Pd/Cu-Catalyzed Oxidative C–H Alkenylation of Imidazo[1,2-*a*]pyridines

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Received 4 September 2008; revised 8 September 2008

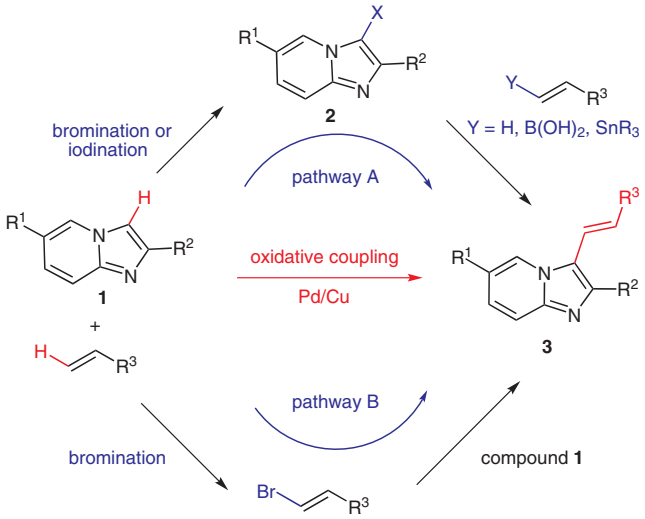
Abstract: A novel direct and regioselective Pd/Cu-catalyzed intermolecular oxidative coupling of imidazo[1,2-*a*]pyridines with alkenes was successfully developed. The scope and limitations of the reaction were further studied by using various alkenes. This method provides a 'green' route to 3-alkenylimidazo[1,2-*a*]pyridine derivatives in high yields.

Key words: palladium/copper-catalyzed oxidative coupling, alkenylation, imidazo[1,2-*a*]pyridines

The ability to form C–C bonds is an indispensable tool in synthetic organic chemistry, and the development of powerful catalytic methods has opened new routes to complex molecule synthesis. Usually, heteroaryl–aryl bonds are formed by the coupling of two functionalized heteroaromatic carbons, but that is not always necessary. It is sometimes possible to directly arylate an aromatic ring by replacing a C–H bond with a C–C bond. In the past three decades, the development of transition-metal-catalyzed C–H activation reactions has received considerable attention.[1] A wide range of metal catalysts, including Ru, Rh, Pt, and Pd catalysts, have been exploited with varying levels of success.

Considering the remarkable progress made in the development of palladium-catalyzed C–C bond-forming reactions of various heterocycles,[2,3] we turned our attention to intermolecular C–H alkenylation via oxidative Pd/Cu-catalyzed reactions. In the recent years a limited number of methods for regioselective couplings of heteroaromatic systems using oxidative palladium-catalyzed reactions of arenes and olefins have been described;[4] however, in some cases, these procedures have shown moderate regioselectivity.[4]

Our group has a long-standing interest in imidazo[1,2-*a*]pyridine derivatives.[5] We have reported a regioselective palladium-catalyzed (hetero)arylation[6] at C-3 of imidazo[1,2-*a*]pyridines and the first examples of one-pot, two-step Suzuki cross-coupling/direct arylation and one-pot, three-step cyclization/Suzuki cross-coupling/regioselective arylation.[7] Herein, we describe recent advances in the direct and regioselective alkenylation of imidazo[1,2-*a*]pyridines by oxidative Pd/Cu-catalyzed C–H bond activation (Scheme 1). As far as we know, this is the first example of intermolecular oxidative C-3 alkenylation of bicyclic heterocycles with a bridgehead nitrogen atom.



Scheme 1

To the best of our knowledge, few approaches, including palladium cross-coupling, are known for preparing 3-alkenylimidazo[1,2-*a*]pyridines **3** from imidazo[1,2-*a*]pyridines **1** (Scheme 1): pathway A, involving halogenation of imidazo[1,2-*a*]pyridines **1**[5a,8–10] followed by Heck,[5a,8,11] Stille,[12] or Suzuki[13] cross-coupling; pathway B, involving bromination of alkene followed by the 'inverse' Heck reaction.[14] Although these sequences were successful, an additional step for the activation of imidazo[1,2-*a*]pyridines and alkenes is required and expensive reagents are used (alkenylboronic acids for Suzuki and alkenylstannanes for Stille couplings). Compared to these methods, the oxidative alkenylation reaction is obviously advantageous in terms of starting material price and byproduct (i.e., brominated alkene) formation.

