EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

Title: A Direct Access to Halogenated Fused Imidazo[1,5-a]N-heteroaromatics via Copper Promoted Double Oxidative C□H Amination and Halogenation

Authors: Sandeep Mummadi, Swati Patil, Sravani Boda, and Rajender Kallu Reddy

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201800628

Link to VoR: http://dx.doi.org/10.1002/ejoc.201800628

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201800628

WILEY-VCH

A Direct Access to Halogenated Fused Imidazo[1,5-*a*]*N*-heteroaromatics *via* Copper Promoted Double Oxidative C–H Amination and Halogenation

Mummadi Sandeep,[a,b] Patil Swati Dushyant, Boda Sravani and Kallu Rajender Reddy.*[a,b]

Dedication ((optional))

Abstract: An aerobic copper promoted double oxidative C–H amination and halogenation tandem reaction of 2- methylazarenes with aliphatic amines or amino acids have been developed, by employing copper salts as catalysts as well as halogen sources and molecular oxygen as a sole oxidant. This protocol is operationally simple and enables the direct access to functionalized fused imidazoles in one pot operation with good functional group tolerance. The synthetic utility of the method has been tested for Suzuki cross coupling reaction and the product obtained in good yield.

Introduction

Fused imidazo[1,5-*a*]*N*-heteroaromatics are important structural motifs in many biologically active compounds such as NK1 receptor ligands,[1] phosphodiesterase10A (PDE10A) inhibitors,[2] tubulin polymerization inhibitors[3] and thromboxane A_2 synthesis inhibitors (Figure 1).[4] Moreover, imidazo[1,5-*a*]isoquinolinedione is a unique example of a naturally occurring tricyclic cribrostatin 6, a highly active antimicrobial and antineoplasic agent.[5] In addition, they have potential applications in organic light-emitting diodes (OLED)[6] and thin-layer field effect transistors (FET).[7] Therefore, method development for accessing these important structural motifs is of highly interest in synthetic organic chemistry. Traditionally, imidazo[1,5-*a*]*N*-heteroaromatics were prepared through Vilsmeier-type cyclization,[8] which involved the use of *N*-2-pyridylmethylamides as substrates. Recent efforts on C-H amination strategy also provided a complementary way to access imidazo[1,5-*a*]*N*-heteroaromatics. Zeng[9a] and Xu[9b] have independently developed copper catalyzed oxidative cyclizations of *N*-heteroaryl aldehydes or ketones with alkylamines to afford imidazo[1,5-*a*]*N*-heteroaromatics (Scheme 1a). Interestingly, Wang has reported a new method to obtain the imidazo[1,5-*a*]*N*-pyridines *via* sequential dual oxidative amination of C(sp3)−H bonds by using stoichiometric amount of *N*-iodobutanimide[9c] (Scheme 1b). A slightly modified version using catalytic amount of CuI was reported later by Adimurthy and co-workers.[9d] Further, Li *et al* has developed a copper promoted cascade reaction of 2-methylquinolines with benzylamines to get the imidazo[1,5-*a*]*N*-quinolines *via* double -oxidative C−H amination strategy (Scheme 1c).[9e] Recently, Zhang has reported an aerobic copper-catalyzed halocyclization reaction of methyl *N*-heteroaromatics with aliphatic amines to obtain imidazo[1,5-*a*]*N*-heteroaryl halides in the presence of excess lithium halides as halogen source (Scheme 1d).[9f]

Aerobic copper catalyzed/mediated C-H bond functionalization is one of the most powerful strategy for carbon-carbon and carbon-heteroatom bond formations.[9e,10] Among which, direct aryl C-H halogenation is of particular importance in organic chemistry. For example, in majority of classical cross-coupling reactions such as Heck, Suzuki and Buchwald–Hartwig reactions aryl halides are used as starting materials.[11] Conventionally, halogenation reactions are done by using various halogen sources such as bromine, hypobromites and iodine, etc.[12] Aerobic copper catalyzed/mediated halogenations of arenes and heteroarenes have also been elegantly demonstrated to obtain green and efficient halogenations.[9f,13] However, direct access to heteroaryl halides from readily available starting materials, *in situ* introduction of halogens to the newly constructed heteroaryl ring in one operation, have not been well explored. In continuation of our efforts on copper catalyzed or mediated oxidative cross coupling reactions,[14] herein we report an aerobic copper mediated double oxidative C-H amination and halogenation reaction for the synthesis of imidazo [1,5-*a*]*N*-heteroarylhalides from 2-methylazarenes and aliphatic amines or amino acid.

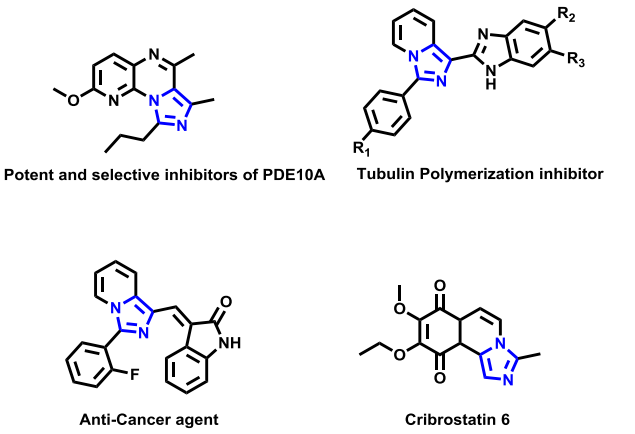


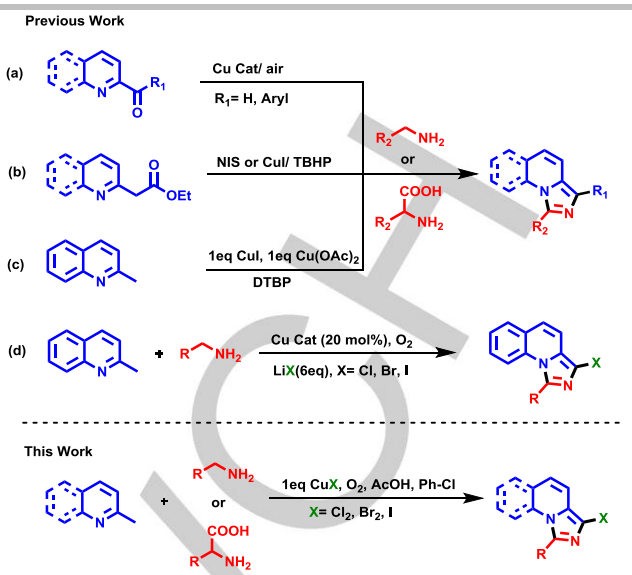
Figure 1: Representative examples of biologically active imidazo[1,5-*a*]*N*-heteroaromatics.

[a] Catalysis and Fine Chemicals Division, CSIR– Indian Institute of Chemical Technology, Tarnaka, Hyderabad– 500007, India
E-mail: rajender@iict.res.in
http://www.iictindia.org/staffprofiles/staffprofile.aspx?qry=1590
[b] Academy of Scientific and Innovative Research, New Delhi-110025, India.
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

Results and Discussion

To indentify the best reaction conditions, we began our studies for aerobic copper mediated halo cyclization reaction with 2-methylquinoline **1a** and benzylamine **2a** as model substrates. First, the reaction was performed with 1 eq of $CuBr_2$, 20 mol% PivOH acid in chlorobenzene at 120 °C under 1atm O_2 for 6 h, and resulted the desired bromimated fused imidazole product **3aa** in 63% yield (Table 1, entry 1). While CuBr gave the desired product in 33% yield (Table 1, entry 2). In the absence of copper salt, the reaction did not proceed at all (Table 1, entry 3). This result indicates the essential role of copper salt in this transformation. Subsequently, the effect of solvents on this reaction were examined with polar and less polar solvents, which were ineffective or less effective for this reaction (Table 1, entries 4-6). Decrease or increase the reaction temperature led the lower yields (Table 1, entry 7). Next, we examined the effect of copper loading on the reaction, increasing the copper salt loading as 1.5 eq, no improvement was observed in the product yield (Table 1, entry 8). In the absence of acid, the reaction gave lower yield, which indicated the necessity of the acid in this reaction (Table 1, entry 9). Then, we examined the role of different acids, in AcOH product yield was improved to 73% (Table 1, entry 10). While in CF_3COOH only 36% product yield was observed (Table 1, entry 11). Further, increasing or lowering the amount of AcOH resulted lower yields (Table 1, entry 12). To verify the role of copper in catalytic amount, we examined the reaction with 20 mol% of $CuBr_2$, $CuCl_2$ and $Cu(OAc)_2$ salts and 2 equiv of KBr as bromine source, unfortunately no product formation was observed (Table 1, entries 13-15).

With the optimal conditions in hand, we next investigated the substrate scope of benzylamine derivatives with 2-methylquinoline under the standard reaction conditions (Table 2). Benzylamine derivatives with electron-donating (-Me, -OMe) and electron-withdrawing (-F, -Cl, $-CF_3$) groups were well tolerated, and the corresponding products were isolated in moderate to good yields (**3aa-3aj**). The electronic effects of the groups on the aromatic ring of benzylamines had little influence on the product yields. Electron donating groups on the aromatic ring gave slightly better yields (**3ab-3af**) than electron withdrawing groups (**3ag-3aj**). However, steric effects had an obvious influence on the reaction since 2-methylbenzylamine gave lower yield (**3ad**) than 4-methylbenzylamine (**3ac**). Moreover, ring fused and heterocyclic benzylamines also could undergo the reaction smoothly and provided the corresponding products in good yields (**3ak, 3al**). Additionally, the present system is applicable to simple aliphatic amines, and the corresponding products were obtained in good yields (**3am-3ao**).



Scheme 1. C-H Amination based strategies for the synthesis of imidazo[1,5-*a*]heteroarenes and imidazo[1,5-a]heteroarylhalides.

