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Annulation of Conjugated Azine-Imine with a Sulfoxonium Ylide in a Noncarbenoid Route to Synthesize Multisubstituted Imidazole-Fused Heterocycles

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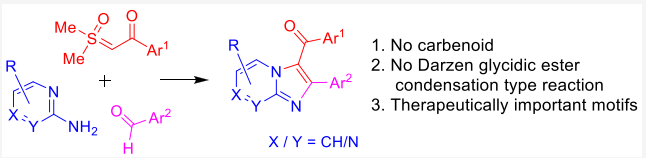
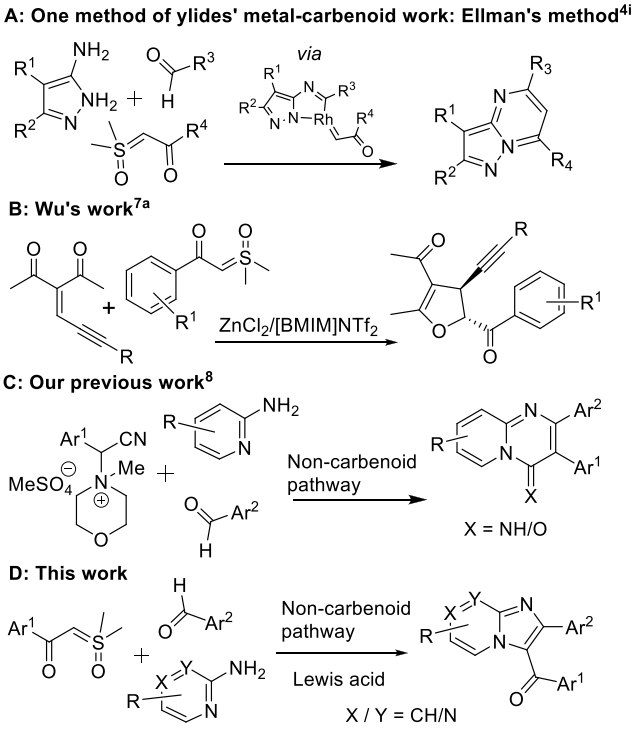
ABSTRACT: A new [4+1]-annulation of in situ generated heterocyclic azine-aldimines with β-keto sulfoxonium ylides has been developed. The reaction constructs N-fused imidazole rings. In the reaction, the ylides play a dual-functional role of a nucleophilic 1,1-dipolar one-carbon synthon and a source of an internal oxidant, dimethyl sulfoxide, that promotes in situ dehydrogenation to product scaffolds. The method enables access to imidazo-pyridine, pyrazine, and pyrimidine heteroaromatics.



Sulfur-based ylides are among the important functional substrates used in various synthetic organic chemistry transformations.[1] Their functions as carbene equivalents in the cyclization reactions with diverse unsaturated electrophilic functional motifs have been widely documented, which afford the synthesis of a range of heterocyclic and carbocyclic compounds.[2] Sulfoxonium ylides are stable, crystalline solids, operationally safe, and, thus, employed as popular carbene surrogates. They are used in X−H (X = C, N, O, S) and other bond insertion reactions.[3] Transition-metal-catalyzed sp^2 C−H activation/insertion−annulation reactions with β-ketosulfoxonium ylides as carbene equivalents are especially appealing and have been widely discovered (Scheme 1A).[4] The β-ketosulfoxonium ylide functions as a traceless bifunctional directing motif in arene C−H functionalization and post-annulation reactions.[4h,5] All of these transformations involve transition-metal-carbenoid chemistry. Recently, a divergent [2+1+1+1]-annulation of Bu^tONO with an aroylsulfoxonium ylide as a carbene precursor has been developed, which provides furoxans and isoxazoles.[6] The study of a sulfoxonium ylide as a 1,1′-dipolar one-carbon synthon, avoiding transition-metal-carbenoid chemistry, is rare in annulation reactions (Scheme 1B)[7] and has not been identified until now for the construction of fused heteroaromatics. In the aspect of a unique feature of ylides, we previously explored nitrile-stabilized ammonium ylide as a masked C−C═N synthon (Scheme 1C).[8] In the study of the β-ketosulfoxonium ylide as a nucleophilic 1,1′-dipolar species toward the preparation of therapeutically important N-fused imidazoles,[9] we realized a [4+1]-annulation reaction of the ylides with a suitable 1,3-conjugated system, heterocyclic amidine-derived imine (Scheme 1D).

Imidazopyridines are important heterocyclic scaffolds because of their versatile applications in the field of medicinal,[10] material,[11] and organometallic chemistry.[12] The

Scheme 1. Sulfoxonium Ylides' Carbenoid and Noncarbenoid Chemistry and Present Work



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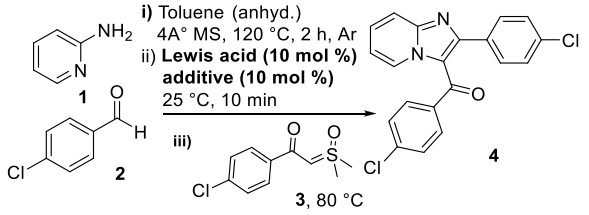
scaffold is present in several drugs including zolpidem,[13] olprinone,[14] minodronic acid[15] and zolimidine,[16] and a clinical candidate Q203.[17] 3-Aroylimidazo[1,2-*a*]pyridines have been ascribed to a broad spectrum of biological activities, such as an anticancer and calcium antagonist.[18] We also have explored synthetic methods and biological properties of various N-fused imidazoles, especially imidazo[1,2-*a*]pyridines/pyrazines.[19] Toward the synthesis of 2-aryl-3-aroylimidazo[1,2-*a*]pyridines, the frequently considered approach is the reaction of aminopyridine with chalcone.[20,21] Other methods include C−H functionalization of N-aryl enamine,[22] CBr_4-mediated oxidative C−N bond formation of 2-aminopyridines with 1,3-dicarbonyls,[23] and a reaction of 2-aminopyridine and benzyl bromide with a terminal alkyne.[24] In light of this synthetic precedence, our envisaged ylide-based [4+1]-annulation approach would afford a new convenient diversity-feasible synthesis of 2-ary-3-aroyl-imidazo[1,2-*a*]pyridines/pyrazines.