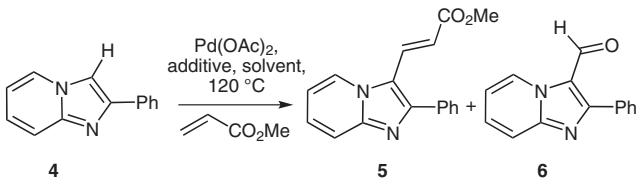
The alkenylation reaction was examined using 2-phenylimidazo[1,2-*a*]pyridine (**4**)[15] and methyl acrylate (Scheme 2, Table 1). The key to success was the optimum combined choice of the catalyst, solvent, and oxidant. Initial investigations consisted of testing the reaction conditions reported for the oxidative dimerization of an imidazotriazine[16] [$Pd(OAc)_2$ (10 mol%), KOAc (2 equiv)]. Under these conditions, the coupling between 2-phenylimidazo[1,2-*a*]pyridine (**4**) and methyl acrylate (4 equiv) in *N*,*N*-dimethylformamide at 120 °C for 60 hours using either O_2 or air as oxidant led to the formation of the

SYNTHESIS 2009, No. 2, pp 0271–0276
Advanced online publication: 12.12.2008
DOI: 10.1055/s-0028-1083252; Art ID: Z20608SS

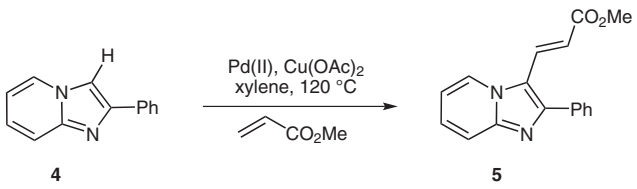
Table 1 Effect of the Oxidant and the Solvent

Entry	Additive[a]	Solvent	Time (h)	Recovered **4** (%)	Yield[b] (%) of **5**	Yield[b] (%) of **6**
1	KOAc, O_2	DMF	60	0	51	0
2	KOAc, air	DMF	60	0	50	0
3	no base, air	DMF	60	0	54	0
4	$Cu(OAc)_2$, air	DMF	3	0	44	11
5	$Cu(OAc)_2$, air	toluene	3	0	62	0
6	$Cu(OAc)_2$, air	xylene	3	0	63	0
7	Ag_2O, argon	xylene	30	23	52	0
8	1,4-benzoquinone, argon	xylene	30	33	25	0
9	CuO, argon	xylene	30	32	41	0
10	$Cu(OAc)_2$, argon	xylene	3	0	85	0

[a] 2 Equivalents of oxidant or base were used.
[b] Yields given are for isolated products.



Scheme 2



Scheme 3

desired compound **5** in 51% and 50% yield, respectively (Table 1, entries 1 and 2). When the same reaction was exposed to atmospheric oxygen in the absence of potassium acetate for 60 hours, product **5** was isolated in 54% yield (entry 3). We found that when copper(II) acetate was used as co-oxidant under air in *N*,*N*-dimethylformamide at 120 °C, the reaction gave the alkenylated product **5** and the formylated byproduct **6**[17] in 44% and 11% yield, respectively (entry 4). The use of toluene or xylene as solvent avoided the formation of this byproduct and furnished the desired compound **5** in 62% and 63% yield, respectively (entries 5 and 6). Then, the effect of the oxidant on the coupling efficacy was investigated. Thus, four oxidants [Ag_2O, 1,4-benzoquinone, CuO, $Cu(OAc)_2$] were tested (Table 1, entries 7–10). First, the use of silver(I) oxide (2 equiv) in the presence of palladium(II) acetate (10 mol%) in xylene at 120 °C resulted in 52% of the desired compound **5** (entry 7). 1,4-Benzoquinone or copper(II) oxide, under similar reaction conditions, gave compound **5** in only 25% and 41% yield, respectively (entries 8 and 9). It is noteworthy that a significant amount of starting material was recovered (entries 7–9). Interestingly, when copper(II) acetate was used as oxidant, the desired methyl 3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (**5**) was isolated in excellent yield (entry 10).

