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Visible Light Organic Photoredox-Catalyzed C−H Alkoxylation of Imidazopyridine with Alcohol

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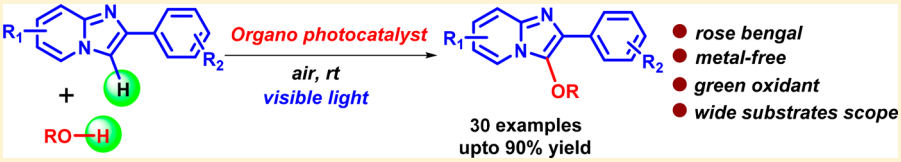
Supporting Information



ABSTRACT: The visible light-mediated C-3 alkoxylation of imidazopyridines with alcohols has been achieved using rose bengal as an organic photoredox catalyst at room temperature. Widely abundant air acts as the terminal oxidant that avoids the use of a stoichiometric amount of peroxo compounds. A wide range of functional groups could be tolerated under the reaction conditions to produce C(sp^2)−H alkoxylated products in high yields.

A visible light photoredox process has emerged as a prominent tool in challenging chemical transformations in recent years.[1] The most common catalysts employed to photoredox reactions are ruthenium and iridium polypyridyl complexes in organic synthesis.[2] However, these precious metal catalysts are potentially toxic on a larger scale.[3] Thus, major efforts have been devoted to utilize organic dyes as metal-free alternatives for their inexpensiveness, nontoxicity, synthetic versatility, and better environmental perspective.[4]

The development of an efficient method for the construction of the C−O bond has gained much attention from the synthetic organic chemists due to their wide occurrence in a large number of biologically active molecules and in natural products.[5] Traditional methods for the synthesis of alkyl ethers involve acid-catalyzed condensation of alcohols, coupling of alkoxides and alkyl halides (Williamson synthesis), alkoxymercuration/demercuration of alkenes, etc.[6] The use of toxic metals and harsh reaction conditions are the disadvantages of these methods in the formation of complex organic molecules.[7] Recently, a number of Pd- and Cu-catalyzed methods have been developed as useful alternatives for the synthesis of alkyl ethers.[8] However, many of these methods still suffer from limited substrate scopes and generate stoichiometric byproducts. Therefore, the development of straightforward and environmentally benign methods for the synthesis of direct C−H alkoxylation is highly demanding in organic synthesis.[9] As a consequence, there are only few methodologies that have been reported recently to construct a new C−O bond through photoredox catalysis.[10]

However, the functionalization of imidazo[1,2-*a*]pyridines is synthetically attractive as this heterocyclic scaffold is widely used in biological and medicinal fields.[11] The nature of the substituents present at the C-3 positions of imidazo[1,2-*a*]pyridines regulates their pharmacological activities. Thus, several methods have been developed for the synthesis and functionalization of imidazoheterocycles.[12] C-3 alkoxyl group-containing imidazo[1,2-*a*]pyridines have been used as selective and potent inhibitors of mycobacterial adenosine triphosphate (ATP) synthesis[13a] and to measure the luciferase activity in living cells (Figure 1).[13b] However, only limited methods for

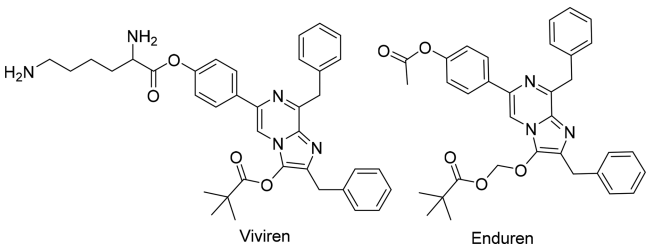


Figure 1. Examples of ether-based live cell substrates.

the construction of imidazo[1,2-*a*]pyridine ethers exists. Very recently, Zhong et al. reported a copper-catalyzed coupling between 2-aminopyridine and 2-phenoxyacetophenone for the synthesis of imidazopyridine ethers.[14] To the best of our knowledge, there is no method for direct C−H alkoxylation on imidazo[1,2-*a*]pyridine moieties. Recently, we have reported a visible light-mediated C-3 thiocyanation of imidazoheterocycles using an eosin Y photocatalyst.[15] On the basis of our previous experiences and continuous efforts on the synthesis of functionalized imidazoheterocycles[16] herein, we report a direct and environmentally benign method for the alkoxylation of imidazopyridines using rose bengal as a photoredox catalyst under ambient air at room temperature (Scheme 1).

We started our investigation by using 2-phenylimidazo[1,2-*a*]pyridine (**1a**) and methanol as model substrates. Initially, we carried out the reaction using 2 equiv of methanol as an

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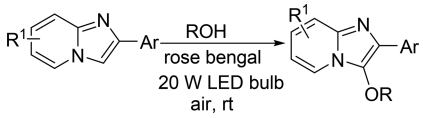
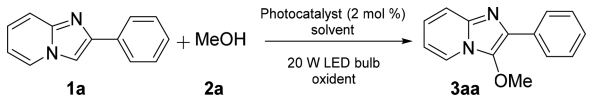
Scheme 1. C-3 Alkoxylation of Imidazopyridine



alkoxylating reagent with eosin Y as an organo photocatalyst in a CH_3CN solvent under a 20 W LED light. The results are summarized in Table 1. To our delight, 2-phenyl-3-methoxy-