In the preliminary investigation, 4-chlorophenacylsulfoxonium ylide **1** was chosen as a model ylide substrate (Table 1).

Table 1. Evaluation of Lewis Acids[a]



entry	equiv of **1** and **2**	Lewis acid (mol %)	yield (%)[b]
1[c]	1	$Cu(OTf)_2$	42
2	1	$Cu(OTf)_2$	56
3	2	$Cu(OTf)_2$	67
4	1.5	$Cu(OTf)_2$	64
5	1.3	$Cu(OTf)_2$	65
6	1		27
7	1.3	$La(OTf)_3$	46
8	1.3	$Sc(OTf)_3$	51
9	1.3	$Y(OTf)_3$	48
10	1.3	$Yb(OTf)_3$	58
11	1.3	$In(OTf)_3$	40
12	1.3	$ZrCl_4$	28
13	1.3	$BF_3.OEt_2$	47
14	1.3	$Cu(OAc)_2$	54
15	1.3	CuO	70
16	1.3	$CuBr_2$	50
17	1.3	$CuCl_2$	76
18	1.3	$Cu(acac)_2$	58
19	1.3	$Cu(BF_4)_2$	56
20	1.3	CuCl	61
21	1.3	CuBr	52

[a]Substrates, reagents, and conditions: sulfoxonium ylide (1 mmol), aldehyde and amine, Lewis acid, additive, reaction temp (oil bath). [b]Isolated yield obtained after carrying out the reaction for maximum conversion in optimum time. [c]*p*-TSA was not used.

An in situ process of the preparation of conjugated imine and its reaction with ylide **1** was examined. After some initial experiments, we found that a sequence of conversion of 2-aminopyridine and 4-chlorobenzaldehyde to imine in toluene (step i), electrophilic activation of imine by $Cu(OTf)_2$ (step ii), and subsequent reaction with the ylide (step iii) provided the desired 2-aryl-3-aroyl-imidazo[1,2-*a*]pyridine in a 42% isolated yield (entry 1). *p*-TSA as an additive along with $Cu(OTf)_2$ improved the yield (entry 2). We observed that imine formation could not be made complete in numerous conditions. Variation in equivalents of aldehyde and amine indicated that 1.3 equiv of each of them were optimal to enhance the yield (entries 3−5). The reaction in the absence of $Cu(OTf)_2$ reduced the yield significantly, indicating the importance of a Lewis acid. A variety of Lewis acids (entries 7−21) were screened. A few Lewis acids (Cu, Yb, Sc-based) were found to be effective, and $CuCl_2$ was found to be the best (entry 17).

Imine formation is reversible and sensitive to pH. In addition, the use of *p*-TSA in the reaction increased the yield. These indicated a possible effect of the pK_a of a Brønsted acid in the reaction. Accordingly, acids with different pK_a values replacing *p*-TSA were evaluated (Table 2A). Acids with pK_a values in the range from −2 to 0.3 were more efficient. Increasing or decreasing pK_a values beyond this range resulted in gradual reducing yields. *p*-TSA and TFA were found to be more effective, and *p*-TSA was considered to be the best choice because of its operational simplicity.

Table 2A. Evaluation of Brønsted Acids[a]

entry	additive (10 mol %)	pK_a	yield (%)[b]
1	TfOH	−13	50
2	HCl	−7	55
3	MsOH	−2	71
4	*p*-TSA	−1.76	76
5	CF_3COOH	0.0	78
6	Picric acid	0.3	69
7	CH_3COOH	4.75	56
8	$PhB(OH)_2$	8.83	48
9	H_3BO_3	9.23	31

The reactions of oxosulfonium ylides catalyzed by transition-metals (Pd, Ru, Rh, Ir) are widely known to occur via the carbenoid pathway. Therefore, in our investigated reaction, we examined the additional use of Pd, Ru, or Rh-based catalysts along with optimized conditions (Table 2B). However, none of them provided an improved yield; rather, the yield was significantly reduced. These indicate that the present reaction undergoes via a noncarbenoid pathway.

Table 2B. Evaluation of Transition Metal Catalysts

entry	catalyst in addition[c]	time (h)	yield (%)[b]
1	$Pd_2(dba)_3$	6	75
2	$RuCl_3$	12	57
3	$RhCl(PPh_3)_3$	6	59

[a]Reaction conditions: **1** (1 mmol), **2** (1 mmol), and **3** (1 mmol), in toluene at 80 °C (oil bath). [b]Isolated yields. [c]10 mol %.

We surmised that, in the reaction, the dimethyl sulfoxide byproduct is generated from sulfoxonium ylide, and it acted as an oxidizing agent for dehydrogenative aromatization of the dihydroimidazo[1,2-*a*]pyridine intermediate converting into imidazo[1,2-*a*]pyridine (Scheme 2).[25]

Therefore, some experiments were performed to identify whether an external oxidant would facilitate the dehydrogenative aromatization and thus the reaction. Three sets of experiments of the reaction were performed, under an O_2

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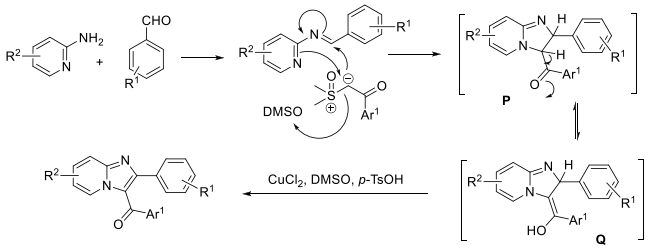
Scheme 2. Plausible Mechanism: Annulation and Dehydrogenative Aromatization

