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Regioselective synthesis of nitrosoimidazoheterocycles using *tert*-butyl nitrite

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A simple and practical method has been developed for the regioselective nitrosylation of imidazopyridines *via* C(sp^2)–H bond functionalization using *tert*-butyl nitrite under mild reaction conditions in short time. A library of 3-nitrosoimidazopyridines with broad functionalities was synthesized in near quantitative yields. The present protocol is also applicable to imidazo[2,1-*b*]thiazole and benzo[*d*]imidazo[2,1-*b*]thiazole.

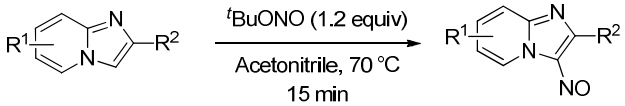
Introduction

The imidazo[1,2-*a*]pyridine moiety is prevalent in biologically active molecules and pharmaceutical compounds.[1] Due to its wide applications in medicinal chemistry, this fused bicyclic 5–6 heterocycle is recognized as a privileged drug scaffold. This heterocycle is also important in the field of material science.[2] The pharmacological activity of imidazo[1,2-*a*]pyridine is shown to be dependent on the nature of substituents and functionalites at different positions. As a result, these 'privileged' fragments have been continuing to gain significant interest in organic synthesis and a number of efficient processes have been developed for the diversified synthesis of functionalized imidazo[1,2-*a*]pyridine derivatives.[3] We are also interested about the chemistry of these derivatives and recently we have reported a number of methods for the synthesis[4] and functionalization[5] of imidazo[1,2-*a*]pyridine derivatives employing readily available starting materials.

On the other hand *C*-nitroso compounds have gained much attention due to their important roles in various biological metabolic processes.[6] In addition nitroso compounds are versatile intermediates in several reactions such as aldol, ene, Diels-Alder, cycloaddition and redox processes, as well as in reactions with radicals and nucleophiles.[7]

Installation of the nitroso functionality in the imidazopyridine moiety renders these compounds more valuable in the subject of drug discovery and material based applications. 3-Nitrosoimidazo[1,2-*a*]pyridine derivatives show potent antibacterial activities against a variety of gram (+), gram (-) bacteria and *Mycobacterium* species.[8] These nitroso derivatives are also excellent organic inhibitors of corrosion for many metals and alloys in aggressive media.[9] Because of these interest a versatile route for the synthesis of 3-nitrosoimidazo[1,2-*a*]pyridine is in demand.[10] Recently ^{t}BuONO has emerged as a mild, safe, easily handled and commercially available nitrating reagent.[11] ^{t}BuONO is known to undergo thermal homolysis to liberate an alkoxyl radical and nitric oxide (NO).[11b,d] Employing this property, direct C–H nitration of olefins and arenes has been growing rapidly using ^{t}BuONO in aerobic reaction conditions.[12] Based on our recent works on the functionalization of imidazo[1,2-*a*]pyridines we envisaged that imidazo[1,2-*a*]pyridine moiety could be functionalized at C-3 position by ^{t}BuONO. Herein we are demonstrating a simple and practical method for the regioselective nitrosylation of imidazo[1,2-*a*]pyridines using ^{t}BuONO under ambient air (Scheme 1).

Scheme 1 Regioselective nitrosylation of imidazo[1,2-*a*]pyridines.

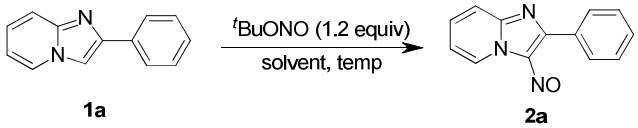


Results and discussion

At the outset of this study, we employed 2-phenylimidazo[1,2-*a*]pyridine as the model substrate with ^{t}BuONO to optimize the reaction conditions. The results are summarized in Table 1. Initially the reaction was carried out in MeCN under room temperature (Table 1, entry 1). Gratifyingly, the 3-nitrosoimidazo[1,2-*a*]pyridine was obtained in 68% yield after 24 hr. With this initial result, we carried out the reaction at different higher temperatures (Table 1, entries 2-4) and best result was obtained in near quantitative yield (98%) by carrying out the reaction at 70 °C for 15 min (Table 1, entry 3). It is worthy to mention that no column chromatography was required for purification. After completion of the reaction the pure product was obtained in near quantitative yield by simply evaporating the solvent under vacuum. The reaction was also carried out in various common solvents such as toluene, dioxane, and 1,2-dichloroethane (DCE) etc (Table 1, entries 5-10). However these are not as effective as MeCN. MeCN was found to be most

