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Synthesis of Imidazopyridines *via* Copper-Catalyzed, Formal Aza-[3 + 2] Cycloaddition Reaction of Pyridine Derivatives with α-Diazo Oxime Ethers

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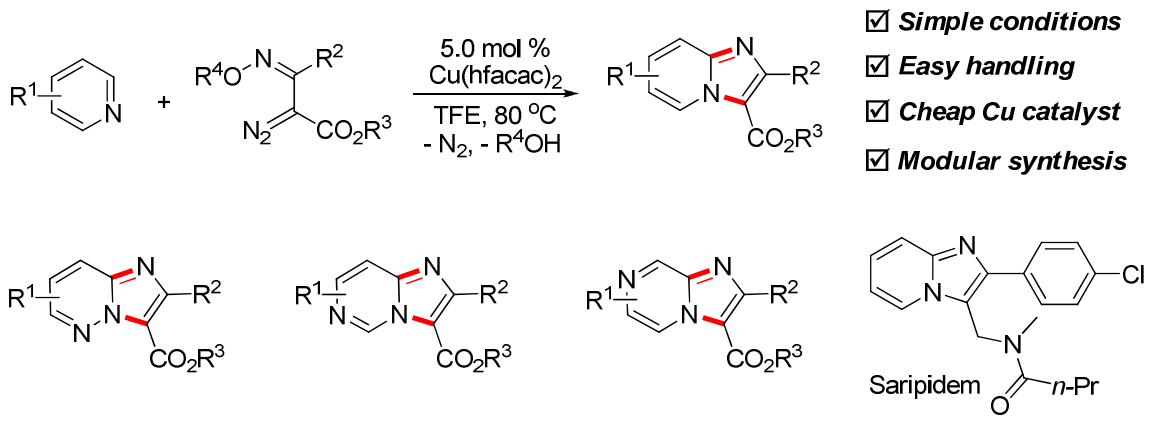


ABSTRACT: The Cu-catalyzed, formal aza-[3 + 2] cycloaddition reaction of pyridine derivatives with α-diazo oxime ethers in trifluoroethanol was used to synthesize imidazopyridines *via* the release of molecular nitrogen and elimination of alcohol. These methods enabled modular synthesis of a wide range of *N*-heterobicyclic compounds such as imidazopyridazines, imidazopyrimidines, and imidazopyrazines with an α-imino Cu-carbenoid generated from the α-diazo oxime ethers and copper.

■ INTRODUCTION

N-Containing heterocyclic compounds are extremely important in the study of biological activity and for pharmaceutical utilization.[1] Especially, imidazopyridines with both pyridine and imidazole moieties, which comprise a typical, privileged scaffold, exhibit antifungal properties and function as antilipases, kinase inhibitors, and H_1-receptor antagonists (Figure 1).[2] For this reason, the development of a synthetic method for imidazopyridine and its derivatives from easily accessible

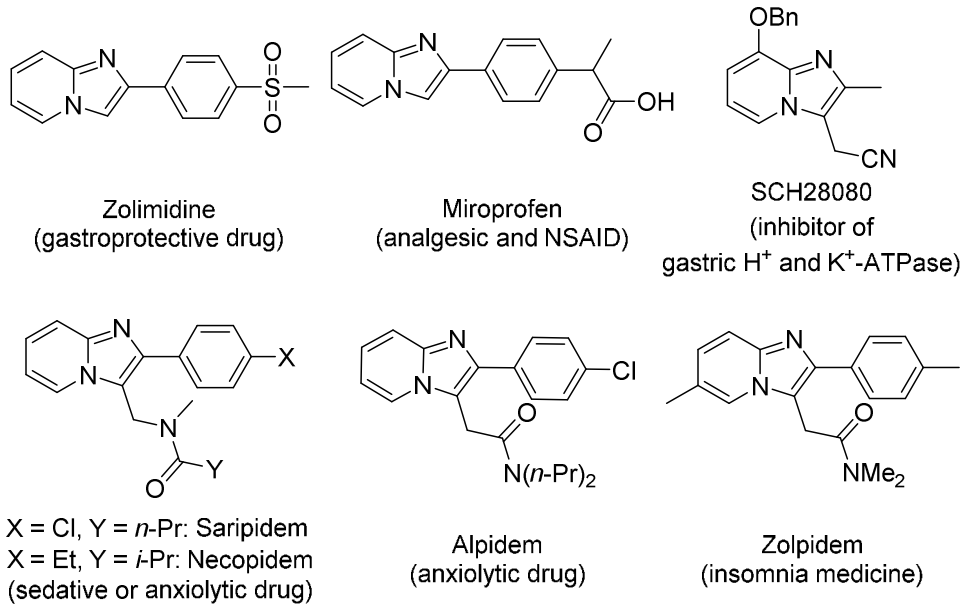
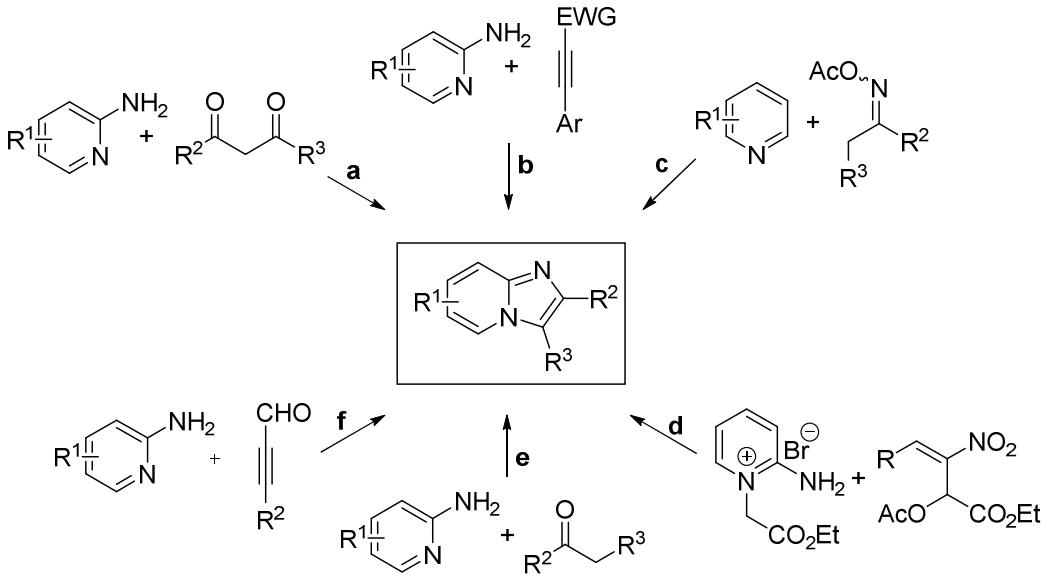


Figure 1. Medicinal Applications of Imidazopyridine Derivatives

compounds is needed. To date, the CBr_4-mediated, oxidative C−N bond formation reaction of 2-aminopyridines with β-keto esters or 1,3-diones (**a**),[3] Cu(II) and Fe(III) co-catalyzed intermolecular diamination of 2-aminopyridines with alkynes (**b**),[4] Cu-catalyzed aerobic dehydrogenative cyclization of pyridines with oxime esters (**c**),[5] aromatic cyclization of Morita-Baylis-Hillman acetates (MBHAs) with 2-amino-1-ethoxycarbonyl-methylpyridium bromide (**d**),[6] I_2/CuO-promoted reaction of 2-aminopyridines with ketones (**e**),[7] and Au-catalyzed reaction of 2-aminopyridines with

propionaldehydes (**f**)[8] have been reported for the synthesis of imidazopyridines (Scheme 1).[9] In particular, it is very important to develop a useful modular method for the synthesis of a variety of *N*-heterobicyclic compounds containing an imidazole ring, such as imidazopyridines, imidazopyridazines, imidazopyrimidines, imidazopyrazines, and imidazotriazines.

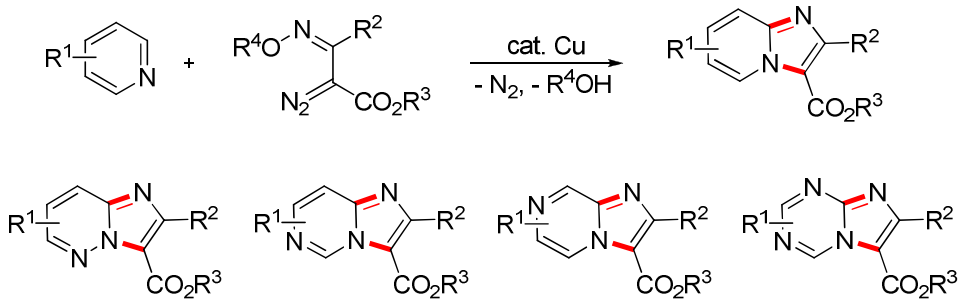
Scheme 1. Previously Reported Synthetic Methods for Imidazopyridine



Recently, a wide range of synthetic methods have been reported for heterocyclic compounds using a metal carbenoid derived from a diazo,[10] triazole,[11] and thiadiazole[12] in the presence of a transition metal catalyst. Encouraged by these results and interested in the potential utilities of *N*- and *S*-heterocyclic compounds in pharmaceuticals, we envisioned that if α-diazo oxime ethers[13] were treated with a variety of *N*-heterocyclic compounds, including pyridine, pyridazine, pyrimidine, pyrazine, and triazine, a large number of *N*-heterobicyclic compounds containing the imidazole ring would be produced through a formal aza-[3 + 2] cycloaddition reaction together with the release of molecular nitrogen and elimination of alcohol. Herein, we demonstrate an efficient synthetic method for imidazopyridines *via* the Cu-catalyzed, formal aza-[3 + 2] cycloaddition

reaction of pyridine derivatives with α-diazo oxime ethers (Scheme 2). These methods enable the modular synthesis of a wide range of *N*-heterobicyclic compounds, such as imidazopyridine, imidazopyridazine, imidazopyrimidine, and imidazopyrazine, bearing the imidazole moiety *via* an α-imino Cu-carbenoid generated from α-diazo oxime ethers and copper.

