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One-pot Cascade Reactions Leading to Pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo-[1,5-*a*]quinolines under Bimetallic Relay Catalysis with Air as the Oxidant

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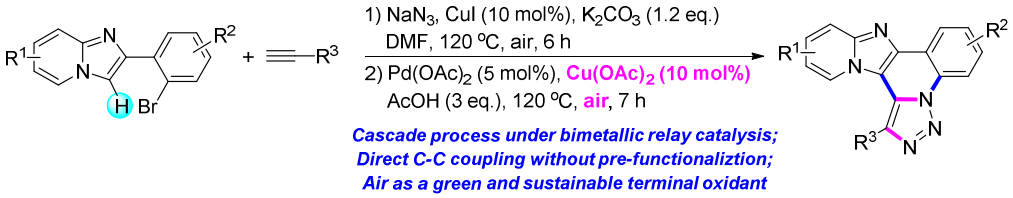


Abstract: In this paper, we report an efficient one-pot synthesis of 1,2,3-triazole/quinoline fused imidazo[1,2-*a*]pyridines starting from 2-(2-bromophenyl)imidazo[1,2-*a*]pyridines, alkynes and sodium azide. This novel method involves a one-pot bimetallic relay catalyzed cascade process combining azide−alkyne cycloaddition, C−N coupling between 1,2,3-triazole and aryl bromide, and intramolecular cross dehydrogenative C−C coupling between 1,2,3-triazole and imidazo-[1,2-*a*]pyridine. Notable features of this protocol include simple starting materials, sustainable oxidant, reduced synthetic steps, and high efficiency.

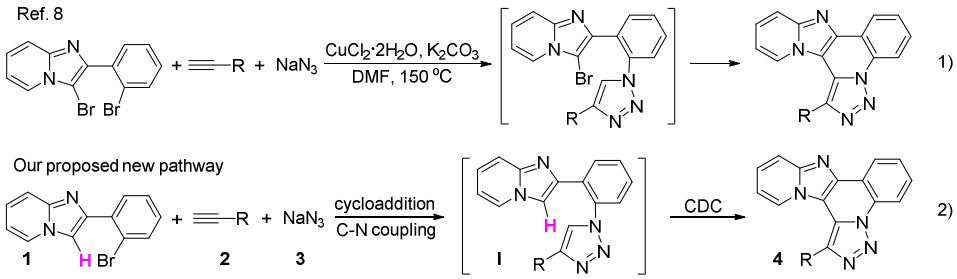
INTRODUCTION

The 1,2,3-triazole scaffold plays an important role in medicinal arena as numerous molecules bearing this framework are endowed with HIV protease inhibiting, anticancer, antituberculosis, antifungal, or antibacterial activities.[1-2] Owing to its stability toward metabolic degradation and capability of hydrogen bonding, 1,2,3-triazole is also an ideal connecting unit in drug design.[2] In a further aspect, 1,2,3-triazole derivatives are frequently used as substrates in organic synthesis[3] and material science.[4] Therefore, the search for highly efficient methods for the preparation of 1,2,3-triazole derivatives has remained as a hot topic in the past several decades.[5]

On the other hand, imidazo[1,2-*a*]pyridine constitutes a valuable skeleton of antiviral, antimicrobial, antitumor, and neuroactive pharmaceuticals.[6] As a result, continuing pursue for efficient and sustainable strategies for the preparation and derivation of imidazo[1,2-*a*]pyridine has been implemented.[7] In this regard, Kumar et al. recently reported a novel protocol for the preparation of 1,2,3-triazole/quinoline-fused imidazo[1,2-*a*]pyridines *via* copper-catalyzed cascade reactions of 3-bromo-2-(2-bromophenyl)imidazo[1,2-*a*]pyridines with alkynes and sodium azide (Scheme 1, eq. 1).[8] While this elegant synthetic method is straightforward and reliable, its use of substrates bearing a bromonated imidazo[1,2-*a*]pyridine scaffold is arguably undesirable in terms of atom economy and environmental aspects as it requires an additional bromonation step to prepare the substrates, and also results in more by-products.

The formation of C−C bond from two simple C−H bonds is highly appreciable as it does not require substrate prefunctionalisation, and holds advantages such as reduced reaction steps, low costs and less wastes.[9] Inspired by the sustainable and environmental benign nature of cross dehydrogenative coupling (CDC),[10] and as part of our continuing interest in imidazo-[1,2-*a*]pyridine derivatives,[11] we envisioned a one pot synthesis of pyrido[2',1':2,3]imidazo-

[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (**4**) from 2-(2-bromophenyl)imidazo[1,2-*a*]pyridine (**1**), alkyne (**2**) and sodium azide (**3**) *via* a cascade process combining azide-alkyne cycloaddition, C−N coupling and cross dehydrogenative C−C coupling as shown in Scheme 1, eq. 2.

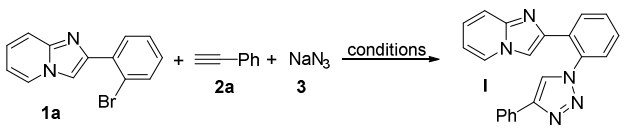


Scheme 1. Different routes leading to 1,2,3-triazole/quinoline-fused imidazo[1,2-*a*]pyridine.

RESULTS AND DISCUSSIONS

To evaluate the feasibility of our proposed synthetic pathway, 2-(2-bromophenyl)imidazo-[1,2-*a*]pyridine (**1a**), ethynylbenzene (**2a**) and sodium azide (**3**) were chosen as model substrates, and they were initially treated with $CuCl_2 \cdot 2H_2O$ and K_2CO_3 in DMF at 80 ºC for 6 h.[8] From this reaction, 2-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)phenyl)imidazo[1,2-*a*]pyridine (**I**), the proposed intermediate for the formation of **4** as shown in Scheme 1, was obtained in 60% yield (Table 1, entry 1). To improve the efficiency, different copper salts were tried (entries 2-5). Among them, CuI was the most efficient. Following studies on the effect of various bases showed that Na_2CO_3, Cs_2CO_3, $K_3PO_4 \cdot 3H_2O$ and DBU were less efficient than K_2CO_3 in promoting this reaction (entries 5-9). When DMSO, 1-methyl-2-pyrrolidinone (NMP), ethanol or CH_3CN was used as the reaction medium, the yield of **I** decreased compared with DMF (entries 5, 10-13). Raising the reaction temperature, to our delight, improved the yield of **I** obviously (entries 5, 14-16). Finally, it was found that reaction period shorter than 6 h gave lower yield (entry 15 *vs* 17). In summary of the optimization study, **I** could be obtained in 92% yield through treatment of **1a**, **2a** and **3** with CuI and K_2CO_3 in DMF at 120 ºC under air for 6 h (entry 15).

