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Diverse Oxidative C(sp²)-N Bond Cleavages of Aromatic Fused Imidazoles for Synthesis of α-Ketoamides and *N*-(pyridin-2-yl)arylamides

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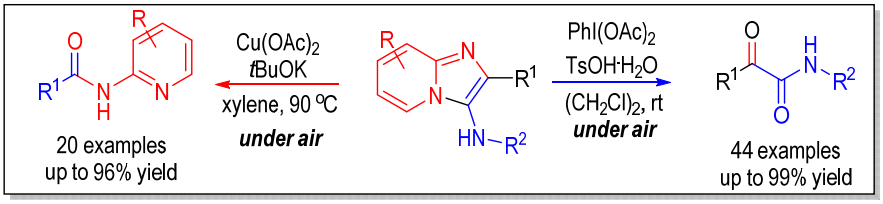
Supporting Information



ABSTRACT: An efficient and chemoselective C(sp²)-N bond cleavage of aromatic imidazo[1,2-a]pyridine molecules is developed. A broad scope of amide compounds such as α-ketoamides and *N*-(pyridin-2-yl)arylamides are afforded as the final products in up to quantitative yields. Diverse C-N bond cleavages are controlled by the oxidative species used in this transformation, with various amide products afforded in chemoselective fashion. Preliminary study indicated that some of α-ketoamides exhibit anti-Tobacco Mosaic Virus (TMV) activity for potential use in plant protection.

KEYWORDS: *aromatic C(sp²)-N bond cleavage, oxidant-based, chemo-selective, inert bond activation, amide*

■ INTRODUCTION

Amides are one class of the fundamental structural units in life science. A vast majority of natural products and bio-active molecules contain amide moieties.[1] Especially, *N*-(pyridin-2-yl)arylamides[2] and α-ketoamides[3] are among the ubiquitous structures that are widely found in medicinal and bio-active compounds (Figure 1). They could not only serve as promising human drug candidates but also as versatile starting materials in various synthetic transformations.[4] To date, numerous methodologies have been developed for the preparation of α-ketoamides and *N*-(pyridin-2-yl)arylamides from various substrates.[5] A variety of functional molecules, such as carboxylic acids,[5d] nitriles,[5e] halides,[5f, 5g] alkynes,[5h] alkenes,[5i] aldehydes,[5j] and ketones,[5k] could be used as the amide precursors. However, most of these protocols have suffered from limitations in low chemical yields or the harsh reaction conditions needed. Therefore, the development of novel methodologies for efficient synthesis of α-ketoamide and *N*-(pyridin-2-yl)arylamide derivatives under mild reaction conditions is still of great interest.

Bond cleavage has attracted considerable attentions due to their significant applications in organic synthesis.[4d,5c,6] Especially, the development of novel synthetic methods for the construction of various functional molecules via inert C(sp²)-N bond cleavage processes has received much interest.[6c, 6d-f] For example, Larock and co-workers have disclosed that the C(sp²)-N bond of an electron-deficient amide substrate could be cleaved and react with benzyne intermediate under basic conditions to afford aromatic amine products (Figure 2a, eq 1).[6f] Kakiuchi and co-workers have reported that the C(sp²)-N

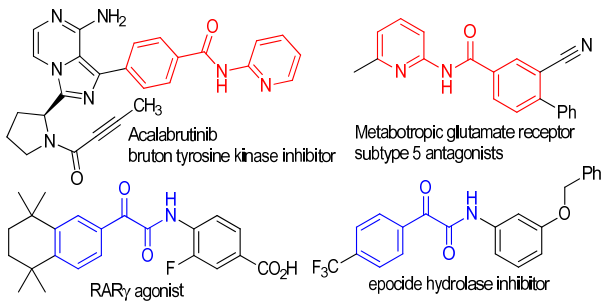


Figure 1. Bio-active *N*-(pyridin-2-yl)arylamides and α-Ketoamides.

bond of an aromatic amine molecule could be cleaved by Ru-complex catalysts and take part in the cross-coupling reactions with aryl borane substrates (Figure 2a, eq 2).[6c] The C(sp²)-N bonds of the foramide molecules could also be broken up by various catalysts under oxidative conditions and serve as the amine sources in the synthesis of various amino-group-containing functional molecules (Figure 2a, eq 3, 4 & 5).[5l,6d,6e]

In 2015, Wang *et al*. reported the ring opening of imidazopyridine via cleavage of C–C and C(sp^2)-N bonds to afford *N*-(pyridin-2-yl)benzamides using TBHP as oxidant (Figure 2a, eq 6).[7] Herein, we report an oxidant-based diverse aromatic C(sp^2)-N bond cleavages of imidazo[1,2-a]pyridine compounds for the efficient preparation of α-ketoamides and *N*-(pyridin-2-yl)arylamides under mild aerobic conditions (Figure 2b).

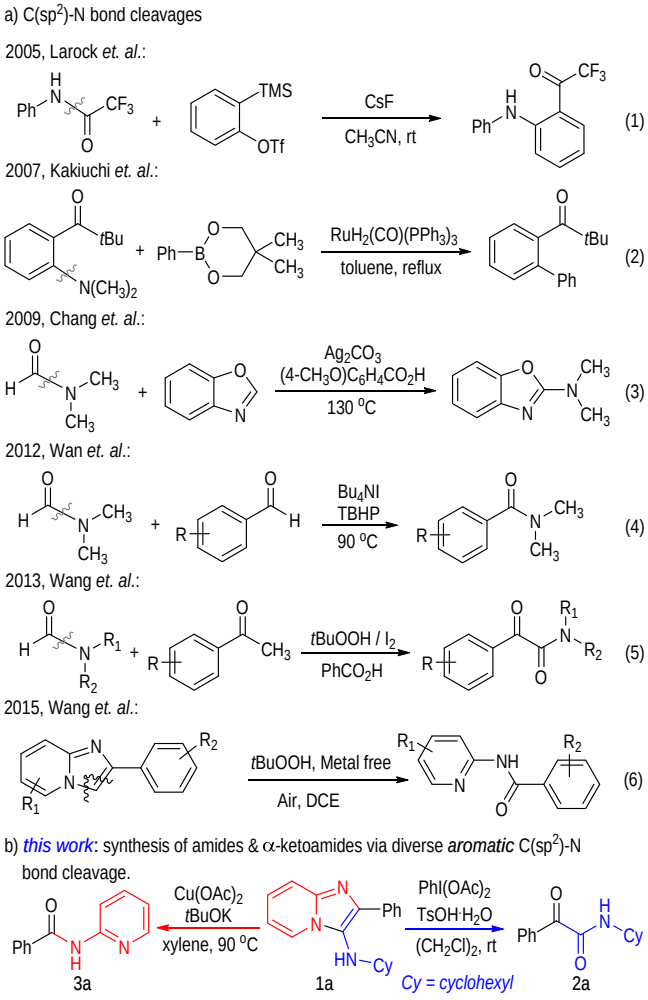
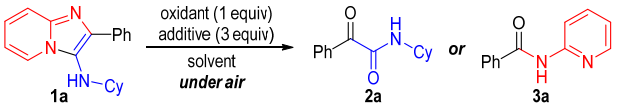


Figure 2. Construction of Functional Molecules via C(sp^2)-N Bond Cleavages.

■ RESULTS AND DISCUSSION

Various common oxidants were first tested for the aromatic C(sp^2)-N bond cleavage reactions of the imidazo[1,2-a]pyridine substrate **1a** at room temperature (Table 1, for more details, see supporting information). Hydroperoxide (Table 1, entry 1), manganese dioxide (entry 2) and iodobenzene diacetate (entry 3) could exclusively give the α-ketoamide **2a** as the oxidizing product in promising yields, while the copper diacetate gave trace amount of *N*-(pyridin-2-yl)benzamide **3a** as the only oxidizing product (entry 4), but while the acidic additives was added, a small amount of **2a** was given (entry 5). Acidic additives were found to significantly improve the yields of **2a** with iodobenzene diacetate used as the external oxidant (e.g., entries 6 to 7). Notably, the product **2a** could be afforded in almost quantitive yield with the assistance of TsOH·H_2O and iodobenzene diacetate (entry 6). Solvents other than dichloroethane generally gave the product **2a** in lower yields (e.g., entries 8 to 9). After that the reaction condition for the formation of *N*-(pyridin-2-yl)benzamide **3a** was also investigated with copper(II) salts used as the catalyst under aerobic atmosphere at a higher temperature in *o*-xylene (entries 10 to 11). Copper(II) diacetate was identified as the most efficient catalyst for this chemoselective C(sp^2)-N bond cleavage (entry 11). The yield of **3a** could be dramatically increased with the help of a variety of inorganic basic additives (entries 12 to 13). Organic bases such as DBU could not facilitate the product formation (entry 14). Finally, the *N*-(pyridin-2-yl)benzamide product **3a** could also be afforded in excellent yield with copper(II) diacetate used as the reaction catalyst and *t*BuOK as the additive at 90 °C in *m*-xylene under aerobic conditions (entry 15).

Table 1. Optimization of reaction conditions [a]



entry	oxidant / catalyst	additive	solvent	yield [%] [b] 2a	3a
1	H_2O_2	-	$(CH_2Cl)_2$	12	0
2	MnO_2	-	$(CH_2Cl)_2$	15	0
3	$PhI(OAc)_2$	-	$(CH_2Cl)_2$	41	0
4	$Cu(OAc)_2$	-	$(CH_2Cl)_2$	0	< 5
5	$Cu(OAc)_2$	TsOH·H_2O	$(CH_2Cl)_2$	23	0
6	$PhI(OAc)_2$	TsOH·H_2O	$(CH_2Cl)_2$	99	0
7	$PhI(OAc)_2$	TsOH·H_2O	THF	82	0
8	$PhI(OAc)_2$	TsOH·H_2O	CH_3OH	22	0
9	$PhI(OAc)_2$	CF_3CO_2H	$(CH_2Cl)_2$	73	0
10[c]	$Cu(OAc)_2$	-	*o*-xylene	0	22
11[c]	$CuCl_2$	-	*o*-xylene	0	17
12[c]	$Cu(OAc)_2$	K_2CO_3	*o*-xylene	0	39
13[c]	$Cu(OAc)_2$	*t*BuOK	*o*-xylene	0	85
14[c]	$Cu(OAc)_2$	DBU	*o*-xylene	0	0
15[d]	$Cu(OAc)_2$	*t*BuOK	*m*-xylene	0	96

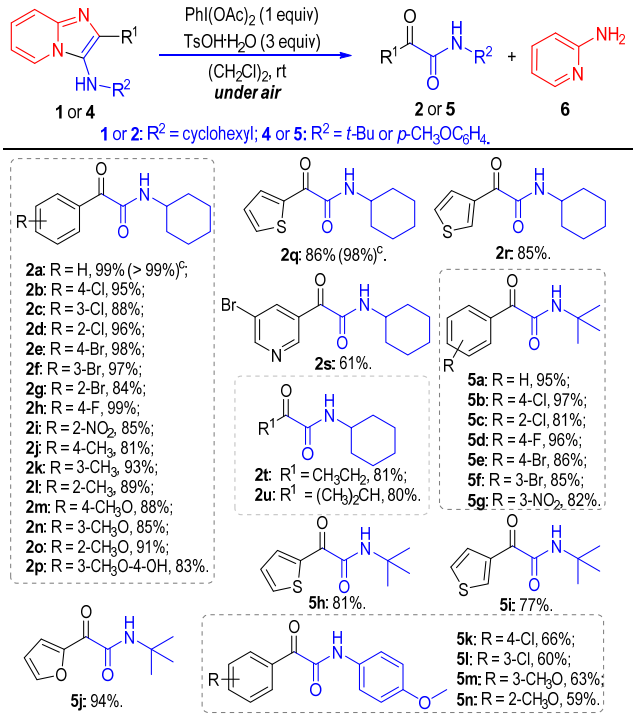
[a]Reaction conditions: **1a** (0.17 mmol), oxidant (0.17 mmol), TsOH·H_2O (0.51 mmol), solvent (2.5 mL), RT, 1 h. [b]Isolated yield. [c]Reaction conditions: **1a** (0.17 mmol), catalysis(0.17 mmol), base (0.51mmol), solvent (3 mL), 120 °C, 1 h. [d]**1a** (0.17 mmol), Cu(II) salt (0.017 mmol), base (0.51 mmol), *m*-xylene (3 mL), 90 °C, 8h. Cy = cyclohexyl.

