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CuI-Catalyzed Aerobic Oxidative α-Aminaton Cyclization of Ketones to Access Aryl or Alkenyl-Substituted Imidazoheterocycles

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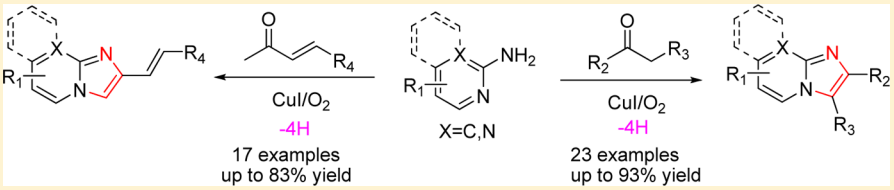
Supporting Information



ABSTRACT: CuI-catalyzed aerobic oxidative synthesis of imidazoheterocycles has been achieved. Four hydrogen atoms were removed in one step. This protocol was compatible with a broad range of functional groups, and it has been also successfully extended to unsaturated ketones, bringing about the formation of alkenyl-substituted imidazoheterocycles, which were difficult to prepare by previous means. Preliminary mechanistic studies indicated that this reaction was most likely to proceed through a catalytic Ortoleva−King reaction. By using this method, the marketed drug Zolimidine could be prepared with 90% yield on a gram scale from commercially available materials.

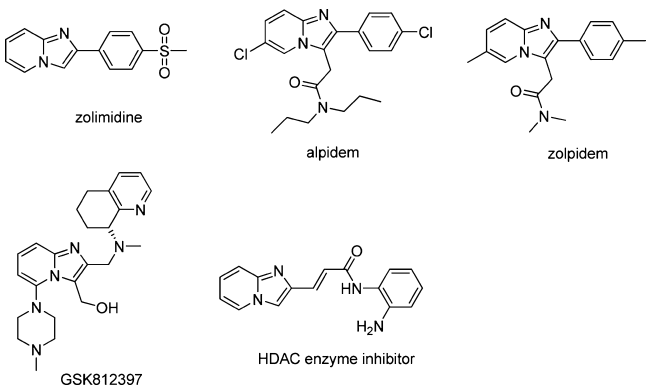
1. INTRODUCTION

Imidazo[1,2-*a*]pyridines are prominent among N-fused heterocycles and are extensively found in biologically active molecules.[1] Several compounds bearing the core structure of imidazo[1,2-*a*]pyridine ring systems have been successfully developed into commercially available drugs, including alpidem, zolpidem, zolimidine, and olprinone (Scheme 1).[2] They are also useful frameworks in material science[3] and in abnormal N-heterocyclic carbenes in organometallic chemistry.[4]

Progress was made to gain access to substituted imidazo[1,2-*a*]pyridines.[5] The reaction of 2-aminopyridines with mono-α-halogenocarbonyl compounds remains the most commonly used means in both laboratory synthesis and industrial manufacture.[3d,5e,6] However, this methodology is still imperfect. Monohalogenation of carbonyl compounds, particularly unsaturated ones, is still challenging.[7] In addition to the difficulties in controlling the monosubstituted product, halogenations using cheap X_2 (mainly bromide) as the halogen source were ineffective for unsaturated ketones.[8] Furthermore, the coupling efficiency was not good enough with respect to halogenated unsaturated ketones.[2h] Because of those intrinsic defects, a wide range of unsaturated ketones cannot be easily incorporated into imidazoheterocycles using this traditional method, severely limiting the structural diversity of imidazoheterocycles. Herein, we describe a CuI-catalyzed aerobic oxidative α-aminaton cyclization of ketones that leads to substituted imidazoheterocycles. Starting from simple and readily available materials, this transformation is straightforward, highly efficient, and applicable to unsaturated ketones.

Toward waste-free synthesis, transition-metal-catalyzed oxidative functionalization of organic molecules involving dioxygen activation presents one of the most powerful means in organic synthesis.[9] Special attention has been paid to the copper/O_2 system, which exhibits broad catalytic activities over a spectrum of substrates.[9e,h,10] Some biomimetic oxidation systems based on copper as cocatalysts have been developed as well.[11] Using CuI as a catalyst under aerobic conditions, the role of iodine anion has been ignored by most authors.[10,11a] In this work, the iodine anion is crucial to the current transformation.

Scheme 1. Biologically Active Compounds Sharing Imidazo[1,2-*a*]pyridine Rings



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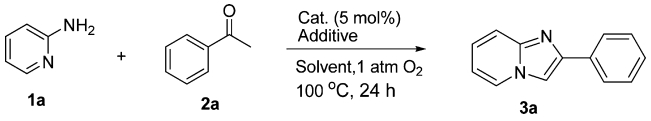
2. RESULTS AND DISCUSSION

Initially, we examined the reaction of 2-aminopyridine (**1a**) and acetophenone (**2a**) in the presence of copper salts (5 mol %) in *N*,*N*-dimethylformamide (DMF) at 100 °C under aerobic conditions. Interestingly, only CuI gave the desired product 2-phenylimidazo[1,2-*a*]pyridine in 66% yield (Table 1, entry 1).

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	additive (equiv)	solvent[b]	yield (%)[c]
1	CuI		DMF	66
2	CuCl		DMF	ND[d]
3	CuBr		DMF	ND[d]
4	$CuCl_2$		DMF	ND[d]
5	$CuBr_2$		DMF	ND[d]
6	$Cu(OAc)_2$		DMF	ND[d]
7	$Cu(CF_3SO_3)_2$		DMF	ND[d]
8	CuO		DMF	ND[d]
9	Cu_2O		DMF	ND[d]
10	CuF_2		DMF	ND[d]
11	$CuSO_4$		DMF	ND[d]
12	$Cu(NO_3)_2{\cdot}3H_2O$		DMF	ND[d]
13	CuI		DMA	68
14	CuI		NMP	69
15	CuI	$In(CF_3SO_3)_3$ (2.5%)	DMA	70[e]
16	CuI	$In(CF_3SO_3)_3$ (2.5%)	NMP	82[e]
17	CuI	$In(CF_3SO_3)_3$ (1%)	NMP	81[e]
18	CuI	$BF_3{\cdot}Et_2O$ (10%)	NMP	50[e]
19	CuI	TsOH (10%)	NMP	71[e]
20	CuI	TsOH (10%)	NMP	46[e,f]
21	CuI	$CuBr_2$ (5%)	NMP	71[e]
22	CuI	$CuBr_2$ (5%)	NMP	80[e,f]

[a]Reaction conditions: **1a** (0.6 mmol), **2a** (0.3 mmol), catalyst (5 mol %), solvent (2 mL), O_2 (1 atm), 100 °C, 24 h. [b]DMF = *N*,*N*-dimethylformamide. DMA = *N*,*N*-dimethylacetamide. NMP = *N*-methyl-2-pyrrolidone. [c]Isolated yield. [d]ND = not detected (by GC-MS). [e]The reaction was carried out for 30 h. [f]**1a** (0.9 mmol).