Table 1. Optimization Study for the Formation of intermediate **I** [a]



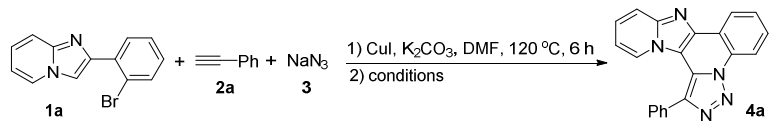
Entry	Catalyst	Base	Solvent	t/h	T/ºC	Yield (%)[b]
1	$CuCl_2·2H_2O$	K_2CO_3	DMF	6	80	60
2	$CuCl_2$	K_2CO_3	DMF	6	80	68
3	$Cu(OAc)_2$	K_2CO_3	DMF	6	80	62
4	CuCl	K_2CO_3	DMF	6	80	66
5	CuI	K_2CO_3	DMF	6	80	81
6	CuI	Na_2CO_3	DMF	6	80	67
7	CuI	Cs_2CO_3	DMF	6	80	70
8	CuI	$K_3PO_4·3H_2O$	DMF	6	80	62
9	CuI	DBU	DMF	6	80	47
10	CuI	K_2CO_3	DMSO	6	80	76
11	CuI	K_2CO_3	NMP	6	80	65
12	CuI	K_2CO_3	ethanol	6	80	58
13	CuI	K_2CO_3	CH_3CN	6	80	57
14	CuI	K_2CO_3	DMF	6	100	86
15	CuI	K_2CO_3	DMF	6	120	92
16	CuI	K_2CO_3	DMF	6	140	90
17	CuI	K_2CO_3	DMF	4	120	80

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), **3** (0.6 mmol), catalyst (0.05 mmol), base (0.6 mmol), solvent (3 mL), air. [b] Isolated yields.

With the highly efficient formation of the key intermediate **I**, we moved forward to study the one pot preparation of 1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (**4a**). Thus, the mixture of **1a**, **2a** and **3** was treated with CuI and K_2CO_3 in DMF at 120 ºC for 6 h. Then, $Pd(OAc)_2$ and $Cu(OAc)_2$ were added, and the resulting mixture was stirred at 120 ºC for 7 h. From this reaction, **4a** was successfully obtained albeit in low yield (Table 2, entry 1). To improve the efficiency, optimizations were carried out by varying the reaction parameters. As a first aspect, inspired by the fact that protonic acids have been frequently used as effective additives for metal-catalyzed C−H functionalizations,[12] we tried acetic acid as an additive for

this transformation. To our delight, addition of AcOH could indeed improve the reaction (entry 2). Gratifyingly, increases in the loading of AcOH till to 3 equiv provided a substantial increase in the yield of **4a** (entries 3-5). Although PivOH has proven to be superior to other organic acids in previous cases of C−H functionalization,[12c] replacing AcOH with PivOH did not lead any improvement in the efficiency of this reaction (entry 4 *vs* 6). In following studies, acetic acid was selected as the additive of choice due to lower cost. Furthermore, to check the effect of different catalysts, $PdCl_2$, $Pd_2(dba)_3$, and $Pd(PPh_3)_2Cl_2$ were tried, and they were found to be less effective than $Pd(OAc)_2$ in promoting this reaction (entries 4, 7-9). Other oxidant such as $Cu(OTf)_2$ was found to be inferior to $Cu(OAc)_2$ (entry 10 *vs* 4). When the reaction was run under O_2 or air in the absence of $Cu(OAc)_2$, its efficiency diminished (entries 11-12). On the other hand, when it was run under air but in the presence of 10 mol% of $Cu(OAc)_2$, the yield of **4a** was comparable with those obtained by using stoichiometric amount of $Cu(OAc)_2$ (entry 13 *vs* 4). In another control experiment, the reaction was run under N_2 in the presence of 10 mol% of $Cu(OAc)_2$. Under this circumstance, only trace amount of **4a** was formed (entry 14). These results indicated that air could act as the terminal oxidant for this CDC reaction. Arguably, this is an interesting and promising finding as in most of the previous CDC reactions stoichiometric or even excess amount of oxidants such as $Cu(OAc)_2$, AgOAc, $PhI(OAc)_2$, BQ etc. were needed.[7] Compared with those oxidants, air is obviously more advantageous, and thus offers attractive industrial prospects in terms of green and sustainable chemistry. Temperature also showed some effect on the yield of **4a**, and the optimum temperature turned out to be 120 ºC (entries 13, 15-17). Finally, it was found that doubling the amount of CuI to 20 mol%, the yield of **2a** was only 46% (entry 18), indicating that addition of Cu(II) is crucial for the CDC process.

Table 2. Optimization Study for the Formation of **4a**[a]



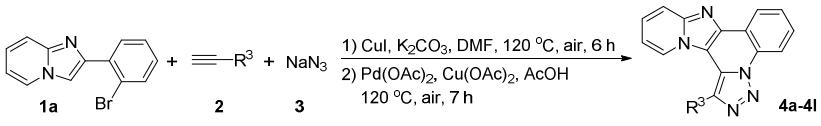
Entry	Catalyst	Oxidant (equiv)	Additive (equiv)	T/°C	Yield (%)[b]
1	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)		120	25
2	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	AcOH (1)	120	36
3	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	AcOH (2)	120	58
4	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	AcOH (3)	120	71
5	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	AcOH (4)	120	70
6	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	PivOH (3)	120	68
7	$PdCl_2$	$Cu(OAc)_2$ (1)	AcOH (3)	120	42
8	$Pd_2(dba)_3$	$Cu(OAc)_2$ (1)	AcOH (3)	120	55
9	$Pd(PPh_3)_2Cl_2$	$Cu(OAc)_2$ (1)	AcOH (3)	120	58
10	$Pd(OAc)_2$	$Cu(OTf)_2$ (1)	AcOH (3)	120	60
11	$Pd(OAc)_2$	O_2	AcOH (3)	120	42
12	$Pd(OAc)_2$		AcOH (3)	120	40
13	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.1)	AcOH (3)	120	69
14[c]	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.1)	AcOH (3)	120	trace
15	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.1)	AcOH (3)	80	58
16	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.1)	AcOH (3)	100	63
17	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.1)	AcOH (3)	130	68
18[d]	$Pd(OAc)_2$		AcOH (3)	120	46

