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ARTICLE

Novel approach in the synthesis of imidazo [1, 2-*a*] pyridine from phenyl acrylic acids

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Abstract

This paper describes highly efficient concise method for the synthesis of imidazo[1,2-*a*] pyridine. It is a first report employing, amino pyridines, copper nitrate, and phenyl acrylic acids in the synthesis of imidazo[1,2-*a*] pyridine. The silent features of the devised protocol include the high yield, milder reaction conditions, and shorter reaction time.

1 | INTRODUCTION

The nitrogen-containing imidazo [1,2-*a*] pyridine compounds have great synthetic applications owing to its varied biological activities viz. anti-inflammatory,[1–4] anticancer,[5–7] antiulcer,[8] anti-viral,[9–13] anti-bacterial,[14–17] and antituberculosis.[18–20] These derivatives act as cardiotonic agents,[21] GABA and benzodiazepine receptor agonists,[22,23] and β-amyloid formation inhibitors.[24] A variety of synthetic strategies have been developed for the construction of imidazo [1,2-*a*]pyridine scaffolds.[25–34] The most explored approaches embrace: (a) condensation of 2-amino pyridine with α-haloketone compounds,[25,33] α-diazoketone compounds,[26] α-tosyloxyketone compounds,[27,34] (b) coupling of 2-amino pyridine with nitroolefins,[28,35] (c) three component coupling of 2-amino pyridine, aldehyde with nitroalkane,[29,36] isonitrile,[30,37,38] alkynes,[31,39] and alkynecarboxylic acid.[32] However, there is scarcity of general methods to synthesize imidazo [1,2-*a*] pyridine derivatives from commercially available or readily accessible materials. The interesting advantage of our protocol compared with the above-mentioned established protocol lies in our starting material cinnamic acid. The established protocol[25] employs 2-bromoacetophenone, which has environmental hazard issues as it is a lachrymatic compound making it difficult to handle, it is toxic upon inhalation, ingestion, and skin absorption and costly when compared with phenyl acrylic acid/cinnamic acid hence we employed cinnamic acid in our protocol. Our protocol is a first report, which provides an alternative synthetic starting material—cinnamic acid for synthesis of such molecules. The fascinating feature of these scaffolds led us[40] toward the development of new methods for their synthesis. The nitroolefins are usually synthesized by using viz. silver nitrate,[41] tert-butyl nitrate,[42] and copper nitrate[43] but its further designing into bioactive molecule was not yet explored. Herein, it prompted us to synthesize nitroimidazopyridines, wherein in situ conversion of nitroolefins to the imidazo[1,2-*a*] pyridine was achieved in ease. In addition, it would open plethora of such

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reaction in synthesizing varied complex bioactive structures like nitroimidazopyridines. The nitroimidazopyridines are used to synthesize polyfused imidazopyridine derivatives, which have varied activities.[44–46] Therefore, we became interested to develop direct and efficient methods to afford functionalized imidazo [1,2-*a*]pyridine employing 2-aminopyridine and phenyl acrylic acid. In this protocol, we synthesized nitroolefins; which in situ was converted to nitroimidazopyridines using copper nitrate. In addition, the 3-nitro-2-phenyl-imidazo[1,2-*a*]pyridine (3bb) was treated with 10% Pd/C in THF to yield 2-phenyl-imidazo[1,2-*a*] pyridin-3-amine that is, whole new series of such amine derivatives could be further synthesized and evaluated for its biological activities. The copper nitrate is known as most common blue crystalline cupric salts with low toxicity, inexpensive, commercially readily available, and operationally very easy to use. Copper nitrate plays an important role in organic synthesis and is widely used as a nitrating reagent and as an oxidant.[47,48]

2 | RESULTS AND DISCUSSION

Herein, we describe a new approach to the synthesis of 3-nitroimidazo[1,2-*a*]pyridines, based on the condensation of phenyl acrylic acid with various 2-aminopyridine (Scheme 1).

