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Electrochemical Oxidative Regioselective C−H Cyanation of Imidazo[1,2-*a*]pyridines

Ting Cui, Yanling Zhan, Changhui Dai, Jun Lin, Ping Liu,* and Peipei Sun*

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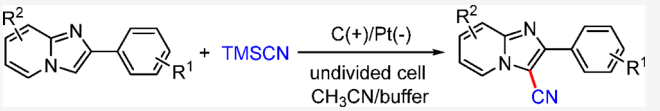
ABSTRACT: Electrochemical oxidative regioselective C−H cyanation of imidazo[1,2-*a*]pyridines was developed using readily available TMSCN as the cyano source. The KH_2PO_4/K_2HPO_4 buffer was essential for this transformation. This protocol was compatible with a broad range of substituted imidazo[1,2-*a*]pyridines and provided the C3 cyanated products in moderate to excellent yields.



INTRODUCTION

Cyano exists in many therapeutic drugs and plays a unique role.[1] Moreover, as a versatile functional group, cyano can be expediently converted into a number of other useful functional groups, such as carbamoyl, carboxyl, aminomethyl, carbonyl, and nitrogen-containing heterocycles, and therefore has extensive applications in organic synthesis.[2] On the other hand, heterocyclic compounds undoubtedly occupy an extremely key position in organic chemistry, especially in medicinal chemistry, so the synthesis of heterocyclic nitriles has aroused great attention of chemists over the past few decades. The direct cyanation of heterocycles is the main approach to obtain heterocyclic nitriles. Palladium-catalyzed cross-coupling of heteroaryl halides with several cyanides such as NaCN, KCN, $Zn(CN)_2$, and $K_4[Fe(CN)_6]$ provided the effective protocols for this purpose (Scheme 1a).[3] However, these methods still have some limitations, e.g., the narrow heterocycle scope and the catalyst deactivation by cyanide.[4] The C−H bond cyanation of arenes provided a new approach for the preparation of aryl nitriles,[5] and this strategy can be used in the cyanation of some heteroarenes. For example, using pyridyl as the directing group, Ackermann et al.[6] and Chang et al.[7] independently demonstrated the cobalt-catalyzed C−H cyanation of (hetero)arenes, in which *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS) and *N*-cyanosuccinimide were employed as the cyano sources, respectively (Scheme 1b). A series of transition metals such as Pd-,[8] Cu-,[9] and Zn-catalyzed[10] cyanations of aromatic heterocycles were developed in recent years, in which DMF, isonitrile, $K_4[Fe(CN)_6]$, NaCN, and nitromethane were employed as the cyanating reagents (Scheme 1c). An electrochemical C−H cyanation of electron-rich (hetero)arenes was reported by Gooßen et al, in which poisonous NaCN was needed (Scheme 1d).[11] Dixon and co-workers[12] used TMSCN as the cyano source, achieving the C−H cyanation of 6-ring *N*-containing heteroaromatics in the presence of Tf_2O and *N*-methylmorpholine (NMM) (Scheme 1e). All the same, in view of the diversity and complexity of heterocyclic compounds, developing the efficient and practical cyanation methods of heterocycles is still a challenging task.

On the other hand, electrochemical synthesis is considered as a clean, environmentally benign, and powerful synthetic strategy in organic transformations and has attracted great attention in recent years in spite of being around for many decades.[13] There are a few examples concerning the $C(sp^2)$−H or $C(sp^3)$−H bond cyanation under the electrochemical conditions.[11,14] The electrocatalytic C−H activation is expected to play an important role in the direct functionalization of heterocyclic compounds. Imidazo[1,2-*a*]pyridine is regarded as a kind of "drug bias" building block in medicinal chemistry;[15] thus, the functional modification of this heterocycle is of great value in pharmaceutical synthesis, and a lot of remarkable works were developed in this area.[16] In continuation of our long-standing interest in the selective direct C−H bond functionalization of imidazo[1,2-*a*]-pyridines,[17] as well as on electrochemical synthesis,[18] herein we want to describe an electrochemical oxidative C−H cyanation of imidazo[1,2-*a*]pyridines using TMSCN as the cyano source to synthesize C3 cyanated products (Scheme 1f).

RESULTS AND DISCUSSION

We began our investigation by using 2-phenylimidazo[1,2-*a*]pyridine (**1a**) and TMSCN (**2**) as the model substrates to explore the reaction conditions (Table 1). The reaction was performed in an undivided cell equipped with a graphite felt electrode as the anode and a platinum plate electrode as the cathode, and $^nBu_4NPF_6$ was employed as the electrolyte. In 10 mL of CH_3CN, under a 5 mA constant current, a trace amount

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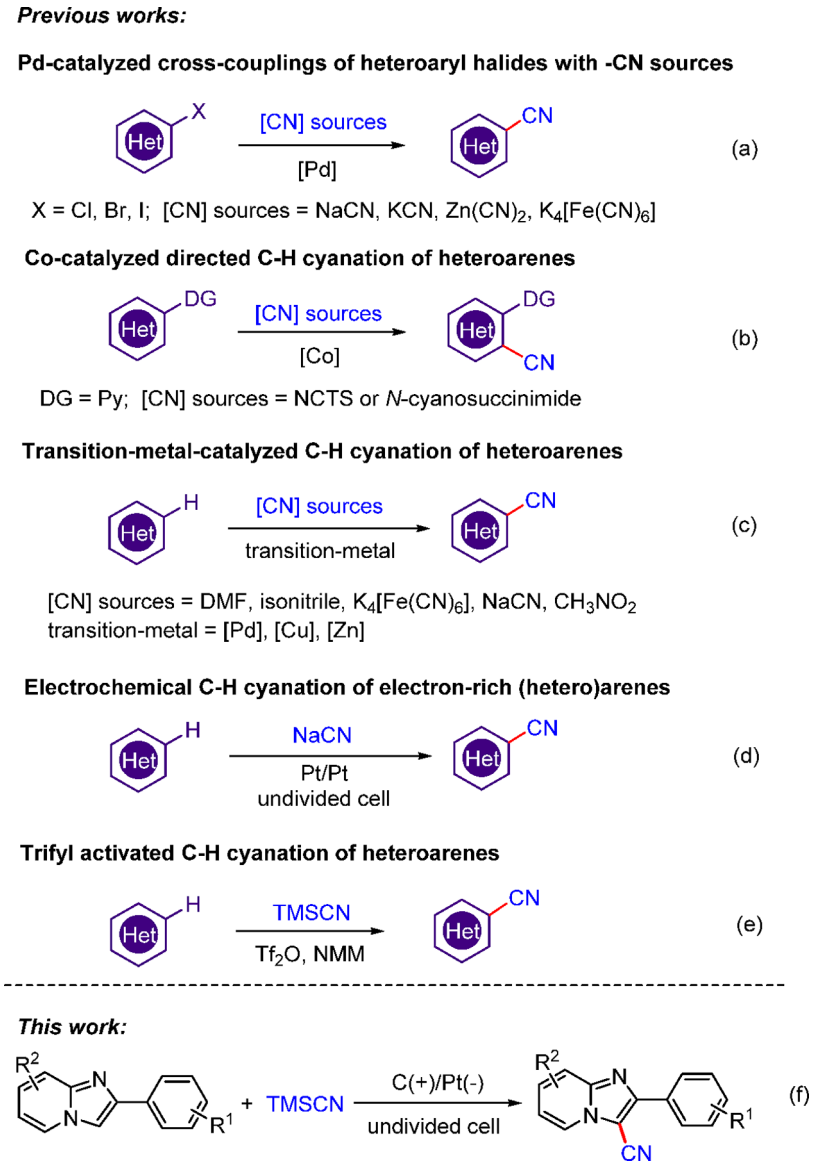
Scheme 1. Cyanation of Heterocycles



of product **3a** was found (entry 1). In CH_2Cl_2, the reaction could not take place at all (entry 2). We were surprised to find that the addition of KH_2PO_4/K_2HPO_4 buffer could effectively promote the reaction. When the cosolvent of CH_3CN and buffer (pH 9) with the ratios (v/v) of 9:1, 1:1, and 1:4 was used, the desired C3-cyanated product **3a** was obtained in 30%, 52%, and 76% yields, respectively (entries 3−5). However, a lower yield of 65% was obtained when a pH 8 buffer was used (entry 6). The supporting electrolyte was then examined. The use of other electrolytes such as $^nBu_4NBF_4$ or $LiClO_4$ did not bring better results (entries 7 and 8). Gratifyingly, the best yield of 82% was obtained in the absence of electrolyte (entry 9). The electrode material has a great influence on the electrochemical reactions. A variety of electrodes were tested (entries 9−13), and C(+)/Pt(−) was proved to be the best one for this transformation (entry 9). Using MeOH or TFE (2,2,2-trifluoroethanol) as the solvent, the yields were reduced (entries 14−16). In other buffer solutions such as $Na_2CO_3/NaHCO_3$ or NH_3/NH_4Cl, the lower yields were obtained (entries 17 and 18). Finally, the reaction did not occur in the absence of an electric current (entry 19).