With the optimized reaction conditions in hand, we next examined the reaction scopes for the diverse chemoselective aromatic C(sp^2)-N bond cleavages in the preparations of both α-ketoamides **2** and *N*-(pyridin-2-yl)arylamide **3** (Table 2 to 4).

Substituents on the benzene group of the substrate **1a** were first tested for the preparation of the α-ketoamides **2** (Table 2, **2a** to **2p**). Both electron-donating and electron-withdrawing groups were well tolerated, with all the products afforded in good to excellent yields. The substituted benzene group on substrate **1** could also be switched to various heteroaromatic groups with little erosion of the product yields (**2q** to **2s**). It is worth noting that the aromatic R^1 group could even be replaced

with various alkyl groups without obvious influence on the product formation (**2t** & **2u**). The *N*-cyclohexyl groups (R^2) on substrate **1** could be switched to other alkyl groups and the corresponding products could also be afforded in good to excellent yields (**5a** to **5j**). Notably, an *N*-aryl substituent could also be used as the R^2 group, although the corresponding products could only be afforded in moderate yields under the current optimized reaction conditions (**5k** to **5n**). We randomly investigated the grams-scale reactions for the synthesis of α-ketoamides, and the products were afforded in even better yields through this protocol (e.g., **2a** & **2q**). Note that, pyridin-2-amine **6**, a key starting material for the synthesis of substrate **1**,[8] was isolated in all the above cases as the major by-product.

Table 2. Scope for the Synthesis of α-Ketoamide 2[a]



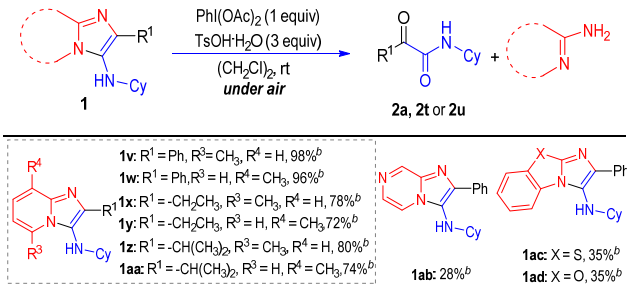
[a]Reaction conditions: 1 (0.17 mmol), oxidant (0.17 mmol), TsOH·H_2O (0.51 mmol), $(CH_2Cl)_2$ (2.5 mL), RT, 1 h. [b]Isolated yield. [c]Yields in parentheses represent the yields of the reactions carried out at 3.4 mmol scale.

Substituents could also be installed on the pyridine moiety of the imidazo[1,2-a]pyridine substrate **1a**, with the excellent yields of the α-ketoamide product **2a** remained (Table 3, **1v** & **1w**). α-Ketoamide products **2t** and **2u** can also been obtained in good yields (**1x**, **1y**, **1z**, **1aa**) when employed alkyl groups on substrate **1**. Interestingly, the pyridine moiety of the fused cyclic **1a** could even be switched to various heteroaromatic structures, although the target products of **2a** could only be afforded in low yields at this moment (**1ab**, **1ac**, **1ad**).

A broad scope of (pyridin-2-yl)arylamides **3** could also be prepared from substituted imidazo[1,2-a]pyridine substrate **1** with the catalysis of $Cu(OAc)_2$ under basic conditions (Table 3). Benzoyl groups with various substituents and substitution types were well tolerated in this transformation and the substituted *N*-(pyridin-2-yl)benzamide products could be formed in moderate to excellent yields (Table 4, **3a** to **3i**). The benzene rings of the benzoyl groups on substrates **1** could also be replaced with a variety of heteroaromatic groups, with the corresponding *N*-(pyridin-2-yl)aryamide products afforded in moderate to good yields (**3j** to **3m**). Moreover, the alkyl group on substrates **1** (R^1 was ethyl) can also give moderate yields of the *N*-(pyridin-2-yl)propionamide (**3n**). As a technical note, the (pyridin-2-yl)arylamide substrates **1** bearing *N*-cyclohexyl groups could facilitate the product formation better than those bearing *N*-*t*Bu groups in this chemoselective C(sp^2)-N bond cleavage reaction.

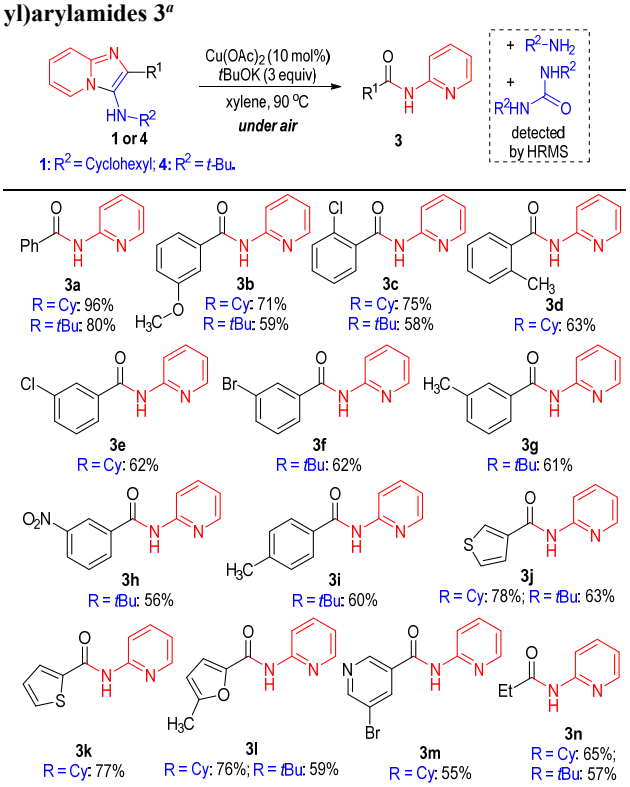
To check the potential mechanism of the reaction, a series of control experiments for α-ketoamide was conducted (**Scheme 1**). We found no reaction occurred in absence of bothiodobenzene diacetate (eq. **1**) and H_2O (eq. **2**), we speculated H_2O might play a pivotal role in formation of α-ketoamide, which may be the source of "O". In order to confirm

Table 3. Scope of Precursors of the α-Ketoamide 2a[a]



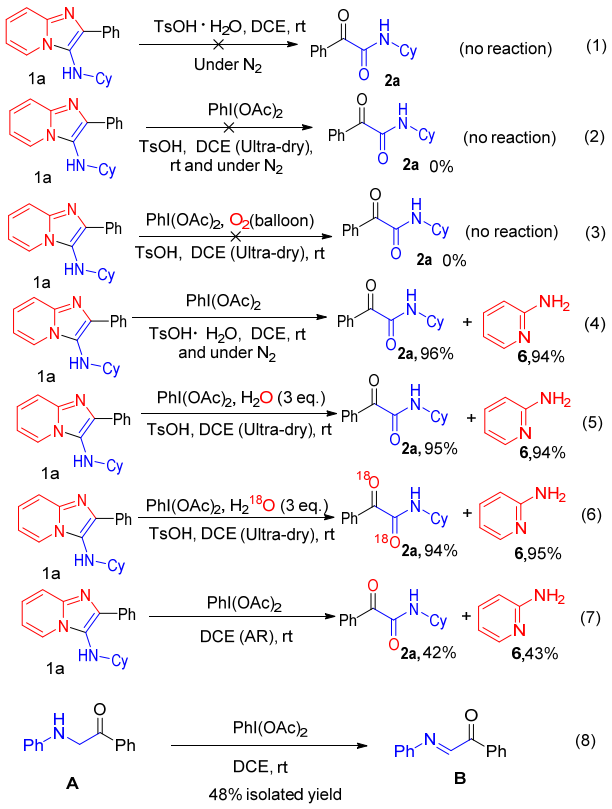
[a]Reaction conditions: **1** (0.17 mmol), oxidant (0.17 mmol), TsOH·H_2O (0.51 mmol), $(CH_2Cl)_2$ (2.5 mL), RT, 1 h. [b]Isolated yield. Cy = cyclohexyl. *t*Bu = *tert*-butyl.

Table 4. Reaction Scope for the Synthesis of (Pyridin-2-yl)arylamides 3[a]



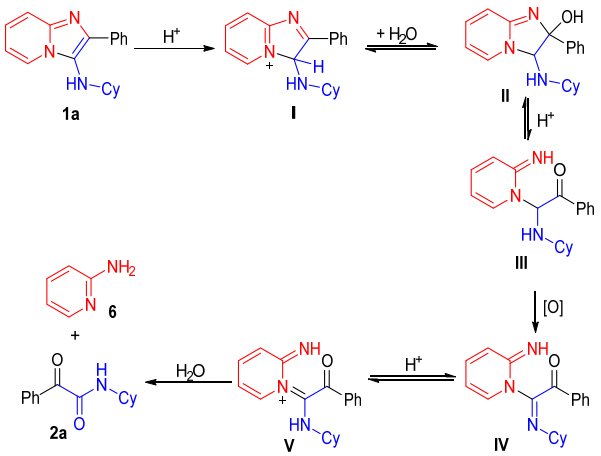
[a]Reaction conditions: **1** (0.17 mmol), Cu(II) salt (0.017 mmol), base (0.51 mmol), m-xylene (3 mL), 90 °C, 8h. Cy = cyclohexyl. *t*Bu = *tert*-butyl.

the source of "O", oxygen and H_2O added as controls, respectively, result revealed that no product was checked under O_2 condition (eq. 3), and surprisingly, an excellent yield was produced by addition of TsOH·H_2O under N_2 (eq. 4, and Figure S2) or by addition of TsOH and H_2O (eq. 5), and pyridin-2-amine was isolated in equivalent of yield as a by-product. Further experiment was carried out using $H_2{}^{18}O$ instead of H_2O, and an excellent yield of α-ketoamide with ^{18}O was obtained and detected by HR-MS (eq. 6, and see Figure S3 in SI). Study (eq. 7) indicated the yield of α-ketoamide could decrease sharply without adding TsOH·H_2O, which indicated that TsOH·H_2O can accelerate the process of the reaction. We have assumed that $PhI(OAc)_2$ could oxidize secondary amine intermediate to imine intermediate.[9] This could be partially supported by the control experiment eq. 8. The imine product **B** could be isolated in 48% yield from oxidation of the secondary amine **A** by $PhI(OAc)_2$ in $(CH_2Cl)_2$ at r.t. (eq. 8, also see Figure S4 – S6 in SI).