suitable for this transformation. Finally, the optimized reaction conditions was obtained using 1.2 equiv of ^{t}BuONO in MeCN at 70 °C temperature for 15 min under ambient air (Table 1, entry 3).

Table 1 Optimization of the reaction conditions[a]



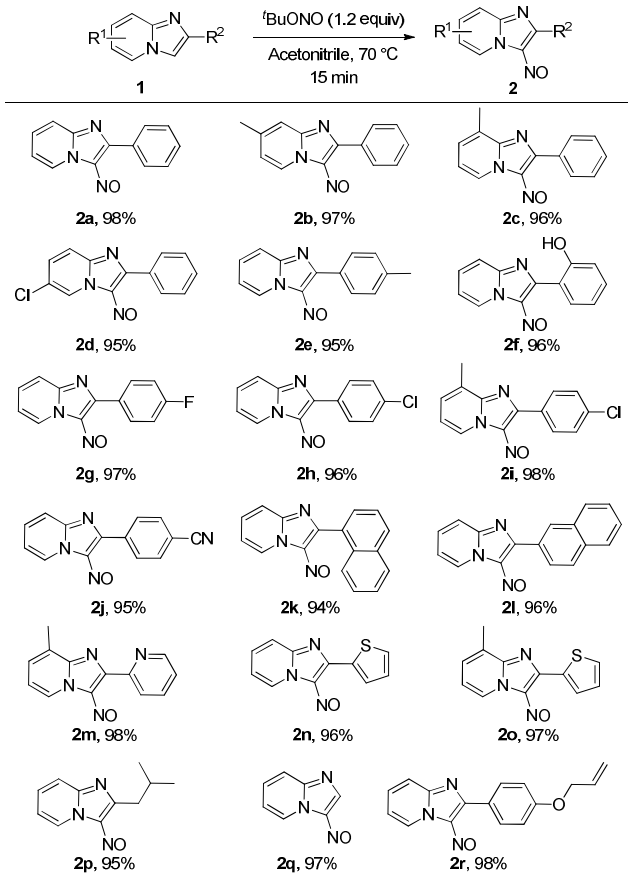
1a **2a**

entry	solvent	temp (°C)	time	yield[b] (%)
1	MeCN	rt	24 hr	68
2	MeCN	60	30 min	96
3	MeCN	70	15 min	98
4	MeCN	80	15 min	96
5	THF	70	15 min	NR[c]
6	DMSO	70	15 min	74
7	DMF	70	15 min	27
8	1,2-DCE	70	15 min	22
9	Toluene	70	15 min	56
10	Dioxane	70	15 min	48

[a]Reaction conditions: 0.2 mmol of **1a** and 0.24 mmol of ^{t}BuONO in acetonitrile (1 mL) at 70 °C. [b]Isolated yields. [c]No reaction.