Table 1. Optimization of the Reaction Conditions[a]



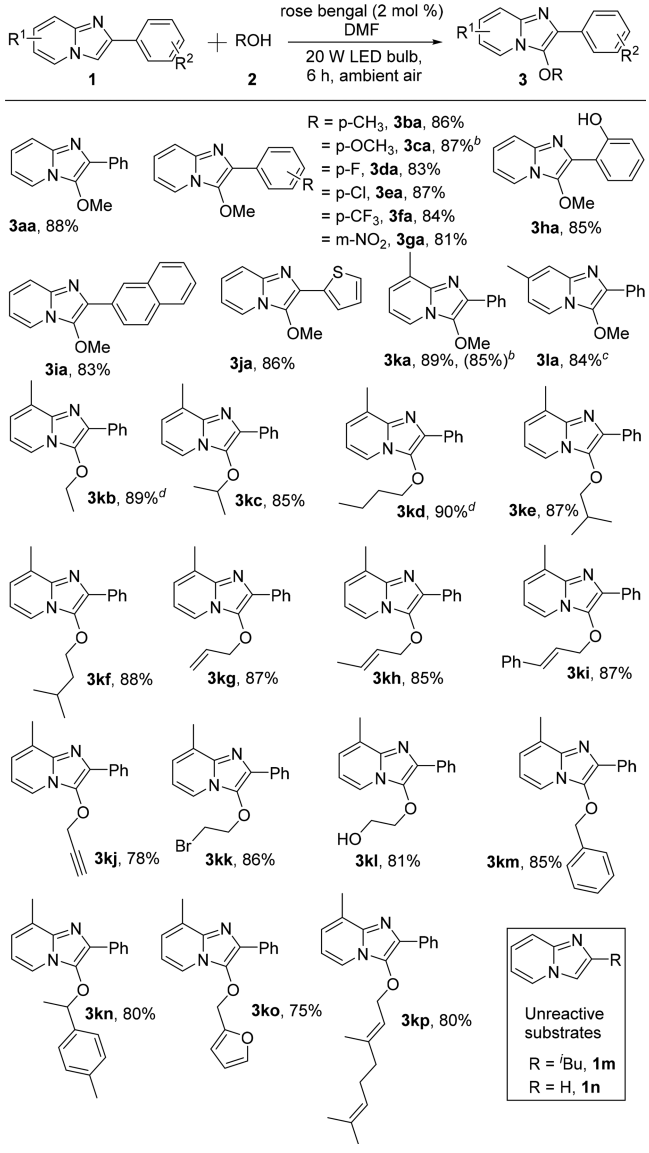
entry	photocatalyst	solvent	oxidant	yield (%)
1	eosin Y	CH_3CN	air	56
2	eosin Y	THF	air	59
3	eosin Y	toluene	air	45
4	eosin Y	1,2-DCE	air	38
5	eosin Y	DCM	air	trace
6	eosin Y	DMF	air	72
7	eosin Y	DMSO	air	65
8	eosin Y	1,4-dioxane	air	68
9	eosin Y	H_2O	air	trace
10	rose bengal	DMF	air	88
11	$Ru(bpy)_3Cl_2·6H_2O$	DMF	air	62
12	$Ir(ppy)_3$	DMF	air	68
13	rose bengal	DMF	O_2	89
14	rose bengal	DMF	TBHP	72
15	rose bengal	DMF	$K_2S_2O_8$	75
16	rose bengal	DMF		trace[b]
17		DMF	air	nd[c]
18	rose bengal	DMF	air	55[d]
19	rose bengal	DMF	air	30[e]

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), photocatalyst (2 mol %), solvent (3 mL), 20 W LED bulb. [b]Under an argon atmosphere. [c]Not detected. [d]Irradiated with a green LED. [e]Irradiated with a blue LED.

imidazo[1,2-*a*]pyridine (**3aa**) was formed in 56% yield after 6 h under ambient air (Table 1, entry 1). Inspired by this initial result, we checked the effect of other solvents such as THF, toluene, 1,2-DCE, DCM, DMF, DMSO, 1,4-dioxane, and H_2O (Table 1, entries 2−9). The best result was obtained in DMF yielding 72% of the desired product (Table 1, entry 6). The screening of other photocatalysts such as rose bengal, $Ru(bpy)_3Cl_2·6H_2O$, and $Ir(ppy)_3$ (Table 1, entries 10−12) revealed that the alkoxylated product could be obtained in an excellent yield by using rose bengal as a photocatalyst (Table 1, entry 10). In presence of molecular O_2, the yield of the alkoxylated product did not improve much (Table 1, entry 13). The use of other stoichiometric oxidants like TBHP and $K_2S_2O_8$ resulted in lower yields (Table 1, entries 14 and 15). No product was formed in the absence of any photocatalyst (Table 1, entry 17). Moreover, the yield decreased significantly when the reaction mixture was irradiated with a green LED and blue LED for 12 h (Table 1, entries 18 and 19). Finally, the optimized reaction conditions were obtained using 2 mol % rose bengal in DMF by irradiation with a 20 W LED for 6 h (Table 1, entry 10).