With the optimized conditions in hand, we turned to examine the scope and limitation of the cyanation of imidazopyridines. As shown in Scheme 2, our method was successfully amenable to a wide range of imidazo[1,2-*a*]pyridines. We first changed the substituents and positions on the phenyl on the C2-position of the imidazo[1,2-*a*]pyridine. The results showed that the reactions of substrates **1** with both electron-donating groups (R^2 = Me, OMe, Ph) and weak electron-withdrawing groups (R^2 = F, Cl, Br, CF_3) on the different position of the benzene ring of 2-phenylimidazo [1,2-*a*]pyridines afforded the C3-cyanated products in moderate to good yields (**3ab**−**3an**, **3f**). Then 2-phenylimidazo [1,2-*a*]pyridines bearing various substituents on the pyridine rings were tested. The position of substituents on the pyridine rings showed no obvious effect on the reaction; substrates with a methyl group at the C-5, C-6, C-7, or C-8 position of 2-phenylimidazo[1,2-*a*]pyridines reacted smoothly with TMSCN and afforded the desired products in 79−85% yields (**3ba**, **3ca**, **3da**, and **3e**). When 8- and 7-methoxyl-

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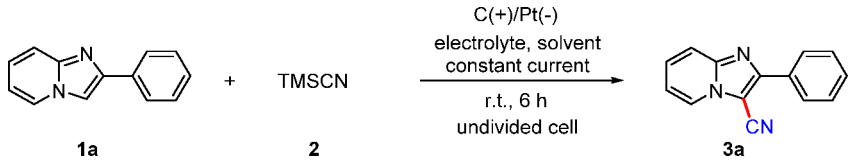
Table 1. Optimization of Reaction Conditions[a]



1a 2 3a

entry	anode/cathode	J/mA cm^{-2}	solvent	buffer[c]	electrolyte	yield (%)[b]
1	C(+)/Pt(−)	5	CH_3CN (10 mL)		$^nBu_4NPF_6$	trace
2	C(+)/Pt(−)	5	DCM (10 mL)		$^nBu_4NPF_6$	0
3	C(+)/Pt(−)	5	CH_3CN (9 mL)	pH 9 (1 mL)	$^nBu_4NPF_6$	30
4	C(+)/Pt(−)	5	CH_3CN (5 mL)	pH 9 (5 mL)	$^nBu_4NPF_6$	52
5	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)	$^nBu_4NPF_6$	76
6	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 8 (8 mL)	$^nBu_4NPF_6$	65
7	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)	$^nBu_4NBF_4$	71
8	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)	$LiClO_4$	40
9	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)		82
10	C(+)/C(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)		23
11	Pt(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)		56
12	C(+)/Fe(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)		29
13	C(+)/Ni(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)		50
14	Pt(+)/Pt(−)	5	MeOH (2 mL)	pH 9 (8 mL)		5
15	C(+)/Pt(−)	5	MeOH (2 mL)	pH 9 (8 mL)		56
16	C(+)/Pt(−)	5	TFE (2 mL)	pH 9 (8 mL)		79
17[d]	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)	$^nBu_4NBF_4$	62
18[e]	C(+)/Pt(−)	5	CH_3CN (2 mL)	pH 9 (8 mL)	$^nBu_4NBF_4$	8
19	C(+)/Pt(−)		CH_3CN (2 mL)	pH 9 (8 mL)		0

[a]Reaction conditions: graphite felt anode, platinum plate cathode (10 mm × 10 mm), constant current (5.0 mA), **1a** (0.2 mmol), **2** (0.6 mmol, 3.0 equiv), supporting electrolyte (0.05 M), solvent (10 mL), undivided cell, under air, rt, 6 h. [b]Isolated yields based on **1a**. [c]Unless otherwise specified, buffer prepared from KH_2PO_4 and K_2HPO_4 at 4 M with respect to phosphate ion. [d]Buffer prepared from Na_2CO_3 and $NaHCO_3$. [e]Buffer prepared from NH_3 and NH_4Cl.

substituted imidazopyridines were treated with TMSCN, the corresponding products could be obtained in 84% and 81% yields, respectively (**3bb** and **3cb**). Besides, the electron-withdrawing groups (R^1 = F, Cl, and CF_3) on pyridine rings were well tolerated and gave the desired products in moderate to good yields (**3bc**, **3cc**−**3ce**, and **3db**). The substrates with 2-naphthyl and 2-thienyl on the 2-position of imidazo[1,2-*a*]pyridines were also investigated and furnished **3g**, **3h**, **3j**, and **3k** in 69−77% yields. Next, imidazopyridines with substituents on both pyridine rings and 2-phenyl were studied. When substrates with a methyl group at the C-6, C-7, or C-8 position of 2-phenylimidazo[1,2-*a*]pyridines, it seemed that electronic effect and the position of substituents on the 2-phenyl showed no obvious impact; various functional groups, including electron-donating (Me, OMe) and electron-withdrawing groups (F, CN, SO_2Me), were well-tolerated, and the reactions gave the desired products **3i**, **3l**, and **3m** in high yields (70−84%). It should be noted that, for the unsubstituted imidazo[1,2-*a*]pyridine and the imidazo[1,2-*a*]pyridines with substituents such as Me, CF_3, or COOEt on the 2-position, almost no corresponding products were obtained, and most of the substrates were recovered (**3q**−**3t**). The cyclic voltammetry (CV) experiments for these reactants **1q**−**1t** were performed, and no obvious oxidation peaks were observed in the 0−2.0 V region (see Supporting Information). In addition, some other imidazo-fused heterocycles such as benzo[*d*]-imidazo[2,1-*b*]thiazole, imidazo[2,1-*b*]thiazole, and imidazo-[1,2-*a*]quinoline were also tested, and the corresponding cyanated products were obtained in 65−75% yields (**3n**−**3p**). Furthermore, when the amount of **1a** was increased to 1 mmol in the same reaction conditions, a 72% yield of **3a** was obtained, indicating that the reaction efficiency did not strikingly decrease.

In order to gain a good insight into the mechanism of this reaction, we conducted several control experiments. When **1a** was employed as the reactant, in the absence of TMSCN, product **3a** was not obtained under the standard reaction conditions (Scheme 3a), which indicated that the cyano in **3a** was derived from TMSCN but not CH_3CN. A kinetic isotope experiment was also done. When **1a** and a 3-deuterated compound **1a′** were used to react with TMSCN separately under standard conditions for 30 min, product **3a** was obtained in 15.3% and 11.9% yields, respectively, and the ratio was nearly 1.29; for 60 min, this ratio was nearly 1.07 (Scheme 3b,c), which suggested that the C−H bond cleavage of imidazo[1,2-*a*]pyridine might not be the rate-determining step of this reaction.

The CV experiments on **1a** and **2** were performed (Figure 1). The oxidation peak of **1a** was observed at 1.30 V (vs SCE), while no obvious oxidation peak of **2** was found in the 0−2.0 V region. These results indicated that our electrochemical oxidative C−H cyanation might begin with the oxidation of **1a** at the anode.