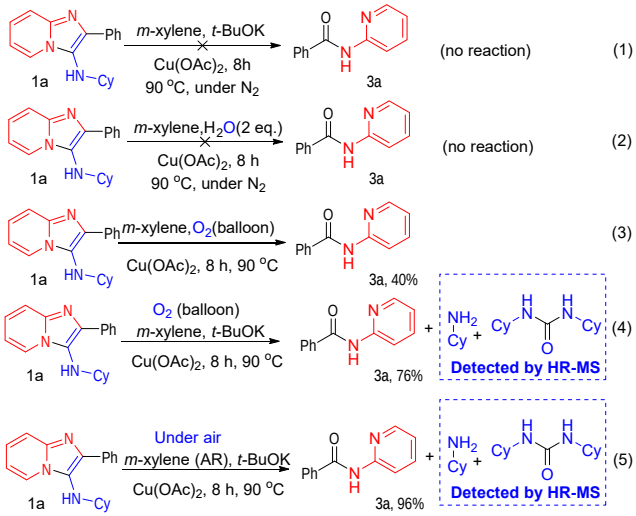
Scheme 1. The Control Experiments for Formation of α-Ketoamide.

As revealed by the control experiments together, the imidazo[1,2-a]pyridine substrate **1a** could be protonated under acidic conditions to form the cation intermediate **I**,[10] which could be hydrolyzed to give the ketone intermediate **III** via an intermediate **II**.[11b] The amine moiety of the intermediate **III** could be oxidized to afford the di-imine intermediate **IV**,[9] which further leads to the iminium intermediate **V** under acidic conditons.[10] Hydrolysis [11] of the iminium **V** gives the α-ketoamide **2a** as the final product and releases the pyridin-2-amine **5** as the main by-product (Scheme 2). Pyridin-2-amine **5** was released and could be reused as the starting material for synthesis of **1a**.[8]



Scheme 2. A Plausible Mechanism for Formation of α-Ketoamide.

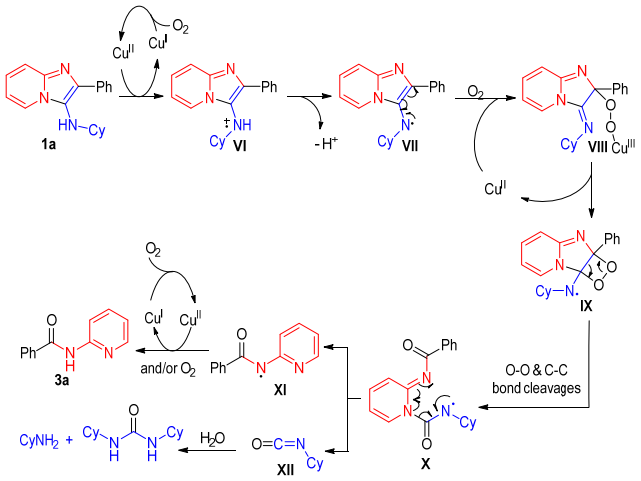
Alternatively, control experiments for formation of N-(pyridin-2-yl)arylamides were also carried out (Scheme 3). The source of oxygen atom still the key step. We firstly deal with the reaction under a nitrogen atmosphere (Scheme 3, eq. 1), and then 2 equivalents of water were added (Scheme 3, eq. 2), unfortunately, no reaction was monitored. Oxygen was then added using a balloon in absence of *t*-BuOK, which led to the amide in 40% yield (Scheme 3, eq. 3). However, the yield of the product was in a large increase by adding base, which was further improved by employing non dry *m*-xylene (Scheme 3, eq. 4), which indicated appropriate water could enhance the yield of product (Scheme 3, eq. 5). Simultaneously, byproducts of cyclohexanamine and 1,3-dicyclohexylurea were detected by HR-MS (eq. 4 and 5). For more details about the mechanism studies could be found in supporting information.



Scheme 3. The Control Experiments for Formation of *N*-(pyridin-2-yl)arylamides

As revealed by the control experiments and shown in **Scheme 4**. The imidazo[1,2-a]pyridine substrate **1a** could be oxidized by Cu(II) to give the radical anion intermediate **VI** [12] and then be deprotonated under base to afford the amine radical **VII**. Amine radical **VII** could be oxidized by air to afford the per-oxidized intermediate **VIII** with the assistance of the Cu(II) catalyst.[5a, 5b, 13] Intramolecular cyclization of per-oxide complex

VIII gives intermediate **IX** and releases the Cu(II) catalyst for additional catalytic oxidative process.[5j,13] Intramolecular rearrangement of intermediate **IX** leads to the di-ketone intermediate **X**,[5j, 7, 13] which could be fragmented into the amide radical **XI** and the isocyanate intermediate **XII**.[7] Arobic oxidation of the amide radical **XI** gives the product **3a**.[5h,13] Hydrolysis of the isocyanate intermediate **XII** leads to various by-products such as the primary amines and urea,[14] as detected by the HR-MS.



Scheme 4. Plausible Mechanism for Formation of *N*-(Pyridin-2-yl)arylamide.

Anti-TMV (Tobacco Mosaic Virus) experiments were carried out in order to show the practical applications of our products (Table 5). Our preliminary results indicated that some of the α-ketoamide products exhibited promising inactivation activity against TMV. For example, compounds **2d**, **2k** and **2l** have shown better anti-TMV activities than the commercially available pesticide of Ribavirin.

Table 5. Anti-TMV Experiments of the Amide Products.

compound	activity (%) [a]	compoun d	activity (%)[a]
2d	73.5	**2l**	71.1
2k	72.7	Ribavirin	70.2

[a] Average data of three replicates. For more details, see Supporting Information.

■ CONCLUSION

In summary, we have developed a series of oxidant-based diverse aromatic C(sp^2)-N bond cleavage reactions for the synthesis of α-ketoamides and *N*-(pyridin-2-yl)arylamides. The inert C(sp^2)-N bonds of the imidazo[1,2-a]pyridine compounds could be broken up in chemoselective fashion and give the target oxidized products in generally good to excellent yields. A broad scope of imidazo[1,2-a]pyridine substrates with different substituents and substitution patterns worked well in these processes. Further investigations into various inert bond cleavages and the bio-activities of the afforded products are currently in progress in our laboratory.

■ EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reactions were carried out in standard Schlenk techniques with magnetic stirring bar under air. The NMR spectra was recorded on a Bruke Avance operating for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz ^{19}F NMR at 376 MHz using TMS as internal standard or JEOL ECX500 NMR spectrometer ^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz ^{19}F NMR at 471 MHz operating at room temperature. The ^{1}H NMR chemical shifts were measured relative to $CDCl_3$ as the internal reference ($CDCl_3$: δ = 7.26 ppm, DMSO-d6: δ = 2.50 ppm). The ^{13}C NMR chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ = 77.16 ppm, DMSO-d6: δ = 39.52 ppm). High-resolution mass spectra (HRMS) were recorded on an Orbitrap LC–MS instrument (Q-Exative, Thermo Scientific™, American). Melting points were determined with X-4 and are uncorrected.

All the materials and solvents were purchased from commercial suppliers and used without additional purification. pyridin-2-amine, 3-methylpyridin-2-amine, 6-methylpyridin-2-amine, isocyanocyclohexane, 2-isocyano-2-methylpropane were purchased from TCI®, series of aldehyde, iodobenzene acetate, *p*-toluenesulfonic acid were purchased from Accela®, $Cu(OAc)_2$, $NiCl_2$ were purchased from Alfa Aesar®. CuI, CuBr, CuCl were purchased from Sigma-Aldrich. $Cu(OTf)_2$, $Pd(OAc)_2$, series of base were purchased from Adamas-beta®. Main solvents were purchased from TCI®.

General Procedure for Synthesis of Substrates. According to our previous work.[8] To a mixture of 2-aminopyridines (1 mmol), aromatic aldehydes (1.4 mmol) and isocyanides in ethanol was added β-cyclodextrin-SO_3H (10 mol%). The reaction mixture was then allowed to stir for 1 hour under 80 °C. After completed of this reaction, the resulting mixture was cooled and the β-cyclodextrin-SO_3H was removed by filtration, the organic phase was concentrated under reduced pressure. Afterwards the residue was washed with ethyl acetate/*n*-hexane (1:3) and dried to give the product in good to excellent yield. The structures of substrates (**1a**, **1q**, **1r**, **1s**, **1ae**, **4a**, **4h**, **4i**, and **4q**) that already known in our previous work[8] can be found in Supporting Information (Figure S1). The rest properties of substrates are listed as follows.

*2-(4-Chlorophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1b**)*: Light yellow solid; m.p. 175 – 177 °C (Lit.[15a] 179 – 181 °C), 410 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 6.9, 1.1 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 2H), 7.54 (dd, *J* = 9.0, 0.9 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.15 (dd, *J* = 8.4, 7.3 Hz, 1H), 6.80 (t, *J* = 6.8 Hz, 1H), 3.07 (d, *J* = 3.9 Hz, 1H), 2.94 (td, *J* = 10.0, 5.2 Hz, 1H), 1.86 – 1.53 (m, 5H), 1.26 – 1.14(m, 5H).

*2-(3-Chlorophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1c**)*: Cream solid, m.p. 164 – 165 °C (Lit.[15b]167 – 169 °C), 384 mg, 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (t, *J* = 1.8 Hz, 1H), 8.10 (dd, *J* = 6.9, 1.1 Hz, 1H), 7.97 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.55 (dd, *J* = 9.0, 1.0 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.16 (ddd, *J* = 7.8, 4.5, 1.0 Hz, 1H), 6.81 (td, *J* = 6.8, 1.1 Hz, 1H), 3.08 (d, *J* = 3.5 Hz, 1H), 2.96 (td, *J* = 10.0, 5.2 Hz, 1H), 1.83-1.55 (m, 5H), 1.30 – 1.21 (m, 5H).

*2-(2-Chlorophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1d**)*: Cream solid, m.p. 104 – 106 °C (Lit.[15b] 107 – 199 °C), 377 mg, 81% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ

8.17 – 8.12 (m, 1H), 7.69 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.47 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.34 (tdd, *J* = 14.6, 7.2, 1.4 Hz, 2H), 7.13 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.80 (td, *J* = 6.8, 1.0 Hz, 1H), 3.30 (d, *J* = 7.3 Hz, 1H), 2.67 (qd, *J* = 9.9, 3.8 Hz, 1H), 1.71 – 1.43 (m, 5H), 1.11 – 0.95 (m, 5H).

*2-(4-Bromophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1e**)*: Pale yellow solid, m.p. 164 – 166 °C (Lit.[15b] 166-168 °C), 384 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 6.9 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 9.1 Hz, 1H), 7.14 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.79 (td, *J* = 6.8, 1.1 Hz, 1H), 3.04 (d, *J* = 4.8 Hz, 1H), 2.93 (ddd, *J* = 14.4, 10.0, 4.6 Hz, 1H), 1.80 – 1.65 (m, 2H), 1.58 (m, 5H), 1.20 (m, 5H).

