Organic & Biomolecular Chemistry

PAPER

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Cite this: *Org. Biomol. Chem.*, 2018, **16**, 8620

Metal-free synthesis of aminomethylated imidazoheterocycles: dual role of *tert*-butyl hydroperoxide as both an oxidant and a methylene source†

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Received 29th September 2018,
Accepted 24th October 2018

DOI: 10.1039/c8ob02432d

rsc.li/obc

A novel and efficient aminomethylation approach has been developed for the regioselective functionalization of imidazoheterocycles under metal-free conditions. A wide range of imidazoheterocycles and 2/4-aminoazaheterocycles successfully provided corresponding aminomethylated imidazoheterocycles in moderate to excellent (33–80%) yields. The isotopic labelling study suggested that TBHP played a dual role as both an oxidant and a methylene source in this transformation. The developed protocol follows a radical pathway which is supported by radical trapping experiments.

Introduction

Transition-metal free construction of C–N and C–C bonds *via* cross-dehydrogenative coupling (CDC) reactions represents an ideal strategy in the perspective of green and sustainable chemistry.[1] These reactions generally demonstrate step- and atom-efficiency and eliminate the use of pre-functionalized substrates for C–H bond functionalization.[2] The oxidative functionalization of sp^3 C–H bonds remains a challenge due to the poor acidity and high bond dissociation energy and is therefore of special interest.[3] Recently, remarkable progress has been realized toward the radical initiated domino approach for the selective functionalization of C–H bonds.[4] Organic peroxides are most commonly used as hydrogen acceptors for the functionalization and synthesis of a diverse range of N-heterocyclic compounds *via* radical addition/cyclization reactions.[5] In recent years, peroxides have been exploited as one carbon source for the methylation of C–H, N–H, OH and S–H bonds.[6] In addition, peroxides have also been used as one carbon source for decarboxylative methylation and the methylation–cyclization strategy.[7] Most of these reactions rely on transition metal-catalysis to produce the methyl radical species from organic peroxides. However, utilization of organic peroxides as a methylene synthon for the aminomethylation reaction has not been reported so far in the literature.

On the other hand, imidazoheterocycles are privileged nitrogen heterocycles as these compounds display a broad range of biological and photophysical properties.[8] It has been observed that the nature of the substituents at the C-2 or C-3 positions of imidazoheterocycles significantly influences their biological activities. Amidomethylated and aminomethylated linkers on imidazo[1,2-*a*]pyridine are found in a number of commercially available drugs such as necopidem, saripidem, GSK812397 and bioactive lead compounds (Fig. 1).[9] Therefore, substantial efforts have been devoted to the synthesis and functionalization of the imidazoheterocycles substituted at the C-3 position of the core ring.[9a,10] Regioselective aminomethylation of imidazoheterocycles may generate diversely substituted imidazoheterocycles for medicinal chemistry application. However, a careful literature survey revealed that the aminomethylated strategy on imidazoheterocycles is rarely explored and limited to only morpholine as an amine coupling partner.[11]

Owing to the valuable applications of organic peroxides in organic synthesis, our previous results on the use of dimethyl sulfoxide (DMSO),[12] and dimethylacetamide (DMA)[13] as the carbon synthon and our efforts towards synthesis and functionalisation of N-heteroaromatics,[14] we herein report a

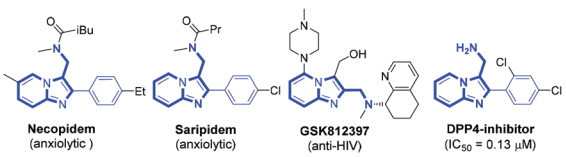

Fig. 1 Representative examples of bioactive imidazo[1,2-*a*]pyridines.

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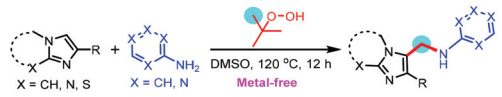
† Electronic supplementary information (ESI) available: Experimental details and characterization of all compounds, copies of ^{1}H and ^{13}C NMR, ESI-HRMS spectra for compounds. See DOI: 10.1039/c8ob02432d



Scheme 1 Aminomethylation of imidazoheterocycles with aminoazaheterocycles.

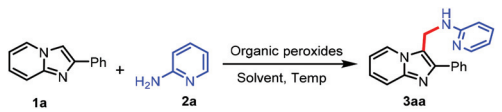
regioselective aminomethylation of imidazoheterocycles with aminoazaheterocycles using TBHP as a mild and eco-friendly oxidant as well as a carbon synthon (Scheme 1). The developed strategy involves sp^3 and sp^2 C–H bond functionalization under metal-free conditions.

Results and discussion

We began our investigation by choosing 2-phenylimidazo[1,2-*a*] pyridine (**1a**) and 2-aminopyridine (**2a**) as model substrates. The results for the optimization of the reaction conditions are given in Table 1. The initial reaction of **1a** and **2a** was performed in DMSO using TBHP (70% aqueous solution; 3 equiv.) as an external oxidant at 120 °C. Pleasingly, the desired product *N*-((2-phenylimidazo[1,2-*a*]pyridin-3yl)methyl)pyridin-2-amine (**3aa**) was obtained in 75% yield after 12 h (Table 1, entry 1). The molecular structure of **3aa** was unambiguously assigned by 1D, 2D-NMR spectroscopy and ESI-HRMS analysis (ESI†).

In light of the above results, various organic peroxides namely di-*tert*-butyl peroxide (DTBP), cumene hydroperoxide (CP), dicumyl peroxide (DCP) and *tert*-butyl peroxybenzoate (TBPB) were used under identical reaction conditions. The desired product **3aa** was obtained in 51%, 70%, 9% and 62% yields by using DTPB, CP, DCP and TBPB, respectively (Table 1, entries 2–5). Acetophenone was also isolated in 75% yield from the reaction of **1a** and **2a** in the presence of CP. Moreover, the use of the TBHP/TBAI oxidative system afforded the desired product (**3aa**) in 72% yield (Table 1, entry 6). Decreasing the reaction temperature to 100 °C resulted in reduced yield (33%) of **3aa** and **1a** was recovered in 59% yield (Table 1, entry 7). The screening of different solvents *viz* H_2O/SLS, 1,4-dioxane, chlorobenzene and DMF revealed that DMSO was the best choice for the present reaction (Table 1, entries 1 *vs.* 8–12). Lower yields of **3aa** were obtained in 1,4-dioxane, chlorobenzene and toluene, whereas the reaction did not proceed in H_2O/SLS. The use of DMF as the solvent resulted in ring opening of **1a** *via* oxidative cleavage of C–C and C–N bonds followed by oxygenation to afford the *N*-(pyridin-2-yl) benzamide[15] in 85% yield after 24 h along with a trace amount of desired product **3aa** (Table 1, entry 12). Further increasing the concentration of TBHP to 4 equiv. under optimal reaction conditions resulted in no significant enhancement in the yield of **3aa** (Table 1, entry 13). In the absence of TBHP as an external oxidant, we could not observe the desired product **3aa**. However, we have isolated 3,3′-bisimidazopyridinylmethane[12] (**4a**) in 32% yield in 24 h under optimal reaction conditions (Table 1, entry 14).

