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PAPER

CuBr catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehydes: Direct access to 3-formyl-2-phenyl-imidazo[1,2-a]pyridines

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Copper bromide catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehyde, directly produced 3-formyl 2-phenyl-imidazo[1,2-a]pyridines. The quantum chemical calculations were performed to trace the reaction mechanism and get insights on the possible reaction pathway. 2-Aminopyridines on coupling with cinnamaldehyde generates (*E*)-3-phenyl-3-(pyridin-2-ylamino)acrylaldehyde IV as a key intermediate which undergoes C-N bond formation reaction to produce 3-formyl-2-phenyl-imidazo[1,2-a]pyridines.

Introduction

Nitrogen heterocycles are known to possess diverse range of pharmacological activities.[1] Imidazo[1,2-a]pyridine is one of the medicinally important *N*-heterocycle[2] and is a pharmacophore of several drugs including zolpidem, alpidem (anxiolytics),[3] and GSK-812397 (anti-HIV) (Figure 1).[4] Furthermore, the radioiodinated imidazo[1,2-a]pyridines have been used for in-vivo SPECT imaging of amyloid-β deposition in mice model of Alzheimer's disease.[5]

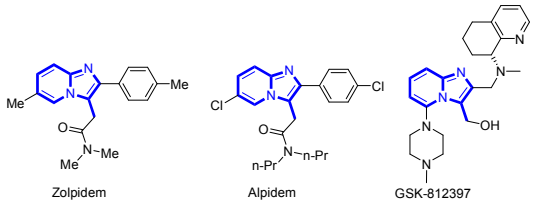

Figure 1. Structures of drugs containing 3-substituted imidazo[1,2-a]pyridine pharmacophore

The synthesis of anxiolytic drugs zolpidem and alpidem requires 3-formyl imidazo[1,2-a]pyridine as one of the key intermediate. There are several reports on the synthesis of imidazo[1,2-a]pyridines,[6] however, the direct access to 3-formyl 2-aryl imidazo[1,2-a]pyridines **3** is somewhat limited. There are only three reports in the literature, which are summarized in Figure 2. These include (a) [$Cu(hfacac)_2 \cdot xH_2O$] catalyzed cyclization of N-(1-phenylallyl)-2-aminopyridine in DMF;[7] (b) two-step approach involving first formation of imidazo[1,2-a]pyridines from 2-aminopyridine and phenacyl bromide, followed by Vilsmeier-Haack formylation.[8] (c) Cu-catalyzed selective C-3 formylation of imidazo[1,2-a]pyridine using DMSO.[9] Chioua *et. al.*[10] reported a silver catalyzed cycloisomerization of *N*-(prop-2-yn-1-yl) pyridine-2-amines leading to formation of non-aryl substituted 3-formyl imidazo[1,2-a]pyridines **3**.

Recently Hajra and coworkers[11] have reported synthesis of 3-aroylimidazo[1,2-*a*]pyridines via $Cu(OAc)_2$-catalyzed oxidative coupling of 2-aminopyridines with chalcones. Herein, we have successfully developed a CuBr catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehydes to produce 3-formyl imidazo[1,2-a]pyridines **3**. The major drawbacks of earlier reports are: (a) preparation of starting material is somewhat difficult[7] (b) synthesis required more than single step[8]; (c) high reaction temperature[7]; and (d) use of expensive silver triflate catalyst.[10] The present method utilizes commercially available starting materials **1a** and **2a** that requires less expensive CuBr catalyst. The plausible reaction mechanism based on the quantum chemical calculations has also been proposed.