Subsequently, we investigated the substrate scope with various 2-methylquinoline and substituted benzylamines to afford the corresponding products under the optimized reaction conditions (**Table 3**). Electron donating (-Me, -OMe) and electron withdrawing groups (-F, -Br) on the aromatic ring of quinolines well reacted with benzylamines, and furnished the corresponding products in moderate to good yields. Comparatively, electron donating groups provided better yields (**3ba-3be**) than electron withdrawing groups (**3bf-3bi, 3bm-3bo**). Interestingly, 6-chloro-2-methylquinoline gave the corresponding products in good yield (**3bj-3bl**).

We next explored the possibility of extending this strategy with 1-methylisoquinoline. The reaction was performed under standard conditions with benzylamine and its derivatives **(Table 4)**. Interestingly the corresponding fused [5,1-a] isomeric products were obtained in good yields **(3ca-3cc)**. In addition, hetero aromatic amine and simple aliphatic amine also well tolerated, and afforded the corresponding products in good yields **(3cd-3ce)**.

Recently, Xu and wang have independently shown copper/iodine co-catalysed and iodine mediated decarboxylative cyclization of α-aminoacids towards the synthesis of fused[1,5-a]*N*-heteroaromatics.[15] To our delight reaction with phenylglycine as an aliphatic amine source also proceeded under the present conditions resulting in halogenated fused[1,5-a] imidazoles in good yields **(3da-3de, Table 5)**. Further, 1-methylisoquinoline also afforded the corresponding [5,1-a] isomer in good yield **(3df)**.

10.1002/ejoc.201800628

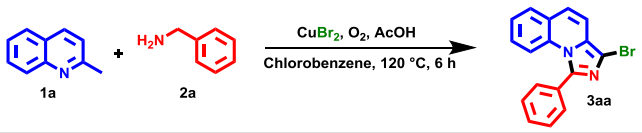
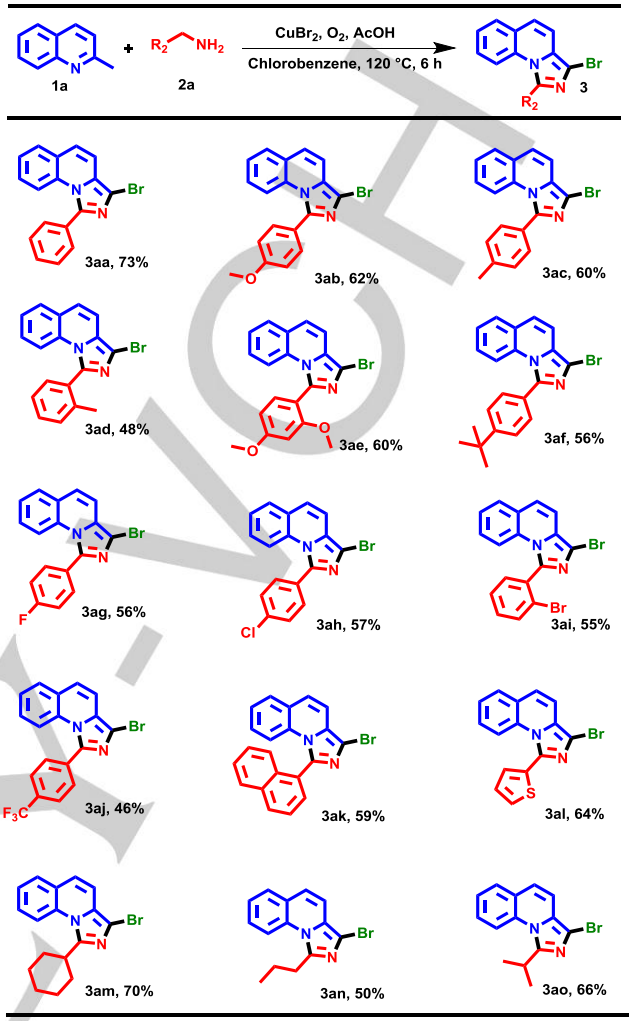


Table 1. Optimization of reaction conditions.[a,b]

Entry	Copper salt	Acid	Solvent	Yields of 3aa[b]
1	$CuBr_2$	PivOH	PhCl	63%
2	CuBr	PivOH	PhCl	33%
3	-	PivOH	PhCl	-
4	$CuBr_2$	PivOH	DMSO	-
5	$CuBr_2$	PivOH	DMF	-
6	$CuBr_2$	PivOH	$t(C_4H_9)Ph$	32%
7[c]	$CuBr_2$	PivOH	PhCl	37, 31%
8[d]	$CuBr_2$	PivOH	PhCl	63%
9	$CuBr_2$	-	PhCl	34%
10	**$CuBr_2$**	**AcOH**	**PhCl**	**73%**
11	$CuBr_2$	CF_3COOH	PhCl	36%
12[e]	$CuBr_2$	AcOH	PhCl	56, 60%
13[f]	$CuBr_2$	AcOH	PhCl	-
14[f]	$CuCl_2$	AcOH	PhCl	-
15[f]	$Cu(OAc)_2$	AcOH	PhCl	-

[a] Reaction conditions: 1a (0.5 mmol, 1equiv), 2a (0.75 mmol, 1.5 equiv), Cu-salt (0.5 mmol), acid (20 mol-%), solvent (4 mL), 120 °C, under 1 atm O_2, 6 h. [b] Isolated yields. [c] Yields are with respect to 110 °C, 130 °C. [d] Yield with respect to 1.5 equiv of $CuBr_2$. [e] Yield with respect to 40, 10 mo-l% of AcOH. [f] 20 mol-% catalyst and 2 equiv of KBr.

Table 2: Scope of benzylamine derivatives.[a, b]



[a] Reaction conditions: 1a (0.5 mmol), 2a (0.75 mmol), $CuBr_2$ (0.5 mmol), AcOH (20 mol-%), Chlorobenzene (4 mL), 120 °C, 6 h, under 1 atm O_2 (using O_2 ballon). [b] Isolated yields.

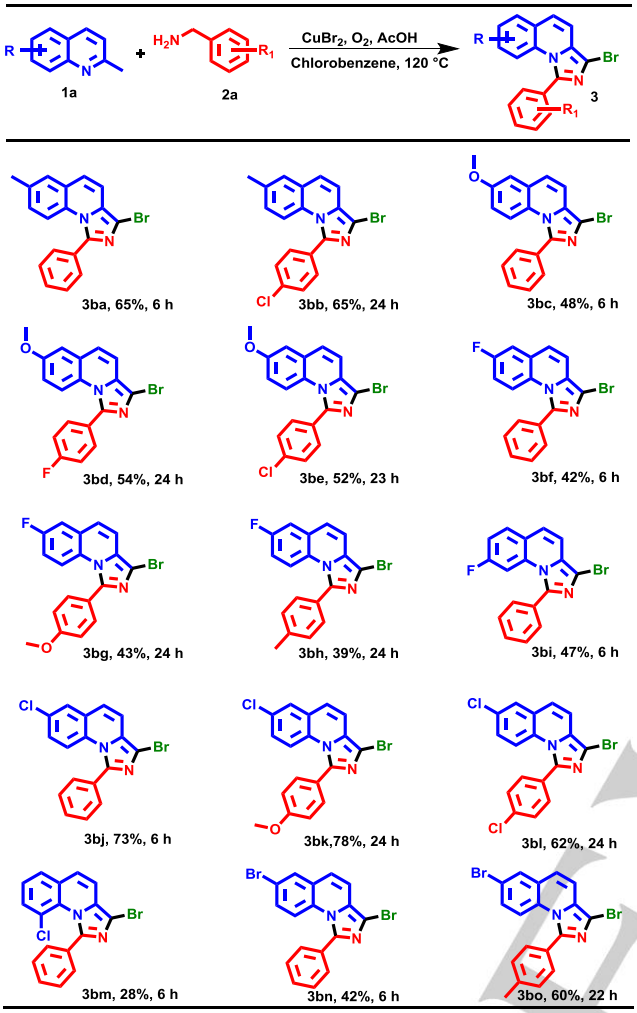
In addition to the above bromocyclization reaction, we further wished to incorporate other halogens into the product by the suitable copper salts. As shown in the **Table-6**, reactions of 2-methylquinoline and benzylamine derivatives using $CuCl_2$ and CuI afforded the chloro- and iodo- cyclized products in good yields **(3ea-3ee)**. Similarly, reaction with 1-methylisoquinoline and benzylamine using CuI resulted the 1-iodo fused imidazole product in good yield **3ef)**.

Further investigations were also attempted to explore the possibility of extending the present strategy to simple 2-methyl pyridine derivatives. Interestingly, reactions with 2-methylpyridine and benzylamine derivatives also underwent the iodocyclization reaction smoothly providing the iodo fused ring produts in moderate yeilds (**3fa-3fk, Table 7)**. On the other hand, the reactions with chloro- and bromo- salts, a trace amount of corresponding products were obtained **(3fl-3fm)**.

To establish a possible mechanism of aerobic copper mediated bromocyclization reaction, several control experiments were carried out (**Scheme 2**). First, the reaction of **1a** and **2a** under the standard condition was interrupted after 15 min and the resulting products were identified as simple cyclized product (**3aa-1** in 30%) and 2-(bromo methyl)quinoline (**1a-1** in 17%). Further **1a-1** was coupled with **2a** to afford the product **3aa** in 80%. Similarly, **3aa-1** underwent the direct bromination to provide the desired product **3aa** in 90%. These results suggest that **1a-1**, and **3aa-1** are the main reaction intermediates. Similalry, the bromination of simple cyclised product **3aa-1** with radical scavenger (**TEMPO**) under standard conditions resulted the quantative formation final product **3aa,** indicating that the transformation from **3aa-1 to 3aa** is mainly ionic and not the radical pathway. The reaction between **1a** and **2a** in the presence of TEMPO also provided the desired **3aa** product in 70%, showing that radical intermediates are not involved in the present halo-cyclizations.