Scheme 2. Synthesis of Imidazopyridines from the Cu-catalyzed, formal Aza-[3 + 2] Cycloaddition of Pyridine Derivatives with α-Diazo Oxime Ethers

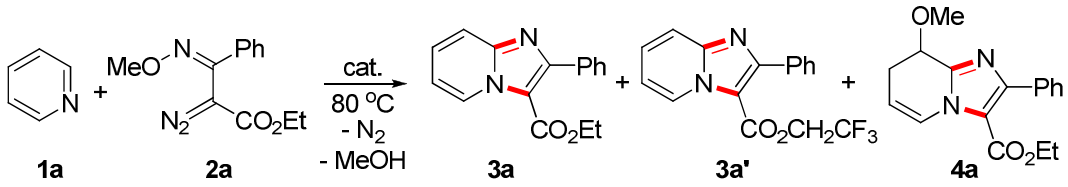


■ RESULTS and DISCUSSION

We initiated our studies with the reaction of pyridine (**1a**) with an α-diazo oxime ether (**2a**) in the presence of a copper catalyst (Table 1). When $Cu(OAc)_2$ (5.0 mol %) was used in the reaction of **1a** with **2a** in dichloroethane (DCE), the desired imidazopyridine (**3a**) was obtained in 3% yield with **4a** (7%) (entry 1). The structure of **4a** was confirmed by X-ray crystallography.[14] Based on these results, a variety of Cu catalysts, such as $Cu(OTf)_2$, $Cu(acac)_2$, $Cu(tfacac)_2$, and $Cu(hfacac)_2$, in DCE were screened to determine that $Cu(hfacac)_2$ (5.0 mol %) was the best catalyst, producing **3a** and **4a** in 15% and 25% yields, respectively (entries 2-5). Further examination of the solvents indicated that trifluoroethanol (TFE) was the optimum solvent, and the other solvents, such as dioxane, acetonitrile, hexane, methanol, and ethanol, gave inferior results (entries 6-11). When TFE was used as the solvent, the desired imidazopyridines, **3a** and **3a'**, were produced in 25% and 39%

yields, respectively, along with **4a** (4%) (entry 11). The imidazopyridine **3a'** bearing a trifluoroethoxycarbonyl group was produced by the transesterification reaction of TFE with **3**. In this case, the imidazopyridines **3a** and **3a'** were easily separated using column chromatography. The best result was achieved *via* the treatment of **1a** (0.2 mmol, 1.0 equiv) with **2a** (2.0 equiv) using $Cu(hfacac)_2$ (5.0 mol %) in TFE at 80 °C for 3 h, which resulted in the imidazopyridines **3a** and **3a'** in 43% and 55% yields, respectively (entry 12).

Table 1. Reaction Optimization[a]



1a **2a** **3a** **3a'** **4a**

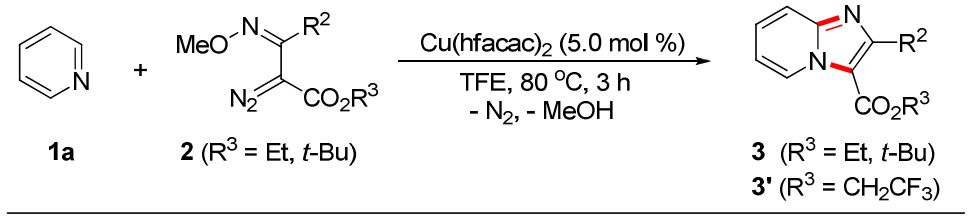
entry	cat.	solvent	time (h)	yield (%)		
				3a	**3a'**	**4a**
1	$Cu(OAc)_2$	DCE	12	3	0	7
2	$Cu(OTf)_2$	DCE	3	7	0	21
3	$Cu(acac)_2$	DCE	12	6	0	2
4	$Cu(tfacac)_2$	DCE	6	3	0	14
5[b]	$Cu(hfacac)_2$	DCE	2	15	0	25
6	$Cu(hfacac)_2$	dioxane	1	6	0	19
7	$Cu(hfacac)_2$	MeCN	12	7	0	13
8	$Cu(hfacac)_2$	hexane	5	13	0	19
9	$Cu(hfacac)_2$	MeOH	5	21	0	4
10	$Cu(hfacac)_2$	EtOH	1	14	0	7
11[b]	$Cu(hfacac)_2$	TFE	6	25	39	4
12[b,c]	$Cu(hfacac)_2$	TFE	3	43	55	0

[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (1.0 equiv), and catalyst (5.0 mol %) were used

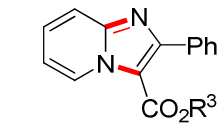
in the solvent (2.0 mL) at 80 °C under N_2 atmosphere. Yields were determined by NMR using CH_2Br_2 as an internal standard. [b]Isolated yield. [c]**2a** (0.4 mmol, 2.0 equiv) was used.

After obtaining the optimum conditions, the scope and limitations of the formal aza-[3 + 2] cycloaddition reaction were investigated using a variety of α-diazo oxime ethers (**2**) (Scheme 3). When methyl and *n*-pentyl-substituted α-diazo oxime ethers were treated with pyridine in the presence of $Cu(hfacac)_2$ (5.0 mol %), the corresponding imidazopyridines **3b** and **3c** were obtained in 96% and 77% yields, respectively. The α-diazo oxime ether with a *tert*-butoxycarbonyl group also underwent the formal aza-[3 + 2] cycloaddition reaction to produce **3d** in 58% yield. Electron-donating groups, including 2-, 3-, and 4-methyl, 4-methoxy, and 3,4-methylenedioxy, on the phenyl ring of the α-diazo oxime ethers did not influence the efficiency of the reaction, and the imidazopyridines **3e-3i** were obtained in good to excellent yields varying from 74% to 98%. However, in the case of the 4-methoxy- and 3,4-methylenedioxy-substituted α-diazo oxime ethers, the ethoxycarbonyl and trifluoroethoxycarbonyl imidazopyridines produced were unable to be separated, and the mixtures of the Et and CH_2CF_3 ester are reported. A large number of electron-withdrawing groups, including chloro-, bromo-, nitro-, and methoxycarbonyl-, on the phenyl ring were well tolerated in the formal aza-[3 + 2] cycloaddition reaction and afforded the desired imidazopyridines (**3j'-3m**) in good to excellent yields ranging from 78% to 89%. Although 2-thiophenyl-substituted α-diazo oxime ether was less reactive, the desired imidazopyridine **3n** was obtained in an acceptable yield.

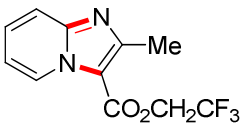
Scheme 3. Scope of α-Diazo Oxime Ethers[a]



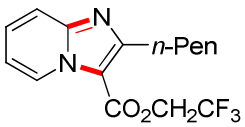
1a **2** (R^3 = Et, *t*-Bu) **3** (R^3 = Et, *t*-Bu) **3'** (R^3 = CH_2CF_3)



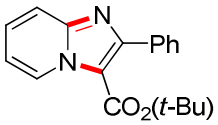
3a (43%, R^3 = Et)
3a' (55%, R^3 = CH_2CF_3)



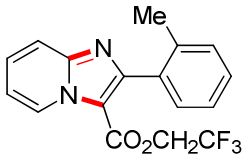
3b (96%)



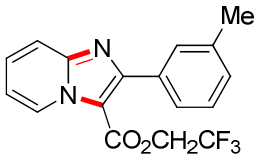
3c (77%)



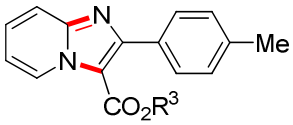
3d (58%)



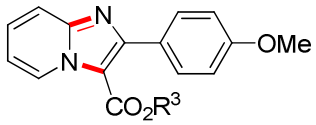
3e (74%)[b]



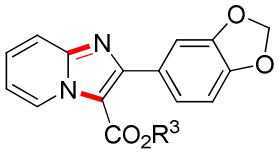
3f (98%)[b]



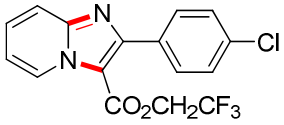
3g (21%, R^3 = Et)
3g' (63%, R^3 = CH_2CF_3)



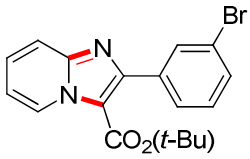
3h (8%, R^3 = Et)[c]
3h' (81%, R^3 = CH_2CF_3)[c]



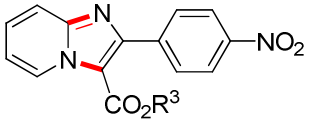
3i (33%, R^3 = Et)[c]
3i' (50%, R^3 = CH_2CF_3)[c]



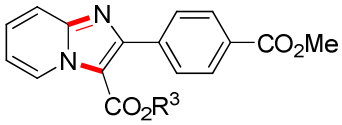
3j' (89%)



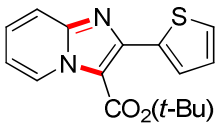
3k (89%)



3l (60%, R^3 = Et)
3l' (18%, R^3 = CH_2CF_3)



3m (41%, R^3 = Et)[c]
3m' (42%, R^3 = CH_2CF_3)[c]

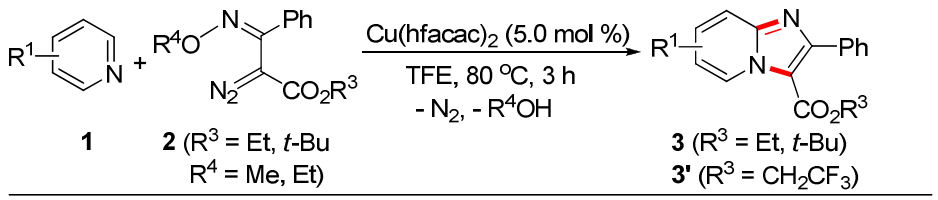


3n (43%)

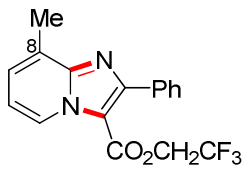
[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2** (2.0 equiv), and $Cu(hfacac)_2$ (5.0 mol %) were used in TFE at 80 °C for 3 h under N_2 atmosphere. [b]Reaction was carried out at 90 °C for 8 h. [c]Et and CH_2CF_3 esters are obtained as mixtures and NMR yields are reported.

Next, a wide range of pyridine derivatives (**1**) were investigated in the formal aza-[3 + 2] cycloaddition reaction with α-diazo oxime ethers (**2**) (Scheme 4). Electronic variation in the substituents on the pyridine ring did not influence the reaction efficiency. 3-Methylpyridine underwent the Cu-catalyzed cycloaddition reaction with α-diazo oxime ether regioselectively at the sterically hindered position to afford imidazopyridine **3o** having methyl group on 8-position in 84% yield. The structure of **3o** was confirmed by X-ray crystallography.[15] The electron-donating 4-methyl and 4-ethyl groups gave the desired imidazopyridines (**3p**, **3p'**, **3q**, and **3q'**) in good yields. The conditions of the Cu-catalyzed formal aza-[3 + 2] cycloaddition reaction were compatible with bromo- and iodo-groups, and **3r** and **3s** were obtained in 78% and 75% yields, respectively. The present method worked equally well with the electron-withdrawing 4-acetyl- and 4-methoxycarbonyl-substituted pyridines and led to the facile construction of imidazopyridines **3t** (95%) and **3u** (68%) and **3u'** (26%). The tolerance of the bromo, iodo, ketone, and ester groups on the pyridine ring is especially useful and provides an opportunity for further functional group transformations. Quinoline underwent the Cu-catalyzed cyclization reaction, producing the desired imidazopyridine (**3v**) in 85% yield. Isoquinoline also provided the desired imidazopyridine (**3w**) in 81% yield. The reaction of 4-phenylpyridine with the α-diazo ethyl oxime ether gave the desired imidazopyridines **3x** (22%) and **3x'** (39%). Likewise, 4-*p*-tolylpyridine and 4-(4-chlorophenyl)pyridine were smoothly converted to the corresponding imidazopyridines in good yields.

