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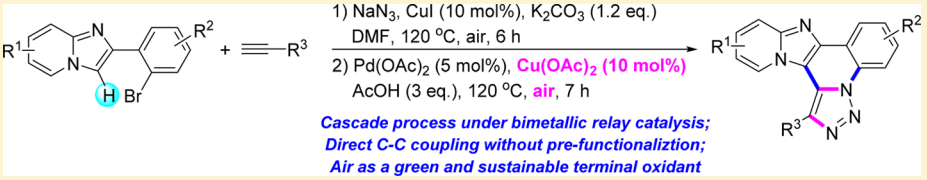
One-Pot Cascade Reactions Leading to Pyrido[2′,1′:2,3]imidazo[4,5-*c*][1,2,3]triazolo[1,5-*a*]quinolines under Bimetallic Relay Catalysis with Air as the Oxidant

Ze Wang, Bin Li, Xinying Zhang, and Xuesen Fan*

School of Chemistry and Chemical Engineering, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, Henan Normal University, Xinxiang, Henan 453007, China

Supporting Information



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 oxidants, reduced synthetic steps, and high efficiency.

INTRODUCTION

The 1,2,3-triazole scaffold plays an important role in the 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] Further, 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 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, a continuing pursuit 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 byproducts.

The formation of a C−C bond from two simple C−H bonds is highly appreciable as it does not require substrate prefunctionalization and holds advantages such as reduced reaction steps, low cost, and less waste.[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.

RESULTS AND DISCUSSION

To evaluate the feasibility of our proposed synthetic pathway, 2-(2-bromophenyl)imidazo[1,2-*a*]pyridine (**1a**), ethynylbenzene (**2a**), and **3** were chosen as model substrates and were initially treated with $CuCl_2 \cdot 2H_2O$ and K_2CO_3 in DMF at 80 °C 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,

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Scheme 1. Different Routes Leading to 1,2,3-Triazole/Quinoline-Fused Imidazo[1,2-*a*]pyridine

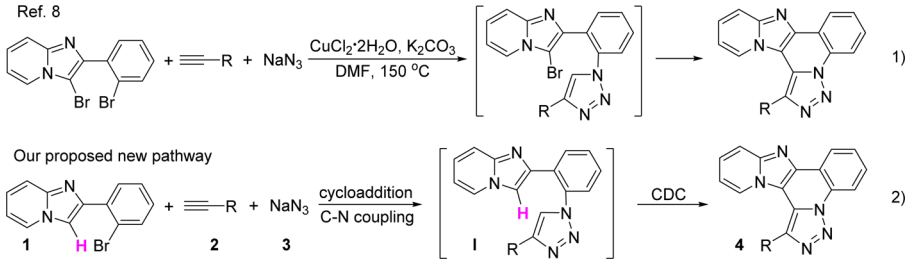
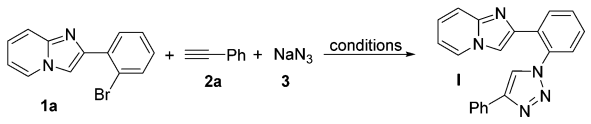


Table 1. Optimization Study for the Formation of Intermediate I[a]



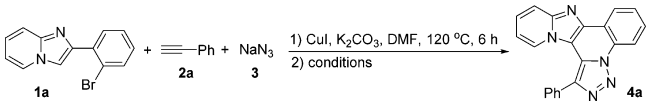
	catalyst	base	solvent	*t* (h)	*T* (°C)	yield (%)[b]
1	$CuCl_2·2H_2O$	K_2CO_3	DMF	6	80	60
2	$CuCl_2$	K_2CO_3	DMF	6	80	68
3	$Cu(OAc)_2$	K_2CO_3	DMF	6	80	62
4	CuCl	K_2CO_3	DMF	6	80	66
5	CuI	K_2CO_3	DMF	6	80	81
6	CuI	Na_2CO_3	DMF	6	80	67
7	CuI	Cs_2CO_3	DMF	6	80	70
8	CuI	$K_3PO_4·3H_2O$	DMF	6	80	62
9	CuI	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.

the yield of **I** decreased compared with DMF (entries 5, 10–13). Raising the reaction temperature, to our delight, improved the yield of **I** notably (entries 5, 14–16). Finally, it was found that a reaction period shorter than 6 h gave a lower yield (entry 15 vs 17). In summary of the optimization study, **I** was obtained in 92% yield through treatment of **1a**, **2a**, and **3** with CuI and K_2CO_3 in DMF at 120 °C under air for 6 h (entry 15).

