Note

An Approach to Quinoline-Fused Imidazopyridines via CDC of Ethers with Imidazopyridines under Metal-Free Conditions

Guifang Lian, Jingyu Li, Ping Liu, and Peipei Sun

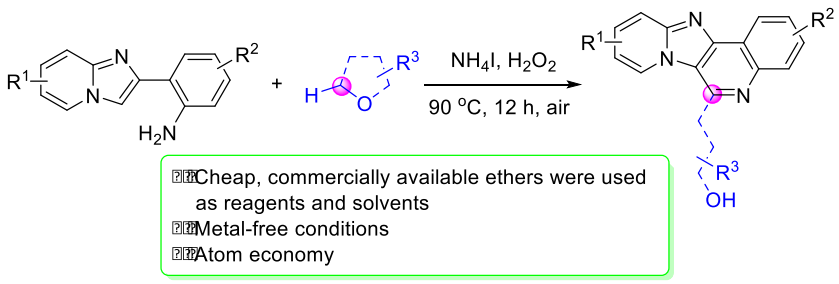
J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02897 • Publication Date (Web): 27 Nov 2019

An Approach to Quinoline-Fused Imidazopyridines via CDC of Ethers with Imidazopyridines under Metal-Free Conditions

Guifang Lian, Jingyu Li, Ping Liu,* and Peipei Sun*

School of Chemistry and Materials Science, Jiangsu Provincial Key Laboratory of Material Cycle Processes and Pollution Control, Jiangsu Collaborative Innovation Center of Biomedical Functional Materials, Nanjing Normal University, Nanjing 210023, China

sunpeipei@njnu.edu.cn; pingliu@njnu.edu.cn



ABSTRACT: A NH_4I-catalyzed cross-dehydrogenative coupling (CDC) reaction of ethers with imidazopyridines cascade cyclization under transition-metal-free conditions has been developed. Cheap, commercially available ethers were used as both reagents and solvents, and green aqueous H_2O_2 was used as oxidizing agent. A series of substituents on the 2-(2-aminoaryl) imidazo[1,2-*a*]pyridines were tolerated and the reaction gave quinoline-fused imidazopyridines in moderate to good yields.

Ethers are widely used as solvents or extracting agents in organic synthesis. As the cheap and easily available reagents, the application of ethers as reactants has also aroused much interest.[1] Many reports focused on the cleavage of α-C(sp^3)–H bond of ethers via cross-dehydrogenative coupling (CDC) to construct C–C bond, *e.g.*, the C–H functionalization of arenes or heteroarenes. Liu et al. introduced a copper-catalyzed oxidative Povarov reaction between *N*, *N*-dialkylanilines and ethers in the presence of peroxide to obtain fused nitrogen and oxygen-containing heterocycles.[2] Wang et al. developed a peroxide-promoted C2-alkoxymethylation on the aromatic heterocyclic compounds such as benzothiazoles and benzimidazoles.[3] These CDC reactions of azoles with ethers can also be catalyzed by Cu,[4] Fe,[5] Pd,[6] or by a visible-light-induced photoredox

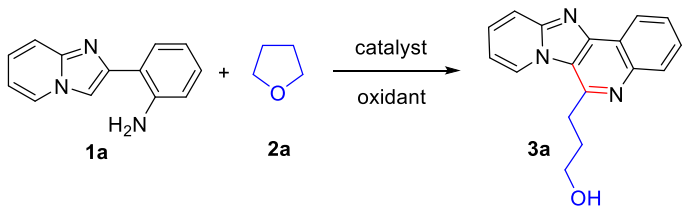
approach using Ir(III) as the catalyst.[7] Meanwhile, some works involved the direct α-C(sp^3)–H amination of ethers to build C–N bonds. This strategy has been employed to construct hemiaminal ether skeletons.[8] Li et al. described an efficient Fe-catalyzed oxidation of ethers to access *N*-substituted azole derivatives.[9] An aminophosphinoylation of ethers via TEMPO-catalyzed α-C(sp^3)–H and C(sp^3)–O bond cleavage was developed for the synthesis of α-aminophosphine oxides.[10] Thus it can be seen that to further exploit the synthetic use of ethers is of great importance.

Imidazo[1,2-*a*]pyridine moiety is known to be "drug prejudice" scaffold due to the extensive biological and pharmacological activities of the compounds based on this heterocycle,[11] such as anticancer,[12] antiinflammatory,[13] antiulcer,[14] antiprotozoal,[15] anti-Alzheimer's disease,[16] and etc. Therefore, the modification and functionalization of imidazo[1,2-*a*]pyridine have attracted attention of many synthetic and pharmaceutical chemists.[17] We have developed a series of methods for the C3-functionalization of imidazo[1,2-*a*]pyridines such as fluorination,[18] cyanomethylation,[19] azolylation,[20] and alkoxycarbonylation[21] in our previous works. Fused heterocycles combined from several heterocycles are expected to exhibit synergistic activities and diverse biological activities. As the continuous study of our group on the selective direct inert C–H bond functionalization, we herein report a cleavage of α-C(sp^3)–H bond of ethers initiated radical CDC/cyclization cascade reaction with imidazo[1,2-*a*]pyridines to assemble quinoline-fused imidazopyridines.

Initially, we employed 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**) and tetrahydrofuran (**2a**, THF) as the model substrates to optimize the reaction conditions (Table 1). To our delight, using NH_4I (20 mol %) as the catalyst and TBHP (3 equiv, 70% in water) as the oxidant at 80 °C, the desired product 3-(pyrido[2',1':2,3]imidazo[4,5-*c*]quinolin-6-yl)propan-1-ol (**3a**) was obtained in 48% yield (entry 1). When the reaction was carried out without NH_4I, no target product was observed (entry 2). Other catalysts such as $^nBu_4NI$ and KI gave inferior yields, and CuI and I_2 were ineffective to this reaction (entries 3–6). The screening experiments also revealed that 20 mol % of NH_4I could give the best result (entries 1, 7 and 8). The oxidants were then explored (entries 9–12). We were delighted to find that the yield of **3a** could be raised to 78% in the presence of H_2O_2 (30% in water), and the appropriate amount of H_2O_2 was 3 equiv (entries 12–14). Temperature was also important for this reaction. Rising the reaction temperature to 90 ^oC brought

a higher yield of 83% (entry 15). At 100 °C, however, the yield no longer had significant change (entry 16).

Table 1. Optimization of the Reaction Conditions[a]



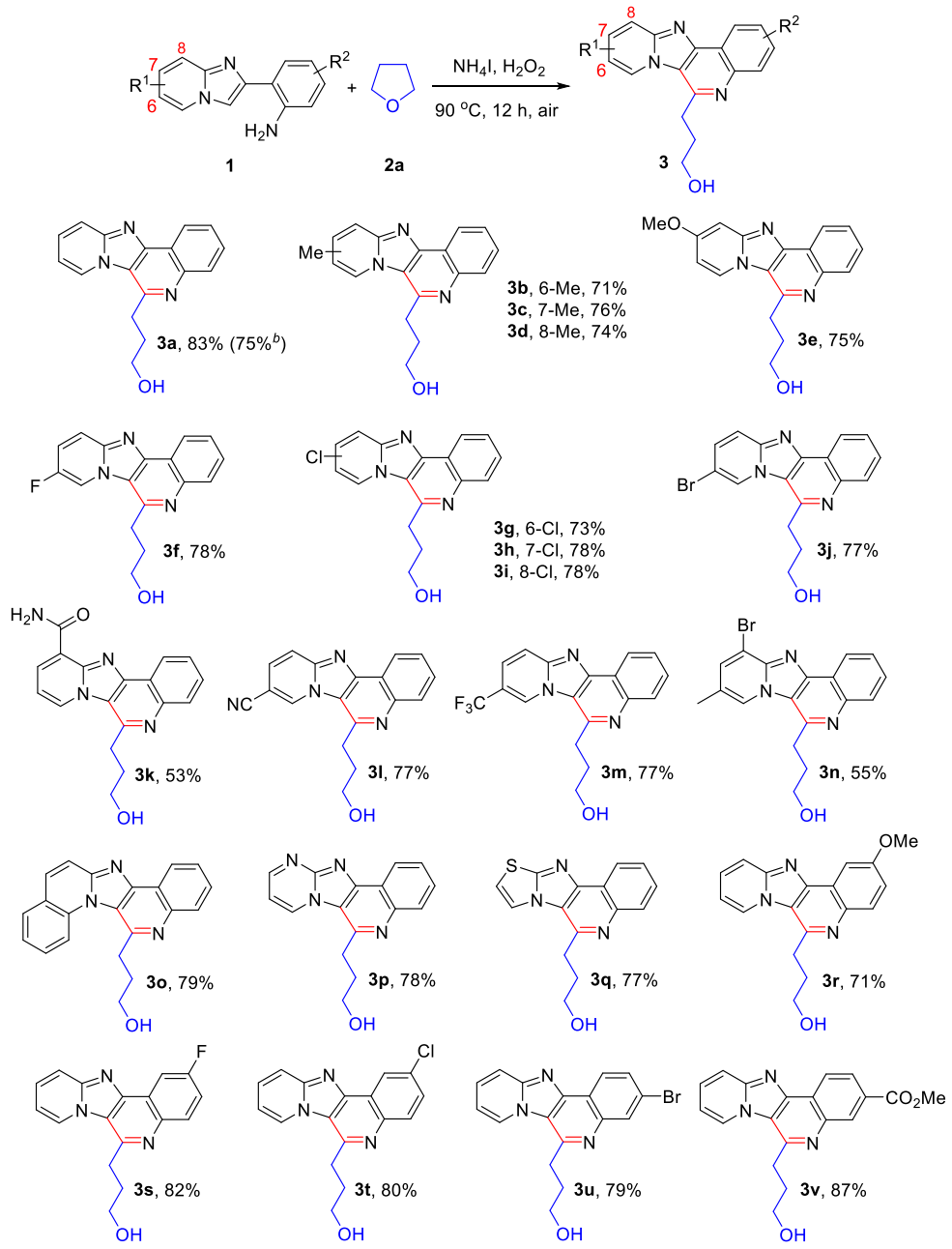
Entry	Catalyst (mol %)	Oxidant (equiv)	Temperature (°C)	Yield (%)[b]
1	NH_4I (20)	TBHP (3)	80	48
2	–	TBHP (3)	80	0
3	$^nBu_4NI$ (20)	TBHP (3)	80	43
4	KI (20)	TBHP (3)	80	38
5	CuI (20)	TBHP (3)	80	0
6	I_2 (20)	TBHP (3)	80	0
7	NH_4I (10)	TBHP (3)	80	37
8	NH_4I (30)	TBHP (3)	80	48
9	NH_4I (20)	DTBP (3)	80	43
10	NH_4I (20)	BPO (3)	80	<10
11	NH_4I (20)	$K_2S_2O_8$ (3)	80	0
12	NH_4I (20)	H_2O_2 (3)	80	78
13	NH_4I (20)	H_2O_2 (4)	80	78
14	NH_4I (20)	H_2O_2 (2)	80	67
15	**NH_4I (20)**	**H_2O_2 (3)**	**90**	**83**
16	NH_4I (20)	H_2O_2 (3)	100	82