Then, we focused our attention on the study of the influence of the palladium catalyst on the cross-coupling alkenylation (Scheme 3, Table 2). The replacement of

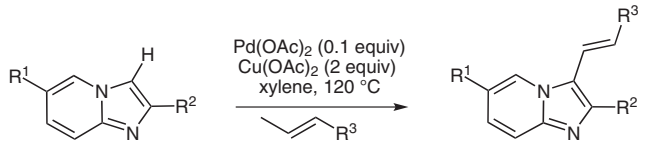
Table 2 Effect of the Palladium Catalyst

Entry	Catalyst	Time (h)	Recovered **4** (%)	Yield[a] (%) of **5**
1	$Pd(OAc)_2$	3	0	85
2	$Pd(PPh_3)_4$	3	0	78
3	$PdCl_2(PPh_3)_2$	3	0	83
4	$PdCl_2(PhCN)_2$	4	0	80
5	$Pd_2(dba)_3$	3	0	77
6	$PdCl_2$	30	28	35
7	$PdCl_2(dppf)_2$	2	0	87

[a] Yields given are for isolated products.

$Pd(OAc)_2$ (entry 1) by $Pd(PPh_3)_4$ afforded compound **5** in 78% yield (entry 2). Similar results were observed using $PdCl_2(PPh_3)_2$, $PdCl_2(PhCN)_2$, or $Pd_2(dba)_3$ (entries 3–5). In contrast, $PdCl_2$ afforded compound **5** in poor yield and starting material was recovered (entry 6). Results comparable to those for $Pd(OAc)_2$ were obtained using $PdCl_2(dppf)_2$ (10 mol%). Under these conditions, the expected compound **5** was obtained in 87% yield (entry 7).

In order to explore the scope and limitations of the oxidative Pd/Cu-catalyzed alkenylation method (Scheme 4),



4, R^1 = H, R^2 = Ph
7, R^1 = Cl, R^2 = Ph
8, R^1 = Cl, R^2 = H
9, R^1= H, R^2 = H

5, 10–13, 15–25

Scheme 4

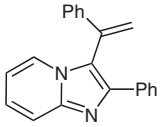
we applied the optimized reaction conditions to imidazo[1,2-*a*]pyridines **4**, **7**,[14] **8**,[14] and **9**,[14] and various alkenes (Table 3). The results showed that compounds **4**, **7**, **8**, and **9** could be efficiently functionalized at the 3-position. Thus, vinyl ketones and alkyl acrylates were successfully used leading to the desired compounds in excellent yields, ranging between 69% and 87%. It is noteworthy that most of the assays gave only regioselective reactions (Table 3) and no starting material was detected in the crude reaction mixtures. In contrast, the reaction between **4** and acrylonitrile, using the same reaction conditions, afforded compound **15** in low yield (45%) after 24 hours (entry 6). In this case, the reaction was not complete and starting material was partially recovered. The coupling reaction between **4** and styrene led to two different compounds **13** and **14** in 39% and 28% yield, respectively (entry 5).

In conclusion, we have developed a new and robust methodology for the direct alkenylation of imidazo[1,2-*a*]pyridines at the 3-position, via a Pd/Cu-catalyzed oxidative process. We found the optimum conditions are the use of palladium(II) acetate [or $PdCl_2(dppf)_2$] as catalyst, copper(II) acetate as oxidant, and xylene (or toluene) as solvent. This method offers several advantages: high yields, a single step (compared to Heck, Stille, or Suzuki cross-coupling), and shorter reaction times. Further work is underway in our laboratory to evaluate the synthetic potential of these products and to develop Pd/Cu-catalyzed oxidative alkenylation reactions involving other classes of heterocycles.