Table 1 Optimization of the reaction conditions[a]

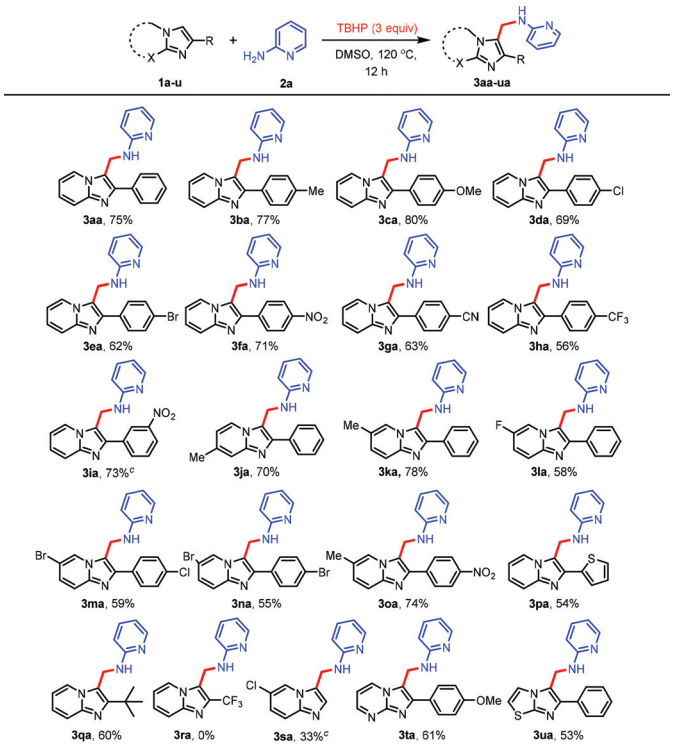


Entry	Peroxide	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	**TBHP**	**DMSO**	**120**	**12**	**75**
2	DTBP	DMSO	120	18	51
3	CP	DMSO	120	12	70[c]
4	DCP	DMSO	120	15	9
5	TBPB	DMSO	120	15	62
6	TBHP	DMSO	120	12	72[d]
7	TBHP	DMSO	100	24	33[e]
8	TBHP	H_2O/SLS	120	24	NR
9	TBHP	1,4-Dioxane	120	24	25
10	TBHP	Chlorobenzene	120	24	33
11	TBHP	Toluene	120	24	17
12	TBHP	DMF	120	24	Trace[f]
13	TBHP[g]	DMSO	120	12	74
14	—	DMSO	120	24	—[h]

[a] Reaction conditions: **1a** (0.8 mmol), **2a** (1.0 mmol), peroxide (2.4 mmol), DMSO (5 mL), 120 °C, 12–24 h. [b] Isolated yield. [c] Acetophenone was isolated in 75% yield. [d] 20 mol% TBAI was used. [e] **1a** was recovered in 59%. [f] *N*-(Pyridine-2-yl)benzamide (**5a**) was isolated in 85% yield. [g] 4 equivalent TBHP was used. [h] Bis(2-phenylimidazo[1,2-*a*]pyridine-3-yl)methane (**4a**) was obtained in 32% yield; NR = no reaction; DTBP = di-*tert*-butyl peroxide; CP = cumene hydroperoxide; DCP = dicumyl peroxide; TBPB = *tert*-butyl peroxybenzoate; SLS = sodium lauryl sulfate.

After establishing the optimal reaction conditions (Table 1, entry 1), we turned our attention to explore the substrate scope of imidazo[1,2-*a*]pyridines having various substitutions for the regioselective aminomethylation with 2-aminopyridine (**2a**) (Table 2). Imidazo[1,2-*a*]pyridines having electron donating groups (*p*-Me, *p*-OMe) on the C-2 phenyl ring (**1b** and **1c**) reacted smoothly with **2a** and afforded respective products **3ba** and **3ca** in 77 and 80% yields, respectively. The substrate with electron withdrawing groups (*p*-Cl, *p*-Br, *p*-NO_2, *p*-CN, *p*-CF_3 and *m*-NO_2) on the C-2 phenyl ring of imidazo[1,2-*a*]pyridines (**1d–i**) also delivered corresponding products (**3da–ia**) in moderate to good yields (56–73%). Furthermore, substrates having the methyl substituent (7-Me and 6-Me) on the pyridine ring of imidazo[1,2-*a*]pyridine (**1j** and **1k**) furnished the desired products **3ja** and **3ka** in 70 and 78% yields, respectively. Interestingly, imidazo[1,2-*a*]pyridine having the fluoro substituent on the pyridine ring (**1l**) also afforded desired product **3la** in 58% yield. The imidazo[1,2-*a*]pyridines with the bromo group on the pyridine ring and chloro or bromo groups on the C-2 phenyl ring also afforded corresponding products **3ma** and **3na** in 59 and 55%, yields, respectively. Similarly, imidazo [1,2-*a*]pyridine with the methyl group at the C-6 position and the nitro group on the C-2 phenyl ring (**1o**) gave the respective product **3oa** in 74% yield. It is worth mentioning that halogens (F, Cl and Br), –NO_2, –CN and pharmaceutically active –CF_3[16] groups were well tolerated under optimized reaction conditions and may serve as crucial substituents for post-functionalization reactions. Imidazo[1,2-*a*]pyridine with C-2 thiophene-yl (**1p**) yielded corresponding product **3pa** in 54%

Table 2 Substrate scope of imidazoheterocycles[a,b]

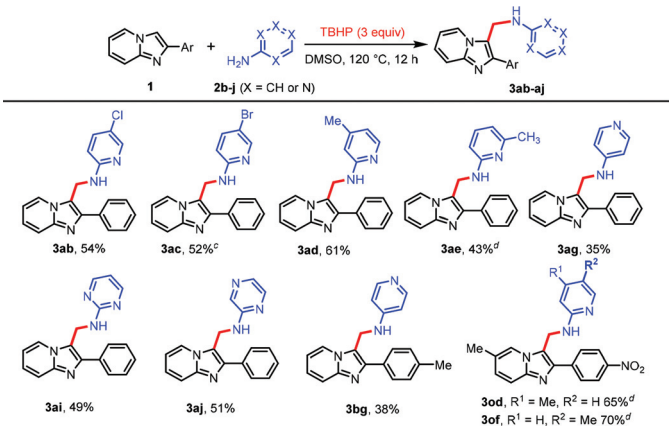


[a] Reaction conditions: **1** (0.8 mmol), **2a** (1.0 mmol), TBHP (2.4 mmol), DMSO (5 mL), 120 °C, 12 h. [b] Isolated yields. [c] 24 h.

yield. Pleasingly, the substrate having the *tert*-butyl group at the C-2 position (**1q**) smoothly delivered the respective product **3qa** in 60% yield under similar reaction conditions. However, the reaction of imidazo[1,2-*a*]pyridine bearing $-CF_3$ substitution at the C-2 position (**1r**) failed to afford the desired product **3ra**. It might be due to the deactivation of the C-3 position due to the strong electron withdrawing nature of the $-CF_3$ group. Notably, unsubstituted imidazo[1,2-*a*]pyridine at the C-2 position (**1s**) afforded the desired product **3sa** in 33% yield along with the recovery of **1s** in 58% yield, which also confirms the C-3 regioselectivity of the present reaction. The low yield in the case of **3sa** might be due to the poor stabilization of the radical intermediate generated in the reaction. 2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyrimidine (**1t**) and 6-phenylimidazo[2,1-*b*]thiazole (**1u**) also reacted smoothly under standard reaction conditions to afford corresponding products **3ta** and **3ua** in 61% and 53% yields, respectively.