Other copper sources, CuCl, CuBr, $CuCl_2$, $CuBr_2$, etc., though under the otherwise identical conditions, failed to produce the product in any detectable amount (Table 1 entries 2−12). Next, we checked the effect of solvents; the yield was not obviously increased in *N*,*N*-dimethylacetamide (DMA) and *N*-methyl-2-pyrrolidone (NMP) (Table 1, entries 13 and 14). Taking into account previous reports concerning the synthesis of imidazo[1,2-*a*]pyridines,[3d,5e,6] we reasoned that this reaction might proceed via an initial α-iodination of acetophenone and a subsequent amination/cyclization sequence, which differs from the C−H bond functionalization mechanism or single electron transfer (SET) process.[12] Thus, the efficiency of α-iodination of acetophenone was decisive for the overall yield. With this hypothesis in mind, we surveyed various Lewis acids to accelerate the α-iodination step (Table 1, entries 15−22). Gratifyingly, a yield of 81% was obtained after adding 1 mol % $In(CF_3SO_3)_3$ in NMP under 1 atm of O_2 (Table 1, entry 17).

With the optimized reaction conditions in hand, we evaluated the scope of the reaction. As depicted in Table 2, the nature of substituents on the benzene ring of (hetero)aryl methyl ketones did not affect the reaction much; good to excellent yields were obtained. Notably, the cyano group was also compatible with the current reaction condition (Table 2, **3c**).[10f] Propiophenone and butyrophenone were transformed into the corresponding products in synthetically useful yields, with some variations from the standard conditions (Table 2, **3t** and **3u**). With regard to 2-aminopyridine counterparts, for those with an electron-withdrawing group, higher temperature was required to achieve satisfying yields (Table 2, **3n**−**3q**), whereas those with an electron-donating group were formed at a relatively lower temperature (Table 2, **3m**). The materials 2-aminopyrimidine and 2-aminothiazole, which were ineffective in prior work, applied to our system as well (Table 2, **3q** and **3r**).[5h]

Surprisingly, the reaction was also amenable to unsaturated ketones, bringing about the formation of alkenyl-substituted imidazoheterocycles (Table 3). Those obtained compounds were rarely investigated due to the difficulties imposed in their preparations.[13] Though α,β-unsaturated ketones are well-recognized as Michael acceptors, the Michael addition cyclization products were not observed.[5i] Extending the conjugated system between carboxyl group and benzene ring had no distinct impact on the yields (Table 3, **4d**, **4g**, **4j**, **4m**, and **4p**). However, the absence of conjugated system was fatal to the reaction (Table 3, **4q**). Note that the alkenyl group can be easily transformed, making the structural diversity of imidazoheterocycles abundant.

Application of this method to the synthesis of zolimidine (**3v**) on a gram scale from commercially available materials was successful, with a 90% isolated yield (Scheme 2). Interestingly, with the protection of the 2′ and 3′ hydroxyl groups, adenosine, which is an important fragment in biochemistry, was converted to imidazo[1,2-*i*]purineheterocycle in 36% yield (Scheme 3). Although this process ran at 120 °C under oxygen atmosphere, the α-hydroxyl group was still intact.[14]

To gain insights into the reaction mechanism, an intramolecular reaction was carried out, and **3a** was produced in only 19% yield (Scheme 4, eq 1), which indicates that both copper-catalyzed tandem condensation−oxidative C−N bond formation cyclization and the SET process are to some degree impossible.[9h,10b,12,15] When quantitative CuI was used, the iodinated product **3x** resulted in good yield (Scheme 4, eq 3), which shows that the release of iodine is possible in the reaction.[16,17] The generation of dehydrogenative product **5a** further confirmed the possibility (Scheme 4, eq 4). The product **3a** was not formed when silver acetate (AgOAc) was used to quench the iodine anion (Scheme 4, eq 5). $Cu(CF_3SO_3)_2$, $CuSO_4$, $Cu(NO_3)_2{\cdot}3H_2O$, etc., which were unreactive, worked well when tetrabutylammonium iodide (TBAI) or NaI was used as additive (Table 4). Recently, the boom of hypervalent iodine chemistry, especially with issues concerning catalytic iodination cascade substitution reactions, convinces us that this transformation proceeds through a similar pathway.[18]

On the basis of the observations and considerations above, a plausible mechanism was postulated in Scheme 5. Cu^I initially coordinates with 2-aminopyridine to form L_nCu^I complex, which is oxidized to L_nCu^{II} species by O_2.[19] The L_nCu^{II} species with a higher oxidation potential cannot coexist with the iodine anion.[16] Subsequently, the release of iodine takes place; iodine may further transform to HOI under the reaction conditions.[18e,19] When iodine or HOI appears in the system, the staring materials are smoothly converted to the products via the Ortoleva−King reaction promoted by Lewis acid (Scheme 4, eq

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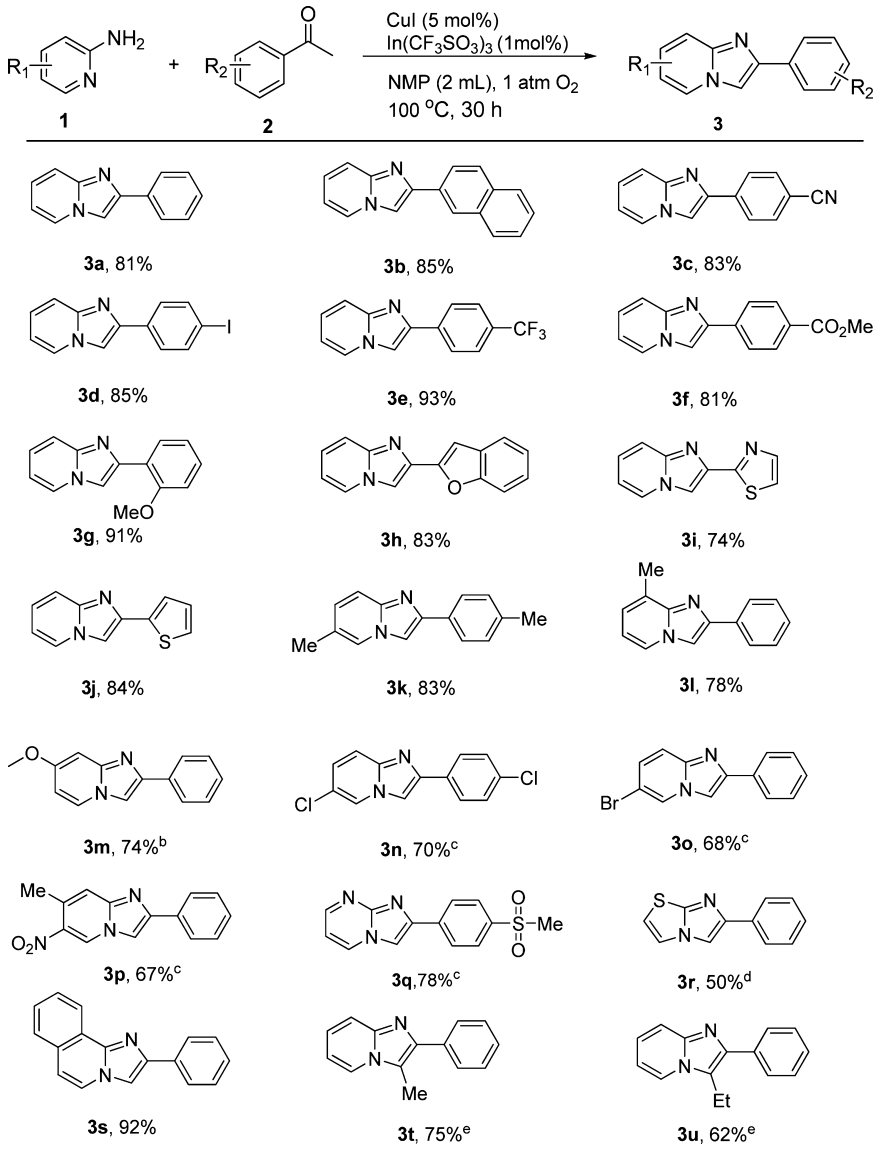
Table 2. CuI-Catalyzed Aerobic Oxidative Reaction of 2-Aminopyridines with Arylketones[a]



[a]Reaction conditions: **1a** (0.6 mmol), **2a** (0.3 mmol), CuI (5 mol %), $In(CF_3SO_3)_3$ (1 mol %), NMP (2 mL), O_2 (1 atm), 100 °C, 30 h. Isolated yields. [b]The reaction was carried out at 90 °C. [c]The reaction was carried out at 120 °C for 48 h. [d]Without $In(CF_3SO_3)_3$. [e]**1a** (0.9 mmol), 5 mol % $CuBr_2$ was used instead of $In(CF_3SO_3)_3$.