With the optimized reaction conditions in hand, we applied this protocol to different imidazo[1,2-*a*]pyridine derivatives. As shown in Scheme 2, a series of 3-nitrosoimidazo[1,2-*a*]pyridines were obtained under the present reaction conditions in excellent yields. At first, the effect of substituent on the pyridine ring was studied. Imidazo[1,2-*a*]pyridines with –Me and –Cl substituents on the pyridine ring afforded the corresponding 3-nitrosoimidazo[1,2-*a*]pyridines with excellent yields (**2b-2d**). Furthermore the effect of the C-2 substituent on the imidazo ring was also examined. Electron-donating substituents like –Me and –OH as well as electron-withdrawing substituent like –F, –Cl, and –CN on the phenyl ring at 2-position of the imidazo[1,2-*a*]pyridine moiety efficiently reacted with ^{t}BuONO to produce the respective 3-nitrosoimidazo[1,2-*a*]pyridine derivatives (**2e-2j**). Imidazo[1,2-*a*]pyridines with heteroaryl moieties like pyridine and thiophene at C-2 position also reacted well and desired nitroso derivatives were obtained in all cases with excellent yields (**2m**, **2n** and **2o**). The alkyl group substituted imidazopyridine also afforded the nitroso product with significant yields (**2p**). In case of 2,3-unsubstituted imidazo[1,2-*a*]pyridine the regioselective nitrosylation took place at the 3-position only (**2q**). It is worthy to mention that the present protocol is highly selective for the regioselective nitrosylation of imidazo-fused heterocycles in presence of alkene substitutent also. The selective 3-nitroso derivative (**2r**) was obtained in excellent yield while alkene part did not react under the present reaction conditions.[12a]

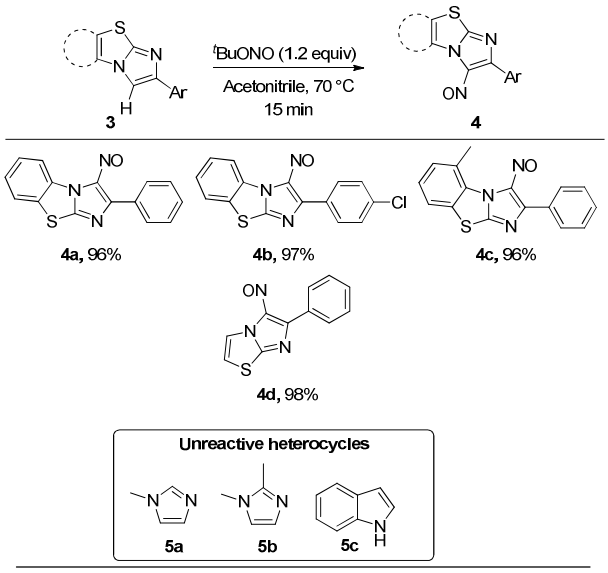
Scheme 2 Substrates scope[a,b]



[a]Reaction conditions: 0.2 mmol of **1** and 0.24 mmol of ^{t}BuONO in acetonitrile (1 mL) at 70 °C for 15 min. [b]Isolated yields.

To extend the scope of our methodology, we employed other imidazoheterocycles (**3**) like imidazo[2,1-*b*]thiazole and benzo[*d*]imidazo[2,1-*b*]thiazoles under the optimized reaction conditions (Scheme 3). To our delight in all cases respective nitroso derivatives (**4**) were obtained regioselectively in excellent yields. In case of imidazo[2,1-*b*]thiazole nitrosilylation occurs regiselectively at the imidazo ring in presence of thiazole ring (**4d**). However, simple imidazoles and indole did not react under the present reaction conditions.

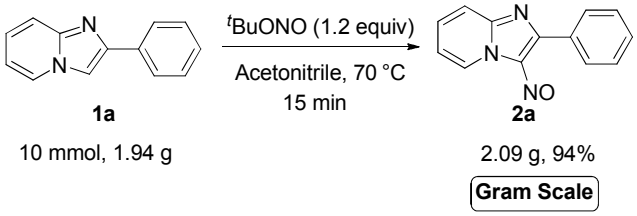
Scheme 3 Nitrosylation of imidazothiazoles[a,b]



[a]Reaction conditions: 0.2 mmol of **3** or **5** and 0.24 mmol of ^{t}BuONO in acetronitrile (1mL) at 70 °C for 15 min. [b]Isolated yields.

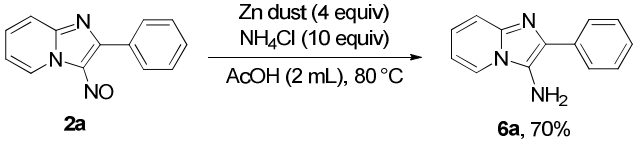
Our present method is also applicable for the gram-scale (10 mmol) synthesis (Scheme 4). 2-Phenylimidazo[1,2-*a*]pyridine (**1a**) afforded the corresponding product with 94% (2.09 g, **2a**) yield. This result proves the efficiency and the practical applicability of this protocol. In general, the reaction is very clean and yields only *tert*-butyl alcohol as a by-product.

