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Copper(II)-Mediated Aerobic Synthesis of Imidazo[1,2-*a*]pyridines via Cascade Aminomethylation/Cycloisomerization of Alkynes

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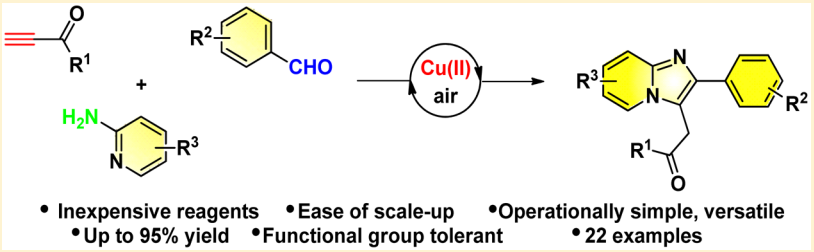
Supporting Information



ABSTRACT: A single copper(II)-catalyzed three-component cascade aminomethylation/cycloisomerization of propiolates to form imidazo[1,2-*a*]pyridines was explored. A straightforward method was developed for the practical synthesis of functionalized imidazo[1,2-*a*]pyridines from benzaldehydes, 2-aminopyridines, and propiolate derivatives catalyzed by $Cu(OAc)_2$ hydrate in the presence of air. The protocol is marked by excellent yields, functional group tolerance, and, above all, adaptability to synthesize imidazo[1,2-*a*]pyridine-based drug molecules such as Alpidem.

Imidazo[1,2-*a*]pyridines are challenging templates in the context of CNS therapies.[1] Many drugs with the imidazo-[1,2-*a*]pyridine scaffold (zolpidem, alpidem, zolimidine, olprinone, saripidem, and necopidem) are extensively prescribed as sedatives, anxiolytics, anticonvulsants, or muscle relaxants.[2] Moreover, the continuous appearance of reports describing novel pharmacological activities of these compounds, e.g., inhibition of farnesyl pyrophosphate synthase (minodronic acid), antimalarial agents,[3] bromodomain,[4] *c*-Met tyrosine kinase inhibitors[5] for cancer treatment, etc.,[6] unequivocally corroborate the ability of imidazopyridines to modulate relevant biomolecules beyond CNS targets (Figure 1).

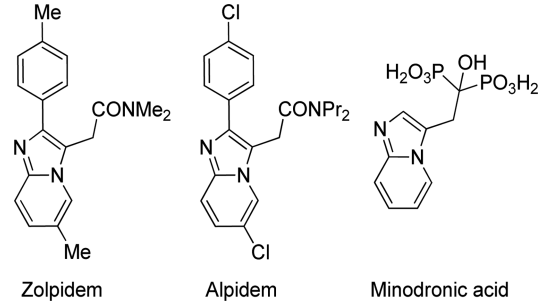


Figure 1. Imidazo[1,2-*a*]pyridine-based drug molecules.

The prevalence of the imidazopyridine scaffold in medically relevant compounds,[6] dyes,[7] ligands for metal catalysts,[8] and materials[9] has inspired the development of many novel methods for their preparation.[10] However, there are only limited protocols for assembling 3-methylenecarbonyl-substituted imidazo[1,2-*a*]pyridine derivatives, important pharmacophores[11] and promising intermediates in organic synthesis.[12] Traditional methods include the heterocyclization of 2-aminopyridines with bromo keto esters[13] and α,β-unsaturated carbonyl compounds.[14] Alternatively, the double aza-Michael addition reaction of Morita−Baylis−Hillman acetates of nitroalkenes with 2-aminopyridines[15] was described. Despite that, it is still a great challenge to synthesize functionalized imidazopyridines from readily available and easily varied starting materials using a simple procedure.

Recently, some of us[16] developed a new three-component copper-catalyzed reaction for the synthesis of imidazo[1,2-*a*]pyridines from conveniently available 2-aminopyridines, aldehydes, and terminal alkynes (Scheme 1). This reaction is believed to undergo three cascade processes, namely (1) Schiff base formation from amine and aldehyde, (2) copper-mediated electrophilic aminomethylation of alkyne with the Schiff base leading to propargylamine, and finally (3) 5-*exo*-*dig* nucleophilic cyclization giving imidazo[1,2-*a*]pyridine. Initially, a mixed Cu(I)/Cu(II) catalysis under an inert atmosphere

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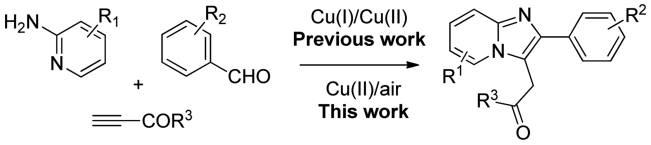
Scheme 1. Synthesis of Imidazo[1,2-*a*]pyridines via the Copper-Catalyzed Cascade Three-Component Reaction of 2-Aminopyridines, Benzaldehydes, and Terminal Alkynes



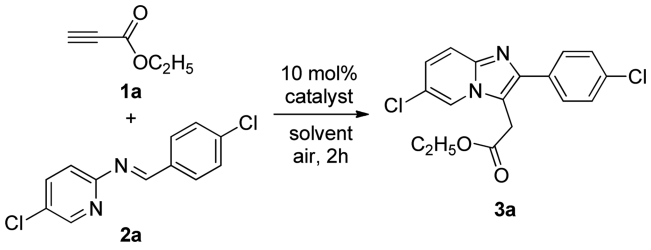
was used to obtain high product yields. To date several modifications of copper(I) catalysts such as CuHal/Cu(OTf)$_2$,[17] $CuSO_4 \cdot 5H_2O$/D-glucose,[18] $CuCl/ZnCl_2$,[19] and $CuI/NaHSO_4/SiO_2$[20] were proposed for this process. However, reactants are generally limited to aryl(alkyl)-acetylenes, while procedures suffer from stringent anaerobic and harsh conditions. Attempts to use a single copper(II) catalysts in this reaction were incompetent.[21] Only the CuHal-Cu(OTf)$_2$ pair was shown to be suitable for heterocyclization of propiolate derivatives providing direct access to the 3-methylenecarbonyl-substituted imidazo[1,2-*a*]pyridine scaffold of drugs (Scheme 1).[16,17] Cascade copper(II)-promoted heterocyclization of propiolates with imines is, to the best of our knowledge, unknown to date.