Next, we evaluated the compatibility of various 2-aminopyridines and related aminoazaheterocycles under the optimized reaction conditions (Table 3). To our delight, different 2-aminopyridines with chloro, bromo and methyl substituents (**2b–e**) reacted smoothly with **1a** to afford corresponding products **3ab–ae** in moderate to good (43–61%) yields. Similarly, the reaction of 2-amino-4-methylpyridine (**2d**) and 2-amino-5-methylpyridine (**2e**) with **1o** having the nitro group on the C-2 phenyl ring gave corresponding products **3od** and **3of** in 65% and 70% yields, respectively. Low yields (35–38%) of pro-

Table 3 Substrate scope of 2/4-aminoazaheterocycles[a,b]



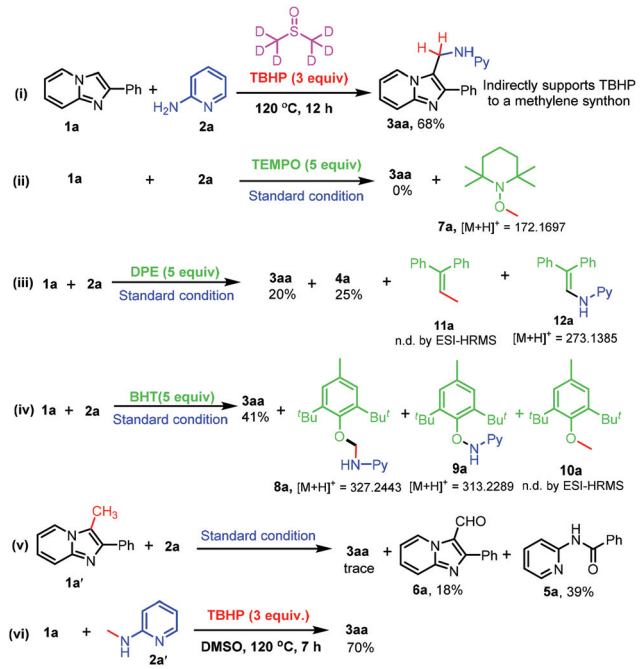
[a] Reaction conditions: **1** (0.8 mmol), **2** (1.0 mmol), TBHP (2.4 mmol), DMSO (5 mL), 120 °C, 12 h. [b] Isolated yields. [c] Reaction time 17 h. [d] Reaction time 20 h.

ducts **3ag** and **3bg** were obtained by the reaction of 4-aminopyridine (**2g**) with **1a** and **1b** along with the recovery of reactants. We were unable to isolate the desired product from the reaction of 3-aminopyridine (**2h**) with **1a** due to multiple side product formation. Finally, the reaction of 2-aminopyrimidine (**2i**) and 2-aminopyrazine (**2j**) with **1a** under optimized reaction conditions resulted in corresponding products **3ai** and **3aj** in 49% and 51% yields, respectively.

To check the practical utility of the present approach, the gram-scale experiment was performed with **1a** (1.5 g) and **2a** (0.870 g) under the standard reaction conditions. To our delight, the desired product **3aa** was formed in 64% yield in 20 h (Scheme 2).

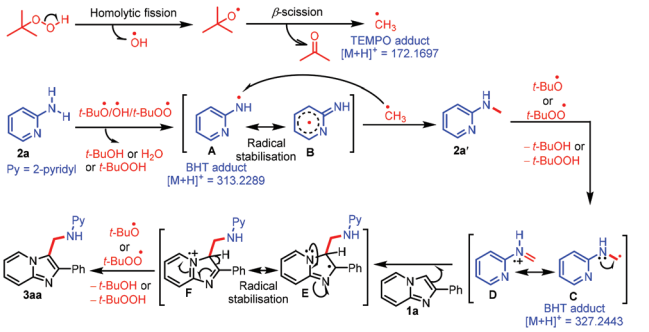
To understand the reaction pathway, we performed a series of control experiments (Scheme 3). The reaction of **1a** and **2a** in the presence of TBHP in DMSO-d_6 as a solvent resulted in the formation of **3aa** in 68% yield (Scheme 3; eqn (i)). This indicated that TBHP acts as a methylene source in this reaction and not DMSO. The radical trapping study with different radical scavengers such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), 1,1-diphenylethylene (DPE), and 2,4-di-*tert*butyl-4-methylphenol (BHT) was performed to shed light on the kind of mechanism involved. The use of TEMPO resulted in complete inhibition of **3aa** formation in the reaction. The methyl adduct of TEMPO (**7a**) was observed in the ESI-HRMS analysis (*m*/*z* 172.1697) indicating the generation of the methyl radical in the reaction mixture (Scheme 3; eqn (ii)). The addition of DPE in the reaction of **1a** and **2a** resulted in reduced yield

Scheme 2 Gram scale application.



Scheme 3 Control experiments.

(20%) of **3aa** along with the formation of **4a** in 25% yield (Scheme 3; eqn (iii)) which is due to homocoupling of **1a** with the methylene synthon *in situ* produced by DMSO under aerobic oxidative conditions.[12] Similarly, addition of BHT in the reaction of **1a** and **2a** also led to reduction in the yield (41%) of **3aa** (Scheme 3; eqn (iv)). The aminomethylated BHT adduct (**8a**) and aminated BHT adduct (**9a**) were also observed in the ESI-HRMS analysis of the reaction mixture. However, in the case of BHT and DPE, the methyl adducts (**10a** and **11a**) were not observed in the ESI-HRMS analysis. Possibly BHT and DPE failed to capture the reactive methyl radical which subsequently reacted with **2a** to produce **3aa** in 41% and 20% yields, respectively. TEMPO exhibited better reactivity than BHT and DPE, captured the reactive methyl radical and therefore completely inhibited the formation of **3aa**. These experiments strongly supported that the reaction involved a substantial amount of radical-mediated pathway. To identify possible intermediates of the present reaction, 3-methyl-2-phenylimidazo[1,2-*a*]pyridine (**1a′**) was allowed to react with **2a** under the optimum reaction conditions. Only traces of **3aa** were observed on TLC along with the formation of imidazopyridine-3-carbaldehyde (**6a**) and *N*-(pyridine-2-yl)benzamide (**5a**) in 18% and 39% yields, respectively (Scheme 3; eqn (v)). These results indicate that **1a′** may not be the intermediate for this transformation. On the other hand, **3aa** was obtained in 70% yield from the reaction of *N*-methylpyridin-2-amine (**2a′**) with **1a** under the standard reaction conditions (Scheme 3; eqn (vi)) which strongly supports the hypothesis that the reaction proceeds *via* methylation of 2-aminopyridine to generate **2a′** as an intermediate which subsequently underwent a radical addition reaction with **1a** to afford **3aa**.



Scheme 4 Proposed mechanism.

Based on preliminary mechanistic studies, ESI-HRMS analysis and relevant literature studies,[6b,c,h,17] a possible mechanism is depicted in Scheme 4. Initially, TBHP undergoes homolytic fission to produce a *tert*-butoxy radical which then produces the methyl radical species *via* β-methyl elimination. The radical species *i.e.* *tert*-butoxy/*tert*-butylperoxy/hydroxy abstracted the hydrogen atom from 2-aminopyridine to give aminyl radical intermediate **A** which may get stabilized with the pyridine ring. The formation of aminyl radical intermediate **A** was supported by radical trapping experiments with BHT and DPE (see the ESI†). Intermediate **A** reacted with the *in situ* generated methyl radical to form intermediate **2a′**. Furthermore, hydrogen atom abstraction from intermediate **2a′** resulted in the formation of radical **C**. Radical addition of **C** to **1a** generated radical intermediate **E** which upon hydrogen atom abstraction in the presence of the *tert*-butoxy/*tert*-butylperoxy radical afforded the desired product **3aa**.

Conclusions

In summary, a highly efficient metal-free method has been developed for the synthesis of aminomethylated imidazoheterocycles that involves intermolecular cross-dehydrogenative coupling and uses TBHP as a methylene source as well as a hydrogen acceptor. The developed protocol follows a radical pathway which is supported by the radical trapping experiments and isotopic labelling study. A series of aminomethylated imidazoheterocycles was synthesized in good to high yields under very simple and practical reaction conditions. Tolerance of various functional groups as well as secondary amine derived products may give an excellent opportunity for post-functionalization in medicinal chemistry application.

