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I_2/KI-Mediated Oxidative N−N Bond Formation for the Synthesis of 1,5-Fused 1,2,4-Triazoles from *N*-Aryl Amidines

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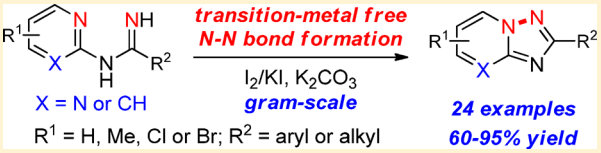
Supporting Information

ABSTRACT: An I_2/KI-mediated oxidative N−N bond formation reaction is described. This new and environmentally benign approach allows for the convenient synthesis of a variety of 1,2,4-triazolo[1,5-*a*]pyridines and other 1,5-fused 1,2,4-triazoles from readily available *N*-aryl amidines in an efficient and scalable fashion.



1. INTRODUCTION

Owing to the numerous advantages associated with this eco-friendly element, molecular iodine plays an important role in organic synthesis.[1] As a catalyst, iodine has been extensively used in transformations, such as esterification, deprotection, Michael addition, and aldol reaction. It can also mediate iodocyclization, domino, and one-pot multicomponent reactions. More importantly, a number of oxidation reactions can be achieved by using iodine, for example, conversion of alcohols/aldehydes to esters, nitriles, or amides,[1b] selective oxidation of alcohols to aldehydes and ketones,[2] and oxidative aromatization.[1e] In particular, this environmentally benign oxidizing reagent has been successfully employed to construct C−C, C−N, C−O, and also C−S bonds.[1h] However, to the best of our knowledge, there is no report of I_2-mediated N−N bond formation reactions. Encouraged by our previous work,[3] in this paper, we envisioned the construction of N−N bonds by employing molecular iodine to synthesize the biologically important 1,2,4-triazole-fused heterocycles.[4]

Oxidative cyclization of *N*-(2-pyridyl) amidines is one of the most straightforward strategies for the construction of the 1,2,4-triazolo[1,5-*a*]pyridine framework, which previously has been achieved by utilizing oxidants, such as NaClO/base,[5] $Pb(OAc)_4$,[6] and MnO_2.[7] Nevertheless, these methods are associated with some disadvantages, including low yields and limited scopes. In 2009, Ueda and Nagasawa[8] reported a copper-catalyzed tandem addition−oxidative cyclization of 2-amino pyridines and aryl nitriles to 2-aryl-1,2,4-triazolo[1,5-*a*]pyridines. Alternatively, Zhao and co-workers[9] developed a recyclable Cu−Zn/Al−Ti catalyst for the same transformation. In 2014, Du, Zhao, and co-workers[10] reported a PIFA-mediated cyclization of *N*-(pyridin-2-yl) amidines to 2-aryl/2-alkyl triazolopyridines. Recently, Bartels, Fantasia, and co-workers[11] described a Cu-catalyzed aerobic oxidation of guanidylpyridines to the ones bearing 2-amino groups. Despite these elegant achievements made, it is still of importance to develop novel and general approaches to access this compound class. Herein, we disclose a new and efficient I_2/KI-mediated methodology for the synthesis of both 2-aryl and 2-alkyl substituted 1,2,4-triazolo[1,5-*a*]pyridines, as well as their pyrazido- and pyrimidotriazole derivatives, from *N*-aryl amidines.

2. RESULTS AND DISCUSSION

The required substrates *N*-aryl amidines **2** were readily prepared via the addition reaction of corresponding aryl amines to substituted nitriles.[8,10,11] Initial screening of a series of laboratory commonly used solvents suggested that dimethyl sulfoxide (DMSO) is the most suitable one for the I_2-mediated oxidative cyclization of substrates **2** to the fused [1,5-*a*]1,2,4-triazoles **1** in the presence of base (e.g., K_2CO_3). As shown in Table 1, full consumption of benzimidamide **2a** required 2.2 equiv of iodine, affording the expected product **1a** and its 6-iodinated derivative **1a′** (confirmed by X-ray; see the Supporting Information) in 52% and 47% yields, respectively (entry 1). When a methyl group was incorporated to the 5-position of the pyridine ring in the substrate, 1.5 equiv of iodine was enough for the complete conversion of **2b** to product **1b**, but still only in moderate yield with some unidentified byproducts formed (entry 2). The reaction also worked with weaker base (e.g., $NaHCO_3$), which, however, slowed down the reaction rate and decreased the yield (entry 3). During the optimization of the reaction conditions, we were pleased to observe that adding a catalytic amount of potassium iodide (KI) to the reaction system is favorable for the formation of product **1b** (entry 4). When a stoichiometric amount of KI was used, the yield was significantly increased up to 92% (entry 5). On this basis, lowering the temperature slowed down the reaction rate with no improvement in the yield (entry 6). Then, we started to investigate if KI would favor the formation of **1a** from substrate **2a**. In the presence of 1 equiv of KI, complete cyclization of **2a** needed only 1.2 equiv of iodine. The desired product **1a** was produced in an improved yield (79%), with less

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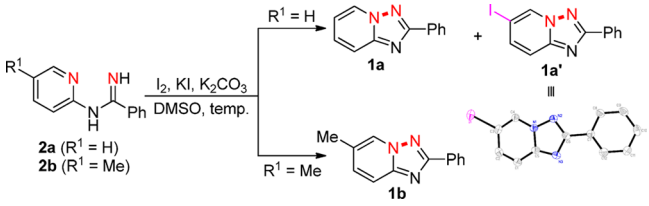
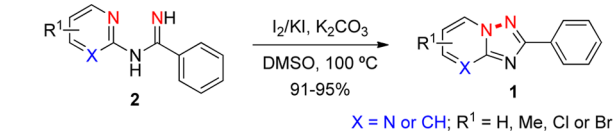
Table 1. Reaction Conditions Optimization for the Oxidative Cyclization of *N*-Aryl Amidines 2[a]