Meanwhile, the aerobic copper(II) catalysis[22] was found to be highly effective in the synthesis of diverse N-heterocycles,[23] including imidazopyridines.[24] Namely, the $CuCl_2$-catalyzed oxidative heterocyclization of functionalized Schiff bases to form imidazo[1,5-*a*]pyridines was also described.[24a] The elegant synthesis of imidazo[1,2-*a*]pyridine-3-carbaldehydes via [Cu(hfacac)$_2 \cdot x$H$_2$O]-catalyzed dehydrogenative amino-oxygenation of allyl-2-amino-5-methylpyrines was reported.[24b] These processes are valued for their mild reaction conditions and functional group tolerance.

Taking into account that Larsen and co-workers showed that aminomethylation of acetylenes with imines (the second step of the above-mentioned cascade reaction) can be successfully performed exclusively under Cu(OTf)$_2$ catalysis,[25] we were prompted to develop a practical efficient approach to imidazo[1,2-*a*]pyridines promoted with a copper(II)−oxygen catalytic system. Research was focused on propiolate derivatives as the most challenging starting materials.

In this regard, we commenced the optimization studies with ethyl propiolate (**1a**) and imine (**2a**), as model substrates, using a series of different copper sources under air (Table 1). Among the copper salts screened, Cu(OTf)$_2$ and Cu(acac)$_2$ showed promising results by providing the desired product **3a** in good yields, 69% and 72%, respectively (Table 1, entries 5 and 6). A comparison of the efficiency of Cu(II) and Cu(I) showed the superior activity of Cu(II) (Table 1, entries 1−3, 5, and 6). The only exception was $CuOTf \cdot C_6H_6$, which produced a comparable yield (67%, Table 1, entry 4). The best results were achieved by performing the reaction with Cu(OAc)$_2$ hydrate in toluene at 120 °C to afford compound **3a** in 95% isolated yield (Table 1, entry 7). The reactions in different solvents, including DCE and acetonitrile, gave low yields of product **3a** (11%, Table 1, entries 10 and 11), whereas neat conditions, DCM, and water were ineffective and led to traces of the product (Table 1, entries 8, 9, and 12). Besides, the reaction of 1 equiv of **1a** with imine **2a** in the presence of Cu(OAc)$_2$ hydrate afforded **3a** in a yield of 39% (Table 1, entry 13) versus 95% when using 2 equiv of **1a**.

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	solvent	*T*, °C	yield **3a**, %
1	CuBr	toluene	120	25[b]
2	CuCl	toluene	120	24[c]
3	$CuSO_4 \cdot 5H_2O$	toluene	120	59[b]
4	$CuOTf \cdot C_6H_6$	toluene	120	67[b]
5	Cu(OTf)$_2$	toluene	120	69[c]
6	Cu(acac)$_2$	toluene	120	72[c]
7	**Cu(OAc)$_2 \cdot$H$_2$O**	**toluene**	**120**	**95**[c]
8	Cu(OAc)$_2 \cdot$H$_2$O	neat	100	5[b]
9	Cu(OAc)$_2 \cdot$H$_2$O	CH_2Cl_2	54	5[b]
10	Cu(OAc)$_2 \cdot$H$_2$O	$C_2H_4Cl_2$	100	11[b]
11	Cu(OAc)$_2 \cdot$H$_2$O	CH_3CN	100	11[b]
12	Cu(OAc)$_2 \cdot$H$_2$O	H_2O	120	–
13	Cu(OAc)$_2 \cdot$H$_2$O	toluene	120	39[d,e]

[a]Reaction conditions: imine **2a** (0.20 mmol), ethyl propiolate **1a** (2 equiv), Cu salt (10 mol %), solvent (1 mL) in a screw-capped vial under air. [b]Determined by ^{1}H NMR. [c]Isolated yield. [d]Reaction with 1 equiv of ethyl propiolate **1a**. [e]Yield with respect to 85% conversion of **2a**.

Based on the above results, then we developed a one-pot three-component protocol using the following standard reaction conditions: 10 mol % of Cu(OAc)$_2$ hydrate, 1.0 equiv of amine, 1.1 equiv of aldehyde, and 2.0 equiv of propiolate in toluene at 120 °C in a screw-capped vial under air in the presence of molecular sieves. Ethyl propiolate and copper catalysts were added to the reaction mixture upon completion of the dehydrocondensation step. The yield of **3a** under one-pot conditions was still quantitative (95% after column chromatography).

Having the optimal conditions in hand, we investigated the scope of the one-pot three-component protocol for the reaction of a series of substituted aryl aldehydes **4** and 2-aminopyridines **5** with ethyl propiolate **1a** as a representative example (Table 2).

Aryl aldehydes containing electron-donating and -withdrawing groups were exposed to the reaction with unsubstituted 2-aminopyridine. The electron-withdrawing substituents in orto-, meta-, and para-positions such as Cl and NO_2 provided high product yields (73−83% for **3b**−**3e**). The employment of 4-fluorobenzaldehyde led to compound **3f** in 59% yield. Electron-donating methoxy groups attached to the aryl moiety decreased the yield to 37% (**3g**). When using benzaldehyde, the desired coupling product **3u** was not obtained although **1a** was entirely consumed (the reaction afforded a complex mixture). The investigation of the substrate scope by employing 2-aminopyridines with electron-donating and -withdrawing groups in the reaction with unsubstituted benzaldehyde showed that the electronic effects of substituents on the pyridine ring are not pronounced. Methyl and chloride derivatives **3i** and **3h** were obtained in 23% and 14% yields, respectively.

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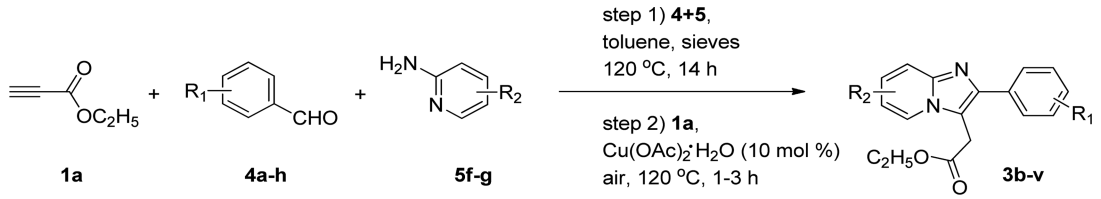
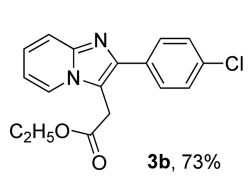
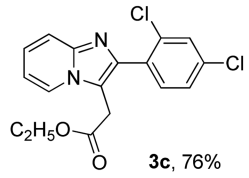
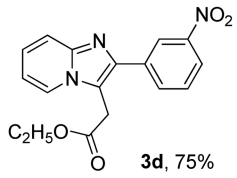
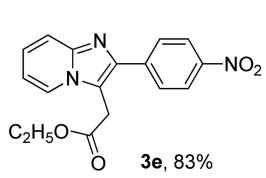
Table 2. One-Pot Synthesis of Imidazo[1,2-*a*]pyridines 3[a,b]