10.1002/ejoc.201800628

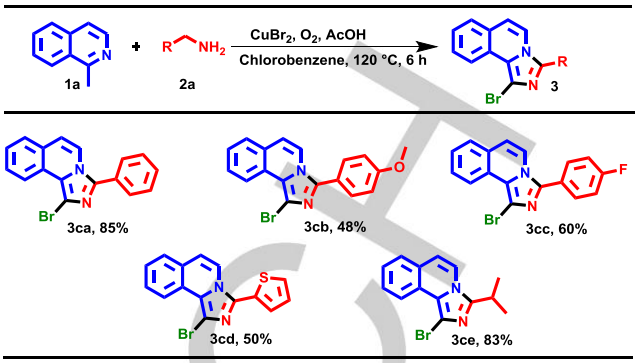
Table 3: Scope of 2-methylquinoline derivatives with different benzylamines.[a,b]



[a] Reaction conditions: 1a (0.5 mmol), 2a (0.75 mmol), $CuBr_2$ (0.5 mmol), AcOH (20 mol-%), Chlorobenzene (4 mL), 120 °C, under 1 atm O_2 (using O_2 ballon). [b] Isolated yields.

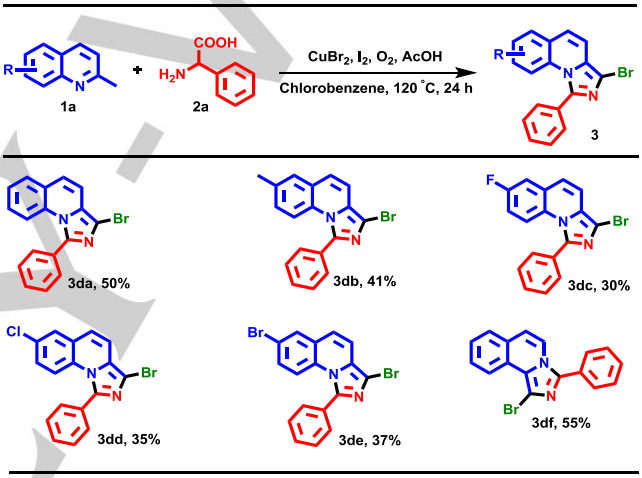
On the basis of previous reports,[9a,9b,9f,10a,10c,10e,16] as well as the present investigations, a possible mechanism is proposed and shown in **Scheme 3**. Initially, 2-(bromomethyl)quinoline **1a-1** is generated from **1a** through a carbocupration intermediate **B,** which is further oxidized to hypervalent species **C** in the presence of HX and O_2, followed by reductive elimination. Further, oxidative coupling of **1a-1** with benzylamine **2a** provides imine **D**, which undergoes intramolecular oxidative cyclization to afford simple cyclised product **3aa-1**. Next, the acidic C-H bond of simple cyclised product **3aa-1** reacts with (CuX_2) forms carbocupration intermediate **E**, which is further oxidized to hypervalent species **F** in the presence of HX and O_2. Then, the hypervalent species **F** undergoes the reductive elimination, and results the halo cyclised product **3aa**.

Table 4: Scope of aliphatic amines with 1-methylisoquinoline.[a,b]



[a] Reaction conditions: 1a (0.5 mmol), 2a (0.75 mmol), $CuBr_2$ (0.5 mmol), AcOH (20 mol-%), Chlorobenzene (4 mL), 120 °C, 6 h, Under 1 atm O_2 (using O_2 ballon). [b] Isolated yields.

Table 5: Scope of Phenylglycine with 2-methylquinoline derivatives.[a,b]

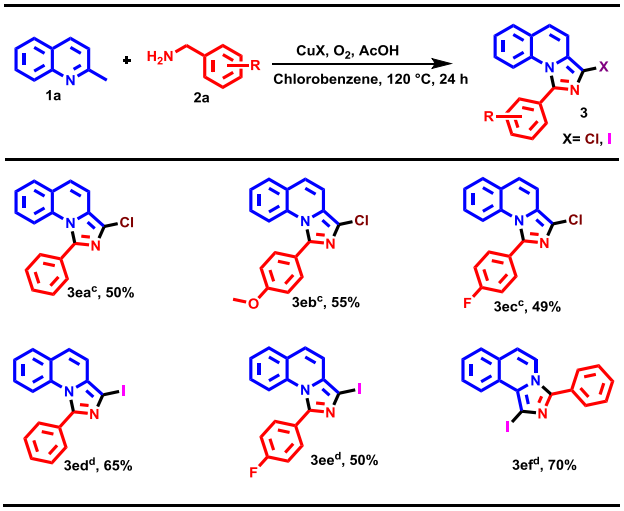


[a] Reaction conditions: 1a (0.5 mmol), 2a (1.5 mmol), $CuBr_2$ (0.5 mmol), I_2 (20 mol-%), AcOH (20 mol-%), Chlorobenzene (4 mL), 120 °C, under 1 atm O_2 (using O_2 ballon), 24 h. [b] Isolated yields.

To check the gram scale applicability of this method, the reaction with 7 mmole (1 gram) of **1a** afforded the product in a good yield (65%). Moreover, we explored the synthetic utility of this halogenated fused hterocylcic compounds by performing Suzuki cross coupling reaction (**Scheme 4**), where the arylated coupled product was obtained in good yield (80%).

10.1002/ejoc.201800628

Table 6: Scope of Halogen Sources.[a,b]



[a] Reaction conditions: 1a (0.5 mmol), 2a (1.5 mmol), catalyst (0.5 mmol), AcOH (0.5 mmol), Chlorobenzene (4 mL), 120 °C, under 1 atm O_2 (using O_2 ballon). [b] Isolated yields. [c] $CuCl_2$ salt was used.[d] CuI salt was used.

Conclusions

In summary, we have developed an aerobic copper promoted double oxidative C–H amination and halogenation tandem reaction for the synthesis of imidazo[1,5-a]*N*-heteroaryl halides from 2-methylazarenes and aliphatic amines or amino acids, by use of cheap and readily available copper salts as catalysts as well as halogen sources, and molecular oxygen as a sole oxidant. This protocol is operationally simple and enables the direct access to functionalized fused imidazoles with good functional group tolerance in one pot operation. The synthetic utility of the method explored by the Suzuki cross coupling reaction, and results the product in good yield. Further investigations on these coupling chemistry and their applications are under investigations.

Experimental Section

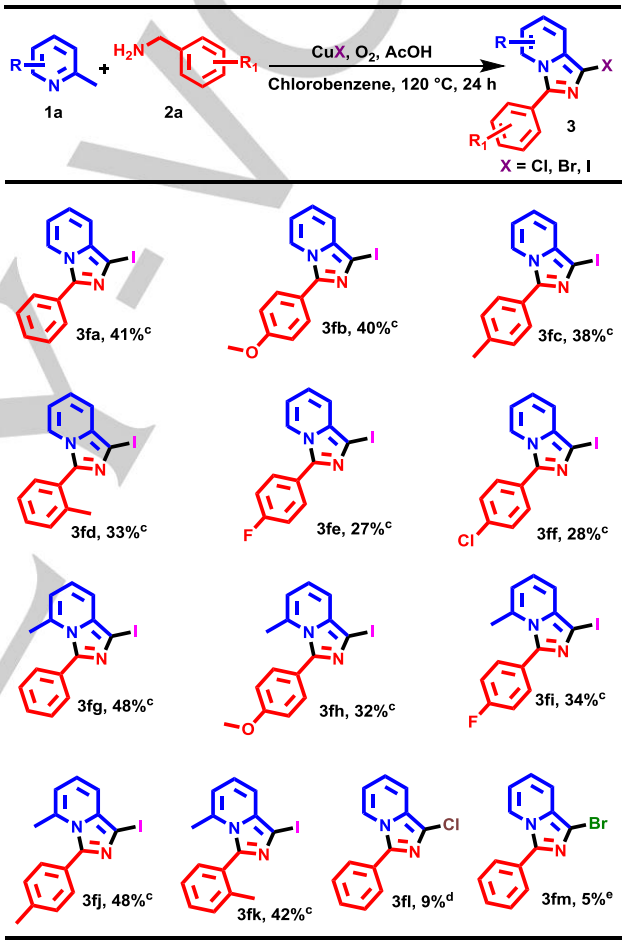
General Information :

All chemicals were purchased from Sigma-Aldrich, Alfa Aesar and S. D. Fine Chemicals, Pvt. Ltd. India and used without further purification. ACME silica gel (100–200 mesh) was used for column chromatography and thin-layer chromatography was performed on Merck-pre-coated silica gel 60-F_{254} plates. TLC plates are visualized by UV-light and developed by Iodine. All the solvents were obtained from commercial sources and purified using standard methods. All ^1H, ^{13}C NMR spectra were recorded on Avance-300, Avance-400 and Avance-500 MHz Spectrometer. Chemical shifts (δ) are reported in ppm, using TMS ($\delta = 0$) as an internal standard in $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; dt, doublet of triplet. The coupling constants (J) are reported in Hertz (Hz). LC-MS samples were recorded on Agilent 1200 series (DAD-Diode Array Detector) using Zorbax (SB-C18, 3.0M x 50mm x 1.8 µm) column. Mass spectral data were compiled using MS (ESI), HRMS mass spectrometers.

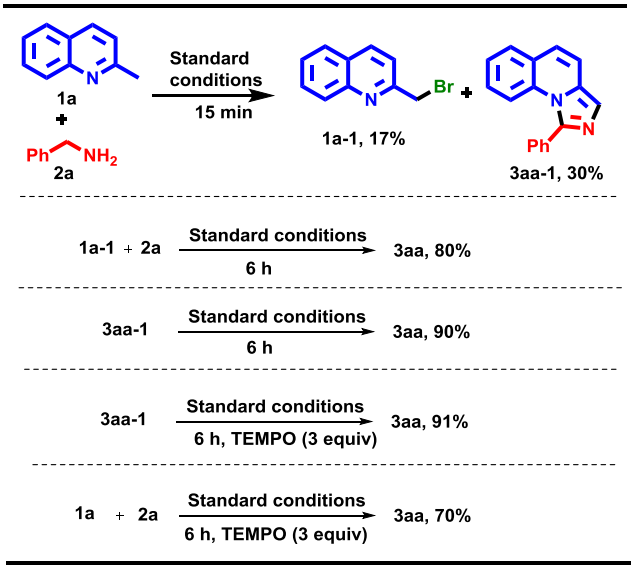
General procedure for the synthesis of 3aa:

The mixture of 2-methylquinoline (0.5 mmol), benzylamine (0.75 mmol), $CuBr_2$(0.5 mmol), and AcOH (20 mol%) in chlorobenzene (4 mL) was stirred at 120 °C for 6 h under 1 atm of O_2 (using O_2 ballon). After being cooled to room temperature, the resulting mixture was extracted with ethylacetate and washed with saturated $NaHCO_3$ solution. The organic layer was dried over $NaSO_4$ and concentrated by removing the solvent under vacuum. Finally, the resulting residue was purified by column chromatography using EtOAc/Hexane as elutants to obtained the product **3aa**.