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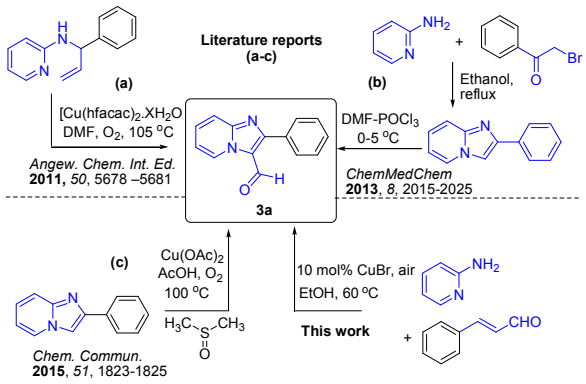
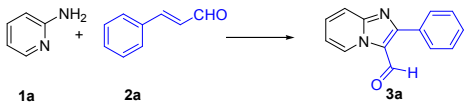


Figure 2. Methods for the preparation of 3-formyl-2-phenyl-imidazo[1,2-a]pyridines **3**.

Results and discussion

The study was initiated with preliminary reaction of 2-aminopyridine **1a** with cinnamaldehyde **2a** in the presence of various catalysts in an air atmosphere and under heating condition. The use of acid catalysts such as triflic acid or TFA did not produce desired product (Table 1, entries 1-2). Next, we screened various other catalysts such as molecular iodine (entry 3), $Pd(OAc)_2$ (entries 4-6), Fe catalysts (entries 7-8), Co catalysts (entries 9-10) and Cu catalysts (entries 11-14). Except copper catalysts (entries 11-14), no other catalyst produced desired product **3a**. $CuSO_4$ and $CuCl_2$ produced moderate yields (25-30%) of product **3a**; however CuBr produced excellent yield (90%) in ethanol as a solvent at 60 °C reaction temperature. This condition (entry 14) was chosen for further experiments. Reaction does not proceed in the case of a control experiment involving CuBr in ethanol under inert atmosphere (in nitrogen atmosphere), indicating the role of air in the reaction.

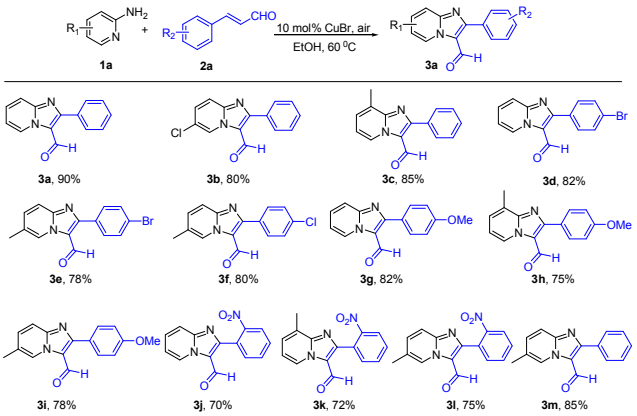
Table 1. Optimization studies[a,b]



Entry	Catalyst (mol%)	Solvent	Temp. (°C)	% yield[c]
1	Triflic acid (100)	EtOH	80	0
2	TFA (100)	none	80	0
3	I_2 (10)	Ethanol	80	0
4	$Pd(OAc)_2$ (10)	Acetic acid	100	0
5	$Pd(OAc)_2$ (10)	Chlorobenzene	100	0
6	$Pd(OAc)_2$ (10)	Dioxane	100	0
7	$Fe(OAc)_2$ (10)	Dioxane	100	0
8	$FeCl_3$ (10)	Dioxane	100	0
9	$CoCl_2$ (10)	DMF	100	0
10	$Co(OAc)_2$ (10)	DMF	100	0
11	$CuSO_4$ (10)	DMF	100	25
12	$CuCl_2$ (10)	DMF	100	30
13	CuBr (10)	DMF	80	60
14[d]	**CuBr** (10)	**EtOH**	**60**	**90**

[a] all reaction were performed in open air atmosphere; [b] **1a** (1.0 equiv.), **2a** (1.2 equiv.) and catalyst (wherever mentioned) in a mentioned solvent; [c] Isolated yields after silica gel column chromatography; [d] optimized reaction condition.