Table 3 Alkenylation of Various Imidazo[1,2-*a*]pyridines

Entry	R^1	R^2	R^3	Product	Yield[a] (%)
1	H	Ph	CO_2Me	**5**	87
2	H	Ph	CO_2Et	**10**	85
3	H	Ph	CO_2Bn	**11**	81
4	H	Ph	COEt	**12**	76
5	H	Ph	Ph	**13** **14**[b]	39 28
6	H	Ph	CN	**15**	45[c]
7	H	Ph	CO_2t-Bu	**16**	74
8	Cl	Ph	CO_2Me	**17**	81
9	Cl	Ph	CO_2Et	**18**	83
10	Cl	Ph	CO_2Bn	**19**	85
11	Cl	Ph	COEt	**20**	73
12	Cl	Ph	CO_2t-Bu	**21**	78
13	Cl	H	CO_2Me	**22**	74
14	Cl	H	CO_2t-Bu	**23**	70
15	H	H	CO_2Me	**24**	71
16	H	H	CO_2Bn	**25**	69

[a] Yields given are for isolated products.
[b] **14**:



[c] 22% of compound **4** was recovered.

All reagents were purchased from Sigma–Aldrich, Acros Organics, and Alfa Aesar and were used without further purification. Melting points were determined with a Büchi SMP-20 melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DPX250 spectrometer (^{1}H, 250.19 MHz; ^{13}C, 62.89 MHz) or a Bruker Avance II 400 spectrometer (^{1}H, 400 MHz; ^{13}C, 100 MHz) using tetramethylsilane as the internal standard; multiplicities were determined using the DEPT 135 sequence. Chemical shifts are reported in parts per million (ppm, δ units). Coupling constants are reported in units of hertz (Hz). Splitting patterns are designated as s: singlet, d: doublet, t: triplet, and m: multiplet. High-resolution mass spectra (HRMS) were recorded with a TOF spectrometer in the electrospray ionization (ESI) mode or with a Finnigan MAT 95 XL spectrometer in the chemical ionization (CI) mode at the Regional Center of Physical Measurement, Blaise Pascal University. All commercial solvents were used without further purification. Column chromatography was carried out using silica gel 60N (spherical, neutral, 40–63 μm, Merck). Thin-layer chromatography was carried out on Merck silica gel $60F_{254}$ precoated plates. Visualization was made with UV light.

Direct C-3 Alkenylation of Imidazo[1,2-*a*]pyridines with Alkenes; General Procedure

$Pd(OAc)_2$ (0.1 equiv) was added to a mixture of an alkene (2 equiv), $Cu(OAc)_2$ (2 equiv), and an imidazo[1,2-*a*]pyridine (0.1 g, 1 equiv) in xylene (3 mL), and the reaction mixture was stirred at 120 °C for 2 to 6 h. The reaction mixture was allowed to cool to r.t., concentrated under reduced pressure, and diluted with CH_2Cl_2 (15 mL), then extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexanes) to give the C-3 alkenylated imidazo[1,2-*a*]pyridine derivatives **5**, **6**, and **10**–**25**.

Methyl (*E*)-3-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (5)

Yield: 87%; yellow solid; mp 150–151 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 6.35 (d, *J* = 16.3 Hz, 1 H), 7.00 (dt, *J* = 3.4, 9.3 Hz, 1 H), 7.28–7.37 (m, 1 H), 7.43–7.54 (m, 3 H), 7.71–7.76 (m, 3 H), 8.04 (d, *J* = 16.3 Hz, 1 H), 8.45 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 51.8, 113.2, 114.1, 117.2, 118.3, 125.4, 126.8, 128.8, 128.9, 129.5, 130.8, 133.7, 147.3, 151.3, 167.9.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{17}H_{15}N_2O_2$: 279.1134; found: 279.1145.

2-Phenylimidazo[1,2-*a*]pyridine-3-carbaldehyde (6)
Yield: 11%; yellow solid; mp 134–135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (t, *J* = 7 Hz, 1 H), 7.51–7.61 (m, 4 H), 7.80–7.85 (m, 3 H), 9.66 (d, *J* = 7 Hz, 1 H), 10.1 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.5, 117.6, 120.9, 128.9, 129.1, 130.0, 130.6, 132.5, 147.9, 158.5, 179.7.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{14}H_{11}N_2O$: 223.0871; found: 223.0877.