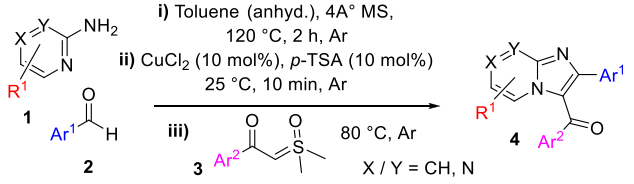


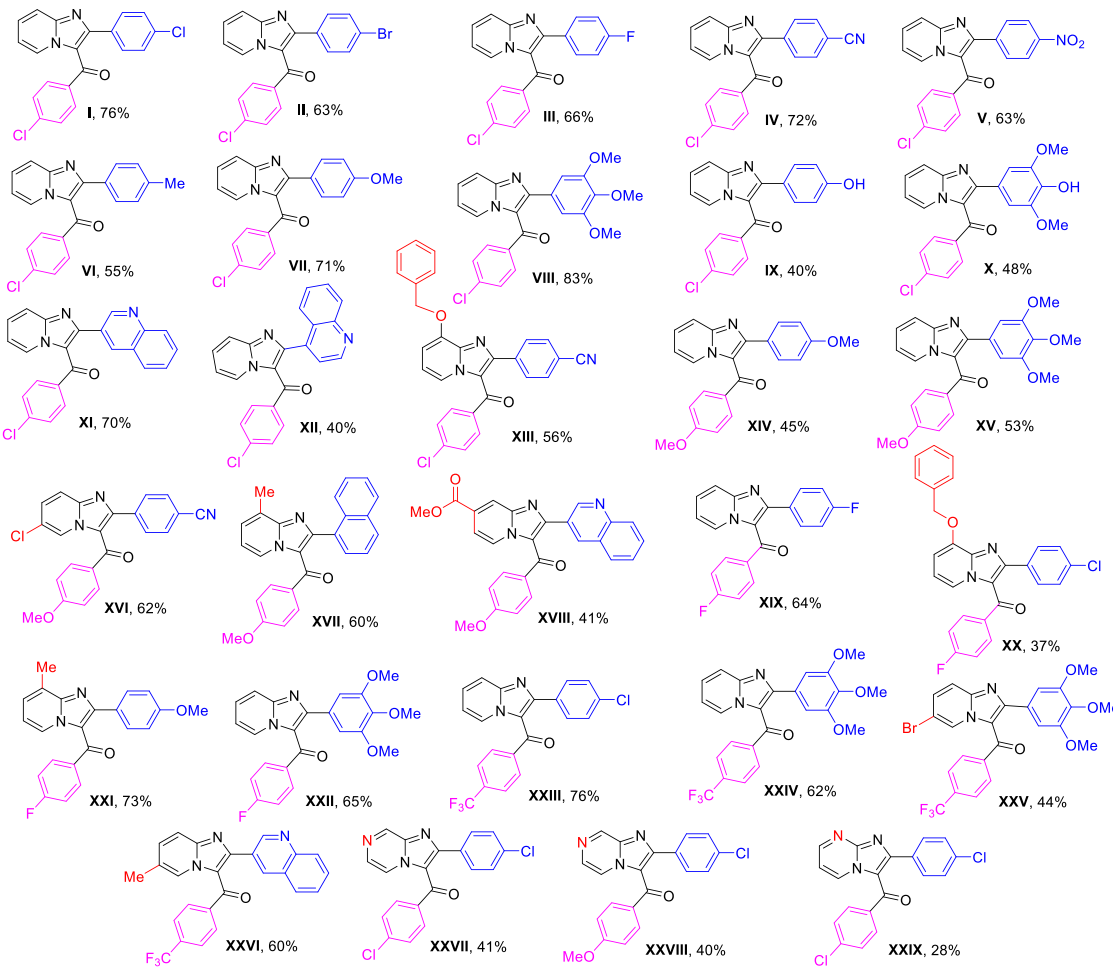
environment, anhydrous aerobic oxygen (with $CaCl_2$ guard tube), and using $K_2S_2O_8$ as an oxidant. However, these oxidative conditions reduced the yield (Table S1). The reaction using DMSO (anhydrous) solvent replacing toluene also resulted in a reduced yield (Table S1). The use of $CuCl_2$, a common oxidant, with increased equivalence (0.1−1 equiv) provided an inferior yield. All of these observations indicate that dimethyl sulfoxide is most effective for dehydrogenative aromatization to the fused imidazole ring, and therefore, sulfoxonium ylide as its source is important for the annulation reaction.

Next, the substrate scope was explored. 2-Aminopyridines, aldehydes, and β-ketosulfoxonium ylides with a variety of electronically varied (withdrawing as well as donating) and diverse substitutions were investigated in the reaction under optimized conditions (Table 3).

Phenacylsulfoxonium ylides with Cl, F, OMe, and CF_3 functionalities on the aromatic ring were examined (**I**–**XXIX**). For all these investigated substrates, the reaction proceeded smoothly and provided imidazo[1,2-*a*]-pyridines in overall good yields. There was no significant electronic effect of substitution motifs. Moreover, the nucleophilic (−OH) as well

Table 3. Substrates Scope: Reactions with a Wide Range of Aldehydes, Azines, and Ylides[a]





[a]Reaction conditions: **1** (1 mmol), **2** (1 mmol), and **3** (1 mmol), in toluene at 80 °C (oil bath); **4** (isolated yields).

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as electrophilic (−CO_2Et, −CN) functional moieties present in the substrates were tolerated in the reaction (**IX**, **XIII**, and **XVIII**). However, the reaction was not feasible for an aliphatic acylsulfoxonium ylide or aliphatic aldehyde. Different classes of heterocyclic-2-amidines, such as 2-aminopyrazine and 2-aminopyrimidine, also proceeded with the reaction smoothly. These enable access to dissimilar classes of N-fused imidazoles, imidazo[1,2-*a*]-pyrazines, and pyrimidines. The compounds that contain amidine functionality, such as benzamidine, guanidine, and bis-guanide, were examined as substrates in place of 2-aminoazine, but they did not undergo the reaction. The conversion of these substrates into imine was found to be nonsignificant. The developed experimental procedure was found to be suitable for the gram-scale (12 mmol) reaction without a significant decrease in yield for product **I** (76% vs 70%).