Based on the above experimental results and previous reports, a plausible mechanism for this electrochemical oxidative C−H cyanation is proposed in Scheme 4. First, **1a** was oxidized at the anode to form the radical cation intermediate **A**.[19] Intermediate **A** was then captured by nucleophile TMSCN to deliver adduct **B**. Further oxidation of **B** on the anode gave the cation intermediate **C**. Final

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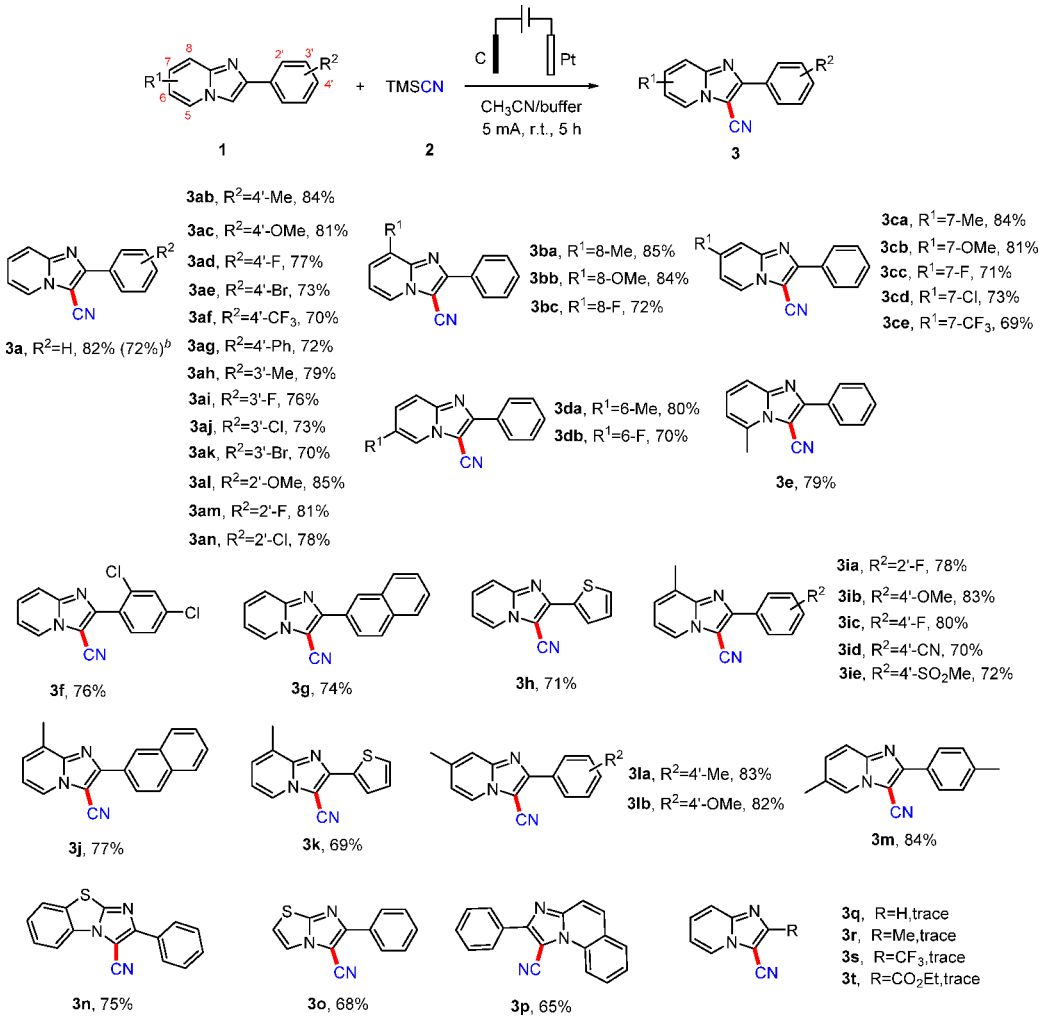
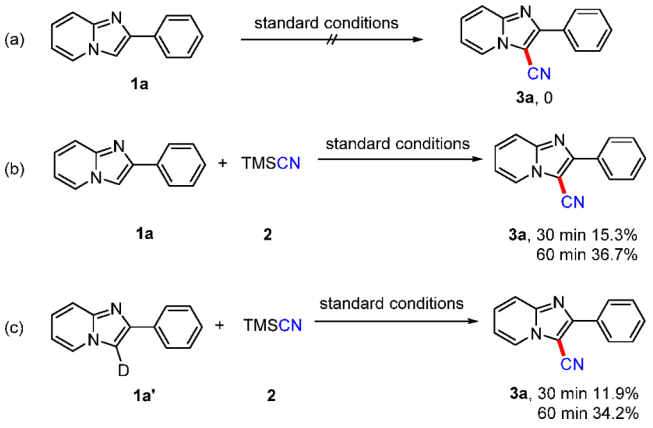
Scheme 2. Substrate Scope for Electrochemical Oxidative Cyanation of Imidazopyridines[a]



[a]Reaction conditions: graphite felt anode, platinum plate cathode (10 mm × 10 mm), constant current (5.0 mA), **1** (0.2 mmol), **2** (0.6 mmol 3.0 equiv), CH_3CN/pH 9 buffer (1:4 (v/v), 10 mL), undivided cell, under air, rt, 6 h. All yields are isolated based on **1**. [b]Compounds **1a** (1 mmol) and **2** (3 mmol 3.0 equiv), CH_3CN/pH 9 buffer (1:4 (v/v), 50 mL), undivided cell, under air, rt, 12 h.

Scheme 3. Control Experiments



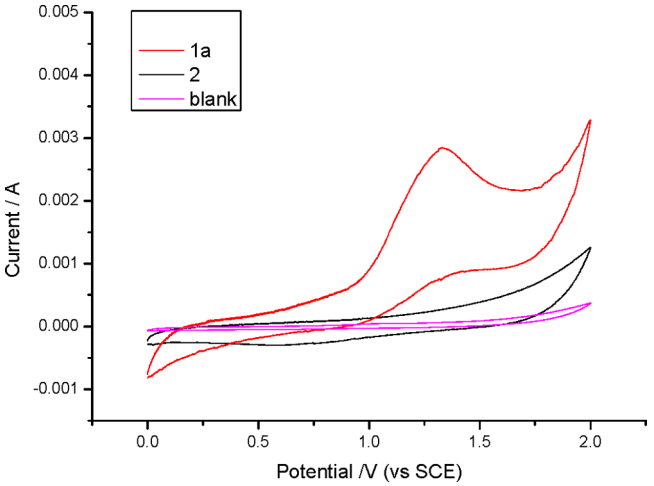


Figure 1. CV scans (scan rate 100 mv s^{-1}) of substrate **1a** (0.01 M) or **2** (0.01 M) in CH_3CN containing $^nBu_4NPF_6$ (0.02 M) at a platinum-wire electrode under air.

deprotonation of the cation intermediate **B** generated the desired product **3a**. At the same time, concomitant cathodic reduction of a proton released hydrogen gas during the reaction.

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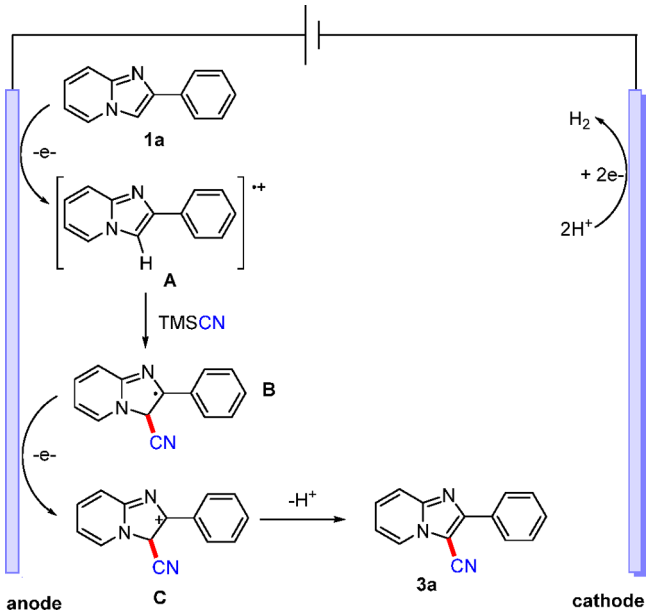
Scheme 4. Proposed Mechanism



In summary, we have developed an efficient method for the electrochemical oxidative C−H thiocyanation of imidazopyridines and similar heterocycles under mild conditions. Commercial readily available TMSCN was utilized as the source of the cyano functional group. A variety of C3 cyanated imidazopyridine products were obtained in satisfactory yields. This electrochemical method may be applied to the field of drug development of imidazopyridine derivatives.