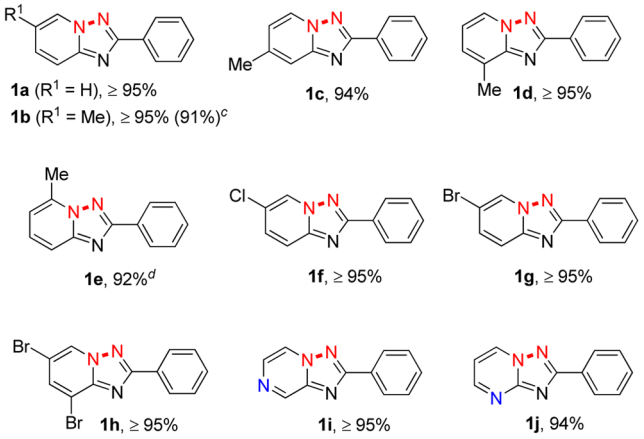


entry	substrate	I_2/equiv	KI/equiv	temp/°C	time/h	product, yield[b]
1	**2a**	2.2		100	1	**1a**, 52%
						1a′, 47%
2	**2b**	1.5		100	1	**1b**, 57%
3[c]	**2b**	1.5		100	12	**1b**, 43%
4	**2b**	1.5	0.2	100	1	**1b**, 69%
5	**2b**	1.5	1	100	0.5	**1b**, 92%
6	**2b**	1.5	1	80	3.5	**1b**, 90%
7	**2a**	1.2	1	100	1	**1a**, 79%
						1a′, 20%
8	**2a**	1.2	5	100	2	**1a**, ≥95%
						1a′, trace
9	**2a**	1.2	1.5	100	1	**1a**, ≥95%
10	**2b**	1.2	1.5	100	1	**1b**, ≥95%

[a]Optimal reaction conditions (entries 9–10): A well-stirred mixture of I_2 (0.6 mmol) and KI (0.75 mmol) in DMSO (5 mL) was treated with substrate **2** (0.5 mmol), followed by the addition of K_2CO_3 (1.5 mmol), and then heated to 100 °C for 1 h. [b]Isolated yields. [c]The same amount of $NaHCO_3$ was used instead of K_2CO_3.

Scheme 1. Substrate Scope for the Synthesis of 2-Phenyl Fused [1,5-*a*]1,2,4-Triazoles 1[a,b]





[a]Optimal reaction conditions: A well-stirred mixture of I_2 (0.6 mmol) and KI (0.75 mmol) in DMSO (5 mL) was treated with substrate **2** (0.5 mmol), followed by the addition of K_2CO_3 (1.5 mmol), and then heated to 100 °C for 1 h. [b]Isolated yields. [c]Yield of gram-scale reaction (6 mmol) in parentheses. [d]The reaction time was 1.5 h.

byproduct **1a′** formed (20%, entry 7). Increasing the dosage of potassium iodide to 5 equiv resulted in the formation of **1a** in excellent yield with only a trace amount of **1a′** observed (entry 8). Nevertheless, excessive KI has a negative impact on the conversion rate (entry 8), as it is also a byproduct formed during this oxidative cyclization process. In view of the above results, we assume that I_2 and KI may form a complex (e.g., KI_3),[2,12] which can mediate this oxidative cyclization process more efficiently. On the basis of this hypothesis, we further optimized the experimental protocol by adding the substrates (**2a** or **2b**) to a well-stirred mixture of I_2 (1.2 equiv) and KI (1.5 equiv) in DMSO. To our delight, both the reactions finished within 1 h and afforded the desired product in excellent yields (entries 9–10). It is noteworthy that this oxidative cyclization reaction is insensitive to air and moisture. Taking substrate **2b** as an example, it was safely conducted on a gram scale (Scheme 1).

Then, a range of *N*-aryl benzimidamides **2** were subjected to the above optimal cyclization conditions to probe the reaction scope and generality (Scheme 1). All the substrates with methyl groups at the different positions of the pyridyl moiety (**2b–e**) were efficiently converted to the corresponding 2-phenyl-1,2,4-triazolo[1,5-*a*]pyridines (**1b–e**). The steric block effect of the 6-methyl group in **2e** could be responsible for the slightly decreased yield of the product (**1e**), and the completeness of this transformation also required a relatively longer reaction time. Substrates bearing electron-withdrawing groups on the pyridine rings (**2f–h**) were also cyclized to the desired products **1f–h**. Additionally, pyrazido- (**1i**) and pyrimidotriazoles (**1j**) were prepared via the oxidative cyclization of *N*-pyrazyl (**2i**) and *N*-pyrimidyl substituted benzimidamides (**2j**), respectively, in good yields.

In light of these encouraging results, we initiated further studies by replacing the phenyl moiety in substrate **2b** with a variety of aromatic and aliphatic substituents (R^2, Scheme 2). When R^2 is an aryl group, this methodology is compatible with both electron-donating and electron-withdrawing groups at *para*-, *meta*-, and *ortho*-positions of the benzene ring (**1k–t**). Even the nitro-group-bearing substrate **2o** was smoothly transformed into the desired 1,2,4-triazolo[1,5-*a*]pyridine **1o** under the optimal reaction conditions. *Ortho*-substitution on the 2-phenyl moiety did not affect either the reaction rate or the yields of the products (**1r–u**). The 2,6-dichlorophenyl substrate (**2u**) was completely cyclized to the expected product **1t** within 1 h in excellent yield, of which the structure is further confirmed by X-ray crystallography (see the Supporting Information). Moreover, 2-pyridyl triazolopyridine (**1v**) was obtained in decent yield from isonicotinimidamide **2v**. This protocol is also amenable to the amidines formed from aliphatic nitriles (R^2CN); however, the presence of α-hydrogens of the R^2 group may prevent the generation of the desired product, as illustrated in the case of **2w** to **1w**. On the other hand, compound **2x** and **2y** were successfully converted into the target products **1x–y**. Noticeably, the sensitive cyclopropane ring in substrate **2x** was untouched under the present cyclization conditions.

A plausible mechanism for the oxidative cyclization process of *N*-aryl amidines **2** is proposed (Scheme 3). Taking the formation of **1a** as an example, the base-promoted oxidative iodination of substrate **2a** gives an iodide intermediate **A** (path a). Then, the N–I bond in iodide **A** cleaves, and consequently, an ammonium ion **B** is generated via an S_N2'-type cyclization of **A** with a new N–N bond formed. Finally, the subsequent deprotonation and rearomatization afford the 1,2,4-triazolo[1,5-*a*]pyridine framework **1a**. To investigate the formation of the