To gain insight into the mechanistic pathway, we analyzed relevant results obtained in the optimization experiments and also did some studies. Optimized conditions with additional use of transition-metal (Pd, Rh, or Ru) catalysts provided a reduced yield of the products, indicating that the reaction did not undergo the carbenoid pathway. No external oxidant is required. The reaction requires a Brønsted acid, *p*-TSA.

In the course of a reaction to the product (**XII**) under optimized conditions, we isolated an intermediate (**Q**), which is dihydro-imidazo[1,2-*a*]pyridine (Schemes 2 and S1). The GC-MS study of the mixtures withdrawn at different intervals of the progress of three sets of reactions using dissimilar substrates was done. They clearly indicated the formation of dimethyl sulfoxide as well as dimethylsulfide in the course of the reaction. The HRMS study suggested the formation of dihydro-imidazo[1,2-*a*]pyridine intermediate (**P** or its tautomeric form **Q**) and the imine (Scheme S1). The phenacylsulfoxonium ylide is a 1,1-ambiphilic functional motif similar to an *α*-halo-ester-*α*-deprotonated conjugated base that undergoes Darzen glycidic ester condensation with an aldehyde. However, in the present reaction, such condensation did not take place since the *α*,*β*-epoxyketone did not form, according to the HRMS study. Therefore, a pathway that involves the reaction of a ylide with an aldehyde to produce epoxyketone and its subsequent reaction with 2-AP to form intermediate **P** or **Q** is ruled out. For dehydrogenation of intermediate **Q** to the product, five sets of control experiments were done (Table S2). The results indicate that the combined role of $CuCl_2$, DMSO, and TsOH is important. On the basis of all of these results, a plausible mechanism has been proposed (Scheme 2). The sulfoxonium ylide carbon undergoes nucleophilic addition to aldimine. The intramolecular substitution with ring-N's nucleophilic attack at *α*-carbon of sulfonium-carbonyl and removal of dimethyl sulfoxide forms annulated C−N bond. This produces a fused imidazoline ring, intermediate **P**, which tautomerizes to intermediate **Q**. Its dehydrogenative aromatization generates imidazo[1,2-*a*]pyridine (Scheme 2).[26]

The transformation pathway provides a formal [4+1]-annulation with the sulfoxonium ylide functioning as a 1,1-ambiphilic one-carbon synthon as well as a source of an internal oxidant.[27] It complements the process of a transition-metal-catalyzed C−H activation−functionalization-based oxidation. This dual role of the ylide demonstrates an unusual pathway compared to common transition-metal-carbenoid processes.

In conclusion, a method for the construction of the N-fused imidazole motif by a new reaction of sulfoxonium ylides with 2-aminoazines and aldehydes has been developed. The behavior of sulfoxonium ylides as a unique dual-purpose substrate has been explored. It provides the ylidic carbon 1,1-ambiphilic reactivity coupled with the source of an internal oxidant, which promotes a formal pathway alternative to the transition-metal carbenoid-based process of C−H activation−functionalization and the insertion of ylidic carbon. This behavior is important for new investigations. The present method enables access to diverse N-fused imidazoles, which are biologically important heterocycles, from easily available substrates.

EXPERIMENTAL SECTION

General. All reagents (analytical grade) were used as purchased without further purification. An oil bath was used for heating to carry out reactions. Reactions were monitored by TLC, which was performed using 0.2 mm precoated silica gel 60 F_{254} aluminum sheets. Compounds were detected under a UV lamp. Column chromatography was performed using silica gel (100−200 mesh, ASTM). ^{1}H NMR (400 or 500 MHz), ^{13}C NMR (100 or 125 MHz), and ^{19}F NMR (470 MHz) spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Bruker Avance III spectrometer. The chemical shifts have been reported in ppm using TMS/$CFCl_3$ as an internal standard. The multiplicity of the signals has been shown (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) with the coupling constant (*J* value) expressed in hertz (Hz). High-resolution mass spectroscopy (HRMS) spectra were obtained using electrospray ionization (ESI) on time-of-flight (TOF) mass spectrometer XEVO G2-XS QTOF equipment. Melting points were determined on a melting point apparatus.

General Procedure for the Synthesis of N-Fused-Imidazoles (Table 3). In a 25 mL two-necked round-bottom flask, heterocyclic amidine (1 mmol, 1.3 equiv) and aldehyde (1 mmol, 1.3 equiv) were taken. To this were added under argon toluene (anhydrous, 8 mL) and 300 mg of 4 Å molecular sieves. The resulting mixture was refluxed (120 °C, oil bath) and stirred for 2 h. The reaction was allowed to cool down to 25 °C. $CuCl_2$ (10 mol %) and *p*-TSA (10 mol %) were added. The resulting mixture was stirred at 25 °C for 10 min. Sulfoxonium ylide (1 mmol) was added, and the mixture was stirred under argon at 80 °C. The reaction progress was monitored by TLC. After completion of the reaction, the solvent was evaporated, and water and ethyl acetate were added to the resultant slurry. The layers were separated, the aqueous layer was washed with ethyl acetate, and the organic layers were combined. The organic solution was dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and evaporated to dryness. The crude mixture was subjected to normal column chromatography over silica gel (100−200 mesh) using EtOAc−hexanes (3:7) to afford the pure products.

Typical Procedure for the Gram-Scale Preparation of Product I. For the gram-scale preparation of product **I**, the general experimental procedure as described above has been followed with 2-aminopyridine (1.13 g, 12 mmol), 4-chlorobenzaldehyde (1.7 g, 12 mmol), $CuCl_2$ (160 mg, 1.2 mmol, 10 mol %), *p*-TSA (0.2 g, 1.2 mmol, 10 mol %), and ylide (**1**, 2.7 g, 12 mmol). The product **I** was isolated in 3 g, 70% yield.