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 °C for 6 h. Then, $Pd(OAc)_2$ and $Cu(OAc)_2$ were added, and the resulting mixture was stirred at 120 °C 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. First, 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 did indeed improve the reaction (entry 2). Gratifyingly, increases in the loading of AcOH up to 3 equiv

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



	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, and then Pd catalyst (0.025 mmol), oxidant, additive, air, 7 h. [b]Isolated yields. [c]Under N_2. [d]0.1 mmol of CuI was used.

provided a substantial increase in the yield of **4a** (entries 3–5). Although PivOH has been proven to be superior to other organic acids in previous cases of C–H functionalization,[12c] replacing AcOH with PivOH did not lead to 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 found to be less effective than $Pd(OAc)_2$ in promoting this reaction (entries 4, 7–9). Other oxidants such as $Cu(OTf)_2$ were 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 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

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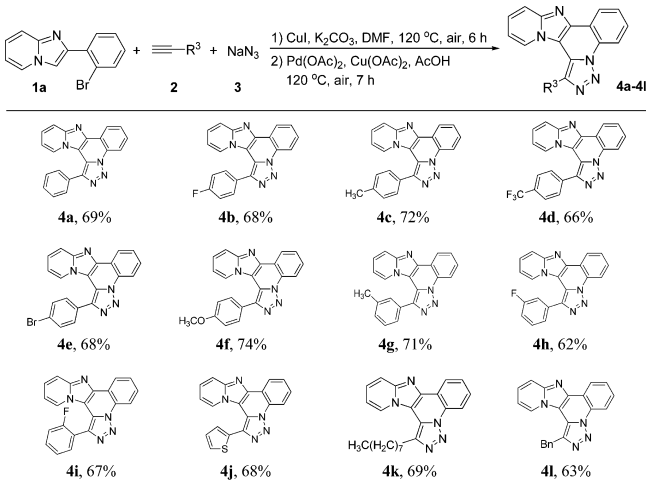
circumstance, only a trace amount of **4a** was formed (entry 14). These results indicated that air could act as the terminal oxidant for this CDC reaction. Arguably, this is an interesting and promising finding, as in most of the previous CDC reactions, stoichiometric or even excess amounts of oxidants 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 °C (entries 13, 15−17). Finally, it was found that when the amount of CuI was doubled to 20 mol %, the yield of **2a** was only 46% (entry 18), indicating that addition of Cu(II) is crucial for the CDC process.

Once the optimization was performed, we next evaluated a series of substrates to determine the influence of steric and electronic parameters on the efficiency of this cascade transformation. First, with **1a** and **3** as model substrates, the scope of alkynes (**2**) was explored. The results listed in Table 3

Table 3. Studies on the Scope of Alkynes (2)[a,b]

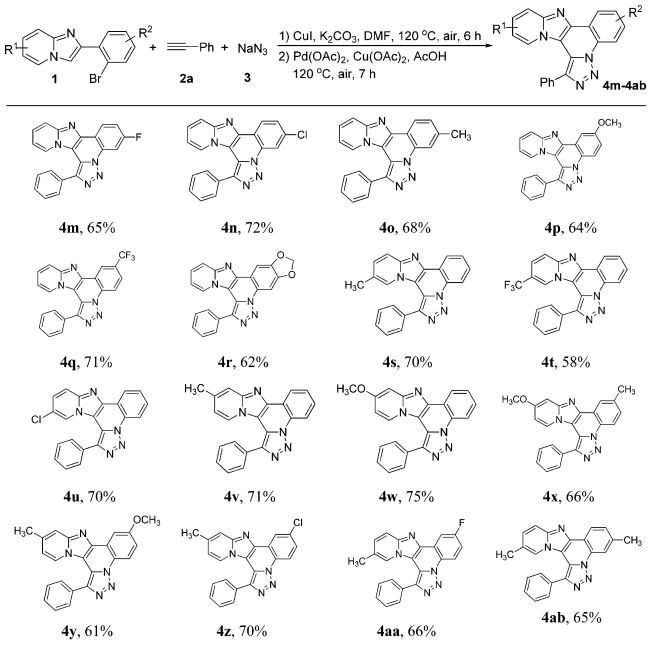


[a]Conditions: **1a** (0.5 mmol), **2** (0.6 mmol), **3** (0.6 mmol), CuI (0.05 mmol), K_2CO_3 (0.6 mmol), DMF (3 mL), air, 120 °C, 6 h, and then $Pd(OAc)_2$ (0.025 mmol), $Cu(OAc)_2$ (0.05 mmol), AcOH (1.5 mmol), air, 120 °C, 7 h. [b]Isolated yields.

indicated that ethynylbenzenes bearing different substituents on the phenyl ring took part in this cascade process smoothly to give **4a−i** in reasonably good yields. Meanwhile, various functional groups such as fluoro, bromo, methyl, methoxy, and trifluoromethyl were tolerated well, and the electronic and steric nature of the substituents did not show an 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 also be suitable substrates for this transformation to afford **4k** and **4l**.

Next, with **2a** and **3** as model substrates, diversely substituted 2-(2-bromophenyl)imidazo[1,2-*a*]pyridines (**1**) were explored, and the results are 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−r** in good yields. No obvious electronic effect was observed. Second, **1** with methyl, methoxy, chloro, or trifluoromethyl groups on

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



[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 °C, 6 h, and then $Pd(OAc)_2$ (0.025 mmol), $Cu(OAc)_2$ (0.05 mmol), AcOH (1.5 mmol), air, 120 °C, 7 h. [b]Isolated yields.

its imidazo[1,2-*a*]pyridine unit were tried, and they were all suitable for this cascade process to give products **4s−w** 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−ab**.