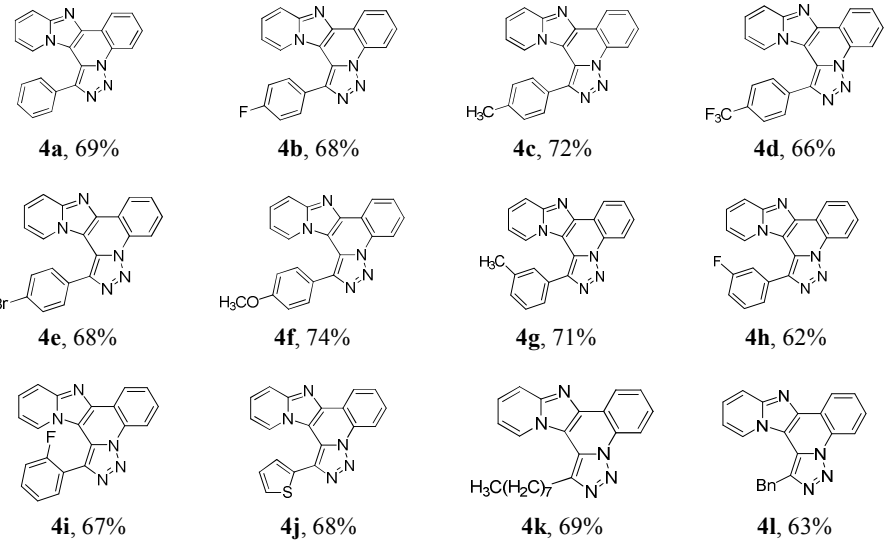
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), **3** (0.6 mmol), CuI (0.05 mmol), K_2CO_3 (0.6 mmol), DMF (3 mL), air, 120 °C, 6 h; then Pd catalyst (0.025 mmol), oxidant, additive, air, 7 h. [b] Isolated yields. [c] Under N_2. [d] 0.1 mmol of CuI were used.

Once the optimization had been performed, we next evaluated a series of substrates to determine the influence of steric and electronic parameters on the efficiency of this cascade transformation. Firstly, with **1a** and **3** as model substrates, the scope of alkynes (**2**) was explored. The results listed in Table 3 indicated that ethynylbenzenes bearing different substituents on the phenyl ring took part in this cascade process smoothly to give **4a**-**4i** in reasonably good yields. Meanwhile, various functional groups such as fluoro, bromo, methyl, methoxy and trifluoromethyl were well tolerable, and the electronic and steric nature of the substituents did

not show obvious effect on the yield of **4**. Moreover, 2-ethynylthiophene could also participate in this cascade process to give the corresponding product **4j** in moderate yield. Interestingly, in addition to aryl substituted alkynes, dec-1-yne and prop-2-ynylbenzene were found to be also suitable substrates for this transformation to afford **4k** and **4l**.

Table 3. Studies on the scope of alkynes (**2**) [a,b]





4a, 69% **4b**, 68% **4c**, 72% **4d**, 66%

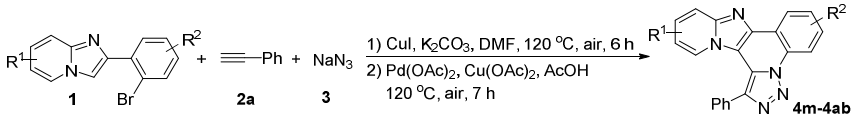
4e, 68% **4f**, 74% **4g**, 71% **4h**, 62%

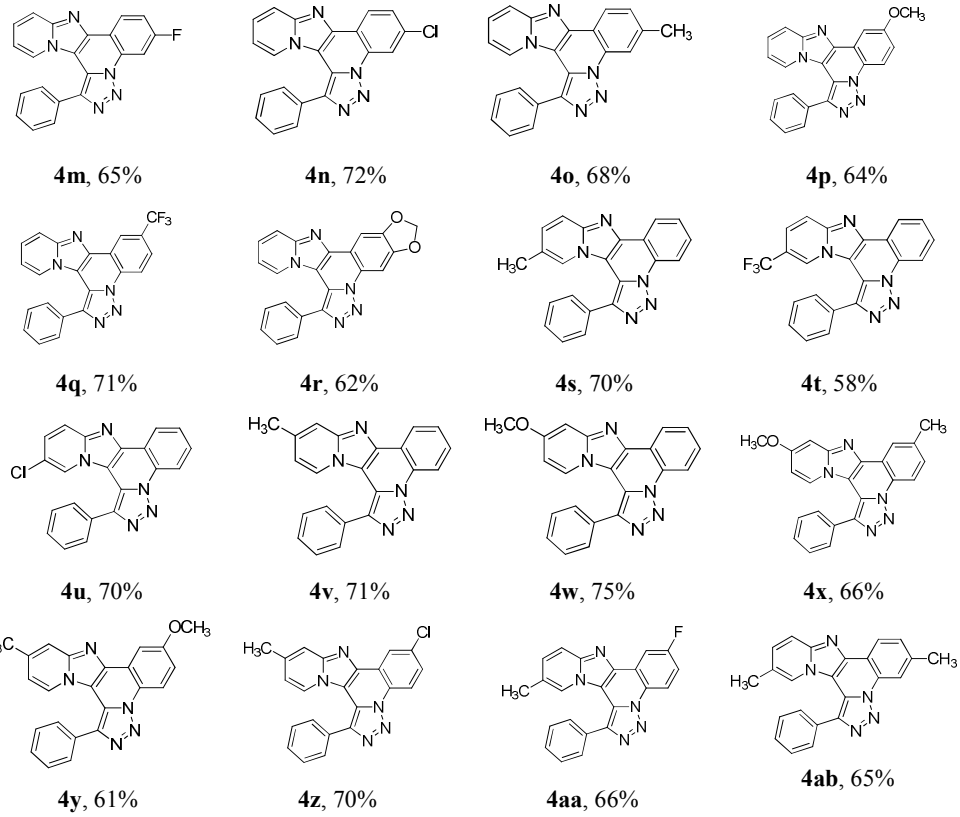
4i, 67% **4j**, 68% **4k**, 69% **4l**, 63%

[a] Conditions: **1a** (0.5 mmol), **2** (0.6 mmol), **3** (0.6 mmol), CuI (0.05 mmol), K_2CO_3 (0.6 mmol), DMF (3 mL), air, 120 ºC, 6 h; then $Pd(OAc)_2$ (0.025 mmol), $Cu(OAc)_2$ (0.05 mmol), AcOH (1.5 mmol), air, 120 ºC, 7 h. [b] Isolated yields.