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (2 mL), oxidant and catalyst were stirred in a sealed tube under air for 12 h upon heating. [b] Based on **1a**.

With the optimized reaction conditions in hand, we started to evaluate the scope of imidazopyridines with THF for this tandem cyclization reaction (Scheme 1). A variety of substituents on the pyridine ring were well tolerated. It seemed that the electronic effect of the substituents had no significant influence to the reaction. Either an electron-donating group (alkyl, alkoxy) or an electron-withdrawing group (halogen, cyano, trifluoromethyl) substituted substrates gave the desired products (**3b–3m**) in moderate to good yields, only the presence of carbamyl led to a decrease of the yield (**3k**). The reaction was also not sensitive to position of the substituents (**3b–3d**, **3g–3i**). The disubstituted substrate **1n** could also be applied in the reaction to give the

product **3n** in 55% yield. Moreover, instead of pyridine ring, the substrates (**1o–1q**) possessing quinoline, pyrimidine or thiazole rings also successfully underwent this transformation and gave the desired products in good yields (**3o**, 79%; **3p**, 78%; **3q**, 77%). The effect of the substituents on benzene ring was then studied. The reactants with electron-withdrawing groups such as halogen (**1s–1u**) or ester (**1v**) group gave higher yields than that with the methoxyl group (**1r**). Finally, when the reaction of **1a** with THF was performed on a gram scale (5 mmol), the product **3a** was still obtained in 75% yield (3.75 mmol, 1.04 g).

Scheme 1. Substrate Scope for Reaction of Imidazopyridines with THF[a]

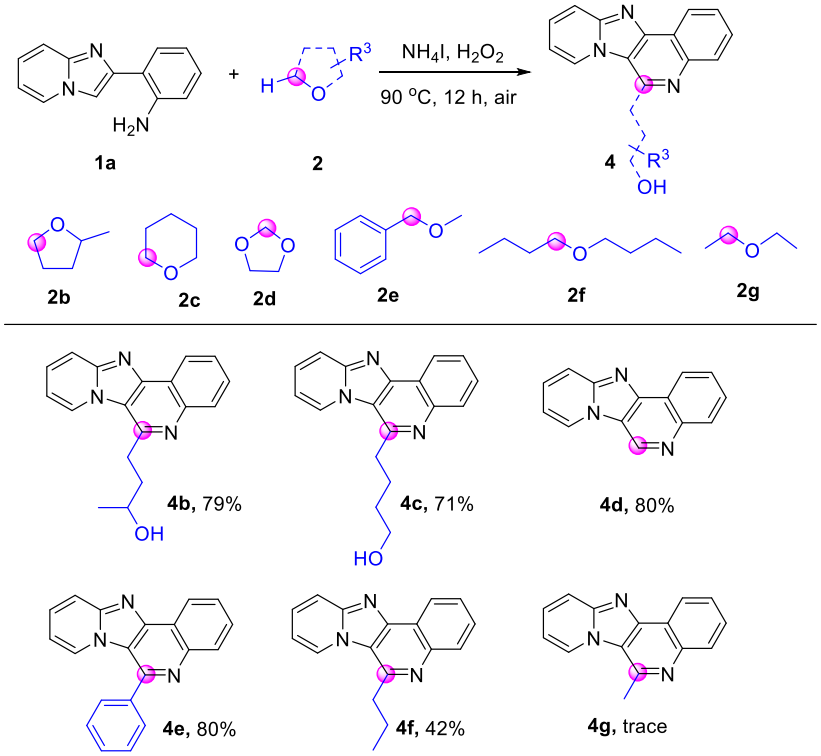


[a]Reaction conditions: **1** (0.2 mmol), **2a** (2 mL), NH_4I (0.04 mmol, 20 mol %) and H_2O_2 (3.0 equiv,

30% in H_2O) were stirred in a sealed tube at 90 °C under air for 12 h. [b]Using 5 mmol of **1a**.

We then turned our attention to a series of other commercial ethers to expand the scope and generality of our reaction (Schemes 2). Employing 2-methyltetrahydrofuran (**2b**), tetrahydropyran (**2c**), 1,3-dioxolane (**2d**) or linear ethers such as benzyl methyl ether (**2e**) and di-*n*-butyl ether (**2f**) to react with **1a** under the standard reaction conditions, the corresponding quinoline-fused imidazopyridines (**4b–4f**) were obtained in good yields (42–80%). For diethyl ether (**2g**), however, almost no desired product **4g** was observed maybe due to the low boiling point of diethyl ether.

Scheme 2. Scope of Ethers 2[a]