Based on the above results and previous reports,[8,9,13] it is supposed that the formation of **4a** should first 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 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 reoxidized 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 neutralizing the resulting mixture of the first phase and stabilizing 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.

CONCLUSION

In conclusion, we 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 using air as a sustainable oxidant.

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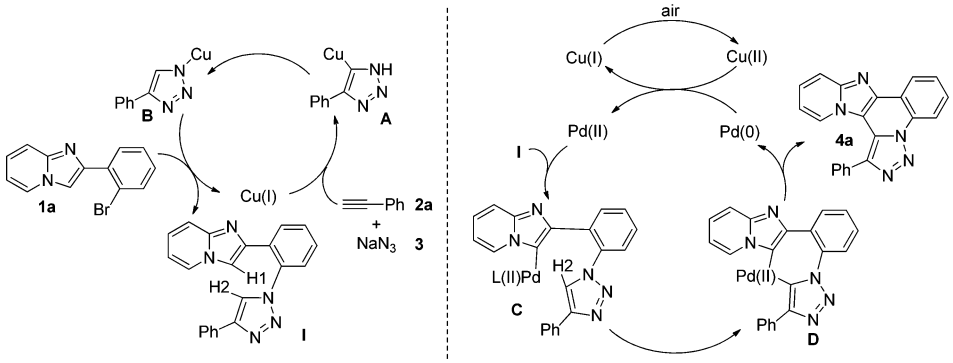
Scheme 2. Plausible Mechanism for the Formation of 4a



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 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 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–ab. 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 °C 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 °C 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–ab** 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, $^2J_{C-F}$ = 21.4 Hz), 117.1, 118.0, 118.9, 122.5, 124.1, 127.4, 127.7, 127.9, 128.1 (d, $^4J_{C-F}$ = 3.2 Hz), 129.8, 131.4, 133.1 (d, $^3J_{C-F}$ = 7.9 Hz), 136.5, 140.0, 148.1, 163.5 (d, $^1J_{C-F}$ = 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, $^1J_{C-F}$ = 233.4 Hz), 124.0, 125.4 (q, $^3J_{C-F}$ = 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),

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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, $^2J_{C-F}$ = 20.7 Hz), 117.1, 117.9, 118.2 (d, $^2J_{C-F}$ = 21.4 Hz), 118.8, 122.4, 124.0, 127.1 (d, $^4J_{C-F}$ = 2.4 Hz), 127.4, 127.7, 127.9, 129.8, 130.0 (d, $^3J_{C-F}$ = 8.7 Hz), 131.4, 134.1 (d, $^3J_{C-F}$ = 8.0 Hz), 136.3, 140.1, 148.1, 162.5 (d, $^1J_{C-F}$ = 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, $^2J_{C-F}$ = 21.1 Hz), 117.2, 118.0, 119.0, 120.5 (d, $^2J_{C-F}$ = 14.6 Hz), 123.8, 124.1, 124.7 (d, $^4J_{C-F}$ = 3.6 Hz), 127.4 (d, $^3J_{C-F}$ = 9.5 Hz), 127.7, 129.7, 130.9, 131.5, 131.7 (d, $^3J_{C-F}$ = 7.3 Hz), 133.1, 133.2, 140.1, 148.3, 160.7 (d, $^1J_{C-F}$ = 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, $^2J_{C-F}$ = 27.0 Hz), 112.3, 112.6, 115.2, 116.0 (d, $^2J_{C-F}$ = 23.8 Hz), 117.6, 122.6, 126.1 (d, $^3J_{C-F}$ = 8.7 Hz), 127.4, 128.1, 128.5, 129.5, 131.3, 131.7, 132.1 (d, $^3J_{C-F}$ = 10.4 Hz), 137.6, 139.5, 148.0, 163.0 (d, $^1J_{C-F}$ = 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, $^3J_{C-F}$ = 4.0 Hz), 124.0 (q, $^1J_{C-F}$ = 227.8 Hz), 126.1 (q, $^3J_{C-F}$ = 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,

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113.8, 114.3, 118.2, 120.8 (q, $^1J_{C-F}$ = 180.8 Hz), 121,3, 123.5, 124.5, 124.8 (q, $^2J_{C-F}$ = 16.0 Hz), 128.7 (q, $^3J_{C-F}$ = 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]quinoline (**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]quinoline (**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, $^2J_{C-F}$ = 24.6 Hz), 113.2, 117.0, 117.5 (d, $^2J_{C-F}$ = 24.6 Hz), 119.4 (d, $^3J_{C-F}$ = 8.7 Hz), 120.9 (d, $^3J_{C-F}$ = 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, $^1J_{C-F}$ = 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.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00996.

Copies of ^{1}H and ^{13}C NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xuesen.fan@htu.cn.

Notes

The authors declare no competing financial interest.

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