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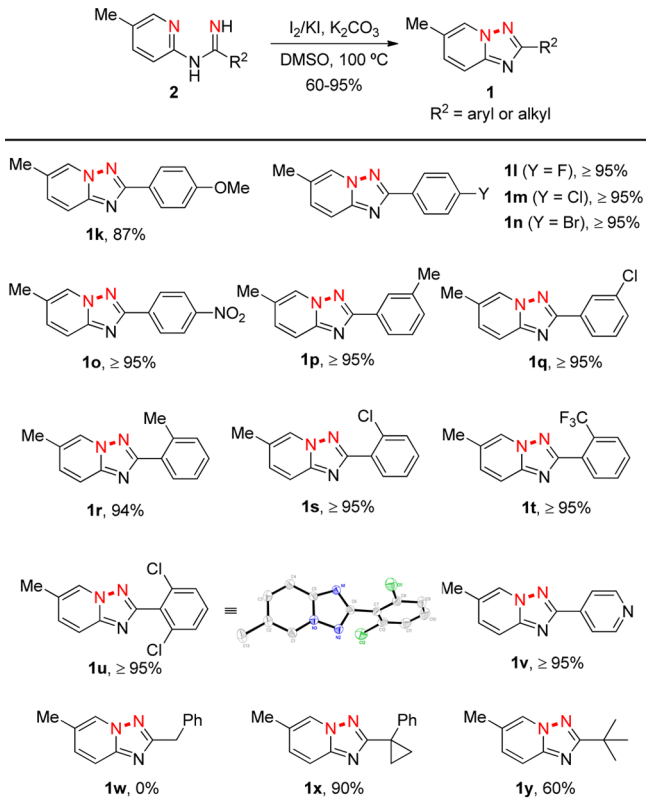
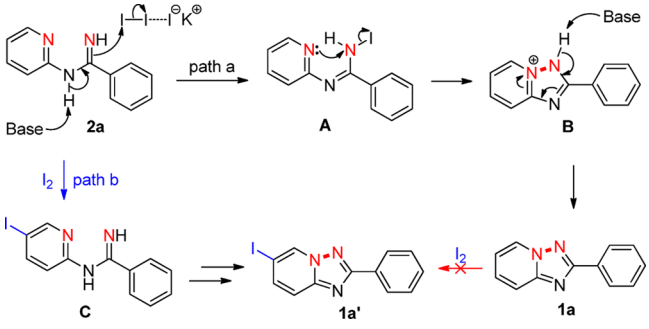
Scheme 2. Substrate Scope for the Synthesis of 2-Substituted 1,2,4-Triazolo[1,5-*a*]pyridines 1[a,b]



[a]Optimal reaction conditions: A well-stirred mixture of I_2 (0.6 mmol) and KI (0.75 mmol) in DMSO (5 mL) was treated with substrate **2** (0.5 mmol), followed by the addition of K_2CO_3 (1.5 mmol), and then heated to 100 °C for 1 h. [b]Isolated yields.

Scheme 3. Proposed Mechanism for the Formation of 1a and 1a′



iodinated byproduct **1a′**, a control experiment was conducted by further treating **1a** with iodine in the presence of K_2CO_3 in DMSO at 100 °C. It turned out that no reaction occurred at all under the above reaction conditions. This result demonstrated that the formation of **1a′** did not undergo **1a** and the iodination on the pyridine ring should take place before the cyclization process (path b). When KI was added to the reaction system, it will complex with I_2 to form KI_3,[2,12] which can mediate the oxidative cyclization of substrate **2a** to the desired product **1a** (path a) more efficiently than free molecular iodine by diminishing the iodination (path b) and other side reactions.

3. CONCLUSIONS

In summary, for the first time, an I_2-mediated oxidative N−N bond formation reaction has been developed for the synthesis of 1,5-fused 1,2,4-triazoles. Addition of KI to the reaction system successfully suppressed the iodination and other side reactions. This facile and transition-metal-free synthetic process works well with a wide range of *N*-aryl substituted amidines and can be safely conducted on a gram scale. The features such as generality, high efficiency, short reaction time, and air- and moisture-insensitive reaction conditions make the present method an attractive alternative for the preparation of 1,2,4-triazolo[1,5-*a*]pyridines and other fused 1,2,4-triazole derivatives.

4. EXPERIMENTAL SECTION

4.1. General Information. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz (100 MHz for ^{13}C NMR) spectrometer. Chemical shift values are given in ppm (parts per million) with tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants (*J*) are reported in hertz (Hz). Melting points were determined on a micromelting point apparatus without corrections. High-resolution mass spectra (HRMS-ESI) were obtained on a Q-TOF mass spectrometer. For the preparation of substrates **2**, analytical grade reagents *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were dried over activated MS 4 Å prior to use; for the oxidative cyclization of **2** to **1**, analytical grade reagent DMSO was used without further treatment. Flash column chromatography was performed over silica gel 200−300 mesh, and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE).

4.2. Preparation of Substrates 2. *4.2.1. General Procedure A.*[8] A solution of substituted 2-aminopyridine (10 mmol) in DMF (5 mL) was treated with NaH (60% dispersion in mineral oil, 0.6 g, 15 mmol) at 0 °C and stirred at the same temperature for 30 min. The corresponding nitrile (R^2CN, 15 mmol) was then added to the reaction mixture, which was stirred at room temperature until TLC indicated the total consumption of the substituted 2-aminopyridine. The reaction was quenched with 5% aqueous $NaHCO_3$ (20 mL) and extracted with EA (3 × 30 mL). The combined organic layers was washed with brine (40 mL), dried over Na_2SO_4, concentrated, and then purified through silica gel column chromatography using a mixture of EA and PE as the eluent enriched with 1% of triethylamine to afford substrates **2a−g**, **2m−n**, **2q**, and **2s**.

4.2.2. General Procedure B.[10] The nitrile (R^2CN, 15 mmol) was taken in a dry sealed tube, to which was added substituted 2-aminopyridine (10 mmol) under a stream of nitrogen. The contents in the sealed tube were stirred at 90 °C for 30 min. The above mixture was treated with $SnCl_4$ (1.76 mL, 15 mmol) and heated to 110 °C for 5 h. After cooling to room temperature, the resulting solid was crushed into powder and dissolved in hot water. The aqueous suspension was made alkaline (pH > 11) with 2 M aqueous NaOH and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography using a mixture of EA and PE as the eluent enriched with 1% of triethylamine to afford substrates **2h**, **2k−l**, **2o−p**, **2r**, and **2t−y**.

4.2.3. General Procedure C.[11] Under a stream of nitrogen, potassium *tert*-butoxide (2.47 g, 22 mmol) was added to a well-stirred solution of 2-pyrazineamine (or 2-pyrimidineamine, 0.95 g, 10 mmol) in anhydrous DMSO (5 mL). After the mixture was stirred at room temperature for 15 min, benzonitrile (2.06 g, 20 mmol) was added dropwise to the above mixture. The reaction mixture was stirred at room temperature for another 30 min and then heated to 50 °C until TLC indicated the total consumption of the aryl amine. After cooling to room temperature, the reaction was quenched with cold water (20 mL), and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic

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layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography using a mixture of EA and PE as the eluent enriched with 1% of triethylamine to afford substrates **2i**–**j**.