3-(4-Chlorobenzoyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (I): light yellow solid; 278 mg, 76% yield, mp = 192−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, *J* = 6.9 Hz, 1H), 7.82 (d, *J* = 8.9 Hz, 1H), 7.56 (dd, *J* = 8.0 Hz, 7.6 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.15−7.11 (m, 5H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.6, 153.5, 147.5, 138.4, 136.9, 134.9, 132.3, 131.4, 130.9, 129.6, 128.8, 128.2, 128.2, 119.8, 117.5, 114.9 ppm; HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{13}Cl_2N_2O$ 367.0407, found 367.0406.

3-(4-Chlorobenzoyl)-2-(4-bromophenyl)imidazo[1,2-a]pyridine (II): light yellow solid; 258 mg, 63% yield, mp = 182−185 °C; ^{1}H

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NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 6.9 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.57 (dd, J = 8.0 Hz, 7.8 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.15−7.12 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.6, 153.6, 147.5, 138.5, 136.9, 132.8, 131.6, 131.1, 130.9, 129.6, 128.2, 123.2, 119.8, 117.6, 114.9 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{13}BrClN_2O$ 410.9900, found 410.9901.

*3-(4-Chlorobenzoyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridine (**III**):* brown solid; 210 mg, 66% yield, mp = 162−165 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 9.50 (d, J = 6.8 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.55 (dd, J = 7.5 Hz, 7.9 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.30−7.27 (m, 2H), 7.12−7.08 (m, 3H), 6.84 (t, J = 8.4 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.7, 162.9 (C−F, $^1J_{C-F}$ = 246 Hz), 153.9, 147.5, 138.3, 136.9, 132.0, 131.9, 130.9, 130.0, 130.0, 129.6, 128.2, 128.2, 119.8, 117.5, 115.0 (C−F, $^2J_{C-F}$ = 21.7 Hz), 114.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −112.05 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{13}ClFN_2O$ 351.0700, found 351.0698.

*3-(4-Chlorobenzoyl)-2-(4-cyanophenyl)imidazo[1,2-a]pyridine (**IV**):* light yellow solid; 256 mg, 72% yield, mp = 185−187 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.49 (d, J = 6.9 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.60 (dd, J = 8.2 Hz, 7.5 Hz, 1H), 7.46 (m, 6H), 7.16 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.4, 152.3, 147.6, 138.9, 138.5, 136.7, 131.6, 130.9, 130.7, 129.9, 128.4, 128.2, 120.1, 118.4, 117.8, 115.4, 112.1 ppm. HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{13}ClN_3O$ 358.0747, found 358.0739.

*3-(4-Chlorobenzoyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridine (**V**):* light yellow solid; 236 mg, 63% yield, mp = 230−233 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.49 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.9 Hz, 1H), 7.62 (dd, J = 8 Hz, 7.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H) 7.20−7.14 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.3, 151.7, 147.6, 147.4, 140.4, 139.0, 136.8, 131.0, 130.9, 129.9, 128.4, 128.2, 123.0, 120.3, 117.8, 115.4 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{13}ClN_3O_3$ 378.0645, found 378.0642.

*3-(4-Chlorobenzoyl)-2-(p-tolyl)imidazo[1,2-a]pyridine (**VI**):* light yellow solid; 190 mg, 55% yield, mp = 167−169 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.54 (dd, J = 7.9 Hz, 7.8 Hz, 1H), 7.45 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.12−7.07 (m, 3H), 6.95 (d, J = 7.8 Hz, 2H), 2.30 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.9, 155.3, 147.5, 138.7, 137.9, 137.1, 130.9, 130.8, 130.1, 129.4, 128.6, 128.2, 128.0, 119.7, 117.4, 114.6, 21.2 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{16}ClN_2O$ 347.0951, found 347.0956.

*3-(4-Chlorobenzoyl)-2-(4-methoxyphenyl)imidazo[1,2-a]-pyridine (**VII**):* light yellow solid; 256 mg, 71% yield, mp = 101−103 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.55 (dd, J = 7.4 Hz, 7.8 Hz 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.7 Hz, 3H), 7.12−7.09 (m, 2H), 6.68 (d, J = 8.7 Hz, 2H), 3.56 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.9, 160.1, 137.8, 137.1, 131.6, 130.9, 129.4, 128.3, 128.0, 126.1, 117.3, 114.6, 113.5, 55.4 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{16}ClN_2O_2$ 363.0900, found 363.0908.

*3-(4-Chlorobenzoyl)-2-(3,4,5-trimethoxyphenyl)imidazo[1,2-a]-pyridine (**VIII**):* white solid; 350 mg, 83% yield, mp = 128−130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.57 (d, J = 7.0 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.59 (ddd, J = 1.2 Hz, 8.3 Hz, 8.8 Hz, 1H), 7.51 (d, J = 8.5 Hz, 2H), 7.22−7.07 (m, 3H), 6.59 (s, 2H), 3.81 (s, 3H), 3.72 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.6, 154.9, 152.8, 147.4, 138.9, 138.2, 137.4, 130.7, 129.6, 129.2, 128.3, 128.0, 119.7, 117.4, 114.9, 107.8, 61.1, 56.0 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{23}H_{20}ClN_2O_4$ 423.1112, found 423.1115.

*3-(4-Chlorobenzoyl)-2-(4-hydroxyphenyl)imidazo[1,2-a]pyridine (**IX**):* light yellow solid; 140 mg, 40% yield, mp = 191−192 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, J = 5.9 Hz, 1H), 7.80 (d, J = 8.6 Hz, 1H), 7.58 (dd, 7.6 Hz, 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.13 (s, 5H), 6.55 (d, J = 7.0 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.0, 157.6, 154.6, 147.2, 138.0, 136.9, 131.7, 131.0, 129.9, 128.3, 128.1, 124.5, 119.4, 116.8, 115.3, 114.9 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{14}ClN_2O_2$ 349.0744, found 349.0737.