Ethyl (*E*)-3-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (10)
Yield: 85%; colorless solid; mp 107–108 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.2 Hz, 3 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 6.36 (d, *J* = 16.4 Hz, 1 H), 7.00 (t, *J* = 6.8 Hz, 1 H), 7.35 (t, *J* = 7.8 Hz, 1 H), 7.42–7.46 (m, 1 H), 7.49–7.52 (m, 2 H), 7.72–7.77 (m, 3 H), 8.05 (d, *J* = 16.4 Hz, 1 H), 8.47 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 60.8, 113.8, 114.1, 117.4, 118.4, 125.6, 126.8, 128.9, 129.1, 129.7, 130.8, 133.8, 147.4, 151.3, 167.6.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{17}N_2O_2$: 293.1290; found: 293.1300.

Benzyl (*E*)-3-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (11)
Yield: 81%; yellow solid; mp 145–146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.26 (s, 2 H), 6.41 (d, *J* = 16.4 Hz, 1 H), 7.00 (t, *J* = 6.8 Hz, 1 H), 7.34–7.52 (m, 9 H), 7.73–7.76 (m, 3 H), 8.12 (d, *J* = 16.4 Hz, 1 H), 8.46 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.5, 112.9, 114.1, 117.3, 118.4, 125.6, 126.9, 128.4, 128.4, 128.7, 128.9, 129.0, 129.6, 131.3, 133.7, 136.2, 147.5, 151.7, 167.4.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{23}H_{19}N_2O_2$: 355.1447; found: 355.1441.

(*E*)-1-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)pent-1-en-3-one (12)
Yield: 76%; yellow solid; mp 115–116 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.3 Hz, 3 H), 2.62 (q, *J* = 7.3 Hz, 2 H), 6.72 (d, *J* = 16.5 Hz, 1 H), 7.00 (t, *J* = 7 Hz, 1 H), 7.32–7.42 (m, 1 H), 7.44–7.54 (m, 3 H), 7.70–7.76 (m, 3 H), 7.94 (d, *J* = 16.5 Hz, 1 H), 8.47 (d, *J* = 7 Hz, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 8.4, 34.5, 114.0, 117.3, 118.2, 121.2, 125.5, 126.8, 128.2, 128.7, 128.9, 129.4, 133.7, 147.4, 151.6, 200.3.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{17}N_2O$: 277.1341; found: 277.1343.

(*E*)-2-Phenyl-3-styrylimidazo[1,2-*a*]pyridine (13)
Yield: 39%; yellow oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.51 (t, *J* = 6.2 Hz, 1 H), 6.76 (d, *J* = 12.5 Hz, 1 H), 6.95 (d, *J* = 12.5 Hz, 1 H), 6.99–7.03 (m, 2 H), 7.10–7.14 (m, 4 H), 7.31–7.48 (m, 4 H), 7.67 (d, *J* = 9.1 Hz, 1 H), 8.04–8.07 (m, *J* = 7.2 Hz, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 111.7, 116.6, 117.3, 124.6, 124.9, 127.9, 127.9, 128.1, 128.2, 128.5, 128.7, 133.9, 134.6, 136.6, 143.8, 145.4.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{21}H_{17}N_2$: 297.1392; found: 297.1398.

2-Phenyl-3-(1-phenylvinyl)imidazo[1,2-*a*]pyridine (14)
Yield: 28%; yellow oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.56 (s, 1 H), 6.15 (s, 1 H), 6.61 (t, *J* = 6.7 Hz, 1 H), 7.14 (t, *J* = 7.7 Hz, 1 H), 7.24–7.35 (m, 8 H), 7.60–7.68 (m, 2 H), 7.92–7.95 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 112.2, 117.5, 120.2, 121.4, 124.3, 126.3, 127.7, 128.4, 128.8, 129.1, 134.2, 137.7, 137.7, 143.6, 144.9.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{21}H_{17}N_2$: 297.1392; found: 297.1398.