*N-(Pyridin-2-yl)benzimidamide (**2a**).* Following General Procedure A, **2a** was obtained as a white solid: yield 1.44 g, 73%; mp 96–97 °C (lit.[8] mp 96–97 °C); R_f = 0.24 (EA/PE 20:80); ^{1}H NMR (400 MHz, CD_3OD) δ 8.34 (dd, J = 5.2, 1.6 Hz, 1H), 7.87–7.85 (m, 2H), 7.73–7.69 (m, 1H), 7.52–7.45 (m, 3H), 7.16 (d, J = 8.0 Hz, 1H), 7.01–6.98 (m, 1H); ^{13}C NMR (400 MHz, CD_3OD) δ 162.3, 161.4, 146.0, 137.6, 136.9, 130.4, 128.1, 127.2, 120.2, 117.8; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{12}N_3$ 198.1026, found 198.1030.

*N-(5-Methylpyridin-2-yl)benzimidamide (**2b**).* Following General Procedure A, **2b** was obtained as a white solid: yield 1.88 g, 89%; mp 86–87 °C (lit.[13] mp 89–90 °C); R_f = 0.24 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.15 (m, 1H), 7.91–7.89 (m, 2H), 7.48–7.43 (m, 4H), 7.20 (d, J = 8.0 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 158.4, 145.8, 138.4, 137.6, 130.4, 128.5, 127.0, 126.9, 121.9, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}N_3$ 212.1182, found 212.1188.

*N-(4-Methylpyridin-2-yl)benzimidamide (**2c**).* Following General Procedure A, **2c** was obtained as a white solid: yield 1.54 g, 73%; mp 124–125 °C (lit.[13] mp 125–126 °C); R_f = 0.23 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 5.2 Hz, 1H), 7.91 (dd, J = 7.2, 1.6 Hz, 2H), 7.45–7.44 (m, 3H), 7.12 (s, 1H), 6.77 (dd, J = 5.2, 1.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 159.0, 148.5, 145.6, 137.5, 130.4, 128.5, 126.9, 122.8, 119.2, 21.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}N_3$ 212.1182, found 212.1185.

*N-(3-Methylpyridin-2-yl)benzimidamide (**2d**).* Following General Procedure A, **2d** was obtained as a white solid: yield 1.54 g, 73%; mp 68–69 °C (lit.[13] mp 68–69 °C); R_f = 0.44 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 4.8, 1.6 Hz, 1H), 8.00–7.97 (m, 2H), 7.50–7.44 (m, 4H), 6.84 (dd, J = 7.2, 4.8 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 157.2, 143.5, 138.0, 137.5, 130.5, 130.4, 128.5, 127.0, 117.8, 18.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}N_3$ 212.1182, found 212.1187.

*N-(6-Methylpyridin-2-yl)benzimidamide (**2e**).* Following General Procedure A, **2e** was obtained as a light yellow solid: yield 1.50 g, 71%; mp 63–65 °C; R_f = 0.26 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.89 (m, 2H), 7.55 (t, J = 8.0 Hz, 1H), 7.46–7.44 (m, 3H), 7.09 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 7.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 158.9, 154.7, 137.8, 137.6, 130.4, 128.6, 126.9, 119.3, 117.2, 24.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{14}N_3$ 212.1182, found 212.1187.

*N-(5-Chloropyridin-2-yl)benzimidamide (**2f**).* Following General Procedure A, **2f** was obtained as a white solid: yield 1.11 g, 48%; mp 155–156 °C (lit.[10] mp 157–158 °C); R_f = 0.39 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 2.4 Hz, 1H), 7.91–7.89 (m, 2H), 7.59 (dd, J = 8.8, 2.8 Hz, 1H), 7.49–7.43 (m, 3H), 7.22 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 159.1, 144.4, 137.3, 137.1, 130.8, 128.6, 126.9, 125.1, 123.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{11}ClN_3$ 232.0636, found 232.0647.

*N-(5-Bromopyridin-2-yl)benzimidamide (**2g**).* Following General Procedure A, **2g** was obtained as a white solid: yield 1.44 g, 52%; mp 158–159 °C; R_f = 0.39 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 2.8 Hz, 1H), 7.91–7.89 (m, 2H), 7.72 (dd, J = 8.4, 2.4 Hz, 1H), 7.48–7.43 (m, 3H), 7.16 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 159.2, 146.7, 140.0, 137.1, 130.8, 128.6, 126.9, 124.1, 113.2; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{11}BrN_3$ 276.1031, found 276.1034.

*N-(3,5-Dibromopyridin-2-yl)benzimidamide (**2h**).* Following General Procedure B, **2h** was obtained as a white solid: yield 2.92 g, 82%; mp 125–126 °C (lit.[10] mp 128–129 °C); R_f = 0.32 (EA/PE 89:11); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (m, 1H), 8.06–8.02 (m, 3H), 7.53–7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 157.9, 145.6, 142.9, 136.4, 131.3, 128.7, 127.3, 119.1, 111.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{10}Br_2N_3$ 355.9216, found 355.9228.

*N-(Pyrazin-2-yl)benzimidamide (**2i**).* Following General Procedure C, **2i** was obtained as a white solid: yield 1.40 g, 71%; mp 160–161 °C; R_f = 0.25 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (br, s, 1H), 8.62 (d, J = 1.2 Hz, 1H), 8.22 (dd, J = 2.8, 1.6 Hz, 1H), 8.14 (d, J = 2.8 Hz, 1H), 7.96–7.93 (m, 2H), 7.51–7.45 (m, 3H), 6.22 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 158.7, 145.8, 139.7, 137.1, 136.6, 131.1, 128.7, 127.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{11}N_4$ 199.0978, found 199.0979.

*N-(Pyrimidin-2-yl)benzimidamide (**2j**).* Following General Procedure C, **2j** was obtained as a white solid: yield 1.33 g, 67%; mp 148–149 °C (lit.[14] mp 149 °C); R_f = 0.27 (EA/PE 99:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.8 Hz, 2H), 8.04–8.02 (m, 2H), 7.49–7.41 (m, 3H), 6.89 (t, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 136.3, 131.1, 128.5, 127.3, 114.6; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{11}N_4$ 199.0978, found 199.0989.