2). Ortoleva–King reaction as the key step in another method for imidazo[1,2-*a*]pyridine synthesis has been proposed recently.[3d,20] The reasons for the transformation available to unsaturated ketones are that only a catalytic amount of iodine or HOI exists in the system and the Ortoleva–King reaction dominates over Michael addition.

3. SUMMARY

In this work, we have developed an efficient and straightforward method for the synthesis of substituted imidazoheterocycles. Compared with the established protocols, this approach presents advantages in the formation of alkenyl-substituted imidazoheterocycles, in which the extended π-conjugated systems are potential optical materials.[3e] By employing dioxygen (1 atm) as the oxidant under approximately neutral condition, this transformation proved to be reliable at the gram scale and reached the goal of waste-free synthesis, which, we suppose, may be applicable to pharmaceutical industrial manufacture. Further studies to fully clarify the role of iodine anion and the application of the CuI/O_2 system in other transformations are in progress.

4. EXPERIMENTAL SECTION

General Methods. All reactions were carried out under dry O_2 with dry solvents under anhydrous conditions. The reagents for experiments were purchased and used as received. DMF, DMA, and NMP were distilled from CaH_2 under nitrogen and stored under nitrogen. (*E*)-*N*-(1-phenylethylidene)pyridin-2-amine[21] and (3*E*,5*E*)-6-phenylhexa-3,5-dien-2-one[22] were prepared according to the reported procedures. ^1H and ^{13}C NMR spectra were measured at 298 K on a 400 MHz spectrometer in $CDCl_3$ solutions unless otherwise noted. Chemical shifts were reported in δ (ppm), relative to the internal standard of TMS.

General Procedure. In a glovebox, a Schlenk tube (25 mL) equipped with a stir bar was charged with CuI (5 mol %),

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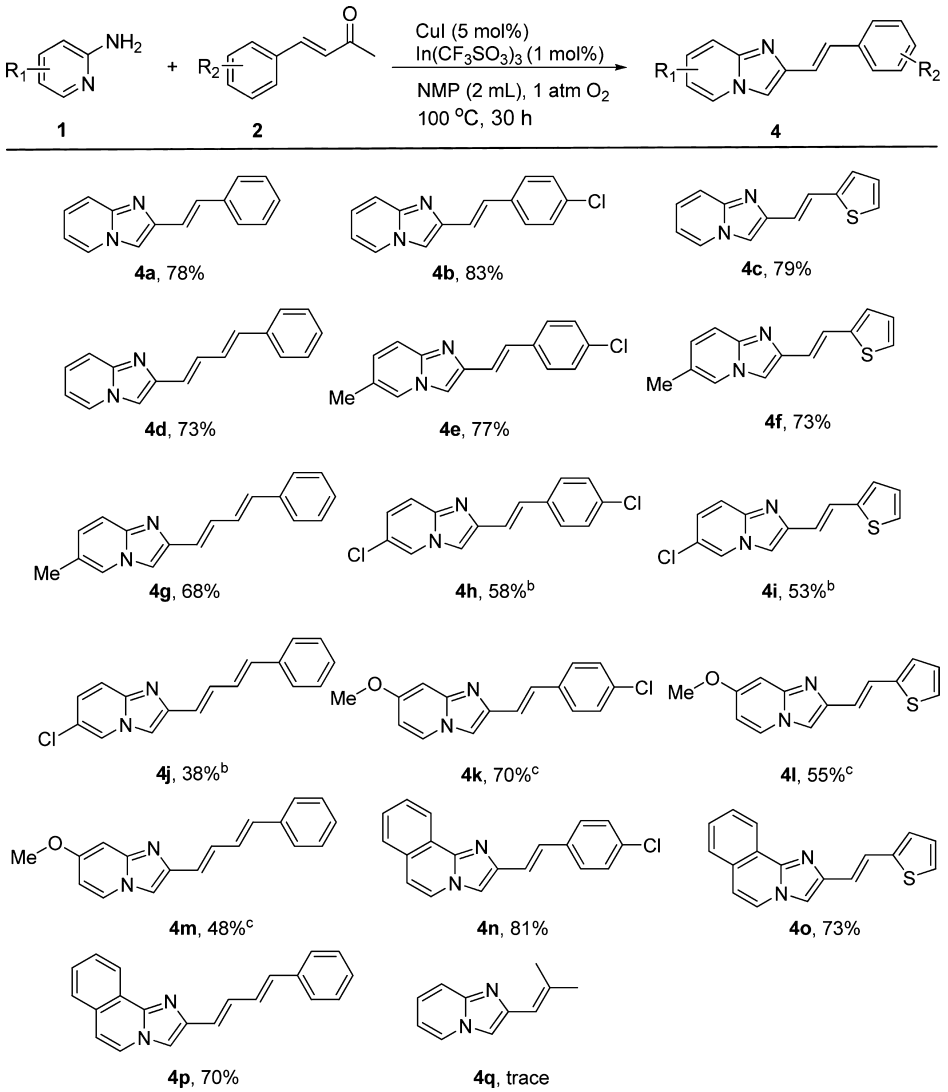
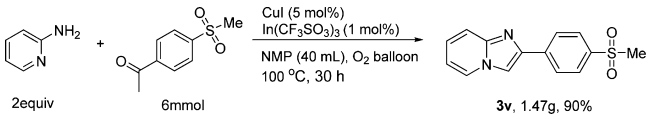
Table 3. CuI-Catalyzed Aerobic Oxidative Reaction of 2-Aminopyridines with Unsaturated Ketones[a]



[a]Reaction conditions: **1a** (0.6 mmol), **2b** (0.3 mmol), CuI (5 mol %), $In(CF_3SO_3)_3$ (1 mol %), NMP (2 mL), O_2 (1 atm), 100 °C, 30 h. Isolated yields. [b]The reaction was carried out at 120 °C for 48 h. [c]The reaction was carried out at 90 °C.

Scheme 2. Gram Scale Synthesis of Zolimidine



$In(CF_3SO_3)_3$ (1 mol %), 2-aminopyridine (2 equiv), and NMP (2 mL). The tube was fitted with a rubber septum and removed from the glovebox. Then, the tube was evacuated and refilled with O_2 three times. Subsequently, acetophenone (0.3 mmol) was added to the Schlenk tube through the rubber septum using syringes, and then the septum was replaced by a Teflon screwcap under an oxygen flow (if the acetophenone was solid, it was added to the tube in glovebox). The reaction mixture was stirred at 100 °C for 30 h. Upon completion, the reaction mixture was diluted with 10 mL of ethyl acetate (EtOAc) and filtered through a pad of silica gel; the pad of silica gel was then washed with additional ethyl acetate (20 mL). The filtrate was washed with water (3 × 15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was then purified by chromatography on silica gel (petroleum ether/EtOAc 1:3) to provide the corresponding product **3** or **4**.