EXPERIMENTAL SECTION

General Information. All reagents were obtained from commercial suppliers and used without further purification. Reactions were monitored by thin-layer chromatography. Column chromatography was performed using silica gel (300−400 mesh). The NMR spectra were recorded on Bruker Avance 400 spectrometers at 400 MHz (^{1}H) and 100 MHz (^{13}C{^{1}H}) in $CDCl_3$ using TMS as an internal standard. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were obtained with an AB Triple 5600 mass spectrometer by ESI on a TOF mass analyzer. Melting points are uncorrected.

General Procedure for the Electrochemical Reaction. To an undivided three-necked flask (25 mL) were added 2-phenylimidazo-[1,2-*a*]pyridine (**1a**, 38.8 mg, 0.2 mmol), TMSCN (**2**, 75 μL, 0.6 mmol, 3 equiv), CH_3CN, and KH_2PO_4/K_2HPO_4 pH 9 buffer (1:4, (v/v), 10 mL). The flask was equipped with a graphite felt electrode as the anode and platinum plate electrode (10 mm × 10 mm) as the cathode. The reaction mixture was electrolyzed and stirred at a constant current (5 mA) under air at room temperature for 6 h. After the reaction was completed, the mixture was diluted with water (30 mL) and then extracted with DCM (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*, and the crude product was obtained. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) as an eluent to give the desired product **3a**.

*2-Phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3a**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (35.9 mg, 82% yield; for 1 mmol of **1a**, 157.7 mg, 72% yield); mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.39−8.37 (m, 1H), 8.22−8.19 (m, 2H), 7.78 (d, J = 9.1 Hz, 1H), 7.56−7.46 (m, 4H), 7.11 (t, J = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.4, 146.9, 131.2, 130.2, 129.1, 128.8, 127.3, 125.6, 118.2, 114.8, 112.8, 93.9.

*2-(p-Tolyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ab**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (39.1 mg, 84% yield); mp 148−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.34 (d, J = 6.7 Hz, 1H), 8.09 (d, J = 8.1 Hz, 2H), 7.74 (d, J = 9.0 Hz, 1H), 7.46−7.42 (m, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.06 (t, J = 6.8 Hz, 1H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.5, 146.8, 140.4, 129.7, 128.7, 128.4, 127.2, 125.6, 118.0, 114.6, 112.9, 93.5, 21.5.

*2-(4-Methoxyphenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ac**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (40.3 mg, 81% yield); mp 204−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.36 (d, J = 6.7 Hz, 1H), 8.17 (d, J = 8.8 Hz, 2H), 7.76 (d, J = 9.0 Hz, 1H), 7.49−7.45 (m, 1H), 7.11−7.04 (m, 3H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 161.2, 153.3, 146.8, 128.8, 128.8, 125.6, 123.7, 117.9, 114.6, 114.4, 113.1, 93.0, 55.4.

*2-(4-Fluorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ad**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (36.5 mg, 77% yield); mp 193−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.35 (d, J = 6.7 Hz, 1H), 8.20−8.16 (m, 2H), 7.75 (d, J = 9.0 Hz, 1H), 7.50−7.46 (m, 1H), 7.20 (t, J = 8.7 Hz, 2H), 7.11 (t, J = 6.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 163.8 (d, J = 250.7 Hz), 152.3, 146.8, 129.3 (d, J = 8.6 Hz), 129.0, 127.4 (d, J = 3.2 Hz), 125.7, 118.1, 116.1 (d, J = 21.9 Hz), 114.9, 112.7, 93.6.

*2-(4-Bromophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ae**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (43.4 mg, 73% yield); mp 165−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.39 (d, J = 6.6 Hz, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.9 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.52 (t, J = 7.8 Hz, 1H), 7.15 (t, J = 6.7 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 152.1, 146.7, 132.3, 130.0, 129.2, 128.8, 125.7, 124.7, 118.2, 115.1, 112.5, 93.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_9BrN_3^+$ 297.9974, found 297.9977.

*2-(4-(Trifluoromethyl)phenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3af**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (40.2 mg, 70% yield); mp 157−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40 (d, J = 6.7 Hz, 1H), 8.32 (d, J = 8.2 Hz, 2H), 7.79 (t, J = 8.3 Hz, 3H), 7.55−7.51 (m, 1H), 7.16 (t, J = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 151.5, 146.9, 134.6, 131.7 (q, J = 32.7 Hz), 129.2, 128.0, 126.0 (q, J = 3.7 Hz), 125.7, 123.9 (q, J = 272.3 Hz), 118.4, 115.2, 112.3, 94.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9F_3N_3^+$ 288.0743, found 288.0743.

*2-([1,1′-Biphenyl]-4-yl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ag**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (42.5 mg, 72% yield); mp 235−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40 (d, J = 6.7 Hz, 1H), 8.30 (d, J = 8.4 Hz, 2H), 7.79 (t, J = 8.8 Hz, 3H), 7.69 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.7 Hz, 3H), 7.41 (t, J = 7.3 Hz, 1H), 7.12 (t, J = 6.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.1, 146.9, 142.9, 140.2, 130.1, 128.9, 128.9, 127.8, 127.7, 127.7, 127.1, 125.7, 118.2, 114.8, 112.9, 93.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{14}N_3^+$ 296.1182, found 296.1183.

*2-(m-Tolyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ah**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (36.8 mg, 79% yield); mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.34 (d, J = 6.7 Hz, 1H), 8.10−7.98 (m, 2H), 7.75 (d, J = 9.0 Hz, 1H), 7.47−7.38 (m, 2H), 7.29 (s, 1H), 7.07 (t, J = 6.5 Hz, 1H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.4, 146.8, 138.8, 131.1, 131.0, 128.9, 128.7, 127.9, 125.6, 124.4, 118.1, 114.7, 112.8, 93.8, 21.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{12}N_3^+$ 234.1026, found 234.1027.

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*2-(3-Fluorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ai**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (36.0 mg, 76% yield); mp 194−196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.39 (dt, J = 6.8, 1.0 Hz, 1H), 8.01−7.99 (m, 1H), 7.94−7.90 (m, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.53−7.48 (m, 2H), 7.21−7.12 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 163.1 (d, J = 246.6 Hz), 151.9, 146.8, 133.3 (d, J = 8.2 Hz), 130.7 (d, J = 8.2 Hz), 129.1, 125.7, 122.9 (d, J = 3.0 Hz), 118.3, 117.1 (d, J = 21.2 Hz), 115.1, 114.3 (d, J = 23.4 Hz), 112.4, 94.2; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9FN_3^+$ 238.0775, found 238.0776.

*2-(3-Chlorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3aj**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (37.0 mg, 73% yield); mp 189−191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.41−8.40 (m, 1H), 8.21 (q, J = 1.2 Hz, 1H), 8.11−8.09 (m, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.54−7.45 (m, 3H), 7.15 (td, J = 6.9, 1.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 151.8, 146.8, 135.2, 132.9, 130.3, 130.2, 129.1, 127.4, 125.7, 125.3, 118.3, 115.1, 112.4, 94.2; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9ClN_3^+$ 254.0480, found 254.0481.