*4-Methoxy-N-(5-methylpyridin-2-yl)benzimidamide (**2k**).* Following General Procedure B, **2k** was obtained as a white solid: yield 2.08 g, 86%; mp 118–119 °C; R_f = 0.32 (EA/PE 99:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 2.4 Hz, 1H), 7.88–7.86 (m, 2H), 7.46 (dd, J = 8.4, 2.4 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.95–6.93 (m, 2H), 3.84 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 156.1, 153.2, 141.0, 133.6, 125.1, 123.7, 122.0, 117.0, 109.0, 50.6, 13.2; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{16}N_3O$ 242.1287, found 242.1296.

*4-Fluoro-N-(5-methylpyridin-2-yl)benzimidamide (**2l**).* Following General Procedure B, **2l** was obtained as a white solid: yield 1.67 g, 73%; mp 149–151 °C; R_f = 0.25 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 2.4 Hz, 1H), 7.92–7.83 (m, 2H), 7.47 (dd, J = 8.4, 2.4 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 7.13–7.09 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (d, J_{C-F} = 248.8 Hz), 160.6, 157.3, 145.8, 138.5, 133.7, 129.0 (d, J_{C-F} = 8.6 Hz), 127.2, 121.9, 115.4 (d, J_{C-F} = 21.6 Hz), 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}FN_3$ 230.1088, found 230.1093.

*4-Chloro-N-(5-methylpyridin-2-yl)benzimidamide (**2m**).* Following General Procedure A, **2m** was obtained as a white solid: yield 1.87 g, 76%; mp 167–168 °C; R_f = 0.28 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.15 (m, 1H), 7.86–7.83 (m, 2H), 7.49–7.46 (m, 1H), 7.42–7.38 (m, 2H), 7.17 (d, J = 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 157.1, 145.8, 138.5, 136.4, 136.0, 128.7, 128.3, 127.3, 122.0, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}ClN_3$ 246.0793, found 246.0795.

*4-Bromo-N-(5-methylpyridin-2-yl)benzimidamide (**2n**).* Following General Procedure A, **2n** was obtained as a white solid: yield 2.21 g, 76%; mp 172–174 °C; R_f = 0.20 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 2.0 Hz, 1H), 7.79–7.77 (m, 2H), 7.58–7.55 (m, 2H), 7.48 (dd, J = 8.0, 2.4 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 157.2, 145.8, 138.5, 136.4, 131.7, 128.5, 127.3, 124.8, 122.0, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}BrN_3$ 290.0287, found 290.0295.

*N-(5-Methylpyridin-2-yl)-4-nitrobenzimidamide (**2o**).* Following General Procedure B, **2o** was obtained as a yellow solid: yield 2.00 g, 78%; mp 147–148 °C; R_f = 0.31 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.26 (m, 2H), 8.19–8.18 (m, 1H), 8.09–8.07 (m, 2H), 7.53–7.50 (m, 1H), 7.20 (d, J = 8.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 155.9, 148.9, 145.9, 143.4, 138.7, 128.1, 128.0, 123.7, 122.3, 18.1; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}N_4O_2$ 257.1033, found 257.1039.

*3-Methyl-N-(5-methylpyridin-2-yl)benzimidamide (**2p**).* Following General Procedure B, **2p** was obtained as a white solid: yield 2.12 g, 94%; mp 54–55 °C; R_f = 0.28 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 2.4 Hz, 1H), 7.75 (s, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.47 (dd, J = 8.4, 2.4 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 158.6, 145.7, 138.4, 138.3, 137.5, 131.2, 128.4, 127.7, 127.0, 123.7, 121.9, 21.5, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{16}N_3$ 226.1339, found 226.1339.

*3-Chloro-N-(5-methylpyridin-2-yl)benzimidamide (**2q**).* Following General Procedure A, **2q** was obtained as a white solid: yield 2.21 g, 90%; mp 129–130 °C; R_f = 0.29 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 2.4 Hz, 1H), 7.93 (t, J = 1.6 Hz, 1H), 7.75 (dt, J = 7.6, 1.2 Hz, 1H), 7.48 (dd, J = 8.4, 2.4 Hz, 1H), 7.44–7.41 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 156.9, 145.8, 139.4, 138.5,

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134.6, 130.4, 129.8, 127.4, 127.3, 124.8, 122.1, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}ClN_3$ 246.0793, found 246.0806.

*2-Methyl-N-(5-methylpyridin-2-yl)benzimidamide (**2r**).* Following General Procedure B, **2r** was obtained as a white solid: yield 0.93 g, 41%; mp 121−122 °C; R_f = 0.27 (EA/PE 99:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (br, s, 1H), 8.16 (d, J = 1.6 Hz, 1H), 7.48−7.44 (m, 2H), 7.31−7.21 (m, 3H), 7.12 (d, J = 8.4 Hz, 1H), 5.51 (br, s, 1H), 2.51 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 160.6, 145.8, 138.7, 138.6, 135.6, 130.9, 129.2, 127.8, 127.3, 126.0, 121.8, 19.8, 18.1; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{16}N_3$ 226.1339, found 226.1348.

*2-Chloro-N-(5-methylpyridin-2-yl)benzimidamide (**2s**).* Following General Procedure A, **2s** was obtained as a white solid: yield 1.57 g, 64%; mp 132−133 °C; R_f = 0.20 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 1.6 Hz, 1H), 7.68 (dd, J = 5.6, 3.6 Hz, 1H), 7.47 (dd, J = 8.4, 2.4 Hz, 1H), 7.42−7.40 (m, 1H), 7.35−7.30 (m, 2H), 7.15 (d, J = 8.0 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.8, 145.7, 138.5, 137.3, 131.3, 130.44, 130.36, 130.1, 127.4, 127.1, 121.8, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{13}ClN_3$ 246.0793, found 246.0793.

*N-(5-Methylpyridin-2-yl)-2-(trifluoromethyl)benzimidamide (**2t**).* Following General Procedure B, **2t** was obtained as a white solid: yield 1.37 g, 49%; mp 162−163 °C; R_f = 0.28 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (br, s, 1H), 8.17 (d, J = 1.6 Hz, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.47 (dd, J = 8.0, 2.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 5.59 (br, s, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 158.2, 145.8, 138.5, 137.3, 132.1, 130.0, 129.2, 127.7 (q, J_{C-F} = 31.3 Hz), 127.6, 126.4 (q, J_{C-F} = 5.0 Hz), 123.9 (q, J_{C-F} = 272.4 Hz), 121.8, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{13}F_3N_3$ 280.1056, found 280.1064.