With the optimized reaction conditions in hand, we investigated the scope of this alkoxylation reaction to show the generality of this methodology (Scheme 2). At first, the

Scheme 2. C-3 Alkoxylation of Imidazopyridines with Alcohols[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), rose bengal (2 mol %), DMF (3 mL), 20 W LED bulb. [b]5 mmol scale. [c]Reaction continued for 9 h. [d]Reaction completed in 4 h.

effect of the C-2 substituents on the phenyl ring was examined. The imidazopyridine moiety with electron-donating substituents ($-CH_3$ and $-OCH_3$) on the phenyl ring afforded the corresponding methoxylated products with excellent yields (**3ba** and **3ca**). Halogens were also well-tolerated under the present reaction conditions (**3da** and **3ea**). Strong electron-withdrawing groups like $-CF_3$ and $-NO_2$ in the phenyl ring also successfully gave the desired products without any difficulties (**3fa** and **3ga**). The hydroxy-substituted phenyl ring of imidazo[1,2-*a*]pyridine also afforded the desired product with a good yield (**3ha**). To our delight, the naphthyl- and thiophene-substituted imidazo[1,2-*a*]pyridines furnished the corresponding methoxylated products with high yields (**3ia** and

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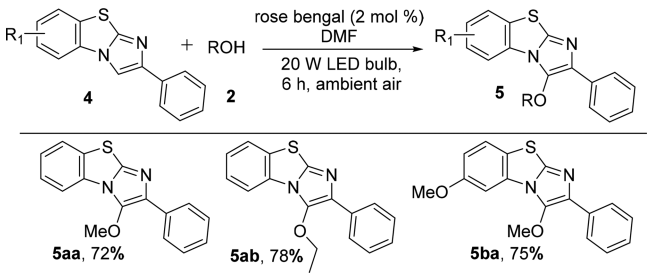
3ja). Also, imidazo[1,2-*a*]pyridines bearing a methyl substituent on the pyridine ring at different positions efficiently reacted with methanol to afford the desired products with good yields (**3ka** and **3la**). Next, to check the feasibility of alcohols, a variety of primary and secondary alcohols were also tested as alkoxylating agents, and in all of the cases, it afforded the corresponding products in moderate to good yields (**3kb**–**3kp**). Saturated alcohols like ethanol, propan-2-ol, 1-butanol, 2-methylpropan-1-ol, and 3-methylbutan-1-ol smoothly reacted with imidazopyridine (**1k**) and gave the desired products with excellent yields (**3kb**–**3kf**). Notably, unsaturated alcohols such as prop-2-en-1-ol, (*E*)-but-2-en-1-ol, (*E*)-3-phenylprop-2-en-1-ol, and prop-2-yn-1-ol were also well-tolerated under the present reaction conditions (**3kg**–**3kj**). Moreover, 2-bromoethanol, a halogenated alcohol, was also found to participate efficiently in this reaction (**3kk**). Surprisingly, when ethylene glycol was used, only one hydroxyl group could be coupled with **1k** to afford the desired product in 81% yield (**3kl**). When phenylmethanol, 1-tolylethanol, and furylmethanol were employed, the corresponding products (**3km**–**3ko**) were obtained in 75–85% yields. More interestingly, the natural product, geraniol, also gave the alkoxylated product with an excellent yield (**3kp**). However, the present methodology is not applicable for the C-2 alkyl-substituted imidazo[1,2-*a*]pyridine, simple imidazo[1,2-*a*]pyridine (**1m** and **1n**), indole, imidazole, sterically hindered tertiary alcohols, and aliphatic thiols. Moreover, no alkoxylated product was obtained when 3-phenylimidazo[1,2-*a*]pyridine was treated with methanol under the standard conditions. This result illustrated that the reaction selectively took place at the 3-position. The gram-scale reaction of the present methodology was also performed in the usual laboratory setup by taking 8-methyl-2-phenylimidazo[1,2-*a*]-pyridine (**1k**) and methanol (**2a**). The corresponding alkoxylated product (**3ka**) was obtained without a significant decrease in yield, which signifies the practical applicability of the present methodology.

To extend the scope of our methodology, we carried out the reaction with substituted benzo[*d*]imidazo[2,1-*b*]thiazoles (Scheme 3). To our delight, in all of the cases, the alkoxylated products were obtained in excellent yields (**5aa**–**5ba**).

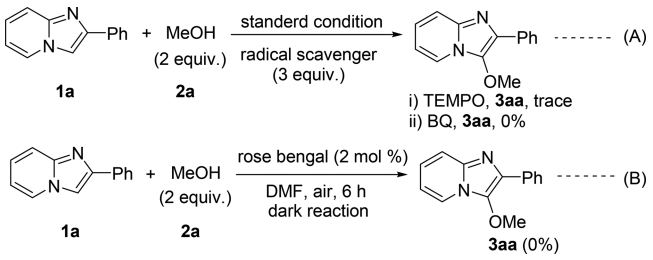
Scheme 3. C-3 Alkoxylation of Benzoimidazothiazoles with Alcohols[a]



[a]Reaction conditions: **4** (0.2 mmol), **2** (0.4 mmol), rose bengal (2 mol %), DMF (3 mL), 20 W LED bulb.