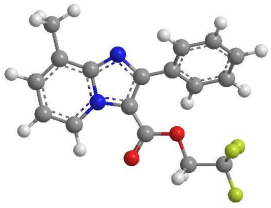
Scheme 4. Scope of the Pyridines[a]

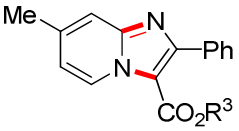


1 **2** (R^3 = Et, *t*-Bu; R^4 = Me, Et) **3** (R^3 = Et, *t*-Bu) **3'** (R^3 = CH_2CF_3)

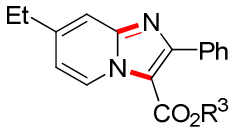


3o (84%)[b]

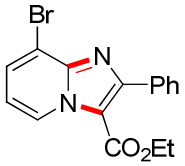




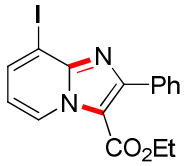
3p (31%, R^3 = Et)
3p' (50%, R^3 = CH_2CF_3)



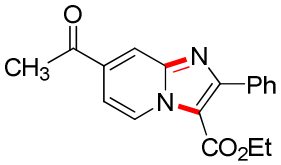
3q (15%, R^3= Et)[c]
3q' (59%, R^3 = CH_2CF_3)[c]



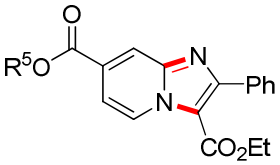
3r (78%)



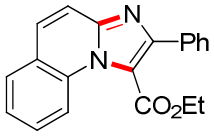
3s (75%)



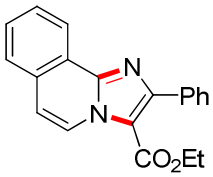
3t (95%)



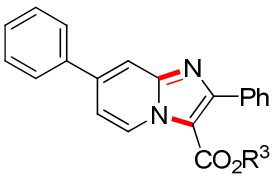
3u (68%, R^5 = Me)
3u' (26%, R^5 = CH_2CF_3)



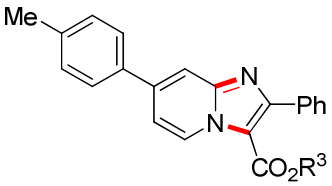
3v (85%)



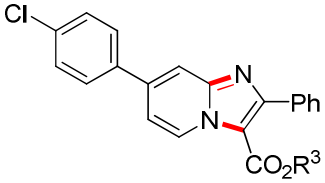
3w (81%)



3x (22%, R^3 = Et)
3x' (39%, R^3 = CH_2CF_3)



3y (20%, R^3 = Et)
3y' (39%, R^3 = CH_2CF_3)



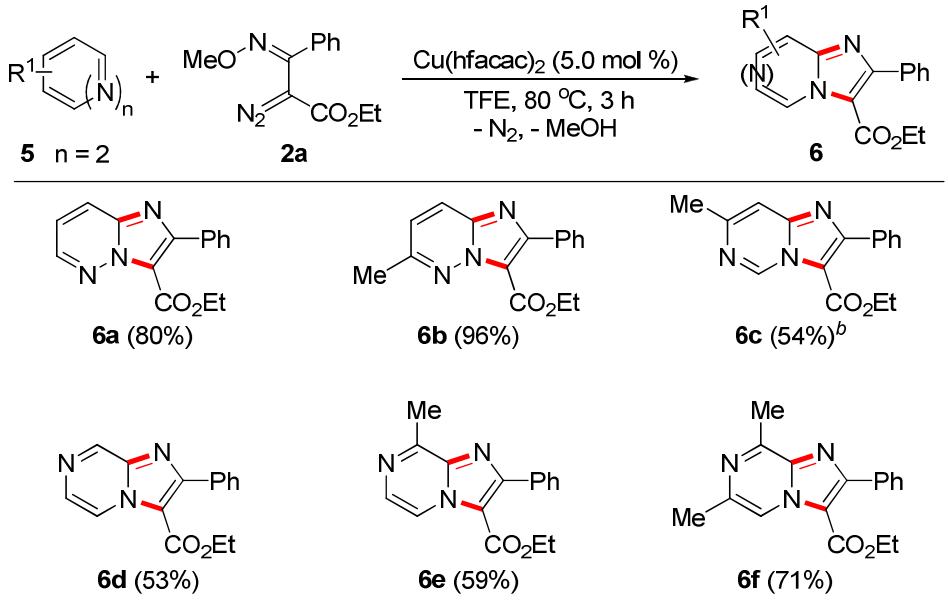
3z (33%, R^3 = Et)
3z' (40%, R^3 = CH_2CF_3)

[a]Reaction conditions: **1** (0.2 mmol, 1.0 equiv), **2** (2.0 equiv), and $Cu(hfacac)_2$ (5.0 mol %) were used in TFE at 80 °C for 3 h under N_2 atmosphere. [b]Reaction was carried out at 90 °C for 8 h. [c]Et and

CH_2CF_3 esters are obtained as mixtures and NMR yields are reported.

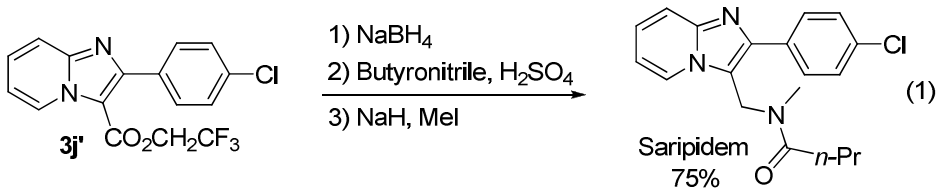
Next, we applied the present method to the synthesis of a variety of *N*-heterobicyclic compounds, including imidazopyridazines, imidazopyrimidines, imidazopyrazines, and imidazotriazines, using pyridazines, pyrimidines, pyrazines, and triazines instead of pyridines in the reaction with the α-diazo oxime ether (Scheme 5). When pyridazine and 3-methylpyridazine were treated with the α-diazo oxime ether **2a** in the presence of $Cu(hfacac)_2$ (5.0 mol %), the formal aza-[3 + 2] cycloaddition reaction occurred, producing the corresponding imidazopyridazines **6a** and **6b** in 80% and 96% yields, respectively. Pyrazine and 2,6-dimethylpyrazine are applicable to the present transformation and provided the corresponding imidazopyrazines **6d** and **6f** in 53% and 71% yields, respectively. It is noteworthy that 2-methylpyrazine is selectively cyclized to produce **6e** in 59% yield. Although 4-methylpyrimidine was less reactive than pyridazine and pyrazine in the cyclization reaction, the imidazopyrimidine **6c** was obtained in an acceptable yield. However, triazine was not efficient. The present method enabled modular synthesis of a wide range of *N*-heterobicyclic compounds, such as imidazopyridines, imidazopyridazines, imidazopyrimidines, and imidazopyrazines, bearing the imidazole moiety *via* an α-imino Cu-carbenoid generated from α-diazo oxime ethers and copper.

Scheme 5. Scope of the *N*-Heterocyclic Compounds in the Reaction with α-Diazo Oxime Ether[a]



[a]Reaction conditions: **5** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), and $Cu(hfacac)_2$ (5.0 mol %) were used in TFE at 80 °C for 3 h under N_2 atmosphere. [b]**5** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), and $Cu(hfacac)_2$ (10.0 mol %) were used in TFE for 12 h under N_2 atmosphere.

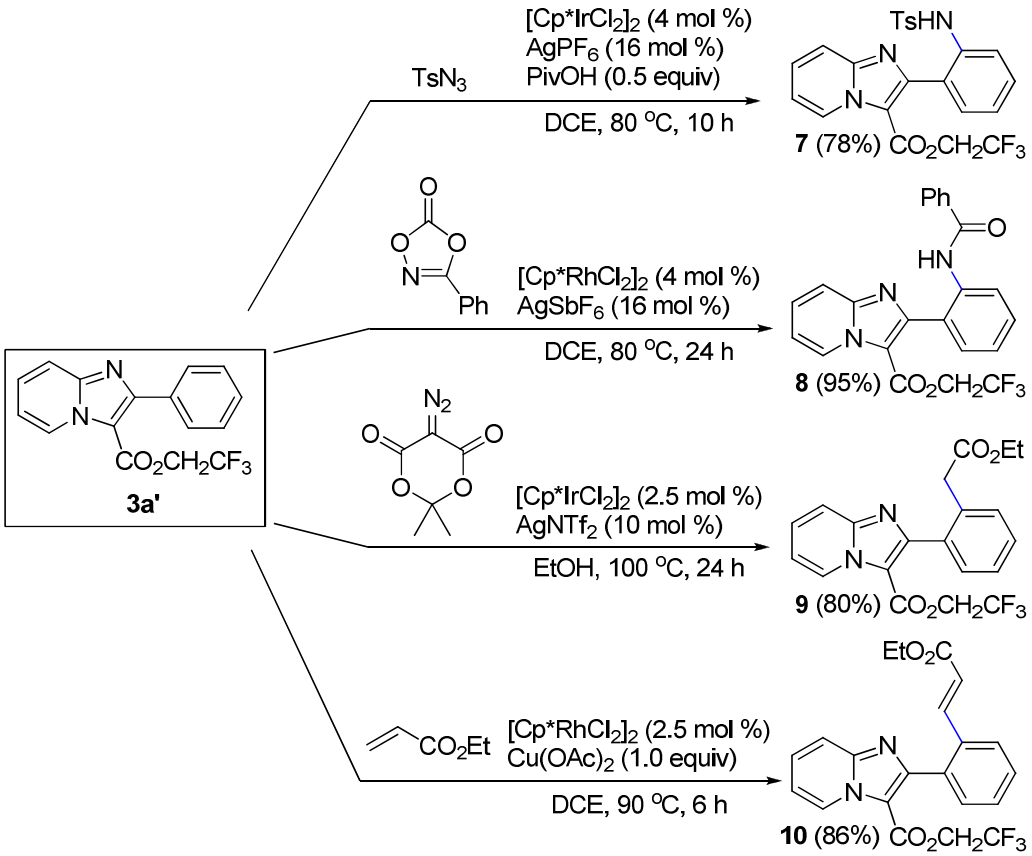
The present method could be applied to the synthesis of Saripidem, which is an anxiolytic drug (eq 1). Imidazopyridine **3j'** was reduced *via* sodium borohydride in methanol and THF to produce the corresponding alcohol in 93% yield.[16] The reaction of alcohol with butyronitrile (Ritter reaction)[17] was followed by methylation and produced Saripidem in 75% yield.