*2,6-Dichloro-N-(5-methylpyridin-2-yl)benzimidamide (**2u**).* Following General Procedure B, **2u** was obtained as a white solid: yield 2.13 g, 76%; mp 179−181 °C; R_f = 0.20 (EA/PE 20:80); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 8.4, 2.4 Hz, 1H), 7.36−7.34 (m, 2H), 7.26−7.22 (m, 1H), 7.16 (d, J = 8.4 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 155.1, 145.9, 138.5, 136.5, 133.6, 130.2, 128.2, 127.8, 121.8, 18.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{12}Cl_2N_3$ 280.0403, found 280.0403.

*N-(5-Methylpyridin-2-yl)isonicotinimidamide (**2v**).* Following General Procedure B, **2v** was obtained as a white solid: yield 1.82 g, 86%; mp 144−145 °C; R_f = 0.30 (EA/PE 99:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (d, J = 6.0 Hz, 2H), 8.22 (s, 1H), 7.97 (d, J = 5.6 Hz, 2H), 7.58 (dd, J = 8.4, 2.0 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 155.6, 150.4, 146.4, 144.2, 139.0, 127.4, 122.0, 121.7, 17.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{13}N_4$ 213.1135, found 213.1134.

*N-(5-Methylpyridin-2-yl)-2-phenylacetimidamide (**2w**).* Following General Procedure B, **2w** was obtained as a white solid: yield 1.92 g, 85%; mp 109−110 °C; R_f = 0.28 (EA/CH_3OH 83:17); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 2.4 Hz, 1H), 7.44 (dd, J = 8.4, 2.4 Hz, 1H), 7.36−7.34 (m, 4H), 7.32−7.27 (m, 1H), 7.07 (d, J = 8.0 Hz, 1H), 3.75 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 160.6, 145.7, 138.5, 136.2, 129.5, 128.9, 127.2, 126.8, 120.9, 44.9, 17.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{16}N_3$ 226.1339, found 226.1353.

*N-(5-Methylpyridin-2-yl)-1-phenylcyclopropanecarboximidamide (**2x**).* Following General Procedure B, **2x** was obtained as a colorless oil: yield 2.18 g, 87%; R_f = 0.23 (EA/PE 34:66); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, 1H), 7.47−7.45 (m, 2H), 7.39−7.33 (m, 3H), 7.30−7.25 (m, 1H), 6.97 (d, J = 8.0 Hz, 1H), 2.23 (s, 3H), 1.77−1.75 (m, 2H), 1.15−1.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.9, 145.7, 140.9, 138.3, 130.7, 128.8, 127.5, 126.1, 120.9, 30.8, 17.9, 16.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{18}N_3$ 252.1495, found 252.1496.

*N-(5-Methylpyridin-2-yl)pivalimidamide (**2y**).* Following General Procedure B, **2y** was obtained as a colorless oil: yield 0.27 g, 14%; R_f = 0.30 (EA/PE 50:50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (m, 1H), 7.42 (dd, J = 8.4, 2.4 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 2.26 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 145.7, 138.5, 126.8, 120.6, 113.4, 37.9, 28.5, 17.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{18}N_3$ 192.1495, found 192.1502.

4.3. Synthesis of Products 1. *4.3.1. Synthesis of 2-Phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1a**) and 7-Iodo-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1a′**).* A stirred solution of *N*-(pyridin-2-yl)benzimidamide (**2a**, 99 mg, 0.5 mmol) in DMSO (5.0 mL) was treated with iodine (279 mg, 1.1 mmol) and K_2CO_3 (311 mg, 2.25 mmol). The reaction mixture was heated to 100 °C for 1 h (TLC indicated that the conversion was complete). After cooling to room temperature, it was quenched with 5% $Na_2S_2O_3$ (0.5 mL), followed by the addition of brine (15 mL), and then extracted with EA (3 × 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through column chromatography using a mixture of EA and PE as the eluent to afford products **1a** (51 mg, 52%, white solid) and **1a′** (76 mg, 47%, white solid).

*7-Iodo-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1a′**).* White solid, mp 176−178 °C; R_f = 0.25 (EA/PE 10:90); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (m, 1H), 8.27−8.25 (m, 2H), 7.69 (dd, J = 9.2, 1.6 Hz, 1H), 7.55 (dd, J = 9.6, 0.8 Hz,1H), 7.51−7.48 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.3, 150.6, 137.7, 133.4, 130.3, 130.2, 128.7, 127.3, 117.2, 75.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_9N_3I$ 321.9836, found 321.9832.

*4.3.2. Synthesis of 1,2,4-Triazolo[1,5-a]pyridines **1** (General Procedure D).* A mixture of KI (125 mg, 0.75 mmol) and iodine (152 mg, 0.6 mmol) in DMSO (5 mL) was stirred at room temperature for 10 min and then treated with *N*-substituted amidine **2** (0.5 mmol), followed by the addition of K_2CO_3 (208 mg, 1.5 mmol). The reaction mixture was heated to 100 °C until TLC indicated the total consumption of the substrate **2** (1−1.5 h). After cooling to room temperature, the reaction was quenched with 5% $Na_2S_2O_3$ (0.5 mL), followed by the addition of brine (15 mL), and then extracted with EA (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography using a mixture of EA and PE as the eluent to afford the desired product **1**.

*2-Phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1a**).* Following General Procedure D, **1a** was obtained as a white solid: yield 97 mg, ≥95%; mp 134−136 °C (lit.[8] mp 134−135 °C); R_f = 0.25 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dt, J = 6.8, 1.2 Hz, 1H), 8.31−8.28 (m, 2H), 7.75 (dt, J = 8.8, 0.8 Hz, 1H), 7.52−7.46 (m, 4H), 6.99 (dt, J = 1.2, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 151.7, 130.7, 130.1, 129.5, 128.7, 128.3, 127.3, 116.4, 113.6; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{10}N_3$ 196.0869, found 196.0873.

*6-Methyl-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1b**).* Following General Procedure D, **1b** was obtained as a white solid: 0.5 mmol scale, yield 103 mg, ≥95%; 6 mmol scale, yield 1.138 g, 91%. mp 118−119 °C (lit.[15] mp 120.5−121.0 °C); R_f = 0.28 (EA/PE 17:83); ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.28−8.26 (m, 2H), 7.64 (d, J = 9.2 Hz, 1H), 7.51−7.45 (m, 3H), 7.33 (dd, J = 9.2, 1.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 150.3, 132.3, 130.9, 129.9, 128.6, 127.1, 126.3, 123.7, 115.5, 18.1; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{12}N_3$ 210.1026, found 210.1034.