*2-(3-Bromophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1f**)*: Brown solid, m.p. 76 – 78 °C (Lit. [15b] 79 – 81 °C), 372 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (t, *J* = 1.7 Hz, 1H), 8.08 (dt, *J* = 6.9, 1.1 Hz, 1H), 8.04 – 7.97 (m, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.43 (ddd, *J* = 7.9, 1.9, 1.0 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.15 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.80 (td, *J* = 6.8, 1.0 Hz, 1H), 3.05 (d, *J* = 4.8 Hz, 1H), 3.01 – 2.90 (m, 1H), 1.86 – 1.56 (m, 5H), 1.31 – 1.05 (m, 5H).

*2-(2-Bromophenyl)-N-cyclohexylimidazo[1,2-a]pyridin-3-amine (**1g**)*: Brown solid, m.p. 139 – 141°C (Lit.[15c] 140 – 142 °C), 365 mg, 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dt, *J* = 6.9, 1.1 Hz, 1H), 7.64 (ddd, *J* = 12.2, 7.9, 1.4 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.40 (td, *J* = 7.5, 1.2 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.13 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.80 (td, *J* = 6.8, 1.0 Hz, 1H), 3.29 (d, *J* = 7.0 Hz, 1H), 2.69 – 2.66 (m, 1H), 1.67 – 1.45 (m, 1H), 1.13 – 0.93 (m, 5H).

*N-Cyclohexyl-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine (**1h**)*: White solid, m.p. 165 – 167°C (Lit.[15b] 167 – 169 °C), 497 mg, 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.07 (m, 1H), 8.07 – 8.01 (m, 2H), 7.53 (dd, *J* = 9.0, 0.9 Hz, 1H), 7.18 – 7.09 (m, 3H), 6.83 – 6.76 (m, 1H), 3.06 (d, *J* = 4.4 Hz, 1H), 2.99 – 2.88 (m, 1H), 1.80 (d, *J* = 11.0 Hz, 2H), 1.69 (d, *J* = 4.1 Hz, 2H), 1.58 (s, 1H), 1.14 – 1.28 (m, 5H.

*N-Cyclohexyl-2-(2-nitrophenyl)imidazo[1,2-a]pyridin-3-amine(**1i**)*: [15c] Yellow solid, m.p. 167 – 169 °C, 412 mg, 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (t, *J* = 1.9 Hz, 1H), 8.52 (d, *J* = 7.8 Hz, 1H), 8.15 (ddd, *J* = 8.2, 2.2, 0.8 Hz, 1H), 8.10 (d, *J* = 6.9 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 9.1 Hz, 1H), 7.19 (ddd, *J* = 9.0, 6.7, 1.1 Hz, 1H), 6.84 (td, *J* = 6.8, 0.9 Hz, 1H), 3.08 (d, *J* = 4.5 Hz, 1H), 3.00 (td, *J* = 10.4, 5.4 Hz, 1H), 1.88 – 1.60 (m, 5H), 1.33 – 1.18 (m, 5H).

*N-Cyclohexyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (**1j**)*: White solid, m.p. 162 – 164 °C (Lit. [15d] 166 – 169 °C), 398 mg, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 6.8 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.30 – 7.25 (d, *J* = 8.2 Hz, 2H), 7.17 – 7.10 (m, 1H), 6.79 (t, *J* = 6.7 Hz, 1H), 3.14 (s, 1H), 3.03 – 2.90 (m, 1H), 1.81 – 1.58 (m, 1H), 1.28 – 1.13 (m, 5H).

*N-Cyclohexyl-2-(m-tolyl)imidazo[1,2-a]pyridin-3-amine (**1k**)*: [15d] Yellow solid, m.p. 114 – 115 °C, 377 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 6.9, 1.0 Hz, 1H), 7.91 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.17 – 7.09 (m, 2H), 6.78 (td, *J* = 6.8, 1.0 Hz, 1H), 3.13 (d, *J* = 4.7 Hz, 1H), 3.04 – 2.93 (m, 1H), 2.43 (s, 3H), 1.87 – 1.55 (m, 5H), 1.30 – 1.11 (m, 5H).

*N-Cyclohexyl-2-(o-tolyl)imidazo[1,2-a]pyridin-3-amine (**1l**)*: [15d] Yellow solid, m.p. 108 – 109 °C, 356 mg, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dt, *J* = 6.9, 1.1 Hz, 1H), 7.53 (dt, *J* = 9.0, 1.0 Hz, 1H), 7.35 (d, *J* = 7.1 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.24 (ddd, *J* = 5.9, 5.1, 3.5 Hz, 1H), 7.13 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.80 (td, *J* = 6.8, 1.1 Hz, 1H), 3.00 (s, 1H), 2.73 (s, 1H), 2.34 (s, 3H), 2.34 (s, 3H), 1.74 – 1.64 (m, 2H), 1.59 (dd, *J* = 9.4, 4.0 Hz, 2H), 1.52 – 1.45 (m, 1H), 1.17 – 0.88 (m, 5H).

*N-Cyclohexyl-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (**1m**)*: White solid, m.p. 153 – 155 °C (Lit. [15d] 154 °C), 358 mg, 79% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 6.8 Hz, 1H), 7.98 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.13 – 7.06 (m, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.74 (t, *J* = 6.7 Hz, 1H), 3.84 (s, 3H), 3.05 (d, *J* = 4.3 Hz, 1H), 2.94 (dt, *J* = 13.5, 6.9 Hz, 1H), 1.79 (d, *J* = 10.7 Hz, 2H), 1.67 (d, *J* = 4.6 Hz, 2H), 1.56 (s, 1H), 1.26 – 1.11 (m, 5H).

*N-Cyclohexyl-2-(3-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (**1n**)*: White solid, m.p. 151 – 152 °C (Lit.[15d] 153 – 155 °C), 382 mg, 84% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 6.9 Hz, 1H), 7.65 (dd, *J* = 2.4, 1.6 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.11 (ddd, J = 9.0, 6.7, 1.2 Hz, 1H), 6.87 (ddd, *J* = 8.2, 2.6, 0.7 Hz, 1H), 6.76 (td, *J* = 6.8, 1.0 Hz, 1H), 3.89 (s, 3H), 3.13 (d, *J* = 5.0 Hz, 1H), 3.02 – 2.92 (m, 1H), 1.67 (m, 5H), 1.30 – 1.07 (m, 5H).

*N-Cyclohexyl-2-(2-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (**1o**)*: Viscous brown oil, 345 mg, 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 6.8, 1.1 Hz, 1H), 7.87 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.55 (dd, *J* = 9.0, 1.0 Hz, 1H), 7.34 (ddd, *J* = 8.9, 3.3, 1.6 Hz, 1H), 7.15 – 7.05 (m, 2H), 7.00 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.79 – 6.73 (m, 1H), 3.96 (d, *J* = 8.3 Hz, 1H), 3.88 (d, *J* = 2.0 Hz, 3H), 2.70 – 2.58 (m, 1H), 1.72 –1.47 (m, 5H), 1.14 – 0.95 (m, 5H).

*4-(3-(Cyclohexylamino)imidazo[1,2-a]pyridin-2-yl)-2-methoxyphenol (**1p**)*: [15e] White solid, m.p. 204 – 205 °C, 398 mg, 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 6.8 Hz, 1H), 7.70 (d, *J* = 1.8 Hz, 1H), 7.58 – 7.46 (m, 2H), 7.17 – 7.10 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.80 (td, *J* = 6.8, 0.8 Hz, 1H), 6.09 (s, 1H), 3.12 (s, 1H), 2.99 (dt, *J* = 13.3, 6.8 Hz, 1H), 1.83 – 1.56 (m, 3H), 1.27-1.14 (m, 5H).

*N-Cyclohexyl-2-ethylimidazo[1,2-a]pyridin-3-amine (**1t**)*: Colorless crystal, m.p. 139 – 141 °C (Lit. [15f] 140 – 142 °C), 293 mg, 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.5 Hz, 1H), 7.22 – 7.15 (m, 1H), 6.97 (t, *J* = 6.8 Hz, 1H), 3.17 (s, 1H), 3.11 (q, *J* = 7.6 Hz, 3H), 2.90 (s, 3H), 2.22 – 1.92 (m, 5H), 1.67 (t, *J* = 7.6 Hz, 3H), 1.59 – 1.48 (m, 5H).

*N-Cyclohexyl-2-isopropylimidazo[1,2-a]pyridin-3-amine (**1u**)*: Yellow viscose oil, 284 mg, 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (s, 1H), 3.76 (tdt, *J* = 12.1, 8.1, 3.9 Hz, 1H), 2.28 (dd, *J* = 13.8, 6.9 Hz, 1H), 1.94 – 1.86 (m, 2H), 1.72 – 1.67 (m, 2H), 1.65 – 1.58 (m, 1H), 1.44 – 1.29 (m, 3H), 1.19 (dd, *J* = 7.6, 4.0 Hz, 1H), 1.15 (s, 3H), 1.13 (s, 3H), 1.12 – 0.97 (m, 2H).

*N-Cyclohexyl-5-methyl-2-phenylimidazo[1,2-a]pyridin-3-amine **(1v)***: Golden red solid, m.p. 74 – 76 °C (Lit. [15d] 76 – 78 °C), 376 mg, yield 87 %; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.3 Hz, 2H), 7.42 – 7.32 (m, 3H), 7.25 – 7.18 (m, 1H), 6.96 (dd, *J* = 8.7, 7.0 Hz, 1H), 6.38 (d, *J* = 6.7 Hz, 1H), 3.09 (s, 1H), 2.87 (s, 3H), 2.68 (s, 1H), 1.61 – 1.41 (m, 5H), 0.94 (t, *J* = 13.0 Hz, 5H).

*N-Cyclohexyl-8-methyl-2-phenylimidazo[1,2-a]pyridin-3-amine **(1w)***: Gray solid, 393 mg, 89% m.p. 123 – 125 °C. 320 mg, 74 % yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.98 (d, *J* = 6.7 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.34 – 7.28 (m, 1H), 6.94 – 6.90 (m, 1H), 6.70 (t, *J* = 6.8 Hz, 1H), 3.15 (s, 1H), 3.00 – 2.89 (m, 1H), 2.63 (s, 3H), 1.81 (d, *J* = 10.7 Hz, 2H), 1.72 – 1.62 (m, 2H), 1.55 (dd, *J* = 6.8, 3.1 Hz, 1H), 1.24 – 1.10 (m, 5H).

*N-Cyclohexyl-2-ethyl-5-methylimidazo[1,2-a]pyridin-3-amine **(1x)***: Yellow solid, 111 – 112 ºC, 317 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.8 Hz, 1H), 6.94 (dd, *J* = 8.9, 6.8 Hz, 1H), 6.37 (d, *J* = 6.8 Hz, 1H), 2.89 (s, 3H), 2.83 (dd, *J* = 10.1, 6.6 Hz, 1H), 2.72 (q, *J* = 7.6 Hz, 2H), 2.63 (d, *J* = 4.9 Hz, 1H), 1.86 (d, J = 8.8 Hz, 2H), 1.79 – 1.69 (m, 2H), 1.64 (dd, *J* = 7.1, 2.2 Hz, 1H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.24 – 1.13 (m, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.1, 142.7, 136.0, 125.6, 123.3, 115.2, 112.8, 59.7, 33.6, 26.0 25.2, 20.7, 19.8, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{24}N_3$ 258.1965; found: 258.1969.