Mechanistic Studies. Intramolecular experiment: In a glovebox, a Schlenk tube (25 mL) equipped with a stir bar was charged with CuI (5 mol %), $In(CF_3SO_3)_3$ (1 mol %), (*E*)-*N*-(1-phenylethylidene)pyridin-2-amine (0.3 mmol), and NMP (2 mL). The tube was fitted with a rubber septum and removed from the glovebox. The tube was evacuated and refilled with O_2 three times. Subsequently, the septum was replaced by a Teflon screwcap under an oxygen flow. The reaction mixture was stirred at 100 °C for 30 h. Upon completion, the reaction mixture was diluted with 10 mL of ethyl acetate and filtered through a pad of silica gel; the pad of silica gel was then washed with additional ethyl acetate (20 mL). The filtrate was washed with water (3 × 15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was then purified by chromatography on silica gel (petroleum ether/EtOAc 1:3) to provide the corresponding product **3a** in 19% yield (see Scheme 4, eq 1). Following the

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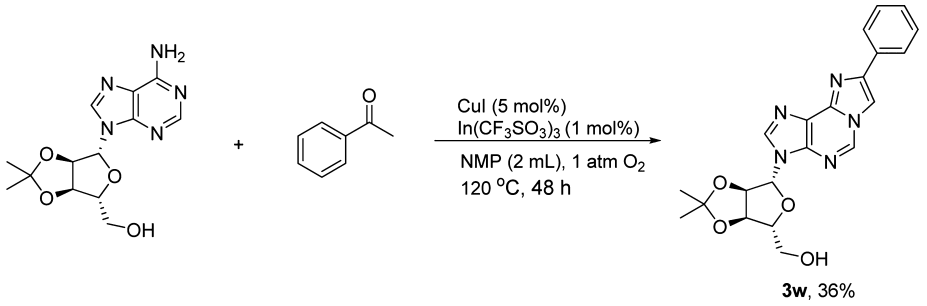
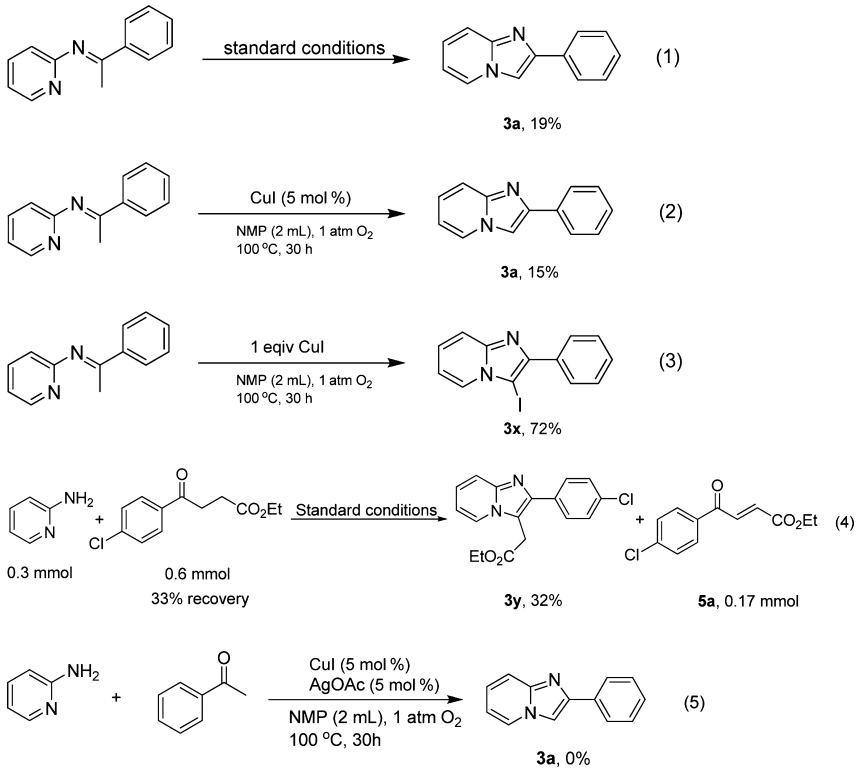
Scheme 3. Reaction of 2′, 3′-*O*-Isopropylideneadenosine with Acetophenone[a]



3w, 36%

[a]Conditions: 2′,3′-*O*-Isopropylideneadenosine (0.6 mmol), acetophenone (0.3 mmol), CuI (5 mol %), $In(CF_3SO_3)_3$ (1 mol %), NMP (2 mL), O_2 (1 atm), 120 °C, 48 h. Isolated yield.

Scheme 4. Mechanistic Studies



procedure above without adding $In(CF_3SO_3)_3$, **3a** was obtained in 15% yield (see Scheme 4, eq 2). Following the procedure above with CuI (1equiv), **3x** was obtained in 72% yield (see Scheme 4, eq 3). Under the standard conditions, **3y** was obtained in 32% yield, with 0.17 mmol of **5a** obtained (see Scheme 4, eq 4). Under the standard conditions, using AgOAc (5 mol %) instead of $In(CF_3SO_3)_3$, **3a** was not obtained (see Scheme 4, eq 5).

*Analytical Data for Compounds **3** and **4**. 2-Phenylimidazo[1,2-a]pyridine (**3a**).* The title compound was prepared according to the general procedure. White solid (47.3 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (d, J = 6.7 Hz, 1H), 7.96 (d, J = 7.4 Hz, 2H), 7.86 (s, 1H), 7.63 (d, J = 9.1 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.77 (t, J = 6.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.9, 145.7, 133.8, 128.7, 127.9, 126.0, 125.5, 124.6, 117.6, 112.4, 108.1. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

*2-(Naphthalen-2-yl)imidazo[1,2-a]pyridine (**3b**).* The title compound was prepared according to the general procedure. White solid (62.5 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (s, 1H), 7.99−7.95 (m, 2H), 7.92−7.90 (m, 1H), 7.86−7.81 (m, 3H), 7.64 (d, J = 9.1 Hz, 1H), 7.50−7.43 (m, 2H), 7.12 (ddd, J = 9.0, 6.8, 1.1 Hz, 1H), 6.68 (td, J = 6.8, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 145.6, 133.7, 133.1, 131.1, 128.2, 128.2, 127.6, 126.2, 125.8, 125.5, 124.7, 124.6, 124.1, 117.3, 112.3, 108.5. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[23]

*4-(Imidazo[1,2-a]pyridin-2-yl)benzonitrile (**3c**).* The title compound was prepared according to the general procedure. White solid (54.7 mg, 83%). ^{1}H NMR (400 MHz, DMSO) δ: 8.54−8.52 (m, 2H), 8.13 (d, J = 7.8 Hz, 3H), 7.86 (d, J = 7.9 Hz, 2H), 7.59 (d, J = 9.1 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 6.91 (t, J = 6.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 145.1, 142.4, 138.4, 132.6, 127.1, 126.0, 125.6, 119.0, 116.9, 112.7,