Experimental section

General information

Melting points were determined in open capillary tubes on EZ-Melt automated melting point apparatus and are uncorrected. All the compounds were fully characterized by ^{1}H, ^{13}C, and IR and further confirmed by ESI-HRMS analysis.

Reactions were monitored by using thin layer chromatography (TLC) on 0.2 mm silica gel F254 plates (Merck). ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz and 100 MHz instruments, respectively, with $CDCl_3$ and DMSO-d_6 as the solvent using TMS as an internal standard. Peak multiplicities of ^{1}H-NMR signals were designated as s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), m (multiplet), *etc*. Chemical shifts (δ) and coupling constants (J) are reported in parts per million (ppm) relative to the residual signal of TMS in deuterated solvents and hertz, respectively. ESI-HRMS were recorded using Q-TOF LC/MS. IR spectra were recorded using an FT-IR spectrophotometer, and values are reported in cm^{-1}. Column chromatography was performed over silica gel (60–120 mesh) using EtOAc–*n*-hexane as an eluent. Imidazoheterocycles were prepared from corresponding methyl ketones and 2-aminopyridines/2-aminopyrimidines/2-aminothiazoles following the reported procedure.[18] All the chemicals were obtained from the commercial suppliers and used without further purification.

Experimental procedure for the preparation of 3aa. To a stirred solution of 2-phenylimidazo[1,2-*a*]pyridine **1a** (0.8 mmol) in DMSO (5 mL) were added 2-aminopyridine **2a** (1 mmol) and *t*-BuOOH (70% aqueous solution) (2.4 mmol) at room temperature and the reaction mixture was stirred at 120 °C for 12 h. After completion of the reaction, observed by TLC, the mixture was allowed to attain room temperature. The reaction mixture was poured into 20 mL of water and extracted with EtOAc (3 × 15 mL). The combined organic layer was dried over Na_2SO_4 and evaporated under vacuum. The resulting crude solid was purified by column chromatography (silica gel 60–120 mesh) using EtOAc–*n*-hexane (4.0 : 6.0, v/v) as an eluent to afford **3aa** in 75% yield as the amorphous white solid.

Procedure for radical trapping experiments. To a stirred solution of 2-phenylimidazo[1,2-*a*]pyridine **1a** (0.8 mmol) in DMSO (5 mL) were added 2-aminopyridine **2a** (1 mmol), *t*-BuOOH (70% aqueous solution) (2.4 mmol) and TEMPO/BHT/DPE (5 equiv.) at room temperature and the reaction mixture was stirred at 120 °C for 12 h. The reaction mixture was allowed to attain room temperature and poured into 20 mL of water and extracted with EtOAc (3 × 15 mL). The combined organic layer was dried over Na_2SO_4 and evaporated under vacuum. The resulting crude solid was purified over silica gel (60–120 mesh) column chromatography by using EtOAc–*n*-hexane (4.0 : 6.0, v/v) to afford **3aa** in 0, 41% and 20% yields in the case of TEMPO, BHT and DPE, respectively. The same reaction mixtures were directly analysed by ESI-HRMS analysis to observe the corresponding intermediates and adducts of radical scavengers such as TEMPO, BHT and DPE.

***N*-((2-Phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3aa).** Off-white solid; 75% yield; mp = 177–178 °C (lit.,[19] 178–179 °C); FT-IR (neat): 3240, 1597, 1481, 1350, 1249, 979, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.13 (m, 2H), 7.75 (d, J = 7.7 Hz, 2H), 7.60 (d, J = 9.0 Hz, 1H), 7.42–7.39 (m, 3H), 7.35 (t, J = 7.3 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 6.75 (t, J = 6.8 Hz, 1H), 6.63 (t, J = 5.9 Hz, 1H), 6.45 (d, J = 8.3 Hz, 1H), 5.00 (d, J = 4.7 Hz, 2H), 4.75 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.3, 148.1, 145.2, 144.7, 137.5, 134.2, 128.7 (2 × CH), 128.5 (2 × CH), 128.0, 124.8, 124.4, 117.5, 117.1, 113.7, 112.4, 108.4, 35.7 ppm; HRMS (ESI) calcd for $C_{19}H_{17}N_4^+$ $[M + H]^+$ 301.1448, found 301.1449.

***N*-((2-(*p*-Tolyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ba).** Off-white solid; 77% yield; mp = 121–122 °C; FT-IR (neat): 3270, 1610, 1517, 1477, 1380, 1343, 1265, 970, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.17 (m, 2H), 7.69–7.64 (m, 3H), 7.43 (t, J = 7.8 Hz, 1H), 7.27–7.22 (m, 3H, overlapped with residual signal), 6.81 (t, J = 6.8 Hz, 1H), 6.66 (t, J = 6.0 Hz, 1H), 6.43 (d, J = 8.4 Hz, 1H), 5.02 (d, J = 4.7 Hz, 2H), 4.65 (s, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 147.9, 145.2, 144.8, 138.0, 137.7, 131.2, 129.6 (2 × CH), 128.4 (2 × CH), 124.9, 124.4, 117.5, 116.8, 113.7, 112.5, 108.4, 35.7, 21.4 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1595.

***N*-((2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ca).** Off-white solid; 80% yield; mp = 160–162 °C; FT-IR (neat): 3232, 1597, 1481, 1242, 1172, 1026, 840, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (dd, J = 5.2, 2 Hz, 1H), 8.10 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 8.7 Hz, 2H), 7.58 (d, J = 9 Hz, 1H), 7.44–7.40 (m, 1H), 7.16 (t, J = 7.1 Hz, 1H), 6.93 (d, J = 8.7 Hz, 2H), 6.74 (t, J = 6.6 Hz, 1H), 6.66–6.62 (m, 1H), 6.48 (d, J = 8.3 Hz, 1H), 4.96 (d, J = 4.7 Hz, 2H), 4.80 (t, J = 4.8 Hz, 1H), 3.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6, 158.2, 148.1, 145.1, 144.5, 137.5, 129.6 (2 × CH), 126.6, 124.7, 124.3, 117.3, 116.3, 114.2 (2 × CH), 113.6, 112.3, 108.4, 55.4, 35.7 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4O^+$ $[M + H]^+$ 331.1553, found 331.1551.

***N*-((2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3da).** Off-white solid; 69% yield; mp = 157–159 °C; FT-IR (neat): 3240, 1597, 1481, 1419, 1357, 1280, 979, 833, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 4.3 Hz, 1H), 8.15 (d, J = 6.7 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 9.1 Hz, 1H), 7.47–7.42 (m, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.22 (t, J = 7.7 Hz, 1H), 6.80 (t, J = 6.6 Hz, 1H), 6.69–6.66 (m, 1H), 6.48 (d, J = 8.3 Hz, 1H), 4.99 (d, J = 4.9 Hz, 2H), 4.66 (t, J = 4.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 148.1, 145.2, 143.5, 137.6, 134.0, 132.6, 129.6 (2 × CH), 129.0 (2 × CH), 125.2, 124.4, 117.6, 117.2, 113.9, 112.7, 108.5, 35.6 ppm; HRMS (ESI) calcd for $C_{19}H_{16}ClN_4^+$ $[M + H]^+$ 335.1058, found 335.1054.