Scheme 4 Gram-scale synthesis



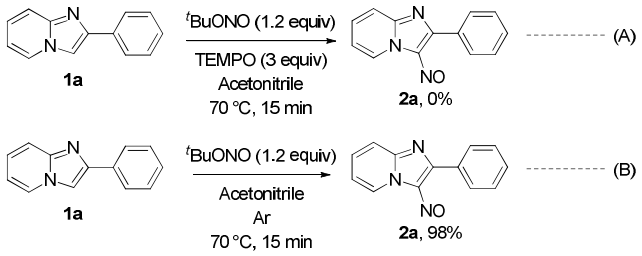
The nitroso derivative could be easily transformed to amino derivative applying common reductive method (Scheme 5). The amino derivatives are key building blocks for synthesis of polyfused heterocycles.[13]

Scheme 5 Reduction of 3-nitroso-2-phenylimidazo[1,2-*a*]pyridine



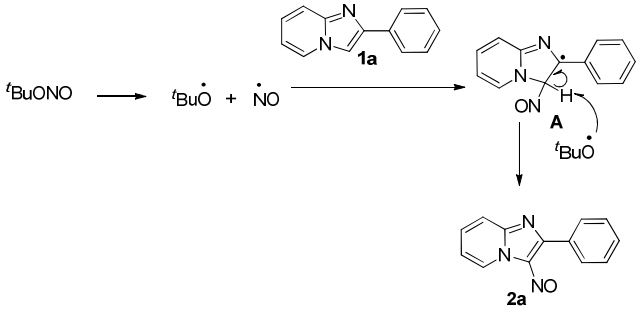
A few control experiments were carried out to understand the reaction pathway. The reaction did not proceed at all in the presence of radical scavenger TEMPO (3 equiv), which signifies that the reaction probably proceeds through a radical pathway (Scheme 6, Eq **A**). Furthermore when the reaction was carried out in argon, no change in yield was observed which suggests that air or oxygen does not play any role in this reaction (Scheme 6, Eq **B**).

Scheme 6 Controlled experiment



A probable mechanism of the reaction is outlined based on the experimental results and literature reports[12] in Scheme 7. At first, the NO radical is generated through homolytic cleavage of ^{t}BuONO and subsequently reacts with the imidazo[1,2-*a*]pyridine to form the radical intermediate **A**. The ^{t}BuO radical subsequently abstract a H· to generate the product. However, the reaction might proceed also through the electrophilic substitution[3g,5c] involving the formation of NO^+, where ^{t}BuONO directly reacts at C3 of imidazopyridine.

Scheme 7 Plausible mechanism



Conclusions

In conclusion, we have developed a direct and straightforward method for the regioselective synthesis of 3-nitrosoimidazo[1,2-*a*]pyridines through C(sp^2)-H bond functionalization employing ^{t}BuONO without any additives or catalyst. An array of 3-nitrosoimidazo[1,2-*a*]pyridine derivatives with broad functionalities were synthesized with near quantitative yields in short times. The present protocol is also applicable for other imidazo-fused heterocycles like imidazo[2,1-*b*]thiazole and benzo[*d*]imidazo[2,1-*b*]thiazole. Clean reaction, ease of product isolation, mild reaction conditions, short reaction times, the use of inexpensive reagent and a simple experimental procedure are the notable advantages of the present method and these features make this procedure practical and synthetically useful.