*N-Cyclohexyl-2-ethyl-5-methylimidazo[1,2-a]pyridin-3-amine **(1y)***: Yellow solid, 92 – 94 ºC, 310 mg, 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.9 Hz, 1H), 6.94 (dd, *J* = 8.9, 6.8 Hz, 1H), 6.38 (d, *J* = 6.8 Hz, 1H), 2.89 (s, 3H), 2.86 – 2.78 (m, 1H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.88-1.85 (m, 2H), 1.75 – 1.73 (m, 2H), 1.65-1.63 (m, 1H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.28 – 1.11 (m, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.1, 142.7, 136.0, 125.6, 123.3, 115.2, 112.8, 59.7, 33.6, 26.0, 25.2, 20.7, 19.8, 13.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{24}N_3$ 258.1965; found: 258.1967.

*N-Cyclohexyl-2-isopropyl-5-methylimidazo[1,2-a]pyridin-3-amine **(1z)***: Yellow solid, m.p. 100 – 101 ºC, 326 mg, 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 6.7 Hz, 1H), 6.85 – 6.81 (m, 1H), 6.62 (t, *J* = 6.8 Hz, 1H), 3.16 (hept, *J* = 6.9 Hz, 1H), 2.84 (s, 1H), 2.79 (s, 1H), 2.57 (s, 3H), 1.88 – 1.59 (m, 5H), 1.38 (s, 3H), 1.37 (s, 3H), 1.26 – 1.17 (m, 5H).

*N-Cyclohexyl-2-isopropyl-8-methylimidazo[1,2-a]pyridin-3-amine **(1aa)***: Yellow solid, m.p. 95 – 97 ºC, 305 mg, 84% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 6.7 Hz, 1H), 6.88 – 6.83 (m, 1H), 6.63 (t, *J* = 6.8 Hz, 1H), 3.17 (hept, *J* = 6.9 Hz, 1H), 2.85 (d, *J* = 4.1 Hz, 1H), 2.81 (s, 1H), 2.58 (s, 3H), 1.91 – 1.81 (m, 2H), 1.74 – 1.61 (m, 3H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.38 (d, J = 6.9 Hz, 3H), 1.26 – 1.16 (m, 5H).

*N-Cyclohexyl-2-phenylimidazo[1,2-a]pyrazin-3-amine **(1ab)***: Light Yellow solid, m.p. 143 – 145 ºC (Lit. [11e] 141 – 142 °C), 306 mg, 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 1.3 Hz, 1H), 8.06 – 7.97 (m, 3H), 7.86 (d, *J* = 4.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.41 – 7.35 (m, 1H), 3.27 (d, *J* = 4.2 Hz, 1H), 3.01 (d, *J* = 3.9 Hz, 1H), 1.83 – 1.59 (m, 1H), 1.21 (dt, *J* = 21.2, 10.0 Hz, 5H).

*N-Cyclohexyl-2-phenylbenzo[d]imidazo[2,1-b]thiazol-3-amine **(1ac)***: White solid, m.p. 189 – 191 ºC, 363 mg, 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.94 (m, 2H), 7.61 – 7.57 (m, 1H), 7.52 – 7.48 (m, 1H), 7.43 – 7.38 (m, 2H), 7.32 (ddd, *J* = 10.3, 7.7, 4.0 Hz, 2H), 7.27 – 7.23 (m, 1H), 3.08 – 2.98 (m, 1H), 1.97 – 1.60 (m, 1H), 1.33 – 1.14 (m, 5H).

*N-Cyclohexyl-2-phenylbenzo[d]imidazo[2,1-b]oxazol-3-amine **(1ad)***: White solid, m.p. 189 – 191 ºC, 264 mg, 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 1.3 Hz, 1H), 8.06 – 7.97 (m, 3H), 7.86 (d, *J* = 4.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.41 – 7.35 (m, 1H), 3.27 (d, *J* = 4.2 Hz, 1H), 3.01 (d, *J* = 3.9 Hz, 1H), 1.83 (d, *J* = 10.5 Hz, 2H), 1.74 – 1.59 (m, 3H), 1.21 (m, 5H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9, 150.7, 128.5, 127.0, 126.6, 126.2, 124.4, 124.0, 112.4, 111.5, 57.9, 34.0, 25.8, 24.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{22}N_3O$ 332.1757; found: 332.1758.

*N-(tert-Butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine **(4b)***: White soild, m.p. 146 – 147 °C (Lit.[15g]146 – 149 °C), 378 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 – 8.25 (m, 1H), 7.72 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.46 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.38 (td, *J* = 7.5, 1.4 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.18 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.82 (td, *J* = 6.8, 1.0 Hz, 1H), 3.21 (brs, 1H), 0.93 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.2, 137.5, 134.7, 132.8, 132.4, 129.5, 129.2, 127.1, 125.1, 124.4, 123.7, 117.4, 111.5, 55.9, 29.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{17}H_{19}ClN_3$ 300.1262; found 300.1259.

*N-(tert-Butyl)-2-(2-chlorophenyl)imidazo[1,2-a]pyridin-3-amine **(4c)**:* White soild, m.p. 154 – 156 °C. 376 mg, 84% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.31 (m, 1H), 7.72 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.46 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.38 (td, *J* = 7.5, 1.4 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.18 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 6.82 (td, *J* = 6.8, 1.0 Hz, 1H), 0.93 (s, 9H).

*N-(tert-Butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine **(4d)***: White soild, m.p. 155-156 °C. (Lit. [15h] 158 – 160 °C), 332 mg, 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.14 (m, 1H), 7.96 – 7.87 (m, 2H), 7.56 – 7.49 (m, 1H), 7.16 – 7.04 (m, 3H), 6.82 – 6.73 (m, 1H), 3.02 (s, 1H), 1.04 (s, 9H).

*2-(4-Bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine **(4e)***: White soild. m.p. 148 – 150 (Lit. [15i] 146 °C), 428 mg, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.9 Hz, 1H), 7.87 (d, *J* = 8.6 Hz, 2H), 7.58 – 7.52 (m, 3H), 7.17 (ddd, *J* = 8.9, 6.7, 1.2 Hz, 1H), 6.80 (td, *J* = 6.8, 1.0 Hz, 1H), 3.05 (s, 1H), 1.06 (s, 9H)

*2-(3-Bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine **(4f)***: White soild, m.p. 138 – 139 ºC, 412 mg, 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.17 (m, 2H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.44 (d, *J* = 9.7 Hz, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.80 (t, *J* = 6.8 Hz, 1H), 3.06 (s, 1H), 1.07 (s, 9H).

*N-(tert-Butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-amine **(4g)***: [15c] Brown solid, m.p. 87 – 88 ºC, 385 mg, yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 1.5 Hz, 1H),

8.48 – 8.39 (m, 1H), 8.22 (d, *J* = 7.0 Hz, 1H), 8.20 – 8.11 (m, 1H), 7.61 (ddd, *J* = 11.2, 7.8, 3.6 Hz, 2H), 7.23 (d, *J* = 6.5 Hz, 1H), 6.93 – 6.80 (m, 1H), 3.08 (brs, 1H), 1.12 (s, 9H).

*N-(tert-Butyl)-2-(furan-2-yl)imidazo[1,2-a]pyridin-3-amine **(4j)***: Brown soild, m.p. 155 – 156 °C (Lit.[15j] 158 – 160 °C), 378 mg, 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 6.9 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.14 (ddd, *J* = 9.0, 6.7, 1.2 Hz, 1H), 6.92 (d, *J* = 3.3 Hz, 1H), 6.76 (td, *J* = 6.8, 0.9 Hz, 1H), 6.53 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.55 (s, 1H), 1.16 (s, 9H).

*2-(4-Chlorophenyl)-N-(4-methoxyphenyl)imidazo[1,2-a] pyridin-3-amine **(4k)***: Brown solid, m.p. 187 – 189 °C (Lit. [15g]190 – 191 °C), 320 mg, yield 64 %; ^{1}H NMR (400 MHz, CDCl3) δ 7.91 (t, *J* = 7.4 Hz, 2H), 7.81 (d, *J* = 6.8 Hz, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.19 (s, 1H), 6.77 (t, *J* = 6.7 Hz, 1H), 6.73 (dd, *J* = 7.2, 5.2 Hz, 2H), 6.52 – 6.47 (m, 2H), 3.68 (s, 3H).

*2-(3-Chlorophenyl)-N-(4-methoxyphenyl)imidazo[1,2-a] pyridin-3-amine **(4l)***: Light yellow solid, 154 – 155 ºC, 236 mg, 47% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 1.8 Hz, 1H), 7.87 (ddd, *J* = 12.3, 5.9, 4.3 Hz, 2H), 7.63 (d, *J* = 9.1 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.26 – 7.21 (m, 2H), 6.82 – 6.76 (m, 3H), 6.60 – 6.52 (m, 2H), 5.40 (s, 1H), 3.75 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.7, 142.7, 138.0, 137.8, 135.3, 134.6, 129.8, 127.8, 127.1, 125.3, 124.9, 122.8, 119.2, 117.8, 115.3, 114.5, 112.4, 55.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{20}H_{17}ClN_3O$ 350.1055; found 350.1056.

*2-(3-Methoxyphenyl)-N-(4-methoxyphenyl)imidazo[1,2-a] pyridin-3-amine **(4m)***: Brown solid, 163 – 165 ºC, 227 mg, 47% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 1H), 7.61 – 7.56 (m, 2H), 7.55 – 7.52 (m, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.17 (ddd, *J* = 9.0, 6.7, 1.2 Hz, 1H), 6.81 (ddd, *J* = 8.2, 2.6, 0.8 Hz, 1H), 6.78 – 6.74 (m, 2H), 6.74 – 6.70 (m, 1H), 6.52 – 6.46 (m, 2H), 5.56 (s, 1H), 3.72 (s, 3H), 3.69 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.8, 153.5, 142.5, 138.7, 138.5, 134.7, 129.6, 125.1, 122.8, 119.4, 119.1, 117.5, 115.3, 114.44, 114.41, 112.2, 111.6, 55.7, 55.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{20}N_3O_2$ [M+H]+: 346.1550; found 346.1560.

*2-(2-Methoxyphenyl)-N-(4-methoxyphenyl)imidazo[1,2-a] pyridin-3-amine **(4n)***: Brown solid, 158 – 160 ºC,189 mg, 39% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.76 (dt, *J* = 6.8, 1.1 Hz, 1H), 7.66 (d, *J* = 9.1 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.20 (ddd, *J* = 9.0, 6.7, 1.2 Hz, 1H), 7.08 (td, J = 7.5, 1.0 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.78 (td, *J* = 6.8, 1.0 Hz, 1H), 6.74 – 6.70 (m, 2H), 6.43 – 6.38 (m, 2H), 6.15 (s, 1H), 3.83 (s, 3H), 3.71 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.2, 153.5, 142.3, 138.4, 134.3, 131.7, 129.3, 123.9, 123.1, 122.1, 121.6, 117.7, 115.5, 114.9, 111.8, 111.6, 56.2, 55.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{20}N_3O_2$ $[M+H]^+$: 346.1550; found 346.1548.