*2-(3-Bromophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ak**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (41.6 mg, 70% yield); mp 175−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40−8.36 (m, 2H), 8.13 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 9.0 Hz, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.53−7.49 (m, 1H), 7.40 (t, J = 7.9 Hz, 1H), 7.14 (t, J = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 151.5, 146.8, 133.1, 130.5, 130.3, 129.1, 125.7, 125.7, 123.3, 118.3, 115.1, 112.4, 94.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9BrN_3^+$ 297.9974, found 297.9974.

*2-(2-Methoxyphenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3al**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (42.3 mg, 85% yield); mp 129−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.37 (d, J = 6.8 Hz, 1H), 8.01 (dd, J = 7.7, 1.5 Hz, 1H), 7.73 (d, J = 9.0 Hz, 1H), 7.46−7.39 (m, 2H), 7.12−7.02 (m, 3H), 3.99 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 157.0, 149.4, 146.2, 131.3, 130.9, 128.2, 125.4, 120.9, 120.6, 117.9, 114.4, 112.6, 111.1, 97.3, 54.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{12}N_3O^+$ 250.0975, found 250.0976.

*2-(2-Fluorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3am**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (38.4 mg, 81% yield); mp 195−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.43 (d, J = 6.7 Hz, 1H), 8.01 (t, J = 7.5 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.54−7.47 (m, 2H), 7.15 (t, J = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 160.1 (d, J = 252.4 Hz), 148.2, 146.6, 131.8 (d, J = 8.4 Hz), 130.9 (d, J = 2.8 Hz), 128.8, 125.7, 124.7 (d, J = 3.6 Hz), 119.4 (d, J = 13.4 Hz), 118.3, 116.4 (d, J = 21.7 Hz), 115.0, 116.4 (d, J = 21.7 Hz), 96.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9FN_3^+$ 238.0775, found 238.0776.

*2-(2-Chlorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3an**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1, v/v): white solid (39.5 mg, 78% yield); mp 170−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.42 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 9.1 Hz, 1H), 7.69−7.67 (m, 1H), 7.57−7.51 (m, 2H), 7.46−7.39 (m, 2H), 7.16 (t, J = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 151.8, 146.4, 133.2, 132.0, 131.0, 130.6, 130.4, 128.8, 127.1, 125.7, 118.5, 115.1, 111.6, 97.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9ClN_3^+$ 254.0480, found 254.0482.

*8-Methyl-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3ba**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (39.6 mg, 85% yield); mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.21−8.17 (m, 3H), 7.53−7.44 (m, 3H), 7.20 (d, J = 7.0 Hz, 1H), 6.95 (t, J = 6.9 Hz, 1H), 2.68 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 152.7, 147.2, 131.5, 129.9, 128.9, 128.6, 127.5, 127.3, 123.3, 114.7, 113.1, 94.1, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{12}N_3^+$ 234.1026, found 234.1027.

*8-Methoxy-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3bb**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (41.8 mg, 84% yield); mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.25−8.23 (m, 2H), 7.99 (d, J = 6.6 Hz, 1H), 7.53−7.44 (m, 3H), 7.01−6.97 (m, 1H), 6.74 (d, J = 7.8 Hz, 1H), 4.08 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 152.4, 149.3, 141.0, 131.0, 130.0, 128.9, 127.4, 118.1, 114.9, 112.8, 104.9, 94.8, 56.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{12}N_3O^+$ 250.0975, found 250.0976.

*8-Fluoro-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3bc**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (34.1 mg, 72% yield); mp 135−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.25−8.22 (m, 3H), 7.57−7.50 (m, 3H), 7.23−7.18 (m, 1H), 7.06 (td, J = 7.7, 7.3, 4.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.4, 151.5 (d, J = 256.5 Hz), 139.5 (d, J = 28.6 Hz), 130.7, 130.5, 129.1, 127.5, 121.9 (d, J = 5.4 Hz), 114.1 (d, J = 6.5 Hz), 112.3 (d, J = 1.5 Hz), 111.6 (d, J = 16.3 Hz), 95.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9FN_3^+$ 238.0775, found 238.0776.

*7-Methyl-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3ca**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (39.1 mg, 84% yield); mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.17−8.14 (m, 3H), 7.52−7.42 (m, 4H), 6.86−6.84 (m, 1H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.3, 147.2, 140.4, 131.3, 130.0, 128.9, 127.2, 124.7, 117.3, 116.7, 113.1, 93.2, 21.6.

*7-Methoxy-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3cb**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (40.3 mg, 81% yield); mp 173−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15−8.09 (m, 3H), 7.51−7.42 (m, 3H), 6.98 (d, J = 2.3 Hz, 1H), 6.72 (dd, J = 7.4, 2.4 Hz, 1H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 160.6, 153.6, 148.7, 131.3, 130.0, 128.9, 127.1, 125.8, 113.2, 109.4, 95.8, 92.6, 55.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{12}N_3O^+$ 250.0975, found 250.0975.

*7-Fluoro-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3cm**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (33.7 mg, 71% yield); mp 185−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.35−8.32 (m, 1H), 8.19−8.17 (m, 2H), 7.56−7.48 (m, 3H), 7.42 (dd, J = 8.6, 2.0 Hz, 1H), 6.98 (td, J = 7.1, 2.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 162.3 (d, J = 257.8 Hz), 154.6, 147.5 (d, J = 14.0 Hz), 130.8, 130.5, 129.1, 127.3, 127.1 (d, J = 11.0 Hz), 112.5, 107.1 (d, J = 29.1 Hz), 102.5 (d, J = 24.0 Hz), 93.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9FN_3^+$ 238.0775, found 238.0776.

*7-Chloro-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3cd**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (36.9 mg, 73% yield); mp 193−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.30−8.28 (m, 1H), 8.19−8.16 (m, 2H), 7.77 (d, J = 1.4 Hz, 1H), 7.56−7.48 (m, 3H), 7.09 (dd, J = 7.2, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 154.2, 146.6, 135.6, 130.7, 130.5, 129.1, 127.3, 125.8, 117.2, 116.4, 112.4, 94.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9ClN_3^+$ 254.0480, found 254.0480.

*2-Phenyl-7-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ce**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (39.6 mg, 69% yield); mp 145−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.50 (d, J = 7.1 Hz, 1H), 8.23−8.20 (m, 2H), 8.08 (s, 1H), 7.59−7.51 (m, 3H), 7.30−7.28 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 154.7, 145.1, 130.8 130.7 (q, J = 34.8 Hz), 130.5, 129.2, 127.4, 126.5, 122.6 (q, J = 272.8 Hz), 116.0 (q, J = 4.7 Hz), 111.9, 110.7 (q, J = 2.9 Hz), 95.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_9F_3N_3^+$ 288.0743, found 288.0744.

*6-Methyl-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3da**).*[20] This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (37.3 mg, 80%

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yield); mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.16 (d, J = 7.9 Hz, 2H), 8.10 (s, 1H), 7.62 (d, J = 9.1 Hz, 1H), 7.52−7.43 (m, 3H), 7.26 (d, J = 9.2 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 152.9, 145.8, 131.8, 131.3, 130.0, 129.0, 127.1, 125.0, 123.4, 117.3, 113.0, 93.4, 18.2.

*6-Fluoro-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3db**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (33.2 mg, 70% yield); mp 194−196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.34 (t, J = 2.5 Hz, 1H), 8.20−8.18 (m, 2H), 7.79 (dd, J = 9.8, 4.8 Hz, 1H), 7.57−7.50 (m, 3H), 7.45−7.40 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 154.3 (d, J = 242.8 Hz), 154.0 (d, J = 2.4 Hz), 144.3, 130.8, 130.4, 129.1, 127.2, 120.9 (d, J = 25.0 Hz), 118.7 (d, J = 8.7 Hz), 113.0 (d, J = 41.4 Hz), 112.2, 95.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_9FN_3^+$ 238.0775, found 238.0776.