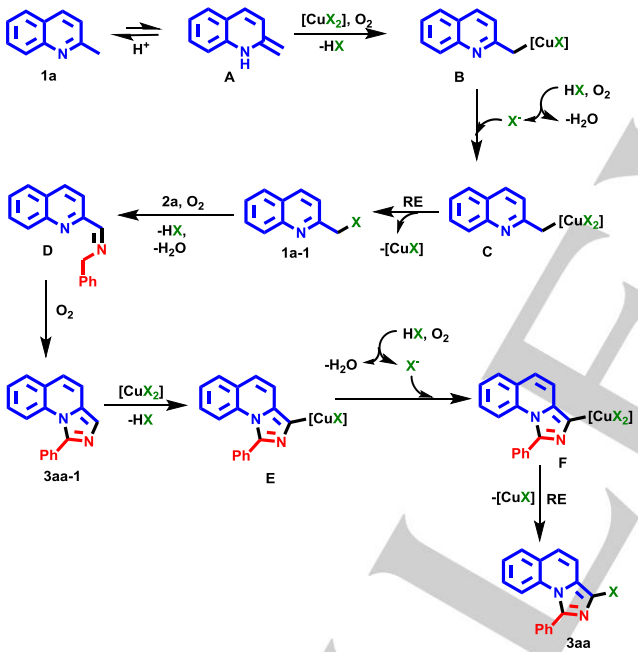
Table 7: Scope of 2-methylpyridine derivatives with benzylamine derivatives.[a,b]



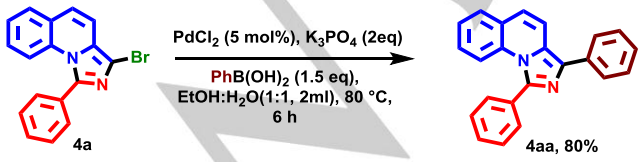
[a] Reaction Conditions: 1a (1 mmol), 2a (4 mmol), CuX (1 mmol), Chlorobenzene (4 mL), 120 °C, 24 h, Under 1 atm O_2 (using O_2 ballon). [b] Isolated yields. [c] CuI, AcOH (3 mmol) were used. [d] $CuCl_2$, AcOH (0.5 mmol) were used. [e] $CuBr_2$, AcOH (0.5 mmol) were used.



Scheme 2: Control experiments.



Scheme 3: Proposed mechanism



Scheme 4: Suzuki Cross Coupling reaction

3-bromo-1-phenylimidazo[1,5-*a*]quinoline (3aa): Pale yellow solid (118 mg, 73% yield), mp 163-164 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 – 7.60 (m, 3H), 7.58 – 7.48 (m, 4H), 7.39 – 7.28 (m, 2H), 7.23 – 7.16 (m, 1H), 7.10 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.5, 132.6, 132.1, 129.7, 129.6, 128.8, 128.8, 127.9, 127.7, 125.7, 125.6, 122.3, 117.2, 116.0, 109.2; IR v = 3060, 2925, 2860, 1958, 1750, 1610, 1550, 1442, 1358, 1296, 1214, 1066, 878, 754, 696, 624 cm^{-1}; MS (ESI, m/z) 323 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{12}N_2Br$ $[M+H]^+$ 323.01784; found 323.01865.

3-bromo-1-(4-methoxyphenyl)imidazo[1,5-*a*]quinoline (3ab): Pale yellow solid (109 mg, 62% yield), mp 147-148 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 3H), 7.40 – 7.27 (m, 2H), 7.25 – 7.17 (m, 1H), 7.12 – 6.97 (m, 3H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 141.5, 132.2, 131.1, 128.9, 127.7, 125.7, 124.6, 122.3, 117.2, 116.0, 114.3, 108.7, 77.3, 77.0, 76.7, 55.4; IR v = 3054, 2999, 2925, 1884, 1736, 1607, 1522, 1447, 1357, 1294, 1245, 1172, 1103, 1017, 960, 884, 744, 660 cm^{-1}; MS (ESI, m/z) 353 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}ON_2Br$ $[M+H]^+$ 353.02840; found 353.02837.

3-bromo-1-(p-tolyl)imidazo[1,5-*a*]quinoline (3ac): Pale yellow solid (101 mg, 60% yield), mp 167-168 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 8.5 Hz, 3H), 7.32 (q, *J* = 9.3 Hz, 4H), 7.25 – 7.16 (m, 1H), 7.08 (d, *J* = 9.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 139.8, 132.2, 129.5, 128.8, 127.6, 125.6, 122.2, 117.3, 116.0, 109.0, 21.5; IR v = 3055, 2918, 1744, 1611, 1562, 1475, 1445, 1362, 1300, 1245, 1105, 1046, 966, 859, 801, 758, 697 cm^{-1}; MS (ESI, m/z) 337 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}N_2Br$ $[M+H]^+$ 337.03349; found 337.03410.

3-bromo-1-(*o*-tolyl)imidazo[1,5-*a*]quinoline (3ad): Pale yellow solid (81 mg, 48% yield), mp 155-156 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.40 – 7.29 (m, 4H), 7.20-7.14 (m, *J* = 8.7 Hz, 2H), 7.09 (d, *J* = 9.5 Hz, 1H), 2.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7, 138.4, 132.6, 132.3, 130.5, 130.5, 130.2, 128.8, 128.3, 127.3, 126.4, 125.7, 125.4, 122.2, 116.0, 115.9, 108.6, 19.6; IR v = 3061, 2923, 2857, 1613, 1452, 1360, 1300, 1247, 1092, 962, 883, 794, 755, 680 cm^{-1}; MS (ESI, m/z) 337 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}N_2Br$ $[M+H]^+$ 337.03349; found 337.03379.

3-bromo-1-(2,4-dimethoxyphenyl)imidazo[1,5-*a*]quinoline (3ae): Pale yellow solid (115 mg, 60% yield), mp 167-168 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 9.0 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.38 – 7.27 (m, 2H), 7.21 (t, *J* = 8.6 Hz, 1H), 7.08 (d, *J* = 9.4 Hz, 1H), 6.65 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.56 (d, *J* = 2.3 Hz, 1H), 3.92 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 159.2, 138.6, 132.8, 128.4, 127.6, 125.4, 122.1, 116.3, 116.0, 114.6, 108.4, 104.8, 98.8, 55.5, 55.3; IR v = 2929, 2844, 1609, 1445, 1296, 1209, 1161, 1030, 797, 751, 666 cm^{-1}; MS (ESI, m/z) 383 $[M+H]^+$; HRMS (ESI) Calcd for $C_{19}H_{16}O_2N_2Br$ $[M+H]^+$ 383.03897; found 383.04055.

3-bromo-1-(4-(*tert*-butyl)phenyl)imidazo[1,5-*a*]quinoline (3af): Honey color semi solid (106 mg, 56% yield); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.71 – 7.48 (m, 6H), 7.40 – 7.16 (m, 3H), 7.07 (d, *J* = 9.4 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 141.7, 132.2, 129.2, 128.8, 127.7, 125.7, 122.4, 117.3, 116.0, 108.8, 34.9, 31.3; IR v = 3066, 2962, 1749, 1607, 1475, 1359, 1249, 1111, 1064, 966, 836, 792, 751, 669, 644 cm^{-1}; MS (ESI, m/z) 379 $[M+H]^+$; HRMS (ESI) Calcd for $C_{21}H_{20}N_2Br$ $[M+H]^+$ 379.08044; found 379.08062.

3-bromo-1-(4-fluorophenyl)imidazo[1,5-*a*]quinoline (3ag): Pale yellow solid (96 mg, 56% yield), mp 170-171 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.59 (m, 3H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 9.4 Hz, 1H), 7.25- 7.19 (m, 3H), 7.11 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 163.5 (d, *J* = 250.2 Hz), 140.5, 132.0, 131.7 (d, *J* = 8.4 Hz), 129.0, 128.7, 128.0, 127.8, 125.9, 125.7, 122.5, 117.0, 116.2, 116.0 (d, *J* = 3.8 Hz), 109.2; IR v = 3058, 2924, 1749, 1612, 1559, 1476, 1368, 1235, 1056, 970, 871, 758, 699, 660 cm^{-1} ; MS (ESI, m/z) 341 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrF$ $[M+H]^+$ 341.00842; found 341.00823.

3-bromo-1-(4-chlorophenyl)imidazo[1,5-*a*]quinoline (3ah): Pale yellow solid (102 mg, 57% yield), mp 213-214 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 10.8 Hz, 3H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.34 – 7.22 (m, 3H), 7.12 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.3, 135.8, 131.9, 130.9, 129.1, 128.2, 127.8, 125.9, 125.7, 122.6, 117.1, 116.0, 109.4; IR v = 3062, 2924, 2856, 1747, 1698, 1598, 1457, 1361, 1250, 1014, 834, 791, 751, 679 cm^{-1}; MS (ESI, m/z) 357 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrCl$ $[M+H]^+$ 356.97887; found 356.97931.