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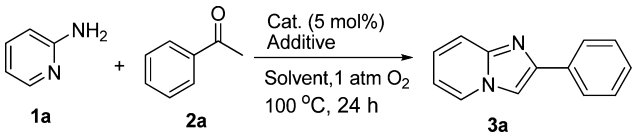
Table 4. Evaluating the Effect of Iodine Anion[a]

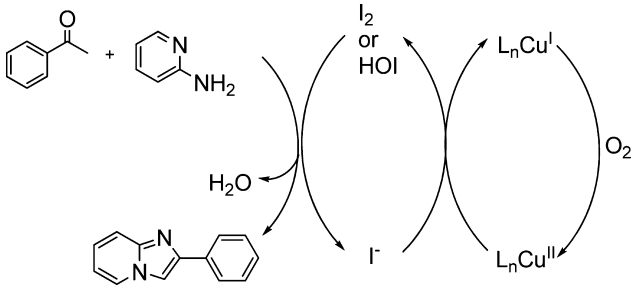


1a 2a 3a

entry	catalyst	additive[b] (equiv)	solvent	yield (%)[c]
1	CuCl	TBAI (5%)	NMP	16
2	CuBr	TBAI (5%)	NMP	0
3	$CuCl_2$	TBAI (5%)	NMP	0
4	$CuBr_2$	TBAI (5%)	NMP	0
5	$Cu(OAc)_2$	TBAI (5%)	NMP	0
6	$Cu(CF_3SO_3)_2$	TBAI (5%)	NMP	52 (55)
7	$CuSO_4$	TBAI (5%)	NMP	33
8	$Cu(NO_3)_2{\cdot}3H_2O$	TBAI (5%)	NMP	40
9	CuCl	NaI (5%)	NMP	9
10	CuBr	NaI (5%)	NMP	<5
11	$CuCl_2$	NaI (5%)	NMP	<5
12	$CuBr_2$	NaI (5%)	NMP	0
13	$Cu(OAc)_2$	NaI (5%)	NMP	0
14	$Cu(CF_3SO_3)_2$	NaI (5%)	NMP	89 (76)
15	$CuSO_4$	NaI (5%)	NMP	56
16	$Cu(NO_3)_2{\cdot}3H_2O$	NaI (5%)	NMP	57

[a]Reaction conditions: **1a** (0.6 mmol), **2a** (0.3 mmol), catalyst (5 mol %), solvent (2 mL), O_2 (1 atm), 100 °C, 24 h. [b]TBAI = tetrabutylammonium iodide. [c]GC yield; isolated yield in parentheses.

Scheme 5. Proposed Reaction Mechanism



111.0, 109.7. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[24]

2-(4-Iodophenyl)imidazo[1,2-a]pyridine (**3d**). The title compound was prepared according to the general procedure. White solid (81.7 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (d, J = 6.6 Hz, 1H), 7.82 (s, 1H), 7.71 (dd, J = 26.4, 8.1 Hz, 4H), 7.60 (d, J = 9.0 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 6.76 (t, J = 6.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 144.7, 137.7, 133.3, 127.7, 125.6, 124.9, 117.6, 112.6, 108.2, 93.4. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[24]

2-(4-(Trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (**3e**). The title compound was prepared according to the general procedure. White solid (73.5 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J = 6.7 Hz, 1H), 8.04 (d, J = 8.0 Hz, 2H), 7.88 (s, 1H), 7.67–7.61 (m, 3H), 7.20–7.16 (m, 1H), 6.78 (t, J = 6.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.8, 144.2, 137.3, 129.7 (q, J = 32 Hz), 126.1, 125.7 (d, J = 2.3 Hz), 125.6, 125.2, 124.3 (q, J = 271 Hz), 117.7, 112.8, 109.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ = −62.5. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[25]

Methyl-4-(imidazo[1,2-a]pyridin-2-yl)benzoate (**3f**). The title compound was prepared according to the general procedure. White solid (61.7 mg, 81%). Mp 209–211 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08–8.06 (m, 3H), 7.99 (d, J = 8.5 Hz, 2H), 7.88 (s, 1H), 7.60 (d, J = 9.1 Hz, 1H), 7.17–7.13 (m, 1H), 6.75 (td, J = 6.8, 0.8 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 145.8, 144.5, 138.1, 130.0, 129.2, 125.7, 125.6, 125.04, 117.6, 112.7, 109.2, 52.0. Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.41; H, 4.79; N, 11.12.

2-(2-Methoxyphenyl)imidazo[1,2-a]pyridine (**3g**). The title compound was prepared according to the general procedure. White solid to colorless oil (61.0 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, J = 7.7 Hz, 1H), 8.18 (s, 1H), 8.09 (d, J = 6.7 Hz, 1H), 7.62 (d, J = 9.1 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.12 (t, J = 7.6 Hz, 2H), 7.00 (d, J = 8.2 Hz, 1H), 6.71 (t, J = 6.7 Hz, 1H), 3.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.6, 144.3, 141.1, 128.7, 128.5, 125.5, 124.3, 122.3, 120.9, 117.1, 112.4, 111.8, 110.7, 55.3. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

2-(Benzofuran-2-yl)imidazo[1,2-a]pyridine (**3h**). The title compound was prepared according to the general procedure. White solid (58.3 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J = 6.8 Hz, 1H), 7.99 (s, 1H), 7.66–7.61 (m, 2H), 7.53 (d, J = 7.7 Hz, 1H), 7.26–7.19 (m, 4H), 6.81 (td, J = 6.8, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.8, 151.5, 145.9, 137.5, 129.0, 125.7, 125.3, 124.3, 122.9, 121.1, 117.6, 112.7, 111.09, 109.5, 102.8. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[26]

2-(Imidazo[1,2-a]pyridin-2-yl)thiazole (**3i**). The title compound was prepared according to the general procedure. White solid (44.9 mg, 74%); mp 159–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (s, 1H), 8.09 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 3.2 Hz, 1H), 7.60 (d, J = 9.1 Hz, 1H), 7.33 (d, J = 3.2 Hz, 1H), 7.19–7.14 (m, 1H), 6.79–6.75 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 163.4, 145.3, 143.5, 140.3, 125.9, 125.4, 119.1, 117.7, 113.1, 109.4. Anal. Calcd for $C_{10}H_7N_3S$: C, 59.68; H, 3.51; N, 20.88. Found: C, 59.59; H, 3.63; N, 20.76.

2-(Thiophen-2-yl)imidazo[1,2-a]pyridine (**3j**). The title compound was prepared according to the general procedure. White solid (50.4 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, J = 6.8 Hz, 1H), 7.71 (s, 1H), 7.58 (d, J = 9.1 Hz, 1H), 7.45 (dd, J = 3.6, 1.0 Hz, 1H), 7.28 (dd, J = 5.0, 1.0 Hz, 1H), 7.14–7.10 (m, 1H), 7.07 (dd, J = 5.0, 3.6 Hz, 1H), 6.72 (td, J = 6.8, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.4, 140.8, 137.5, 127.8, 125.4, 125.0, 124.7, 123.6, 117.2, 112.5, 107.4. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

6-Methyl-2-p-tolylimidazo[1,2-a]pyridine (**3k**). The title compound was prepared according to the general procedure. White solid (55.2 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82–7.78 (m, 3H), 7.65 (s, 1H), 7.49 (d, J = 9.1 Hz, 1H), 7.21 (d, J = 7.7 Hz, 2H), 6.95 (d, J = 9.1 Hz, 1H), 2.37 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.5, 144.6, 137.4, 131.1, 129.3, 127.5, 125.7, 123.2, 121.7, 116.6, 107.4, 21.2, 18.0. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

8-Methyl-2-phenylimidazo[1,2-a]pyridine (**3l**). The title compound was prepared according to the general procedure. White solid (48.7 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, J = 7.7 Hz, 2H), 7.94 (d, J = 6.7 Hz, 1H), 7.80 (s, 1H),

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7.44 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 6.8 Hz, 1H), 6.65 (t, J = 6.8 Hz, 1H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.2, 145.2, 134.1, 128.6, 127.7, 127.5, 126.1, 123.3, 123.2, 112.2, 108.5, 17.0. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[27]

*7-Methoxy-2-phenylimidazo[1,2-a]pyridine (**3m**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 90 °C for 30 h. White solid (49.7 mg, 74%); mp 93−95 °C .^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93−7.88 (m, 3H), 7.67 (s, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 6.90 (d, J = 2.4 Hz, 1H), 6.48 (dd, J = 7.4, 2.5 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.9, 147.1, 145.5, 133.9, 128.6, 127.6, 125.9, 125.7, 107.4, 106.8, 94.7, 55.4. Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.15; H, 5.52; N, 12.30.