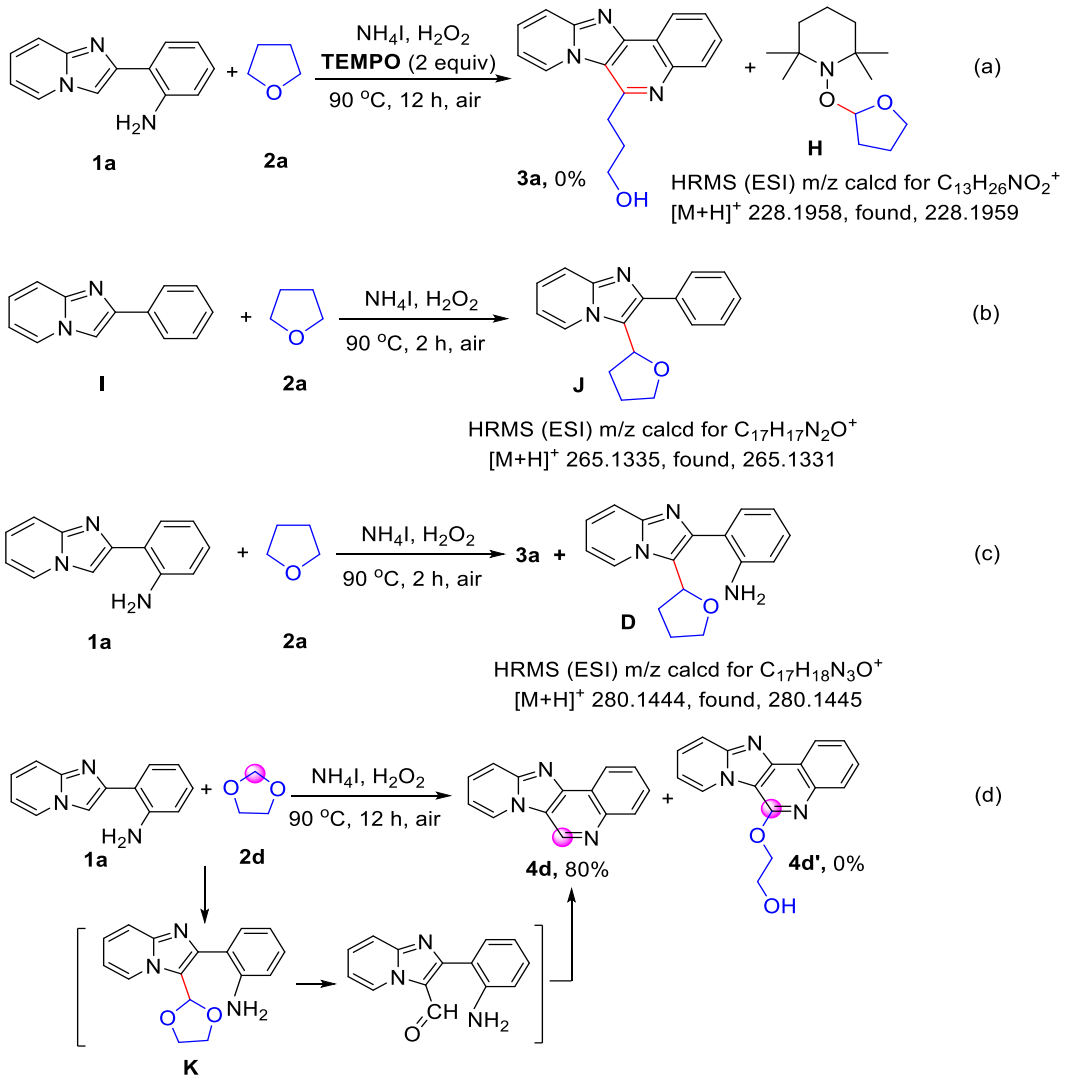


[a]Reaction conditions: **1a** (0.2 mmol), **2** (2 mL), NH_4I (0.04 mmol, 20 mol %) and H_2O_2 (3.0 equiv, 30% in H_2O) were stirred in a sealed tube at 90 °C under air for 12 h.

A set of experiments were performed to investigate the mechanism (Scheme 3). When a radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 2 equiv) was added to the reaction mixture of **1a** and **2a**, the cyclization reaction was obviously suppressed, and a coupling product (**H**) was detected, which indicated that the reaction might proceed via a radical pathway (Scheme 3(a)). Moreover, Using 2-phenylimidazo[1,2-*a*]pyridine (**I**) or 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline (**1a**) to react with THF under the standard reaction

conditions for 2 h, the possible intermediate product 2-phenyl-3-(tetrahydrofuran-2-yl)imidazo[1,2-*a*]pyridine (**J**) or 2-(3-(tetrahydrofuran-2-yl)imidazo[1,2-*a*]pyridin-2-yl)aniline (**D**) was detected by HRMS analysis from the mixture(Scheme 3(b) and 3(c)). In addition, when 1,3-dioxolane (**2d**) was used as a reaction partner under the standard reaction conditions, **4d** was the only product and no another product **4d'** was found. This result further demonstrated that the intermediate **K** generated from the CDC of 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline with ether was likely to be involved in this transformation (Scheme 3(d)).

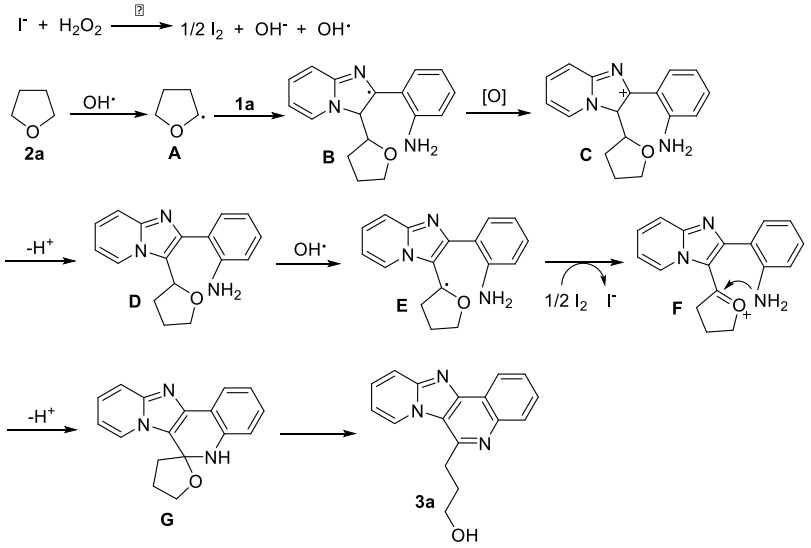
Scheme 3. Control Experiments



According to above results and previous reports, a plausible mechanism is depicted in Scheme 4. Initially, the reaction might begin with the decomposition of H_2O_2 catalyzed by NH_4I to generate hydroxyl radical, along with the generation of I_2. Subsequently, the hydroxyl radical

captured α-hydrogen atom from THF to give the tetrahydrofuran radical (**A**). The radical **A** attacked **1a** to afford the radical intermediate **B**. The oxidation of **B** gave the carbocation **C**, which was converted into **D** through the proton elimination. A further hydrogen abstraction by hydroxyl radical and one-electron oxidation with iodine resulted in the oxonium **F**.[22] Finally, the cation **F** underwent an intramolecular nucleophilic cyclization to give the unstable intermediate product **G**, which could be easily transformed into **3a** via the aromatization owing to the electron-donating property of the nitrogen atom.[10]

Scheme 4. Possible Mechanism



In summary, we have developed a NH_4I-catalyzed CDC cascade cyclization reaction of imidazopyridines with ethers for the synthesis of quinoline-fused imidazopyridines. A "green" oxidant H_2O_2 was used in this process. The operational simplicity and metal-free conditions are the key features of our methodology, which increase its utility in the construction of pharmaceutically important heterocycles.

■ EXPERIMENTAL SECTION

General Information. All reagents and solvents were obtained from chemical suppliers, and were used without further purification. The NMR spectra were recorded at 400 MHz (^{1}H) and 100 MHz (^{13}C{^{1}H}) in $CDCl_3$ or DMSO-d_6 using TMS as an internal standard. Chemical shifts are given relative to $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C{^{1}H} NMR) or DMSO-d_6 (2.50 ppm for ^{1}H NMR, 39.6 ppm for ^{13}C{^{1}H} NMR). The following abbreviations were used to explain

the multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, dt = doublet of triplet, m = multiplet. High-resolution mass spectra (HRMS) were obtained by ESI on TOF mass analyzer. Melting points are uncorrected.

General Procedure for the Synthesis of 1. Some starting materials were known compounds and were prepared according to known methods (**1a**, **1k**;[23] **1c**;[24] **1j**, **1o**;[25]). Compounds **1b**, **1d−1i**, **1l−1n** and **1p−1v** were new compounds and all of them were prepared according to the literature (10 mmol of substituted 2-amino pyridines were used).[24]

2-(6-Methylimidazo[1,2-a]pyridin-2-yl)aniline (**1b**). White solid (1.61 g, 72% yield). mp 150−152 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.30 (s, 1H), 8.18 (s, 1H), 7.56–7.49 (m, 2H), 7.11–7.00 (m, 2H), 6.75 (d, J = 8.0 Hz, 1H), 6.61–6.56 (m, 3H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.1, 146.1, 143.1, 128.7, 128.0, 127.8, 124.2, 122.1, 116.5, 116.1, 116.0, 115.8, 108.9, 18.0. HRMS (ESI) m/z calcd for $C_{14}H_{14}N_3^+$ $[M+H]^+$ 224.1182, found 224.1180.

2-(8-Methylimidazo[1,2-a]pyridin-2-yl)aniline (**1d**). White solid (1.54 g, 69% yield). mp 90−92 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.38 (d, J = 6.4 Hz, 1H), 8.27 (s, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.06–7.01 (m, 2H), 6.82 (t, J = 6.8 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 6.67 (s, 2H), 6.59 (t, J = 7.4 Hz, 1H), 2.53 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.1, 145.6, 144.4, 128.8, 128.1, 126.0, 124.5, 123.5, 116.5, 116.0, 115.8, 112.8, 109.6, 17.0. HRMS (ESI) m/z calcd for $C_{14}H_{14}N_3^+$ $[M+H]^+$ 224.1182, found 224.1187.

2-(8-Methylimidazo[1,2-a]pyridin-2-yl)aniline (**1e**). White solid (1.77 g, 74% yield). mp 147−149 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.38 (d, J = 7.2 Hz, 1H), 8.07 (s, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.00 (s, 2H), 6.73 (d, J = 8.0 Hz, 1H), 6.65–6.55 (m, 4H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 157.7, 147.0, 145.8, 145.5, 128.6, 127.9, 127.4, 116.5, 116.1, 107.8, 107.2, 94.6, 56.0. HRMS (ESI) m/z calcd for $C_{14}H_{14}N_3O^+$ $[M+H]^+$ 240.1131, found 240.1131.

2-(6-Fluoroimidazo[1,2-a]pyridin-2-yl)aniline (**1f**). White solid (1.54 g, 68% yield). mp 129−131 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.77 (s, 1H), 8.31 (s, 1H), 7.67 (dd, J = 9.6, 5.2 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 8.4 Hz, 1H), 7.04 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 6.60 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 153.1 (d, J = 231.1 Hz), 147.3, 146.9, 141.9, 129.1, 128.2, 117.2 (d, J = 9.4 Hz), 116.7, 116.6 (d, J = 25.5 Hz), 116.2, 115.3, 113.6 (d, J = 41.3 Hz), 110.8. HRMS (ESI) m/z calcd for $C_{13}H_{11}FN_3^+$ $[M+H)]^+$ 228.0932,

found 228.0931.