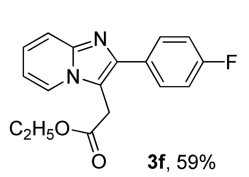


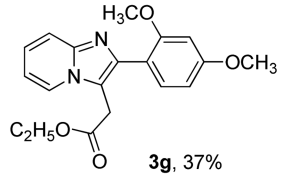


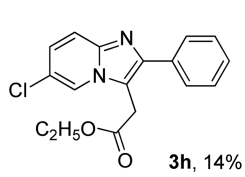


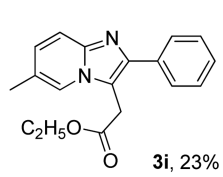


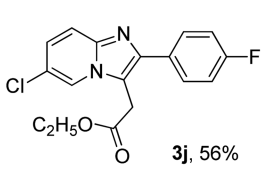


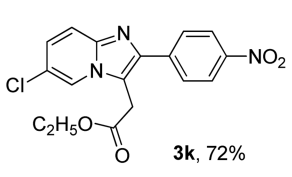


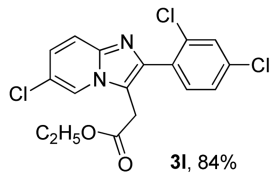


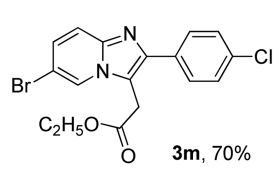


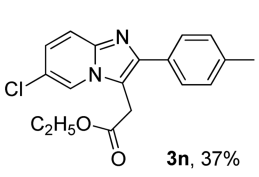


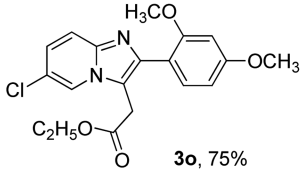


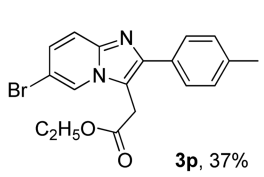


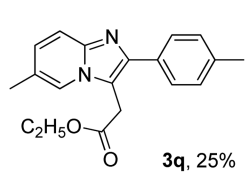


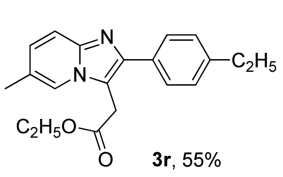


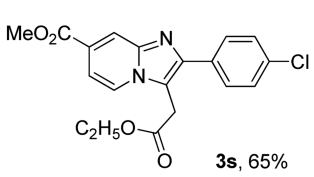


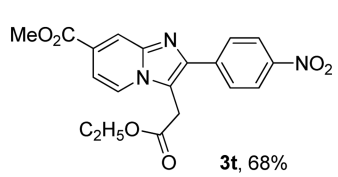


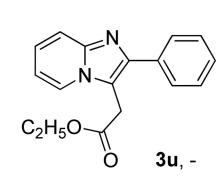












[a]Reaction conditions: (step 1) aldehyde **4** (0.36 mmol) and 2-aminopyridine **5** (0.30 mmol) with molecular sieves (300 mg) in toluene (1.5 mL) at 120 °C for 14 h; (step 2) ethyl propiolate **1a** (2 equiv) and $Cu(OAc)_2$ hydrate (10 mol %) at 120 °C for 1−3 h. [b]Isolated yield.

The three-component coupling of 5-halo-2-aminopyridines with ethyl propiolate **1a** and benzaldehydes containing both electron-donating and -withdrawing substituents on the benzoyl group proceeded smoothly in 56−95% yield (**3a,j−o**). Weak electron-donating *p*-tolylaldehyde showed moderate yields (37%, 37%, and 25% for **3n**, **3p**, and **3q**, respectively). However, for *p*-ethylbenzaldehyde, improvement was observed; compound **3r** was isolated in 55% yield. The reaction can also be performed with carboxy-substituted pyridines, namely, ethyl 2-aminoisonicotinate, producing the corresponding imidazo[1,2-*a*]pyridines **3s,t** in good yields.

All these reactions were carried out at a 0.3 mmol scale, but they could easily be scaled-up. Indeed, imidazo[1,2-*a*]pyridine **3a** was prepared in an 88% isolated yield (2.7 g, recrystallization from EtOH) at the 8 mmol scale from 1.0 equiv (2.0 g) of the imine **2a**.

The synthetic utility of the process described in this study was demonstrated by its use in a concise route for the preparation of Alpidem, an anxyolytic drug (Scheme 2). Starting from the propiolamide **1b** and Schiff base generated *in situ* from *p*-chlorbenzaldehyde **4b** and 5-chloro-2-aminopyridine **5b**, the target Alpidem **6** was produced. The isolated yield of **6** achieved in the one-pot two-step procedure was 91% compared with the reported overall yields of 83% (two steps)[16] and 72% (four steps).[15]

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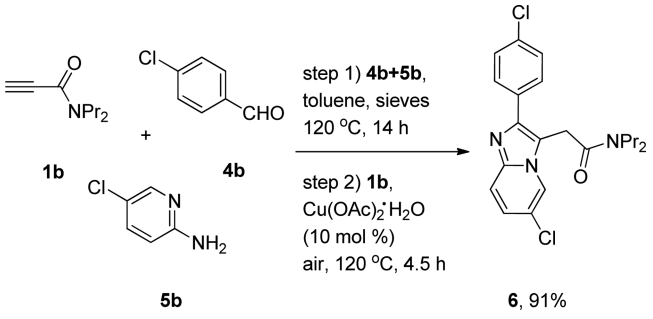
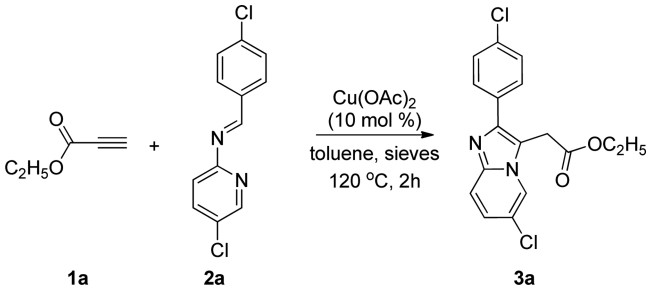
Scheme 2. Synthesis of Alpidem