3-bromo-1-(2-bromophenyl)imidazo[1,5-*a*]quinoline (3ai): Pale yellow solid (110 mg, 55% yield), mp 158-159 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.59 (m, 1H), 7.53 – 7.49 (m, 1H), 7.47 – 7.43 (m, 1H), 7.38 – 7.30 (m, 2H), 7.25 – 7.17 (m, 2H), 7.13 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 134.5, 133.0, 132.6, 132.2, 131.6, 128.9, 128.4, 128.0, 127.5, 125.8, 125.3, 125.2, 122.6, 115.9, 115.9, 108.7; IR v = 3059, 2924, 2857, 1612, 1557, 1434, 1365, 1300, 1249, 1069, 1029, 964, 885, 750, 662 cm^{-1}; MS (ESI, m/z) 401 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2Br_2$ $[M+H]^+$ 400.92835; found 400.92824.

3-bromo-1-(4-(trifluoromethyl)phenyl)imidazo[1,5-*a*]quinoline (3aj): Pale yellow solid (90 mg, 46% yield), mp 173-174 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.76 (m, 4H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 9.4 Hz, 1H), 7.31 – 7.24 (m, 2H), 7.16 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 136.1, 131.7, 129.9, 129.2, 128.5, 127.9, 126.1, 125.8, 125.7, 122.8, 117.1, 116.0, 109.9; MS (ESI, m/z) 391 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrF_3$ $[M+H]^+$ 391.00522; found 391.00589.

3-bromo-1-(naphthalen-2-yl)imidazo[1,5-*a*]quinoline (3ak): Pale yellow solid (110 mg, 59% yield), mp 167-168 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.71 (d, *J* = 7.0 Hz, 1H), 7.65 – 7.54 (m, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.29 (m, 3H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 9.5 Hz, 1H), 6.96 – 6.88 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 133.6, 132.2, 132.0, 130.6, 130.1, 129.1, 128.8, 128.5, 128.1, 127.8, 127.3, 126.6, 125.6, 125.5, 125.4, 125.3, 122.6, 116.9, 115.9, 108.9; IR v = 3055, 2924, 1743, 1611, 1462, 1360, 1301, 1247, 1077, 948, 893, 743, 667 cm^{-1}; MS (ESI, m/z) 373 $[M+H]^+$; HRMS (ESI) Calcd for $C_{21}H_{14}N_2Br$ $[M+H]^+$ 373.03349; found 373.03341.

3-bromo-1-(thiophen-2-yl)imidazo[1,5-*a*]quinoline (3al): Pale yellow solid (105 mg, 64% yield), mp 156-157 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.43 – 7.35 (m, 2H), 7.34 – 7.27 (m, 2H), 7.23 – 7.20 (m, 1H), 7.13 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.2, 132.7, 132.1, 130.1, 128.9, 128.7, 128.5, 128.1, 127.4, 125.9, 125.6, 122.9, 116.8, 115.8, 109.2; IR v = 3069, 2924, 2856, 1741, 1695, 1614, 1470, 1361, 1302, 1251, 1217, 1084, 935, 846, 793, 748, 703 cm^{-1}; MS (ESI, m/z) 329 $[M+H]^+$; HRMS (ESI) Calcd for $C_{15}H_{10}N_2BrS$ $[M+H]^+$ 328.97426; found 328.97508.

3-bromo-1-cyclohexylimidazo[1,5-*a*]quinoline (3am): Pale yellow solid (115 mg, 70% yield), mp 178-179 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 8.6 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 9.4 Hz, 1H), 6.97 (d, *J* = 9.4 Hz, 1H), 3.40 (t, *J* = 11.5 Hz, 1H), 2.21 (d, *J* = 12.4 Hz, 2H), 1.96 (d, *J* = 13.3 Hz, 2H), 1.91 – 1.80 (m, 3H), 1.60 – 1.33 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 132.9, 129.0, 128.1, 127.0, 126.0, 125.3, 121.4, 116.7, 116.3, 107.8, 39.9, 31.7, 26.4, 25.9; IR v = 3051, 2926, 2852, 1699, 1456, 1381, 1343, 1255, 1077, 983, 895, 795, 749, 690 cm^{-1}; MS (ESI, m/z) 329 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{18}N_2Br$ $[M+H]^+$ 329.06479; found 329.06447.

3-bromo-1-propylimidazo[1,5-*a*]quinoline (3an): yellow semi solid (72 mg, 50% yield); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 9.4 Hz, 1H), 6.99 (d, *J* = 9.4 Hz, 1H), 3.41 – 3.24 (m, 2H), 2.05 – 1.95 (m, 2H), 1.14 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 132.8, 129.0, 128.2, 127.5, 125.9, 125.5, 121.7, 116.5, 116.1, 33.9, 29.7, 20.6, 13.9; IR v = 2923, 2858, 1710, 1615, 1462, 1378, 1248, 1060, 912, 783, 757, 692 cm^{-1}; MS (ESI, m/z) 289 $[M+H]^+$; HRMS (ESI) Calcd for $C_{14}H_{14}N_2Br$ $[M+H]^+$ 289.03349; found 289.03422.

3-bromo-1-isopropylimidazo[1,5-*a*]quinoline (3ao): Dulish white solid (75 mg, 66% yield), mp 140-141 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 9.4 Hz, 1H), 6.98 (d, *J* = 9.4 Hz, 1H), 3.85 – 3.75 (m, 1H), 1.56 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.8, 132.8, 129.0, 128.1, 127.3, 126.1, 125.4, 121.5, 116.9, 116.3, 107.6, 30.0, 21.5; IR v = 3052, 2966, 2925, 1615, 1463, 1374, 1254, 1068, 794, 750, 692 cm^{-1}; MS (ESI, m/z) 289 $[M+H]^+$; HRMS (ESI) Calcd for $C_{14}H_{14}N_2Br$ $[M+H]^+$ 289.03349; found 289.03424.

3-bromo-7-methyl-1-phenylimidazo[1,5-*a*]quinoline (3ba): Gray solid (110 mg, 65% yield), mp 189-190 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.60 (m, 2H), 7.54 – 7.49 (m, 3H), 7.43 (s, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 7.28 (d, *J* = 9.4 Hz, 1H), 7.06 – 6.99 (m, 2H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.1, 135.7, 132.2, 130.0, 129.8, 129.7, 128.8, 127.9, 125.6, 122.5, 117.1, 115.8, 108.6; IR v = 3055, 2918, 1744, 1611, 1562, 1475, 1445, 1362, 1300, 1245, 1105, 1046, 966, 859, 801, 758, 697 cm^{-1}; MS (ESI, m/z) 337 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}N_2Br$ $[M+H]^+$ 337.03349; found 337.03322.

3-bromo-1-(4-chlorophenyl)-7-methylimidazo[1,5-*a*]quinoline (3bb): Pale yellow solid (121 mg, 65%), mp 194-195 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.32 (m, 4H), 7.25 (d, *J* = 6.8 Hz, 1H), 7.06 – 7.03 (m, 2H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 135.8, 135.7, 131.1, 130.9, 129.9, 129.1, 128.9, 128.1, 125.6, 122.5, 116.9, 115.8, 109.3, 20.5; IR v = 3047, 2920, 2857, 1617, 1563, 1496, 1441, 1403, 1366, 1304, 1244, 1098, 1050, 1013, 805, 754, 676 cm^{-1}; MS (ESI, m/z) 371$[M+H]^+$, HRMS (ESI) Calcd for $C_{18}H_{13}N_2BrCl$ $[M+H]^+$ 370.99452; found 370.99643.

3-bromo-7-methoxy-1-phenylimidazo[1,5-*a*]quinoline (3bc): Pearl white solid (85 mg, 48% yield), mp 175-176 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.59 (m, 2H), 7.53 – 7.50 (m, 3H), 7.42 (d, *J* = 9.3 Hz, 1H), 7.30 (d, *J* = 9.4 Hz, 1H), 7.11 – 7.01 (m, 2H), 6.78 (dd, *J* = 9.3, 2.9 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 140.9, 132.5, 129.7, 128.8, 127.6, 127.0, 126.3, 122.1, 118.5, 116.4, 115.3, 111.0, 109.0, 55.5; IR v = 3055, 2997, 2925, 1743, 1609, 1557, 1475, 1447, 1323, 1237, 1024, 962, 845, 759, 698, 637 cm^{-1}; MS (ESI, m/z) 353 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}ON_2Br$ $[M+H]^+$ 353.02840; found 353.02963.

3-bromo-1-(4-fluorophenyl)-7-methoxyimidazo[1,5-*a*]quinoline (3bd): Pale yellow solid (100 mg, 54% yield), mp 184-185 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.58 (m, 2H), 7.38 (d, *J* = 9.3 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.22 (t, *J* = 8.5 Hz, 2H), 7.10 – 7.01 (m, 2H), 6.81 (d, *J* = 9.3 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5 (d, *J* = 250.3 Hz), 157.0, 139.8, 131.7 (d, *J* = 8.4 Hz), 128.6, 127.7, 127.1, 126.2, 122.2, 118.2, 116.4, 116.1 (d, *J* = 21.9 Hz), 115.4, 111.1, 109.0, 55.6; IR v = 3064, 2934, 2844, 1608, 1561, 1524, 1453, 1233, 1160, 1061, 839, 664 cm^{-1}; MS (ESI, m/z) 371 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{13}N_2BrOF$ $[M+H]^+$ 371.01898; found 371.01825.