Next, we examined the synthetic application of trifluoroethyl 2-phenylimidazo[1,2-a]pyridine-3-carboxylate (**3a'**) on C–H activation (Scheme 6). When **3a'** was treated with a tosyl azide in the

presence of $[Cp^*IrCl_2]_2$, $AgPF_6$, and pivalic acid, the sulfonyl amidated imidazopyridine **7** was obtained in 78% yield.[18] Additionally, the Rh-catalyzed C–H activation reaction of **3a'** with dioxazolone produced the benzoyl-amidated product **-8** in 95% yield.[19] The use of diazo Meldrum's acid in the presence of an iridium catalyst smoothly converted **3a'** to the ethoxycarbonyl methylated imidazo-pyridine **9** in 80% yield.[20] The Rh-catalyzed alkenylation of **3a'** with ethyl acrylate was successful and gave **10** in 86% yield.[21]

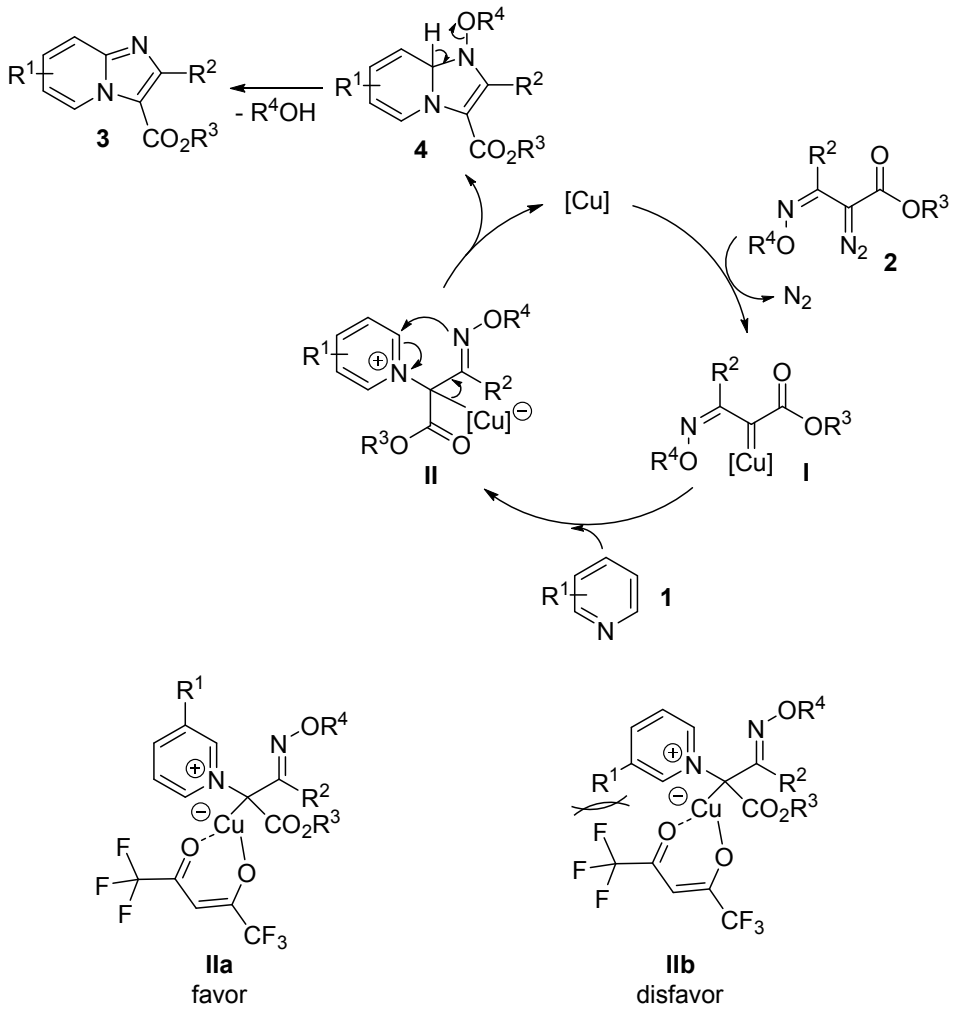
Scheme 6. Applications of Imidazopyridine to C–H Activation



A plausible mechanism for the formation of the imidazopyridines (**3**) from the pyridine derivatives (**1**) and α-diazo oxime ethers (**2**) *via* Cu-catalyzed, formal aza-[3 + 2] cycloaddition is

suggested in Scheme 7. First, the α-diazo oxime ethers (**2**) were converted to a Cu-carbenoid (**I**) in the presence of the Cu catalyst, and this was accompanied by the release of molecular nitrogen.[13] The nucleophilic addition of the nitrogen atom in the pyridine derivatives to the electrophilic carbene center of **I** generates the copper-bound, zwitterionic intermediate **II**. Then, the anionic copper of **II** releases an electron pair that flows into the *N*-alkoxy imine moiety and makes the nitrogen atom sufficiently nucleophilic to react with the cationic pyridinium to afford dihydroimidazopyridine **4** and regenerate the copper(II) catalyst. Intermediate **IIa** is more favor than **IIb** due to the steric hindrance and then, 3-methylpyridine, isoquinoline, and 2-methylpyrazine underwent the Cu-catalyzed cycloaddition reaction with α-diazo oxime ether regioselectively at the sterically hindered position. Finally, **4** is smoothly transformed to the imidazopyridine **3** through the elimination of alcohol.

Scheme 7. A Plausible Mechanism



■ CONCLUSION

In conclusion, we developed a Cu-catalyzed, formal aza-[3 + 2] cycloaddition reaction with pyridine derivatives and α-diazo oxime ethers in trifluoroethanol to synthesize imidazopyridines with the release of molecular nitrogen and elimination of alcohol. This method enabled modular synthesis of a wide range of *N*-heterobicyclic compounds such as imidazopyridazines, imidazopyrimidines, and imidazopyrazines.

Experimental Section

General: Reactions were carried out in oven-dried glassware under a nitrogen atmosphere. $Cu(hfacac)_2$ were purchased and was used as received. Commercial available reagents were used without purification. Trifluoroethanol was dried with CaH_2. All reaction mixtures were stirred magnetically and were monitored by thin-layer chromatography using Silica gel pre-coated glass plates, which were visualized with UV light and then developed using either iodine or a solution of anisaldehyde. Flash column chromatography was carried out using Silica gel (230-400 mesh). ^1H NMR (400 MHz) and $^{13}C\{^1H\}$ NMR (100 MHz) spectra were recorded on NMR spectrometer. Deuterated chloroform was used as the solvent, and chemical shift values (δ) are reported in parts per million relative to the residual signals of solvent [δ 7.26 for ^1H (chloroform-d_3) and δ 77.2 for $^{13}C\{^1H\}$ (chloroform-d_3)]. Infrared spectra were recorded on FT-IR spectrometer as either a thin neat pressed between two sodium chloride plates or as a solid suspended in a potassium bromide disk. High resolution mass spectra (HRMS) were obtained by electron impact (EI) ionization technique (magnetic sector - electric sector double focusing mass analyzer). Melting points were determined in open capillary tube.

General Procedure for the Synthesis of α-diazo oxime ether

To a solution of oxime ether (2.0 mmol) and 4-methylbenzenesulfonyl azide (1.2 equiv) in CH_3CN (4 mL) at 0 °C was added dropwise DBU (1.2 equiv). The resulting orange solution was stirred for 30 min at 0 °C and allowed to warm to room temperature. The reaction mixture was concentrated and the crude material was purified by column chromatography to afford the desired diazo compound. All procedures should routinely be carried out behind a safety shield in a fume hood.

General Procedure for the Synthesis of Imidazopyridines

$Cu(hfacac)_2$ (5.0 mol %) and trifluoroethanol (1.0 mL) were added to an oven-dried test tube equipped with a stirring bar. To the solution was added α-diazo oxime ether (0.4 mmol) in

trifluoroethanol (1.0 mL) and then was added pyridine derivatives (0.2 mmol). The mixture was stirred at 80 ^{o}C for 3 h. To remove Cu(hfacac)$_2$, the residue was passed through a pad of Silica gel filter and eluted with CH_2Cl_2. The filtrate was concentrated under reduced pressure and the residue was purified by Silica gel flash column chromatography to give imidazopyridine.

Ethyl 2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3a): yield 22.9 mg (43%), white solid; mp 53−55 ^{o}C; R_f= 0.2 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (td, J = 1.1 Hz, 7.0 Hz, 1H), 7.78-7.72 (m, 3H), 7.45-7.40 (m, 4H), 7.02 (dt, J = 1.2 Hz, 10.4 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.2, 153.7, 147.2, 134.6, 130.3, 128.8, 128.4, 128.0, 127.8, 127.6, 117.6, 114.2, 60.5, 14.1; IR (KBr) 3058, 2979, 2929, 1684, 1400, 1225, 1155, 1050 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{14}N_2O_2$ 266.1055, Found 266.1051.

2,2,2-Trifluoroethyl 2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3a´): yield 35.2 mg (55%), white solid; mp 99−101 ^{o}C; R_f = 0.15 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (td, J = 1.1 Hz, 7.0 Hz, 1H), 7.79 (td, J = 1.1 Hz, 9.0 Hz, 1H), 7.74-7.72 (m, 2H), 7.54-7.49 (m, 1H), 7.47-7.43 (m, 3H), 7.10 (dt, J = 1.3 Hz, 10.4 Hz, 1H), 4.62 (q, J = 8.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.0, 155.4, 147.8, 133.9, 130.0, 129.0, 128.8, 128.4, 128.0, 127.8, 122.9 (J = 277.6 Hz), 117.7, 114.7, 110.4, 59.8 (J = 36.9 Hz); ^{19}F NMR δ -73.1 ppm; IR (KBr) 3058, 2970, 1699, 1494, 1414, 1281, 1148 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{11}F_3N_2O_2$ 320.0773, Found 320.0773.

2,2,2-Trifluoroethyl 2-methylimidazo[1,2-a]pyridine-3-carboxylate (3b): yield 49.6 mg (96%), white solid; mp 100−102 ^{o}C; R_f = 0.2 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, J = 6.9 Hz, 1H), 7.66 (d, J = 8.9 Hz, 1H), 7.47-7.43 (m, 1H), 7.03 (dt, J = 1.0 Hz, 10.4 Hz, 1H), 4.76 (q, J = 8.4 Hz, 2H), 2.74 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.3, 154.7, 147.8, 128.6, 128.1, 123.3 (J = 277.2 Hz), 117.0, 114.4, 111.3, 60.0 (J = 36.7 Hz) 16.9; ^{19}F

NMR δ -73.7 ppm; IR (KBr) 3036, 2963, 2926, 1698, 1425, 1278, 1155 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{11}H_9F_3N_2O_2$ 258.0616, Found 258.0613.