*5-Methyl-2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (**3e**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (36.8 mg, 79% yield); mp 148−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.20−8.17 (m, 2H), 7.66 (d, J = 8.9 Hz, 1H), 7.55−7.47 (m, 3H), 7.37 (dd, J = 8.9, 7.1 Hz, 1H), 6.77 (d, J = 7.0 Hz, 1H), 3.05 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 155.3, 147.8, 138.1, 131.4, 130.0, 129.1, 128.9, 127.7, 116.0, 115.5, 115.3, 93.0, 20.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{12}N_3^+$ 234.1026, found 234.1027.

*2-(2,4-Dichlorophenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3f**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 6:1, v/v): white solid (43.6 mg, 76% yield); mp 210−212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.44 (d, J = 6.5 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.66−7.53 (m, 3H), 7.43−7.41 (m, 1H), 7.19 (t, J = 6.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 150.7, 146.4, 136.5, 134.0, 132.8, 130.3, 129.2, 129.0, 127.5, 125.7, 118.6, 115.3, 111.3, 97.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_8Cl_2N_3^+$ 288.0090, found 288.0090.

*2-(Naphthalen-2-yl)imidazo[1,2-a]pyridine-3-carbonitrile (**3g**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 6:1, v/v): white solid (39.8 mg, 74% yield); mp 202−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.72 (s, 1H), 8.38 (d, J = 6.7 Hz, 1H), 8.31 (dd, J = 8.6, 1.7 Hz, 1H), 7.99 (dd, J = 8.9, 4.6 Hz, 2H), 7.91−7.88 (m, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.58−7.53 (m, 2H), 7.51−7.46 (m, 1H), 7.13−7.07 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.2, 146.9, 134.1, 133.3, 128.9, 128.9, 128.8, 128.5, 127.8, 127.2, 126.7, 125.6, 124.2, 118.1, 114.8, 113.0, 94.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{12}N_3^+$ 270.1026, found 270.1027.

*2-(Thiophen-2-yl)imidazo[1,2-a]pyridine-3-carbonitrile (**3h**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (31.9 mg, 71% yield); mp 145−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.34 (d, J = 6.7 Hz, 1H), 7.94 (dd, J = 3.7, 0.9 Hz, 1H), 7.76 (d, J = 9.1 Hz, 1H), 7.53−7.46 (m, 2H), 7.21 (dd, J = 5.0, 3.8 Hz, 1H), 7.13−7.10 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 148.5, 146.7, 134.4, 129.0, 128.4, 128.4, 127.3, 125.6, 117.9, 114.9, 112.3, 92.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{12}H_8N_3S^+$ 226.0433, found 226.0434.

*2-(2-Fluorophenyl)-8-methylimidazo[1,2-a]pyridine-3-carbonitrile (**3ia**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (39.2 mg, 78% yield); mp 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.26 (d, J = 6.7 Hz, 1H), 8.02 (td, J = 7.5, 1.7 Hz, 1H), 7.50−7.44 (m, 1H), 7.33−7.22 (m, 3H), 7.02 (t, J = 6.9 Hz, 1H), 2.70 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 160.0 (d, J = 252.0 Hz), 147.5 (d, J = 1.8 Hz), 147.0, 131.6 (d, J = 8.3 Hz), 131.1 (d, J = 2.9 Hz), 128.7, 127.5, 124.7 (d, J = 3.6 Hz), 123.3, 119.7 (d, J = 13.7 Hz), 116.3 (d, J = 21.7 Hz), 114.9, 111.8 (d, J = 2.2 Hz), 97.2, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{11}FN_3^+$ 252.0932, found 252.0933.

*2-(4-Methoxyphenyl)-8-methylimidazo[1,2-a]pyridine-3-carbonitrile (**3ib**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (43.7 mg, 83% yield); mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.18−8.14 (m, 3H), 7.20 (dt, J = 7.0, 1.0 Hz, 1H), 7.04−7.00 (m, 2H), 6.94 (t, J = 6.9 Hz, 1H), 3.88 (s, 3H), 2.67 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 161.0, 152.7, 147.1, 128.8, 128.3, 127.4, 124.1, 123.2, 114.4, 114.3, 113.4, 93.2, 55.4, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3O^+$ 264.1131, found 264.1133.

*2-(4-Fluorophenyl)-8-methylimidazo[1,2-a]pyridine-3-carbonitrile (**3ic**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (40.2 mg, 80% yield); mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.22−8.17 (m, 3H), 7.25−7.17 (m, 3H), 6.99 (t, J = 6.9 Hz, 1H), 2.68 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 163.7 (d, J = 250.3 Hz), 151.8, 147.2, 129.3 (d, J = 8.5 Hz), 128.6, 127.7 (d, J = 3.2 Hz), 127.6, 123.3, 116.0 (d, J = 21.8 Hz), 114.8, 113.0, 93.8, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{11}FN_3^+$ 252.0932, found 252.0932.

*2-(4-Cyanophenyl)-8-methylimidazo[1,2-a]pyridine-3-carbonitrile (**3id**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (36.1 mg, 70% yield); mp 255−257 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.36 (d, J = 8.5 Hz, 2H), 8.27 (d, J = 6.7 Hz, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 7.0 Hz, 1H), 7.07 (t, J = 6.9 Hz, 1H), 2.72 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 150.2, 147.4, 135.8, 132.7, 129.1, 128.0, 127.8, 123.4, 118.6, 115.4, 113.2, 112.5, 95.1, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{11}N_4^+$ 259.0978, found 259.0979.

*8-Methyl-2-(4-(methylsulfonyl)phenyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3ie**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (44.8 mg, 72% yield); mp 202−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40 (d, J = 8.5 Hz, 2H), 8.25 (d, J = 6.7 Hz, 1H), 8.07 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 7.1 Hz, 1H), 7.06 (t, J = 6.9 Hz, 1H), 3.12 (s, 3H), 2.70 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 150.1, 147.3, 141.2, 136.7, 129.1, 128.1, 128.1, 128.0, 123.4, 115.5, 112.4, 95.1, 44.6, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3O_2S^+$ 312.0801, found 312.0804.

*8-Methyl-2-(naphthalen-2-yl)imidazo[1,2-a]pyridine-3-carbonitrile (**3j**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (43.6 mg, 77% yield); mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.69 (s, 1H), 8.31 (dd, J = 8.5, 1.5 Hz, 1H), 8.17 (d, J = 6.6 Hz, 1H), 7.99−7.94 (m, 2H), 7.87 (dd, J = 6.0, 3.3 Hz, 1H), 7.54 (dt, J = 6.2, 3.4 Hz, 2H), 7.18 (d, J = 6.9 Hz, 1H), 6.92 (t, J = 6.8 Hz, 1H), 2.70 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 152.5, 147.2, 134.0, 133.2, 128.9, 128.8, 128.6, 128.5, 127.8, 127.5, 127.0, 127.0, 126.5, 124.4, 123.2, 114.7, 113.3, 94.3, 17.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{14}N_3^+$ 284.1182, found 284.1183.

*8-Methyl-2-(thiophen-2-yl)imidazo[1,2-a]pyridine-3-carbonitrile (**3k**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (33.0 mg, 69% yield); mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.20 (d, J = 6.7 Hz, 1H), 7.93 (dd, J = 3.7, 0.9 Hz, 1H), 7.50 (dd, J = 5.0, 0.9 Hz, 1H), 7.25 (d, J = 7.0 Hz, 1H), 7.20 (dd, J = 5.0, 3.8 Hz, 1H), 7.00 (t, J = 6.9 Hz, 1H), 2.70 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 147.9, 147.1, 134.6, 128.4, 128.3, 128.1, 127.7, 127.2, 123.3, 114.8, 112.6, 93.0, 16.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{13}H_{10}N_3S^+$ 240.0590, found 240.0592.

*7-Methyl-2-(p-tolyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3la**).* This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (41.0 mg, 83% yield); mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.21 (d, J = 6.9 Hz, 1H), 8.07 (d, J = 8.2 Hz, 2H), 7.50 (s, 1H), 7.32 (d, J = 8.0 Hz, 2H), 6.90 (dd, J = 6.9, 1.3 Hz, 1H), 2.48 (s, 3H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.6, 147.2, 140.3, 140.3, 129.7, 128.5, 127.1, 124.7, 117.1, 116.6, 113.2, 92.9, 21.6, 21.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3^+$ 248.1182, found 248.1183.