3-bromo-1-(4-chlorophenyl)-7-methoxyimidazo[1,5-*a*]quinoline (3be): Pale yellow solid (101 mg, 52% yield), mp 209- 210 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 9.3 Hz, 1H), 7.29 (d, *J* = 9.4 Hz, 1H), 7.09 (d, *J* = 2.9 Hz, 1H), 7.05 (d, *J* = 9.4 Hz, 1H), 6.84 (dd, *J* = 9.3, 2.9 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 139.7, 135.8, 130.9, 130.8, 129.2, 127.8, 127.1, 126.1, 122.4, 118.4, 116.4, 115.5, 111.2, 109.2, 55.6; IR v = 3060, 2932, 1614, 1563, 1488, 1452, 1329, 1246, 1096, 1060, 863, 757, 650 cm^{-1}; MS (ESI, m/z) 388 $[M+H]^+$

3-bromo-7-fluoro-1-phenylimidazo[1,5-*a*]quinoline (3bf): pale yellow solid (72 mg, 42% yield), mp 173-174 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.67 – 7.59 (m, 2H), 7.58 – 7.50 (m, 3H), 7.48 (dd, *J* = 9.3, 4.7 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.03 (d, *J* = 9.5 Hz, 1H), 6.97 – 6.83 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7 (d, *J* = 246.7 Hz), 141.5, 132.3, 129.9, 129.5, 129.0, 128.5, 127.6, 127.5 (d, *J* = 8.4 Hz), 121.4, 119.0 (d, *J* = 8.3 Hz), 117.3, 115.2 (d, *J* = 23.7 Hz), 113.9 (d, *J* = 22.6 Hz), 109.8; IR v = 3058, 2924, 1749, 1612, 1559, 1476, 1368, 1235, 1056, 970, 871, 758, 699, 660 cm^{-1}; MS (ESI, m/z) 341 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrF$ $[M+H]^+$ 341.00842; found 341.00942.

3-bromo-7-fluoro-1-(4-methoxyphenyl)imidazo[1,5-*a*]quinoline (3bg): Pale yellow solid (80 mg, 43% yield); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 – 7.50 (m, 3H), 7.35 – 7.27 (m, 2H), 7.07 – 6.97 (m, 3H), 6.97 – 6.89 (m, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (d, *J* = 8.6 Hz), 158.5, 141.5, 131.0, 128.6, 127.6 (d, *J* = 8.6 Hz), 124.1, 121.4, 118.9 (d, *J* = 8.3 Hz), 117.3, 115.2 (d, *J* = 23.6 Hz), 114.4, 113.9 (d, *J* = 22.6 Hz), 109.2, 55.4; IR v = 3069, 2928, 1611, 1564, 1478, 1296, 1246, 1180, 1023, 870, 825, 785, 660 cm^{-1}; MS (ESI, m/z) 371 $[M+H]^+$, HRMS (ESI) Calcd for $C_{18}H_{13}N_2BrOF$ $[M+H]^+$ 371.01898; found 371.01833.

3-bromo-7-fluoro-1-(p-tolyl)imidazo[1,5-*a*]quinoline (3bh): Pale yellow solid (70 mg, 39% yield), mp 187-188 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.49 (m, 3H), 7.34 – 7.29 (m, 4H), 7.01 (d, *J* = 9.4, 1H), 6.92 (t, *J* = 8.6 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (d, *J* = 246.3 Hz), 141.7, 140.0, 129.7, 129.4, 128.6, 127.5, 121.3, 119.0 (d, *J* = 8.3 Hz), 117.4, 115.1 (d, *J* = 23.7 Hz), 113.9 (d, *J* = 22.6 Hz), 109.7, 21.5; IR v = 3060, 2924, 2859, 1614, 1561, 1478, 1369, 1241, 1054, 972, 873, 822, 786, 659 cm^{-1}; MS (ESI, m/z) 355 $[M+H]^+$, HRMS (ESI) Calcd for $C_{18}H_{13}N_2BrF$ $[M+H]^+$ 355.02407; found 355.02320.

3-bromo-8-fluoro-1-phenylimidazo[1,5-*a*]quinoline (3bi): Pale yellow solid (80 mg, 47% yield), mp 150-151 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.60 (m, 3H), 7.58 – 7.52 (m, 3H), 7.27 (d, *J* = 9.7 Hz, 2H), 7.17 (d, *J* = 11.1 Hz, 1H), 7.11 -7.05 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2 (d, *J* = 248.6 Hz), 141.6, 138.4, 133.0, 132.8 (d, *J* = 10.9 Hz), 131.8, 130.5 (d, *J* = 9.5 Hz), 130.2, 129.7, 129.0, 127.8 (d, *J* = 15.8 Hz), 121.9 (d, *J* = 47.0 Hz), 115.2, 113.8 (d, *J* = 22.8 Hz), 109.0, 104.7 (d, *J* = 28.6 Hz); IR v = 3064, 2926, 1605, 1526, 1467, 1363, 1233, 969, 841, 788, 674 cm^{-1}; MS (ESI, m/z) 341 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrF$ $[M+H]^+$ 341.00842; found 341.00940.

3-bromo-7-chloro-1-phenylimidazo[1,5-*a*]quinoline (3bj): Pale yellow solid (130 mg, 73% yield), mp 178-179 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.66 – 7.59 (m, 3H), 7.58 – 7.50 (m, 3H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.34 (d, *J* = 9.4 Hz, 1H), 7.15 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.01 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.7, 132.0, 131.3, 130.5, 130.0, 129.5, 129.0, 128.0, 127.7, 127.1, 121.2, 118.5, 117.3, 109.7; IR v = 3055, 2923, 1750, 1552, 1461, 1366, 1249, 1206, 1106, 966, 885, 764, 699, 637 cm^{-1}; MS (ESI, m/z) 357 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrCl$ $[M+H]^+$ 356.97887; found 356.98020.

3-bromo-7-chloro-1-(4-methoxyphenyl)imidazo[1,5-*a*]quinoline (3bk): Pale yellow solid (151 mg, 78% yield), mp 221-222 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 2.3 Hz, 1H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.32 (d, *J* = 9.4 Hz, 1H), 7.16 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 9.5 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 141.6, 131.3, 131.0, 130.6, 128.0, 127.7, 127.6, 127.2, 123.7, 121.3, 118.5, 117.3, 114.5, 109.0, 55.4; IR v = 3023, 2928, 1606, 1522, 1461, 1365, 1298, 1247, 1175, 1105, 1022, 963, 887, 816, 761, 669 cm^{-1}; MS (ESI, m/z) 387 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{13}N_2BrOCl$ $[M+H]^+$ 386.98943; found 386.98919.

3-bromo-7-chloro-1-(4-chlorophenyl)imidazo[1,5-*a*]quinoline (3bl): Pale yellow solid (122 mg, 62% yield), mp 187-188 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 2.4 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.53 – 7.49 (m, 2H), 7.44 (d, *J* = 9.1 Hz, 1H), 7.34 (d, *J* = 9.4 Hz, 1H), 7.20 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.03 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 136.1, 131.5, 130.8, 130.5, 130.3, 129.3, 128.1, 128.0, 127.8, 127.1, 121.4, 118.4, 117.4, 110.1; IR v = 3044, 2924, 2855, 1595, 1461, 1368, 1300, 1252, 1204, 1097, 1015, 964, 877, 834, 753, 644 cm^{-1}; MS (ESI, m/z) 391 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{10}N_2BrCl_2$ $[M+H]^+$ 390.93989; found 390.93963.

3-bromo-9-chloro-1-phenylimidazo[1,5-*a*]quinoline (3bm): Yellow solid (50 mg, 28% yield), mp 178-179 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 (s, 3H), 7.43 – 7.19 (m, 6H), 7.07 – 6.92 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 134.2, 130.3, 129.8, 129.6, 129.0, 128.6, 126.9, 126.3, 125.3, 124.6, 121.8, 117.4, 111.8; IR v = 3062, 2923, 1750, 1602, 1540, 1431, 1355, 1250, 1207, 1101, 950, 805, 736, 693 cm^{-1}; MS (ESI, m/z) 357 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrCl$ $[M+H]^+$ 356.97887; found 356.98019.

3,7-dibromo-1-phenylimidazo[1,5-*a*]quinoline (3bn): Pale yellow solid (85 mg, 42% yield), mp 190-191 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 2.2 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.58 – 7.49 (m, 3H), 7.41 – 7.27 (m, 3H), 7.00 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 132.0, 131.0, 130.9, 130.5, 130.1, 129.5, 129.0, 127.7, 127.5, 121.2, 119.0, 118.7, 117.4, 109.7; IR v = 3063, 2925, 2856, 1751, 1606, 1548, 1463, 1365, 1299, 1250, 1205, 1103, 1056, 964, 883, 761, 702, 669 cm^{-1}; MS (ESI, m/z) 401 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2Br_2$ $[M+H]^+$ 400.92835; found 400.92859.

3,7-dibromo-1-(p-tolyl)imidazo[1,5-*a*]quinoline (3bo): Pale yellow solid (125 mg, 60% yield), mp 190-191 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.2 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 9.1 Hz, 1H), 7.33 – 7.27 (m, 4H), 6.97 (d, *J* = 9.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 140.2, 131.0, 130.9, 130.4, 129.7, 129.4, 129.1, 127.6, 127.5, 121.0, 118.9, 118.8, 117.4, 109.7, 21.5; IR v = 3039, 2921, 1613, 1544, 1461, 1365, 1298, 1246, 1207, 1106, 965, 894, 830, 801, 759, 668 cm^{-1}; MS (ESI, m/z) 417 $[M+H]^+$

1-bromo-3-phenylimidazo[5,1-*a*]isoquinoline (3ca): Pale yellow solid (137 mg, 85%), mp 158-159 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (d, *J* = 7.9 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.65 – 7.42 (m, 6H), 6.81 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 129.4, 129.0, 128.9, 128.6, 128.4, 127.49, 127.3, 127.0, 124.7, 124.2, 122.5, 120.2, 114.9, 108.3. IR v = 3062, 2925, 2853, 1606, 1454, 1365, 1303, 1237, 969, 763, 694 cm $^{-1}$; MS (ESI, m/z) 323 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2Br$ $[M+H]^+$ 323.01784; found 323.01769.

1-bromo-3-(4-methoxyphenyl)imidazo[5,1-*a*]isoquinoline (3cb) : Pale yellow solid (85 mg, 48% yield), mp 135-136 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (d, *J* = 8.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.46 (t, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.79 (d, *J* = 7.5 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 140.1, 129.8, 128.3, 127.4, 127.1, 126.9, 124.7, 123.9, 122.4, 121.3, 120.3, 114.7, 114.4, 108.0, 55.1; IR v = 3063, 2932, 1610, 1528, 1466, 1364, 1249, 1178, 1029, 968, 838, 787, 666 cm^{-}1; MS (ESI, m/z) 353 $[M+H]^+$, HRMS (ESI) Calcd for $C_{18}H_{14}N_2BrO$ $[M+H]^+$ 353.02840; found 353.02850.