2-(6-Chloroimidazo[1,2-a]pyridin-2-yl)aniline (**1g**). White solid (1.63 g, 67% yield). mp 159−161 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.79 (s, 1H), 8.27 (s, 1H), 7.64 (d, J = 9.6 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.29 (dd, J = 9.6, 1.6 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 6.62–6.55 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.2, 147.2, 142.5, 129.2, 128.2, 125.7, 124.7, 119.6, 117.4, 116.6, 116.2, 115.2, 109.9. HRMS (ESI) m/z calcd for $C_{13}H_{11}ClN_3^+$ $[M+H]^+$ 244.0636, found 244.0636.

2-(7-Chloroimidazo[1,2-a]pyridin-2-yl)aniline (**1h**). White solid (1.58 g, 65% yield). mp 168−170 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.62 (d, J = 5.6 Hz, 1H), 8.38 (s, 1H), 7.76 (s, 1H), 7.56 (d, J = 6.8 Hz, 1H), 7.07–7.02 (m, 2H), 6.81 (d, J = 7.2 Hz, 1H), 6.62 (t, J = 6.6 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 146.3, 146.3, 143.6, 130.4, 129.3, 128.3, 127.9, 117.1, 116.8, 115.5, 115.1, 114.2, 110.0. HRMS (ESI) m/z calcd for $C_{13}H_{11}ClN_3^+$ $[M+H]^+$ 244.0636, found 244.0633.

2-(8-Chloroimidazo[1,2-a]pyridin-2-yl)aniline (**1i**). White solid (1.51 g, 62% yield). mp 141−143 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.55 (d, J = 6.4 Hz, 1H), 8.45 (s, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.06 (t, J = 7.0 Hz, 1H), 6.94 (t, J = 6.8 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.63–6.59 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.2, 146.5, 141.1, 129.3, 128.2, 126.0, 124.1, 121.0, 116.7, 116.1, 115.0, 112.7, 111.2. HRMS (ESI) m/z calcd for $C_{13}H_{11}ClN_3^+$ $[M+H]^+$ 244.0636, found 244.0634.

2-(2-Aminophenyl)imidazo[1,2-a]pyridine-6-carbonitrile (**1l**). White solid (1.50 g, 64% yield). mp 185−187 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.37 (s, 1H), 8.44 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 6.8 Hz, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.06 (t, J = 6.2 Hz, 1H), 6.78 (d, J = 7.2 Hz, 1H), 6.62–6.55 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 148.1, 147.4, 143.4, 133.9, 129.6, 128.5, 124.9, 117.7, 117.4, 116.8, 116.2, 114.5, 110.5, 97.5. HRMS (ESI) m/z calcd for $C_{14}H_{11}N_4^+$ $[M+H]^+$ 235.0978, found 235.0975.

2-(6-(Trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)aniline (**1m**). White solid (1.83 g, 66% yield). mp 150−152 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.23 (s, 1H), 8.44 (s, 1H), 7.79 (d, J = 9.6 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.47 (d, J = 9.2 Hz, 1H), 7.06 (t, J = 7.2 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.62–6.57 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.9, 147.3, 143.8, 129.4, 128.4, 126.5 (q, J = 5.7 Hz), 124.4 (q, J = 269.1 Hz), 120.3 (q, J = 2.4 Hz), 117.5,

116.7, 116.2, 115.2 (q, J = 33.1 Hz), 114.9, 110.8. HRMS (ESI) m/z calcd for $C_{14}H_{11}F_3N_3^+$ $(M+H)^+$ 278.0900, found 278.0899.

2-(8-Bromo-6-methylimidazo[1,2-a]pyridin-2-yl)aniline (**1n**). White solid (1.57 g, 52% yield). mp 148−150 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.34 (s, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.48 (s, 1H), 7.04 (t, J = 7.2 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.59 (t, J = 7.2 Hz, 1H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 147.1, 146.3, 140.8, 130.0, 129.1, 128.1, 124.0, 122.8, 116.7, 116.1, 115.1, 110.9, 109.3, 17.7. HRMS (ESI) m/z calcd for $C_{14}H_{13}BrN_3^+$ $[M+H]^+$ 302.0287, found 302.0288.

2-(Imidazo[1,2-a]pyrimidin-2-yl)aniline (**1p**). White solid (1.11 g, 53% yield). mp 164−166 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.98 (dd, J = 6.6, 1.8 Hz, 1H), 8.52 (dd, J = 4.0, 2.0 Hz, 1H), 8.29 (s, 1H), 7.60 (dd, J = 7.8, 1.4 Hz, 1H), 7.11–7.04 (m, 2H), 6.78 (dd, J = 8.2, 1.0 Hz, 1H), 6.63–6.58 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 150.0, 147.4, 147.4, 147.2, 134.8, 129.5, 128.1, 116.7, 116.1, 115.0, 109.5, 107.5. HRMS (ESI) m/z calcd for $C_{12}H_{11}N_4^+$ $[M+H]^+$ 211.0978, found 211.0975.

2-(Imidazo[2,1-b]thiazol-6-yl)aniline (**1q**). Brown solid (1.31 g, 61% yield). mp 115−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.53 (s, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.20 (d, J = 4.4 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.77–6.73 (m, 2H), 6.63 (d, J = 4.4 Hz, 1H), 5.51 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 148.7, 147.8, 145.2, 128.5, 127.6, 118.7, 117.7, 117.5, 116.8, 112.2, 108.6. HRMS (ESI) m/z calcd for $C_{11}H_{10}N_3S^+$ $[M+H]^+$ 216.0590, found 216.0588.

2-(Imidazo[1,2-a]pyridin-2-yl)-4-methoxyaniline (**1r**). White solid (1.60 g, 67% yield). mp 145−147 °C. ^{1}H NMR (400 MHz, CDCl3) δ (ppm) 7.97 (d, J = 6.4 Hz, 1H), 7.71 (s, 1H), 7.52 (d, J = 9.2 Hz, 1H), 7.12–7.04 (m, 2H), 6.77–6.70 (m, 2H), 6.64 (t, J = 6.6 Hz, 1H), 5.41 (s, 2H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl3) δ (ppm) 151.8, 146.0, 144.5, 139.9, 125.4, 124.3, 118.1, 117.8, 116.9, 115.4, 113.2, 112.4, 108.8, 55.9. HRMS (ESI) m/z calcd for $C_{14}H_{14}N_3O^+$ $[M+H]^+$ 240.1131, found 240.1134.

4-Fluoro-2-(imidazo[1,2-a]pyridin-2-yl)aniline (**1s**). White solid (1.48 g, 65% yield). mp 141−143 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.53 (d, J = 6.4 Hz, 1H), 8.39 (s, 1H), 7.61 (d, J = 9.2 Hz, 1H), 7.44 (dd, J = 10.4, 2.8 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 6.96–6.88 (m, 2H), 6.76 (dd, J = 8.8, 5.2 Hz, 1H), 6.46 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 154.4 (d, J = 228.3 Hz), 145.0 (d, J = 2.5 Hz), 144.1, 143.7, 126.9, 125.3, 117.5 (d, J = 7.5 Hz), 116.8,

116.2 (d, J = 7.1 Hz), 115.6 (d, J = 22.1 Hz), 113.5 (d, J = 22.7 Hz), 113.1, 110.0. HRMS (ESI) m/z calcd for $C_{13}H_{11}FN_3^+$ $[M+H]^+$ 228.0932, found 228.0931.

4-Chloro-2-(imidazo[1,2-a]pyridin-2-yl)aniline (**1t**). Yellow solid (1.51 g, 62% yield). mp 165−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.14 (d, J = 6.4 Hz, 1H), 7.82 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.50 (d, J = 2.0 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.06 (dd, J = 8.4, 2.4 Hz, 1H), 6.82 (t, J = 6.6 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 5.46 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 144.9, 144.4, 128.6, 127.5, 125.4, 124.8, 121.7, 118.0, 117.7, 117.1, 112. 9, 112.8, 108.7. HRMS (ESI) m/z calcd for $C_{13}H_{11}ClN_3^+$ $[M+H]^+$ 244.0636, found 244.0635.

5-Bromo-2-(imidazo[1,2-a]pyridin-2-yl)aniline (**1u**). White solid (1.75 g, 61% yield). mp 144−146 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.54 (d, J = 5.2 Hz, 1H), 8.33 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 6.6 Hz, 1H), 6.96–6.91 (m, 4H), 6.72 (d, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 148.7, 145.1, 144.0, 129.8, 126.9, 125.3, 121.7, 118.4, 118.2, 116.7, 114.8, 113.1, 109.5. HRMS (ESI) m/z calcd for $C_{13}H_{11}BrN_3^+$ $[M+H]^+$ 288.0131, found 288.0137.