Control experiments were performed to gain insights into the reaction mechanism (Table 3). The reaction of **1a** with

Table 3. Studies of the Heterocyclization of Propiolates[a–d]



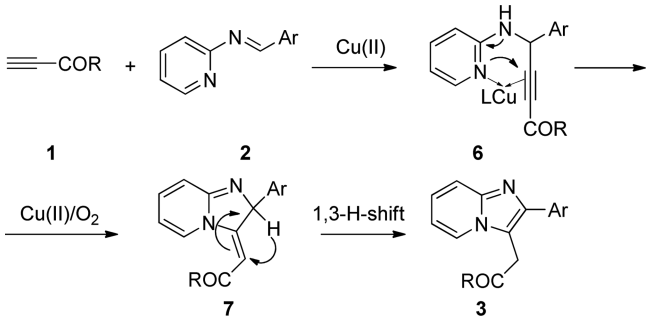
entry	deviation from standard conditions	yield **3a**, %
1	–	95[b]
2	inert atmosphere	51[c]
3	inert atmosphere, CuCl (10 mol %)	75[c]
4	inert atmosphere, 2-aminophenol (5 mol %)	47[c]

[a]Standard reaction conditions: imine **2a** (0.20 mmol), ethyl propiolate **1a** (2 equiv), $Cu(OAc)_2$ hydrate (10 mol %), toluene (1 mL) in a screw-capped vial under air. [b]Isolated yield. [c]Determined by ^1H NMR with internal standard. [d]In all experiments, the conversion of starting imine **2a** was complete.

imine **2a** under an inert atmosphere of argon under standard conditions for 2 h afforded **3a** in 51% yield (Table 3, entry 2) versus 95% in air (Table 3, entry 1). Since the imine alkynylation generally proceeds with Cu(I),[16−21] the possibility of oxidative disproportionation of Cu(II) as a source of active Cu(I) species was addressed with a mixed catalyst study. The direct addition of Cu(I) as the CuCl salt (Table 3, entry 3) or the *in situ* generation of Cu(I) with an 2-aminophenol[26] additive (Table 3, entry 4) led to a significant reduction of the **3a** yield accompanied by the formation of a complex mixture. More importantly, a comparison of the initial rate of the formation of product **3a** in experiments 1 and 3 (^1H NMR monitoring, aliquots every 10−20 min, corrected for the known amount of dibromomethane as the internal standard) showed that the CuCl additive reduces the reaction rate (see Supporting Information). Reaction acceleration was not observed even at the first reaction moment, prompting suggestions that copper(I) is not a key reactive species.

The possible mechanism for the formation of imidazo[1,2-*a*]pyridines **3** by the reaction of Schiff bases **2** with alkynes **1** suggested by literature precedents is shown in Scheme 3. The process is initiated by the Cu(II)-mediated aminomethylation of alkyne **1** with the Schiff base−copper complex[27] leading to

Scheme 3. Proposed Mechanistic Pathway



propargylamines **6**. The subsequent cyclization of **6** into intermediate **7** and the rearomatization of the former provide imidazo[1,2-*a*]pyridines **3**.[19]

In this case, most likely copper(II) alone provides the formation of propargylamines **6**[25] in contrast to mixed catalysis applying Cu(I) species. Moreover, the findings described above (Table 3) admit transformations of **6** into **7** involving radical coupling processes via the aminyl radical[28] by either peroxy-copper(III) active species.[24b]

CONCLUSION

In conclusion, we have explored the catalytic efficiency of a copper(II)−oxygen catalytic system in the three-component coupling reaction of aryl aldehydes with 2-aminopyridines and terminal alkynes toward imidazo[1,2-*a*]pyridines. Unlike previous processes, the present practical method avoids the requirement of an anaerobic procedure, uses an inexpensive $Cu(OAc)_2$ catalyst, tolerates an array of functional groups, and is effective for propiolate derivateves. This simple, additive-free methodology was successfully applied for the efficient synthesis of the anxiolytic drug Alpidem starting from readily available starting materials.

EXPERIMENTAL SECTION

General Information. NMR spectra were acquired at room temperature; the chemical shifts δ were measured in ppm relative to the solvent (^1H: $CDCl_3$, δ = 7.27 ppm; ^{13}C: $CDCl_3$, δ = 77.00 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, double doublet; ddd, double double doublet. The coupling constants (J) are in hertz (Hz). The structures of all compounds were established using 1D NMR (^1H, ^{13}C) spectroscopy. High-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) with Q-TOF detection and electron ionization (EI) techniques. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with an infrared spectrometer. Melting points (mp) are uncorrected. Analytical thin layer chromatography (TLC) was carried out on silica gel plates (silica gel 60 F254 aluminum supported plates); the visualization was accomplished with a UV lamp (365 nm). Column chromatography was performed on silica gel 60 (230−400 mesh) treated with 1% triethylamine solution in petroleum benzene. Alkynes, aldehydes, and 2-aminopyridines were commercially available and were used without additional purification. All reactions were carried out using freshly distilled and dry solvents. Parent *N*,*N*-dipropylpropiolamide was prepared according to published procedures.[29]

General Procedure for the Synthesis of Imidazo[1,2-*a*]pyridines 3. A screw-capped vial (2.0 mL) was charged with 2-aminopyridine (0.3 mmol, 1.0 equiv), aldehyde (0.36 mmol, 1.2 equiv), 4 Å molecular sieves (300 mg), and dry toluene (1.5 mL, 0.5 M). The microreactor was stored at 120 °C for 14 h. The resulting mixture containing imine was cooled down to room temperature and

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charged with $Cu(OAc)_2$ hydrate (6 mg, 0.03 mmol, 10 mol % on anhydrous basis) and alkyne (0.6 mmol, 2 equiv). The reaction mixture was stirred additionally at 120 °C for 1−3 h. Upon completion, the mixture was filtered through a plug of silica treated with 1% triethylamine solution in petroleum benzene (eluent−EtOAc). The filtrate was concentrated under reduced pressure to give a crude material, which was purified by column chromatography on silica gel to give product (eluent: Et_3N/EtOAc/petroleum ether).