*7-Methyl-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1c**).* Following General Procedure D, **1c** was obtained as a white solid: yield 98 mg, 94%; mp 141−142 °C (lit.[16] mp 140−142 °C); R_f = 0.28 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 7.2 Hz, 1H), 8.28−8.26 (m, 2H), 7.51−7.45 (m, 4H), 6.80 (dd, J = 7.2, 2.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 151.9, 141.0, 130.9, 129.9, 128.6, 127.2, 116.0, 115.0, 21.6; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{12}N_3$ 210.1026, found 210.1029.

*8-Methyl-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1d**).* Following General Procedure D, **1d** was obtained as a white solid: yield 100 mg, ≥95%; mp 96−97 °C (lit.[10] mp 100−101 °C); R_f = 0.44 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 6.8 Hz, 1H), 8.31−8.29 (m, 2H), 7.51−7.45 (m, 3H), 7.26−7.22 (m, 1H), 6.87(t, J = 6.8 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 152.2, 131.0, 129.9, 128.6, 128.1, 127.3, 127.0, 125.9, 113.4, 17.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{12}N_3$ 210.1026, found 210.1033.

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*5-Methyl-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1e**).* Following General Procedure D, **1e** was obtained as a white solid: yield 96 mg, 92%; mp 84−85 °C (lit.[17] mp 83−85 °C); R_f = 0.33 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34−8.32 (m, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.52−7.40 (m, 4H), 6.81 (dt, J = 7.2, 0.8 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 151.8, 138.9, 131.2, 129.9, 129.3, 128.6, 127.3, 113.5, 112.8, 17.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{12}N_3$ 210.1026, found 210.1025.

*6-Chloro-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1f**).* Following General Procedure D, **1f** was obtained as a white solid: yield 114 mg, ≥95%; mp 165−167 °C (lit.[10] mp 168−169 °C); R_f = 0.47 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.27−8.25 (m, 2H), 7.69 (d, J = 9.6 Hz, 1H) 7.52−7.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 150.3, 130.9, 130.34, 130.31, 128.7, 127.3, 126.6, 121.5, 116.4; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_9ClN_3$ 230.0479, found 230.0481.

*6-Bromo-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1g**).* Following General Procedure D, **1g** was obtained as a white solid: yield 136 mg, ≥95%; mp 165−167 °C (lit.[10] mp 165−166 °C); R_f = 0.32 (EA/PE 11:89); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 1.6 Hz, 1H), 8.27−8.25 (m, 2H), 7.66−7.63 (m, 1H), 7.58−7.55 (m, 1H), 7.52−7.47 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 150.4, 133.1, 130.34, 130.29, 128.8, 128.7, 127.3, 116.8, 107.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_9BrN_3$ 275.9955, found 275.9955.

*6,8-Dibromo-2-phenyl-[1,2,4]triazolo[1,5-a]pyridine (**1h**).*[10] Following General Procedure D, **1h** was obtained as a white solid: yield 176 mg, ≥95%; mp 149−151 °C; R_f = 0.32 (EA/PE 5:95); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 1.6 Hz, 1H), 8.30−8.28 (m, 2H), 7.84 (d, J = 1.6 Hz, 1H), 7.50−7.48 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 149.7, 135.0, 130.6, 129.8, 128.7, 127.9, 127.6, 110.1, 106.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_8Br_2N_3$ 353.9059, found 353.9056.

*2-Phenyl-[1,2,4]triazolo[1,5-a]pyrazine (**1i**).* Following General Procedure D, **1i** was obtained as a white solid: yield 98 mg, ≥95%; mp 179−180 °C; R_f = 0.33 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 1.2 Hz, 1H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H), 8.32−8.30 (m, 2H), 8.18 (d, J = 4.4 Hz, 1H), 7.54−7.51 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 147.3, 142.7, 131.6, 130.8, 129.8, 128.9, 127.6, 121.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_9N_4$ 197.0822, found 197.0822.

*2-Phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**1j**).* Following General Procedure D, **1j** was obtained as a white solid: yield 92 mg, 94%; mp 184−185 °C (lit.[14] mp 184 °C); R_f = 0.33 (EA/PE 50:50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, J = 6.4, 2.0 Hz, 1H), 8.80 (dd, J = 4.4, 2.0 Hz, 1H), 8.36−8.34 (m, 2H), 7.53−7.50 (m, 3H), 7.09 (dd, J = 6.8, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 156.1, 154.4, 135.5, 130.8, 130.2, 128.8, 127.5, 110.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{11}H_8N_4Na$ 219.0641, found 219.0656.

*2-(4-Methoxyphenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1k**).* Following General Procedure D, **1k** was obtained as a white solid: yield 104 mg, 87%; mp 166−167 °C; R_f = 0.26 (EA/PE 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36−8.35 (m, 1H), 8.22−8.18 (m, 2H), 7.61 (d, J = 9.2 Hz, 1H), 7.32 (dd, J = 8.8, 1.6 Hz, 1H), 7.03−6.99 (m, 2H), 3.87 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 161.0, 150.3, 132.3, 128.6, 126.2, 123.5, 123.4, 115.3, 114.0, 55.3, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{14}H_{14}N_3O$ 240.1131, found 240.1142.

*2-(4-Fluorophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1l**).* Following General Procedure D, **1l** was obtained as a white solid: yield 113 mg, ≥95%; mp 163−164 °C; R_f = 0.22 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (m, 1H), 8.27−8.22 (m, 2H), 7.62 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 9.2, 1.6 Hz, 1H), 7.19−7.14 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J_{C-F} = 247.8 Hz), 163.0, 150.3, 132.4, 129.1 (d, J_{C-F} = 8.4 Hz), 127.2 (d, J_{C-F} = 3.1 Hz), 126.3, 123.8, 115.7 (d, J_{C-F} = 21.6 Hz), 115.5, 18.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}FN_3$ 228.0932, found 228.0938.

*2-(4-Chlorophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1m**).* Following General Procedure D, **1m** was obtained as a white solid: yield 119 mg, ≥95%; mp 169−171 °C; R_f = 0.28 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.21−8.18 (m, 2H), 7.63 (d, J = 9.2 Hz, 1H), 7.46−7.44 (m, 2H), 7.35 (dd, J = 9.2, 1.6 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 150.3, 135.9, 132.5, 129.5, 128.9, 128.4, 126.3, 123.9, 115.5, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}ClN_3$ 244.0636, found 244.0644.

*2-(4-Bromophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1n**).* Following General Procedure D, **1n** was obtained as a white solid: yield 143 mg, ≥95%; mp 179−181 °C; R_f = 0.25 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.14−8.11 (m, 2H), 7.64−7.59 (m, 3H), 7.35 (dd, J = 9.2, 1.6 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 150.3, 132.5, 131.8, 130.0, 128.7, 126.3, 124.2, 123.9, 115.6, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}BrN_3$ 288.0131, found 288.0128.

