133.8, 130.7, 129.9, 129.4, 129.4, 128.5, 128.1, 127.9, 126.1, 121.7, 121.2, 120.7, 118.1 ppm. HRMS (ESI): *m/z* [M + H]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>14</sub>ClN<sub>2</sub> 305.084003; found 305.084282.

**Supporting Information** (see footnote on the first page of this article): Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra for compounds **1a–1p**, **2a–2g**, **2i–2p**, **2s**, **2t** and **2v**.

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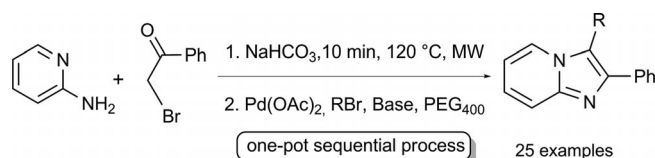
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PEG<sub>400</sub> was found to be a suitable solvent for condensation of various 2-amino pyridines with  $\alpha$ -bromo ketones. 2-Arylimidazo[1,2-*a*]pyridines were obtained in a short time through microwave irradiation.

A combination of the previous condensation with a C–H arylation reaction was developed to access various 2,3-diarylimidazo[1,2-*a*]pyridines with a reduced amount of palladium catalyst and no ligand.

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Straightforward Synthesis of Various 2,3-Diarylimidazo[1,2-*a*]pyridines in PEG<sub>400</sub> Medium through One-Pot Condensation and C–H Arylation 

**Keywords:** Synthetic methods / Nitrogen heterocycles / C–H activation