*N-(tert-Butyl)-2-(o-tolyl)imidazo[1,2-a]pyridin-3-amine **(4o)***: Yellow solid, m.p. 118 – 120 ºC, 326 mg, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 6.8 Hz, 1H), 7.77 (s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.17 – 7.08 (m, 2H), 6.76 (t, *J* = 6.7 Hz, 1H), 3.12 (s, 1H), 2.41 (s, 3H), 1.04 (s, 9H).

*N-(tert-Butyl)-2-(3-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine **(4p)***: White solid, m.p. 103 – 105 °C, 356 mg, 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dt, *J* = 6.9, 1.1 Hz, 1H), 7.54 (dt, *J* = 9.0, 1.0 Hz, 1H), 7.50 (dd, *J* = 2.5, 1.5 Hz, 1H), 7.48 – 7.44 (m, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.13 (ddd, *J* = 9.0, 6.6, 1.3 Hz, 1H), 6.87 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.77 (td, *J* = 6.8, 1.1 Hz, 1H), 3.88 (s, 3H), 3.12 (s, 1H), 1.04 (s, 9H).

General Procedure for Preparation of *α*-Ketoamide. A reaction tube vial was charged with 1 (0.17 mmol), and $TsOH·H_2O$ (0.51 mmol), followed by addition of DCE (2.5 mL), Adding iodobenzene acetate (0.17 mmol) during the stirring process. The resulting mixture was allowed to stir at room temperature for 1h. After the reaction was completed, the reaction mixture was evaporated under reduced pressure to leave a crude mixture, which was purified by column chromatography on silica gel (eluting with petroleum ether/ethyl acetate = 5: 1) to afford **2** or **5**.

*N-Cyclohexyl-2-oxo-2-phenylacetamide **(2a)**:* White solid, m.p. 93 – 94°C, 39.3 mg, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 6.97 (s, 1H), 3.96 – 3.72 (m, 1H), 2.04 – 1.94 (m, 2H), 1.81 – 1.71 (m, 2H), 1.70 – 1.61 (m, 1H), 1.49 – 1.34 (m, 2H), 1.30 – 1.21 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 188.2, 160.9, 134.3, 133.7, 131.2, 128.5, 48.49, 32.7, 25.4, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{18}O_2N$ 232.1332; found 232.1335.

*2-(4-Chlorophenyl)-N-cyclohexyl-2-oxoacetamide **(2b)***: White solid, m.p. 90 – 91°C, 42.9 mg, 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 6.99 (s, 1H), 3.82 (m,1H), 2.03 – 1.92 (m, 2H), 1.79 – 1.71 (m, 2H), 1.73 – 1.56 (m, 1H), 1.45 – 1.34 (m, 2H), 1.24 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 189.9, 164.4, 140.0, 132.2, 132.0, 129.8, 48.3, 32.5, 25.6, 25.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NCl$ 266.0942; found 266.0938.

*2-(3-Chlorophenyl)-N-cyclohexyl-2-oxoacetamide **(2c)**:* White solid, m.p. 95 – 96 °C, 38.4 mg, 88% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (t, *J* = 1.8 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 6.96 (s, 1H), 3.88 – 3.78 (m, 1H), 1.97 (dd, *J* = 12.5, 3.5 Hz, 2H), 1.80 – 1.73 (m, 2H), 1.67 – 1.62 (m, 1H), 1.45 – 1.36 (m, 2H), 1.31 – 1.19 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.8, 160.3, 135.0, 134.8, 134.3, 131.2, 129.8, 129.5, 48.7, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NCl$ 266.0942; found 266.0939.

*2-(2-Chlorophenyl)-N-cyclohexyl-2-oxoacetamide **(2d)***: White solid, m.p. 95 – 96 °C, 43.4 mg, 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.1 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 6.82 (s, 1H), 3.90 – 3.76 (m, 1H), 1.99 (d, *J* = 12.4 Hz, 2H), 1.81 – 1.72 (m, 2H), 1.65 (dd, *J* = 9.1, 3.9 Hz, 1H), 1.47 – 1.35 (m, 2H), 1.34 – 1.21 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 190.6, 159.8, 134.2, 133.1, 133.0, 131.3, 130.4, 126.5, 48.7, 32.6, 25.4, 24.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NCl$ 266.0942; found 266.09391.

*2-(4-Bromophenyl)-N-cyclohexyl-2-oxoacetamide **(2e)**:* White solid, m.p. 93 – 94 °C, 51.7 mg, 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 – 8.23 (m, 2H), 7.63 – 7.60 (m, 2H), 6.97 (d, *J* = 6.3 Hz, 1H), 3.88 – 3.79 (m, 1H), 1.97 (dd, *J* = 12.6, 3.6 Hz,

2H), 1.78 – 1.73 (m, 2H), 1.67 – 1.62 (m, 1H), 1.45 – 1.36 (m, 2H), 1.30 – 1.20 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 187.0, 160.5, 132.9, 132.3, 131.9, 130.1, 48.6, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NBr$ 310.0437; found 310.0432.

2-(3-Bromophenyl)-N-cyclohexyl-2-oxoacetamide (**2f**): White solid, m.p. 102 – 103 °C, 51.2 mg, 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.78 – 7.70 (m, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 5.7 Hz, 1H), 3.91 – 3.76 (m, 1H), 1.98 (dd, *J* = 12.4, 3.3 Hz, 2H), 1.79 – 1.74 (m, 2H), 1.68 – 1.62 (m, 1H), 1.41 (m, 2H), 1.32 – 1.18 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 186.7, 160.2, 137.2, 135.2, 134.1, 130.1, 130.0, 122.7, 48.7, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NBr$ 310.0437; found 310.0433.

*2-(2-Bromophenyl)-N-cyclohexyl-2-oxoacetamide (**2g**)*: White solid, 101 – 102 °C, 44.3 mg, 84% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 7.4, 1.9 Hz, 2H), 7.38 (dtd, *J* = 17.1, 7.5, 1.6 Hz, 2H), 6.88 (d, *J* = 5.7 Hz, 1H), 3.87 – 3.77 (m, 1H), 1.99 (dd, *J* = 12.4, 3.3 Hz, 2H), 1.82 – 1.72 (m, 2H), 1.68 – 1.58 (m, 1H), 1.45 – 1.34 (m, 2H), 1.32 – 1.19 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 191.3, 159.5, 136.3, 133.6, 133.0, 131.3, 127.2, 121.0, 48.8, 32.7, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_2NBr$ 310.0437; found 310.0431.

*N-Cyclohexyl-2-(4-fluorophenyl)-2-oxoacetamide (**2h**)*: White solid, m.p. 84 – 85 °C, 42.1 mg, 99% yield; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (d, *J* = 7.9 Hz, 1H), 8.00 (dd, *J* = 8.6, 5.6 Hz, 2H), 7.39 (t, *J* = 8.8 Hz, 2H), 3.74 – 3.63 (m, 1H), 1.79 (d, *J* = 9.7 Hz, 2H), 1.68 (dd, *J* = 9.5, 3.1 Hz, 2H), 1.55 (d, *J* = 12.8 Hz, 1H), 1.32 – 1.19 (m, 4H), 1.15 – 1.05 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO- d_6) δ 189.6, 166.2 (d, *J* = 254.1 Hz). 164.6, 133.3 (d, *J* = 10.0 Hz), 130.3, 116.8 (d, *J* = 22.3 Hz), 48.3, 32.6, 25.6, 25.0; $^{19}F\{^{1}H\}$ NMR (471 MHz, DMSO-d_6) δ -98.53 (s); HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}FNO_2$ 250.1238; found 250.1234.

*N-Cyclohexyl-2-(3-nitrophenyl)-2-oxoacetamide (**2i**)*: White solid, m.p. 91 – 92 °C, 39.9 mg, 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.20 – 9.19 (t, 1H), 8.72 (tt, *J* = 7.8, 1.3 Hz, 1H), 8.46 (m, *J* = 8.2, 2.3, 1.1 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 6.1 Hz, 1H), 3.89 – 3.81 (m, 1H), 1.99 (dd, *J* = 12.4, 3.4 Hz, 2H), 1.81 – 1.75 (m, 2H), 1.69 – 1.63 (m, 1H), 1.47 – 1.37 (m, 2H), 1.33 – 1.20 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 185.8, 159.7, 148.3, 137.0, 134.8, 129.8, 128.4, 126.3, 48.9, 32.8, 25.4, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{14}H_{17}O_4N_2$ 277.1183; found 277.1178.

*N-Cyclohexyl-2-oxo-2-(p-tolyl)acetamide (**2j**)*: Light yellow solid, m.p. 95 – 96 °C, 33.8 mg, 81% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.95 (s, 1H), 3.90 – 3.77 (m, 1H), 2.41 (s, 3H), 1.97 (dd, *J* = 12.5, 3.3 Hz, 2H), 1.79 – 1.71 (m, 2H), 1.69 – 1.62 (m, 1H), 1.44 – 1.36 (m, 2H), 1.25 (m, *J* = 16.1, 12.7, 3.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 187.7, 161.2, 145.6, 131.5, 131.1, 129.3, 48.5, 32.8, 25.5, 24.8, 22.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_2$ 246.1489; found 246.1484.

*N-Cyclohexyl-2-oxo-2-(m-tolyl)acetamide (**2k**)*: White solid, m.p. 97 – 98 °C, 38.9 mg, 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.11 (m, 2H), 7.44 – 7.40 (m, 1H), 7.38 – 7.33 (m, 1H), 6.93 (d, *J* = 5.4 Hz, 1H), 3.89 – 3.80 (m, 1H), 2.40 (s, 3H), 1.98 (dd, *J* = 12.6, 3.6 Hz, 2H), 1.81 – 1.73 (m, 2H), 1.69 – 1.61 (m, 1H), 1.46 – 1.35 (m, 2H), 1.25 (m, *J* = 25.1, 16.1, 12.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 188.4, 161.1, 138.3, 135.2, 133.5, 131.7, 128.5, 128.4, 48.6, 32.8, 25.5, 24.9, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_2$ 246.1489; found 246.1484.

*N-Cyclohexyl-2-oxo-2-(o-tolyl)acetamide (**2l**)*: Light yellow solid, 100 – 101 °C, 37.2 mg, 89% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.26 (dd, *J* = 10.5, 4.6 Hz, 2H), 6.90 (s, 1H), 3.93 – 3.76 (m, 1H), 2.48 (s, 3H), 1.99 (dd, *J* = 12.3, 3.1 Hz, 2H), 1.80 – 1.72 (m, 2H), 1.69 – 1.61 (m, 1H), 1.47 – 1.35 (m, 2H), 1.34 – 1.20 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 191.9, 161.2, 140.1, 133.1, 132.7, 132.0, 131.7, 125.4, 48.7, 32.8, 25.5, 24.8, 20.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_2$ 246.1489; found 246.1482.