To optimize the reaction conditions, 4-methyl cinnamic acid (1a) and 2-amino 4-methyl pyridine (2a) were chosen as test substrates for this cyclization using different nitrating reagents and solvents, which are summarized in Table 1. Initially, reaction was performed employing $AgNO_3$, $NaNO_3$, $Pb(NO_3)_2$, $Co(NO_3)_2$, $Cu(NO_3)_2$ in MeCN at 85°C to achieve the transformation in $Cu(NO_3)_2$ (Table 1, entry 1-5). The desired 7-methyl-3-nitro-2-*p*-tolyl-imidazo[1,2-*a*]pyridine (3aa) was obtained in 95% yield after 6 hours (Table 1, entry 5). The yield decreased to 85% at lower temperature 75°C (Table 1, entry 6) and when temperature increased to 95°C (Table 1, entry 7) yield remained 95% same as at 85°C (Table 1, entry 5). Furthermore, solvents' changes such as ethyl acetate (EtOAc), *N*,*N*-dimethylformamide (DMF), dioxane, methanol (MeOH), and tetrahydrofuran (THF) were also evaluated, and better results were not obtained (Table 1, entries 8-12). When $Cu(NO_3)_2$ loading was decreased (1.0 mmol) yield decreased to 73% and it took more duration for completion of reaction (Table 1, entry 13). However, further increment of $Cu(NO_3)_2$ (1.5 mmol) did not affect the yield 95% and rate of the reaction substantially (Table 1, entry 14). With these optimized reaction conditions, we examined a series of cinnamic acids and 2-amino pyridines to establish the scope and limitations of this process. A wide range of substituted cinnamic acids and 2-aminopyridines were subjected to prove the general applicability of our present procedure.

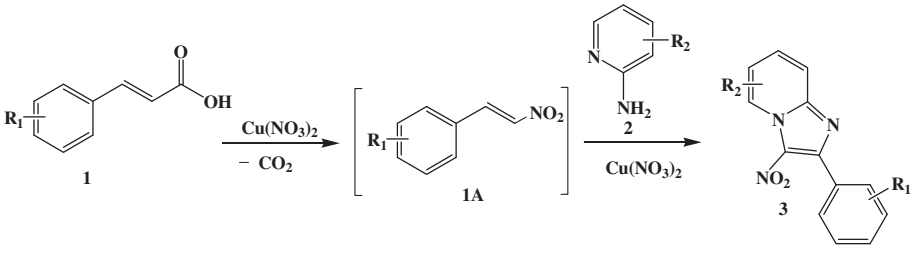
Generally, the reaction of cinnamic acid and 2-amino pyridine proceeded smoothly and afforded the corresponding 3-nitroimidazo[1,2-*a*]pyridines with great efficiency (Table 2, entry 1).

To our delight, a wide range substituted groups of cinnamic acid and 2-aminopyridines all gave the desired products in good yields, which include methyl, methoxy, bromo, and chloro groups. We tried reaction of cinnamic acid directly with 2-amino pyridine to yield 3-nitroimidazo

TABLE 1 Optimization of the reaction condition[a]

Entry	Reagent	Solvent	Temp (°C)	Yield (%)[b]
1	$AgNO_3$	MeCN	85	Trace
2	$NaNO_3$	MeCN	85	ND
3	$Pb(NO_3)_2$	MeCN	85	ND
4	$Co(NO_3)_2$	MeCN	85	ND
5	$Cu(NO_3)_2$	MeCN	85	95
6	$Cu(NO_3)_2$	MeCN	75	85
7	$Cu(NO_3)_2$	MeCN	95	95
8	$Cu(NO_3)_2$	EtOAC	85	75
9	$Cu(NO_3)_2$	DMF	110	ND
10	$Cu(NO_3)_2$	Dioxane	110	88
11	$Cu(NO_3)_2$	MeOH	70	ND
12	$Cu(NO_3)_2$	THF	70	ND
13	$Cu(NO_3)_2$	MeCN	85	73[c]
14	$Cu(NO_3)_2$	MeCN	85	95[d]