Methyl 3-amino-4-(imidazo[1,2-a]pyridin-2-yl)benzoate (**1v**). Yellow solid (1.39 g, 52% yield). mp 185−187 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.57 (d, J = 6.8 Hz, 1H), 8.44 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.2 Hz, 1H), 7.43 (s, 1H), 7.29 (t, J = 7.8 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.97–6.90 (m, 3H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 166.9, 147.1, 144.9, 144.1, 129.5, 128.2, 127.0, 125.5, 119.7, 117.2, 116.8, 116.5, 113.2, 110.5, 52.3. HRMS (ESI) m/z calcd for $C_{15}H_{14}N_3O_2^+$ $[M+H]^+$ 268.1081, found 268.1081.

General Procedure for the Synthesis of 3 and 4. To a sealed tube were added imidazopyridines **1** (0.2 mmol), NH_4I (5.8 mg, 0.04 mmol, 20 mol %), ether (2 mL) and H_2O_2 (61 μL, 3.0 equiv, 30% in H_2O). The reaction mixture was stirred at 90 °C (using oil bath as the heat source) for 12 h. After cooled to room temperature, the resulting solution was diluted with DCM (15 mL). The organic layer was washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate as eluent to afford the desired products **3** or **4**.

3-(Pyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3a**). White solid (46.0 mg, 83% yield; 1.04 g, 75% yield (**1a** 1.05 g (5 mmol), NH_4I 0.145 g (1 mmol), H_2O_2 1.7 mL (3.0 equiv, 30% in H_2O), THF 30 mL)). mp 170−172 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.13 (d, J = 6.4

Hz, 1H), 8.56 (d, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 7.74–7.64 (m, 3H), 7.24 (t, *J* = 6.6 Hz, 1H), 4.85 (s, 1H), 3.68 (t, *J* = 5.0 Hz, 2H), 3.52 (t, *J* = 7.6 Hz, 2H), 2.09–2.02 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.8, 149.1, 146.3, 144.6, 130.7, 129.4, 129.0, 128.7, 126.1, 122.6, 121.3, 117.8, 113.4, 60.7, 33.0, 30.8. HRMS (ESI) m/z calcd for $C_{17}H_{16}N_3O^+$ $[M+H]^+$ 278.1288, found 278.1290.

3-(9-Methylpyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3b**). White solid (41.3 mg, 71% yield). mp 198−200 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.93 (s, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 9.2 Hz, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 9.2 Hz, 1H), 5.01 (s, 1H), 3.69 (t, *J* = 5.8 Hz, 2H), 3.51 (t, *J* = 7.8 Hz, 2H), 2.43 (s, 3H), 2.07–2.00 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.8, 148.2, 146.3, 144.3, 133.5, 128.8, 128.6, 126.7, 126.0, 122.8, 122.6, 121.4, 121.1, 117.1, 60.6, 32.9, 30.9, 18.2. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O^+$ $[M+H]^+$ 292.1444, found 292.1448.

3-(10-Methylpyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3c**). White solid (44.3 mg, 76% yield). mp 225−227 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.92 (d, *J* = 5.2 Hz, 1H), 8.71 (d, *J* = 7.6 Hz, 1H), 8.48 (d, *J* = 7.2 Hz, 1H), 7.85–7.73 (m, 3H), 7.09 (d, *J* = 4.8 Hz, 1H), 5.32 (s, 1H), 3.91–3.89 (m, 4H), 2.61 (s, 3H), 2.33–2.27 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.4, 149.8, 146.7, 144.3, 144.3, 142.1, 128.8, 128.7, 128.5, 126.1, 122.7, 121.3, 121.2, 116.0, 60.7, 32.7, 30.9, 21.6. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O^+$ $[M+H]^+$ 292.1444, found 292.1448.

3-(11-Methylpyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3d**). White solid (43.1 mg, 74% yield). mp 179−181 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.95 (d, *J* = 6.8 Hz, 1H), 8.56 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.2 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 6.8 Hz, 1H), 7.13 (t, *J* = 6.8 Hz, 1H), 3.67 (t, *J* = 6.0 Hz, 2H), 3.48 (t, *J* = 7.8 Hz, 2H), 2.69 (s, 3H), 2.07–2.00 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.7, 149.6, 145.9, 144.3, 129.0, 128.7, 127.3, 126.9, 126.1, 122.7, 121.8, 121.4, 113.3, 60.7, 32.8, 30.8, 17.7. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O^+$ $[M+H]^+$ 292.1444, found 292.1448.

3-(10-Methoxypyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3e**). White solid (46.1 mg, 75% yield). mp 201−203 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.95 (d, *J* = 7.2 Hz, 1H), 8.50 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 6.8 Hz, 1H), 7.62 (t, *J* = 6.8 Hz, 1H), 7.31 (s, 1H), 6.90 (d, *J* = 6.0 Hz, 1H), 4.85 (s, 1H), 3.97 (s, 3H), 3.66 (t, *J* = 5.8 Hz, 2H), 3.46

(t, J = 7.0 Hz, 2H), 2.07–2.00 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 161.2, 151.7, 149.9, 147.1, 144.7, 129.8, 128.9, 128.4, 125.7, 122.5, 121.2, 121.2, 107.7, 95.3, 60.7, 56.6, 32.7, 30.9. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O_2^+$ $[M+H]^+$ 308.1394, found 308.1397.

3-(9-Fluoropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3f**). White solid (46.0 mg, 78% yield). mp 218−220 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.29 (d, J = 2.8 Hz, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.09–8.02 (m, 2H), 7.90–7.85 (m, 1H), 7.76 (t, J = 7.0 Hz, 1H), 7.67 (t, J = 7.2 Hz, 1H), 4.94 (s, 1H), 3.68 (t, J = 5.8 Hz, 2H), 3.52 (t, J = 7.8 Hz, 2H), 2.08–1.99 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 152.8 (d, J = 232.6 Hz), 150.9, 146.8, 144.4, 129.0, 128.9, 126.3, 122.6, 122.5, 122.3 (d, J = 3.3 Hz), 121.4, 118.5 (d, J = 8.8 Hz), 118.4, 118.5 (d, J = 41.5 Hz), 60.6, 32.6, 30.7. HRMS (ESI) m/z calcd for $C_{17}H_{15}FN_3O^+$ $[M+H]^+$ 296.1194, found 296.1198.

3-(9-Chloropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3g**). White solid (45.4 mg, 73% yield). mp 211−213 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.23 (s, 1H), 8.53 (d, J = 7.6 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 9.2 Hz, 1H), 7.79–7.74 (m, 2H), 7.66 (t, J = 7.0 Hz, 1H), 4.96 (s, 1H), 3.67 (t, J = 5.4 Hz, 2H), 3.51 (t, J = 7.2 Hz, 2H), 2.08–2.01 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 151.0, 147.4, 146.5, 144.6, 131.4, 129.1, 129.0, 127.3, 126.4, 122.6, 121.6, 121.2, 119.9, 118.5, 60.6, 32.7, 30.6. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_3O^+$ $[M+H]^+$ 312.0898, found 312.0900.

3-(10-Chloropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3h**). White solid (48.5 mg, 78% yield). mp 177−179 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.09 (d, J = 7.6 Hz, 1H), 8.51 (d, J = 7.6 Hz, 1H), 8.10–8.06 (m, 2H), 7.75 (t, J = 7.2 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 7.27 (dd, J = 7.2, 2.0 Hz, 1H), 4.86 (s, 1H), 3.67 (t, J = 6.0 Hz, 2H), 3.48 (t, J = 7.8 Hz, 2H), 2.08–2.01 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.7, 148.9, 146.7, 144.7, 135.8, 130.3, 129.1, 129.0, 126.3, 122.6, 121.3, 121.1, 116.4, 114.2, 60.7, 32.8, 30.6. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_3O^+$ $[M+H]^+$ 312.0898, found 312.0901.

3-(11-Chloropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3i**). White solid (48.5 mg, 78% yield). mp 152−154 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.96 (d, J = 6.8 Hz, 1H), 8.48 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.81–7.58 (m, 3H), 7.11 (t, J = 7.0 Hz, 1H), 4.88 (s, 1H), 3.67 (t, J = 5.6 Hz, 2H), 3.39 (t, J = 7.4 Hz, 2H), 2.06–1.98 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.6, 146.0, 145.7, 144.5, 129.2, 128.9, 128.8, 128.2, 126.2,

122.5, 122.2, 122.1, 121.0, 112.8, 60.7, 32.8, 30.5. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_3O^+$ $[M+H]^+$ 312.0898, found 312.0902.

3-(9-Bromopyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3j**). White solid (54.7 mg, 77% yield). mp 203−205 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.26 (s, 1H), 8.52 (d, J = 7.6 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.93–7.65 (m, 4H), 4.94 (s, 1H), 3.67 (t, J = 7.4 Hz, 2H), 3.49 (t, J = 7.0 Hz, 2H), 2.07–2.01 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 151.1, 147.5, 146.3, 144.6, 133.5, 129.4, 129.1, 129.0, 126.4, 122.6, 121.5, 121.2, 118.8, 106.9, 60.6, 32.7, 30.6. HRMS (ESI) m/z calcd for $C_{17}H_{15}BrN_3O^+$ $[M+H]^+$ 356.0393, found 356.0398.