2,2,2-Trifluoroethyl 2-pentylimidazo[1,2-a]pyridine-3-carboxylate (3c): yield 37.5 mg (77%), white solid; mp 71-73 °C; R_f = 0.3 (EtOAc:DCM:Hexane = 1:10:10); white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 9.27 (dd, *J* = 0.7 Hz, 6.9 Hz, 1H), 7.68 (dd, *J* = 0.7 Hz, 8.9 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.04 (t, *J* = 6.9 Hz, 1H), 4.75 (q, *J* = 8.4 Hz, 2H), 3.09 (t, *J* = 7.9 Hz, 2H), 1.82-1.74 (m, 2H), 1.45-1.32 (m, 4H) 0.91 (t, *J* = 6.86 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 159.1, 148.0, 128.6, 128.2, 123.4 (*J* = 277.2 Hz), 117.2, 114.3, 110.8, 60.1 (*J* = 36.7 Hz), 32.0, 30.7, 29.5, 22.6, 14.1; ^{19}F NMR δ -73.5 ppm; IR (KBr) 2959, 2923, 2861, 1702, 1415, 1335, 1278, 1170, 1080 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{15}H_{17}F_3N_2O_2$ 314.1242, Found 314.1239.

***tert*-Butyl 2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3d):** yield 34.2 mg (58%), colorless oil; R_f= 0.3 (EtOAc:DCM:Hexane = 1:10:10); ^1H NMR (400 MHz, $CDCl_3$) δ 9.41 (td, *J* = 1.1 Hz, 7.0 Hz, 1H), 7.72-7.69 (m, 3H), 7.45-7.38 (m, 4H), 6.99 (dt, 1.2 Hz, 10.4 Hz, 1H), 1.43 (s. 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7, 153.2, 146.8, 135.0, 130.2, 128.4, 128.3, 127.6, 127.6, 117.5, 113.9, 113.2, 82.0, 28.3; IR (KBr) 3069, 2978, 2930, 1682, 1496, 1391, 1338, 1227, 1150 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{18}N_2O_2$ 294.1368, Found 294.1368.

2,2,2-Trifluoroethyl 2-(o-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3e): yield 49.5 mg (74%), colorless oil; R_f = 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^1H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, *J* = 6.9 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.55-7.50 (m, 1H), 7.34-7.21 (m, 4H), 7.13 (t, *J* = 10.4 Hz, 1H), 4.49 (q, *J* = 8.4 Hz, 2H), 2.21 (s, 3H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 155.6, 147.9, 136.6, 134.2, 129.8, 129.6, 128.8, 128.7, 128.3, 125.2, 122.8 (*J* = 277.5 Hz), 117.9, 114.8, 111.6 ,59.9 (*J* = 36.9 Hz) 19.9; ^{19}F NMR δ -73.8 ppm; IR (KBr) 3028, 2968, 2927, 1702, 1494, 1414, 1280, 1152 cm-1; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_2$ 334.0929, Found 334.0927.

2,2,2-Trifluoroethyl 2-(*m*-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3f): yield 65.8 mg (98%), white solid; mp 75-77 ^{o}C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (td, J = 1.1 Hz, 7.0 Hz, 1H), 7.78 (td, J = 1.1 Hz, 8.9 Hz, 1H), 7.55-7.49 (m, 3H), 7.34 (t, J = 7.6 Hz, 1H), 7.25 (d, J = 7.0 Hz, 1H), 7.09 (dt, J = 1.3 Hz, 10.4 Hz, 1H), 4.62 (q, J = 8.5 Hz, 2H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.3, 155.7, 148.0, 137.6, 133.9, 130.7, 129.9, 128.9, 128.6, 127.8, 127.3, 123.1 (J = 277.5 Hz), 117.8, 114.8, 110.4, 59.9 (J = 36.9 Hz), 21.4; ^{19}F NMR δ -73.1 ppm; IR (KBr) 3054, 2978, 2930, 1685, 1496, 1384, 1227, 1150 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_2$ 334.0929, Found 334.0930.

Ethyl 2-(*p*-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3g):[23] yield 11.8 mg (21%), white solid; mp 86-88 ^{o}C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (td, J = 1.1, 7.0 Hz, 1H), 7.73 (td, J = 1.1 Hz, 8.9 Hz, 1H), 7.68 (dd, J = 1.7 Hz, 6.4 Hz, 2H), 7.45-7.40 (m, 1H), 7.24 (dd, J = 0.6 Hz, 8.5 Hz, 2H), 7.02 (dt, J = 1.3 Hz, 10.4 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 153.9, 147.2, 138.7, 131.6, 130.2, 128.5, 128.4, 127.9, 117.6, 114.0, 111.9, 60.5, 21.5, 14.2

2,2,2-Trifluoroethyl 2-(*p*-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3g´): yield 42.1 mg (63%), white solid; mp 154-157 ^{o}C; R_f = 0.35 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, ´$CDCl_3$) δ 9.37 (d, J = 7.0 Hz, 1H), 7.77 (d, J = 8.9 Hz, 1H), 7.65 (d, J= 8.1 Hz, 2H), 7.52-7.48 (m, 1H), 7.25 (d, J = 6.5 Hz, 2H), 7.09 (dt, J = 1.2 Hz, 10.4 Hz, 1H), 4.63 (q, J = 8.5 Hz, 2H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 155.7, 148.0, 139.1, 131.0, 130.1, 128.8, 128.6, 123.1 (J = 277.8Hz), 117.8, 114.7, 110.4, 59.8 (J = 36.9 Hz), 21.5; ^{19}F NMR δ -73.0 ppm; IR (KBr) 2980, 2924, 1683, 1497, 1404, 1336, 1223, 1155 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_2$ 334.0929, Found 334.0930.

Ethyl 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carboxylate (3h, minor): NMR yield 8%, white solid; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (d, J =

7.0 Hz, 1H), 7.76-7.70 (m, 3H), 7.43-7.39 (m, 1H), 7.02-7.00 (m, 1H), 7.00-6.95 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 160.2, 153.6, 131.8, 128.5, 128.0, 127.0, 117.4, 114.0, 113.4, 60.5, 14.3; IR (KBr) 2967, 2839, 1697, 1612, 1484, 1417, 1387, 1281, 1250, 1176 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{16}N_2O_3$ 296.1161, Found 296.1162.

2,2,2-Trifluoroethyl 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carboxylate (3h', major): NMR yield 81%, white solid; R_f = 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, *J* = 7.0 Hz, 1H), 7.72 (dd, *J* = 2.1 Hz, *J* = 6.8 Hz, 1H), 7.51-7.47 (m, 1H), 7.07 (dd, *J* = 1.1 Hz, 10.4 Hz, 1H), 6.98(dd, *J* = 2.1 Hz, *J* = 6.8 Hz 2H), 4.64 (q, *J* = 8.5 Hz, 2H), 3.87 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 160.5, 159.2, 155.4, 148.0, 131.6, 128.9, 128.6, 126.3, 123.1 (*J* = 277.7 Hz), 117.7, 114.6, 113.4, 110.1, 59.9 (*J* = 36.9 Hz), 55.5; ^{19}F NMR δ -73.0 ppm; IR (KBr) 2967, 2839, 1697, 1612, 1484, 1417, 1387, 1281, 1250, 1176 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_3$ 350.0878, Found 350.0880.

Ethyl 2-(benzo[d][1,3]dioxol-5-yl)imidazo[1,2-a]pyridine-3-carboxylate (3i, minor): NMR yield 33%, white solid; R_f = 0.2 (EtOAc:DCM:Hexane = 1:3:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (td, *J* = 1.1 Hz, 7.0 Hz, 1H), 7.70 (td, *J* = 1.1 Hz, 9.0 Hz, 1H), 7.43-7.39 (m, 1H), 7.34-7.23 (m, 2H), 7.00 (dt, *J* = 1.3 Hz, 10.4 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 159.0, 155.1, 153.2, 148.5, 148.1, 147.8, 147.3, 147.0, 128.9, 128.5, 128.4, 128.3, 128.0, 127.7, 124.5, 123.1 (*J* = 277.6 Hz), 117.6, 117.7, 114.4, 114.0, 111.7, 110.9, 110.6, 110.2, 107.9, 107.7, 101.30, 101.26, 101.2, 60.5, 59.9 (*J* = 36.8 Hz), 14.1; IR (KBr) 3051, 2978, 2898, 1696, 1472, 1394, 1342, 1242, 1170, 1040 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{14}N_2O_4$ 310.0954, Found 310.0953.

2,2,2-Trifluoroethyl 2-(benzo[d][1,3]dioxol-5-yl)imidazo[1,2-a]pyridine-3-carboxylate (3i', major): NMR yield 50%, white solid; R_f = 0.2 (EtOAc:DCM:Hexane = 1:3:3); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 9.34 (td, J = 1.1 Hz, 7.0 Hz, 1H), 7.73 (td, J = 1.1 Hz, 9.0 Hz, 1H), 7.50-7.46 (m, 1H), 7.34-7.23 (m, 2H), 7.06 (dt, J = 1.2 Hz, 10.4 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 5.99 (s, 2H), 4.65 (q, J = 8.5 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 159.0, 155.1, 153.2, 148.5, 148.1, 147.8, 147.3, 147.0, 128.9, 128.5, 128.4, 128.3, 128.0, 127.7, 124.5, 123.1 (J = 277.6 Hz), 117.6, 117.7, 114.4, 114.0, 111.7, 110.9, 110.6, 110.2, 107.9, 107.7, 101.30, 101.26, 101.2, 60.5, 59.9 (J = 36.8 Hz), 14.1; ^{19}F NMR δ -73.1 ppm; IR (KBr) 3051, 2978, 2898, 1696, 1472, 1394, 1342, 1242, 1170, 1040 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{11}F_3N_2O_4$ 364.0671, Found 364.0671.

2,2,2-Trifluoroethyl 2-(4-chlorophenyl)imidazo[1,2-a]pyridine-3-carboxylate (3j'): yield 63.3 mg (89%), white solid; mp 118-120 ^oC; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^1H NMR (400 MHz, $CDCl_3$) δ 9.38 (d, J = 7.0 Hz, 1H), 7.78 (d, 9.0 Hz 1H), 7.69 (dd, J = 1.9 Hz, 6.6 Hz, 2H), 7.55-7.51 (m, 1H), 7.43 (dd, J = 1.9 Hz, 6.7 Hz, 2H), 7.12 (dt, J = 1.1 Hz, 10.4 Hz, 1H), 4.63 (q, J = 8.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 154.3, 148.0, 135.3, 132.5, 131.5, 129.2, 128.6, 128.2, 123.0 (J = 277.6 Hz), 117.9, 115.0, 110.6, 60.0 (J = 36.9 Hz); ^{19}F NMR δ -73.1 ppm; IR (KBr) 2970, 2917, 1700, 1409, 1384, 1336, 1280, 1147 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{10}ClF_3N_2O_2$ 354.0383, Found 354.0386.