[a]Reaction conditions: 1 mmol of 1a and 1.5 mmol of 2a in the presence of reactant (1.2 mmol) in solvent (2 mL) at 85°C for 6 h.
[b]Isolated yields. ND, not detected in TLC.
[c]$Cu(NO_3)_2$ used (1.0 mmol) reaction completed in 10 h.
[d]$Cu(NO_3)_2$ used (1.5 mmol) reaction completed in 6 h.



SCHEME 1 Present work approach for the synthesis of 3-nitroimidazo[1,2-*a*]pyridines

TABLE 2 Synthesis of 3-nitroimidazo[1,2-*a*]pyridines from 2-aminopyridines and phenyl acrylic acids[a]

Entry	1 (R^1)	2 (R^2)	Product	Yield (%)[b]
1	1a (4-Me)	2a (4-Me)	3aa	95
2	1a (4-Me)	2b (H)	3ab[49]	78
3	1a (4-Me)	2c (5-Br)	3ac	81
4	1a (4-Me)	2d (3-Me)	3ad[49]	70
5	1b (H)	2a (4-Me)	3ba	85
6	1b (H)	2b (H)	3bb[49]	93
7	1b (H)	2c (5-Br)	3bc	89
8	1b (H)	2d (3-Me)	3bd[49]	78
9	1c (4-OMe)	2a (4-Me)	3ca	65
10	1c (4-OMe)	2b (H)	3cb[49]	91
11	1c (4-OMe)	2c (5-Br)	3cc	60
12	1c (4-OMe)	2d (3-Me)	3cd	63
13	1d (3-Cl)	2a (4-Me)	3da	90
14	1d (3-Cl)	2b (H)	3db[49]	94
15	1d (3-Cl)	2c (5-Br)	3dc	88
16	1d (3-Cl)	2d (3-Me)	3dd	93
17	1e (2-OMe)	2a (4-Me)	3ea	90
18	1e (2-OMe)	2b (H)	3eb[49]	83
19	1e (2-OMe)	2c (5-Br)	3ec	93
20	1e (2-OMe)	2d (3-Me)	3ed	65

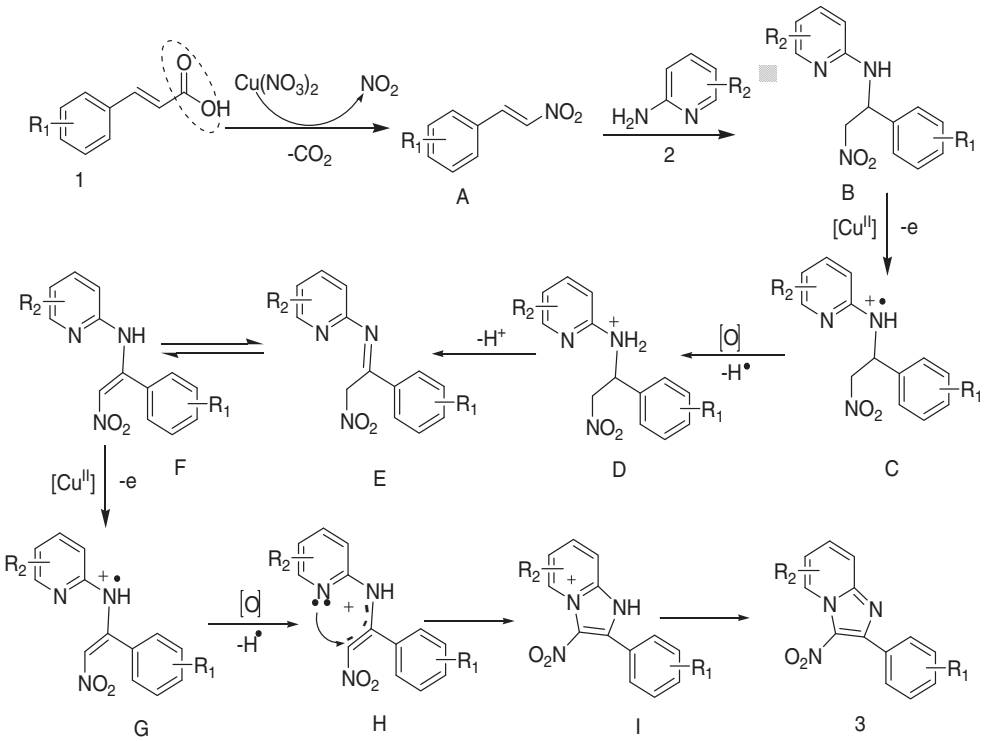
[a]Reaction conditions: 1 mmol of 1 and 1.5 mmol of 2 in the presence of Copper nitrate (1.2 mmol) in MeCN (2 mL) at 85°C for 6 h.
[b]Isolated yields.