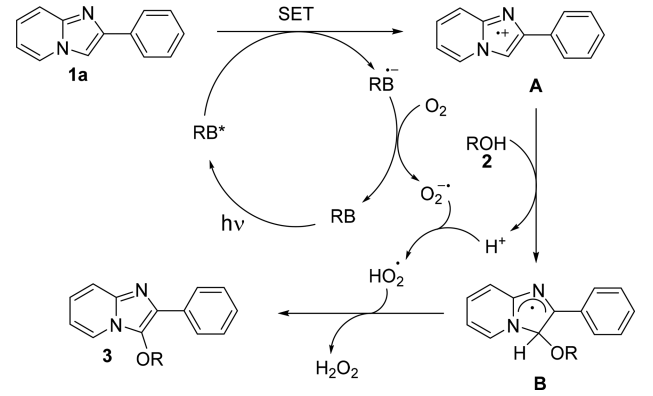
To unravel the mechanistic path for the alkoxylation reaction of imidazopyrines with alcohols, a few control experiments were carried out as shown in Scheme 4. In the presence of radical scavenger 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), only a trace amount of product was obtained (Scheme 4, eq A, (i)). No formation of the desired product was found in the presence of benzoquinone (BQ) (Scheme 4, eq A, (ii)). These results signify that the reaction possibly proceeds through a radical pathway. The reaction did not proceed at all in the dark (Scheme 4, eq B), which strongly supports the radical mechanism.

Scheme 4. Control Experiments



On the basis of our experimental observations and literature reports,[4f,10a] a plausible mechanistic pathway has been proposed in Scheme 5. A single electron transfer (SET) from imidazopyridine to the excited state of rose bengal (RB*) afforded the imidazopyridine radical cation (**A**) and photocatalyst radical anion ($RB^{\bullet-}$). The resulting imidazopyridine radical cation reacts with alcohol (ROH) to yield the alkoxide-adduct radical (**B**). The photoredox cycle is completed by the reduction of O_2 to $O_2^{\bullet-}$, which can abstract a proton to produce $HO_2^{\bullet}$. Hydrogen abstraction by $HO_2^{\bullet}$ from intermediate **B** affords the alkoxylation product with H_2O_2, which is detected by the starch–iodine test. Benzoquinone, which acts as a scavenger of the superoxide radical anion, completely stopped the formation of the desired product.[4i]

Scheme 5. Probable Mechanistic Pathway



In summary, we have developed a direct C-3 alkoxylation of imidazopyridines using visible light organophotoredox catalysis at ambient temperature. This methodology exploits a commercially available organic dye (rose bengal) as the inexpensive and nontoxic photocatalyst using air as the sole green oxidant. A wide range of functional groups present in the substrates could be tolerated under the mild reaction conditions to provide the corresponding alkoxylated products in moderate to excellent yields. To the best of our knowledge, this is the first report for the direct C–H alkoxylation of imidazopyridines. We believe this visible light-driven organophotocatalytic C–H alkoxylation strategy will add prospective luminescence over expensive and toxic metal-catalyzed reactions in organic synthesis.

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EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources and used without further purification. ^{1}H NMR spectra were determined on a 400 MHz spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (δ), and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet). Coupling constants (J) were given in Hz. $^{13}C\{^1H\}$ NMR spectra were recorded at 100 MHz in a $CDCl_3$ solution. Chemical shifts are referenced to $CDCl_3$ (δ = 7.26 for ^{1}H and δ = 77.16 for $^{13}C\{^1H\}$ NMR) as the internal standard. TLC was done on silica gel-coated glass slides. All solvents were dried and distilled before use. Commercially available solvents were freshly distilled before the reaction. All reactions involving moisture-sensitive reactants were executed using oven-dried glassware. All of the imidazoheterocycles were prepared by our reported method.[16b]

General Experimental Procedure for the Synthesis of Compound 3aa−3kp. Imidazo[1,2-*a*]pyridine (**1**, 0.2 mmol), alcohol (**2**, 0.4 mmol), rose bengal (2.0 mol %), and DMF (3.0 mL) were added to an oven-dried reaction vessel equipped with a magnetic stir bar, and the reaction vessel was irradiated using a 20 W LED bulb at room temperature under ambient air for 6 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the crude residue, which was purified by column chromatography on silica gel (60−120 mesh) using petroleum ether/ethyl acetate as an eluent to afford the pure alkoxylated products (**3aa−3kp**).

*3-Methoxy-2-phenylimidazo[1,2-a]pyridine (**3aa**).* Colorless oil (39 mg, 88% yield), R_f = 0.6 (PE/EA = 84:16). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41−8.39 (m, 1H), 7.97−7.94 (m, 2H), 7.77−7.73 (m, 1H), 7.53−7.51 (m, 1H), 7.48−7.45 (m, 2H), 7.29 (d, J = 8.0 Hz, 1H), 7.15−7.12 (m, 1H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.9, 160.7, 159.5, 148.3, 138.1, 134.2, 132.2, 128.8, 128.6, 121.7, 119.6, 52.1. Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49%. Found: C, 74.82; H, 5.46; N, 12.59%.

*3-Methoxy-2-(p-tolyl)imidazo[1,2-a]pyridine (**3ba**).* Yellow oil (41 mg, 86% yield), R_f = 0.6 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.39−8.38 (m, 1H), 7.85−7.83 (m, 2H), 7.75−7.70 (m, 1H), 7.28−7.25 (m, 3H), 7.12−7.09 (m, 1H), 3.79 (s, 3H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.9, 160.6, 159.6, 148.2, 142.9, 138.0, 131.5, 129.5, 128.6, 121.5, 119.5, 52.0, 21.7. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76%. Found: C, 75.80; H, 5.87; N, 11.89%.