***tert*-Butyl 2-(3-bromophenyl)imidazo[1,2-a]pyridine-3-carboxylate (3k):** yield 66.4 mg (89%), colorless oil; R_f= 0.4 (EtOAc:DCM:Hexane = 1:10:10); ^1H NMR (400 MHz, $CDCl_3$) δ 9.42 (td, J = 1.1 Hz, 7.0 Hz, 1H), 7.86 (t, J = 1.7 Hz, 1H), 7.72 (td, J = 1.0 Hz, 8.9 Hz, 1H), 7.68 (td, J = 1.3 Hz, 7.7 Hz, 1H), 7.53 (qd, J = 1.0 Hz, 8.0 Hz, 1H), 7.45-7.41 (m, 1H) 7.31 (t, J = 7.9 Hz, 1H), 7.02 (dt, J = 1.2 Hz, 10.4 Hz, 1H), 1.47 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.5, 151.3, 146.9, 137.1, 133.5, 131.4, 129.3, 128.8, 128.4, 128.0, 121.5, 117.6, 114.2, 113.3, 82.3, 28.4; IR (KBr) 2978, 2930, 1684, 1496, 1384, 1227, 1150 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{17}{}^{79}BrN_2O_2$ 372.0473, $C_{18}H_{17}{}^{81}BrN_2O_2$, 374.0455 Found 372.0470, 374.0461.

Ethyl 2-(4-nitrophenyl)imidazo[1,2-a]pyridine-3-carboxylate (3l): yield 37.4 mg (60%), white

solid; mp 174-176 °C; R_f= 0.15 (EtOAc:Hexane = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (td, J = 1.1 Hz, 7.0 Hz, 1H), 8.31 (dd, J = 2.0 Hz, 6.9 Hz, 2H), 7.97 (dd, J = 2.0 Hz, 6.9 Hz, 2H), 7.77 (td, J = 1.1 Hz, 9.0 Hz, 1H), 7.52-7.48 (m, 1H), 7.10 (dt, J = 1.2 Hz, 10.4 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.6, 150.9, 148.0, 147.4, 141.2, 131.4, 128.6, 128.5, 122.9, 117.9, 114.8, 112.7, 61.0, 14.2; IR (KBr) 2997, 2918, 1687, 1516, 1380, 1344, 1225, 1169 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{13}N_3O_4$ 311.0906 Found 311.0904.

Ethyl 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carboxylate (3m): NMR yield 41%, white solid; R_f = 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (dd, J = 0.9 Hz, J = 7.0 Hz, 1H), 8.12-8.11 (m, 2H), 7.80-7.74 (m, 3H), 7.48-7.44 (m, 1H), 7.13 (t, J = 6.9 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 3.96 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 160.2, 153.6, 131.8, 128.5, 128.0, 127.0, 117.4, 114.0, 113.4, 60.5, 14.3; IR (KBr) 2967, 2839, 1697, 1612, 1484, 1417, 1387, 1281, 1250, 1176 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{16}N_2O_4$ 324.1110, Found 324.1108.

2,2,2-Trifluoroethyl 2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carboxylate (3m‘): NMR yield 42%, white solid; R_f = 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, CDCl3) δ 9.39 (d, J = 0.9 Hz, J = 7.0 Hz, 1H), 8.14-8.12 (m, 2H), 7.86-7.82 (m, 3H), 7.55-7.51 (m, 1H), 7.06 (t, J = 6.9 Hz, 1H), 4.62 (q, J = 8.4 Hz, 2H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 159.2, 155.4, 148.0, 131.6, 128.9, 128.6, 126.3, 123.1 (J = 277.7 Hz), 117.7, 114.6, 113.4, 110.1, 59.9 (J = 36.9 Hz), 55.5; ^{19}F NMR δ -73.0 ppm; IR (KBr) 2967, 2839, 1697, 1612, 1484, 1417, 1387, 1281, 1250, 1176 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{13}F_3N_2O_4$ 378.0827, Found 378.0831.

***tert*-Butyl 2-(thiophen-2-yl)imidazo[1,2-a]pyridine-3-carboxylate (3n):** yield 25.9 mg (43%), brown solid; mp 116−119 °C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (td, J = 1.1 Hz, 7.2 Hz, 1H), 7.93 (dd, J = 1.1 Hz, 3.7 Hz, 1H), 7.68 (d, J = 9.0 Hz,

1H), 7.44 (dd, *J* = 1.1 Hz, 5.1 Hz, 1H), 7.40-7.36 (m, 1H), 7.12 (dd, *J* = 3.7 Hz, 5.1 Hz, 1H), 6.95 (dt, *J* = 1.2 Hz, 10.4 Hz, 1H), 1.63 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 160.5, 146.7, 146.4, 136.8, 129.9, 129.0, 128.6, 127.9, 127.8, 127.3, 117.4, 113.9, 82.8, 28.7; IR (KBr) 2963, 2928, 2855, 1725, 1680, 1497, 1381, 1342, 1132 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{16}N_2O_2S$ 300.0932, Found 300.0930.

2,2,2-Trifluoroethyl 8-methyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3o): yield 56.4 mg (84%), white solid; mp 110−113 ^{o}C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, *J* = 6.8 Hz, 1H), 7.72-7.70 (m, 2H), 7.45-7.42 (m, 3H), 7.30 (td, *J* = 1.0 Hz, 7.0 Hz, 1H), 7.01 (t, *J* = 7.0 Hz, 1H), 4.59 (q, *J* = 8.4 Hz, 2H), 2.70 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 155.1, 148.2, 134.4, 130.2, 129.0, 127.9, 127.8, 126.2, 123.0 (*J* = 266.8 Hz), 114.8, 110.9, 59.8 (*J* = 36.8 Hz), 17.2; ^{19}F NMR δ -73.2 ppm; IR (KBr) 3033, 2970, 1698, 1490, 1381, 1281, 1234, 1169, 1108 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_2$ 334.0929, Found 334.0927.

Ethyl 7-methyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3p): yield 17.4 mg (31%), white solid; mp 48−51 ^{o}C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, *J* = 7.1 Hz, 1H), 7.77-7.75 (m, 2H), 7.49 (s, 1H), 7.44-7.41 (m, 3H), 6.87 (dd, *J* = 1.7 Hz, 7.1 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.48 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3, 153.9, 147.7, 139.4, 134.8, 130.3, 130.2, 128.7, 127.8, 127.7, 116.7, 116.2, 60.5, 21.6, 14.1; IR (KBr) 3058, 2979, 2929, 1684, 1400, 1225, 1155, 1050 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{16}N_2O_2$ 280.1212, Found 280.1213.

2,2,2-Trifluoroethyl 7-methyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3p´): yield 33.5 mg (50%), white solid; mp 108−111 ^{o}C; R_f= 0.2 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, *J* = 7.1 Hz, 1H), 7.73-7.71 (m, 2H), 7.53 (s, 1H), 7.45-7.43 (m, 3H), 6.94 (dd, *J* = 1.7 Hz, 7.1 Hz, 1H), 4.60 (q, *J* = 8.5 Hz, 2H), 2.50 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz,

$CDCl_3$) δ 159.2, 155.7, 148.4, 140.5, 134.1, 130.1, 129.1, 127.9, 127.7, 123.1 (J = 277.7 Hz), 117.3, 116.5, 110.1, 59.8 (J = 36.9 Hz), 21.6; ^{19}F NMR δ -73.1 ppm; IR (KBr) 3036, 2969, 2925, 1693, 1413, 1281, 1169, 1069 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{13}F_3N_2O_2$ 334.0929, Found 334.0926.

Ethyl 7-ethyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3q, minor): NMR yield 15%, white solid; R_f= 0.4 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 7.2 Hz, 1H), 7.78-7.75 (m, 2H), 7.52 (s, 1H), 7.44-7.42 (m, 3H), 6.91 (d, J = 6.8 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 2.76 (q, J = 8.0 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); IR (KBr) 3138, 3062, 2971, 2931, 1692, 1406, 1283, 1163 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{18}N_2O_2$ 294.1368, Found 294.1368.

2,2,2-Trifluoroethyl 7-ethyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3q', major): NMR yield 59%, white solid; R_f= 0.4 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (d, J = 7.1 Hz, 1H), 7.74-7.71 (m, 2H), 7.56 (s, 1H), 7.44-7.42 (m, 3H), 6.97 (d, J = 7.1 Hz, 1H), 4.60 (q, J = 8.5 Hz, 2H), 2.80 (q, J = 7.6 Hz, 2H), 1.33 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 155.8, 148.6, 146. 5, 134.2, 130.3, 130.1, 129.0, 127.9, 127.7, 120.1 (J = 295.8 Hz), 116.3, 115.1, 59.8 (J = 37.0 Hz), 28.6, 14.4; ^{19}F NMR δ -73.1 ppm; IR (KBr) 3138, 3062, 2971, 2931, 1692, 1406, 1283, 1163 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{15}F_3N_2O_2$ 348.1086, Found 348.1085.

Ethyl 8-bromo-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3r): yield 53.9 mg (78%), white solid; mp 109-110 ^{o}C; R_f= 0.5 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (dd, J = 1.0 Hz, 7.0 Hz, 1H), 7.77-7.75 (m, 2H), 7.69 (dd, J = 1.0 Hz, 7.4 Hz, 1H), 7.44-7.42 (m, 3H), 6.92 (t, J = 7.2 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.2, 154.0, 145.1, 134.2, 130.5, 130.4, 128.9, 127.7, 114.2, 113.8, 111.7, 60.9, 14.0; IR (KBr) 2980, 1685, 1490, 1402, 1322, 1239, 1156 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd

for $C_{16}H_{13}{}^{79}BrN_2O_2$ 344.0160, $C_{16}H_{13}{}^{81}BrN_2O_2$ 346.0142, Found 344.0158, 346.0140.

Ethyl 8-iodo-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3s): yield 58.8 mg (75%), white solid; mp 109-110 ^oC; R_f= 0.5 (EtOAc:DCM:Hexane = 1:20:20); ^1H NMR (400 MHz, $CDCl_3$) δ 9.43 (dd, J = 1.0 Hz, 6.9 Hz, 1H), 7.92 (dd, J = 1.0 Hz, 7.3 Hz, 1H), 7.78-7.76 (m, 2H), 7.44-7.41 (m, 3H), 6.78 (t, J = 7.1 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 153.8, 146.4, 137.2, 134.3, 130.6, 128.9, 128.5, 127.7, 114.8, 113.9, 84.0, 60.8, 14.0; IR (KBr) 2979, 1685, 1488, 1400, 1320, 1238, 1202, 1163, 1054 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{13}N_2O_2I$ 392.0022, Found 392.0019.

Ethyl 7-acetyl-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3t): yield 58.6 mg (95%), white solid, mp 148-150 ^oC; R_f = 0.4 (EtOAc:DCM:Hexane = 1:20:20); ^1H NMR (400 MHz, $CDCl_3$) δ 9.43 (d, J = 0.8 Hz, 7.3 Hz, 1H), 8.29 (q, J = 0.8 Hz, 1H), 7.79-7.77 (m, 2H), 7.60 (dd, J = 1.8 Hz, 7.3 Hz, 1H), 7.47-7.45 (m, 3H), 4.34 (q, J = 7.1 Hz, 2H), 2.70 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.8, 161.0, 155.0, 146.2, 135.4, 134.0, 130.3, 129.2, 128.3, 127.8, 119.0, 113.6, 111.7, 61.0, 26.4, 14.1; IR (KBr) 3057, 2988, 2926, 1684, 1403, 1381, 1312, 1231 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{16}N_2O_3$ 308.1161, Found 308.1162.