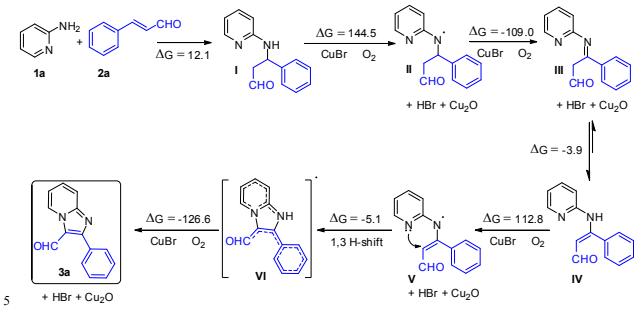
With the optimized reaction conditions in hand, the utility of this approach was investigated for coupling of various substituted 2-aminopyridines and cinnamaldehydes. As shown in Scheme 1, various substituted 2-aminopyridines were well tolerated in the reaction. 2-Aminopyridines with electron-donating groups such as 3-methyl, 5-methyl (examples **3c, 3e, 3f, 3h, 3i, 3k, 3l, 3m**), as well as electron-withdrawing groups such as Cl (example **3b**) participated well in the reaction. The reaction also worked well with cinnamaldehydes substituted with electron-donating groups (e.g. methoxy – examples **3g**, **3h**, **3i**), as well as electron-withdrawing groups (e.g. Br, Cl, NO_2 – examples **3d, 3e, 3f, 3j, 3k, 3l**) producing corresponding 3-formyl-2-phenyl-imidazo[1,2-a]pyridines in good yields. Next, we investigated the scope of this reaction for crotonaldehyde (aliphatic enal); however reaction does not proceeded.



Scheme 1. Substrate scope for synthesis of 3-formyl-2-phenyl-imidazo[1,2-a]pyridines **3a-m** by variation of 2-aminopyridine and cinnamaldehydes. Reagents and conditions: **1** (1.0 equiv.), **2** (1.2 equiv.), CuBr (10 mol%)/ air, ethanol, 60 °C, 8 h.

On the basis of the results obtained above, we proposed a plausible reaction mechanism for coupling of 2-aminopyridines and cinnamaldehydes as illustrated in Scheme 2, and verified its feasibility using quantum chemical analysis (B3LYP/6-311+G(d,p)). The reaction may undergo the following steps. The first step involves a coupling of 2-aminopyridine **1a** and cinnamaldehyde **2a** to produce the Michael addition intermediate **I**. This step is slightly endoergic with a Gibbs free energy difference (ΔG) of 12.1 kcal/mol. The intermediate **I** in the presence of copper catalyst loose a hydrogen radical and generate a radical intermediate **II** with HBr and Cu_2O as side products. This step is highly endoergic and requires free energy of 144.5 kcal/mol. The radical intermediate **II** further looses one hydrogen radical to give neutral imine intermediate **III**. Formation of **III** from **II** is highly exergonic (109.0 kcal/mol). The imine **III** then equilibrates to enamine **IV**, which is more stable by 3.9 kcal/mol. Similarly, H-radical abstraction from intermediate **IV** in the presence of copper catalyst generates a radical **V**, which is endoergic by 112.8 kcal/mol. The radical **V** undergoes 1,3-H shift and cyclize to give an intermediate **VI** which is stable by 5.1 kcal/mol. Finally, intermediate **VI** looses one more hydrogen radical to give the product **3a**. This step is exoergic by 126.6 kcal/mol.

The formation of Cu_2O as a byproduct in the reaction was also supported by experimental observations. The initial green color of the reaction was changed to red at the completion (after 8 h), indicating the conversion of CuBr (green) to Cu_2O (red).



Scheme 2. Plausible mechanism for the preparation of 3-formyl-2-phenyl-imidazo[1,2-a]pyridine **3a**. The Gibbs free energy values at each step are given in kcal/mol.

Conclusions

In conclusion, we have successfully developed a copper (II) catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehydes for one-pot synthesis of 3-formyl-2-phenyl-imidazo[1,2-a]pyridines. Developed method is operationally simple and could be used efficiently for the preparation of biologically important drugs. This may also serve as an excellent method for C-N bond formation to study its scope in other reactions.