[1,2-*a*]pyridines, but we were unable to synthesize the desired product in absence of copper nitrate. In addition, we also tried reaction of cinnamic acid, 2-amino pyridine, and copper nitrate to yield 3-nitroimidazo[1,2-*a*]pyridines, but we were unable to synthesize the desired product upon simultaneous addition of reactants. Hence, we firstly synthesized the nitroolefin by reacting cinnamic acid and copper nitrate. The nitroolefin was directly treated with 2-amino pyridine to synthesize 3-nitroimidazo[1,2-*a*]pyridines with greater efficiency.

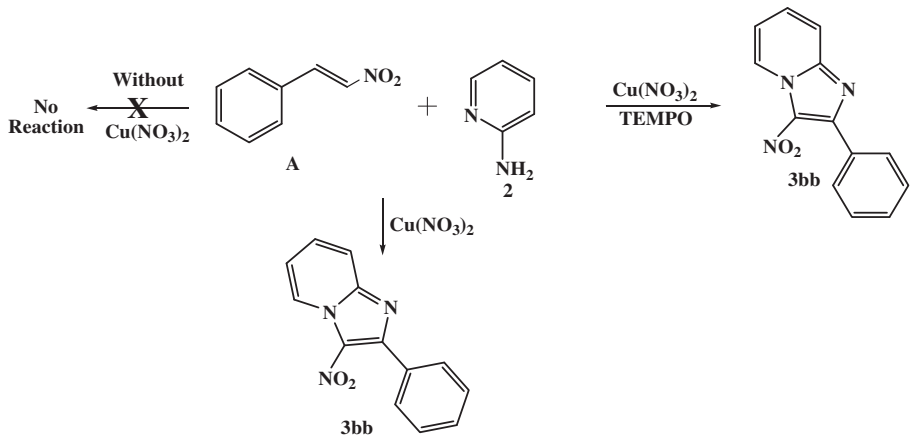
On the basis of the reaction condition, a plausible mechanism[49] of this reaction is illustrated in Scheme 2.

The reaction may undergo the following steps; first step involves formation of nitroolefin (A) by copper nitrate and its decarboxylation. Second, the nitroolefin (A) couple with 2-amino pyridine (2) to produce the Michael addition intermediate (B), one-electron oxidation of intermediate (B) with copper generates radical cation (C), which is followed by hydrogen abstraction with oxidation resulting in the formation of nitrenium ion D. The imine (E) is then formed by proton elimination and equilibrates to enamine (F). Similarly, intermediate (G) produced by one-electron oxidation with copper from enamine (F) and generates the nitrenium ion (H) by hydride abstraction with oxidation. Finally, intermediate (H) undergoes intramolecular nucleophilic addition to give intermediate (I) and the subsequent proton elimination to afford product 3.