6-(3-Hydroxypropyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-11-carboxamide (**3k**). White solid (33.9 mg, 53% yield). mp 245−247 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.80 (s, 1H), 9.28 (d, J = 6.8 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.46 (d, J = 7.2 Hz, 1H), 8.24 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.0 Hz, 1H), 4.79 (t, J = 4.8 Hz, 1H), 3.68 (q, J = 5.2 Hz, 2H), 3.50 (t, J = 7.8 Hz, 2H), 2.09–2.03 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 164.0, 150.7, 147.2, 145.0, 144.7, 133.2, 132.5, 129.1, 129.0, 126.3, 122.8, 121.2, 121.0, 120.6, 113.1, 60.7, 32.9, 30.6. HRMS (ESI) m/z calcd for $C_{18}H_{17}N_4O_2^+$ $[M+H]^+$ 321.1346, found 321.1347.

6-(3-Hydroxypropyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-9-carbonitrile (**3l**). White solid (46.5 mg, 77% yield). mp 239−241 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.70 (s, 1H), 8.49 (d, J = 7.6 Hz, 1H), 8.07–7.99 (m, 2H), 7.91 (d, J = 9.2 Hz, 1H), 7.77 (t, J = 7.2 Hz, 1H), 7.67 (t, J = 7.0 Hz, 1H), 4.93 (s, 1H), 3.69 (t, J = 5.2 Hz, 2H), 3.50 (t, J = 7.0 Hz, 2H), 2.11–2.04 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 150.9, 148.1, 146.9, 144.8, 136.7, 130.1, 129.4, 129.1, 126.6, 122.6, 121.4, 120.8, 118.4, 117.3, 98.0, 60.6, 32.5, 30.3. HRMS (ESI) m/z calcd for $C_{18}H_{15}N_4O^+$ $[M+H]^+$ 303.1240, found 303.1246.

3-(9-(Trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3m**). White solid (53.1 mg, 77% yield). mp 202−204 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.45 (s, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.14–8.08 (m, 2H), 7.97 (d, J = 9.6 Hz, 1H), 7.78 (t, J = 7.0 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 4.94 (t, J = 3.8 Hz, 1H), 3.66 (q, J = 4.7 Hz, 2H), 3.53 (t, J = 7.8 Hz, 2H), 2.07–2.00 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 151.2, 148.8, 147.2, 144.8, 129.3, 129.2 (q, J = 5.4 Hz), 129.1, 126.6, 126.0 (q, J = 2.4 Hz), 124.2 (q, J = 269.5 Hz), 122.7, 121.9, 121.1, 118.8, 115.3 (q, J = 33.7 Hz), 60.4, 32.7, 30.8. HRMS (ESI) m/z calcd for $C_{18}H_{15}F_3N_3O^+$

$[M+H]^+$ 346.1162, found 346.1162.

3-(11-Bromo-9-methylpyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3n**). White solid (40.6 mg, 55% yield). mp 221−223 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.94 (s, 1H), 8.55 (d, J = 5.6 Hz, 1H), 8.06–7.95 (m, 2H), 7.76–7.65 (m, 2H), 5.03 (s, 1H), 3.68 (t, J = 10.6 Hz, 2H), 3.48 (t, J = 7.6 Hz, 2H), 2.43 (s, 3H), 2.06–1.98 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 151.1, 145.8, 145.7, 144.5, 135.5, 129.0, 128.9, 126.4, 126.3, 123.1, 122.6, 122.4, 121.3, 110.4, 60.6, 32.9, 30.8, 17.9. HRMS (ESI) m/z calcd for $C_{18}H_{17}BrN_3O^+$ $[M+H]^+$ 370.0550, found 370.0549.

3-(Imidazo[1,2-a:5,4-c']diquinolin-6-yl)propan-1-ol (**3o**). White solid (51.7 mg, 79% yield). mp 180−182 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.58 (dd, J = 8.0, 0.8 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 8.13–8.08 (m, 3H), 7.86–7.82 (m, 2H), 7.78–7.74 (m, 1H), 7.68–7.61 (m, 2H), 4.52 (s, 1H), 3.48 (t, J = 7.6 Hz, 2H), 3.38 (t, J = 5.8 Hz, 2H), 2.08–2.02 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 150.6, 149.6, 147.2, 144.6, 134.6, 132.9, 129.5, 129.5, 128.8, 128.5, 126.2, 125.7, 124.5, 124.0, 122.5, 120.7, 120.5, 117.4, 60.7, 35.4, 31.9. HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O^+$ $[M+H]^+$ 328.1444, found 328.1450.

3-(Pyrimido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3p**). White solid (43.4 mg, 78% yield). mp 210−212 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.53 (d, J = 6.4 Hz, 1H), 8.95 (s, 1H), 8.55 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 5.0 Hz, 1H), 3.66 (t, J = 5.4 Hz, 2H), 3.47 (t, J = 7.4 Hz, 2H), 2.08–2.01 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 155.9, 151.2, 151.1, 146.3, 144.6, 138.2, 129.2, 126.3, 122.8, 120.9, 119.6, 109.7, 60.6, 32.7, 30.5. HRMS (ESI) m/z calcd for $C_{16}H_{15}N_4O^+$ $[M+H]^+$ 279.1240, found 279.1246.

3-(Thiazolo[2',3':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3q**). White solid (43.6 mg, 77% yield). mp 185−187 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.53 (d, J = 4.4 Hz, 1H), 8.42 (d, J = 7.2 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.70–7.59 (m, 3H), 4.87 (s, 1H), 3.62 (t, J = 5.8 Hz, 2H), 3.38 (t, J = 7.8 Hz, 2H), 2.04–1.97 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) 158.0, 149.4, 148.9, 144.2, 129.1, 128.0, 126.1, 122.8, 122.0, 121.4, 121.2, 114.7, 60.6, 31.9, 31.4. HRMS (ESI) m/z calcd for $C_{15}H_{14}N_3OS^+$ $[M+H]^+$ 284.0852, found 284.0854.

3-(2-Methoxypyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3r**). Brown solid (43.6 mg, 71%). mp 173−175 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.10 (d, J = 6.8 Hz, 1H),

7.99–7.87 (m, 3H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.35 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.23 (t, *J* = 6.6 Hz, 1H), 3.97 (s, 3H), 3.67 (t, *J* = 6.0 Hz, 2H), 3.47 (t, *J* = 7.8 Hz, 2H), 2.06–2.00 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 157.5, 148.9, 148.0, 145.8, 139.7, 130.6, 130.4, 129.4, 122.1, 121.4, 119.9, 117.7, 113.3, 101.7, 60.7, 55.9, 32.7, 30.9. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O_2^+$ $[M+H]^+$ 308.1394, found 308.1397.

3-(2-Fluoropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3s**). White solid (48.4 mg, 82% yield). mp 214−216 °C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.09 (d, *J* = 7.2 Hz, 1H), 8.12–8.07 (m, 2H), 7.92 (d, *J* = 9.2 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.58 (td, *J* = 8.9, 2.9 Hz, 1H), 7.24 (t, *J* = 6.8 Hz, 1H), 4.81 (s, 1H), 3.67 (t, *J* = 6.0 Hz, 2H), 3.47 (t, *J* = 7.8 Hz, 2H), 2.06–1.99 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 160.0 (d, *J* = 245.1 Hz), 150.2, 149.1, 145.8, 141.6, 131.8 (d, *J* = 9.2 Hz), 130.8, 129.4, 122.1 (d, *J* = 12.0 Hz), 121.5, 117.8, 117.8 (d, *J* = 24.0 Hz), 113.6, 106.5 (d, *J* = 22.7 Hz), 60.7, 32.9, 30.7. HRMS (ESI) m/z calcd for $C_{17}H_{15}FN_3O^+$ $[M+H]^+$ 296.1194, found 296.1199.

3-(2-Chloropyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3t**). White solid (49.8 mg, 80% yield). mp 208−210 °C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.07 (d, *J* = 6.8 Hz, 1H), 8.38 (d, *J* = 2.0 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.75–7.66 (m, 2H), 7.25 (t, *J* = 6.6 Hz, 1H), 4.81 (s, 1H), 3.67 (q, *J* = 5.3 Hz, 2H), 3.45 (t, *J* = 7.8 Hz, 2H), 2.06–1.99 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 151.3, 149.2, 145.2, 142.9, 131.1, 131.0, 130.4, 129.4, 128.9, 122.1, 121.7, 121.4, 117.8, 113.6, 60.7, 32.9, 30.6. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_3O^+$ $[M+H]^+$ 312.0898, found 312.0902.

3-(3-Bromopyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)propan-1-ol (**3u**). White solid (56.1 mg, 79% yield). mp 219−221 °C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.11 (s, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.19 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 6.0 Hz, 1H), 4.83 (s, 1H), 3.67 (t, *J* = 4.8 Hz, 2H), 3.48 (t, *J* = 6.2 Hz, 2H), 2.06–1.99 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 151.8, 149.2, 145.8, 145.1, 130.8, 130.7, 129.2, 128.6, 124.4, 121.5, 121.3, 119.9, 117.7, 113.5, 60.7, 32.8, 30.5. HRMS (ESI) m/z calcd for $C_{17}H_{15}BrN_3O^+$ $[M+H]^+$ 356.0393, found 356.0398.