1-bromo-3-(4-fluorophenyl)imidazo[5,1-*a*]isoquinoline (3cc): Pale yellow solid (102 mg, 60% yield), mp 189-190 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.62 – 7.56 (m, 2H), 7.51 – 7.45 (m, 1H), 7.26 – 7.19 (m, 2H), 6.82 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, *J* = 250.3 Hz), 139.1, 130.6 (d, *J* = 8.4 Hz), 128.5, 127.2 (d, *J* = 36.3 Hz), 125.1, 124.5 (d, *J* = 34.3 Hz), 122.6, 120.0, 116.2 (d, *J* = 21.9 Hz), 115.2, 108.2; IR v = 3064, 2926, 1605, 1526, 1467, 1363, 1233, 969, 841, 788, 674 cm^{-1}; MS (ESI, m/z) 341 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{11}N_2Br$ $[M+H]^+$ 341.00842; found 341.00774.

1-bromo-3-(thiophen-2-yl)imidazo[5,1-*a*]isoquinoline (3cd): Pale yellow solid (82 mg, 50% yield), mp 125-126 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 7.55-7.42 (m, 5H), 7.20 – 7.13 (m, 1H), 6.83 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.5, 130.6, 128.5, 127.7, 127.4, 127.3, 127.0, 126.6, 124.4, 122.4, 120.1, 115.4, 108.3; IR v = 3073, 2926, 1607, 1521, 1469, 1410, 1337, 1238, 963, 847, 776, 704 cm^{-1}; MS (ESI, m/z) 329 $[M+H]^+$; HRMS (ESI) Calcd for $C_{15}H_{10}N_2BrS$ $[M+H]^+$ 328.97426; found 328.97508.

1-bromo-3-isopropylimidazo[5,1-*a*]isoquinoline (3ce): Pale yellow solid (120 mg, 83% yield), mp 70-71 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 (d, *J* = 8.1 Hz, 1H), 7.59 – 7.47 (m, 3H), 7.40 (t, *J* = 7.9 Hz, 1H), 6.74 (d, *J* = 7.3 Hz, 1H), 3.30 – 3.23 (m, 1H), 1.43 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 128.2, 127.0, 126.9, 124.7, 122.9, 122.2, 119.1, 114.1, 106.0, 26.0, 20.7; IR v = 3062, 2970, 2929, 1608, 1486, 1455, 1355, 1308, 1232, 1086, 971, 778, 678 cm^{-}1; MS (ESI, m/z) 289 $[M+H]^+$, HRMS (ESI) Calcd for $C_{14}H_{12}N_2Br$ $[M+H]^+$ 289.03349; found 289.03330.

3-bromo-1-phenylimidazo[1,5-*a*]quinoline (3da): Pale yellow solid (80 mg, 50% yield), mp 159-160 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 – 7.3 (m, 3H), 7.56 – 7.48 (m, 4H), 7.37 – 7.28 (m, 2H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.10 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 132.6, 132.1, 129.7, 129.6, 128.9, 128.8, 127.9, 127.7, 125.7, 125.6, 122.3, 117.2, 116.0, 109.2; IR v = 3060, 2925, 2860, 1958, 1750, 1610, 1550, 1442, 1358, 1296, 1214, 1066, 878, 754, 696, 624 cm^{-1}; MS (ESI, m/z) 323 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2Br$ $[M+H]^+$ 323.01784; found 323.01685.

3-bromo-7-methyl-1-phenylimidazo[1,5-*a*]quinoline (3db): Pale yellow solid (69 mg, 41% yield), mp 185-186 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.60 (m, 2H), 7.54 – 7.48 (m, 3H), 7.46 – 7.42 (m, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 1H), 7.05 – 7.00 (m, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 135.6, 132.5, 130.1, 129.6, 128.8, 127.9, 125.6, 122.3, 117.1, 115.9, 108.9, 20.8; IR v = 3055, 2918, 1744, 1611, 1562, 1475, 1445, 1362, 1300, 1245, 1105, 1046, 966, 859, 801, 758, 697 cm^{-1}; MS (ESI, m/z) 337 $[M+H]^+$; HRMS (ESI) Calcd for $C_{18}H_{14}N_2Br$ $[M+H]^+$ 337.03349; found 337.03322.

3-bromo-7-fluoro-1-phenylimidazo[1,5-a]quinoline (3dc): Pale yellow solid (51 mg, 30% yield), mp 173-174 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 – 7.60 (m, 2H), 7.56 – 7.51 (m, 3H), 7.49 – 7.46 (m, 1H), 7.37 – 7.29 (m, 2H), 7.03 (d, *J* = 9.5 Hz, 1H), 6.92 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (d, *J* = 246.6 Hz), 141.5, 132.3, 129.9, 129.6, 129.0, 128.5, 127.7, 127.5 (d, *J* = 8.6 Hz), 121.5, 119.0 (d, *J* = 8.3 Hz), 117.4, 115.2 (d, *J* = 23.8 Hz), 114.0 (d, *J* = 22.6 Hz), 109.8; IR v = 3062, 2925, 2856, 1894, 1733, 1612, 1560, 1478, 1369, 1237, 1137, 1056, 971, 872, 769, 701, 650 cm^{-1}; MS (ESI, m/z) 341 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrF$ $[M+H]^+$ 341.00842; found 341.00942.

3-bromo-7-chloro-1-phenylimidazo[1,5-a]quinoline (3dd): Pale yellow solid (63 mg, 35% yield), mp 178-179 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 3H), 7.56 – 7.49 (m, 3H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.34 (d, *J* = 9.5 Hz, 1H), 7.15 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.01 (d, *J* = 9.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 132.2, 131.2, 130.5, 130.0, 129.5, 129.0, 128.0, 127.7, 127.1, 121.2, 118.5, 117.4, 109.9; IR v = 3056, 2925, 2856, 1730, 1601, 1553, 1473, 1368, 1301, 1250, 1207, 1106, 1053, 966, 882, 841, 769, 700, 669 cm^{-1}; MS (ESI, m/z) 357 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2BrCl$ $[M+H]^+$ 356.97887; found 356.98020.

3,7-dibromo-1-phenylimidazo[1,5-*a*]quinoline (3de): Pale yellow solid (74 mg, 37% yield), mp 190-191 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 2.2 Hz, 1H), 7.63 – 7.60 (m, 2H), 7.55- 7.52 (m, 3H), 7.35 (dd, *J* = 14.1, 9.3 Hz, 2H), 7.29 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.00 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 132.2, 131.0, 130.5, 130.0, 129.5, 129.0, 127.4, 127.5, 121.2, 119.0, 118.8, 117.4, 110.0; IR v = 3063, 2924, 2856, 1730, 1610, 1451, 1362, 1301, 1251, 1217, 1099, 1067, 965, 886, 796, 763, 701, 670 cm^{-1}; MS (ESI, m/z) 401 $[M+H]^+$; HRMS (ESI) Calcd for $C_{17}H_{11}N_2Br_2[M+H]^+$ 400.92835; found 400.92859.

1-bromo-3-phenylimidazo[5,1-*a*]isoquinoline (3df): Pale yellow solid (89 mg, 55% yield), mp 158-159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 14.4 Hz, 2H), 7.61- 7.58 (m, 2H), 7.55 – 7.52 (m, 2H), 7.50 – 7.46 (m, 2H), 6.81 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 129.5, 129.0, 128.6, 128.4, 127.5, 127.3, 127.0, 124.7, 124.2, 124.1, 122.5, 120.3, 115.0, 108.3; IR v = 3062, 2925, 2853, 1606, 1454, 1365, 1303,1237, 969, 763, 694 cm $^{-1}$; MS (ESI, m/z) 323 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2Br$ $[M+H]^+$ 323.01784; found 323.01769.

3-chloro-1-phenylimidazo[1,5-*a*]quinoline (3ea): Yellow solid (70 mg, 50% yield), mp 157-158 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.66 – 7.63 (m, 3H), 7.55 – 7.48 (m, 4H), 7.37 – 7.31 (m, 2H), 7.22 – 7.18 (m, 1H), 7.08 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 132.5, 132.1, 129.7, 129.6, 128.9, 128.8, 127.7, 125.7, 125.6, 125.3, 122.1, 121.9, 117.3, 115.4; IR v = 3062, 2922, 1961, 1754, 1610, 1552, 1446, 1362, 1303, 1258, 1104, 963, 800, 759, 698 cm^{-1}; MS (ESI, m/z) 279 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2Cl$ $[M+H]^+$ 279.06835; found 279.06844.

3-chloro-1-(4-methoxyphenyl)imidazo[1,5-*a*]quinoline (3eb): Yellow solid (85 mg, 55% yield), mp 133-134 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 7.8, 1H), 7.57 – 7.54 (m, 3H), 7.38 – 7.29 (m, 2H), 7.23 – 7.19 (m 1H), 7.06 – 7.02 (m, 3H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 140.1, 132.3, 131.0, 128.8, 127.6, 125.6, 125.1, 124.8, 121.9, 121.7, 117.2, 115.5, 114.2, 55.4; IR v = 3068, 2926, 2852, 1610, 1528, 1453, 1363, 1296, 1251, 1176, 1107, 1071, 1030, 837, 797, 755, 669; MS [ESI, m/z] 309 $[M+H]^+$, HRMS (ESI) Calcd for $C_{18}H_{14}N_2ClO$ $[M+H]^+$ 309.07892; found 309.07891.