*3-Methoxy-2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (**3ca**).* Yellow oil (44 mg, 87% yield), R_f = 0.45 (PE/EA = 80:20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.40−8.38 (m, 1H), 7.94−7.92 (m, 2H), 7.76−7.71 (m, 1H), 7.27−7.25 (m, 1H), 7.13−7.09 (m, 1H), 6.99−6.96 (m, 2H), 3.88 (s, 3H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.0, 163.0, 160.0, 159.8, 148.2, 138.0, 130.6, 126.9, 121.3, 119.4, 114.2, 55.6, 52.0. Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%. Found: C, 70.70; H, 5.61, N, 10.98%.

*2-(4-Fluorophenyl)-3-methoxyimidazo[1,2-a]pyridine (**3da**).* Yellow oil (40 mg, 83% yield), R_f = 0.5 (PE/EA = 86:14). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.40−8.38 (m, 1H), 7.99−7.96 (m, 2H), 7.77−7.72 (m, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.17−7.12 (m, 3H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.7, 165.3 (J_{C-F} = 252 Hz), 159.3, 159.2, 148.2, 138.2, 130.9 (J_{C-F} = 8 Hz), 130.4 (J_{C-F} = 3 Hz), 121.8, 119.7, 116.0 (J_{C-F} = 22 Hz), 52.2. Anal. Calcd for $C_{14}H_{11}FN_2O$: C, 69.41; H, 4.58; N, 11.56%. Found: C, 69.62; H, 4.62; N, 11.46%.

*2-(4-Chlorophenyl)-3-methoxyimidazo[1,2-a]pyridine (**3ea**).* Brown oil (45 mg, 87% yield), R_f = 0.6 (PE/EA = 86:14). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.40−8.39 (m, 1H), 7.92−7.89 (m, 2H), 7.77−7.73 (m, 1H), 7.45−7.42 (m, 2H), 7.29 (d, J = 8.0 Hz, 1H), 7.16−7.13 (m, 1H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.6, 159.3, 159.1, 148.3, 138.5, 138.2, 132.6, 129.9, 129.1, 122.0, 119.9, 52.2. Anal. Calcd for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; N, 10.83%. Found: C, 65.18; H, 4.23; N, 10.95%.

*3-Methoxy-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (**3fa**).* Yellow oil (49 mg, 84% yield), R_f = 0.6 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.42−8.41 (m, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.80−7.76 (m, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.6 Hz, 1H), 7.19−7.16 (m, 1H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.4, 159.1, 158.8, 148.3, 138.3, 137.4, 133.5 (J_{C-F} = 32 Hz), 128.9, 125.7 (J_{C-F} = 8 Hz), 123.8 (J_{C-F} = 284 Hz), 122.3, 120.2, 52.3. Anal. Calcd for $C_{15}H_{11}F_3N_2O$: C, 61.65; H, 3.79; N, 9.59%. Found: C, 61.48; H, 3.72; N, 9.70%.

*3-Methoxy-2-(3-nitrophenyl)imidazo[1,2-a]pyridine (**3ga**).* Brown gummy mass (44 mg, 81% yield), R_f = 0.55 (PE/EA = 80:20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.85 (d, J = 2 Hz, 1H), 8.43−8.41 (m, 1H), 8.38−8.36 (m, 1H), 8.29−8.27 (m, 1H), 7.82−7.78 (m, 1H), 7.66 (t, J = 8.4 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.22−7.18 (m, 1H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 158.3, 157.9, 148.7, 148.3, 138.5, 136.0, 134.2, 129.8, 126.4, 123.5, 122.6, 120.5, 52.5. Anal. Calcd for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61%. Found: C, 62.25; H, 4.17; N, 15.48%.

*2-(3-Methoxyimidazo[1,2-a]pyridin-2-yl)phenol (**3ha**).* Yellow oil (41 mg, 85% yield), R_f = 0.6 (PE/EA = 82:18). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 13.67 (s, 1H), 8.43−8.42 (m, 1H), 7.79−7.75 (m, 1H), 7.44−7.38 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.20−7.17 (m, 1H), 7.05−7.03 (m, 1H), 6.93−6.89 (m, 1H), 3.91 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.3, 163.4, 162.8, 155.7, 148.3, 138.5, 134.6, 130.8, 122.7, 120.8, 119.2, 118.3, 116.2, 52.3. Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%. Found: C, 69.80; H, 5.08; N, 11.78%.

*3-Methoxy-2-(naphthalen-2-yl)imidazo[1,2-a]pyridine (**3ia**).* Brown gummy mass (45 mg, 83% yield), R_f = 0.5 (PE/EA = 84:16). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44−8.42 (m, 1H), 8.29 (s, 1H), 8.23−8.21 (m, 1H), 7.94−7.90 (m, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.79−7.75 (m, 1H), 7.59−7.51 (m, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.17−7.13 (m, 1H), 3.86 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 167.0, 160.7, 159.5, 148.3, 138.2, 135.3, 132.8, 131.6, 130.6, 129.4, 128.7, 128.2, 127.9, 126.8, 124.2, 121.8, 119.8, 52.2. Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21%. Found: C, 78.97; H, 5.10; N, 10.30%.