Experimental section

General Information: ^{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 are referenced to tetramethylsilane (TMS) as internal standard and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet) and coupling constants *J* were given in Hz. ^{13}C NMR spectra were

recorded at 100 MHz. HRMS analysis was performed in a Qtof mass analyzer using the ESI ionization method. Petroleum ether refers to the fraction boiling in the range of 60-80 ºC unless otherwise mentioned. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. All reactions involving moisture sensitive reactants were executed using oven dried glassware. All the imidazoheterocycles were prepared by our reported methods.[4a,c]

General procedure for nitrosylation of imidazoheterocycles: A mixture of **1** (or 3) (0.2 mmol) and ^{t}BuONO (28 mg, 33μL, 0.24 mmol) in acetonitrile (1 mL) was taken in a screw cap reaction tube and the reaction mixture was stirred for 15 min at 70 °C temperature. After completion of the reaction the product was obtained in pure form with near quantitative yield by simply evaporating the solvent, by-product ^{t}BuOH and excess ^{t}BuONO under vacuum.

Synthesis of 2-phenylimidazo[1,2-*a*]pyridin-3-amine (6a): In a dry sealed tube a mixture of **2a** (0.2 mmol, 45 mg), Zn dust (6 equiv, 76 mg), and NH_4Cl (10 equiv, 108 mg) in acetic acid (2 mL) was taken and heated at 80 °C for 1 hr. After completion the reaction mixture was neutralized with saturated solution of $NaHCO_3$ and was extracted with dichloromethane (5 mL). The organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography to obtain the pure product (**6a**).

3-Nitroso-2-phenylimidazo[1,2-*a*]pyridine (2a):[9] Green solid, (98%, 45 mg), mp 164-165 ºC (lit. mp 165 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.77 (d, *J* = 8.0 Hz, 1H), 8.54-8.51 (m, 2H), 7.77-7.65 (m, 2H), 7.44-7.40 (m, 3H), 7.13-7.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 153.2, 145.6, 136.1, 131.5, 131.5, 130.7, 128.8, 126.4, 119.5, 117.4.

7-Methyl-3-nitroso-2-phenylimidazo[1,2-*a*]pyridine (2b):[10] Green solid, (97%, 45 mg), mp 200-201 ºC; (lit. mp 202 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (d, *J* = 7.2 Hz, 1H), 8.58-8.56 (m, 2H), 7.52-7.44 (m, 4H), 6.99 (d, *J* = 7.2 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 153.3, 149.0, 146.5, 131.7, 131.6, 130.9, 128.9, 126.2, 121.4, 116.2, 22.4. HRMS calcd for $C_{14}H_{12}N_3O$ $[M+H]^+$: 238.0980, found $[M+H]^+$: 238.0956.

8-Methyl-3-nitroso-2-phenylimidazo[1,2-*a*]pyridine (2c):[10] Green solid, (96%, 45 mg), mp 134-135 ºC; (lit. mp 136 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, *J* = 6.8 Hz, 1H), 8.62-8.59 (m, 2H), 7.56-7.44 (m, 4H), 7.07 (t, *J* = 6.8 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 153.8, 145.7, 135.5, 131.9, 131.4, 130.9, 128.7, 128.0, 124.3, 119.5, 16.6. HRMS calcd for $C_{14}H_{12}N_3O$ [M+H]+: 238.0980, found [M+H]+ : 238.0975.

6-Chloro-3-nitroso-2-phenylimidazo[1,2-*a*]pyridine (2d): Green Solid, (95%, 49 mg) ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.59-8.56 (m, 2H), 7.72 (d, *J* = 3.2 Hz, 2H), 7.52-7.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 153.2, 143.9, 136.8, 133.6, 131.9, 131.3, 130.9, 129.0, 124.5, 117.9; HRMS calcd for $C_{13}H_9ClN_3O$ [M+H]+: 258.0434, found [M+H]+: 258.0432.

3-Nitroso-2-(*p*-tolyl)imidazo[1,2-*a*]pyridine (2e): Green solid, (95%, 45 mg), mp 145-146 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (d, *J* = 8.0 Hz, 1H), 8.56 (d, *J* = 8.0 Hz, 2H), 7.83-7.80 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.24-7.20 (m, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 153.3, 145.9, 142.3, 136.2, 130.8, 129.7, 128.8, 126.5, 119.3, 117.4, 21.7. HRMS calcd for $C_{14}H_{12}N_3O$ $[M+H]^+$: 238.0980, found $[M+H]^+$: 238.0954.