Next, with **2a** and **3** as model substrates, diversely substituted 2-(2-bromophenyl)imidazo-[1,2-*a*]pyridines (**1**) were explored, and the results were included in Table 4. First, **1** with either electron-donating or electron-withdrawing group(s) on its 2-phenyl moiety reacted smoothly with **2a** and **3** to give **4m**-**4r** in good yields. No obvious electronic effect was observed. Second, **1** having a methyl, methoxy, chloro, or trifluoromethyl group on its imidazo[1,2-*a*]pyridine unit were tried, and they were all suitable for this cascade process to give products **4s**-**4w** in an efficient manner. Finally, **1** bearing substituents attached on both the 2-phenyl and the imidazo[1,2-*a*]pyridine units took part in this reaction smoothly to afford **4x**-**4ab**.

Table 4. Studies on the scope of 2-(2-bromophenyl)imidazo[1,2-*a*]pyridines (**1**) [a,b]





4m, 65% **4n**, 72% **4o**, 68% **4p**, 64%

4q, 71% **4r**, 62% **4s**, 70% **4t**, 58%

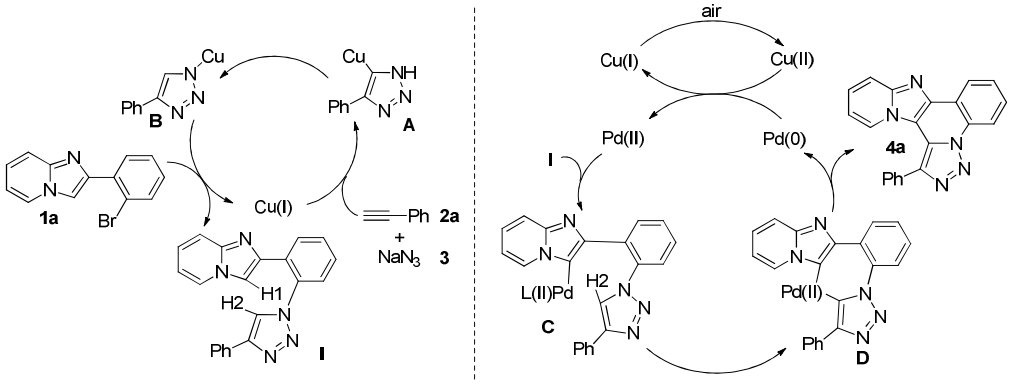
4u, 70% **4v**, 71% **4w**, 75% **4x**, 66%

4y, 61% **4z**, 70% **4aa**, 66% **4ab**, 65%

[a] Conditions: **1** (0.5 mmol), **2a** (0.6 mmol), **3** (0.6 mmol), CuI (0.05 mmol), K_2CO_3 (0.6 mmol), DMF (3 mL), air, 120 ºC, 6 h; then $Pd(OAc)_2$ (0.025 mmol), $Cu(OAc)_2$ (0.05 mmol), AcOH (1.5 mmol), air, 120 ºC, 7 h. [b] Isolated yields.

Based on the above results and previous reports,[8,9,13] it is supposed that the formation of **4a** should firstly involve a CuI-catalyzed azide−alkyne cycloaddition of **2a** with **3** to afford intermediate **A**, which then undergoes a copper-hydrogen exchange to give intermediate **B** (Scheme 2). Arylation of **B** with **1a** through a C−N coupling results in the formation of the key intermediate **I**. In the second phase of this cascade process, aromatic palladation of **I** through cleavage of the C−H1 bond affords intermediate **C**. Subsequently, palladation of **C** by the cleavage of the C−H2 bond affords a seven-membered palladacycle intermediate **D**. Finally, reductive elimination occurs with **D** to generate **4a** together with Pd(0), which is re-oxidized into the Pd(II) species by $Cu(OAc)_2$(cat.)/air. While the precise role played by the carboxylic

acid additive is still unclear at this stage, it is postulated that it might have contributed to neutralize the resulting mixture of the first phase and stabilize the Pd complex formed in the second phase of this cascade procedure. Meanwhile, an alternative pathway, in which the Cu-catalyzed azidation[14] may occur in the initial step for the subsequent click reaction with alkynes, could not be eliminated at this stage.



Scheme 2. Plausible mechanism for the formation of **4a**

CONCLUSION

In conclusion, we have discovered an efficient one-pot approach for the synthesis of 1,2,3-triazole/quinoline-fused imidazo[1,2-*a*]pyridines *via* bimetallic relay catalyzed cascade reactions of simple and readily available starting materials featured with a CDC of two C−H bonds by using air as a sustainable oxidant. With this method, a series of diversely substituted fused heterocycles were successfully constructed. Given its straightforward and sustainable nature, and the importance of 1,2,3-triazole- and imidazo[1,2-*a*]pyridine-related heterocycles, this new synthetic strategy is expected to find wide applications in both heterocyclic and medicinal chemistry.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all the commercial reagents were used without

further purification. 2-(2-Bromophenyl)imidazo[1,2-*a*]pyridines (**1**) were synthesized through condensation of the corresponding 2-aminopyridines with 2-bromophenacyl bromides.[15] Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H NMR spectra were recorded at 400 MHz. The ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts (in ppm) were referenced to tetramethylsilane in $CDCl_3$ or TFA-d_1. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), etc. Coupling constants were given in hertz. High-resolution mass spectra (HRMS) were obtained *via* an ESI mode by using a MicrOTOF mass spectrometer. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

Typical procedure for the synthesis of 4a and spectroscopic data of 4a-4ab

To a flask containing 2-(2-bromophenyl)imidazo[1,2-*a*]pyridine (**1a**, 137 mg, 0.5 mmol), phenylacetylene (**2a**, 61 mg, 0.6 mmol) and sodium azide (**3**, 39 mg, 0.6 mmol) in DMF (3 mL) were added CuI (10 mg, 0.05 mmol) and K_2CO_3 (83 mg, 0.6 mmol). The mixture was then stirred at 120 ºC for 6 h. Upon cooling to ambient temperature, $Pd(OAc)_2$ (6 mg, 0.025 mmol), $Cu(OAc)_2$ (9 mg, 0.05 mmol) and AcOH (88 μL, 1.5 mmol) were added. The resulting mixture was stirred at 120 ºC for 7 h. Then, it was quenched with saturated NH_4Cl (10 mL), and extracted with EtOAc (6 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (1:1) as eluent to give **4a** in 69% yield. Other 1,2,3-triazole/quinoline-fused imidazo[1,2-*a*]pyridine derivatives **4b**-**4ab** were obtained in a

similar manner.

Phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4a): Eluent: petroleum ether/ethyl acetate (1:1); white solid (116 mg, 69%), mp 248-250 °C (lit.[8] 248-250 °C); ^{1}H NMR (400 MHz, TFA-d_1) δ 6.99 (t, J = 6.8 Hz, 1H), 7.39 (d, J = 6.8 Hz, 1H), 7.46 (t, J = 7.2 Hz, 4H), 7.60 (t, J = 6.8 Hz, 1H), 7.83-7.93 (m, 4H), 8.38 (d, J = 7.6 Hz, 1H), 8.72 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, TFA-d_1) δ 109.7, 109.8, 112.6, 113.5, 115.4, 117.8, 118.0, 118.2, 118.8, 123.8, 129.4, 130.7, 132.1, 133.2, 134.2, 137.8, 142.0. MS: 336 $[M+H]^+$.

1-(4-Fluorophenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4b): Eluent: petroleum ether/ethyl acetate (1:1); white solid (120 mg, 68%), mp 267-269 °C (lit.[8] 268-270 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (td, J_1 = 7.2 Hz, J_2 = 0.8 Hz, 1H), 7.30-7.34 (m, 2H), 7.40-7.44 (m, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.71 (td, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H), 7.74-7.78 (m, 1H), 7.80-7.88 (m, 2H), 8.69 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 8.92 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.8, 115.6 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 117.1, 118.0, 118.9, 122.5, 124.1, 127.4, 127.7, 127.9, 128.1 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 129.8, 131.4, 133.1 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 136.5, 140.0, 148.1, 163.5 (d, $^1J_{C\text{-}F}$ = 248.5 Hz). MS: 354 $[M+H]^+$.

1-(*p*-Tolyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4c): Eluent: petroleum ether/ethyl acetate (1:1); white solid (126 mg, 72%), mp 265-267 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (s, 3H), 6.68 (td, J_1 = 7.2 Hz, J_2 = 0.8 Hz, 1H), 7.34-7.41 (m, 3H), 7.59 (d, J = 8.0 Hz, 3H), 7.68-7.73 (m, 1H), 7.76-7.81 (m, 2H), 8.62 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 8.87 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 112.5, 113.0, 117.0, 117.7, 118.8, 122.3, 123.9, 127.2, 127.5, 128.3, 129.0, 129.1, 129.6, 131.2, 131.4, 137.7, 139.3, 139.7, 148.0. HRMS calcd for $C_{22}H_{15}N_5Na$: 372.1220 $[M+Na]^+$, found: 372.1202.

1-(4-(Trifluoromethyl)phenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4d): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (133 mg, 66%), mp 307-308 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (td, J_1 = 6.8 Hz, J_2 = 0.8 Hz, 1H), 7.41-7.45 (m, 1H), 7.53 (d, J = 6.8 Hz, 1H), 7.72-7.76 (m, 1H), 7.78-7.83 (m, 1H), 7.84-7.90 (m, 5H), 8.64 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 8.87 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.5, 112.9, 117.1, 118.0, 118.8, 122.3, 123.8 (q, $^1J_{C\text{-}F}$ = 233.4 Hz), 124.0, 125.4 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 127.5, 127.8, 127.9, 129.9, 131.1, 131.3, 131.4, 135.7, 136.1, 140.3, 148.2. HRMS calcd for $C_{22}H_{13}F_3N_5$: 404.1118 $[M+H]^+$, found: 404.1104.

1-(4-Bromophenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4e): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (141 mg, 68%), mp 273-274 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (t, J = 6.8 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.58-7.62 (m, 3H), 7.71-7.76 (m, 3H), 7.78-7.85 (m, 2H), 8.64 (d, J = 8.0 Hz, 1H), 8.86 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.7, 112.8, 117.0, 117.9, 118.8, 122.2, 123.7, 124.0, 127.4, 127.7, 128.0, 129.8, 130.9, 131.3, 131.7, 132.7, 136.4, 140.1, 148.1. HRMS calcd for $C_{21}H_{12}BrN_5Na$: 436.0168 $[M+Na]^+$, found: 436.0158.

1-(4-Methoxyphenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4f): Eluent: petroleum ether/ethyl acetate (1:1); white solid (135 mg, 74%), mp 228-230 °C (lit.[8] 231-232 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 3H), 6.72 (t, J = 6.8 Hz, 1H), 7.12 (d, J = 8.4 Hz, 2H), 7.38 (t, J = 8.0 Hz, 1H), 7.62-7.65 (m, 3H), 7.73 (t, J = 7.6 Hz, 1H), 7.78-7.84 (m, 2H), 8.66 (d, J = 7.2 Hz, 1H), 8.91 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 112.7, 113.1, 113.8, 117.1, 117.8, 118.9, 122.4, 124.0, 124.2, 127.2, 127.5, 128.2, 129.6, 131.5, 132.6, 137.4, 139.7, 148.0, 160.5. MS: 366 $[M+H]^+$.

1-(*m*-Tolyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4g): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (124 mg, 71%), mp 216-217 °C (lit.[8] 218-219 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.48 (s, 3H), 6.65 (t, J = 6.8 Hz, 1H), 7.34 (t, J = 8.0, 1H), 7.41 (d, J = 4.0 Hz, 1H), 7.46 (t, J = 7.6, 2H), 7.53 (d, J = 5.6 Hz, 2H), 7.67 (t, J = 8.0,

1H), 7.75 (t, J = 8.8, 2H), 8.58 (d, J = 7.6 Hz, 1H), 8.83 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 112.4, 112.9, 117.0, 117.6, 118.8, 122.3, 123.9, 127.1, 127.5, 128.3, 128.4, 129.5, 130.0, 131.4, 131.8, 131.9, 137.8, 138.2, 139.7, 147.9. MS: 350 $[M+H]^+$.