*3-Methoxy-2-(thiophen-2-yl)imidazo[1,2-a]pyridine (**3ja**).* Brown oil (40 mg, 86% yield), R_f = 0.5 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.38−8.36 (m, 1H), 7.74−7.70 (m, 1H), 7.57−7.56 (m, 1H), 7.54−7.53 (m, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.13−7.09 (m, 2H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.9, 158.8, 154.8, 148.1, 141.1, 138.1, 132.8, 132.3, 128.2, 121.7, 120.0, 52.3. Anal. Calcd for $C_{12}H_{10}N_2OS$: C, 62.59; H, 4.38; N, 12.16%. Found: C, 62.41; H, 4.44; N, 12.30%.

*3-Methoxy-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3ka**).* Brown oil (42 mg, 89% yield), R_f = 0.55 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.22−8.20 (m, 1H), 8.01−7.98 (m, 2H), 7.55−7.50 (m, 2H), 7.48−7.44 (m, 2H), 7.06−7.03 (m, 1H), 3.78 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.8, 159.5, 158.1, 145.5, 138.9, 134.3, 132.0, 130.1, 128.7, 128.6, 121.8, 52.0, 17.5. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76%. Found: C, 75.76; H, 5.99; N, 11.64%.

*3-Methoxy-7-methyl-2-phenylimidazo[1,2-a]pyridine (**3la**).* Yellow oil (40 mg, 84% yield), R_f = 0.5 (PE/EA = 84:16). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.25 (d, J = 4.8 Hz, 1H), 7.96−7.93 (m, 2H), 7.54−7.49 (m, 1H), 7.47−7.43 (m, 2H), 7.13 (s, 1H), 6.55 (d, J = 5.2 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.9, 160.6, 159.5, 149.4, 147.9, 134.3, 132.1, 128.7, 128.5, 122.9, 120.3, 52.1, 21.1. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76%. Found: C, 75.42; H, 5.97; N, 11.65%.

*3-Ethoxy-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kb**).* Yellow oil (45 mg, 89% yield), R_f = 0.6 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.02−7.99 (m, 2H), 7.53−7.49 (m, 2H), 7.48−7.44 (m, 2H), 7.04−7.01 (m, 1H), 4.25 (q, J = 14.4 Hz, 2H), 2.38 (s, 3H), 1.14 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.0, 159.9, 158.7, 145.5, 138.6, 134.4, 131.9, 128.7, 128.6, 127.9, 121.6, 61.4, 17.5, 14.0. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10%. Found: C, 75.99; H, 6.35; N, 11.20%.

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*3-Isopropoxy-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kc**).* Yellow oil (45 mg, 85% yield), R_f = 0.5 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.17 (m, 1H), 8.01−7.99 (m, 2H), 7.54−7.50 (m, 2H), 7.48−7.44 (m, 2H), 7.04−7.01 (m, 1H), 5.20−5.11 (m, 1H), 2.36 (s, 3H), 1.14 (d, J = 6.0 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.2, 160.2, 159.0, 145.4, 138.5, 134.4, 131.9, 128.7, 128.6, 127.5, 121.4, 69.4, 21.6, 17.5. Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52%. Found: C, 76.86; H, 6.88; N, 10.39%.

*3-Butoxy-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kd**).* Yellow oil (50 mg, 90% yield), R_f = 0.6 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.02−7.99 (m, 2H), 7.54−7.50 (m, 2H), 7.48−7.44 (m, 2H), 7.04−7.01 (m, 1H), 4.18 (t, J = 6.8 Hz, 2H), 2.38 (s, 3H), 1.52−1.45 (m, 2H), 1.25−1.15 (m, 2H), 0.84 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 159.9, 158.6, 145.5, 138.6, 134.4, 131.9, 128.7, 128.6, 127.8, 121.6, 65.2, 30.3, 19.0, 17.5, 13.7. Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99%. Found: C, 77.27; H, 7.13; N, 10.08%.

*3-Isobutoxy-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3ke**).* Yellow oil (49 mg, 87% yield), R_f = 0.5 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.03−8.00 (m, 2H), 7.52−7.49 (m, 2H), 7.48−7.44 (m, 2H), 7.03−7.00 (m, 1H), 3.95 (d, J = 6.8 Hz, 2H), 2.39 (s, 3H), 1.84−1.77 (m, 1H), 0.78 (d, J = 6.8 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 159.8, 158.6, 145.5, 138.6, 134.4, 131.9, 128.68, 128.66, 127.8, 121.6, 71.5, 27.4, 19.0, 17.5. Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99%. Found: C, 77.29; H, 7.15; N, 10.13%.

*3-(Isopentyloxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kf**).* Yellow oil (52 mg, 88% yield), R_f = 0.6 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.20−8.18 (m, 1H), 8.02−7.99 (m, 2H), 7.53−7.49 (m, 2H), 7.48−7.44 (m, 2H), 7.04−7.01 (m, 1H), 4.21 (t, J = 6.8 Hz, 2H), 2.37 (s, 3H), 1.52−1.144 (m, 1H), 1.41−1.36 (m, 2H), 0.83 (d, J = 6.4 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 159.8, 158.6, 145.5, 138.6, 134.3, 131.9, 128.67, 128.63, 127.8, 121.6, 63.9, 37.0, 24.8, 22.4, 17.5. Anal. Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52%. Found: C, 77.39; H, 7.60; N, 9.41%.