Ethyl 2-(6-Chloro-2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3a). Yield 102 mg (95%), yellow solid, mp 154−162 °C; R_f = 0.32 (petroleum ether−EtOAc, 5:1). The spectral data and melting point matched those reported by Ley and co-workers.[14b] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.78 (d, *J* = 8.07 Hz, 2H), 7.64 (d, *J* = 9.53 Hz, 1H), 7.47 (d, *J* = 8.07 Hz, 2H), 7.25 (d, *J* = 9.53 Hz, 1H), 4.26 (q, *J* = 7.35 Hz, 2H), 4.00 (s, 2H), 1.31 (t, *J* = 7.35 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8 (CO), 144.4 (C), 143.4 (C), 134.3 (C), 132.1 (C), 129.8 (2 × CH), 128.9 (2 × CH), 126.2 (CH), 121.8 (CH), 120.9 (C), 117.9 (CH), 113.8 (C), 61.9 (CH_2), 30.8 (CH_2), 14.2 (CH_3); IR (KBr) 3087 (s), 1727 (s), 1199 (s), 841 (w), 802 (w) cm^{-1}; MS (ESI) 348 $[M]^+$.

Ethyl 2-(2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3b). Yield 76 mg (73%), yellow solid, mp 68−77 °C; R_f = 0.35 (petroleum ether−EtOAc, 1:1). The spectral data and melting point matched those reported by Namboothiri and co-workers.[15] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 6.60 Hz, 1H), 7.79 (d, *J* = 8.07 Hz, 2H), 7.64 (d, *J* = 8.81 Hz, 1H), 7.43 (d, *J* = 8.07 Hz, 2H), 7.22 (dd, *J* = 6.50, 8.81 Hz, 1H), 6.85 (dd, *J* = 6.50, 6.60 Hz, 1H), 4.21 (q, *J* = 7.34 Hz, 2H), 3.99 (s, 2H), 1.26 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2 (CO), 145.1 (C), 143.6 (C), 134.0 (C), 132.7 (C), 129.9 (2 × CH), 128.9 (2 × CH), 124.8 (CH), 123.8 (CH), 117.7 (CH), 113.1 (C), 112.6 (CH), 61.8 (CH_2), 30.9 (CH_2), 14.2 (CH_3); IR (KBr) 3140 (w), 1728 (s), 1489 (s), 1198 (w) cm^{-1}; MS (ESI) 314 $[M]^+$.

Ethyl 2-(2-(2,4-Dichlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3c). Yield 79 mg (76%), yellow solid, mp 106−109 °C; R_f = 0.40 (petroleum ether−EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, *J* = 6.60 Hz, 1H), 7.67 (d, *J* = 9.50 Hz, 1H), 7.50−7.53 (m, 2H), 7.33−7.37 (m, 1H), 7.23−7.28 (m, 1H), 6.90 (dd, *J* = 6.50, 6.60 Hz, 1H), 4.16 (q, *J* = 7.37 Hz, 2H), 3.86 (s, 2H), 1.23 (t, *J* = 7.37 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0 (CO), 145.2 (C), 135.0 (C), 134.6 (2 × C), 133.6 (CH), 132.0 (C), 129.7 (CH), 127.2 (CH), 124.7 (CH), 124.0 (CH), 118.0 (CH), 115.1 (C), 112.7 (CH), 61.6 (CH_2), 30.6 (CH_2), 14.2 (CH_3); IR (KBr) 1729 (s), 1472 (s), 1205 (w), 1158 (w) cm^{-1}; HRMS (ESI) 371.0328, calcd for $C_{17}H_{14}Cl_2N_2O_2Na^+$ ($[M + Na]^+$) 371.0325.

Ethyl 2-(2-(3-Nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3d). Yield 78 mg (75%), yellow solid, mp 103−109 °C; R_f = 0.40 (petroleum ether−EtOAc, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (s, 1H), 8.22−8.28 (m, 3H), 7.64−7.72 (m, 2H), 7.31 (dd, *J* = 6.41, 8.50 Hz, 1H), 6.95 (dd, *J* = 6.05, 6.69 Hz, 1H), 4.28 (q, *J* = 7.59 Hz, 2H), 4.07 (s, 2H), 1.33 (t, *J* = 7.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9 (CO), 148.7 (C), 145.2 (C), 142.0 (C), 135.8 (C), 134.6 (CH), 129.8 (CH), 125.6 (CH), 124.1 (CH), 123.3 (CH), 122.8 (CH), 117.8 (CH), 114.0 (C), 113.2 (CH), 62.2 (CH_2), 31.0 (CH_2), 14.2 (CH_3); IR (KBr) 1730 (s), 1521 (w), 1346 (s), 753 (w) cm^{-1}; MS (ESI) 325 $[M]^+$; HRMS (ESI-TOF) 348.0949, calcd for $C_{17}H_{15}N_3O_4Na^+$ ($[M + Na]^+$) 348.0955.

Ethyl 2-(2-(4-Nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3e). Yield 87 mg (83%), yellow solid, mp 151−156 °C; R_f = 0.20 (petroleum ether−EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.07 Hz, 2H), 8.21 (d, *J* = 6.60 Hz, 1H), 8.09 (d, *J* = 8.07 Hz, 2H), 7.77 (d, *J* = 8.80 Hz, 1H), 7.32−7.38 (m, 1H), 6.96−7.00 (m, 1H), 4.25 (q, *J* = 7.38 Hz, 2H), 4.06 (s, 2H), 1.30 (t, *J* = 7.38 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9 (CO), 147.4 (C), 145.4 (C), 142.1 (C), 140.6 (C), 129.2 (2 × CH), 125.7 (CH), 124.0 (3 × CH), 118.0 (CH), 114.6 (C), 113.3 (CH), 62.1 (CH_2), 31.0 (CH_2), 14.3 (CH_3); IR (KBr) 1734 (s), 1601 (s), 1509 (s), 1341 (s), 1234 (w), 734 (w) cm^{-1}; MS (ESI) 325 $[M]^+$; HRMS (ESI-TOF) 348.0960, calcd for $C_{17}H_{15}N_3O_4Na^+$ ($[M + Na]^+$) 348.0955.

Ethyl 2-(2-(4-Fluorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3f). Yield 62 mg (59%), yellow oil; R_f = 0.30 (petroleum ether−EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, *J* = 6.61 Hz, 1H), 7.77−7.82 (m, 2H), 7.61 (d, *J* = 8.81 Hz, 1H), 7.10−7.21 (m, 3H), 6.82 (dd, *J* = 6.48, 6.61 Hz, 1H), 4.18 (q, *J* = 7.34 Hz, 2H), 3.97 (s, 2H), 1.23 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4 (CO), 162.9 (d, J_{C-F} = 246 Hz, C), 145.0 (C), 143.8 (C), 130.4 (d, J_{C-F} = 8 Hz, 2 × CH), 124.8 (CH), 123.8 (CH), 117.7 (CH), 115.5 (d, J_{C-F} = 21.1 Hz, 2 × CH), 112.9 (C), 112.6 (CH), 61.8 (CH_2), 30.9 (CH_2), 14.3 (CH_3) (the signal of the one C atom was not observed); IR (film) 3141 (w), 1733 (s), 1503 (s), 1223 (w), 844 (w) cm^{-1}; HRMS (ESI-TOF) 321.1015, calcd for $C_{17}H_{15}FN_2O_2Na^+$ ($[M + Na]^+$) 321.1010.