*N-Cyclohexyl-2-(4-methoxyphenyl)-2-oxoacetamide (**2m**)* : White solid, m.p. 102 – 103 °C, 39.3 mg, 88% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 – 8.35 (m, 2H), 7.00 (d, *J* = 7.0 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H), 3.85 – 3.78 (m, 1H), 2.00 – 1.93 (m, 2H), 1.79 – 1.71 (m, 2H), 1.67 – 1.60 (m, 1H), 1.44 – 1.35 (m, 2H), 1.25 (ddd, *J* = 26.9, 13.5, 10.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 186.1, 164.7, 161.4, 134.0, 126.6, 113.9, 55.6, 48.5, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_3$ 262.1438; found 262.1434.

N-Cyclohexyl-2-(3-methoxyphenyl)-2-oxoacetamide (**2n**): Light yellow solid, m.p. 79 – 80°C, 37.9 mg, 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.7 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.16 (dd, *J* = 8.2, 2.7 Hz, 1H), 6.94 (d, *J* = 5.7 Hz, 1H), 3.88 – 3.79 (m, 4H), 1.98 (dd, *J* = 12.4, 3.4 Hz, 2H), 1.83 – 1.71 (m, 2H), 1.67 – 1.61 (m, 1H), 1.45 – 1.35 (m, 2H), 1.31 – 1.18 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 187.9, 161.0, 159.6, 134.7, 129.6, 124.2, 121.5, 114.8, 55.5, 48.6, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_3$ $[M+H]^+$: 262.1438; found 262.1434.

N-Cyclohexyl-2-(2-methoxyphenyl)-2-oxoacetamide (**2o**): White solid, m.p. 80 – 81 °C, 40.6 mg, 91% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.50 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H), 7.02 (td, *J* = 7.5, 0.8 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.50 (s, 1H), 3.89 – 3.79 (m, 4H), 1.99 (dd, *J* = 12.4, 3.3 Hz, 2H), 1.80 – 1.70 (m, 2H), 1.68 – 1.59 (m, 1H), 1.45 – 1.35 (m, 2H), 1.33 – 1.19 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 191.9, 162.3, 159.6, 134.6, 131.3, 124.8, 120.8, 112.1, 56.2, 48.5, 32.8, 25.6, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_3$ $[M+H]^+$: 262.1438; found 262.1433.

N-Cyclohexyl-2-(4-hydroxy-3-methoxyphenyl)-2-oxoacetamide (**2p**): Light yellow oil, 39.2 mg, 83% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.5 Hz, 1H), 8.01 (s, 1H), 7.01 (d, *J* = 6.6 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.19 (s, 1H), 3.96 (s, 3H), 3.87 – 3.76 (m, 1H), 1.98 (ddd, *J* = 7.5, 3.4, 1.2 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.64 – 1.61 (m, 1H), 1.43 – 1.36 (m, 2H), 1.24 (dt, *J* = 15.7, 12.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 185.7, 161.5, 151.9, 146.3, 127.7, 126.3, 114.3, 113.1, 56.2, 48.5, 32.8, 25.5, 24.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{20}NO_4$ $[M+H]^+$: 248.1387; found 248.1381.

N-Cyclohexyl-2-oxo-2-(thiophen-2-yl)acetamide (***2q***): Light yellow solid, m.p. 100 – 101 °C, 34.3 mg, 86% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 3.0 Hz, 1H), 7.82 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.18 (dd, *J* = 4.8, 4.1 Hz, 2H), 3.96 – 3.59 (m, 1H), 1.96 (dd, *J* = 12.4, 3.1 Hz, 2H), 1.78 – 1.73 (m, 2H), 1.66 – 1.62 (m, 1H), 1.44 – 1.35 (m, 2H), 1.32 – 1.19 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.8, 159.9, 138.8, 138.1, 136.8, 128.2, 48.8, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}NO_2S$ 238.0896; found 238.0891.

*N-Cyclohexyl-2-oxo-2-(thiophen-3-yl)acetamide (**2r**)*: Light yellow solid, m.p. 79 – 80°C, 34.3 mg, 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (dt, *J* = 2.8, 1.3 Hz, 1H), 7.76 (dt, *J* = 5.1, 1.3 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.14 (s, 1H), 3.85 – 3.77 (m, 1H), 1.95 (d, *J* = 12.3 Hz, 2H), 1.78 – 1.72 (m, 2H), 1.64 (dd, *J* = 8.8, 4.3 Hz, 1H), 1.45 – 1.34 (m, 2H), 1.31 – 1.18 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 180.5, 160.4, 139.7, 137.3, 128.8, 125.8, 48.6, 32.8, 25.5, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}NO_2S$ 238.0896; found 238.0892.

*2-(5-Bromopyridin-3-yl)-N-cyclohexyl-2-oxoacetamide (**2s**)*: Light yellow solid, m.p. 96 – 97 °C, 32.4 mg, 61% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.45 (d, *J* = 1.1 Hz, 1H), 8.87 (d, *J* = 2.1 Hz, 1H), 8.80 (t, *J* = 1.9 Hz, 1H), 7.00 (s, 1H), 3.83 (ddd, *J* = 10.6, 8.7, 4.4 Hz, 1H), 1.97 (dd, *J* = 12.4, 3.4 Hz, 2H), 1.79 – 1.74 (m, 2H), 1.68 – 1.63 (m, 1H), 1.40 (ddd, *J* = 15.3, 9.3, 5.9 Hz, 2H), 1.33 – 1.20 (m, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 185.7, 159.4, 155.3, 150.3, 140.9, 130.5, 120.8, 48.9, 32.7, 25.4, 24.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{16}BrN_2O_2$ 311.0390; found 311.0383.

*N-Cyclohexyl-2-oxobutanamide (**2t**)*: Light yellow solid, m.p. 100 – 101 °C, 25.3 mg, 81% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (s, 1H), 3.77 – 3.67 (m, 1H), 2.94 (q, *J* = 7.3 Hz, 2H), 1.88 (dd, *J* = 12.6, 3.5 Hz, 2H), 1.75 – 1.69 (m, 2H), 1.65 – 1.58 (m, 1H), 1.41 – 1.31 (m, 2H), 1.20 (ddd, *J* = 15.4, 11.9, 3.0 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.3, 159.2, 48.4, 32.8, 30.4, 25.5, 24.8, 7.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_{18}NO_2$ 184.1332; found 184.1329.

*N-Cyclohexyl-3-methyl-2-oxobutanamide (**2u**)*: White solid, m.p. 61 – 62 °C, 26.9 mg, 80% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 1H), 3.79 – 3.69 (m, 1H), 3.61 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.90 (dd, *J* = 12.5, 3.6 Hz, 2H), 1.75 – 1.69 (m, 2H), 1.65 – 1.59 (m, 1H), 1.38 – 1.32 (m, 2H), 1.20 (ddd, *J* = 24.6, 12.3, 3.7 Hz, 3H), 1.12 (d, *J* = 0.7 Hz, 3H), 1.11 (d, *J* = 0.7 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 203.0, 158.9, 48.4, 34.0, 32.8, 25.5, 24.8, 17.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{11}H_{20}NO_2$ 198.1489; found 198.1485.

General Procedure for Papration of *N*-(Pyridin-2-yl)arylamides (3). A reaction tube vial was charged with 1 (0.17 mmol), and $Cu(OAc)_2$ (0.017 mmol), followed by addition of m-xylene (3 ml), Adding *t*-BuOK (0.51 mmol) during the stirring process. and then stirred at 120 °C for 8 h. After cooling to room temperature, the mixture was diluted with dichloromethane, purified by silica gel coiumn chromagraphy using petroleum ether/ethyl acetate (10:1) to give **3**.

*N-(Pyridin-2-yl)benzamide (**3a**)*: Light yellow solid, m.p. 73 – 75 °C, 32.4 mg, 96% yield (R = cy); 27 mg, 80% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 4.5 Hz, 1H), 7.98 – 7.88 (m, 2H), 7.83 – 7.69 (m, 1H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.10 – 6.93 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.9, 151.7, 147.8, 138.6, 134.3, 132.3, 128.8, 127.3, 119.9, 114.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{11}N_2O$ 199.0866; found 199.0862.

*2-Methoxy-N-(pyridin-2-yl)benzamide (**3b**)*: Light yellow solid, m.p. 146 – 147 °C. 27.6 mg, 71% yield (R = cy); 22.9 mg, 59% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.27 (dd, *J* = 4.9, 0.9 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.51 – 7.44 (m, 2H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.14 – 7.04 (m, 2H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.6, 160.0, 151.6, 147.8, 138.6, 135.7, 129.9, 120.0, 119.1, 118.7, 114.3, 112.4, 55.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{13}N_2O_2$ 229.0972; found 229.0968.

*2-Chloro-N-(pyridin-2-yl)benzamide (**3c**)*: White solid, m.p. 121 – 122 °C, 29.7 mg, 75% yield (R = cy); 23 mg, 58% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 7.96 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.80 – 7.72 (m, 1H), 7.70 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.36 (ddd, *J* = 7.4, 6.6, 2.2 Hz, 1H), 7.01 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.2, 151.3, 147.5, 138.7, 135.2, 131.8, 131.1, 130.5, 129.9, 127.2, 120.1, 114.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{10}ClN_2O$ 233.0476; found 233.0472.

*2-Methyl-N-(pyridin-2-yl)benzamide (**3d**)*: Yellowish-brown solid, m.p. 80 – 81 °C, 22.8 mg, 63% yield (R = cy); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 4.9 Hz, 1H), 7.90 – 7.59 (m, 3H), 7.37 (d, *J* = 4.9 Hz, 2H), 7.06 (ddd, *J* = 7.3, 5.0, 0.7 Hz, 1H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4, 151.7, 147.7, 138.5, 136.5, 136.0, 131.3, 130.5, 126.9, 126.0, 119.8, 114.2, 19.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{13}N_2O$ 213.1022; found 213.1018.

*3-Chloro-N-(pyridin-2-yl)benzamide (**3e**)*: Light yellow solid, m.p. 96 – 97 °C, 24.5 mg, 62% yield (R = cy); ^{1}H NMR (400 MHz, $CDCl_3$) δ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.38 (d, *J* = 8.3 Hz, 1H), 8.22 (s, 1H), 7.93 (t, *J* = 1.7 Hz, 1H), 7.83 – 7.71 (m, 2H), 7.54 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 6.8, 5.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.5, 151.4, 147.9, 138.7, 136.1, 135.1, 132.3, 130.1, 127.8, 125.3, 120.2, 114.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{10}ClN_2O$ 232.0481; found 232.0485.

*2-Bromo-N-(pyridin-2-yl)benzamide (**3f**)*: Light yellow solid, m.p. 96 – 97 °C, 29.3 mg, 62% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 4.0 Hz, 1H), 8.14 (t, *J* = 1.7 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.73 – 7.64 (m, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.11 (dd, *J* = 6.6, 5.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.5, 151.4, 147.4, 139.0, 136.2, 135.2, 130.7, 130.3, 125.9, 123.0, 120.2, 114.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{10}BrN_2O$ 276.9971; found 276.9975.

*3-Methyl-N-(pyridin-2-yl)benzamide (**3g**)*: Light yellow solid, m.p. 42-44 °C, 25 mg, 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.25 – 8.18 (m, 1H), 7.79 – 7.69 (m, 4H), 7.36 (d, *J* = 4.9 Hz, 3H), 7.05 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1H), 2.41 (s, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.0, 151.7, 147.7, 138.8, 138.6, 134.2, 133.0, 128.7, 128.0,

124.3, 119.9, 114.3, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{13}N_2O$ 213.1022; found 213.1019.