*6-Chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (**3n**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (55.4 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (s, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.78 (s, 1H), 7.55 (d, J = 9.5 Hz, 1H), 7.39 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 144.1, 134.0, 131.8, 129.0, 127.3, 126.3, 123.4, 120.7, 117.8, 108.5. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[28]

*6-Bromo-2-phenylimidazo[1,2-a]pyridine (**3o**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (55.7 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.24 (s, 1H), 7.93 (d, J = 7.4 Hz, 2H), 7.80 (s, 1H), 7.52 (d, J = 9.5 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.22 (dd, J = 9.5, 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.7, 144.1, 133.2, 1288, 128.3, 128.0, 126.1, 125.5, 118.1, 108.2, 106.9. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

*7-Methyl-6-nitro-2-phenylimidazo[1,2-a]pyridine (**3p**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. Yellow solid (50.7 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.09 (s, 1H), 7.93−7.89 (m, 3H), 7.44−7.37 (m, 4H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.2, 145.4, 138.7, 132.5, 130.2, 128.9, 128.9, 126.3, 126.2, 117.9, 109.0, 21.1. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[29]

*2-(4-(Methylsulfonyl)phenyl)imidazo[1,2-a]pyrimidine (**3q**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. Light yellow solid (64.2 mg, 78%); mp 261−263 °C. ^{1}H NMR (400 MHz, DMSO) δ: 9.00 (dd, J = 6.7, 1.8 Hz, 1H), 8.59−8.56 (m, 1H), 8.56 (s, 1H), 8.26 (d, J = 8.3 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H), 7.11−7.08 (m, 1H), 3.26 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 151.3, 148.2, 143.2, 139.9, 138.3, 135.4, 127.6, 126.2, 109.4, 109.3, 43.5. Anal. Calcd for $C_{13}H_{11}N_3O_2S$: C, 57.13; H, 4.06; N, 15.37. Found: C, 57.41; H, 4.28; N, 15.13.

*6-Phenylimidazo[2,1-b]thiazole (**3r**).* The title compound was prepared according to the general procedure without adding 1 mol % $In(CF_3SO_3)_3$. Yellow to white solid (30.6 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, J = 7.4 Hz, 2H), 7.71 (s, 1H), 7.42−7.38 (m, 3H), 7.28 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 4.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.2, 147.8, 134.0, 128.6, 127.3, 125.2, 118.4, 112.4, 107.9. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[30]

*2-Phenylimidazo[2,1-a]isoquinoline (**3s**).* The title compound was prepared according to the general procedure. White solid (67.6 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (d, J = 7.9 Hz, 1H), 8.01 (d, J = 7.4 Hz, 2H), 7.79 (d, J = 7.2 Hz, 1H), 7.74 (s, 1H), 7.64 (dd, J = 11.3, 7.8 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 6.95 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.9, 143.2, 134.0, 129.4, 128.6, 128.0, 128.0, 127.5, 126.8, 125.8, 123.8, 123.4, 122.8, 112.9, 109.8. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

*3-Methyl-2-phenylimidazo[1,2-a]pyridine (**3t**).* The title compound was prepared according to the general procedure using **1a** (3 equiv) and 5 mol % $CuBr_2$ instead of 1 mol % $In(CF_3SO_3)_3$. White solid (47.1 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, J = 6.9 Hz, 1H), 7.81−7.78 (m, 2H), 7.64 (d, J = 9.1 Hz, 1H), 7.48−7.44 (m, 2H), 7.36−3.32 (m, 1H), 7.18−7.14 (m, 1H), 6.82 (td, J = 6.8, 1.0 Hz, 1H), 2.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.2, 142.3, 134.7, 128.4, 128.3, 127.3, 123.4, 122.8, 117.3, 115.8, 112.0, 9.5. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[31]

*3-Ethyl-2-phenylimidazo[1,2-a]pyridine (**3u**).* The title compound was prepared according to the general procedure using **1a** (3 equiv) and 5 mol % $CuBr_2$ instead of 1 mol % $In(CF_3SO_3)_3$. Colorless oil (41.1 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J = 6.9 Hz, 1H), 7.79 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 9.1 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.83 (t, J = 6.7 Hz, 1H), 3.12 (q, J = 7.5 Hz, 2H), 1.37 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.4, 142.0, 135.0, 128.5, 128.2, 127.4, 123.5, 122.8, 121.8, 117.7, 112.0, 17.1, 12.2. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[31]

*2-(4-(Methylsulfonyl)phenyl)imidazo[1,2-a]pyridine (**3v**).* The title compound was prepared according to the general procedure at 6 mmol scale. Light yellow solid (1.47 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15−8.13 (m, 3H), 7.99−7.97 (m, 3H), 7.64 (d, J = 9.1 Hz, 1H), 7.24−7.20 (m, 1H), 6.84−6.81 (m, 1H), 3.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.9, 143.6, 139.3, 127.8, 126.6, 125.8, 125.4, 117.8, 113.0, 109.6, 44.6. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5f]

*((3aR,4R,6R,6aR)-2,2-dimethyl-6-(8-phenyl-3H-imidazo-[1,2-i]purin-3-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-methanol (**3w**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (43.6 mg, 36%); mp 257−259 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.78 (s, 1H), 8.17 (s, 1H), 8.00 (d, J = 7.3 Hz, 2H), 7.89 (s, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 6.06 (d, J = 4.2 Hz, 1H), 5.26−5.23 (m, 1H), 5.14 (dd, J = 6.0, 1.5 Hz, 1H), 4.55 (d, J = 1.7 Hz, 1H), 4.03 (dd, J = 12.4, 1.9 Hz, 1H), 3.88 (dd, J = 12.4, 2.4 Hz, 1H), 1.66 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.5, 141.2, 140.5, 137.7, 135.2, 132.6, 128.7, 128.5, 126.3, 124.8, 114.24, 105.9, 93.3, 86.3, 83.9, 81.5, 63.0, 27.5, 25.3. Anal. Calcd for $C_{21}H_{21}N_5O_4$: C, 61.91; H, 5.20; N, 17.19. Found: C, 62.19; H, 5.26; N, 17.23.