***N*-((2-(4-Bromophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ea).** Off-white solid; 62% yield; mp = 167–169 °C; FT-IR (neat): 3240, 1597, 1504, 1481, 1357, 1280, 979, 825, 771, 725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18–8.16 (m, 1H), 8.13 (dt, J = 6.9, 1.2 Hz, 1H), 7.63–7.58 (m, 3H), 7.53–7.49 (m, 2H), 7.47–7.42 (m, 1H), 7.23–7.18 (m, 1H), 6.79 (td, J = 6.8, 1.2 Hz, 1H), 6.69–6.65 (m, 1H), 6.50 (dt, J = 8.3, 1.0 Hz, 1H), 4.96 (d, J = 4.8 Hz, 2H), 4.78 (t, J = 4.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 148.1, 145.2, 143.4, 137.6, 133.0, 131.9 (2 × CH), 129.8 (2 × CH), 125.2, 124.4, 122.2, 117.5, 117.3, 113.8, 112.7, 108.5, 35.6 ppm; HRMS (ESI) calcd for $C_{19}H_{16}BrN_4^+$ $[M + H]^+$ 379.0553, found 379.0549.

***N*-((2-(4-Nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3fa).** Yellow solid; 71% yield; mp = 196–198 °C; FT-IR

(neat): 3232, 1597, 1512, 1334, 1111, 979, 858, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.7 Hz, 2H), 8.20–8.17 (m, 2H), 7.94 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 9.1 Hz, 1H), 7.49–7.45 (m, 1H), 7.28–7.23 (m, 1H, overlapped with the residual signal), 6.83 (t, J = 6.7 Hz, 1H), 6.71–6.68 (m, 1H), 6.53 (d, J = 8.3 Hz, 1H), 5.03 (d, J = 4.9 Hz, 2H), 4.79 (d, J = 4.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 148.1, 147.2, 145.5, 142.0, 140.6, 137.7, 128.8 (2 × CH), 125.8, 124.6, 124.0 (2 × CH), 118.9, 117.8, 114.1, 113.1, 108.7, 35.5 ppm; HRMS (ESI) calcd for $C_{19}H_{16}N_5O_2^+$ $[M + H]^+$ 346.1299, found 346.1318.

4-((3-((Pyridin-2-ylamino)methyl)imidazo[1,2-*a*]pyridin-2-yl) benzonitrile (3ga). Off-white solid; 63% yield; mp = 134–136 °C; FT-IR (neat): 3263, 2229, 1604, 1504, 1481, 1280, 979, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.12 (m, 2H), 7.83 (d, J = 8.3 Hz, 2H), 7.61–7.57 (m, 3H), 7.47–7.43 (m, 1H), 7.24–7.20 (m, 1H), 6.80 (t, J = 6.8 Hz, 1H), 6.68 (t, J = 5.2 Hz, 1H), 6.53 (d, J = 8.3 Hz, 1H), 4.96 (s, 3H, overlapped with the NH signal); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 148.1, 145.3, 142.2, 138.6, 137.6, 132.4 (2 × CH), 128.6 (2 × CH), 125.7, 124.5, 118.9, 118.5, 117.6, 114.0, 113.0, 111.2, 108.7, 35.4; HRMS (ESI) calcd for $C_{20}H_{16}N_5^+$ $[M + H]^+$ 326.1400, found 326.1399.

***N*-((2-(4-(Trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridin-3-yl) methyl)pyridin-2-amine (3ha).** White solid; 56% yield; mp = 175–177 °C; FT-IR (neat): 3240, 1597, 1481, 1319, 1242, 1165, 1064, 910, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15–8.14 (m, 1H), 8.04 (d, J = 6.9 Hz, 1H), 7.77 (d, J = 8.1 Hz, 2H), 7.55–7.51 (m, 3H), 7.46–7.42 (m, 1H), 7.15 (t, J = 8.0 Hz, 1H), 6.72–6.64 (m, 2H), 6.59 (d, J = 8.3 Hz, 1H), 5.26 (br s, 1H), 4.92 (d, J = 4.6 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.2, 148.0, 145.1, 142.6, 137.5, 137.4, 129.6 (q, J_{C-F} = 32 Hz), 128.2 (2 × CH), 125.5 (q, J_{C-F} = 4 Hz), 125.4, 124.4, 122.9 (J_{C-F} = 270 Hz), 118.0, 117.4, 113.7, 112.8, 108.7, 35.4 ppm; HRMS (ESI) calcd for $C_{20}H_{16}F_3N_4$ $[M + H]^+$ 369.1322, found 369.1324.

***N*-((2-(3-Nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ia).** White solid; 73% yield; mp = 135–137 °C; FT-IR (neat): 3302, 3248, 3086, 1604, 1504, 1473, 1342, 1280, 1149, 1072, 987, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.63 (t, J = 1.8 Hz, 1H), 8.19–8.13 (m, 3H), 8.07 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 9 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.24–7.20 (m, 1H), 6.80 (t, J = 7.1 Hz, 1H), 6.69–6.66 (m, 1H), 6.54 (d, J = 8.4 Hz, 1H), 5.02 (d, J = 4.5 Hz, 2H), 4.97 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 148.6, 148.0, 145.3, 141.9, 137.6, 135.9, 134.1, 129.6, 125.6, 124.6, 123.1, 122.6, 118.2, 117.6, 114.0, 113.0, 108.8, 35.4 ppm; HRMS (ESI) calcd for $C_{19}H_{16}N_5O_2^+$ $[M + H]^+$ 346.1299, found 346.1292.

***N*-((7-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ja).** Off-white solid; 70% yield; mp = 189–191 °C; FT-IR (neat): 3240, 1597, 1481, 1350, 1080, 771, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.15 (m, 1H), 7.98 (d, J = 7.0 Hz, 1H), 7.73 (d, J = 6.9 Hz, 2H), 7.45–7.37 (m, 3H), 7.35–7.27 (m, 2H, overlapped with the residual signal), 6.67–6.63 (m, 1H), 6.58 (dd, J = 7.0, 1.8 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 4.95 (s, 3H, overlapped with the N–H signal), 2.38 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.2, 147.9, 145.6, 144.3, 137.6, 136.0, 134.2, 128.7 (2 × CH), 128.5 (2 × CH), 127.9, 123.7, 116.4, 115.9, 115.2, 113.6, 108.4, 35.7, 21.5 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1598.

***N*-((6-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ka).** Off-white solid; 78% yield; mp = 209–211 °C; FT-IR (neat): 3240, 1597, 1473, 1388, 1242, 771, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.17 (m, 1H), 7.93 (s, 1H), 7.76–7.74 (m, 2H), 7.54 (d, J = 9.2 Hz, 1H), 7.45–7.40 (m, 3H), 7.36–7.32 (m, 1H), 7.06 (dd, J = 9.2, 1.4 Hz, 1H), 6.68–6.65 (m, 1H), 6.48 (d, J = 8.3 Hz, 1H), 4.95 (d, J = 4.8 Hz, 2H), 4.69 (t, J = 5.0 Hz, 1H), 2.29 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.3, 148.1, 144.5, 144.3, 137.6, 134.2, 128.7 (2 × CH), 128.4 (2 × CH), 128.1, 127.9, 122.2, 122.0, 116.9, 116.6, 113.7, 108.4, 35.9, 18.5 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1619.