*2-(4-Methoxyphenyl)-7-methylimidazo[1,2-a]pyridine-3-carbonitrile (**3lb**).* This compound was purified by silica gel column

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chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (43.1 mg, 82% yield); mp 159−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.18 (d, J = 6.9 Hz, 1H), 8.14−8.10 (m, 2H), 7.46 (s, 1H), 7.04−7.00 (m, 2H), 6.87 (dd, J = 6.9, 1.5 Hz, 1H), 3.88 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 161.0, 153.4, 147.2, 140.3, 128.7, 124.6, 123.9, 117.0, 116.4, 114.3, 113.4, 92.3, 55.4, 21.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3O^+$ 264.1131, found 264.1132.

6-Methyl-2-(p-tolyl)imidazo[1,2-a]pyridine-3-carbonitrile (**3m**). This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (41.5 mg, 84% yield); mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.16 (s, 1H), 8.09 (d, J = 8.2 Hz, 2H), 7.66 (d, J = 9.1 Hz, 1H), 7.32 (t, J = 7.9 Hz, 3H), 2.44 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 153.2, 145.8, 140.3, 131.8, 129.7, 128.5, 127.1, 124.8, 123.5, 117.3, 113.2, 93.1, 21.5, 18.2; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3^+$ 248.1182, found 248.1184.

2-Phenylbenzo[d]imidazo[2,1-b]thiazole-3-carbonitrile (**3n**). This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (41.3 mg, 75% yield); mp 176−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15−8.10 (m, 3H), 7.75 (d, J = 8.0 Hz, 1H), 7.54−7.41 (m, 5H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 156.0, 151.4, 131.9, 131.2, 130.0, 129.9, 129.0, 127.1, 126.6, 126.1, 124.5, 113.4, 113.2, 94.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{10}N_3S^+$ 276.0590, found 276.0590.

6-Phenylimidazo[2,1-b]thiazole-5-carbonitrile (**3o**). This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (30.6 mg, 68% yield); mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.10−8.08 (m, 2H), 7.66 (d, J = 4.4 Hz, 1H), 7.53−7.44 (m, 3H), 7.10 (d, J = 4.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 155.8, 153.0, 131.4, 129.8, 129.0, 126.7, 118.5, 115.2, 112.7, 94.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{12}H_8N_3S^+$ 226.0433, found 226.0434.

2-Phenyl-1,2-dihydroimidazo[1,2-a]quinoline-1-carbonitrile (**3p**). This compound was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 8:1, v/v): white solid (35.0 mg, 65% yield); mp 156−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.93 (d, J = 8.6 Hz, 1H), 8.20 (d, J = 7.1 Hz, 2H), 7.81 (d, J = 7.9 Hz, 1H), 7.68 (t, J = 7.3 Hz, 2H), 7.60 (d, J = 9.4 Hz, 1H), 7.55−7.46 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6, 145.7, 133.5, 131.2, 130.7, 130.0, 129.9, 129.6, 129.0, 127.4, 126.1, 124.0, 116.6, 115.8, 115.4, 94.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{12}N_3^+$ 270.1026, found 270.1027.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c03026.

Control experiments and copies of ^{1}H NMR, ^{13}C{^{1}H} NMR, and HRMS spectra for products **3** (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Ping Liu − *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 and Changzhou Innovation and Development Institute, Nanjing Normal University, Nanjing 210023, China*; Email: pingliu@njnu.edu.cn

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*; orcid.org/0000-0002-1716-2343; Email: sunpeipei@njnu.edu.cn

Authors

Ting Cui − *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*

Yanling Zhan − *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*

Changhui Dai − *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*

Jun Lin − *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 and Changzhou Innovation and Development Institute, Nanjing Normal University, Nanjing 210023, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c03026

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Fleming, F. F.; Yao, L.; Ravikumar, P. C.; Funk, L.; Shook, B. C. Nitrile-Containing Pharmaceuticals: Efficacious Roles of the Nitrile Pharmacophore. *J. Med. Chem.* **2010**, *53*, 7902−7917. (b) Wang, J.; Liu, H. Application of Nitrile in Drug Design. *Youji Huaxue* **2012**, *32*, 1643−1652.

(2) Fatiadi, A. J. In *Preparation and Synthetic Applications of Cyano Compounds*; Patai, S., Rappaport, Z., Eds.; Wiley-VCH: New York, 1983.

(3) For partial reviews and examples, see: (a) Ellis, G. P.; Romney-Alexander, T. M. Cyanation of Aromatic Halides. *Chem. Rev.* **1987**, *87*, 779−794. (b) Anbarasan, P.; Schareina, T.; Beller, M. Recent Developments and Perspectives in Palladium-Catalyzed Cyanation of Aryl Halides: Synthesis of Benzonitriles. *Chem. Soc. Rev.* **2011**, *40*, 5049−5067. (c) Littke, A.; Soumeillant, M.; Kaltenbach III, R. F.; Cherney, R. J.; Tarby, C. M.; Kiau, S. Mild and General Methods for the Palladium-Catalyzed Cyanation of Aryl and Heteroaryl Chlorides. *Org. Lett.* **2007**, *9*, 1711−1714. (d) Ushkov, A. V.; Grushin, V. V. Rational Catalysis Design on the Basis of Mechanistic Understanding: Highly Efficient Pd-Catalyzed Cyanation of Aryl Bromides with NaCN in Recyclable Solvents. *J. Am. Chem. Soc.* **2011**, *133*, 10999−11005. (e) Zhang, D.; Sun, H.; Zhang, L.; Zhou, Y.; Li, C.; Jiang, H.; Chen, K.; Liu, H. An Expedient Pd/DBU Mediated Cyanation of Aryl/Heteroaryl Bromides with $K_4[Fe(CN)_6]$. *Chem. Commun.* **2012**, *48*, 2909−2911. (f) Senecal, T. D.; Shu, W.; Buchwald, S. L. A General, Practical Palladium-Catalyzed Cyanation of (Hetero)Aryl Chlorides and Bromides. *Angew. Chem., Int. Ed.* **2013**, *52*, 10035−10039. (g) Cohen, D. T.; Buchwald, S. L. Mild Palladium-Catalyzed