*3-(4-Chlorobenzoyl)-2-(4-hydroxy-3,5-dimethoxyphenyl)-imidazo[1,2-a]pyridine (**X**):* yellow solid; 194 mg, 48% yield, mp > 200 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 5.0 Hz, 1H), 7.82 (d, J = 7.2 Hz, 1H), 7.56 (d, J = 7.8 Hz, 3H), 7.17 (d, J = 8.1 Hz, 2H), 7.11 (dd, J = 6.7 Hz, 6.6 Hz, 1H), 6.65 (s, 2H), 3.73 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.6, 154.6, 147.4, 146.7, 138.4, 137.3, 135.7, 130.9, 129.5, 128.2, 124.7, 119.4, 117.3, 114.7, 107.6, 97.9, 56.2 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{18}ClN_2O_4$ 409.0955, found 409.0956.

*3-(4-Chlorobenzoyl)-2-(quinolin-3-yl)imidazo[1,2-a]pyridine (**XI**):* light yellow solid; 268 mg, 70% yield, mp = 186−189 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.60 (d, J = 6.8 Hz, 1H), 8.80 (s, 1H), 8.24 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.9 Hz, 1H), 7.76−7.69 (m, 2H), 7.64 (dd, J = 8 Hz, 7.8 Hz, 1H), 7.56 (dd, J = 7.5 Hz, 7.4 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.20 (dd, J = 6.8 Hz, 6.9 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.6, 150.8, 147.9, 147.2, 138.5, 137.0, 136.7, 130.8, 130.3, 129.9, 129.1, 128.4, 128.4, 127.9, 127.1, 127.0, 120.5, 117.6, 115.2 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{23}H_{15}ClN_3O$ 384.0904, found 384.0901.

*3-(4-Chlorobenzoyl)-2-(quinolin-4-yl)imidazo[1,2-a]pyridine (**XII**):* faint white solid; 153 mg, 40% yield, mp = 178−179 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.33 (d, J = 6.8 Hz, 1H), 8.41 (d, J = 4.3 Hz, 1H), 7.76 (d, J = 8.9 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.57 (dd, J = 7.9, 7.5 Hz 1H), 7.51 (dd, J = 7.4, 7.3 Hz, 1H), 7.32 (dd, J = 8.3, 7.4 Hz, 1H), 7.20 (dd, J = 6.8, 6.7 Hz, 1H), 7.08 (d, J = 4.3 Hz, 1H), 6.99 (d, J = 8.2 Hz, 2H), 6.55 (d, J = 8.2 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 190.1, 155.6, 154.2, 152.5, 152.3, 145.2, 142.6, 141.1, 135.7, 135.0, 134.6, 134.1, 133.5, 132.2, 132.1, 131.3, 130.9, 128.7, 126.9, 122.6, 121.0 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{23}H_{15}ClN_3O$ 384.0904, found 384.0910.

*8-(Benzyloxy)-3-(4-chlorobenzoyl)-2-(4-cyanophenyl)imidazo-[1,2-a]pyridine (**XIII**):* brown solid; 253 mg, 56% yield, mp = 206−208 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, J = 6.8 Hz, 1H), 7.53−7.50 (m, 4H), 7.47−7.34 (m, 7H), 7.14 (d, J = 8.4 Hz, 2H), 6.97 (dd, J = 7.6, 7.0 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 5.46 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.5, 151.2, 147.8, 141.9, 138.9, 138.4, 136.6, 135.6, 131.4, 130.9, 128.8, 128.3, 127.2, 121.0, 120.7, 118.4, 115.1, 111.9, 108.3, 71.1 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{28}H_{19}ClN_3O_2$ 464.1166, found 464.1161.

*3-(4-Methoxybenzoyl)-2-(4-methoxyphenyl)imidazo[1,2-a]-pyridine (**XIV**):* brown solid; 161 mg, 45% yield, mp = 198−200 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 6.8 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 7.4 Hz, 2H), 7.47 (dd, J = 7.8, 7.8, 1H), 7.33 (d, J = 7.8 Hz, 2H), 7.03 (dd, J = 6.8, 6.8 Hz, 1H), 6.67 (d, J = 7.9 Hz, 2H), 6.64 (d, J = 7.5 Hz, 2H), 3.75 (s, 3H), 3.74 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.2, 162.5, 159 6, 153.4, 147.1, 131.9, 131.5, 131.1, 128.6, 127.9, 126.4, 119.6, 117.1, 114.0, 113.4, 113. 2, 55.3, 55.2 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3$ 359.1396, found 359.1384.

*3-(4-Methoxybenzoyl)-2-(3,4,5-trimethoxyphenyl)imidazo[1,2-a]pyridine (**XV**):* off-white solid; 221 mg, 53% yield, mp = 125−127 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.41 (d, J = 6.9 Hz, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.51 (ddd, J = 6.9, 6.8, 1.1, 1H), 7.08 (ddd, J = 6.9, 6.9, 1.0 Hz, 1H), 6.69−6.67 (m, 4H), 3.79 (s, 3H), 3.77 (s, 3H), 3.70 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.9, 162.9, 153.4, 152.7, 147.0, 138.3, 131.8, 131.3, 129.3, 128.8, 128.0, 119.8, 117.2, 114.3, 113.2, 107.6, 60.8, 55.9, 55.4 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{24}H_{23}N_2O_5$ 419.1607, found 419.1604.

*6-Chloro-3-(4-methoxybenzoyl)-2-(4-cyanophenyl)imidazo[1,2-a]pyridine (**XVI**):* light yellow solid; 238 mg, 62% yield, mp = 198−200 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.74 (d, J = 9.4 Hz, 1H), 7.54−7.44 (m, 7H), 6.65 (d, J = 8.56, 2H), 3.79 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.4, 163.5, 151.0, 145.5, 138.3, 132.0, 131.6, 130.6, 130.4, 130.2, 125.9, 123.2, 120.6, 118.5,

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117.9, 113.5, 111.9, 55.5 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{15}ClN_3O_2$ 388.0853, found 388.0849.