*3-(Allyloxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kg**).* Brown gummy mass (46 mg, 87% yield), R_f = 0.6 (PE/EA = 86:14). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.02−8.00 (m, 2H), 7.54−7.50 (m, 2H), 7.48−7.44 (m, 2H), 7.05−7.02 (m, 1H), 5.84−5.74 (m, 1H), 5.27−5.21 (m, 1H), 5.20−5.17 (m, 1H), 4.70−4.68 (m, 2H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.9, 159.4, 158.3, 145.4, 138.7, 134.3, 132.0, 131.4, 128.7, 128.6, 128.2, 121.8, 119.2, 66.0, 17.5. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60%. Found: C, 77.06; H, 6.15; N, 10.48%.

*(E)-3-(But-2-en-1-yloxy)-8-methyl-2-phenylimidazo[1,2-a]-pyridine (**3kh**).* Brown gummy mass (47 mg, 85% yield), R_f = 0.6 (PE/EA = 86:14). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.17 (m, 1H), 8.01−7.99 (m, 2H), 7.53−7.49 (m, 2H), 7.47−7.43 (m, 2H), 7.04−7.01 (m, 1H), 5.75−5.69 (m, 1H), 5.46−5.42 (m, 1H), 4.64−4.62 (m, 2H), 2.38 (s, 3H), 1.68−1.66 (m, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.9, 159.7, 158.4, 145.4, 138.7, 134.4, 132.3, 131.9, 128.7, 128.6, 128.0, 124.4, 121.6, 66.0, 17.9, 17.5. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06%. Found: C, 77.82; H, 6.46; N, 10.16%.

*3-(Cinnamyloxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3ki**).* Brown gummy mass (59 mg, 87% yield), R_f = 0.5 (PE/EA = 84:16). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12−8.11 (m, 1H), 8.04−8.02 (m, 2H), 7.53−7.45 (m, 4H), 7.35−7.27 (m, 5H), 6.96−6.93 (m, 1H), 6.57 (d, J = 16.0 Hz, 1H), 6.17−6.10 (m, 1H), 4.87−4.85 (m, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.9, 159.5, 158.3, 145.5, 138.7, 136.2, 135.0, 134.3, 132.0, 128.76, 128.71, 128.2, 128.1, 126.7, 122.2, 121.7, 65.8, 17.5. Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23%. Found: C, 81.32; H, 5.88; N, 8.10%.

*8-Methyl-2-phenyl-3-(prop-2-yn-1-yloxy)imidazo[1,2-a]pyridine (**3kj**).* Brown gummy mass (41 mg, 78% yield), R_f = 0.6 (PE/EA = 93:7). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21−8.19 (m, 1H), 8.03−8.00 (m, 2H), 7.55−7.50 (m, 2H), 7.49−7.45 (m, 2H), 7.06−7.03 (m, 1H), 4.83 (d, J = 2.4 Hz, 2H), 2.47 (t, J = 2.4 Hz, 1H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.7, 158.3, 157.5, 145.4, 139.0, 134.3, 132.1, 128.9, 128.7, 128.6, 122.1, 75.4, 74.6, 52.4, 17.5. Anal. Calcd for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68%. Found: C, 77.64; H, 5.31; N, 10.77%.

*3-(2-Bromoethoxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kk**).* Brown gummy mass (57 mg, 86% yield), R_f = 0.45 (PE/EA = 86:14). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.04−8.01 (m, 2H), 7.55−7.51 (m, 2H), 7.49−7.45 (m, 2H), 7.07−7.04 (m, 1H), 4.51 (t, J = 6.4 Hz, 1H), 3.41 (t, J = 6.4 Hz, 1H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.8, 158.7, 157.9, 145.3, 139.0, 134.0, 132.1, 128.8, 128.7, 128.6, 122.1, 64.5, 27.7, 17.5. Anal. Calcd for $C_{16}H_{15}BrN_2O$: C, 58.02; H, 4.57; N, 8.46%. Found: C, 58.18; H, 4.63; N, 8.32%.

*2-((8-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)oxy)ethan-1-ol (**3kl**).* Brown gummy mass (43 mg, 81% yield), R_f = 0.45 (PE/EA = 70:30). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.17 (m, 1H), 7.99−7.97 (m, 2H), 7.57−7.52 (m, 2H), 7.49−7.45 (m, 2H), 7.09−7.05 (m, 1H), 4.47−4.44 (m, 2H), 3.81−3.79 (m, 2H), 2.65 (br, 1H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.3, 159.4, 157.9, 145.4, 139.3, 134.1, 132.2, 129.0, 128.8, 128.6, 122.2, 67.0, 60.3, 17.6. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%. Found: C, 71.44; H, 6.06; N, 10.34%.

*3-(Benzyloxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3km**).* Yellow oil (53 mg, 85% yield), R_f = 0.6 (PE/EA = 84:16). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02−8.01 (m, 1H), 8.00−7.97 (m, 2H), 7.53−7.48 (m, 2H), 7.46−7.42 (m, 2H), 7.31−7.29 (m, 3H), 7.22−7.20 (m, 2H), 6.99−6.96 (m, 1H), 5.23 (s, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 159.3, 158.1, 145.5, 138.7, 135.1, 134.4, 132.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 121.8, 67.1, 17.5. Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91%. Found: C, 80.37; H, 5.73; N, 9.04%.