(*E*)-3-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)acrylonitrile (15)
Yield: 45%; yellow solid; mp 163–164 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (d, *J* = 16.8 Hz, 1 H), 7.06 (t, *J* = 6.8 Hz, 1 H), 7.41 (t, *J* = 7.8 Hz, 1 H), 7.48–7.54 (m, 3 H), 7.64 (d, *J* = 16.8 Hz, 1 H), 7.67–7.70 (m, 2 H), 7.76 (d, *J* = 9.2 Hz, 1 H), 8.31 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 91.1, 114.6, 116.9, 118.6, 119.1, 124.9, 127.4, 129.1, 129.4, 129.5, 133.3, 135.7, 147.6, 151.7.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{16}H_{12}N_3$: 246.1031; found: 246.1033.

***tert*-Butyl (*E*)-3-(2-Phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (16)**
Yield: 74%; red oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 6.20 (d, *J* = 16.5 Hz, 1 H), 6.85–6.91 (m, 1 H), 7.18–7.26 (m, 1 H), 7.33–7.44 (m, 3 H), 7.61–7.69 (m, 3 H), 7.90 (d, *J* = 16.5 Hz, 1 H), 8.37 (d, *J* = 7 Hz, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 38.3, 80.6, 113.9, 115.5, 117.3, 118.2, 125.6, 126.5, 128.7, 128.8, 129.5, 129.8, 133.7, 147.2, 150.9, 166.7.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{20}H_{21}N_2O_2$: 321.1603; found: 321.1597.

Methyl (*E*)-3-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (17)
Yield: 81%; yellow oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 6.37 (d, *J* = 16.3 Hz, 1 H), 7.27–7.34 (m, 1 H), 7.45–7.53 (m, 3 H), 7.66–7.74 (m, 3 H), 8.00 (d, *J* = 16.3 Hz, 1 H), 8.47 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 52.0, 114.7, 117.6, 118.6, 122.4, 123.2, 127.9, 128.9, 129.2, 129.5, 130.3, 133.3, 145.5, 151.5, 167.6.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{17}H_{14}N_2O_2{}^{35}Cl$: 313.0744; found: 313.0732.

Ethyl (*E*)-3-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (18)
Yield: 83%; yellow solid; mp 144–145 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 8.0 Hz, 3 H), 4.29 (q, *J* = 8.0 Hz, 2 H), 6.37 (d, *J* = 16.0 Hz, 1 H), 7.32 (m, 1 H), 7.43–7.53 (m, 3 H), 7.66–7.69 (m, 1 H), 7.73–7.75 (m, 2 H), 8.00 (d, *J* = 16.0 Hz, 1 H), 8.49 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.5, 60.9, 115.1, 118.6, 122.3, 123.3, 127.9, 128.9, 129.2, 129.5, 130.2, 133.4, 145.5, 151.3, 167.2.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{16}N_2O_2{}^{35}Cl$: 327.0900; found: 327.0885.

Benzyl (*E*)-3-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (19)
Yield: 85%; yellow solid; mp 166–167 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.27 (s, 2 H), 6.41 (d, *J* = 16.3 Hz, 1 H), 7.29–7.52 (m, 9 H), 7.65–7.74 (m, 3 H), 8.06 (d, *J* = 16.3 Hz, 1 H), 8.47–8.49 (m, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 66.7, 114.2, 117.7, 118.6, 122.4, 123.4, 128.0, 128.5, 128.7, 128.9, 129.2, 129.5, 130.7, 133.3, 136.0, 145.7, 151.9, 167.1.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{23}H_{18}N_2O_2{}^{35}Cl$: 389.1057; found: 389.1046.