1-(3-Fluorophenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4h): Eluent: petroleum ether/ethyl acetate (1:1); white solid (109 mg, 62%), mp 270-272 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (t, J = 6.8 Hz, 1H), 7.33 (t, J = 8.0, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6, 1H), 7.51 (d, J = 9.6 Hz, 1H), 7.57 (d, J = 7.2, 2H), 7.74 (t, J = 7.6, 1H), 7.79-7.85 (m, 2H), 8.65 (d, J = 7.6 Hz, 1H), 8.88 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 112.8, 116.3 (d, $^2J_{C\text{-}F}$ = 20.7 Hz), 117.1, 117.9, 118.2 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 118.8, 122.4, 124.0, 127.1 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 127.4, 127.7, 127.9, 129.8, 130.0 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 131.4, 134.1 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 136.3, 140.1, 148.1, 162.5 (d, $^1J_{C\text{-}F}$ = 247.8 Hz). HRMS calcd for $C_{21}H_{13}FN_5$: 354.1150 $[M+H]^+$, found: 354.1138.

1-(2-Fluorophenyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4i): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (118 mg, 67%), mp 246-248 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (t, J = 6.8 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.39-7.46 (m, 2H), 7.62 (d, J = 6.4 Hz, 1H), 7.67 (d, J = 6.0 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.81-7.91 (m, 3H), 8.71 (d, J = 7.6 Hz, 1H), 8.94 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.8, 113.2, 115.8 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 117.2, 118.0, 119.0, 120.5 (d, $^2J_{C\text{-}F}$ = 14.6 Hz), 123.8, 124.1, 124.7 (d, $^4J_{C\text{-}F}$ = 3.6 Hz), 127.4 (d, $^3J_{C\text{-}F}$ = 9.5 Hz), 127.7, 129.7, 130.9, 131.5, 131.7 (d, $^3J_{C\text{-}F}$ = 7.3 Hz), 133.1, 133.2, 140.1, 148.3, 160.7 (d, $^1J_{C\text{-}F}$ = 246.5 Hz). HRMS calcd for $C_{21}H_{13}FN_5$: 354.1150 $[M+H]^+$, found: 354.1141.

1-(Thiophen-2-yl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4j): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (116 mg, 68%), mp 252-254 °C; ^{1}H NMR (400 MHz, TFA-d_1) δ 7.23 (t, J = 6.8 Hz, 1H), 7.30 (s, 1H), 7.56 (d, J = 6.0 Hz, 2H), 7.80 (d, J =

3.2 Hz, 1H), 7.95-8.00 (m, 1H), 8.02-8.09 (m, 3H), 8.51 (d, J = 8.0 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (100 MHz, TFA-d_1) δ 111.1, 111.6, 112.3, 112.5, 112.9, 113.5, 114.4, 115.4, 116.3, 116.7, 117.2, 119.2, 128.3, 129.8, 131.6, 132.6, 134.5, 137.9, 142.4. HRMS calcd for $C_{19}H_{11}N_5SNa$: 364.0627 $[M+Na]^+$, found: 364.0620.

1-Octylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4k): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (128 mg, 69%), mp 121-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, J = 6.8 Hz, 3H), 1.25-1.37 (m, 8H), 1.45-1.52 (m, 2H), 1.82-1.90 (m, 2H), 3.28 (t, J = 8.0 Hz, 2H), 6.93 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.31-7.35 (m, 1H), 7.53-7.57 (m, 1H), 7.60-7.67 (m, 2H), 8.38 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 8.58-8.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 28.3, 29.2, 29.3, 29.4, 31.5, 31.8, 113.2, 113.4, 116.6, 118.1, 118.3, 122.0, 123.6, 125.5, 127.0, 127.2, 129.2, 131.2, 136.9, 138.6, 147.3. HRMS calcd for $C_{23}H_{25}N_5Na$: 394.2002 $[M+Na]^+$, found: 394.1983.

1-Benzylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4l): Eluent: petroleum ether/ethyl acetate (1:1); white solid (110 mg, 63%), mp 238-239 °C; ^{1}H NMR (400 MHz, TFA-d_1) δ 5.04 (s, 2H), 7.06 (d, J = 6.8 Hz, 2H), 7.16-7.21 (m, 3H), 7.36-7.40 (m, 1H), 7.94-8.01 (m, 2H), 8.04 (d, J = 3.2 Hz, 2H), 8.48 (d, J = 8.0 Hz, 1H), 8.78 (d, J = 8.4 Hz, 1H), 8.95 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, TFA-d_1) δ 109.8, 112.1, 112.6, 112.8, 113.5, 115.4, 117.9, 118.1, 118.2, 119.2, 123.8, 127.4, 128.4, 128.7, 129.7, 132.2, 132.3, 134.3, 138.1, 142.1. HRMS calcd for $C_{22}H_{15}N_5Na$: 372.1220 $[M+Na]^+$, found: 372.1236.

6-Fluoro-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4m): Eluent: petroleum ether/ethyl acetate (1:1); brown solid (115 mg, 65%), mp 260-262 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (t, J = 6.8 Hz, 1H), 7.33-7.42 (m, 2H), 7.46 (d, J = 6.8 Hz, 1H), 7.61 (s, 3H), 7.69 (d, J = 5.6 Hz, 2H), 7.74 (d, J = 8.8 Hz, 1H), 8.48 (d, J = 9.6 Hz, 1H), 8.54 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.9 (d, $^2J_{C\text{-}F}$ = 27.0 Hz), 112.3, 112.6, 115.2,

116.0 (d, $^{2}J_{C\text{-}F}$ = 23.8 Hz), 117.6, 122.6, 126.1 (d, $^{3}J_{C\text{-}F}$ = 8.7 Hz), 127.4, 128.1, 128.5, 129.5, 131.3, 131.7, 132.1 (d, $^{3}J_{C\text{-}F}$ = 10.4 Hz), 137.6, 139.5, 148.0, 163.0 (d, $^{1}J_{C\text{-}F}$ = 248.5 Hz). HRMS calcd for $C_{21}H_{13}FN_5$: 354.1150 $[M+H]^+$, found: 354.1136.