*8-Methyl-3-(4-Methoxybenzoyl)-2-(naphthalen-1-yl)imidazo-[1,2-a]pyridine (**XVII**):* faint white solid; 235 mg, 60% yield, mp = 177−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (d, J = 6.8 Hz, 1H), 8.08−8.06 (m, 1H), 7.74−7.72 (m, 1H), 7.65 (d, J = 8.1, 1H), 7.46−7.41(m, 2H), 7.37 (d, J = 6.9 Hz, 1H), 7.30 (dd, J = 7.0, 1.1 Hz, 1H), 7.28−7.19 (m, 3H), 7.06 (dd, J = 6.9, 6.9 Hz, 1H), 6.18 (d, J = 8.8 Hz, 2H), 3.58 (s, 3H), 2.77 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 186.5, 161.9, 152.7, 147.6, 133.4, 132.2, 132.1, 131.5, 130.6, 129.7, 128.6, 127.9, 127.8, 127.5, 126.3, 126.0, 125.7, 125.6, 124.7, 122.5, 114.5, 112.2, 55.1, 17.2 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_2$ 393.1603, found 393.1598.

*7-Methyl-carboxylate-3-(4-methoxybenzoyl)-2-(quinolin-3-yl)-imidazo[1,2-a]pyridine (**XVIII**):* yellow solid; 178 mg, 41% yield, mp = 180−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 7.2 Hz, 1H), 8.89 (d, J = 2.0 Hz, 1H), 8.53 (s, 1H), 8.31 (d, J = 1.7 Hz, 1H), 8.02 (d, J = 8.8 Hz, 1H), 7.72−7.65 (m, 3H), 7.61 (d, J = 8.8 Hz, 2H), 7.52 (dd, J = 7.5 Hz, 6.9 Hz, 1H), 6.55 (d, J = 8.8 Hz, 2H), 4.04 (s, 3H), 3.57 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.8, 164.9, 163.4, 150.9, 150.8, 147.2, 146.5, 136.9, 132.1, 130.2, 130.1, 130.0, 129.1, 128.1, 127.6, 127.2, 126.9, 126.8, 121.5, 119.7, 113.7, 113.6, 55.3, 52.9 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{20}N_3O_4$ 438.1454, found 438.1458.

*3-(4-Fluorobenzoyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridine (**XIX**):* light yellow solid; 213 mg, 64% yield, mp = 116−119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.47(d, J = 6.9 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.55−7.50 (m, 3H), 7.31−7.28 (m, 2H), 7.11−7.08 (m, 1H), 6.84−6.78 (m, 4H), ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.5, 164.9 (C−F, $^1J_{C-F}$ = 252 Hz), 162.8 (C−F, $^1J_{C-F}$ = 248 Hz), 153.6, 147.4, 134.8 (C−F, $^4J_{C-F}$ = 3 Hz), 132.0 (C−F, $^3J_{C-F}$ = 9 Hz), 131.9 (d, C−F, $^3J_{C-F}$ = 8 Hz), 130.0 (C−F, $^4J_{C-F}$ = 3 Hz), 129.4, 128.2, 119.7, 117.4, 115.0 (d, C−F, $^2J_{C-F}$ = 22 Hz), 115.0 (C−F, $^2J_{C-F}$ = 22 Hz), 114.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −105.84, −112.32 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{13}F_2N_2O$ 335.0996, found 335.0995.

*8-(Benzyloxy)-3-(4-fluorobenzoyl)-2-(4-chlorophenyl)imidazo-[1,2-a]pyridine (**XX**):* light yellow solid; 166 mg, 37% yield, mp = 196−198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, J = 6.8 Hz, 1H), 7.58−7.52 (m, 4H), 7.41 (dd, J = 7.0 Hz, 7.5 Hz, 2H), 7.37−7.33 (m, 3H), 7.13 (d, J = 8.4 Hz, 2H), 6.93 (dd, J = 7.5 Hz, 7.2 Hz, 1H), 6.87−6.82 (m, 3H), 5.48 (s, 2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.7, 165.0 (C−F, $^1J_{C-F}$ = 253 Hz), 152.2, 147.6, 141.8, 135.8, 134.7, 134.6, 132.4, 132.1, 132.0, 131.6, 128.8, 128.3, 128.0, 127.2, 120.8, 120.7, 115.1 (C−F, $^2J_{C-F}$ = 21.1 Hz), 114.6, 108.1, 71.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −105.94 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{19}ClFN_2O_2$ 457.1119, found 457.1113.

*8-Methyl-3-(4-fluorobenzoyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (**XXI**):* light yellow solid; 262 mg, 73% yield, mp = 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (d, J = 6.8 Hz, 1H), 7.56−7.52 (m, 2H), 7.34−7.27 (m, 3H), 7.00 (dd, J = 6.9, 6.9, 1H), 6.81 (dd, J = 8.6, 8.6 Hz, 2H), 6.67 (d, J = 8.7 Hz, 2H), 3.76 (s, 3H), 2.74 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.8, 164.6 (C−F, $^1J_{C-F}$ = 252 Hz), 159 8, 154.3, 147.3, 135.1 (C−F, $^4J_{C-F}$ = 3 Hz), 132.0 (C−F, $^3J_{C-F}$ = 9 Hz), 131.6, 128.1, 127.3, 126.5, 125.8, 120.0, 114.8 (C−F, $^2J_{C-F}$ = 22 Hz), 114.5, 113.4, 55.3, 17.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −112.30 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{18}FN_2O_2$ 361.1352, found 361.1350.

*3-(4-Fluorobenzoyl)-2-(3,4,5-trimethoxyphenyl)imidazo[1,2-a]-pyridine (**XXII**):* faint white, solid; 263 mg, 65% yield, mp = 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (d, J = 6.8 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.62−7.54 (m, 3H), 7.12 (dd, J = 6.8, 5.9, 1H), 6.85 (dd, J = 8.6, 8.4 Hz, 2H), 6.59 (s, 2H), 3.78 (s, 3H), 2.71 (s, 6H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.5, 164.8 (C−F, $^1J_{C-F}$ = 252 Hz), 154.5, 152.8, 147.3, 138.7, 135.1 (C−F, $^4J_{C-F}$ = 3 Hz), 131.8 (C−F, $^3J_{C-F}$ = 9 Hz), 129.4, 129.2, 128.2 119.7, 117.4, 114.9 (C−F, $^2J_{C-F}$ = 22 Hz), 114.7, 107.7, 60.9, 56.0 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −106.34 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{23}H_{20}FN_2O_4$ 407.1407, found 407.1413.