*6-Methyl-2-(4-nitrophenyl)-[1,2,4]triazolo[1,5-a]pyridine (**1o**).* Following General Procedure D, **1o** was obtained as a light yellow solid: yield 126 mg, ≥95%; mp decomposed at 277−280 °C; R_f = 0.25 (EA/PE 17:83); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.89 (s, 1H), 8.45−8.37 (m, 4H), 7.84 (d, J = 8.8 Hz, 1H), 7.62 (dd, J = 9.2, 1.6 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, CF_3COOD) δ 153.3, 150.3, 141.8, 141.4, 132.5, 128.8, 128.7, 128.4, 124.5, 110.8, 16.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}N_4O_2$ 255.0876, found 255.0875.

*6-Methyl-2-(m-tolyl)-[1,2,4]triazolo[1,5-a]pyridine (**1p**).* Following General Procedure D, **1p** was obtained as a white solid: yield 111 mg, ≥95%; mp 129−131 °C; R_f = 0.27 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38−8.37 (m, 1H), 8.10 (s, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 9.2 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.33 (dd, J = 9.2, 1.6 Hz, 1H), 7.27 (d, J = 7.2 Hz, 1H), 2.45 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 150.3, 138.4, 132.4, 130.8, 130.7, 128.6, 127.8, 126.3, 124.3, 123.7, 115.5, 21.4, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{14}H_{14}N_3$ 224.1182, found 224.1182.

*2-(3-Chlorophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1q**).* Following General Procedure D, **1q** was obtained as a white solid: yield 121 mg, ≥95%; mp 153 °C; R_f = 0.31 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.28−8.27 (m, 1H), 8.17−8.12 (m, 1H), 7.64 (d, J = 8.8 Hz, 1H), 7.42−7.41 (m, 2H), 7.36 (dd, J = 9.2, 1.6 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 150.3, 134.7, 132.8, 132.6, 129.9, 129.8, 127.3, 126.3, 125.2, 124.1, 115.6, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}ClN_3$ 244.0636, found 244.0639.

*6-Methyl-2-(o-tolyl)-[1,2,4]triazolo[1,5-a]pyridine (**1r**).* Following General Procedure D, **1r** was obtained as a white solid: yield 105 mg, 94%; mp 95−96 °C; R_f = 0.35 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (m, 1H), 8.06−8.03 (m, 1H), 7.66 (d, J = 9.2 Hz, 1H), 7.36−7.30 (m, 4H), 2.70 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 144.8, 132.9, 127.4, 126.4, 125.6, 125.4, 124.5, 121.5, 121.0, 118.7, 110.8, 17.0, 13.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{14}H_{14}N_3$ 224.1182, found 224.1194.

*2-(2-Chlorophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1s**).* Following General Procedure D, **1s** was obtained as a white solid: yield 121 mg, ≥95%; mp 109−110 °C; R_f = 0.22 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.00−7.98 (m, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.55−7.52 (m, 1H), 7.39−7.37 (m, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 149.6, 133.1, 132.5, 132.0, 130.7, 130.5, 130.2, 126.7, 126.4, 124.0, 115.8, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}ClN_3$ 244.0636, found 244.0647.

*6-Methyl-2-(2-(trifluoromethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridine (**1t**).* Following General Procedure D, **1t** was obtained as a white solid: yield 138 mg, ≥95%; mp 80 °C; R_f = 0.31 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44−8.43 (m, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.65 (t, J = 7.6 Hz 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.40 (dd, J = 9.2, 2.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 149.7, 132.6, 132.3, 131.5, 130.5 (q, J_{C-F} = 2.0 Hz), 129.4, 129.2 (q, J_{C-F} = 31.4 Hz), 126.6 (q, J_{C-F} = 5.4 Hz), 126.4, 124.1, 123.8 (q, J_{C-F} = 272.1 Hz), 115.9, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{14}H_{11}F_3N_3$ 278.0899, found 278.0909.

*2-(2,6-Dichlorophenyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1u**).* Following General Procedure D, **1u** was obtained as a white solid: yield 138 mg, ≥95%; mp 171 °C; R_f = 0.28 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.73 (d, J = 9.2 Hz, 1H), 7.44−7.41 (m, 3H), 7.36−7.32 (m, 1H), 2.45 (s, 3H); ^{13}C NMR (100

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MHz, $CDCl_3$) δ 160.2, 149.8, 136.0, 132.6, 131.0, 130.9, 127.9, 126.6, 124.2, 116.1, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{10}Cl_2N_3$ 278.0246, found 278.0246.

*6-Methyl-2-(pyridin-4-yl)-[1,2,4]triazolo[1,5-a]pyridine (**1v**).* Following General Procedure D, **1v** was obtained as a white solid: yield 105 mg, ≥95%; mp 181−182 °C; R_f = 0.25 (EA/PE 67:33); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76−8.75 (m, 2H), 8.40 (s, 1H), 8.13−8.11 (m, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.40 (dd, J = 8.8, 1.6 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 150.4, 138.4, 132.9, 126.4, 124.6, 121.2, 115.9, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_{11}N_4$ 211.0978, found 211.0978.

*6-Methyl-2-(1-phenylcyclopropyl)-[1,2,4]triazolo[1,5-a]pyridine (**1x**).* Following General Procedure D, **1x** was obtained as a white solid: yield 112 mg, 90%; mp 77−78 °C; R_f = 0.25 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.22 (m, 1H), 7.52−7.49 (m, 3H), 7.38−7.34 (m, 2H), 7.30−7.24 (m, 2H), 2.33 (s, 3H), 1.71−1.68 (m, 2H), 1.41−1.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 149.8, 142.2, 132.0, 130.1, 128.4, 126.9, 126.2, 122.8, 115.0, 25.2, 18.0, 16.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{16}H_{16}N_3$ 250.1339, found 250.1341.

*2-(tert-Butyl)-6-methyl-[1,2,4]triazolo[1,5-a]pyridine (**1y**).* Following General Procedure D, **1y** was obtained as a white solid: yield 57 mg, 60%; mp 69−70 °C; R_f = 0.30 (EA/PE 17:83); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32−8.31 (m, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.30 (dd, J = 8.8, 1.6 Hz, 1H), 2.38 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 149.7, 131.9, 126.2, 122.9, 115.2, 33.2, 29.7, 18.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_{16}N_3$ 190.1339, found 190.1340.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of compounds **1** and **2**, and X-ray structures and data of compounds **1a′** and **1u** (CIF). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01183.

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Notes

The authors declare no competing financial interest.

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