*3-Iodo-2-phenylimidazo[1,2-a]pyridine (**3x**).* White solid (68.8 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, J = 6.9 Hz, 1H), 8.10 (d, J = 7.3 Hz, 2H), 7.63 (d, J = 9.0 Hz, 1H),

7.51 (t, J = 7.5 Hz, 2H), 7.42 (t, J = 7.4 Hz, 1H), 7.28−7.24 (m, 1H), 6.92 (t, J = 6.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.1, 148.0, 133.6, 128.5, 128.3, 128.3, 126.5, 125.5, 117.5, 113.1, 59.4. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[3e]

*1-(2-(4-Chlorophenyl)imidazo[1,2-a]pyridin-3-yl)butan-2-one (**3y**).* Light yellow oil (30.0 mg, 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.06 (d, J = 7.0 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.50−7.46 (m, 1H), 7.41 (d, J = 8.5 Hz, 2H), 7.08 (t, J = 6.7 Hz, 1H), 3.97 (q, J = 7.1 Hz, 2H), 1.01 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.2, 162.7, 146.4, 142.5, 139.2, 138.0, 130.2, 129.2, 128.7, 127.4, 122.3, 118.6, 115.7, 61.8, 13.6. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[5h]

*(E)-ethyl 4-(4-chlorophenyl)-4-oxobut-2-enoate (**5a**).* White solid (40.4 mg, 0.17 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 15.5 Hz, 1H), 7.47 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 15.5 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 188.2, 165.4, 140.4, 135.8, 134.9, 133.0, 130.2, 129.2, 61.4, 14.1. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[32]

*(E)-2-styrylimidazo[1,2-a]pyridine (**4a**).* The title compound was prepared according to the general procedure. White solid (51.3 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J = 6.8 Hz, 1H), 7.58−7.55 (m, 5H), 7.36 (t, J = 7.5 Hz, 2H), 7.28−7.25 (m, 1H), 7.17−7.12 (m, 2H), 6.71 (t, J = 6.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.6, 144.0, 137.1, 130.4, 128.6, 127.6, 126.5, 125.4, 124.9, 119.9, 117.0, 112.1, 110.5. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[14b]

*(E)-2-(4-chlorostyryl)imidazo[1,2-a]pyridine (**4b**).* The title compound was prepared according to the general procedure. White solid (63.3 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, J = 6.6 Hz, 1H), 7.57−7.55 (m, 2H), 7.50−7.44 (m, 3H), 7.30 (d, J = 8.2 Hz, 2H), 7.17−7.07 (m, 2H), 6.73 (t, J = 6.6 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 143.7, 135.7, 133.2, 129.1, 128.8, 127.7, 125.5, 125.2, 120.4, 117.2, 112.3, 110.8. This compound is known. The ^{1}H and ^{13}C NMR spectral data are in agreement with the literature data.[14b]

*(E)-2-(2-(thiophen-2-yl)vinyl)imidazo[1,2-a]pyridine (**4c**).* The title compound was prepared according to the general procedure. White solid (53.6 mg, 79%). Mp 165−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (d, J = 6.8 Hz, 1H), 7.66 (d, J = 15.8 Hz, 1H), 7.53 (dd, J = 9.1, 0.5 Hz, 1H), 7.49 (s, 1H), 7.17 (d, J = 5.1 Hz, 1H), 7.14−7.08 (m, 2H), 6.98 (dd, J = 5.0, 3.6 Hz, 1H), 6.92 (d, J = 15.8 Hz, 1H), 6.69 (td, J = 6.8, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.6, 143.6, 142.6, 127.6, 126.4, 125.4, 125.0, 124.4, 123.6, 119.4, 117.0, 112.1, 110.5. Anal. Calcd for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.45; N, 12.38. Found: C, 68.72; H, 4.43; N, 12.34.

*2-((1E,3E)-4-phenylbuta-1,3-dienyl)imidazo[1,2-a]pyridine (**4d**).* The title compound was prepared according to the general procedure. White solid (53.8 mg, 73%). Mp 191−193 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J = 6.8 Hz, 1H), 7.54 (d, J = 9.1 Hz, 1H), 7.51 (s, 1H), 7.44 (d, J = 7.4 Hz, 2H), 7.37−7.30 (m, 3H), 7.22 (t, J = 7.3 Hz, 1H), 7.13 (ddd, J = 9.0, 6.8, 1.2 Hz, 1H), 6.97 (dd, J = 15.5, 10.8 Hz, 1H), 6.73−6.68 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 144.1, 137.3, 133.3, 131.2, 128.9, 128.6, 127.5, 126.4, 125.4, 124.9, 123.9, 117.08, 112.2, 110.4. Anal. Calcd for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37. Found: C, 82.94; H, 5.76; N, 11.41.

*(E)-2-(4-chlorostyryl)-6-methylimidazo[1,2-a]pyridine (**4e**).* The title compound was prepared according to the general procedure. White solid (61.9 mg, 77%); mp 233−235 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (s, 1H), 7.50−7.46 (m, 5H), 7.32 (d, J = 7.0 Hz, 2H), 7.12−7.06 (m, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.8, 143.4, 135.8, 133.1, 128.8, 128.4, 127.7, 123.0, 121.9, 120.6, 116.5, 110.5, 18.1. Anal. Calcd for $C_{16}H_{13}N_2Cl$: C, 71.51; H, 4.88; N, 10.42. Found: C, 71.66; H, 4.92; N, 10.52.

*(E)-6-methyl-2-(2-(thiophen-2-yl)vinyl)imidazo[1,2-a]-pyridine (**4f**).* The title compound was prepared according to the general procedure. White solid (52.8 mg, 73%); mp 167−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.63 (d, J = 15.8 Hz, 1H), 7.43 (d, J = 9.9 Hz, 2H), 7.17 (d, J = 5.1 Hz, 1H), 7.08 (d, J = 3.4 Hz, 1H), 6.99−6.96 (m, 2H), 6.91 (d, J = 15.8 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.8, 143.3, 142.8, 128.20, 127.6, 126.3, 124.2, 123.2, 121.7, 119.6, 116.3, 110.3, 18.0. Anal. Calcd for $C_{14}H_{12}N_2S$: C, 69.97; H, 5.03; N, 11.66. Found: C, 69.89; H, 5.23; N, 11.68.

*6-Methyl-2-((1E,3E)-4-phenylbuta-1,3-dienyl)imidazo[1,2-a]pyridine (**4g**).* The title compound was prepared according to the general procedure. White solid (52.9 mg, 68%); mp 216−218 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.45−7.42 (m, 4H), 7.34−7.28 (m, 3H), 7.21 (t, J = 7.3 Hz, 1H), 6.96 (dd, J = 15.1, 10.7 Hz, 2H), 6.69 (dd, J = 15.4, 7.2 Hz, 2H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.8, 143.9, 137.4, 133.0, 130.7, 129.0, 128.6, 128.1, 127.4, 126.4, 124.2, 123.1, 121.8, 116.4, 110.2, 18.0. Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.04; H, 6.19; N, 10.76. Found: C, 82.79; H, 6.19; N, 10.64.

*(E)-6-chloro-2-(4-chlorostyryl)imidazo[1,2-a]pyridine (**4h**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (50.8 mg, 58%); mp 251−253 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (s, 1H), 7.55 (s, 1H), 7.52−7.45 (m, 4H), 7.32 (d, J = 8.4 Hz, 2H), 7.14 (dd, J = 9.6, 1.7 Hz, 1H), 7.08 (d, J = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.8, 144.1, 135.5, 133.5, 129.8, 128.9, 127.8, 126.6, 123.3, 120.4, 120.0, 117.5, 111.0. Anal. Calcd for $C_{15}H_{10}N_2Cl_2$: C, 62.30; H, 3.49 N, 9.69. Found: C, 62.28; H, 3.66; N, 9.45.