*3-(4-Trifluoromethylbenzoyl)-2-(4-chlorophenyl)imidazo[1,2-a]-pyridine (**XXIII**):* white solid; 304 mg, 76% yield, mp = 175−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (d, J = 6.9 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.63 (ddd, J = 1.2 Hz, 8.3 Hz, 8.8 Hz, 1H), 7.56 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.22−7.18 (m, 3H), 7.09−7.07 (m, 2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.6, 154.7, 147.7, 141.8, 135.0, 132.9, 132.2, 131.3, 130.1, 129.6, 128.5, 128.0, 124.8 (C−F, $^3J_{C-F}$ = 3.73 Hz), 120.0, 117.6, 115.3 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.01 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{13}ClF_3N_2O$ 401.0669, found 401.0667.

*3-(4-Trifluoromethylbenzoyl)-2-(3,4,5-trimethoxyphenyl)-imidazo[1,2-a]pyridine (**XXIV**):* light yellow solid; 282 mg, 62% yield, mp = 108−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, J = 6.9 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.66−7.59 (m, 3H), 7.44 (d, J = 8.2 Hz, 2H), 7.17(ddd, J = 6.9, 6.9, 1.8 Hz, 1H), 6.54(s, 2H), 3.74 (s, 3H), 3.68 (s, 6H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.3, 155.5, 152.7, 147.6, 142.1, 138.8, 133.1 (C−F, $^2J_{C-F}$ = 32 Hz), 130.0, 129.8, 129.5, 128.4, 124.6 (C−F, $^3J_{C-F}$ = 3 Hz) 124.4 (C−F, $^1J_{C-F}$ = 271 Hz) 122.0, 119.6, 117.4, 115.1, 107.7, 60.7, 56.0 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.01 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{24}H_{20}F_3N_2O_4$ 457.1375, found 457.1379.

*6-Bromo-3-(4-trifluoromethylbenzoyl)-2-(3,4,5-trimethoxyphenyl)imidazo[1,2-a]pyridine (**XXV**):* yellow solid; 234 mg, 44% yield, mp = 162−164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.73 (d, J = 9.36 Hz, 1H), 7.69−7.64 (m, 3H), 7.46 (d, J = 8.0 Hz, 2H), 6.52 (s, 2H), 3.75 (s, 3H), 3.68 (s, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 185.4, 155.5, 152.9, 146.0, 141.7, 139.2, 133.6, 133.3, 133.2, 129.6, 128.5, 124.7 (C−F, $^3J_{C-F}$ = 3.57 Hz), 122.0, 119.8, 118.0, 109.9, 107.8, 60.8, 56.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.01 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{24}H_{19}BrF_3N_2O_4$ 535.0480, found 535.0481.

*6-Methyl-3-(4-trifluoromethylbenzoyl)-2-(quinolin-3-yl)imidazo-[1,2-a]pyridine (**XXVI**):* light yellow solid; 260 mg, 60% yield, mp = 179−181 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.73 (s, 1H), 8.03 (s, 1H), 7.95 (d, J = 10 Hz, 1H), 7.76 (s, 1H), 7.67 (dd, J = 10, 5 Hz, 1H), 7.57 (d, J = 5 Hz, 1H), 7.52 (d, J = 5 Hz, 2H), 7.47 (dd, J = 10, 5 Hz, 2H), 7.18 (d, J = 10 Hz, 2H), 2.47 (s, 3H) ppm ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 185.5, 150.5, 147.2, 141.8, 136.9, 133.2, 130.3, 132.8, 130.3, 129.5 (C−F, $^2J_{C-F}$ = 48 Hz), 127.7, 127.1, 126.6, 125.8, 124.9 (C−F, $^3J_{C-F}$ = 2.97 Hz), 124.2 (C−F, $^1J_{C-F}$ = 271 Hz), 122.0, 116.9, 18.6 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.49 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{25}H_{17}F_3N_3O$ 432.1324, found 432.1321.

*3-(4-Chlorobenzoyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyrazine (**XXVII**):* brown solid; 150 mg, 41% yield, mp = 152−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 9.19 (d, J = 4.4 Hz, 1H), 8.22 (d, J = 4.5 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 4H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.9, 152.9, 143.9, 141.5, 139.5, 135.7, 135.6, 132.3, 131.4, 131.3, 130.9, 128.6, 128.5, 120.1 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{19}H_{12}Cl_2N_3O$ 368.0357, found 368.0351.

*3-(4-Methoxybenzoyl)-2-(4-chlorophenyl)imidazo[1,2-a]-pyrazine (**XXVIII**):* brown solid; 145 mg, 40% yield, mp = 192−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 9.95 (d, J = 4.4 Hz, 1H), 8.18 (d, J = 4.6 Hz, 1H), 7.57 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.7, 163.6, 150.6, 143.3, 141.1, 133.9, 132.5, 132.4, 131.9, 131.8, 130.1, 128.5, 120.66, 120.60, 114.0, 56.0, ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{15}ClN_3O_2$ 364.0853, found 364.0850.

*3-(4-Chlorobenzoyl)-2-(4-Chlorophenyl)imidazo[1,2-a]-pyrimidine (**XXIX**):* faint white solid; 103 mg, 28% yield, mp = 157−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 1.8 Hz, 1H), 8.41−8.36 (m, 3H), 7.57 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.4, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.00−6.98 (m, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 187.7, 152.3, 146.6, 140.4, 139.5, 136.0, 135.4, 132.6, 131.8, 131.7, 129.5, 128.5, 126.6, 125.5, 110.3 ppm; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{19}H_{12}Cl_2N_3O$ 368.0357, found 368.0363.

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■ ASSOCIATED CONTENT

Supporting Information

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Additional experiments and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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