***N*-((6-Fluoro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3la).** Off-white solid; 58% yield; mp = 187–189 °C; FT-IR (neat): 3248, 3008, 1604, 1489, 1334, 1219, 848, 763, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (dd, J = 4.4, 2.4 Hz, 1H), 8.16 (dd, J = 5.1, 1.8 Hz, 1H), 7.72–7.70 (m, 2H), 7.56 (dd, J = 9.8, 5.1 Hz, 1H), 7.43–7.39 (m, 3H), 7.36–7.32 (m, 1H), 7.11–7.06 (m, 1H), 6.65 (dd, J = 6.8, 5.5 Hz, 1H), 6.48 (d, J = 8.3 Hz, 1H), 4.98 (d, J = 5.2 Hz, 2H), 4.83 (t, J = 4.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.14, 153.3 (J_{C-F} = 235 Hz), 148.0, 145.86, 145.84, 142.7, 137.6, 133.8, 128.8 (2 × CH), 128.3 (2 × CH), 128.1, 118.9 (J_{C-F} = 2.0 Hz), 117.8 (J_{C-F} = 9.0 Hz), 116.8 (J_{C-F} = 25 Hz), 113.8, 111.7, 111.3, 108.6, 35.5 ppm; HRMS (ESI) calcd for $C_{19}H_{16}FN_4^+$ $[M + H]^+$ 319.1354, found 319.1350.

***N*-((6-Bromo-2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl) methyl)pyridin-2-amine (3ma).** Off-white solid; 59% yield; mp = 177–179 °C; FT-IR (neat): 3232, 1597, 1411, 1327, 1280, 1095, 771, 732, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, J = 1.0 Hz, 1H), 8.19 (dd, J = 5.1, 1.0 Hz, 1H), 7.67–7.63 (m, 2H), 7.48–7.44 (m, 2H), 7.38–7.35 (m, 2H), 7.26–7.23 (m, 1H, overlapped with the residual signal), 6.70–6.67 (m, 1H), 6.53 (d, J = 8.4 Hz, 1H), 4.93 (d, J = 4.9 Hz, 2H), 4.88 (t, J = 4.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 148.1, 144.0, 143.5, 137.6, 134.3, 132.1, 129.5 (2 × CH), 129.0 (2 × CH), 128.6, 124.9, 118.08, 118.03, 114.1, 108.7, 107.4, 35.5 ppm; HRMS (ESI) calcd for $C_{19}H_{15}BrClN_4^+$ $[M + H]^+$ 413.0163, found 413.0154.

***N*-((6-Bromo-2-(4-bromophenyl)imidazo[1,2-*a*]pyridin-3-yl) methyl)pyridin-2-amine (3na).** White solid; 55% yield; mp = 183–185 °C; FT-IR (neat): 3248, 1597, 1481, 1411, 1327, 1273, 1080, 833, 771, 545 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.85 (s, 1H), 8.03 (d, J = 5.1 Hz, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 7.9 Hz, 2H), 7.59 (d, J = 9.4 Hz, 1H), 7.44–7.38 (m, 2H), 6.57 (t, J = 6.2 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 4.89 (s, 2H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 147.9, 144.1, 143.6, 137.7, 132.6, 132.0 (2 × CH), 129.8 (2 × CH), 128.6, 125.0, 122.6, 118.1, 114.1, 108.8, 107.4, 35.5 ppm; HRMS (ESI) calcd for $C_{19}H_{15}Br_2N_4^+$ $[M + H]^+$ 456.9658, found 456.9640.

***N*-((6-Methyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl) pyridin-2-amine (3oa).** Yellow solid; 74% yield; mp =

206–208 °C; FT-IR (neat): 3248, 1597, 1512, 1481, 1334, 1265, 1111, 979, 856, 771, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.17 (m, 1H), 8.16–8.13 (m, 2H), 7.97 (d, J = 7.0 Hz, 1H), 7.88–7.84 (m, 2H), 7.50–7.45 (m, 1H), 7.33–7.32 (m, 1H), 6.71–6.68 (m, 1H), 6.62–6.58 (m, 2H), 5.06 (t, J = 4.6 Hz, 1H), 4.94 (d, J = 4.8 Hz, 2H), 2.40 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 148.1, 146.9, 145.8, 141.4, 140.6, 137.6, 137.0, 128.5 (2 × CH), 123.9 (2 × CH), 123.6, 118.4, 116.0, 115.8, 113.9, 108.8, 35.4, 21.5 ppm; HRMS (ESI) calcd for $C_{20}H_{18}N_5O_2^+$ $[M + H]^+$ 360.1455, found 360.1439.

***N*-((2-(Thiophen-2-yl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3pa).** Off-white solid; 54% yield; mp = 149–151 °C; FT-IR (neat): 3224, 3055, 1597, 1388, 1280, 1149, 771, 725, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.21–8.18 (m, 2H), 7.59 (d, J = 9.1 Hz, 1H), 7.45–7.41 (m, 2H), 7.35 (dd, J = 5.1, 1.2 Hz, 1H), 7.21–7.16 (m, 1H), 7.09 (dd, J = 5.0, 3.7 Hz, 1H), 6.78 (t, J = 6.7 Hz, 1H), 6.67–6.64 (m, 1H), 6.48 (d, J = 8.4 Hz, 1H), 5.10 (d, J = 4.4 Hz, 2H), 4.76 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 147.9, 145.1, 138.9, 137.6, 137.0, 128.0, 127.9, 125.27, 125.21, 124.5, 117.3, 116.7, 113.7, 112.6, 108.7, 35.3 ppm; HRMS (ESI) calcd for $C_{17}H_{15}N_4S^+$ $[M + H]^+$ 307.1012, found 307.1014.

***N*-((2-(*tert*-Butyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3qa).** White solid; 60% yield; mp = 195–197 °C; FT-IR (neat): 3209, 2962, 1589, 1427, 1319, 1273, 779, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.14 (m, 1H), 8.01 (d, J = 6.8 Hz, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.43–7.39 (m, 1H), 7.14–7.10 (m, 1H), 6.71 (td, J = 6.8, 1.2 Hz, 1H), 6.65–6.62 (m, 1H), 6.43 (d, J = 8.4 Hz, 1H), 4.96 (d, J = 4.8 Hz, 2H), 4.33 (t, J = 4.8 Hz, 1H), 1.48 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 153.7, 148.1, 143.7, 137.4, 123.9, 123.6, 117.2, 115.4, 113.5, 112.0, 108.4, 36.0, 33.4, 31.2 ppm; HRMS (ESI) calcd for $C_{17}H_{21}N_4^+$ $[M + H]^+$ 281.1761, found 281.1761.

***N*-((6-Chloroimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3sa).** Brownish semi-solid; 33% yield; FT-IR (neat): 3248, 3079, 1597, 1481, 1288, 1072, 771, 732, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, J = 1.2 Hz, 1H), 8.15–8.13 (m, 1H), 7.54 (s, 1H), 7.49 (dd, J = 9.5, 0.9 Hz, 1H), 7.43–7.39 (m, 1H), 7.10 (dd, J = 9.6, 2.0 Hz, 1H), 6.65–6.62 (m, 1H), 6.46 (dt, J = 8.4, 1.0 Hz, 1H), 4.91 (t, J = 5.8 Hz, 1H), 4.85 (d, J = 5.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 157.6, 146.9, 143.4, 136.4, 133.0, 124.6, 122.8, 122.4, 119.5, 117.2, 112.4, 108.1, 34.2 ppm; HRMS (ESI) calcd for $C_{13}H_{12}ClN_4^+$ $[M + H]^+$ 259.0745, found 259.0744.

***N*-((2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyrimidin-3-yl)methyl) pyridin-2-amine (3ta).** Off-white solid; 61% yield; mp = 155–157 °C; FT-IR (neat): 3255, 1705, 1604, 1504, 1481, 1342, 1249, 1180, 1026, 840, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, J = 6.0 Hz, 1H), 8.43 (d, J = 2.2 Hz, 1H), 8.09 (d, J = 4.4 Hz, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.76–6.73 (m, 1H), 6.63 (t, J = 5.9 Hz, 1H), 6.52 (d, J = 8.3 Hz, 1H), 5.96 (br s, 1H), 4.94 (s, 2H), 3.81 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.8, 157.9, 149.7, 148.0, 146.9, 145.5, 138.1, 132.3, 129.8 (2 × CH), 125.7, 115.2, 114.2 (2 × CH), 113.5, 108.9, 108.5, 55.4, 35.2 ppm; HRMS (ESI) calcd for $C_{19}H_{18}N_5O^+$ $[M + H]^+$ 332.1506, found 332.1510.