*(E)-6-chloro-2-(2-(thiophen-2-yl)vinyl)imidazo[1,2-a]-pyridine (**4i**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (41.6 mg, 53%); mp 194−196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, J = 1.3 Hz, 1H), 7.64 (d, J = 15.8 Hz, 1H), 7.47 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 5.0 Hz, 1H), 7.11−7.08 (m, 2H), 6.99 (dd, J = 5.0, 3.6 Hz, 1H), 6.89 (d, J = 15.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.7, 144.0, 142.4, 127.6, 126.8, 126.4, 124.7, 124.3, 123.2, 120.2, 118.9, 117.26, 110.7. Anal. Calcd for $C_{13}H_9N_2SCl$: C, 59.88; H, 3.48; N, 10.74. Found: C, 59.83; H, 3.67; N, 10.78.

*6-Chloro-2-((1E,3E)-4-phenylbuta-1,3-dienyl)imidazo[1,2-a]pyridine (**4j**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 120 °C for 48 h. White solid (31.6 mg, 38%); mp 210−212 °C . ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08−8.07 (m, 1H), 7.50−7.44 (m, 4H), 7.36−7.29 (m, 3H), 7.23 (t, J = 7.3 Hz, 1H), 7.11 (dd, J = 9.7, 2.0 Hz, 1H), 6.96 (dd, J = 15.3, 10.9 Hz, 1H), 6.70 (dd, J = 20.8, 15.5 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 144.1, 137.2, 133.9, 131.8, 128.7, 128.6, 127.7, 126.5, 126.3, 123.4, 123.2, 120.3, 117.4, 110.6. Anal. Calcd for $C_{17}H_{13}N_2Cl$: C, 72.73; H, 4.67; N, 9.98. Found: C, 72.91; H, 4.66; N, 9.98.

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*(E)-2-(4-chlorostyryl)-7-methoxyimidazo[1,2-a]pyridine (**4k**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 90 °C for 30 h. White solid (60.2 mg, 70%); mp 222−224 °C . ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, J = 7.4 Hz, 1H), 7.43 (dd, J = 12.1, 3.6 Hz, 3H), 7.37 (s, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 16.1 Hz, 1H), 6.82 (d, J = 2.2 Hz, 1H), 6.45 (dd, J = 7.4, 2.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.3, 147.3, 143.4, 135.9, 132.9, 128.7, 128.3, 127.6, 125.8, 120.5, 109.8, 107.3, 94.2, 55.4. Anal. Calcd for $C_{16}H_{13}N_2OCl$: C, 67.49; H, 4.60; N, 9.84. Found: C, 67.32; H, 4.67; N, 9.59.

*(E)-7-methoxy-2-(2-(thiophen-2-yl)vinyl)imidazo[1,2-a]-pyridine (**4l**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 90 °C for 30 h. Brown solid (42.0 mg, 55%); mp 144−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, J = 7.4 Hz, 1H), 7.61 (d, J = 15.8 Hz, 1H), 7.33 (s, 1H), 7.16 (d, J = 5.1 Hz, 1H), 7.06 (d, J = 3.4 Hz, 1H), 6.97 (dd, J = 5.0, 3.6 Hz, 1H), 6.86 (d, J = 15.8 Hz, 1H), 6.80 (d, J = 2.4 Hz, 1H), 6.42 (dd, J = 7.4, 2.5 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.2, 147.2, 143.3, 142.9, 127.5, 126.2, 125.8, 124.1, 122.9, 119.5, 109.5, 107.2, 94.2, 55.4. Anal. Calcd for $C_{14}H_{12}N_2OS$: C, 65.60; H, 4.72; N, 10.93. Found: C, 65.88; H, 4.93; N, 11.05.

*7-Methoxy-2-((1E,3E)-4-phenylbuta-1,3-dienyl)imidazo-[1,2-a]pyridine (**4m**).* The title compound was prepared according to the general procedure. The reaction mixture was stirred at 90 °C for 30 h. Light yellow solid (40.2 mg, 48%); mp 160−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (d, J = 7.4 Hz, 1H), 7.43 (d, J = 7.5 Hz, 2H), 7.32−7.29 (m, 4H), 7.20 (t, J = 7.3 Hz, 1H), 6.95 (dd, J = 15.5 Hz, 10.9, 1H), 6.81 (d, J = 2.3 Hz, 1H), 6.65 (dd, J = 20.3, 15.4 Hz, 2H), 6.42 (dd, J = 7.4, 2.4 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 147.2, 143.8, 137.4, 132.8, 130.4, 129.0, 128.5, 127.4, 126.3, 125.7, 124.0, 109.4, 107.2, 94.2, 55.4. Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.05; H, 6.06; N, 10.35.

*(E)-2-(4-chlorostyryl)imidazo[2,1-a]isoquinoline (**4n**).* The title compound was prepared according to the general procedure. Light yellow solid (73.9 mg, 81%); mp 192−194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.68 (d, J = 7.9 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.64 (dd, J = 16.5, 7.9 Hz, 2H), 7.57−7.45 (m, 5H), 7.31 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 16.1 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.4, 142.1, 135.9, 132.9, 129.6, 128.7, 128.3, 128.2, 128.1, 127.6, 126.9, 123.5, 123.4, 122.7, 120.7, 113.0, 112.3. Anal. Calcd for $C_{19}H_{13}N_2Cl$: C, 74.88; H, 4.30; N, 9.19. Found: C, 74.92; H, 4.35; N, 9.20.

*(E)-2-(2-(thiophen-2-yl)vinyl)imidazo[2,1-a]isoquinoline (**4o**).* The title compound was prepared according to the general procedure. White solid (60.3 mg, 73%); mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.71 (d, J = 15.8 Hz, 1H), 7.64 (dd, J = 12.4, 7.8 Hz, 2H), 7.58−7.54 (m, 1H), 7.47 (s, 1H), 7.21 (d, J = 5.0 Hz, 1H), 7.14 (d, J = 3.4 Hz, 1H), 7.07−7.95 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.3, 142.9, 141.9, 129.5, 128.2, 128.0, 127.6, 126.9, 126.0, 124.1, 123.4, 123.3, 122.7, 122.7, 119.8, 112.8, 112.0. Anal. Calcd for $C_{17}H_{12}N_2S$: C, 73.88; H, 4.38; N, 10.14. Found: C, 74.04; H, 4.38; N, 10.18.

*2-((1E,3E)-4-phenylbuta-1,3-dienyl)imidazo[2,1-a]-isoquinoline (**4p**).* The title compound was prepared according to the general procedure. Light yellow solid (61.8 mg, 70%); mp 197−199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.68 (d, J = 7.9 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.67−7.61 (m, 2H), 7.55 (td, J = 7.6, 1.2 Hz, 1H), 7.48−7.45 (m, 3H), 7.41−7.32 (m, 3H), 7.23 (t, J = 7.3 Hz, 1H), 7.03−6.95 (m, 2H), 6.74 (dd, J = 15.4, 4.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.4, 142.5, 137.5, 132.8, 130.3, 129.5, 129.1, 128.6, 128.2, 128.0, 127.4, 126.9, 126.36, 124.2, 123.5, 123.4, 122.7, 112.9, 112.1. Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 84.85; H, 5.25; N, 9.25.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectral data of all compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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