6-Chloro-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4n): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (133 mg, 72%), mp 274-276 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (t, *J* = 6.8 Hz, 1H), 7.40 (t, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 6.8 Hz, 1H), 7.61-7.66 (m, 4H), 7.70-7.71 (m, 2H), 7.79 (d, *J* = 8.8 Hz, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.86 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.8, 112.9, 117.1, 117.3, 117.8, 122.6, 125.3, 127.5, 128.1, 128.2, 128.5, 129.5, 131.3, 131.67, 131.71, 135.7, 137.7, 139.3, 148.1. HRMS calcd for $C_{21}H_{12}ClN_5Na$: 392.0673 $[M+Na]^+$, found: 392.0660.

6-Methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4o): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (119 mg, 68%), mp 215-217 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (s, 3H), 6.59 (td, J_1 = 7.2 Hz, J_2 = 0.8 Hz, 1H), 7.27-7.31 (m, 1H), 7.41-7.46 (m, 2H), 7.58 (dd, J_1 = 5.2 Hz, J_2 = 2.0 Hz, 3H), 7.68-7.71 (m, 3H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 112.3, 116.2, 116.8, 117.5, 122.3, 123.6, 127.0, 128.1, 128.4, 128.9, 129.3, 131.2, 131.3, 132.0, 135.2, 137.4, 139.8, 140.3, 147.8. HRMS calcd for $C_{22}H_{15}N_5Na$: 372.1220 $[M+Na]^+$, found: 372.1186.

7-Methoxy-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4p): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (117 mg, 64%), mp 225-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.04 (s, 3H), 6.67 (t, *J* = 6.8 Hz, 1H), 7.33-7.39 (m, 2H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.59-7.60 (m, 3H), 7.69-7.71 (m, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 2.8 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.0, 104.4, 112.5, 113.3, 117.7, 118.7, 119.3, 120.1, 121.6, 125.8, 127.3, 128.2, 128.4, 129.3, 131.3, 132.1, 137.5, 139.6, 147.9, 159.0. HRMS calcd for $C_{22}H_{16}N_5O$: 366.1349 $[M+H]^+$, found: 366.1361.

1-Phenyl-7-(trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4q): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (143 mg, 71%), mp 283-284 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.42-7.46 (m, 1H), 7.55 (d, J = 7.2 Hz, 1H), 7.62-7.66 (m, 3H), 7.71-7.73 (m, 2H), 7.88 (d, J = 8.8 Hz, 1H), 8.05 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 1H), 9.04 (s, 1H), 9.07 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.1, 113.6, 117.98, 118.03, 119.0, 122.0 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 124.0 (q, $^{1}J_{C\text{-}F}$ = 227.8 Hz), 126.1 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 127.8, 128.2, 128.6, 129.6, 129.7, 129.9, 131.3, 131.5, 133.0, 138.0, 139.3, 148.4. HRMS calcd for $C_{22}H_{13}F_3N_5$: 404.1118 $[M+H]^+$, found: 404.1132.

8-Phenyl-[1,3]dioxolo[4,5-*g*]pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4r): Eluent: petroleum ether/ethyl acetate (1:1); pale brown solid (118 mg, 62%), mp 224-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (s, 2H), 6.67 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.37 (td, J_1 = 6.8 Hz, J_2 = 0.8 Hz, 1H), 7.53 (d, J = 7.2 Hz, 1H), 7.60 (dd, J_1 = 5.2 Hz, J_2 = 1.6 Hz, 3H), 7.70-7.72 (m, 2H), 7.79 (d, J = 9.2 Hz, 1H), 7.97 (s, 1H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 97.6, 101.9, 102.4, 112.1, 112.3, 113.9, 117.5, 122.0, 127.2, 127.3, 128.3, 128.4, 129.3, 131.3, 132.1, 137.2, 140.1, 147.9, 148.1, 149.9. HRMS calcd for $C_{22}H_{13}N_5O_2Na$: 402.0961 $[M+Na]^+$, found: 402.0966.

12-Methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4s): Eluent: petroleum ether/ethyl acetate (1:1); white solid (122 mg, 70%), mp 224-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (s, 3H), 7.20-7.27 (m, 2H), 7.59-7.65 (m, 3H), 7.70-7.77 (m, 4H), 7.81 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 8.69 (dd, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H), 8.94 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 112.7, 116.9, 117.1, 119.1, 122.4, 122.9, 124.0, 126.1, 127.6, 128.3, 129.3, 129.5, 130.4, 131.4, 131.7, 132.2, 137.5, 139.7, 147.1. HRMS calcd for $C_{22}H_{16}N_5$: 350.1400 $[M+H]^+$, found: 350.1385.

1-Phenyl-12-(trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline

(4t): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (117 mg, 58%), mp 271-272 °C; ^{1}H NMR (400 MHz, TFA-d_1) δ 7.57 (t, J = 7.6 Hz, 2H), 7.65 (d, J = 6.8 Hz, 2H), 7.73 (d, J = 7.6 Hz, 1H), 7.96 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 8.03-8.10 (m, 2H), 8.30 (d, J = 9.2 Hz, 1H), 8.66 (d, J = 7.6 Hz, 1H), 8.83 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, TFA-d_1) δ 112.8, 113.8, 114.3, 118.2, 120.8 (q, $^1J_{C\text{-}F}$ = 180.8 Hz), 121,3, 123.5, 124.5, 124.8 (q, $^2J_{C\text{-}F}$ = 16.0 Hz), 128.7 (q, $^3J_{C\text{-}F}$ = 2.9 Hz), 130.0, 130.9, 131.0, 131.9, 132.6, 133.5, 134.0, 134.9, 135.9, 142.9. HRMS calcd for $C_{22}H_{13}F_3N_5$: 404.1118 $[M+H]^+$, found: 404.1122.

12-Chloro-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4u): Eluent: petroleum ether/ethyl acetate (1:1); brown solid (129 mg, 70%), mp 245-247 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, J_1 = 9.6 Hz, J_2 = 1.6 Hz, 1H), 7.40 (s, 1H), 7.62-7.68 (m, 3H), 7.70-7.75 (m, 4H), 7.82 (t, J = 7.6 Hz, 1H), 8.63 (d, J = 8.0 Hz, 1H), 8.91 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.2, 117.2, 117.9, 118.7, 120.8, 122.3, 124.1, 126.1, 127.7, 128.5, 128.6, 129.8, 129.9, 131.5, 131.55, 131.57, 138.0, 140.4, 146.2. HRMS calcd for $C_{21}H_{13}ClN_5$: 370.0854 $[M+H]^+$, found: 370.0853.