Experimental Section

General. All chemicals were obtained from Sigma-Aldrich Company and used as received. ^{1}H, ^{13}C and DEPT NMR spectra were recorded on Brucker-Avance DPX FT-NMR 500 and 400 MHz instruments. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvent ($CDCl_3$, 7.26 ppm). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 125 MHz or 100 MHz: chemical data for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent ($CDCl_3$, 77 ppm). ESI-MS and HRMS spectra were recorded on Agilent 1100 LC-Q-TOF and HRMS-6540-UHD machines. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. Melting points were recorded on digital melting point apparatus.

General procedure for synthesis of imidazo[1,2-a]pyridine carbaldehydes (3a-3m). To the mixture of 2-aminopyridine (1.0 equiv.) and cinnamaldehyde (1.2 equiv.) in ethanol was added 10 mol% CuBr and reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction (monitored by TLC), the reaction mixture was filtered using Whatman paper. The filtrate was dried on rotavapor and was then extracted between water ethyl acetate. EtOAc layer was dried over anhydrous sodium sulphate and evaporated on vacuo rotavapor to get crude product. The crude product was purified by silica gel (#100-200) column chromatography using n-hexane and EtOAc as an eluent to get pure products **3a-m** in 70-90% yield.

*2-Phenyl-imidazo[1,2-a]pyridine-3-carbaldehyde (**3a**).*[12] Yellow solid; m.p. 122-123 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.07 (s, 1H), 9.68 (d, J = 8.0 Hz, 1H), 7.85-7.81 (m, 3H), 7.61-7.53 (m, 4H), 7.14 (t, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 179.7, 158.4, 147.8, 132.3, 130.5, 129.9, 129.8, 128.9, 128.8, 120.8, 117.5, 115.4; IR ($CHCl_3$): ν_{max} 2924, 1646, 1634, 1494, 1407, 1326, 1248 cm^{-1}; ESI-MS: *m/z* 223.00 $[M+H]^+$; HR-ESIMS: *m/z* 223.0878 calcd for $C_{14}H_{10}N_2O+H^+$ (223.0866).

*7-Chloro-2-phenyl-imidazo[1,2-a]pyridine-3-carbaldehyde (**3b**):*[13] Yellow solid; m.p. 149-150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.07 (s, 1H), 9.75 (s, 1H), 7.85-7.81 (m, 2H), 7.76 (d, J = 12.0 Hz, 1H), 7.56-7.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.8, 158.4, 146.0, 131.9, 131.6, 130.1, 129.8, 129.0, 126.8, 123.5, 120.8, 117.7; IR ($CHCl_3$): ν_{max} 2921, 1641, 1406, 1018 cm^{-1}; ESI-MS: *m/z* 256.90 $[M+H]^+$; HR-ESIMS: *m/z* 257.0471 calcd for $C_{14}H_9ClN_2O+H^+$ (257.0476).

*8-Methyl-2-phenyl-imidazo[1,2-a]pyridine-3-carbaldehyde (**3c**):*[14, 15] Yellow solid; m.p. 169-170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.04 (s, 1H), 9.53 (d, J = 8.0 Hz, 1H), 7.85 (dd, J = 4.0, 8.0 Hz, 2H), 7.53 (m, 3H), 7.39 (d, J = 8.0 Hz, 1H), 7.04 (t, J = 8.0 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.6, 158.0, 148.0, 132.7, 130.0, 129.7, 129.4, 128.8, 127.6, 126.5, 121.2, 115.2, 115.3, 17.0; IR ($CHCl_3$): ν_{max} 2925, 1638, 1409, 1018 cm^{-1}; ESI-MS: *m/z* 236.90 $[M+H]^+$; HR-ESIMS: *m/z* 237.1005 calcd for $C_{15}H_{12}N_2O+H^+$ (237.1022).