3-Ethyl 7-methyl 2-phenylimidazo[1,2-a]pyridine-3,7-dicarboxylate (3u): yield 44.1 mg (68%), white solid, mp 123-125 ^oC; R_f = 0.2 (EtOAc:DCM:Hexane = 1:10:10); ^1H NMR (400 MHz, $CDCl_3$) δ 9.45 (d, J = 7.3 Hz, 1H), 8.42 (s, 1H), 7.78-7.76 (m, 2H), 7.62 (dd, J = 1.7 Hz, 7.3 Hz, 1H), 7.47-7.43 (m, 3H), 4.33 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.3, 161.0, 155.0, 146.2, 134.1, 130.3, 129.2, 129.1, 128.1, 127.8, 119.8, 113.4, 113.3, 61.0, 52.9, 14.1; IR (KBr) 3136, 3068, 2983, 2953, 1725, 1688, 1489, 1406, 1324 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{16}N_2O_4$ 324.1110, Found 324.1107.

Ethyl 2-phenylimidazo[1,2-a]quinoline-1-carboxylate (3v): yield 53.8 mg (85%), white solid; mp

89−91 °C; R_f= 0.4 (EtOAc:DCM:Hexane = 1:10:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.7 Hz, 1H), 7.85-7.81 (m, 3H), 7.70 (d, J = 9.3 Hz, 1H), 7.65-7.61 (m, 2H), 7.52-7.40 (m, 4H), 4.38 (q, J = 7.1 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 150.9, 146.0, 134.0, 133.5, 129.8, 129.7, 129.4, 128.8, 128.7, 128.1, 125.4, 124.6, 118.3, 117.0, 116.2, 61.9, 14.0; IR (KBr) 3058, 2979, 1710, 1445, 1370, 1193 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{16}N_2O_2$ 316.1212, Found 316.1209.

Ethyl 2-phenylimidazo[2,1-a]isoquinoline-3-carboxylate (3w): yield 51.3 mg (81%), white solid; mp 125−127 °C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (d, J = 7.5 Hz, 1H), 8.80 (q, J = 3.1 Hz, 1H), 7.82-7.79 (m, 3H), 7.69-7.67 (m, 2H), 7.48–7.42 (m, 3H), 7.27 (d, J = 8.7 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 152.0, 145.2, 134.8, 130.6, 130.4, 129.6, 128.6, 128.4, 127.8, 126.8, 124.6, 124.5, 123.2, 114.3, 113.8, 60.7, 14.1; IR (KBr) 3134 ,3056, 2979, 2904, 1692, 1516, 1400, 1369, 1222, 1163 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{16}N_2O_2$ 316.1212, Found 316.1209.

Ethyl 2,7-diphenylimidazo[1,2-a]pyridine-3-carboxylate (3x): yield 15.1 mg (22%), white solid; mp 168−170 °C; R_f= 0.35 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (dd, J = 0.9 Hz, 7.3 Hz, 1H), 7.94 (q, J = 0.9 Hz, 1H), 7.81-7.79 (m, 2H), 7.72-7.70 (m, 2H), 7.53-7.49 (m, 2H), 7.47-7.42 (m, 4H), 7.33 (dd, J = 1.9 Hz, 7.3 Hz 1H), 4.33 (q, J = 8.4 Hz, 2H) 1.24 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.2, 154.4, 147.8, 141.0, 138.1, 134.6, 130.3, 129.4, 129.0, 128.8, 128.3, 127.7, 127.1, 114.2, 113.8, 111.9, 60.6, 14.1; IR (KBr) 3033, 2985, 2904, 1671, 1406, 1381, 1227, 1165, 1049 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{18}N_2O_2$ 342.1368, Found 342.1370.

2,2,2-Trifluoroethyl 2,7-diphenylimidazo[1,2-a]pyridine-3-carboxylate (3x′): yield 30.9 mg (39%), white solid; mp 195−197 °C; R_f= 0.4 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (dd, J = 0.7 Hz, 7.3 Hz, 1H), 7.98 (q, J = 0.9 Hz, 1H), 7.77-7.75 (m, 2H), 7.73-7.70

(m, 2H), 7.55-7.51 (m, 2H), 7.48-7.45 (m, 4H), 7.39 (dd, J = 1.9 Hz, J = 7.3 Hz, 1H), 4.63 (q, J = 8.4 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 156.2, 148.5, 141.9, 137.8, 134.0, 130.1, 129.4, 129.2, 129.1, 128.4, 127.9, 127.1, 123.1 (J = 277.6 Hz), 114.4, 114.3, 110.3, 59.9 (J = 36.9 Hz); ^{19}F NMR δ -73.1 ppm; IR (KBr) 3033, 2985, 2904, 1671, 1406, 1381, 1227, 1165, 1049 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{15}F_3N_2O_2$ 396.1086, Found 396.1088.

Ethyl 2-phenyl-7-(*p*-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3y): yield 14.3 mg (20%), white solid; mp 176−178 ^{o}C; R_f = 0.25 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (dd, J = 0.6 Hz, 7.3 Hz, 1H), 7.92 (q, J = 0.9 Hz, 1H), 7.81-7.78 (m, 2H) 7.61 (d, J = 8.2 Hz, 2H), 7.45-7.42 (m, 3H), 7.33-7.30 (m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 2.43 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3, 154.4, 147.9, 141.0, 139.1, 135.2, 134.7, 130.3, 130.1, 128.8, 128.3, 127.7, 126.9, 113.8, 111.8, 60.6, 29.8, 21.4, 14.2; IR (KBr) 2988, 2921, 1674, 1382, 1226, 1163, 1050 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{23}H_{20}N_2O_2$ 356.1525, Found 356.1522.

2,2,2-Trifluoroethyl 2-phenyl-7-(*p*-tolyl)imidazo[1,2-a]pyridine-3-carboxylate (3y′): yield 32.0 mg (39%), white solid; mp 191−193 ^{o}C; R_f = 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 7.3 Hz, 1H), 7.95 (s, 1H), 7.77-7.74 (m, 2H), 7.61 (d, J = 8.2 Hz, 2H), 7.47-7.44 (m, 3H), 7.37 (dd, J = 1.9 Hz, 7.3 Hz, 1H), 7.33 (q, J = 8.0 Hz, 2H), 4.62 (q, J = 8.5 Hz, 2H), 2.43 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 156.2, 148.6, 141.9, 139.4, 134.9, 134.1, 130.1, 129.2, 128.3, 127.9, 127.2, 126.9, 123.1 (J = 277.7 Hz), 114.3, 113.9, 110.2, 59.9 (J = 36.9 Hz), 21.4, 1.2; ^{19}F NMR δ -73.1 ppm; IR (KBr) 2960, 2351, 1675, 1385, 1286, 1176, 1156, 1067 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{23}H_{17}F_3N_2O_2$ 410.1242, Found 410.1242.

Ethyl 7-(4-chlorophenyl)-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3z): yield 24.9 mg (33%), white solid; mp 213−215 ^{o}C; R_f = 0.25 (EtOAc:DCM:Hexane = 1:20:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (dd, J = 0.8 Hz, 7.3 Hz, 1H), 7.90 (q, J = 0.9 Hz, 1H) 7.80-7.78 (m, 2H), 7.63

(dd, J = 1.9 Hz, 6.6 Hz, 2H) 7.50-7.43 (m, 5H), 7.28-7.26 (m, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.2, 154.5, 147.6, 139.6, 136.6, 135.2, 134.5, 130.3, 129.6, 128.9, 128.5, 128.3, 127.7, 114.2, 113.5, 112.0, 60.7, 14.1; IR (KBr) 3028, 2966, 2925, 2349, 1668, 1488, 1226, 1168 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{17}ClN_2O_2$ 376.0979, Found 376.0981.

2,2,2-Trifluoroethyl 7-(4-chlorophenyl)-2-phenylimidazo[1,2-a]pyridine-3-carboxylate (3z´): yield 34.5 mg (40%), white solid; mp 199−201 ^oC; R_f= 0.3 (EtOAc:DCM:Hexane = 1:20:20); ^1H NMR (400 MHz, $CDCl_3$) δ 9.40 (d, J = 7.2 Hz, 1H), 7.93 (s, 1H), 7.75 (q, J = 3.2 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 7.50-7.45 (m, 5H), 7.33 (dd, J = 1.8 Hz, 7.3 Hz, 1H), 4.63 (q, J = 8.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 156.3, 148.3, 140.6, 136.3, 135.5, 133.9, 130.1, 129.7, 129.3, 128.6, 128.3, 128.0, 123.0 (J = 278.0 Hz), 114.4, 114.0, 110.4, 60.0 (J = 36.9 Hz); ^{19}F NMR δ -73.1 ppm; IR (KBr) 2964, 2920, 1670, 1387, 1290, 1224, 1166, 1068 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{14}ClF_3N_2O_2$ 430.0696, Found 430.0694.

Ethyl 8-methoxy-2-phenyl-7,8-dihydroimidazo[1,2-a]pyridine-3-carboxylate (4a): yield 14.9 mg (25%), white solid; mp 70−72 ^oC; R_f= 0.1 (EtOAc:Hexane = 1:5); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77-7.74 (m, 1H), 7.69-7.67 (m, 2H), 7.43-7.36 (m, 3H), 5.69-5.65 (m, 1H), 4.52 (ddd, J = 0.8 Hz, 2.4 Hz, 5.3 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.42 (s, 3H), 2.81-2.64 (m, 2H), 1.21(t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 144.7, 134.1, 129.8, 128.3, 127.7, 123.5, 116.9, 112.0, 70.1, 60.9, 57.1, 28.2, 14.0; IR (KBr) 2981, 2928, 2824, 1701, 1437, 1373, 1226, 1146, 1087 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{18}N_2O_3$ 298.1317, Found 298.1317.

Ethyl 2-phenylimidazo[1,2-b]pyridazine-3-carboxylate (6a): yield 42.9 mg (80%), white solid; mp 89−91 ^oC; R_f= 0.2 (EtOAc:DCM:Hexane = 1:3:3); ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, J = 1.6 Hz, 4.4 Hz, 1H), 8.05 (dd, J = 1.6 Hz, 9.2 Hz, 1H), 7.82-7.80 (m, 2H), 7.49-7.43 (m, 3H), 7.24 (q, J = 4.5 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz,

$CDCl_3$) δ 159.9, 151.2, 144.0, 140.7, 133.8, 129.8, 129.1, 128.0, 125.7, 119.4, 116.9, 61.2, 14.1; IR (KBr) 2980, 2917, 1714, 1531, 1485, 1415, 1329, 1279, 1183 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{15}H_{13}N_3O_2$ 267.1008, Found 267.1009.