2-(3-nitrosoimidazo[1,2-*a*]pyridin-2-yl)phenol (2f): Green solid, (96%, 45 mg), mp 167-168 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.62 (br, 1H); 10.03 (d, *J* = 6.4 Hz, 1H), 9.10 (d, *J* = 8.0 Hz, 1H), 7.92-7.81 (m, 2H), 7.52-7.41 (m, 1H), 7.34-7.28 (m, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 158.4, 152.7, 143.8, 136.9, 134.2, 132.7, 126.6, 120.4, 120.0, 118.3, 116.6, 115.0. HRMS calcd for $C_{13}H_{10}N_3O_2$ $[M+H]^+$: 240.0773, found $[M+H]^+$: 240.0768.

2-(4-Fluorophenyl)-3-nitrosoimidazo[1,2-*a*]pyridine (2g): Green solid, (97%, 46 mg), mp 120-121 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (d, *J* = 6.4 Hz, 1H), 8.76-8.69 (m, 2H), 7.90-7.83 (m, 2H), 7.31-7.22 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4 (d, $^1J_{C\text{-}F}$ = 252 Hz), 158.9, 153.3, 145.8, 136.3, 133.1 (d, $^3J_{C\text{-}F}$ = 9 Hz), 127.9 (d, $^4J_{C\text{-}F}$ = 3 Hz), 126.6, 119.7, 117.5, 116.2 (d, $^2J_{C\text{-}F}$ = 21 Hz). HRMS calcd for $C_{13}H_9FN_3O$ $[M+H]^+$: 242.0729, found $[M+H]^+$: 242.0741.

2-(4-Chlorophenyl)-3-nitrosoimidazo[1,2-*a*]pyridine (2h): Green gummy mass, (96%, 49 mg), ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (d, *J* = 6.4 Hz, 1H), 8.66-8.63 (m, 2H), 7.87-7.86 (m, 2H), 7.55-7.52 (m, 2H), 7.31-7.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ158.7, 153.1, 145.8, 138.4, 136.5, 132.1, 130.0, 129.3, 126.7, 119.9, 117.6. HRMS calcd for $C_{13}H_9ClN_3O$ $[M+H]^+$: 258.0434, found $[M+H]^+$: 258.0432.

2-(4-Chlorophenyl)-8-methyl-3-nitrosoimidazo[1,2-*a*]pyridine (2h): Green solid, (98%, 53 mg), mp 135-136 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (d, *J* = 6.8 Hz, 1H), 8.68-8.64 (m, 2H), 7.66-7.63 (m, 1H), 7.53-7.49 (m, 2H), 7.17 (t, *J* = 6.8 Hz, 1H), 2.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 153.5, 145.5, 137.9, 135.5, 131.9, 130.3, 129.0, 127.9, 124.2, 119.6, 16.5. HRMS calcd for $C_{14}H_{11}ClN_3O$ $[M+H]^+$: 272.0590, found $[M+H]^+$: 272.0580.

4-(3-Nitrosoimidazo[1,2-*a*]pyridin-2-yl)benzonitrile (2j): Green solid, (95%, 47 mg), mp 252-253 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (d, *J* = 6.8 Hz, 1H), 8.85 (d, *J* = 8.4 Hz, 2H), 7.93-7.90 (m, 2H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.38-7.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 153.2, 145.2, 136.2, 135.6, 132.3, 131.0, 126.3, 120.3, 118.1, 117.7, 114.6. HRMS calcd for $C_{14}H_9N_4O$ $[M+H]^+$: 249.0776, found $[M+H]^+$: 249.0776.

2-(Naphthalen-1-yl)-3-nitrosoimidazo[1,2-*a*]pyridine (2k): Gummy Mass, (94%, 51 mg), ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.85 (d, *J* = 6.8 Hz, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* =

7.6Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.88-7.84 (m, 2H), 7.77-7.73 (m, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.51-7.45 (m, 2H), 7.21-7.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 154.,4 145.,3 135.9, 134.0, 133.4, 131.9, 131.4, 128.6, 128.2, 127.3, 126.3, 126.3, 126.0, 125.1, 119.7, 117.8. HRMS calcd for $C_{17}H_{12}N_3O$ $[M+H]^+$: 274.0980, found $[M+H]^+$: 274.0963.