*2-(4-Bromophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**3d**):*[7] Yellow solid; m.p. 175-176 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.05 (s, 1H), 9.67 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 12.0 Hz, 1H), 7.73 (dd, J = 8.0, 16.0 Hz, 4H), 7.61 (t, J = 8.0 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6, 156.5, 147.3, 131.7, 130.7, 130.1, 128.4, 124.1, 117.0, 115.0; IR ($CHCl_3$): ν_{max} 2912, 2852, 1730, 1636, 1400, 1257, 1210 cm^{-1}; ESI-MS: *m/z* 300.90 $[M+H]^+$; HR-ESIMS: *m/z* 300.9980 calcd for $C_{14}H_9BrN_2O+H^+$ (300.9971).

*2-(4-Bromophenyl)-6-methylimidazo[1,2-a]pyridine-3-carbaldehyde (**3e**):* Yellow solid; m.p. 173-174 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.01 (s, 1H), 9.48 (s, 1H), 7.72-7.68 (m, 5H), 7.47 (dd, J = 4.0, 8.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.0, 156.8, 146.7, 133.6, 132.1, 131.5, 131.2, 126.9, 125.8, 124.4, 120.5, 116.7, 18.4; IR ($CHCl_3$): ν_{max} 2924, 2843, 1726, 1633, 1420, 1256, 809 cm^{-1}; ESI-MS: *m/z* 314.80 $[M+H]^+$; HR-ESIMS: *m/z* 315.0130 calcd for $C_{15}H_{11}BrN_2O+H^+$ (315.0128).

*2-(4-Chlorophenyl)-6-methylimidazo[1,2-a]pyridine-3-carbaldehyde (**3f**):*[16] Pale yellow solid; m.p. 167-168 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.01 (s, 1H), 9.48 (s, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.1, 156.8, 146.7, 136.1, 133.6, 131.0, 129.2, 126.9, 125.8, 120.5, 116.7, 18.4; IR ($CHCl_3$): ν_{max} 3436, 1633, 1413, 1020 cm^{-1}; ESI-MS: *m/z* 271.06 $[M+H]^+$; HR-ESIMS: *m/z* 271.0600 calcd for $C_{15}H_{11}ClN_2O+H^+$ (271.0633).

*2-(4-Methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**3g**)*:[8] White solid; m.p. 171-172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.06 (s, 1H), 9.67 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 3H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 179.6, 161.1, 158.4, 147.8, 131.2, 130.5, 128.9, 124.8, 120.5, 117.2, 115.1, 114.4, 55.5; IR ($CHCl_3$): ν_{max} 2918, 2850, 1733, 1634, 1409, 1253, 1215 cm^{-1}; ESI-MS: *m/z* 253.10 $[M+H]^+$; HR-ESIMS: *m/z* 253.1000 calcd for $C_{15}H_{12}N_2O_2$ +H^+ (253.0972).

*2-(4-Methoxyphenyl)-8-methylimidazo[1,2-a]pyridine-3-carbaldehyde (**3h**)*:[14] Brown solid; m.p. 165-166 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.02 (s, 1H), 9.48 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 12.0 Hz, 2H), 3.88 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 179.4, 161.0, 158.1, 146.8, 133.2, 131.1, 126.9, 125.2, 125.0, 120.3, 116.5, 114.4, 55.4, 18.3; IR ($CHCl_3$): ν_{max} 3436, 1636, 1415, 1219, 1020 cm^{-1}; ESI-MS: *m/z* 266.90 $[M+H]^+$; HR-ESIMS: *m/z* 267.1125 calcd for $C_{16}H_{14}N_2O_2$+H^+ (267.1128).

*2-(4-Methoxyphenyl)-6-methylimidazo[1,2-a]pyridine-3-carbaldehyde (**3i**)*:[7] Yellow solid; m.p. 119-120 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.01 (s, 1H), 9.47 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 12.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 180.7, 162.3, 159.4, 148.0, 134.5, 132.4, 128.2, 126.5, 126.3, 117.7, 115.7, 56.7, 19.6; IR ($CHCl_3$): ν_{max} 2916, 1733, 1633, 1383, 1019 cm^{-1}; ESI-MS: *m/z*; 267.00 $[M+H]^+$; HR-ESIMS: *m/z* 267.1100 calcd for $C_{16}H_{14}N_2O_2$ + H^+ (267.1128).