Ethyl 2-(2-(2,4-Dimethoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3g). Yield 39 mg (37%), yellow oil; R_f = 0.16 (petroleum ether−EtOAc, 1:4). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, *J* = 6.60 Hz, 1H), 7.67 (d, *J* = 8.54 Hz, 1H), 7.47 (d, *J* = 1.47 Hz, 1H), 7.38 (dd, *J* = 1.47, 8.07 Hz, 1H), 7.23 (dd, *J* = 7.15, 8.54 Hz, 1H), 6.99 (d, *J* = 8.07 Hz, 1H), 6.87 (dd, *J* = 6.60, 7.15 Hz, 1H), 4.22 (q, *J* = 7.31 Hz, 2H), 4.04 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 1.27 (t, *J* = 7.31 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6 (CO), 149.3 (C), 149.1 (C), 144.9 (C), 144.6 (C), 126.9 (C), 124.6 (CH), 123.8 (CH), 121.1 (CH), 117.5 (CH), 112.5 (CH), 112.0 (CH), 111.4 (CH), 110.1 (C), 61.7 (CH_2), 56.1 (CH_3O), 56.0 (CH_3O), 31.1 (CH_2), 14.3 (CH_3); IR (film) 1732 (s), 1508 (s), 1397 (s), 1251 (w), 1025 (s), 753 (w) cm^{-1}; HRMS (ESI-TOF) 341.1498, calcd for $C_{19}H_{21}N_2O_4^+$ ($[M + H]^+$) 341.1496.

Ethyl 2-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-acetate (3h). Yield 14 mg (14%), yellow solid, mp 111−117 °C; R_f = 0.35 (petroleum ether−EtOAc, 1:1). The spectral data and melting point matched those reported by Ley and co-workers.[14b] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.83 (d, *J* = 7.34 Hz, 2H), 7.62 (d, *J* = 9.54 Hz, 1H), 7.47−7.52 (m, 2H), 7.39−7.44 (m, 1H), 7.25 (d, *J* = 9.54 Hz, 1H), 4.26 (q, *J* = 7.34 Hz, 2H), 4.04 (s, 2H), 1.32 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0 (CO), 145.7 (C), 143.4 (C), 133.7 (C), 128.7 (2 × CH), 128.6 (2 × CH), 128.2 (CH), 125.9 (CH), 121.8 (CH), 120.7 (C), 118.0 (CH), 113.7 (C), 61.8 (CH_2), 30.8 (CH_2), 14.2 (CH_3); IR (KBr) 2966 (w), 1724 (s), 1198 (s), 1159 (s) cm^{-1}; MS (ESI) 314 $[M]^+$.

Ethyl 2-(6-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-acetate (3i). Yield 24 mg (23%), yellow solid, mp 95−100 °C; R_f = 0.20 (petroleum ether−EtOAc, 3:1). The spectral data and melting point matched those reported by Ley and co-workers.[14b] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.83 (d, *J* = 7.34 Hz, 2H), 7.57 (d, *J* = 8.81 Hz, 1H), 7.44−7.49 (m, 2H), 7.34−7.39 (m, 1H), 7.08 (d, *J* = 8.81 Hz, 1H), 4.23 (q, *J* = 7.34 Hz, 2H), 4.02 (s, 2H), 2.37 (s, 3H), 1.28 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5 (CO), 144.0 (C), 134.1 (C), 130.3 (C), 128.7 (3 × CH), 127.9 (2 × CH), 122.3 (CH), 121.5 (CH), 116.9 (CH), 112.8 (C), 108.1 (C), 61.7 (CH_2), 30.9 (CH_2), 18.5 (CH_3), 14.2 (CH_3); IR (KBr) 3148 (w), 1728 (s), 1180 (s), 796 (w), 702 (w) cm^{-1}; MS (ESI) 294 $[M]^+$.

Ethyl 2-(6-Chloro-2-(4-fluorophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3j). Yield 63 mg (56%), yellow solid, mp 145−150 °C; R_f = 0.15 (petroleum ether−EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.78−7.83 (m, 2H), 7.60 (d, *J* = 8.78 Hz, 1H), 7.15−7.22 (m, 3H), 4.25 (q, *J* = 7.34 Hz, 2H), 3.99 (s, 2H), 1.31 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0 (CO), 162.8 (d, J_{C-F} = 247 Hz, C), 144.9 (C), 143.5 (C), 130.4 (d, J_{C-F} = 9 Hz, 2 × CH), 129.8 (C), 126.1 (CH), 121.9 (CH), 120.9 (C), 118.0 (CH), 115.7 (d, J_{C-F} = 22.1 Hz, 2 × CH), 113.5 (C), 62.0 (CH_2), 30.9 (CH_2), 14.3 (CH_3); IR (KBr) 3131 (w), 1726 (s), 1501 (s), 1254 (w), 844 (w) cm^{-1}; HRMS (ESI-TOF) 333.0804, calcd for $C_{17}H_{15}ClFN_2O_2^+$ ($[M + H]^+$) 333.0801.

Ethyl 2-(6-Chloro-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3k). Yield 75 mg (72%), yellow solid, mp 202−206 °C; R_f = 0.35 (petroleum ether−EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.24 Hz, 2H), 8.26 (s, 1H), 8.06 (d, *J* = 8.24 Hz, 2H), 7.64 (d, *J* = 9.15 Hz, 1H), 7.27 (d, *J* = 9.15 Hz, 1H), 4.28 (q, *J* = 7.29 Hz, 2H), 4.05 (s, 2H), 1.33 (t, *J* = 7.29 Hz, 3H); ^{13}C

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NMR (75 MHz, $CDCl_3$): δ 168.6 (CO), 147.6 (C), 143.8 (C), 143.3 (C), 140.2 (C), 129.2 (2 × CH), 127.0 (CH), 124.1 (2 × CH), 122.0 (CH), 121.6 (C), 118.4 (CH), 115.1 (C), 62.3 (CH_2), 31.0 (CH_2), 14.3 (CH_3); IR (KBr) 1722 (s), 1602 (s), 1514 (w), 1343 (w), 1212 (s), 860 (w) cm^{-1}; HRMS (ESI-TOF) 360.0748, calcd for $C_{17}H_{15}ClN_3O_4^+$ ($[M + H]^+$) 360.0746.