To support this mechanism, we performed additional experiments. First, we treated cinnamic acid with



SCHEME 2 Plausible reaction mechanism[49]



SCHEME 3 Control experiments supporting our reaction mechanism

$Cu(NO_3)_2$ and isolated the nitroolefin intermediate A confirmed with the literature.[43,50]

This nitroolefin intermediate A was treated with 2-aminopyridine in absence of $Cu(NO_3)_2$, the reaction did not yield the desired product, highlighting the importance of $Cu(NO_3)_2$ in reaction (Scheme 3)

When the nitroolefin intermediate A was treated with 2-aminopyridine in presence of $Cu(NO_3)_2$, we got the desired product (3bb) which is in agreement with our proposed mechanism and shows the importance of $Cu(NO_3)_2$ in completion of reaction. When reacting nitroolefin intermediate A with 2-aminopyridine in presence of $Cu(NO_3)_2$ and TEMPO, we got the desired product (3bb) which is in agreement with our proposed mechanism.

3 | CONCLUSIONS

In summary, we have developed an efficient in situ synthesis of 3-nitroimidazo[1,2-*a*]pyridine derivatives. To the best of our knowledge, this is the first report on the synthesis of 3-nitroimidazo[1,2-*a*]pyridine from phenyl acrylic acids and 2-amino pyridine under $Cu(NO_3)_2$ with high regioselectivity. This protocol offers several significant advantages including operational simplicity, superior atom economy, shorter reaction time, easily available basic chemicals as the starting materials, a less expensive metal, tolerance of a wide range of functional groups, and good to excellent yields. These advantages render this protocol facile and suitable to create a diversified library of 3-nitroimidazo[1,2-*a*]pyridine derivatives.

4 | EXPERIMENTAL SECTION

4.1 | General information

All reagents were purchased from commercial sources and used without further purification. ^{1}H NMR spectra were determined on 400 MHz spectrometer as solutions in DMSO/$CDCl_3$. Chemical shifts are expressed in parts per million (δ) and the signals were reported as s (singlet), d (doublet), and t (triplet) and coupling constants (*J*) were given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in DMSO/$CDCl_3$ solution. Chemical shifts are referenced to DMSO (δ = 2.50/3.3 for ^{1}H and δ = 39.5 for ^{13}C NMR) as internal standard. Thin-layer chromatography (TLC) was performed on 60 F254 silica gel, precoated on aluminum plates and revealed with a UV lamp (λmax = 254 nm). All the melting points were determined on Labstar melting point apparatus and are uncorrected.

4.2 | General experimental procedure for the synthesis of 3

Charged phenyl acrylic acid (1 mmol) in acetonitrile (2 mL) under nitrogen followed by addition of copper nitrate (1.2 mmol) and the reaction mixture was stirred for 5 hours at 85°C. The progress of the reaction was monitored by TLC. After completion, charged 2-aminopyridine (1.5 mmol) and the reaction mixture were stirred for 1 hour at 85°C. Reaction was monitored by TLC. After completion reaction mass cool to room temperature then added water (8 mL) and extracted with dichloromethane (8 mL × 3 times) and the organic phase was dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude residue was obtained. Finally, it was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/*n*-hexane as an eluent to afford the pure products.

2-nitrovinyl benzene (1A)

Yellow solid (1.94 g, 97%), mp 56°C-58°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (d, *J* = 13.6 Hz, 1H), 7.60 (d, *J* = 13.6 Hz, 1H), 7.57-7.51 (m, 2H), 7.49-7.44 (m, 3H).

7-methyl-3-nitro-2-p-tolyl-imidazo[1,2-a]pyridine (3aa)

Yellow solid (1.56 g, 95%), mp 169°C-171°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.25 (d, J = 9.5 Hz, 1H), 7.72 (d, J = 10.8 Hz, 3H), 7.28 (d, J = 6.5 Hz, 3H), 2.45 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (DMSO, 100 MHz): δ 150.1, 145.5, 143.9, 140.1, 130.3, 129.8, 129.3, 128.9, 128.4, 128.1, 119.5, 116.8, 21.5, 21.3. MS (ES^+): m/z = 268.1 $[M + H]^+$.