Ethyl 6-methyl-2-phenylimidazo[1,2-b]pyridazine-3-carboxylate (6b): yield 54.0 mg (96%), white solid; mp 107−109 °C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:3:3); ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.2 Hz, 1H), 7.80-7.78 (m, 2H), 7.46-7.42 (m, 3H), 7.10 (d, *J* = 9.3 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.69 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.1, 153.2, 150.6, 139.8, 134.0, 129.8, 128.9, 128.0, 125.2, 121.5, 116.8, 61.1, 22.3, 14.1; IR (KBr) 2981, 1715, 1616, 1547, 1338 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{15}N_3O_2$ 281.1164, Found 281.1161.

Ethyl 7-methyl-2-phenylimidazo[1,2-c]pyrimidine-3-carboxylate (6c): yield 30.4 mg (54%), white solid; mp 73−76 °C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:3:3); ^1H NMR (400 MHz, $CDCl_3$) δ 10.05 (d, *J* = 1.1 Hz, 1H), 7.81-7.78 (m, 2H), 7.46-7.42 (m, 4H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.62 (d, *J* = 0.4 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.6, 154.8, 152.9, 147.9, 140.4, 133.5, 130.4, 129.4, 127.8, 110.8, 109.9, 61.1, 23.9, 14.1; IR (KBr) 2980, 1758, 1685, 1580, 1334 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{15}N_3O_2$ 281.1164, Found 281.1166.

Ethyl 2-phenylimidazo[1,2-a]pyrazine-3-carboxylate (6d): yield 28.4 mg (53%), white solid; mp 89−91 °C; R_f= 0.3 (EtOAc:Hexane = 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.25-9.23 (m, 2H), 8.15 (d, *J* = 4.6 Hz, 1H), 7.81-7.78 (m, 2H), 7.47-7.46 (m, 3H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7, 154.1, 143.9, 141.5, 133.5, 131.8, 130.4, 129.4, 127.9, 120.7, 113.2, 61.3, 14.1; IR (KBr) 3138, 3065, 2992, 1685, 1487, 1474, 1402, 1383, 1254, 1209, 1164 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{15}H_{13}N_3O_2$ 267.1008, Found 267.1006.

Ethyl 8-methyl-2-phenylimidazo[1,2-a]pyrazine-3-carboxylate (6e): yield 33.1 mg (59%), white solid; mp 130−132 °C; R_f= 0.3 (EtOAc:DCM:Hexane = 1:3:3); ^1H NMR (400 MHz, $CDCl_3$) δ 9.10

(d, J = 4.7 Hz, 1H), 8.00 (d, J = 4.7 Hz, 1H), 7.78-7.76 (m, 2H), 7.47-7.44 (m, 3H), 4.34 (q, J = 7.1 Hz, 2H), 2.97 (s, 3H) 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8, 153.3, 153.2, 141.2, 133.9, 131.1, 130.4, 129.2, 127.9, 119.1, 113.6, 61.2, 20.9, 14.1; IR (KBr) 2997, 2983, 1684, 1481, 1409, 1257, 1168 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{16}H_{15}N_3O_2$ 281.1164, Found 281.1163.

Ethyl 6,8-dimethyl-2-phenylimidazo[1,2-a]pyrazine-3-carboxylate (6f): yield 41.9 mg (71%), yllow solid; mp 128−130 ^oC; R_f= 0.2 (EtOAc:DCM:Hexane = 1:5:5); ^1H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.76-7.74 (m, *2*H), 7.46-7.43 (m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 2.95 (s, 3H), 2.58 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.0, 153.3, 151.9, 140.1, 134.2, 130.3 (2C), 129.0, 127.8 (2C), 116.2, 61.0, 21.4, 20.8, 14.1; IR (KBr) 2981, 2925, 1690, 1488, 1406, 1379, 1290, 1171, 1132 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{17}N_3O_2$ 295.1321, Found 295.1324.

General Procedure for the C–H Activations

2,2,2-Trifluoroethyl 2-(2-((4-methylphenyl)sulfonamido)phenyl)imidazo[1,2-a]pyridine-3-carboxylate (7): To an oven-dried test tube equipped with a stirring bar, **3a´** (64.1 mg, 0.2 mmol), tosyl azide (47.3 mg, 0.24 mmol), $[Cp^*IrCl_2]_2$ (4.0 mol %), $AgPF_6$ (16.0 mol %), and dichloroethane (1.0 mL) were added and then pivalic acid (11.0 μL, 0.1 mmol) was added. The resulting mixture was stirred at 80 ^oC for 10 h. After celite filtration with dichloromehane and evaporation of the solvents in vacuo, the residue was purified by Silica gel flash column chromatography (EtOAc:Hexane = 1:2) to give **7** (76.4 mg, 78%). white solid; mp 178−180 ^oC; R_f= 0.2 (EtOAc:Hexane = 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.32-9.30 (m, 2H), 7.79 (d, J = 8.9 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.64-7.59 (m, 1H), 7.47-7.42 (m, 2H), 7.24-7.16 (m, 2H), 7.07 (d, J = 8.2 Hz, 2H), 6.64 (d, J = 8.0 Hz, 2H), 4.44 (q, J = 8.4 Hz, 2H), 2.21 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.1, 151.4, 147.1, 143.0, 136.5, 135.1, 132.3, 130.5, 129.7, 128.6, 128.3, 127.0,

126.6, 126.2, 125.5, 122.9 (J = 280.7 Hz), 117.6, 115.3, 110.9, 60.1 (J = 37.0 Hz), 21.5; ^{19}F NMR δ -72.8 ppm; IR (KBr) 3148, 2965, 2923, 1701, 1417, 1385, 1334, 1281, 1166 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{23}H_{18}F_3N_3O_4S$ 489.0970, Found 489.0972.

2,2,2-Trifluoroethyl 2-(2-benzamidophenyl)imidazo [1,2-a]pyridine-3-carboxylate (8): To an oven-dried test tube equipped with a stirring bar, **3a´** (64.1 mg, 0.2 mmol), dioxazolone (48.9 mg, 0.3 mmol), $[Cp^*RhCl_2]_2$ (4.0 mol %), and $AgSbF_6$ (16.0 mol %) were added in dichloroethane (1.0 mL). The resulting mixture was stirred at 80 ^{o}C for 24 h. After celite filtration with EtOAc and evaporation of the solvents in vacuo, the residue was purified by Silica gel flash column chromatography (EtOAc:Hexane = 1:5) to give **8** (83.5 mg, 95%). white solid; mp 146−148 ^{o}C; R_f= 0.3 (EtOAc:Hexane = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1H), 9.44 (td, J = 1.0 Hz, J = 7.0 Hz, 1H), 8.61 (d, J = 8.2, 1H), 7.93-7.91 (m, 2H), 7.80 (td, J = 1.0 Hz, J = 8.9 Hz, 1H), 7.64-7.57 (m, 2H), 7.52-7.41 (m, 4H), 7.20-7.15 (m, 2H), 4.62 (q, J = 8.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.1, 158.8, 152.7, 147.3, 136.8, 135.3, 132.7, 131.7, 130.5, 129.8, 128.9, 128.7, 127.2, 123.2, 122.9 (J = 277.8 Hz), 121.5, 117.0, 115.3, 111.5, 59.9 (J = 37 Hz); ^{19}F NMR δ -72.8 ppm; IR (KBr) 3301, 3063, 2248, 1701, 1675, 1587, 1495, 1450, 1308, 1150 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{23}H_{16}F_3N_3O_3$ 439.1144, Found 439.1147.

2,2,2-Trifluoroethyl 2-(2-(2-ethoxy-2-oxoethyl)phenyl) imidazo[1,2-a]pyridine-3-carboxylate (9): To an oven-dried test tube equipped with a stirring bar, **3a´** (64.1 mg, 0.2 mmol), diazo Meldrum's acid (51.0 mg, 0.3 mmol), $[Cp^*IrCl_2]_2$ (2.5 mol %), and $AgNTf_2$ (10 mol %) were added in ethyl alcohol (2.0 mL). The resulting mixture was stirred at 100 ^{o}C for 24 h. After celite filtration with EtOAc and evaporation of the solvents in vacuo, the residue was purified by Silica gel flash column chromatography (EtOAc:Hexane = 1:5) to give **9** (64.9 mg, 80%). yellow liquid; R_f= 0.25 (EtOAc:Hexane = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, J = 6.9 Hz, 1H), 7.76 (d, J = 8.9 Hz, 1H), 7.55-7.51 (m, 1H), 7.43-7.31 (m, 4H), 7.13 (dt, J = 1.1 Hz, J = 10.4 Hz, 1H), 4.47 (q, J = 8.4

Hz, 2H), 3.97 (q, J = 7.1 Hz, 2H), 3.60 (s, 2H), 1.08(t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.4, 158.9, 154.6, 147.8, 134.4, 133.1, 130.5, 130.2, 129.0, 128.9, 128.3, 126.7, 122.8 (J = 277.3 Hz), 117.9, 114.9, 112.0, 60.6, 59.9 (J = 36.9 Hz), 39.2, 14.1; ^{19}F NMR δ -73.7 ppm; IR (KBr) 2981, 2931, 1734, 1702, 1414, 1281, 1152 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{17}F_3N_2O_4$ 406.1140, Found 406.1137.

2,2,2-Trifluoroethyl (*E*)-2-(2-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)imidazo[1,2-a]pyridine-3-carboxylate (10): To an oven-dried test tube equipped with a stir bar, **3a´** (64.1 mg, 0.2 mmol), ethyl acrylate (0.026 mL, 0.24 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), and $Cu(OAc)_2$ (1.0 equiv) were added in dichloroethane (2.0 mL). The resulting mixture was stirred at 90 ^oC for 6 h. After celite filtration with EtOAc and evaporation of the solvents in vacuo, the residue was purified by Silica gel flash column chromatography (EtOAc:Hexane = 1:2) to give **10** (72.0 mg, 86%). white solid; mp 96−98 ^oC; R_f= 0.3 (EtOAc:Hexane = 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 6.4 Hz, 1H), 7.82-7.75 (m, 2H), 7.62-7.54 (m, 2H), 7.47-7.45 (m, 3H), 7.17 (t, J = 6.9 Hz, 1H), 6.41 (d, J = 15.8 Hz, 1H), 4.45 (q, J = 8.4 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.0, 158.7, 153.5, 147.7, 142.5, 135.3, 133.7, 130.9, 129.4, 129.2, 128.3, 126.0, 122.7 (J = 277.5 Hz), 119.3, 118.1, 115.2, 112.4, 72.8, 60.6, 60.0 (J = 36.9 Hz), 14.4; ^{19}F NMR δ -73.7 ppm; IR (KBr) 2981, 1710, 1635, 1389, 1317, 1280, 1177, 1153 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{17}F_3N_2O_4$ 418.1140, Found 418.1142.

ASSOCIATED CONTENT

Supporting Information

X-ray crystallographic data (**3o** and **4a**) and copies of the NMR spectra for all products (PDF). This material is available free of charge *via* the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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DEDICATION

This paper is dedicated to Professor Hee-Yoon Lee (KAIST) on the occasion of his 60th birthday.

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14. CCDC 1548507 (**4a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/ data_request/cif.

15. CCDC 1523575 (**3o**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/ data_request/cif.

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