Ethyl 2-(6-Chloro-2-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3l). Yield 88 mg (84%), yellow solid, mp 141−146 °C; R_f = 0.20 (petroleum ether−EtOAc, 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.63 (d, *J* = 9.54 Hz, 1H), 7.52 (s, 1H), 7.49 (d, *J* = 8.81 Hz, 1H), 7.35 (d, *J* = 8.81 Hz, 1H), 7.24 (d, *J* = 9.54 Hz, 1H), 4.18 (q, *J* = 7.39 Hz, 2H), 3.84 (s, 2H), 1.25 (t, *J* = 7.39 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.6 (CO), 143.4 (C), 142.2 (C), 135.3 (C), 134.4 (C), 133.5 (CH), 131.2 (C), 129.9 (CH), 127.3 (CH), 126.4 (CH), 122.1 (CH), 121.2 (C), 118.2 (CH), 115.9 (C), 61.8 (CH_2), 30.5 (CH_2), 14.2 (CH_3); IR (KBr) 3134 (s), 1725 (s), 1372 (s), 1325 (s), 1204 (w), 1155 (w), 1100 (w), 808 (w) cm^{-1}; HRMS (ESI-TOF) 383.0121, calcd for $C_{17}H_{14}Cl_3N_2O_2^+$ ($[M + H]^+$) 383.0115.

Ethyl 2-(6-Bromo-2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3m). Yield 73 mg (70%), yellow solid, mp 159−173 °C; R_f = 0.32 (petroleum ether−EtOAc, 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.77 (d, *J* = 8.07 Hz, 2H), 7.55 (d, *J* = 8.81 Hz, 1H), 7.45 (d, *J* = 8.07 Hz, 2H), 7.30 (d, *J* = 8.81 Hz, 1H), 4.25 (q, *J* = 7.06 Hz, 2H), 3.99 (s, 2H), 1.30 (t, *J* = 7.06 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9 (CO), 144.1 (C), 143.4 (C), 134.4 (C), 131.9 (C), 129.9 (2 × CH), 129.1 (2 × CH), 128.5 (CH), 124.1 (CH), 118.2 (CH), 113.7 (C), 107.6 (C), 62.0 (CH_2), 30.9 (CH_2), 14.2 (CH_3); IR (KBr) 1724 (s), 1296 (w), 803 (w) cm^{-1}; MS (ESI) 393 $[M]^+$; HRMS (ESI-TOF) 416.9790, calcd for $C_{17}H_{14}BrClN_2O_2Na^+$ ($[M + Na]^+$) 416.9799.

Ethyl 2-(6-Chloro-2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3n). Yield 39 mg (37%), yellow oil; R_f = 0.32 (petroleum ether−EtOAc, 5:1). The spectral data matched those reported by Ley and co-workers.[14b] ^1H NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.71 (d, *J* = 7.32 Hz, 2H), 7.59 (d, *J* = 9.54 Hz, 1H), 7.29 (d, *J* = 7.32 Hz, 2H), 7.19 (d, *J* = 9.54 Hz, 1H), 4.24 (q, *J* = 7.36 Hz, 2H), 4.01 (s, 2H), 2.41 (s, 3H), 1.30 (t, *J* = 7.36 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1 (CO), 145.8 (C), 143.4 (C), 138.1 (C), 130.8 (C), 129.5 (2 × CH), 128.5 (2 × CH), 125.7 (CH), 121.8 (C), 120.6 (CH), 117.9 (CH), 113.4 (C), 61.8 (CH_2), 30.9 (CH_2), 21.3 (CH_3), 14.2 (CH_3); IR (film) 1734 (s), 1573 (s), 1025 (w), 823 (w) cm^{-1}; MS (ESI) 328 $[M]^+$.

Ethyl 2-(6-Chloro-2-(2,4-dimethoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)acetate (3o). Yield 78 mg (75%), yellow oil; R_f = 0.38 (petroleum ether−EtOAc, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.66 (d, *J* = 9.54 Hz, 1H), 7.46 (s, 1H), 7.37 (d, *J* = 8.07 Hz, 1H), 7.24 (d, *J* = 9.54 Hz, 1H), 7.00 (d, *J* = 8.07 Hz, 1H), 4.25 (q, *J* = 7.46 Hz, 2H), 4.03 (s, 2H), 3.99 (s, 3H), 3.95 (s, 3H), 1.31 (t, *J* = 7.46 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2 (CO), 149.3 (C), 146.4 (C), 145.7 (C), 143.3 (C), 126.4 (C), 125.8 (CH), 121.8 (CH), 121.0 (CH), 120.6 (C), 117.7 (CH), 113.1 (CH), 111.8 (C), 111.3 (CH), 61.9 (CH_2), 56.0 (2 × OCH_3), 31.0 (CH_2), 14.2 (CH_3); IR (film) 3021 (w), 1734 (s), 1509 (s), 1258 (w), 1102 (w) cm^{-1}; HRMS (ESI-TOF) 375.1099, calcd for $C_{19}H_{20}ClN_2O_4^+$ ($[M + H]^+$) 375.1106.

Ethyl 2-(6-Bromo-2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3p). Yield 39 mg (37%), yellow solid, mp 172−176 °C; R_f = 0.35 (petroleum ether−EtOAc, 4:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.71 (d, *J* = 8.24 Hz, 2H), 7.54−7.57 (m, 1H), 7.27−7.30 (m, 3H), 4.24 (q, *J* = 7.20 Hz, 2H), 4.01 (s, 2H), 2.41 (s, 3H), 1.30 (t, *J* = 7.20 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 169.1 (CO), 145.3 (C), 143.3 (C), 138.3 (C), 130.4 (C), 129.6 (2 × CH), 128.5 (2 × CH), 128.2 (CH), 124.1 (CH), 118.1 (CH), 113.3 (C), 107.3 (C), 61.9 (CH_2), 30.9 (CH_2), 21.4 (CH_3), 14.2 (CH_3); IR (KBr) 3181 (w), 1731 (s), 1619 (w), 801 (w) cm^{-1}; HRMS (ESI-TOF) 395.0341, calcd for $C_{18}H_{17}BrN_2O_2Na^+$ ($[M + Na]^+$) 395.0366.