3-nitro-2-p-tolylimidazo[1,2-a]pyridine (3ab)

Yellow solid (1.22 g, 78%), mp 195°C-197°C; ^{1}H NMR (DMSO, 400 MHz) δ 9.39 (d, J = 9.3 Hz, 1H), 7.93 (d, J = 11.2 Hz, 1H), 7.80 (t, J = 12 Hz, 1H), 7.73 (d, J = 10.8 Hz, 2H), 7.44 (t, J = 12 Hz, 1H), 7.30 (d, J = 10.5 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (DMSO, 100 MHz): δ 149.7, 145.1, 140.1, 132.3, 130.3, 129.7, 128.9, 118.1, 117.4, 21.5.

MS (ES^+): m/z = 253.9 $[M + H]^+$.

6-bromo-3-nitro-2-p-tolyl-imidazo[1,2-a]pyridine (3ac)

Yellow solid (1.62 g, 81%), mp 172°C-174°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.44 (s, 1H), 7.96 (d, J = 12.5 Hz, 1H), 7.90 (d, J = 12.5 Hz, 1H), 7.72 (d, J = 10.8 Hz, 2H), 7.30 (d, J = 10.6 Hz, 2H), 2.37 (s, 3H); ^{13}CNMR (DMSO, 100 MHz): δ 149.5, 143.6, 140.3, 134.9, 130.2, 129.3, 129, 128.5, 119.2, 111, 21.5.

MS (ES^+): m/z = 333.8 $[M + H]^+$.

8-methyl-3-nitro-2-p-tolyl-imidazo[1,2-a]pyridine (3ad)

Yellow solid (1.15 g, 70%), mp 126°C-128°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.37 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.2 Hz, 1H), 7.32 (d, J = 8 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 2.72 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz):δ 149.9, 145.2, 140.3, 130, 129.9, 129.2, 128.8, 128.4, 125.9, 116.3, 21.5, 16.6. MS (ES^+): m/z = 268.8 $[M + H]^+$.

7-methyl-3-nitro-2-phenyl-imidazo[1,2-a]pyridine (3ba)

Yellow solid (1.45 g, 85%), mp 169°C-171°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.25 (d, J = 9.5 Hz, 1H), 7.82-7.79 (m, 2H), 7.72 (s, 1H), 7.50-7.46 (m, 3H), 7.29 (d, J = 9.5 Hz, 1H), 2.46 (s, 3H); ^{13}CNMR (DMSO, 100 MHz): δ 149.9, 145.5, 144, 132.7, 130.3, 130.2, 129, 128.3, 128, 119.7, 116.9, 21.3.

MS (ES^+): m/z = 253.9 $[M + H]^+$.

3-nitro-2-phenyl-imidazo[1,2-a]pyridine (3bb)

Yellow solid (1.5 g, 93%), mp 167°C-169°C; ^{1}H NMR (400 MHz, DMSO): δ 9.40 (d, J = 9.3 Hz, 1H), 7.94 (d, J = 11.4 Hz, 1H), 7.84-7.78 (m, 3H), 7.52-7.43 (m, 4H), ^{13}CNMR (DMSO, 100 MHz): δ 149.6, 145.1, 132.7, 132.3, 130.3, 130.2, 128.9, 128.3, 118.2, 117.5.

MS (ES^+): m/z = 239.8 $[M + H]^+$.

6-bromo-3-nitro-2-phenyl-imidazo[1,2-a]pyridine (3bc)

Yellow solid (1.90 g, 89%), mp 166°C-168°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.43 (s, 1H), 7.97-7.89 (m, 2H), 7.81-7.78 (m, 2H), 7.50-7.45 (m, 3H); ^{13}C NMR (DMSO, 100 MHz): δ 150.1, 145.5, 143.9, 140, 130.3, 129.8, 129.3, 128.9, 128.4, 128, 119.5, 116.8, 21.4. MS (ES^+): m/z = 319.8 $[M + H]^+$.