Methyl 6-(3-hydroxypropyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-3-carboxylate (**3v**). White solid (58.3 mg, 87% yield). mp 247−249 °C. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.15 (d, *J* = 5.2 Hz, 1H), 8.62 (s, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 6.0 Hz,

1H), 7.27 (t, *J* = 6.4 Hz, 1H), 3.96 (s, 3H), 3.70 (t, *J* = 5.6 Hz, 2H), 3.55 (t, *J* = 5.8 Hz, 2H), 2.15–2.09 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 166.1, 151.6, 148.9, 145.1, 143.2, 130.5, 130.2, 129.0, 124.7, 123.8, 122.7, 121.8, 117.4, 113.2, 60.2, 52.3, 32.4, 29.9. HRMS (ESI) m/z calcd for $C_{19}H_{18}N_3O_3^+$ $[M+H]^+$ 336.1343, found 336.1347.

4-(Pyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)butan-2-ol (**4b**). Yellow solid (46.0 mg, 79% yield). mp 102−104 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.17 (s, 1H), 8.57 (s, 1H), 8.09–7.96 (m, 2H), 7.75–7.66 (m, 3H), 7.26 (s, 1H), 4.94 (s, 1H), 3.91 (s, 1H), 3.62 (t, *J* = 10.4 Hz, 2H), 1.97–1.88 (m, 2H), 1.20 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 151.0, 149.1, 146.3, 144.6, 130.7, 129.4, 129.0, 128.7, 126.1, 122.6, 121.3, 117.8, 113.4, 66.0, 37.0, 32.8, 24.2. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O^+$ $[M+H]^+$ 292.1444, found 292.1446.

4-(Pyrido[2',1':2,3]imidazo[4,5-c]quinolin-6-yl)butan-1-ol (**4c**). White solid (41.3 mg, 71% yield). mp 182−184 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.08 (d, *J* = 6.8 Hz, 1H), 8.57 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 7.75 (t, *J* = 7.0 Hz, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 6.6 Hz, 1H), 4.52 (s, 1H), 3.54–3.46 (m, 4H), 1.97–1.89 (m, 2H), 1.73–1.66 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 150.9, 149.1, 146.3, 144.7, 130.7, 129.4, 129.1, 128.7, 126.1, 122.6, 121.4, 121.3, 117.8, 113.5, 60.9, 36.0, 32.4, 24.1. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3O^+$ $[M+H]^+$ 292.1444, found 292.1447.

Pyrido[2',1':2,3]imidazo[4,5-c]quinoline (**4d**).[26] White solid (38.6 mg, 88% yield). mp 253−255 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.82 (s, 1H), 9.39 (d, *J* = 6.8 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 9.2 Hz, 1H), 7.81–7.71 (m, 3H), 7.25 (t, *J* = 6.8 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 149.0, 145.7, 145.6, 138.3, 131.7, 130.0, 128.7, 128.0, 126.9, 122.8, 122.7, 122.1, 117.6, 113.1. HRMS (ESI) m/z calcd for $C_{14}H_{10}N_3^+$ $[M+H]^+$ 220.0869, found 220.0869.

6-Phenylpyrido[2',1':2,3]imidazo[4,5-c]quinoline (**4e**).[27] White solid (47.2 mg, 80% yield). mp 221−223 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.65 (d, *J* = 7.6 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 6.8 Hz, 1H), 7.96 (d, *J* = 9.2 Hz, 1H), 7.83–7.68 (m, 8H), 7.03 (t, *J* = 7.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm) 149.7, 148.6, 147.0, 144.8, 138.5, 131.3, 130.0, 129.6, 129.5, 129.2, 127.5, 126.9, 122.8, 121.5, 120.5, 118.1, 113.0. HRMS (ESI) m/z calcd for $C_{20}H_{14}N_3^+$ $[M+H]^+$ 296.1182, found 296.1187.

6-Propylpyrido[2',1':2,3]imidazo[4,5-c]quinoline (**4f**).[28] White solid (21.9 mg, 42% yield). mp

124−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73–8.71 (m, 2H), 8.25 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.78 (t, J = 7.4 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 6.6 Hz, 1H), 3.47 (t, J = 7.8 Hz, 2H), 2.04–1.95 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 149.7, 149.4, 147.2, 144.3, 129.5, 128.8, 128.4, 127.4, 126.1, 122.6, 121.2, 121.1, 118.4, 112.9, 38.7, 21.5, 14.2. HRMS (ESI) m/z calcd for $C_{17}H_{16}N_3^+$ $[M+H]^+$ 262.1339, found 262.1337.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Control experiments, copies of ^{1}H NMR and ^{13}C{^{1}H} NMR spectra for all products.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sunpeipei@njnu.edu.cn

*E-mail: pingliu@njnu.edu.cn

ORCID

Peipei Sun: 0000-0002-1716-2343

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Project 21672104, 21502097), the Natural Science Foundation of the Education Department of Jiangsu province (15KJB150015), and the Priority Academic Program Development of Jiangsu Higher Education Institutions. The authors also thank Mr. Hailong Liu for the determination of HRMS.

■ REFERENCES

(1) Liu, P.; Zhang, G.; Sun, P. In *Solvents as Reagents in Organic Synthesis*, ed. Wu, X.-F. Wiley-VCH, Weinheim, **2018**, pp. 81−123.

(2) Kawade, R. K.; Huple, D. B.; Lin, R.-J.; Liu, R.-S. Cu-Catalyzed Oxidative Povarov Reactions

Between *N*-Alkyl *N*-Methylanilines and Saturated Oxa- and Thiacycles. *Chem. Commun*. **2015**, *51*, 6625−6628.

(3) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. Direct C2-Alkylation of Azoles with Alcohols and Ethers through Dehydrogenative Cross-Coupling under Metal-Free Conditions. *Org. Lett.* **2011**, *13*, 5016−5019.

(4) (a) Xie, Z.; Cai, Y.; Hu, H.; Lin, C.; Jiang, J.; Chen, Z.; Wang, L.; Pan, Y. Cu-Catalyzed Cross-Dehydrogenative Coupling Reactions of (Benzo)thiazoles with Cyclic Ethers. *Org. Lett.* **2013**, *15*, 4600−4603. (b) Zhou, J.; Zou, Y.; Zhou, P.; Chen, Z.; Li, J. Copper-Catalyzed Versatile C(sp^3)–H Arylation: Synthetic Scope and Regioselectivity Investigations. *Org. Chem. Front.* **2019***, 6,* 1594−1598.

(5) (a) Correa, A.; Fiser, B.; Gómez-Bengoa, E. Iron-Catalyzed Direct *α*-Arylation of Ethers with Azoles. *Chem. Commun.* **2015**, *51*, 13365−13368. (b) An, Z.; Zhao, L.; Wu, M.; Ni, J.; Qi, Z.; Yu, G.; Yan, R. $FeCl_3$-Catalyzed Synthesis of Pyrrolo[1,2-*a*]quinoxaline Derivatives from 1-(2-Aminophenyl)pyrroles Through Annulation and Cleavage of Cyclic Ethers. *Chem. Commun.* **2017**, *53*, 11572−11575. (c) Guo, X.; Pan, S.; Liu, J.; Li, Z. One-Pot Synthesis of Symmetric and Unsymmetric 1,1-Bis-indolylmethanes via Tandem Iron-Catalyzed C−H Bond Oxidation and C−O Bond Cleavage. *J. Org. Chem.* **2009***, 74,* 8848−8851.

(6) Wu, Z.; Pi, C.; Cui, X.; Bai, J.; Wu, Y. Direct C-2 Alkylation of Quinoline *N*-Oxides with Ethers via Palladium-Catalyzed Dehydrogenative Cross-Coupling Reaction. *Adv. Synth. Catal.* **2013**, *355*, 1971−1976.

(7) Jin, J.; MacMillan, D. W. C. Direct *α*-Arylation of Ethers through the Combination of Photoredox-Mediated C−H Functionalization and the Minisci Reaction. *Angew. Chem. Int. Ed.* **2015**, *54*, 1565−1569.

(8) Dian, L.; Xing, Q.; Zhang-Negreriea, D.; Du, Y. Direct Functionalization of Alkyl Ethers to Construct Hemiaminal Ether Skeletons (HESs). *Org. Biomol. Chem*. **2018**, *16*, 4384–4398.

(9) Pan, S.; Liu, J.; Li, H.; Wang, Z.; Guo, X.; Li, Z. Iron-Catalyzed *N*-Alkylation of Azoles via Oxidation of C−H Bond Adjacent to an Oxygen Atom. *Org. Lett.* **2010**, *12*, 1932−1935.

(10) Huang, Q.; Dong, K.; Bai, W.; Yi, D.; Ji, J.-X.; Wei, W. TEMPO-Catalyzed Aminophosphinoylation of Ethers via Tandem C(sp^3)–H and C(sp^3)–O Bond Cleavage. *Org. Lett.* **2019**, *21*, 3332−3336.