Ethyl 2-(6-Methyl-2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)-acetate (3q). Yield 26 mg (25%), yellow solid, mp 85−99 °C; R_f = 0.20 (petroleum ether−EtOAc, 3:1). The spectral data and melting point matched those reported by Namboothiri and co-workers.[15] ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.74 (d, *J* = 8.07 Hz, 2H), 7.62 (d, *J* = 8.80 Hz, 1H), 7.29 (d, *J* = 8.07 Hz, 2H), 7.11 (d, *J* = 8.80 Hz, 1H), 4.24 (q, *J* = 7.39 Hz, 2H), 4.02 (s, 2H), 2.41 (s, 3H), 2.38 (s, 3H), 1.29 (t, *J* = 7.39 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6 (CO), 144.5 (C), 144.0 (C), 137.6 (C), 131.4 (C), 129.4 (2 × CH), 128.4 (2 × CH), 127.6 (CH), 122.0 (C), 121.4 (CH), 116.8 (CH), 112.5 (C), 61.6 (CH_2), 30.9 (CH_2), 21.3 (CH_3), 18.5 (CH_3), 14.2 (CH_3); IR (KBr) 3429 (w), 1722 (s), 1185 (w), 789 (w) cm^{-1}; MS (ESI) 308 $[M]^+$.

Ethyl 2-(2-(4-Ethylphenyl)-6-methylimidazo[1,2-*a*]pyridin-3-yl)acetate (3r). Yield 57 mg (55%), yellow oil; R_f = 0.20 (petroleum ether−EtOAc, 3:1). ^1H NMR (300 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.76 (d, *J* = 7.34 Hz, 2H), 7.57 (d, *J* = 8.81 Hz, 1H), 7.31 (d, *J* = 7.34 Hz, 2H), 7.08 (d, *J* = 8.81 Hz, 1H), 4.23 (q, *J* = 7.34 Hz, 2H), 4.02 (s, 2H), 2.71 (q, *J* = 7.34 Hz, 2H), 2.37 (s, 3H), 1.28 (t, *J* = 7.34 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6 (CO), 144.5 (C), 144.1 (C), 144.0 (C), 131.6 (C), 128.6 (2 × CH), 128.2 (2 × CH), 127.6 (CH), 122.0 (C), 121.4 (CH), 116.9 (CH), 112.5 (C), 61.6 (CH_2), 31.0 (CH_2), 28.7 (CH_3), 18.5 (CH_3), 15.6 (CH_3), 14.2 (CH_3); IR (film) 1734 (s), 1252 (w), 1027 (w), 839 (w) cm^{-1}; HRMS (ESI-TOF) 323.1763, calcd for $C_{20}H_{23}N_2O_2^+$ ($[M + H]^+$) 323.1754.

Ethyl 2-(4-Carbomethoxy-2-(4-chlorophenyl)imidazo[1,2-*a*]-pyridin-3-yl)acetate (3s). Yield 68 mg (65%), yellow solid, mp 128−131 °C; R_f = 0.23 (petroleum ether−EtOAc, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.17 (d, *J* = 7.47 Hz, 1H), 7.80 (d, *J* = 8.47 Hz, 2H), 7.46−7.49 (m, 3H), 4.24 (q, *J* = 7.43 Hz, 2H), 4.05 (s, 2H), 3.98 (s, 3H), 1.29 (t, *J* = 7.43 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8 (CO), 165.7 (CO), 146.0 (C), 144.1 (C), 134.5 (C), 132.1 (C), 129.9 (2 × CH), 129.0 (2 × CH), 126.2 (C), 123.4 (CH), 120.3 (CH), 115.1 (C), 111.9 (CH), 62.0 (CH_2), 52.7 (CH_3), 30.9 (CH_2), 14.2 (CH_3); HRMS (ESI-TOF) 395.0756, calcd for $C_{19}H_{17}ClN_2O_4Na^+$ ($[M + Na]^+$) 395.0769.

Ethyl 2-(4-Carbomethoxy-2-(4-nitrophenyl)imidazo[1,2-*a*]-pyridin-3-yl)acetate (3t). Yield 71 mg (68%), yellow solid, mp 161−164 °C; R_f = 0.20 (petroleum ether−EtOAc, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.35 (d, *J* = 7.82 Hz, 2H), 8.22 (d, *J* = 7.43 Hz, 1H), 8.07 (d, *J* = 7.82 Hz, 2H), 7.52 (d, *J* = 7.43 Hz, 1H), 4.27 (q, *J* = 7.42 Hz, 2H), 4.10 (s, 2H), 3.98 (s, 3H), 1.31 (t, *J* = 7.42 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5 (CO), 165.5 (CO), 147.6 (C), 144.5 (C), 144.3 (C), 140.1 (C), 129.2 (2 × CH), 126.9 (C), 124.1 (2 × CH), 123.6 (CH), 120.5 (CH), 116.3 (C), 112.3 (CH), 62.2 (CH_2), 52.8 (CH_3), 31.0 (CH_2), 14.2 (CH_3); HRMS (ESI-TOF) 384.1184, calcd for $C_{19}H_{18}N_3O_6^+$ ($[M + H]^+$) 384.1190.

2-(6-Chloro-2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-*N*,*N*-dipropylacetamide (6). Yield 95 mg (91%), yellow solid, mp 133−135 °C; R_f = 0.20 (petroleum ether−EtOAc, 3:1). The spectral data and melting point matched those reported by Ley and co-workers.[14b] ^1H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, *J* = 1.47 Hz, 1H), 7.58 (d, *J* = 8.07 Hz, 2H), 7.55 (d, *J* = 9.53 Hz, 1H), 7.43 (d, *J* = 8.07 Hz, 2H), 7.18 (dd, *J* = 1.47, 9.53 Hz, 1H), 4.05 (s, 2H), 3.30 (q, *J* = 7.34 Hz, 2H), 3.13 (q, *J* = 7.34 Hz, 2H), 1.48−1.59 (m, 4H), 0.86 (t, *J* = 7.34 Hz, 3H), 0.77 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.3 (CO), 143.8 (C), 143.6 (C), 134.2 (C), 132.8 (C), 129.9 (2 × CH), 129.0 (2 × CH), 126.1 (CH), 122.7 (CH), 120.6 (C), 117.8 (CH), 115.7 (C), 50.0 (CH_2), 48.1 (CH_2), 30.1 (CH_2), 22.3 (CH_2), 21.0 (CH_2), 11.4 (CH_3), 11.1 (CH_3); MS (ESI) 404 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02102.

Copies of ^1H, ^{13}C NMR spectra, full data concerning optimization of reaction conditions and kinetic experiments (PDF)

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Notes

The authors declare no competing financial interest.

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