Cyanation of (Hetero)aryl Halides and Triflates in Aqueous Media. *Org. Lett.* **2015**, *17*, 202−205.
(4) Erhardt, S.; Grushin, V. V.; Kilpatrick, A. H.; Macgregor, S. A.; Marshall, W. J.; Roe, D. C. Mechanisms of Catalyst Poisoning in Palladium-Catalyzed Cyanation of Haloarenes. Remarkably Facile C-N Bond Activation in the $[(Ph_3P)_4Pd]/[Bu_4N]^+CN^-$ System. *J. Am. Chem. Soc.* **2008**, *130*, 4828−4845.
(5) Ping, Y.; Ding, Q.; Peng, Y. Advances in C-CN Bond Formation via C-H Bond Activation. *ACS Catal.* **2016**, *6*, 5989−6005.
(6) Li, J.; Ackermann, L. Cobalt-Catalyzed C-H Cyanation of Arenes and Heteroarenes. *Angew. Chem., Int. Ed.* **2015**, *54*, 3635−3638.
(7) Pawar, A. B.; Chang, S. Cobalt-Catalyzed C-H Cyanation of (Hetero)arenes and 6-Arylpurines with *N* -Cyanosuccinimide as a New Cyanating Agent. *Org. Lett.* **2015**, *17*, 660−663.
(8) (a) Ding, S.; Jiao, N. Direct Transformation of *N*, *N* -Dimethylformamide to -CN: Pd-Catalyzed Cyanation of Heteroarenes via C-H Functionalization. *J. Am. Chem. Soc.* **2011**, *133*, 12374−12377. (b) Xu, S.; Huang, X.; Hong, X.; Xu, B. Palladium-Assisted Regioselective C-H Cyanation of Heteroarenes Using Isonitrile as Cyanide Source. *Org. Lett.* **2012**, *14*, 4614−4617. (c) Yan, G.; Kuang, C.; Zhang, Y.; Wang, J. Palladium-Catalyzed Direct Cyanation of Indoles with $K_4[Fe(CN)_6]$. *Org. Lett.* **2010**, *12*, 1052−1055.
(9) Do, H.-Q.; Daugulis, O. Copper-Catalyzed Cyanation of Heterocycle Carbon-Hydrogen Bonds. *Org. Lett.* **2010**, *12*, 2517−2519.
(10) Nagase, Y.; Sugiyama, T.; Nomiyama, S.; Yonekura, K.; Tsuchimoto, T. Zinc-Catalyzed Direct Cyanation of Indoles and Pyrroles: Nitromethane as a Source of a Cyano Group. *Adv. Synth. Catal.* **2014**, *356*, 347−352.
(11) Hayrapetyan, D.; Rit, R. K.; Kratz, M.; Tschulik, K.; Gooßen, L. J. Electrochemical C-H Cyanation of Electron-Rich (Hetero)Arenes. *Chem. - Eur. J.* **2018**, *24*, 11288−11291.
(12) Elbert, B. L.; Farley, A. J. M.; Gorman, T. W.; Johnson, T. C.; Genicot, C.; Lallemand, B.; Pasau, P.; Flasz, J.; Castro, J. L.; MacCoss, M.; Paton, R. S.; Schofield, C. J.; Smith, M. D.; Willis, M. C.; Dixon, D. J. C-H Cyanation of 6-Ring N-Containing Heteroaromatics. *Chem. - Eur. J.* **2017**, *23*, 14733−14737.
(13) For partial reviews, see: (a) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, *117*, 13230−13319. (b) Sauermann, N.; Meyer, T. H.; Qiu, Y.; Ackermann, L. Electrocatalytic C-H Activation. *ACS Catal.* **2018**, *8*, 7086−7103. (c) Wiebe, A.; Gieshoff, T.; Möhle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S. R. Electrifying Organic Synthesis. *Angew. Chem., Int. Ed.* **2018**, *57*, 5594−5619. (d) Yuan, Y.; Lei, A. Electrochemical Oxidative Cross-Coupling with Hydrogen Evolution Reactions. *Acc. Chem. Res.* **2019**, *52*, 3309−3324. (e) Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. Recent Advances in Oxidative R^1-H/R^2-H Cross-Coupling with Hydrogen Evolution via Photo-/Electrochemistry. *Chem. Rev.* **2019**, *119*, 6769−6787. (f) Yamamoto, K.; Kuriyama, M.; Onomura, O. Anodic Oxidation for the Stereoselective Synthesis of Heterocycles. *Acc. Chem. Res.* **2020**, *53*, 105−120. (g) Xiong, P.; Xu, H.-C. Chemistry with Electrochemically Generated *N* -Centered Radicals. *Acc. Chem. Res.* **2019**, *52*, 3339−3350. (h) Listratova, A. V.; Sbei, N.; Voskressensky, L. G. Catalytic Electrosynthesis of *N*,*O*-Heterocycles-Recent Advances. *Eur. J. Org. Chem.* **2020**, *2020*, 2012−2027.
(14) Libendi, S. S.; Demizu, Y.; Onomura, O. Direct Electrochemical *a*-Cyanation of *N*-Protected Cyclic Amines. *Org. Biomol. Chem.* **2009**, *7*, 351−356.
(15) (a) Enguehard-Gueiffier, C.; Gueiffier, A. Recent Progress in the Pharmacology of Imidazo[1,2-*a*]pyridines. *Mini-Rev. Med. Chem.* **2007**, *7*, 888−899. (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) 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. *MedChemComm* **2010**, *1*, 355−360.
(16) For partial reviews, see: (a) Fbagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. Synthesis of Imidazo[1,2-*a*]pyridines: A Decade Update. *Chem. Commun.* **2015**, *51*, 1555−1575. (b) Bagdi, A. K.; Hajra, A. Visible Light Promoted C-H Functionalization of Imidazoheterocycles. *Org. Biomol. Chem.* **2020**, *18*, 2611−2631. (c) Tashrifi, Z.; Mohammadi-Khanaposhtani, M.; Larijani, B.; Mahdavi, M. C3-Functionalization of Imidazo[1,2-*a*]pyridines. *Eur. J. Org. Chem.* **2020**, *2020*, 269−284. (d) Jin, C.; Xu, Q.; Feng, G.; Jin, Y.; Zhang, L. Progress in C-H Bond Functionalization on C-3 Position of Imidazo[1,2-*a*]pyridines. *Youji Huaxue* **2018**, *38*, 775−790. (e) Yu, Y.; Su, Z.; Cao, H. Strategies for Synthesis of Imidazo[1,2-*a*]pyridine Derivatives: Carbene Transformations or C-H Functionalizations. *Chem. Rec.* **2019**, *19*, 2105−2118. (f) Patel, O. P. S.; Nandwana, N. K.; Legoabe, L. J.; Das, B. C.; Kumar, A. Recent Advances in Radical C-H Bond Functionalization of Imidazoheterocycles. *Adv. Synth. Catal.* **2020**, *362*, 4226−4255. (g) Pericherla, K.; Kaswan, P.; Pandey, K.; Kumar, A. Recent Developments in the Synthesis of Imidazo[1,2-*a*]pyridines. *Synthesis* **2015**, *47*, 887−912.
(17) For the partial work of our group on the functionalization of imidazo[1,2-*a*]pyridines, see: (a) 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. (b) Gao, Y.; Lu, W.; Liu, P.; Sun, P. Iron-Catalyzed Regioselective Alkoxycarbonylation of Imidazoheterocycles with Carbazates. *J. Org. Chem.* **2016**, *81*, 2482−2487. (c) 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. (d) Lian, G.; Li, J.; Liu, P.; Sun, P. An Approach to Quinoline-Fused Imidazopyridines via CDC of Ethers with Imidazopyridines under Metal-Free Conditions. *J. Org. Chem.* **2019**, *84*, 16346−16354. (e) Zhang, J.; Xie, S.; Liu, P.; Sun, P. Mild and Regioselective Three-component Heteroarylation-Nitration of Alkenes with Imidazo[1,2-*a*]pyridines and *tert*-Butyl Nitrite. *Adv. Synth. Catal.* **2020**, *362*, 2173−2177. (f) Li, Y.; Shu, K.; Liu, P.; Sun, P. Selective C-5 Oxidative Radical Silylation of Imidazopyridines Promoted by Lewis Acid. *Org. Lett.* **2020**, *22*, 6304−6307.
(18) (a) Zhang, X.; Cui, T.; Zhao, X.; Liu, P.; Sun, P. Electrochemical Difunctionalization of Alkenes by a Four-Component Reaction Cascade Mumm Rearrangement: Rapid Access to Functionalized Imides. *Angew. Chem., Int. Ed.* **2020**, *59*, 3465−3469. (b) Zhang, X.; Cui, T.; Zhang, Y.; Gu, W.; Liu, P.; Sun, P. Electrochemical Oxidative Cross-Coupling Reaction to Access Unsymmetrical Thiosulfonates and Selenosulfonates. *Adv. Synth. Catal.* **2019**, *361*, 2014−2019.
(19) Yu, Y.; Yuan, Y.; Liu, H.; He, M.; Yang, M.; Liu, P.; Yu, B.; Dong, X.; Lei, A. Electrochemical Oxidative C-H/N-H Cross-Coupling for C-N Bond Formation with Hydrogen Evolution. *Chem. Commun.* **2019**, *55*, 1809−1812.
(20) Wen, Q.; Lu, P.; Wang, Y. Copper-mediated Three-Component Synthesis of 3-Cyanoimidazo[1,2-*a*]pyridines. *Chem. Commun.* **2015**, *51*, 15378−15381.

https://dx.doi.org/10.1021/acs.joc.0c03026
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