8-methyl-3-nitro-2-phenyl-imidazo [1,2-a]pyridine (3bd)

Yellow solid (1.33 g, 78%), mp 167°C-169°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (d, J = 7.2 Hz, 1H), 7.92-7.90 (m, 2H), 7.52-7.49 (m, 3H), 7.46 (d, J = 7.2 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ149.7, 145.1, 132.2, 130.1, 130, 129.9, 128.6, 128.1, 125.9, 116.4. 16.6. MS (ES^+): m/z = 253.9 $[M + H]^+$.

2-(4-methoxyphenyl)-7-methyl-3-nitro-imidazo[1,2-a] pyridine (3ca)

Yellow solid (1 g, 65%), mp 165°C-167°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.26 (d, J = 9.5 Hz, 1H), 7.83 (d, J = 11.7 Hz, 2H), 7.70 (s, 1H), 7.27 (d, J = 8.6 Hz, 1H), 7.03 (d, J = 11.7 Hz, 2H), 3.82 (s, 3H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.1, 149.9, 145.6, 144, 132.1, 128.1, 124.7, 119.4, 116.7, 113.7, 55.7, 21.3. MS (ES^+): m/z = 283.9 $[M + H]^+$.

2-(4-methoxyphenyl)-3-nitro-imidazo[1,2-a]pyridine (3cb)

Yellow solid (1.37 g, 91%), mp 179°C-181°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.39 (d, J = 8.6 Hz, 1H), 7.92-7.76 (m, 4H), 7.42 (t, J = 9.3 Hz, 1H), 7.04 (d, J = 12.6 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.6, 145.2, 132.4, 132.1, 128.9, 124.6, 118, 117.3, 113.8, 55.7. MS (ES^+): m/z = 269.9 $[M + H]^+$.

6-bromo-2-(4-methoxyphenyl)-3-nitro-imidazo[1,2-a] pyridine (3cc)

Yellow solid (1.17 g, 60%), mp 162°C-164°C; ^{1}H NMR (DMSO, 400 MHz): δ 9.43 (s, 1H), 7.96-7.80 (m, 4H), 7.03 (d, J = 11.8 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.2, 149.3, 143.6, 134.9, 132.1, 129.1, 128.5, 124.2, 119, 113.9, 110.8, 55.7. MS (ES^+): m/z = 349.8 $[M + H]^+$.

2-(4-methoxyphenyl)-8-methyl-3-nitro-imidazo[1,2-a] pyridine (3cd)

Yellow solid (1 g, 63%), mp 161°C-163°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.38 (d, J = 6.8 Hz, 1H), 7.95 (d, J = 6.8 Hz, 2H), 7.44 (d, J = 7.2 Hz, 1H), 7.15 (t, J = 6.8 Hz, 1H), 7.03 (d, J = 6.8 Hz, 2H), 3.89 (s, 3H), 2.72 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.1, 149.7, 145.2, 131.8, 129.9, 128.3, 126.1, 124.4, 116.2, 113.6, 55.4, 16.6. MS (ES^+): m/z = 283.9 $[M + H]^+$.

2-(3-chlorophenyl)-7-methyl-3-nitro-imidazo[1,2-a]pyridine (3da)

Yellow solid (1.41 g, 90%), mp 179°C-181°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.37 (d, J = 7.2 Hz, 1H), 7.89 (s, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.60 (s, 1H), 7.47-7.41 (m, 2H), 7.13 (d, J = 7.2 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.9, 145.5, 143.3, 134.1, 133.7, 130.1, 130, 129.3128.2, 127.3, 119.2, 117.1, 21.6. MS (ES^+): m/z = 288.8 $[M + H]^+$.