*2-(2-Nitrophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**3j**)*:[17] Pale yellow solid; m.p. 197-198 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.80 (s, 1H), 9.62 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.80 (dd, *J* = 8.0, 20 Hz, 2H), 7.71-7.60 (m, 3H), 7.19 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.9, 154.3, 149.7, 148.2, 133.1, 132.7, 130.7, 130.6, 128.7, 127.3, 125.0, 121.4, 117.8, 115.9; IR ($CHCl_3$): ν_{max} 3436, 1643, 1533, 1494, 1323, 1117 cm^{-1}; ESI-MS: *m/z* 267.90 $[M+H]^+$; HR-ESIMS: *m/z* 268.0710 calcd for $C_{14}H_9N_3O_3$ + H^+ (268.0717).

*8-Methyl-2-(2-nitrophenyl)H-imidazo[1,2-a]pyridine-3-carbaldehyde (**3k**)*: Brown solid; m.p. 142-143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.77 (s, 1H), 9.47 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 4.0 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 2.66 (s, 3H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 177.0, 153.8, 150.1, 148.0, 133.2, 132.7, 132.6, 130.5, 129.7, 128.0, 126.3, 124.9, 115.8, 16.9; IR ($CHCl_3$): ν_{max} 3436, 2917, 1733, 1639, 1465, 1377, 1019 cm^{-1}; ESI-MS: *m/z* 282.09 $[M+H]^+$; HR-ESIMS: *m/z* 282.0900 calcd for $C_{15}H_{11}N_3O_3$+H^+ (282.0873).

*6-Methyl-2-(2-nitrophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (**3l**)*: Yellow solid; m.p. 135-136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.76 (s, 1H), 9.43 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.69-7.64 (m, 3H), 7.48 (d, *J* = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.8, 154.2, 150.1, 146.7, 133.6, 133.1, 132.6, 130.5, 126,7, 126.2, 124.9, 121.1, 117.0, 18.4; IR ($CHCl_3$): ν_{max} 3435, 2918, 1731, 1641, 1534, 1215 cm^{-1}; ESI-MS: *m/z* 282.09 $[M+H]^+$; HR-ESIMS: *m/z* 282.0900 calcd for $C_{15}H_{11}N_3O_3$+H^+ (282.0873).

*6-Methyl-2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (**3m**)*: Yellow sticky solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.70 (s, 1H), 9.48 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.51 (s, 3H), 7.45 (d, *J* = 8.0 Hz, 1H), 2.44 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.6, 158.1, 146.6, 133.4, 132.3, 129.9, 129.8, 128.9, 126.8, 125.7, 120.5, 116.6, 18.4; IR ($CHCl_3$): ν_{max} 3436, 2924, 1724, 1594, 1442, 1275, 1018 cm^{-1}; ESI-MS: *m/z* 237.20 $[M+H]^+$; HR-ESIMS: *m/z* 237.1020 calcd for $C_{15}H_{12}N_2O$+H^+ (237.1022).

DFT studies. Density functional (DFT) analysis was carried out to explore the reaction mechanism for CuBr catalyzed synthesis of 3-formyl-2-phenyl-imidazo[1,2-a]pyridines from 2-aminopyridine and cinnamaldehyde. The GAUSSIAN09 suite of programs was used to carry out the geometry optimization of all the structures on the possible reaction mechanism pathways and to estimate the Gibbs free energy values at each step. Complete optimizations without any symmetry constraints were carried out using Becke−Lee−Yang−Parr (B3LYP) method with the 6-311+G(d,p) basis set. Same basis set was used to analytically compute frequencies to characterize the stationary points to minima and the transition states. Each transition state is a first-order saddle point with only one imaginary vibrational mode on the potential energy surface.

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