(*E*)-1-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)pent-1-en-3-one (20)
Yield: 73%; yellow oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (t, *J* = 7.2 Hz, 3 H), 2.65 (q, *J* = 7.2 Hz, 2 H), 6.31 (d, *J* = 16.5 Hz, 1 H), 7.31 (m, 1 H), 7.44–7.54 (m, 3 H), 7.65–7.73 (m, 3 H), 7.95 (d, *J* = 16.5 Hz, 1 H), 8.49 (m, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 8.4, 34.7, 117.8, 118.5, 122.3, 122.4, 123.4, 127.7, 128.0, 128.9, 129.2, 129.4, 133.4, 145.6, 151.9, 200.2.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{16}N_2O^{35}Cl$: 311.0951; found: 311.0939.

***tert*-Butyl (*E*)-3-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)acrylate (21)**
Yield: 78%; yellow oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.56 (s, 9 H), 6.31 (d, *J* = 16.5 Hz, 1 H), 7.31 (m, 1 H), 7.44–7.54 (m, 3 H), 7.69–7.75 (m, 3 H), 7.95 (d, *J* = 16.5 Hz, 1 H), 8.49 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.5, 81.2, 117.1, 118.7, 122.3, 123.6, 127.9, 129.1, 129.2, 129.5, 129.6, 133.5, 145.6, 151.4, 166.6.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{20}H_{20}N_2O_2{}^{35}Cl$: 355.1213; found: 355.1218.

Methyl (*E*)-3-(6-Chloroimidazo[1,2-*a*]pyridin-3-yl)acrylate (22)
Yield: 74%; yellow solid; mp 215–216 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 6.42 (d, *J* = 16.0 Hz, 1 H), 7.26–7.30 (m, 1 H), 7.64 (d, *J* = 9.5 Hz, 1 H), 7.82 (d, *J* = 16.0 Hz, 1 H), 8.04 (s, 1 H), 8.33 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 52.0, 115.1, 118.8, 122.2, 122.5, 127.4, 128.1, 137.7, 146.2, 167.3.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{11}H_{10}N_2O_2{}^{35}Cl$: 237.0431; found: 237.0428.

***tert*-Butyl (*E*)-3-(6-Chloroimidazo[1,2-*a*]pyridin-3-yl)acrylate (23)**
Yield: 70%; yellow solid; mp 119–120 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.56 (s, 9 H), 6.36 (d, *J* = 16.0 Hz, 1 H), 7.24–7.29 (m, 1 H), 7.63 (d, *J* = 9.5 Hz, 1 H), 7.67 (d, *J* = 16.0 Hz, 1 H), 7.99 (s, 1 H), 8.31 (s, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.3, 81.0, 117.7, 118.8, 122.2, 122.3, 126.9, 127.1, 137.1, 146.0, 166.2.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{14}H_{16}N_2O_2{}^{35}Cl$: 279.0900; found: 279.0918.

Methyl (*E*)-3-(Imidazo[1,2-*a*]pyridin-3-yl)acrylate (24)
Yield: 71%; yellow solid; mp 142–143 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 6.41 (d, *J* = 16.0 Hz, 1 H), 7.28 (t, *J* = 6.8 Hz, 1 H), 7.30–7.34 (m, 1 H), 7.70 (d, *J* = 9.2 Hz, 1 H), 7.89 (d, *J* = 16.0 Hz, 1 H), 8.05 (s, 1 H), 8.31 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.9, 113.8, 114.1, 118.7, 121.7, 124.2, 126.2, 128.8, 137.3, 148.1, 167.7.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{11}H_{11}N_2O_2$: 203.0821; found: 203.0820.

Benzyl (*E*)-3-(Imidazo[1,2-*a*]pyridin-3-yl)acrylate (25)
Yield: 69%; yellow solid; mp 129–130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.28 (s, 2 H), 6.46 (d, *J* = 16.0 Hz, 1 H), 6.99 (t, *J* = 6.8 Hz, 1 H), 7.31–7.45 (m, 6 H), 7.71 (d, *J* = 8.8 Hz, 1 H), 7.93 (d, *J* = 16.0 Hz, 1 H), 8.06 (s, 1 H), 8.31 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.6, 113.7, 114.1, 118.7, 124.3, 126.3, 128.5, 128.8, 129.1, 136.2, 137.5, 167.1.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{17}H_{15}N_2O_2$: 279.1134; found: 279.1150.

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