*8-Methyl-2-phenyl-3-(1-(p-tolyl)ethoxy)imidazo[1,2-a]pyridine (**3kn**).* Yellow oil (55 mg, 80% yield), R_f = 0.5 (PE/EA = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02−8.01 (m, 1H), 7.95−7.92 (m, 2H), 7.52−7.46 (m, 2H), 7.44−7.40 (m, 2H), 7.14−7.09 (m, 4H), 6.97−6.94 (m, 1H), 6.02 (q, J = 13.2 Hz, 1H), 2.36 (s, 3H), 2.33 (s, 3H), 1.41 (d, J = 6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.1, 159.8, 158.7, 145.5, 138.5, 137.8, 137.6, 134.4, 131.9, 129.2, 128.6, 127.5, 126.4, 125.4, 121.4, 73.7, 21.7, 21.2, 17.5. Anal. Calcd for $C_{23}H_{22}N_2O$: C, 80.67; H, 6.48; N, 8.18%. Found: C, 80.82; H, 6.42; N, 8.07%.

*3-(Furan-2-ylmethoxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3ko**).* Brown gummy mass (46 mg, 75% yield), R_f = 0.6 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05−8.04 (m, 1H), 7.98−7.95 (m, 2H), 7.51−7.49 (m, 2H), 7.46−7.42 (m, 2H), 7.38−7.37 (m, 1H), 7.01−6.98 (m, 1H), 6.37 (d, J = 3.2 Hz, 1H), 6.35−6.33 (m, 1H), 5.20 (s, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.9, 158.0, 145.5, 143.4, 138.8, 134.4, 132.0, 130.2, 129.0, 128.7, 128.6, 128.4, 121.8, 111.4, 110.7, 58.5, 17.5. Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20%. Found: C, 74.79; H, 5.37; N, 9.32%.

*(E)-3-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-8-methyl-2-phenylimidazo[1,2-a]pyridine (**3kp**).* Brown gummy mass (58 mg, 80% yield), R_f = 0.5 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19−8.18 (m, 1H), 8.01−7.98 (m, 2H), 7.53−7.49 (m, 2H), 7.47−7.43 (m, 2H), 7.04−7.01 (m, 1H), 5.23−5.19 (m, 1H), 5.09−5.04 (m, 1H), 4.71 (d, J = 7.2 Hz, 2H), 2.38 (s, 3H), 2.09−2.03 (m, 2H), 2.01−1.97 (m, 2H), 1.66 (s, 3H), 1.63 (s, 3H), 1.59 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 159.8, 158.5, 145.5, 143.3, 138.6, 134.4, 132.0, 131.9, 128.6, 127.9, 125.1, 123.8, 121.6, 117.5, 62.1, 39.6, 26.3, 25.8, 17.8, 17.5, 16.5. Anal. Calcd for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83; N, 7.77%. Found: C, 80.13; H, 7.88; N, 7.63%.

*3-Methoxy-2-phenylbenzo[d]imidazo[2,1-b]thiazole (**5aa**).* Yellow oil (40 mg, 72% yield), R_f = 0.6 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78−7.76 (m, 1H), 7.75−7.71 (m, 2H), 7.43−7.37 (m, 4H), 7.33−7.28 (m, 1H), 7.25−7.20 (m, 1H), 3.43 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 173.2, 167.3, 135.3, 130.9, 129.8, 128.7, 127.5, 126.8, 126.5, 126.1, 123.5, 113.8, 103.9, 52.9. Anal. Calcd for $C_{16}H_{12}N_2OS$: C, 68.55; H, 4.31; N, 9.99%. Found: C, 68.77; H, 4.25; N, 9.87%.

*3-Ethoxy-2-phenylbenzo[d]imidazo[2,1-b]thiazole (**5ab**).* Yellow oil (46 mg, 78% yield), R_f = 0.55 (PE/EA = 90:10). ^{1}H NMR ($CDCl_3$,

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400 MHz): δ 7.78−7.76 (m, 1H), 7.75−7.72 (m, 2H), 7.42−7.38 (m, 4H), 7.32−7.28 (m, 1H), 7.24−7.20 (m, 1H), 3.68−3.61 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 173.5, 166.9, 135.8, 131.0, 129.7, 128.7, 127.4, 126.8, 126.6, 126.1, 123.4, 113.8, 103.8, 61.2, 15.4. Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.17; H, 4.73; N, 9.65%.

3,6-Dimethoxy-2-phenylbenzo[d]imidazo[2,1-b]thiazole (**5ba**). Yellow gummy mass (46 mg, 75% yield), R_f = 0.5 (PE/EA = 86:14). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, *J* = 8.8 Hz, 1H), 7.55−7.52 (m, 2H), 7.43−7.39 (m, 1H), 7.31−7.28 (m, 2H), 7.12 (d, *J* = 2.8 Hz, 1H), 6.97−6.95 (m, 1H), 4.07 (s, 3H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 165.8, 164.7, 156.7, 146.1, 135.6, 131.5, 130.2, 129.3, 128.9, 128.5, 122.3, 114.3, 104.7, 55.8, 55.5. Anal. Calcd for $C_{17}H_{14}N_2O_2S$: C, 65.79; H, 4.55; N, 9.03%. Found: C, 65.99; H, 4.61; N, 8.90%.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02582.

Starch−idodine test for the detection of hydrogen peroxide and scanned copies of ^1H and $^{13}C\{^1H\}$ NMR spectra of the synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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