2-(Naphthalen-2-yl)-3-nitrosoimidazo[1,2-*a*]pyridine (2l): Green solid, (96%, 52 mg), mp 232-233 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.01 (d, *J* = 6.4 Hz, 1H), 8.77 (d, *J* = 8.0 Hz, 1H), 8.31 (d, *J* = 7.2 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.09-7.90 (m, 3H), 7.69-7.57 (m, 3H), 7.38-7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 154.2, 145.3, 135.3, 134.0, 133.4, 131.8, 131.4, 128.5, 128.0, 127.3, 126.3, 126.2, 125.9, 125.1, 119.6, 117.7. HRMS calcd for $C_{17}H_{12}N_3O$ $[M+H]^+$: 274.0980, found $[M+H]^+$: 274.0963.

8-Methyl-3-nitroso-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (2m): Green solid, (98%, 46 mg), mp 212-213 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (d, *J* = 6.4 Hz, 1H), 8.99 (d, *J* = 4.4Hz, 1H), 8.80 (d, *J* = 8.0 Hz, 1H), 7.96-7.91 (m, 1H), 7.70 (d, *J* = 7.2 Hz, 1H); 7.55-7.51 (m, 1H), 7.28-7.24 (m, 1H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 153.9, 150.4, 149.9, 145.3, 137.0, 135.6, 128.8, 127.9, 125.3, 124.0, 120.5, 16.8. HRMS calcd for $C_{13}H_{11}N_4O$ $[M+H]^+$: 239.0933, found $[M+H]^+$: 239.0908.

3-Nitroso-2-(thiophen-2-yl)imidazo[1,2-*a*]pyridine (2n): Green solid, (96%, 44 mg), mp 201-202 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88-9.85 (m, 1H), 8.47-8.46 (m, 1H), 7.83-7.76 (m, 2H), 7.74-7.72 (m, 1H), 7.27-7.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 151.5, 146.4, 136.5, 134.3, 133.3, 133.0, 129.2, 126.6, 119.3, 117.2. HRMS calcd for $C_{11}H_8N_3OS$ $[M+H]^+$: 230.0388, found $[M+H]^+$: 230.0383.

8-Methyl-3-nitroso-2-(thiophen-2-yl)imidazo[1,2-*a*]pyridine (2o): Green solid, (97%, 47 mg), mp 219-220 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (d, *J* = 6.4 Hz, 1H), 8.37-8.36 (m, 1H), 7.68-7.67 (m, 1H), 7.52-7.51 (m, 1H), 7.22-7.20 (m, 1H), 7.02 (t, *J* = 7.2 Hz, 1H) 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ154.8, 151.5, 146.0, 135.7, 134.4, 132.7, 132.6, 128.7, 127.5, 124.0, 119.0, 16.3. HRMS calcd for $C_{12}H_{10}N_3OS$ $[M+H]^+$: 244.0544, found $[M+H]^+$: 244.0529.

2-Isobutyl-3-nitrosoimidazo[1,2-*a*]pyridine (2p): Green solid, (95%, 38 mg), mp 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78-9.76 (m, 1H), 7.75-7.73 (m, 2H), 7.21-7.18 (m, 1H), 3.35 (d, *J* = 7.2 Hz, 2H), 2.47-2.37 (m, 1H), 1.02 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 154.0, 145.9, 135.7, 126.3, 119.1, 117.1, 37.3, 29.3, 22.7. Anal Calcd for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.68%; Found: C, 65.25; H, 6.26; N, 20.79%.

3-Nitrosoimidazo[1,2-*a*]pyridine (2q): Green solid, (97%, 28 mg), mp 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65-9.63 (m, 1H), 9.21 (s, 1H), 7.84-7.76 (m, 2H), 7.29-7.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 153.7, 146.5, 135.5, 127.2, 120.0, 118.0. HRMS calcd for $C_7H_6N_3O$ $[M+H]^+$: 148.0511, found $[M+H]^+$: 148.0476.