***N*-((6-Phenylimidazo[2,1-*b*]thiazol-5-yl)methyl)pyridin-2-amine (3ua).** White solid; 53% yield; mp = 123–125 °C; FT-IR (neat): 3271, 3008, 1604, 1489, 1334, 1141, 918, 763, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15–8.13 (m, 1H), 7.71–7.68 (m, 2H), 7.58 (d, J = 4.5 Hz, 1H), 7.43–7.38 (m, 3H), 7.34–7.29 (m, 1H), 6.76 (d, J = 4.5 Hz, 1H), 6.65–6.62 (m, 1H), 6.40 (d, J = 8.4 Hz, 1H), 4.93 (d, J = 5.4 Hz, 2H), 4.74 (t, J = 4.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.1, 149.2, 147.9, 145.3, 137.6, 134.3, 128.7 (2 × CH), 127.7 (2 × CH), 127.5, 119.7, 118.5, 113.7, 112.2, 108.4, 36.3 ppm; HRMS (ESI) calcd for $C_{17}H_{15}N_4S^+$ $[M + H]^+$ 307.1012, found 307.1006.

5-Chloro-*N*-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ab). Off-white solid; 54% yield; mp = 158–160 °C; FT-IR (neat): 3242, 1597, 1470, 1413, 1328, 1281, 979, 842, 731cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, J = 5.2, 1.8 Hz, 1H), 8.09 (dd, J = 6.9 Hz, 1H), 7.81 (dd, J = 8.0 Hz, 2H), 7.59–7.56 (m, 3H), 7.47–7.43 (m, 1H), 7.20–7.16 (m, 1H), 6.74 (t, J = 6.8 Hz, 1H), 6.68–6.65 (m, 1H), 6.56 (d, J = 8.3 Hz, 1H), 5.07 (t, J = 5.0 Hz, 1H), 4.95 (d, J = 4.6 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5, 146.4, 145.2, 144.7, 137.4, 134.0, 128.8 (2 × CH), 128.4 (2 × CH), 128.1, 125.0, 124.3, 120.7, 117.5, 116.9, 112.6, 109.4, 35.7 ppm; HRMS (ESI) calcd for $C_{19}H_{16}ClN_4^+$ $[M + H]^+$ 335.1058, found 335.1061.

5-Bromo-*N*-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ac). Off-white solid; 52% yield; mp = 220–222 °C; FT-IR (neat): 3263, 1589, 1496, 1465, 1357, 1273, 987, 925, 817, 748, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 2.1 Hz, 1H), 8.11 (d, J = 6.8 Hz, 1H), 7.73 (d, J = 7.1 Hz, 2H), 7.63 (d, J = 9.0 Hz, 1H), 7.49 (dd, J = 8.8, 2.5 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.23–7.19 (m, 1H) 6.80 (t, J = 6.8 Hz, 1H), 6.39 (d, J = 8.8 Hz, 1H), 4.99 (d, J = 5.0 Hz, 2H), 4.70 (t, J = 5.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.7, 148.7, 145.2, 144.8, 139.9, 134.0, 128.8 (2 × CH), 128.5 (2 × CH), 128.1, 125.1, 124.3, 117.6, 116.8, 112.6, 110.0, 108.1, 35.6 ppm; HRMS (ESI) calcd for $C_{19}H_{16}BrN_4^+$ $[M + H]^+$ 379.0553, found 379.0549.

4-Methyl-*N*-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3ad). Off-white solid; 61% yield; mp = 190–192 °C; FT-IR (neat): 3278, 1612, 1519, 1481, 1396, 1342, 1257, 1172, 979, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, J = 6.9 Hz, 1H), 7.99 (d, J = 5.2 Hz, 1H), 7.77–7.57 (m, 2H), 7.62 (d, J = 9.0 Hz, 1H), 7.45–7.41 (m, 2H), 7.37–7.33 (m, 1H), 7.21–7.17 (m, 1H), 6.76 (t, J = 6.7 Hz, 1H), 6.49 (d, J = 5.1 Hz, 1H), 6.24 (s, 1H), 4.98 (d, J = 4.8 Hz, 2H), 4.72 (br s, 1H), 2.20 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.4, 148.7, 147.6, 145.2, 144.7, 134.2, 128.7 (2 × CH), 128.5 (2 × CH), 128.0, 124.9, 124.5, 117.5, 117.2, 115.4, 112.4, 108.5, 35.7, 21.2 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1596.

6-Methyl-*N*-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)methyl) pyridin-2-amine (3ae). Off-white solid; 43% yield; mp = 148–150 °C; FT-IR (neat): 3271, 2924, 1597, 1458, 1257, 1172, 779, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, J = 6.9 Hz, 1H), 7.79 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.38–7.32 (m, 2H), 7.21 (t, J = 7.6 Hz, 1H), 6.79 (t, J = 6.8 Hz, 1H), 6.53 (d, J = 7.3 Hz, 1H), 6.26 (d, J = 8.2 Hz, 1H), 4.99 (d, J = 5.1 Hz, 2H), 4.53 (br s, 1H), 2.42 (s, 3H)

ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.8, 157.1, 145.2, 144.8, 138.0, 134.3, 128.8 (2 × CH), 128.6 (2 × CH), 128.0, 124.9, 124.7, 117.6, 117.4, 113.0, 112.4, 104.6, 35.9, 24.5 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1604.

4-Methyl-*N*-((6-methyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3od). Yellow solid; 65% yield; mp = 220–222 °C; FT-IR (neat): 3248, 1604, 1512, 1481, 1342, 1172, 856, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.4 Hz, 2H), 8.05 (d, J = 8.1 Hz, 2H), 7.95 (d, J = 8.4 Hz, 2H), 7.38 (s, 1H), 6.67 (d, J = 7.0 Hz, 1H), 6.55 (d, J = 5.3 Hz, 1H), 6.32 (s, 1H), 4.98 (d, J = 4.8 Hz, 2H), 4.59 (t, J = 5.2 Hz, 1H), 2.42 (s, 3H), 2.25 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.2, 148.8, 147.7, 147.1, 145.9, 141.6, 140.8, 137.0, 128.6 (2 × CH), 124.0 (2 × CH), 123.7, 118.4, 116.1, 115.8, 115.7, 108.8, 35.6, 21.5, 21.2 ppm; HRMS (ESI) calcd for $C_{21}H_{20}N_5O_2^+$ $[M + H]^+$ 374.1612, found 374.1609.

5-Methyl-*N*-((6-methyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-2-amine (3of). Yellow solid; 70% yield; mp = 225–227 °C; FT-IR (neat): 3271, 1604, 1504, 1334, 1257, 1172, 856, 709 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.5 Hz, 2H), 7.95 (s, 1H), 7.90 (d, J = 6.9 Hz, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.30–7.24 (m, 2H), 6.54 (d, J = 7.9 Hz, 2H), 5.11 (t, J = 5.1 Hz, 1H), 4.85 (d, J = 5.0 Hz, 2H), 2.35 (s, 3H), 2.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.3, 147.5, 146.8, 145.7, 141.1, 140.5, 138.7, 136.9, 128.3 (2 × CH), 123.7 (2 × CH), 123.6, 122.7, 118.6, 115.8, 115.6, 108.4, 35.6, 21.4, 17.5 ppm; HRMS (ESI) calcd for $C_{21}H_{20}N_5O_2^+$ $[M + H]^+$ 374.1612, found 374.1610.