3-Nitro-N-(pyridin-2-yl)benzamide ***(3h)***: Light yellow solid, m.p. 85 – 87 °C, 23.2 mg, 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.79 (t, *J* = 1.8 Hz, 1H), 8.47 – 8.33 (m, 2H), 8.31 – 8.26 (m, 1H), 8.22 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.80 (td, *J* = 8.5, 1.8 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.10 (ddd, *J* = 7.3, 5.0, 0.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 151.2, 148.4, 147.8, 138.8, 136.0, 133.2, 130.1, 126.7, 122.5, 120.5, 114.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{10}N_3O_3$ 244.0717; found 244.0721.

Methyl-N-(pyridin-2-yl)benzamide ***(3i)***: White solid, m.p. 139 – 140 °C, 28.4 mg, 60% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.39 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.26 (d, *J* = 4.8 Hz, 1H), 7.87 – 7.80 (m, 2H), 7.78 – 7.70 (m, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.05 (ddd, *J* = 7.3, 4.9, 0.8 Hz, 1H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 151.7, 147.8, 142.9, 138.5, 131.4, 129.5, 127.3, 119.8, 114.2, 21.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{13}N_2O$ 213.1022; found 213.1019.

N-(Pyridin-2-yl)thiophene-3-carboxamide ***(3j)***: m.p. 90 – 91 °C, 27.1 mg, 78% yield (R = cy); 21.8 mg, 63% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 4.9 Hz, 1H), 8.11 – 8.04 (m, 1H), 7.80 – 7.71 (m, 1H), 7.56 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.40 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.07 (dd, *J* = 6.9, 5.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.1, 151.5, 147.6, 138.7, 137.3, 129.6, 127.0, 126.3, 119.9, 114.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_9N_2OS$ 205.0430; found 205.0428.

N-(Pyridin-2-yl)thiophene-2-carboxamide ***(3k)***: Light yellow solid, m.p. 110 – 111 °C, 26.8 mg, 77% yield (R = cy); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.29 – 8.26 (m, 1H), 7.80 – 7.71 (m, 1H), 7.69 (dd, *J* = 3.8, 0.6 Hz, 1H), 7.58 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.06 (ddd, *J* = 7.3, 4.9, 0.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 151.3, 147.8, 138.9, 138.6, 131.6, 129.0, 128.0, 119.9, 114.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_9N_2OS$ 205.0430; found 205.0428.

5-Methyl-N-(pyridin-2-yl)furan-2-carboxamide ***(3l)***: Light yellow solid, m.p. 93 – 94 °C, 26.1 mg, 76% yield (R = cy); 20.3 mg, 59% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.35 – 8.29 (m, 2H), 7.73 (t, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 3.4 Hz, 1H), 7.05 (dd, *J* = 6.9, 5.4 Hz, 1H), 6.17 (d, *J* = 3.3 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.2, 155.6, 151.2, 147.8, 145.7, 138.5, 119.7, 117.2, 114.1, 109.2, 13.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{11}H_{11}N_2O_2$ 203.0815; found 203.0813.

5-Bromo-N-(pyridin-2-yl)nicotinamide ***(3m)***: Light yellow solid, m.p. 181 – 182 °C, 20.6 mg, 55% yield (R = cy); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 9.07 (s, 1H), 8.86 (s, 1H), 8.40 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 8.24 (d, *J* = 4.0 Hz, 1H), 7.80 (t, *J* = 7.2 Hz, 1H), 7.12 (dd, *J* = 6.7, 5.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 154.0, 150.9, 147.7, 146.3, 139.0, 138.0, 131.4, 121.1, 120.7, 114.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{11}H_9BrN_3O$ 277.9924; found 277.9927.

N-(pyridin-2-yl)propionamide ***(3n)***: White solid, m.p. 64 – 65 °C, 16.5 mg, 65% yield (R = Cy); 14.5 mg, 57% yield (R = *t*Bu); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.26 (dd, *J* = 6.8, 4.1 Hz, 2H), 7.72 (t, *J* = 8.5 Hz, 1H), 7.08 – 7.00 (m, 1H), 2.44 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 151.8, 147.5, 138.6, 119.6, 114.4, 30.7, 9.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_8H_9N_2O$ 151.0866; found 151.0870.

N-(tert-Butyl)-2-oxo-2-phenylacetamide ***(5a)***: White solid, m.p. 37 – 38°C, 33.2 mg, 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 – 8.25 (m, 2H), 7.62 – 7.53 (m, 1H), 7.49 – 7.39 (m, 2H), 6.94 (s, 1H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.7, 161.3, 134.3, 133.5, 131.3, 128.5, 51.8, 28.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}NO_2$ 206.1176; found 206.1172.

N-(tert-Butyl)-2-(4-chlorophenyl)-2-oxoacetamide ***(5b)***: Yellow solid, m.p. 51 – 52 °C, 39.6 mg, 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 6.96 (s, 1H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.2, 160.8, 141.0, 132.9, 131.8, 128.9, 51.8, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}ClNO_2$ 240.0786; found 240.0783.

N-(tert-Butyl)-2-(2-chlorophenyl)-2-oxoacetamide ***(5c)****:* Yellow solid, m.p. 64 – 65°C, 33 mg, 81% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 1H), 7.46 – 7.40 (m, 2H), 7.37 – 7.32 (m, 1H), 6.82 (s, 1H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 191.4, 160.1, 134.4, 132.9, 131.2, 130.4, 126.6, 51.9, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}ClNO_2$ 240.0786; found 240.0785.

N-(tert-Butyl)-2-(4-fluorophenyl)-2-oxoacetamide ***(5d)***: Yellow solid, m.p. 59 – 60°C, 36.2 mg, 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (dd, *J* = 9.0, 5.6 Hz, 2H), 7.10 (dd, *J* = 9.0, 8.5 Hz, 2H), 6.98 (s, 1H), 1.43 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.8, 166.5 (d, *J* = 257.0 Hz), 161.0, 134.3 (d, *J* = 9.5 Hz), 129.9, 115.7 (d, *J* = 21.7 Hz), 51.8, 28.4; ^{19}F{^{1}H}NMR (476MHz, $CDCl_3$) δ -102.61 (s); HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}FNO_2$ 224.1081; found 224.1079.

2-(4-Bromophenyl)-N-(tert-butyl)-2-oxoacetamide ***(5e)***: Light yellow solid, m.p. 40 – 41 °C, 41.6 mg, 86% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 6.94 (s, 1H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.4, 160.7, 132.9, 132.2, 131.8, 129.9, 51.8, 28.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}BrNO_2$ 284.0281; found 284.0274.

2-(3-Bromophenyl)-N-(tert-butyl)-2-oxoacetamide ***(5f)***: Light yellow oil, 41.2 mg, 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 – 8.42 (m, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 6.95 (s, 1H), 1.43 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.1, 160.5, 137.1, 135.1, 134.0, 130.0, 129.9, 122.6, 51.9, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}NO_2Br$ 284.0281; found 284.0275.

N-(tert-Butyl)-2-(3-nitrophenyl)-2-oxoacetamide ***(5g)***: Light yellow oil, 34.9 mg, 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 – 9.11 (t, 1H), 8.66 (tt, *J* = 7.8, 1.3 Hz, 1H), 8.42 (m, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 1.45 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.3, 159.9, 148.2, 137.0, 134.7, 129.7, 128.2, 126.2, 52.1, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}O_4N_2$ 251.1026; found 251.1022.

*N-(tert-Butyl)-2-oxo-2-(thiophen-2-yl)acetamide (**5h**)*: Yellow oil, 29.1 mg, 81% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.81 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.25 (s, 1H), 7.16 (dd, *J* = 4.9, 4.0 Hz, 1H), 1.45 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 179.2, 160.0, 138.6, 137.9, 136.2, 128.0, 51.5, 28.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_{14}O_2NS$ 212.0740; found 212.0737.

*N-(tert-Butyl)-2-oxo-2-(thiophen-3-yl)acetamide (**5i**)*: Yellow solid, m.p. 35 – 36 °C, 27.7 mg, 77% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.21 – 8.91 (m, 1H), 7.73 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.32 – 7.23 (m, 1H), 7.12 (s, 1H), 1.42 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 181.1, 160.6, 139.4, 137.1, 128.9, 125.6, 51.5, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_{14}O_2NS$ 212.0740; found 212.0735.

*N-(tert-Butyl)-2-(furan-2-yl)-2-oxoacetamide (**5j**)*: Yellow oil, 31.2 mg, 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.15 (m, 1H), 7.75 (d, *J* = 0.9 Hz, 1H), 7.16 (s, 1H), 6.62 (dd, *J* = 3.6, 1.6 Hz, 1H), 1.44 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.6, 159.3, 149.5, 149.2, 126.8, 113.1, 51.6, 28.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_{14}NO_3$ 196.0968; found 196.0966.

*2-(4-Chlorophenyl)-N-(4-methoxyphenyl)-2-oxoacetamide (**5k**)*: Yellow solid, m.p. 110 – 111°C, 32.5 mg, 66% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.41 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.6 Hz, 2H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.3, 158.4, 157.3, 141.5, 133.0, 131.6, 129.7, 129.0, 121.6, 114.5, 55.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{13}ClNO_3$ 290.0579; found 290.0573.

*2-(3-Chlorophenyl)-N-(4-methoxyphenyl)-2-oxoacetamide (**5l**)*: Yellow solid, m.p. 132 – 133 °C, 29.6 mg, 60% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.41 (s, 1H), 8.34 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 8.9 Hz, 3H), 7.45 (t, *J* = 7.9 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 2H), 3.82 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.4, 158.1, 157.3, 134.9, 134.7, 134.6, 131.4, 130.0, 129.7, 129.6, 121.6, 114.5, 55.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{13}ClNO_3$ 290.0579; found 290.0574.

*2-(3-Methoxyphenyl)-N-(4-methoxyphenyl)-2-oxoacetamide (**5m**)*: Yellow solid, m.p. 78 – 79 °C, 30.6 mg, 63% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.91 (s, 1H), 7.61 (d, *J* = 8.9 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.4, 159.7, 158.8, 157.2, 134.4, 129.9, 129.7, 124.5, 121.71, 121.66, 115.1, 114.5, 55.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{16}O_4N$ 286.1074; found 286.1068.

*2-(2-Methoxyphenyl)-N-(4-methoxyphenyl)-2-oxoacetamide (**5n**)*: White solid, m.p. 127 – 128 °C, 28.6 mg, 59% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.61 – 7.57 (d, 2H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.93 – 6.88 (d, 2H), 3.85 (s, 3H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 191.6, 159.73, 159.67, 157.0, 134.7, 131.3, 130.2, 124.5, 121.5, 120.8, 114.4, 112.1, 56.3, 55.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{16}O_4N$ 286.1074; found 286.1068.

■ ASSOCIATED CONTENT

Supporting Information

Details for the optimization of reaction conditions, the structures of known substrates in our previous work, mechanistic studies, anti-TMV activity, as well as the copies of spectral data for all the compounds. 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 interests.

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