2-(4-(Allyloxy)phenyl)-3-nitrosoimidazo[1,2-*a*]pyridine (2r): Green solid, (98%, 54 mg), mp 241-242 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.85 (d, *J* = 5.6 Hz, 1H), 8.56 (d, *J* = 6.8 Hz, 2H), 7.70-7.61 (m, 1H), 7.12-7.08 (m, 1H), 6.98-6.95 (m, 3H), 6.01-5.96 (m, 1H), 5.38 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* = 10.4 Hz, 1H), 4.56-4.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 159.6, 151.6, 146.0, 138.8, 136.2, 132.5, 126.5, 124.2, 118.9, 118.0, 117.1, 115.0, 68.0. HRMS calcd for $C_{16}H_{14}N_3O_2$ $[M+H]^+$: 280.1086, found $[M+H]^+$: 280.1076.

3-Nitroso-2-phenylbenzo[*d*]imidazo[2,1-*b*]thiazole (4a): Green solid, (96%, 53 mg), mp 124-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (d, *J* = 8.4 Hz, 1H), 8.57 (d, *J* = 6.8 Hz, 2H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.60-7.52 (m, 4H), 7.46-7.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 158.4, 157.2, 132.7, 131.8, 131.4, 130.9, 129.9, 128.8, 126.6, 123.2, 118.8. HRMS calcd for $C_{15}H_{10}N_3OS$ $[M+H]^+$: 280.0545, found $[M+H]^+$: 280.0539.

2-(4-Chlorophenyl)-3-nitrosobenzo[*d*]imidazo[2,1-*b*]thiazole (4b): Green solid, (97%, 60 mg), mp 178-179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.93 (d, *J* = 8.4 Hz, 1H), 8.54 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.59-7.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 158.4, 157.0, 138.2, 132.6, 132.0, 130.2, 130.0, 129.1, 126.8, 126.8, 123.3, 118.8. HRMS calcd for $C_{15}H_9ClN_3OS$ $[M+H]^+$: 314.0155, found $[M+H]^+$: 314.0149.

5-Methyl-3-nitroso-2-phenylbenzo[*d*]imidazo[2,1-*b*]thiazole (4c): Green solid, (96%, 56 mg), mp 124-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, *J* = 8.8 Hz, 1H), 8.57 (d, *J* = 6.8 Hz, 2H), 7.60-7.52 (m, 4H), 7.47-7.28 (m, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 158.1, 157.2, 137.1, 131.9, 131.3, 130.8, 130.6, 130.1, 128.8, 127.7, 123.1, 118.4, 21.1. HRMS calcd for $C_{16}H_{12}N_3OS$ $[M+H]^+$: 294.0701, found $[M+H]^+$: 294.0694.

5-Nitroso-6-phenylimidazo[2,1-*b*]thiazole (4d): Green solid, (98%, 45 mg), mp 147-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57-8.54 (m, 2H), 8.32 (d, *J* = 4.4 Hz, 1H), 7.51-7.42 (m, 3H), 6.98 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ159.0, 158.8, 156.8, 131.6, 131.5, 130.1, 128.9, 121.8, 116.8. HRMS calcd for $C_{11}H_8N_3OS$ $[M+H]^+$: 230.0388, found $[M+H]^+$: 230.0390.

2-Phenylimidazo[1,2-*a*]pyridin-3-amine (6a): Gummy Mass, (70%, 29 mg), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00-7.94 (m, 1H), 7.91-7.87 (m, 2H), 7.51 (d, *J* = 9.2 Hz, 1H), 7.45-7.37 (m, 2H), 7.35-7.30 (m, 1H), 7.30-7.19 (m, 1H), 7.08-7.04 (m, 1H), 6.76 (t, *J* = 6.4 Hz, 1H), 3.42 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.7, 132.3, 128.7, 127.3, 127.1, 123.8, 122.7, 122.5, 121.9, 117.0, 112.0. HRMS calcd for $C_{13}H_{12}N_3$ $[M+H]^+$: 210.1031, found $[M+H]^+$: 210.1007.

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