***N*-((2-Phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-4-amine (3ag).** White solid; 35% yield; mp = 166–168 °C; FT-IR (neat): 3240, 3024, 2862, 1597, 1481, 1388, 1180, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 4.1 Hz, 2H), 7.78 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 9.1 Hz, 1H), 7.45–7.41 (m, 3H), 7.36 (t, J = 7.3 Hz, 1H), 7.21 (*t*, J = 7.6 Hz, 1H), 6.79 (t, J = 6.8 Hz, 1H), 6.66 (t, J = 5.8 Hz, 1H), 6.45 (d, J = 8.4 Hz, 1H), 5.02 (d, J = 5 Hz, 2H), 4.59 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.2, 148.1, 145.3, 144.8, 137.6, 134.2, 128.8 (2 × CH), 128.6 (2 × CH), 128.1, 124.9, 124.5, 117.6, 117.1, 113.8, 112.5, 108.4, 35.7 ppm; HRMS (ESI) calcd for $C_{19}H_{17}N_4^+$ $[M + H]^+$ 301.1448, found 301.1452.

***N*-((2-(*p*-Tolyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)pyridin-4-amine (3bg).** Yellow semi-solid; 38% yield; FT-IR (neat): 3248, 3022, 2861, 1597, 1478, 1380, 1181, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 6.8 Hz, 2H), 7.69–7–63 (m, 3H), 7.43 (t, J = 7.2 Hz, 1H), 7.27–7.25 (m, 2H, overlapped with the residual signal), 7.21 (t, J = 7.5 Hz, 1H), 6.80 (t, J = 6.8 Hz, 1H), 6.66 (t, J = 6.2 Hz, 1H), 6.44 (d, J = 8.3 Hz, 1H), 5.02 (d, J = 4.4 Hz, 2H), 4.63 (br s, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.2, 147.9, 145.1, 144.7, 137.9, 137.6, 131.1, 129.5 (2 × CH), 128.4 (2 × CH), 124.9, 124.4, 117.4, 116.8, 113.6, 112.4, 108.4, 35.7, 21.4 ppm; HRMS (ESI) calcd for $C_{20}H_{19}N_4^+$ $[M + H]^+$ 315.1604, found 315.1606.

***N*-((2-Phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyrimidin-2-amine (3ai).** White solid; 49% yield; mp = 109–111 °C; FT-IR (neat): 3224, 3062, 1589, 1527, 1450, 1419, 1357, 1265, 1180, 802, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 6.6 Hz, 3H), 7.79 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.46 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 6.80 (t, J = 6.7 Hz, 1H), 6.56 (t, J = 4.8 Hz, 1H), 5.82 (t, J = 5.2 Hz, 1H), 5.09 (d, J = 5.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.0, 158.0 (2 × CH), 145.1, 144.8, 134.0, 128.7 (2 × CH), 128.5 (2 × CH), 128.0, 124.9, 124.3, 117.5, 116.7, 112.4, 111.3, 35.3 ppm; HRMS (ESI) calcd for $C_{18}H_{16}N_5^+$ $[M + H]^+$ 302.1400, found 302.1398.

***N*-((2-Phenylimidazo[1,2-*a*]pyridin-3-yl)methyl)pyrazin-2-amine (3aj).** Off-white solid; 51% yield; mp = 153–155 °C; FT-IR (neat): 3217, 3070, 1589, 1504, 1537, 1273, 1141, 1072, 995, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.04 (m, 2H), 7.99 (s, 1H), 7.86 (s, 1H), 7.68 (d, J = 7.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 1H), 7.38–7.31 (m, 3H), 7.19 (t, J = 7.3 Hz, 1H), 6.78 (t, J = 6.4 Hz, 1H), 5.28 (t, J = 5.0 Hz, 1H), 4.99 (d, J = 5.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.4, 145.2, 144.8, 141.8, 133.7, 133.4, 133.3, 128.8 (2 × CH), 128.3 (2 × CH), 128.1, 125.2, 124.2, 117.5, 116.5, 112.7, 34.8 ppm; HRMS (ESI) calcd for $C_{18}H_{16}N_5^+$ $[M + H]^+$ 302.1400, found 302.1395.

Bis(2-phenylimidazo[1,2-*a*]pyridin-3-yl)methane (4a). White solid; 32% yield; mp = 214–216 °C (lit.,[12] 216–218 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, J = 7.8 Hz, 4H), 7.54–7.49 (m, 6H), 7.44–7.40 (m, 2H), 7.33 (d, J = 6.8 Hz, 2H), 7.05 (t, J = 7.4 Hz, 2H), 6.47 (t, J = 6.7 Hz, 2H), 4.99 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.0, 144.1, 134.3, 129.0 (2 × CH), 128.9 (2 × CH), 128.3, 124.5, 123.9, 117.5, 114.3, 112.4, 19.8 ppm; HRMS (ESI) calcd for $C_{27}H_{21}N_4^+$ $[M + H]^+$ 401.1761, found 401.1756.

***N*-(Pyridin-2-yl)benzamide (5a).** White solid; 85% yield; mp = 83–85 °C (lit.,[15b] 82–84 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.22 (br s, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.12–8.11 (m, 1H), 7.93–7.90 (m, 2H), 7.75–7.70 (m, 1H), 7.55–7.51 (m, 1H), 7.47–7.43 (m, 2H), 7.01 (dd, J = 7.1, 5.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.1, 151.8, 147.8, 138.5, 134.4, 132.2, 128.8 (2 × CH), 127.4 (2 × CH), 119.9, 114.4 ppm; HRMS (ESI) calcd for $C_{12}H_{11}N_2O^+$ $[M + H]^+$ 199.0866, found 199.0861.

2-Phenylimidazo[1,2-*a*]pyridine-3-carbaldehyde (6a). White solid; 18% yield; mp = 129–131 °C (lit.,[15b] 128–130 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.06 (s, 1H), 9.65 (dt, J = 6.9, 1.2 Hz, 1H), 7.83–7.78 (m, 3H), 7.59–7.49 (m, 4H), 7.11 (td, J = 6.8, 1.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.6, 158.4, 147.8, 132.5, 130.4, 129.9 (2 × CH), 129.9, 128.99 (2 × CH), 128.93, 120.9, 117.5, 115.3 ppm; HRMS (ESI) calcd for $C_{14}H_{11}N_2O^+$ $[M + H]^+$ 223.0866, found 223.0862.

3-Methyl-2-phenylimidazo[1,2-*a*]pyridine (1a′). White solid; 75% yield; mp = 155–157 °C (lit.,[20] 157 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dt, J = 6.9, 1.2 Hz, 1H), 7.80–7.77 (m, 2H), 7.62 (dt, J = 9.0, 1.1 Hz, 1H), 7.47–7.43 (m, 2H), 7.35–7.31 (m, 1H), 7.16–7.12 (m, 1H), 6.80 (td, J = 6.8, 1.2 Hz, 1H), 2.60 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.4, 142.5, 135.0, 128.5 (2 × CH), 128.4 (2 × CH), 127.4, 123.5, 122.9, 117.5, 115.9, 112.0, 9.7 ppm; HRMS (ESI) calcd for $C_{14}H_{13}N_2^+$ $[M + H]^+$ 209.1073, found 209.1075

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

Financial support by the DST-FIST [SR/FST/CSI-270/2015] for the HRMS facility and central analytical lab BITS Pilani for NMR studies is acknowledged. O. P. S. Patel is thankful to SERB-New Delhi for national post-doctorate fellowship (File No. PDF/2017/001910) to carry out the research work. N. K. N. is thankful to CSIR, New Delhi, India for SRF.

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