(11) (a) Katritzky, A. R.; Rees, C. W. In *Comprehensive Heterocyclic Chemistry*, ed. Potts, K. T. Pergamon Press: Oxford, UK, **1984**, vol. 5, part 4A. (b) Devi, N.; Singh, D.; Rawal, R. K.; Bariwal, J.; Singh, V. Medicinal Attributes of Imidazo[1,2-*a*]pyridine Derivatives: An Update. *Curr. Top. Med. Chem*. **2016**, *16*, 2963−2994. (c) Deep, A.; Bhatia, R. K.; Kaur, R.; Kumar, S.; Jain, U. K.; Singh, H.; Batra, S.; Kaushik, D.; Deb, P. K. Imidazo[1,2-*a*]pyridine Scaffold as Prospective Therapeutic Agents. *Curr. Top. Med. Chem*. **2017**, *17*, 238−250.

(12) (a) Kim, O.; Jeong, Y.; Lee, H.; Hong, S.-S.; Hong, S. Design and Synthesis of Imidazopyridine Analogues as Inhibitors of Phosphoinositide 3-Kinase Signaling and Angiogenesis. *J. Med. Chem*. **2011**, *54*, 2455−2466. (b) Kamal, A.; Reddy, J. S.; Ramaiah, M. J.; Dastagiri, D.; Bharathi, E. V.; Sagar, M. V. P.; Pushpavalli, S. N. C. V. L; Ray, P.; Pal-Bhadra, M. Design, Synthesis and Biological Evaluation of Imidazopyridine/pyrimidine-chalcone Derivatives as Potential Anticancer Agents. *Med. Chem. Commun*. **2010**, *1*, 355−360. (c) El-Sayed, W. M.; Hussin, W. A.; Al-Faiyz, Y. S.; Ismail, M. A. The Position of Imidazopyridine and Metabolic Activation Are Pivotal Factors in the Antimutagenic Activity of Novel Imidazo[1,2-*a*]pyridine Derivatives. *Eur. J. Pharmacol*. **2013**, *715*, 212−218.

(13) (a) Almirante, L.; Polo, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Biancotti, A.; Gamba, A.; Murmann, W. Derivatives of Imidazole. I. Synthesis and Reactions of Imidazo[1,2-*a*]pyridines with Analgesic, Antiinflammatory, Antipyretic, and Anticonvulsant Activity. *J. Med. Chem.* **1965**, *8*, 305−312. (b) Lacerda, R. B.; de Lima, C. K. F.; da Silva, L. L.; Romeiro, N. C.; Miranda, A. L. P.; Barreiro, E. J.; Fraga, C. A. M. Discovery of Novel Analgesic and Anti-inflammatory 3-Arylamine-imidazo[1,2-*a*]pyridine Symbiotic Prototypes. *Bioorg. Med. Chem*. **2009**, *17*, 74−84.

(14) (a) Starrett Jr., J. E.; Montzka, T. A.; Crosswell, A. R.; Cavanagh, R. L. Synthesis and Biological Activity of 3-Substituted Imidazo[1,2-*a*]pyridines as Antiulcer Agents. *J. Med. Chem.* **1989**, *32*, 2204−2210. (b) Kaminski, J. J.; Doweyko, A. M. Antiulcer Agents. 6. Analysis of the in Vitro Biochemical and in Vivo Gastric Antisecretory Activity of Substituted Imidazo[1,2-*a*]pyridines and Related Analogues Using Comparative Molecular Field Analysis and Hypothetical Active Site Lattice Methodologies. *J. Med. Chem*. **1997**, *40*, 427−436.

(15) Ismail, M. A.; Arafa, R. K.; Wenzler, T.; Brun, R.; Tanious, F. A.; Wilson, W. D.; Boykin, D. W. Synthesis and Antiprotozoal Activity of Novel Bis-benzamidino Imidazo[1,2-*a*]pyridines and 5,6,7,8-Tetrahydro-imidazo[1,2-*a*]pyridines. *Bioorg. Med. Chem*. **2008**, *16*, 683−691.

(16) Zhuang, Z.-P.; Kung, M.-P.; Wilson, A.; Lee, C.-W.; Plössl, K.; Hou, C.; Holtzman, D. M.; Kung, H. F. Structure−Activity Relationship of Imidazo[1,2-*a*]pyridines as Ligands for Detecting β-Amyloid Plaques in the Brain. *J. Med. Chem.* **2003**, *46*, 237−243.

(17) (a) Koubachi, J.; Kazzouli, S. E.; Bousmina, M.; Guillaumet, G. Functionalization of Imidazo[1,2-*a*]pyridines by Means of Metal-Catalyzed Cross-Coupling Reactions. *Eur. J. Org. Chem.* **2014**, 5119−5138. (b) Pericherla, K.; Kaswan, P.; Pandey, K.; Kumar, A. Recent Developments in the Synthesis of Imidazo[1,2-*a*]pyridines. *Synthesis* **2015**, *47*, 887−912. (c) Bagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. Synthesis of Imidazo[1,2-*a*]pyridines: A Decade Update. *Chem. Commun.* **2015**, *51*, 1555−1575.

(18) Liu, P.; Gao, Y.; Gu, W.; Shen, Z.; Sun, P. Regioselective Fluorination of Imidazo[1,2-*a*]pyridines with Selectfluor in Aqueous Condition. *J. Org. Chem*. **2015**, *80*, 11559−11565.

(19) Chang, Q.; Liu, Z.; Liu, P.; Yu, L.; Sun, P. Visible-Light-Induced Regioselective Cyanomethylation of Imidazopyridines and Its Application in Drug Synthesis. *J. Org. Chem*. **2017**, *82*, 5391−5397.

(20) Chang, Q.; Wu, Z.; Yu, L.; Liu, P.; Sun, P. Visible-Light-Mediated C3-Azolylation of Imidazo[1,2-*a*]pyridines with 2-Bromoazoles. *Org. Biomol. Chem*. **2017**, *15*, 5318−5324.

(21) Gao, Y.; Lu, W.; Liu, P.; Sun, P. Iron-Catalyzed Regioselective Alkoxycarbonylation of Imidazoheterocycles with Carbazates. *J. Org. Chem*. **2016**, *81*, 2482−2487.

(22) (a) Majji, G.; Guin, S.; Rout, S. K.; Behera, A.; Patel, B. K. Cyclic Ethers to Esters and Monoesters to Bis-esters with Unconventional Coupling Partners under Metal Free Conditions *via* sp^3 C–H Functionalisation. *Chem. Commun*. **2014**, *50*, 12193−12196. (b) Zhang, J.; Song, C.; Sheng, L.; Liu, P.; Sun, P. Annulation of 1-(2-Aminoaryl)pyrroles, Ethers with Elemental Sulfur To Give 1,3,6-Benzothiadiazepine Derivatives through Double C−S Bond Formation and C−O Cleavage of Ethers. *J. Org. Chem*. **2019**, *84*, 2191−2199.

(23) Sharma, S.; Saha, B.; Sawant, D.; Kundu, B. Synthesis of Novel N-Rich Polycyclic Skeletons Based on Azoles and Pyridines. *J. Comb. Chem.* **2007***, 9,* 783−792.

(24) Pandey, A. K.; Sharma, R.; Singh, A.; Shukla, S.; Srivastava, K.; Puri, S. K.; Kumar, B.; Chauhan, P. M. S. Synthesis of Biologically Active Pyridoimidazole/imidazobenzothiazole Annulated Polyheterocycles Using Cyanuric Chloride in Water. *RSC Adv.* **2014***, 4,* 26757–26770.

(25) Kielesiński, L.; Tasior, M.; Gryko, D. T. Polycyclic Imidazo[1,2-*a*]pyridine Analogs – Synthesis *via* Oxidative Intramolecular C–H Amination and Optical Properties. *Org. Chem. Front.* **2015***, 2,* 21−28.

(26) Nandwana, N. K.; Dhiman, S.; Saini, H. K.; Kumar, I.; Kumar, A. Synthesis of Quinazolinones, Imidazo[1,2-*c*]quinazolines and Imidazo[4,5-*c*]quinolines through Tandem Reductive Amination of Aryl Halides and Oxidative Amination of C(sp^3)–H Bonds. *Eur. J. Org. Chem.* **2017***,* 514−522.

(27) Mani, G. S.; Rao, A. V. S.; Tangella, Y.; Sunkari, S.; Sultana, F.; Namballa, H. K.; Shankaraiah, N.; Kamal, A. Molecular Iodine-Catalysed Oxidative CO–C(alkyl) Bond Cleavage of Aryl/Heteroaryl Alkyl Aetones: An Efficient Strategy to Access Fused Polyheterocycles. *New J. Chem.* **2018***, 42,* 15820−15829.

(28) Fan, X.-S.; Zhang, J.; Li, B.; Zhang, X.-Y. One-pot Sequential Reactions Featuring a Copper-catalyzed Amination Leading to Pyrido[2',1':2,3]imidazo[4,5-*c*]quinolines and Dihydropyrido[2',1':2,3]imidazo[4,5-*c*]quinolines. *Chem. Asian J.* **2015***, 10,* 1281−1285.