2-(3-chlorophenyl)-3-nitro-imidazo[1,2-a]pyridine (3db)

Yellow solid (1.41 g, 94%), mp 166°C-168°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.51 (d, J = 6.8 Hz, 1H), 7.90 (s, 1H),

7.85 (d, J = 9.6 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.49-7.42 (m, 2H), 7.32 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.6, 145.1, 134.1, 133.5, 131.1, 130.1, 129.4, 128.1, 124.1, 118.4, 117.6, 116.8. MS (ES^+): m/z = 274.3 $[M + H]^+$.

6-bromo-2-(3-chlorophenyl)-3-nitro-imidazo[1,2-a]pyridine (3dc)

Yellow solid (1.7 g, 88%), mp 188°C-190°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.65 (s, 1H), 7.88 (s, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.74 (s, 2H), 7.50-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.5, 143.4, 134.3, 133.1, 130.4, 130, 129.4, 128.2, 118.8, 111.8. MS (ES^+): m/z = 353.4 $[M + H]^+$.

2-(3-chlorophenyl)-8-methyl-3-nitro-imidazo[1,2-a]pyridine (3dd)

Yellow solid (1.46 g, 93%), mp 167°C-169°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.37 (d, J = 6.8 Hz, 1H), 7.90 (s, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.49-7.42 (m, 3H), 7.21(t, J = 7.2 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.1, 145.1, 134.1, 130.1, 129.3, 128.7, 128.3, 125.8, 116.7, 16.6. MS (ES^+): m/z = 288.6 $[M + H]^+$.

2-(2-methoxyphenyl)-7-methyl-3-nitro-imidazo[1,2-a]pyridine (3ea)

Yellow solid (1.42 g, 90%), mp 152°C-154°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.34 (d, J = 6.8 Hz, 1H), 7.56 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 8 Hz, 1H), 7.08 (t, J = 6.8 Hz, 2H), 7.02 (d, J = 8.4 Hz, 1H), 3.81 (s, 3H), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.6, 147.4, 145.5, 142.3, 131.3, 130.5, 126.9, 122, 120.5, 118.6, 116.9, 110.8, 55.6, 21.5. MS (ES^+): m/z = 283.9 $[M + H]^+$.

2-(2-methoxyphenyl)-3-nitroimidazo[1,2-a]pyridine (3eb)

Yellow solid (1.25 g, 83%), mp 171°C-173°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.47 (d, J = 7.2 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.63-7.57 (m, 2H), 7.50-7.46 (m, 1H), 7.27-7.23 (m, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 8 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.6, 147.9, 147, 145.1, 131.4, 130.5, 127.6, 121.8, 120.6, 118.2, 116.2, 110.9, 55.5.

MS (ES^+): m/z = 269.9 $[M + H]^+$.

6-bromo-2-(2-methoxyphenyl)-3-nitro-imidazo[1,2-a]pyridine (3ec)

Yellow solid (1.81 g, 93%), mp 170°C-172°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.63 (s, 1H), 7.70 (d, J = 5.6 Hz, 2H), 7.57 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 8.2 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.5, 146.9, 143.3, 133.5, 131.6, 130.5, 127.6, 121.3, 120.6, 118.7, 111.1, 55.6. MS (ES^+): m/z = 248.9 $[M + H]^+$.

2-(2-methoxyphenyl)-8-methyl-3-nitro-imidazo[1,2-a]pyridine (3ed)

Yellow solid (1.03 g, 65%), mp 188°C-190°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.35 (d, J = 6.8 Hz, 1H), 7.58 (d, J = 7.2 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 7.2 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 3.81 (s, 3H), 2.72 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.7, 146.5, 145.1, 131.2, 130.6, 129.3, 128.4, 125.4, 122.2, 120.6, 116.2, 110.8, 55.6, 16.7. MS (ES^+): m/z = 283.9 $[M + H]^+$.

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