11-Methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4v): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (124 mg, 71%), mp 275-276 °C (lit.[8] 273-274 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 6.35 (d, J = 6.8 Hz, 1H), 7.22(d, J = 6.8 Hz, 1H), 7.32 (s, 1H), 7.56-7.62 (m, 4H), 7.66-7.70 (m, 3H), 8.42 (d, J = 8.0 Hz, 1H), 8.73 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 112.3, 115.0, 115.7, 116.8, 118.6, 122.3, 123.7, 127.1, 127.3, 128.4, 129.20, 129.23, 131.0, 131.3, 132.0, 137.1, 138.6, 139.5, 148.2. MS: 350 $[M+H]^+$.

11-Methoxy-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4w): Eluent: petroleum ether/ethyl acetate (1:1); pale brown solid (137 mg, 75%), mp 260-261 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 6.35 (dd, J_1 = 7.6 Hz, J_2 = 2.4 Hz, 1H), 7.08 (d, J = 2.4

Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.58-7.61(m, 3H), 7.70-7.73 (m, 2H), 7.75 (d, J = 7.6 Hz, 1H), 7.78-7.82 (m, 1H), 8.64 (d, J = 7.6 Hz, 1H), 8.93 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 94.8, 107.6, 112.4, 117.1, 118.8, 122.5, 123.9, 127.5, 128.4, 128.5, 129.3, 131.15, 131.21, 132.1, 136.9, 140.1, 150.2, 159.6. HRMS calcd for $C_{22}H_{15}N_5ONa$: 388.1169 $[M+Na]^+$, found: 388.1158.

11-Methoxy-7-methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinolin e (4x): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (125 mg, 66%), mp 234-236 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H), 3.89 (s, 3H), 6.33 (dd, J_1 = 7.6 Hz, J_2 = 2.8 Hz, 1H), 7.08 (d, J = 2.4 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.58-7.60 (m, 3H), 7.69-7.72 (m, 2H), 8.48 (d, J = 8.0 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 55.7, 94.8, 107.3, 111.9, 116.4, 116.9, 122.6, 123.6, 128.4, 128.5, 128.9, 129.3, 131.16, 131.21, 132.2, 136.8, 140.1, 140.3, 150.2, 159.4. HRMS calcd for $C_{23}H_{18}N_5O$: 380.1506 $[M+H]^+$, found: 380.1499.

7-Methoxy-11-methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinolin e (4y): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (116 mg, 61%), mp 217-218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 4.03 (s, 3H), 6.48 (dd, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.31-7.36 (m, 2H), 7.51 (s, 1H), 7.57-7.58 (m, 1H), 7.59 (d, J = 2.0 Hz, 2H), 7.69-7.71 (m, 2H), 7.92 (d, J = 2.8 Hz, 1H), 8.74 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 56.0, 104.3, 112.9, 115.2, 116.0, 118.6, 119.1, 120.1, 121.7, 125.7, 127.3, 128.4, 129.2, 131.3, 132.2, 137.1, 138.7, 139.6, 148.3, 158.9. HRMS calcd for $C_{23}H_{17}N_5ONa$: 402.1325 $[M+Na]^+$, found: 402.1309.

7-Chloro-11-methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4z): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (134 mg, 70%), mp 230-232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.94 (s, 3H), 7.10 (s, 1H), 7.16 (dd, J_1 = 6.0 Hz, J_2 = 0.8

Hz, 1H), 7.54 (t, J = 5.2 Hz, 2H), 7.58 (d, J = 5.2 Hz, 1H), 7.62-7.64 (m, 3H), 7.66 (dd, J_1 = 6.0 Hz, J_2 = 1.6 Hz, 1H), 8.58 (d, J = 1.2 Hz, 1H), 8.78 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 113.3, 117.0, 118.7, 120.4, 122.7, 122.8, 123.6, 126.1, 128.3, 129.5, 129.67, 129.70, 130.7, 131.7, 132.0, 133.7, 137.6, 138.7, 147.2. HRMS calcd for $C_{22}H_{14}ClN_5Na$: 406.0830 $[M+Na]^+$, found: 406.0828.

7-Fluoro-12-methyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4aa): Eluent: petroleum ether/ethyl acetate (1:1); yellow solid (121 mg, 66%), mp 197-199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.94 (s, 3H), 7.10 (s, 1H), 7.16 (dd, J_1 = 8.8 Hz, J_2 = 1.2 Hz, 1H), 7.41-7.46 (m, 1H), 7.52-7.59 (m, 3H), 7.62 (d, J = 1.6 Hz, 2H), 7.64-7.65 (m, 1H), 8.23 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 8.83-8.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 109.6 (d, $^2J_{C\text{-}F}$ = 24.6 Hz), 113.2, 117.0, 117.5 (d, $^2J_{C\text{-}F}$ = 24.6 Hz), 119.4 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 120.9 (d, $^3J_{C\text{-}F}$ = 9.6 Hz), 122.5, 122.7, 126.1, 127.8, 128.3, 129.4, 130.6, 131.7, 132.1, 137.6, 138.9, 147.1, 161.6 (d, $^1J_{C\text{-}F}$ = 246.1 Hz). HRMS calcd for $C_{22}H_{15}FN_5$: 368.1306 $[M+H]^+$, found: 368.1309.

6,12-Dimethyl-1-phenylpyrido[2',1':2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinoline (4ab): Eluent: petroleum ether/ethyl acetate (1:1); pale yellow solid (118 mg, 65%), mp 252-254 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (s, 3H), 2.64 (s, 3H), 7.11 (s, 1H), 7.13-7.16 (m, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.58-7.64 (m, 4H), 7.70-7.72 (m, 2H), 8.43 (d, J = 8.0 Hz, 1H), 8.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 22.0, 112.1, 116.4, 116.6, 116.9, 122.1, 122.8, 123.6, 126.0, 128.2, 128.9, 129.2, 130.1, 131.2, 131.7, 132.3, 137.3, 139.7, 140.1, 146.9. HRMS calcd for $C_{23}H_{17}N_5Na$: 386.1376 $[M+Na]^+$, found: 386.1377.

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Supporting Information. Copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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