3-chloro-1-(4-fluorophenyl)imidazo[1,5-*a*]quinoline (3ec): Pale yellow solid (73 mg, 49% yield), mp 161-162 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.75 – 7.57 (m, 3H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.29 – 7.17 (m, 4H), 7.09 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5 (d, *J* = 250.1 Hz), 139.0, 132.0, 131.7 (d, *J* = 8.4 Hz), 129.0, 128.8, 127.8, 125.8, 125.6 (d, *J* = 20.7 Hz), 122.1 (d, *J* = 20.6 Hz), 117.1, 116.1 (d, *J* = 21.8 Hz), 115.5; IR v = 3070, 2925, 1750, 1604, 1526, 1454, 1366, 1305, 1229, 1158, 1103, 968, 893, 843, 796, 764, 669 cm^{-1}; MS (ESI, m/z) 297 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{11}N_2FCl$ $[M+H]^+$ 297.05893; found 297.05937.

3-iodo-1-phenylimidazo[1,5-*a*]quinoline (3ed): Pale yellow solid (120 mg, 65% yield), mp 142-143 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.60 (m, 3H), 7.55 – 7.47 (m, 4H), 7.36 – 7.32 (m, 1H), 7.25 (d, *J* = 9.3 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.11 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 132.7, 132.4, 132.3, 129.7, 129.6, 128.8, 127.7, 125.7, 122.9, 117.1, 117.1, 77.8; IR v = 3061, 2972, 2856, 1609, 1475, 1449, 1359, 795, 756, 699, 668 cm^{-1}; MS (ESI, m/z) 371 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2I$ $[M+H]^+$ 371.00397; found 371.00420.

1-(4-fluorophenyl)-3-iodoimidazo[1,5-*a*]quinoline (3ee): Pale yellow solid (97 mg, 50% yield), mp 191-192 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.56 (m, 3H), 7.46 (d, *J* = 8.6 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.20 (m, 4H), 7.12 (d, *J* = 9.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5 (d, *J* = 250.2 Hz), 143.1, 132.5, 132.2, 131.7 (d, *J* = 8.4 Hz), 129.0, 128.9, 127.7, 125.8 (d, *J* = 5.9 Hz), 123.0, 117.0 (d, *J* = 21.7 Hz), 116.1 (d, *J* = 21.9 Hz), 77.8; IR v = 3066, 2924, 2856, 1605, 1522, 1450, 1359, 1298, 1228, 1158, 1094, 963, 885, 839, 764, 659 cm^{-1}; MS (ESI, m/z) 389 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{11}N_2FI$ $[M+H]^+$ 388.99455; found 388.99486.

1-iodo-3-phenylimidazo[5,1-*a*]isoquinoline (3ef): Pale yellow solid (130 mg, 70% yield), mp 141-142 °C; ^{1}H NMR (400 MHz,) δ 9.16 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.80 – 7.71 (m, 2H), 7.62 – 7.46 (m, 6H), 6.80 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 129.5, 129.0, 128.7, 128.1, 127.7, 127.5, 127.1, 124.7, 122.0, 120.3, 114.9, 74.3; IR v = 3061, 2972, 2856, 1609, 1475, 1449, 1359, 795, 756, 699, 668 cm^{-1}; MS (ESI, m/z) 371 $[M+H]^+$, HRMS (ESI) Calcd for $C_{17}H_{12}N_2I$ $[M+H]^+$ 371.00397; found 371.00420.

1-iodo-3-phenylimidazo[1,5-*a*]pyridine (3fa): Green solid (131 mg, 41% yield), mp 142-143 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 7.2 Hz, 1H), 7.77 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.37 (d, *J* = 9.2 Hz, 1H), 6.83 – 6.79 (m, 1H), 6.61 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.4, 133.4, 129.3, 129.0, 129.0, 128.0, 121.8, 120.2, 119.0, 113.9, 74.1; IR v = 3062, 2924, 2857, 1713, 1631, 1508, 1454, 1358, 1258, 1170, 1000, 943, 740, 689, 626 cm^{-1}; MS (ESI, m/z) 321 $[M+H]^+$, HRMS (ESI) Calcd for $C_{13}H_{10}N_2I$ $[M+H]^+$ 320.98832; found 320.98823.

1-iodo-3-(4-methoxyphenyl)imidazo[1,5-*a*]pyridine (3fb): Green solid (140 mg, 40% yield), mp 90-91 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 10.8 Hz, 2H), 7.33 (d, *J* = 11.2 Hz, 1H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.77 (t, *J* = 9.0 Hz, 1H), 6.57 (t, *J* = 7.5 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2, 140.4, 133.0, 129.4, 121.8, 121.6, 120.0, 118.9, 114.4, 113.8, 73.4, 55.4; IR v = 2930, 2840, 1611, 1526, 1459, 1358, 1252, 1179, 1031, 945, 838, 739, 684, 636 cm^{-1}; MS (ESI, m/z) 351 $[M+H]^+$

1-iodo-3-(p-tolyl)imidazo[1,5-*a*]pyridine (3fc): Green solid (127 mg, 38% yield), mp 110-111 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 7.3 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.37 – 7.29 (m, 3H), 6.80 – 6.77 (m, 1H), 6.58 (t, *J* = 6.3 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 139.1, 133.2, 129.6, 127.9, 126.4, 121.9, 120.0, 119.0, 113.7, 73.8, 21.4; IR v = 2925, 2858, 1727, 1628, 1464, 1361, 1261, 1124, 1008, 947, 826, 742, 687, 627 cm^{-1}; MS (ESI, m/z) 335 $[M+H]^+$, HRMS (ESI) Calcd for $C_{14}H_{12}N_2I$ $[M+H]^+$ 335.00397; found 335.00356.

1-iodo-3-(o-tolyl)imidazo[1,5-*a*]pyridine (3fd): Green solid (110 mg, 33% yield), mp 103-104 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.33 (m, 4H), 7.31 (t, *J* = 7.7 Hz, 1H), 6.82 – 6.79 (m, 1H), 6.56 (t, *J* = 6.8 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 138.3, 132.5, 130.8, 130.5, 129.7, 128.4, 126.0, 121.9, 120.0, 118.7, 113.5, 72.8, 19.7; IR v = 3062, 2925, 1632, 1461, 1355, 1258, 1106, 1004, 945, 772, 738, 691, 629 cm^{-1}; MS (ESI, m/z) 335 $[M+H]^+$, HRMS (ESI) Calcd for $C_{14}H_{12}N_2I$ $[M+H]^+$ 335.00397; found 335.00403.

3-(4-fluorophenyl)-1-iodoimidazo[1,5-*a*]pyridine (3fe): Green solid (91 mg, 27% yield), mp 92-93 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 7.2 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.37 (d, *J* = 9.2 Hz, 1H), 7.24 – 7.18 (m, 2H), 6.84 – 6.80(m, 1H), 6.63 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.0 (d, *J* = 249.9 Hz), 139.5, 133.4, 130.0 (d, *J* = 8.3 Hz), 125.6, 121.5, 120.2, 119.1, 116.2 (d, *J* = 21.9 Hz), 114.1, 74.0; IR v = 3071, 2924, 2856, 1724, 1602, 1524, 1459, 1359, 1301, 1231, 1161, 1007, 843, 739, 684, 626 cm^{-1}; MS (ESI, m/z) 339 $[M+H]^+$, HRMS (ESI) Calcd for $C_{13}H_9N_2FI$ $[M+H]^+$ 338.97890; found 338.97865.

3-(4-chlorophenyl)-1-iodoimidazo[1,5-*a*]pyridine (3ff): Green solid (100 mg, 28% yield), mp 94-95 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 6.85 – 6.81 (m, 1H), 6.65 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 134.9, 133.6, 129.3, 129.1, 127.8, 121.6, 120.3, 119.1, 114.3, 74.4; IR v = 2926, 2857, 1727, 1466, 1366, 1289, 1081, 769, 625 cm^{-1}; MS (ESI, m/z) 355 $[M+H]^+$, HRMS (ESI) Calcd for $C_{13}H_9N_2ClI$ $[M+H]^+$ 354.94935; found 354.94929.

1-iodo-5-methyl-3-phenylimidazo[1,5-*a*]pyridine (3fg): Green solid (160 mg, 48% yield), mp 125-126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.47 (m, 2H), 7.45 (d, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.30 (d, *J* = 9.1 Hz, 1H), 6.75 (dd, *J* = 9.1, 6.5 Hz, 1H), 6.34 (d, *J* = 6.5 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.1, 134.2, 133.6, 132.8, 131.0, 129.1, 127.4, 120.5, 116.9, 114.6, 73.6, 21.7; IR v = 3060, 2924, 1637, 1531, 1444, 1322, 1256, 1078, 986, 860, 767, 701, 661 cm^{-1}; MS (ESI, m/z) 335 $[M+H]^+$; HRMS $C_{14}H_{12}N_2I$ $[M+H]^+$ Calcd 335.00397; found 335.00369.

1-iodo-3-(4-methoxyphenyl)-5-methylimidazo[1,5-*a*]pyridine (3fh): Green solid (116 mg, 32% yield), mp 90-91 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 8.8 Hz, 2H), 7.31 – 7.23 (m, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.75 – 6.71 (m, 1H), 6.32 (d, *J* = 6.5 Hz, 1H), 3.87 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 141.1, 134.1, 133.7, 132.3, 125.1, 120.3, 117.0, 114.4, 112.8, 73.4, 55.2, 21.6; IR v = 2930, 2840, 1611, 1526, 1459, 1358,

1252, 1179, 1031, 945, 838, 739, 684, 636 cm^{-1}; MS (ESI, m/z) 365 $[M+H]^+$, HRMS (ESI) Calcd for $C_{15}H_{14}N_2OI$ $[M+H]^+$ 365.01453; found 365.01455.

3-(4-fluorophenyl)-1-iodo-5-methylimidazo[1,5-*a*]pyridine(3fi): Green solid (120 mg, 34% yield), mp 115-116 °C; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.45 (m, 2H), 7.31 (d, *J* = 9.2 Hz, 1H), 7.12 (t, *J* = 8.7 Hz, 2H), 6.78 – 6.75 (m, 1H), 6.36 (d, *J* = 8.6 Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, *J* = 249.6 Hz), 139.9, 134.3, 133.4, 132.8 (d, *J* = 8.4 Hz), 128.9, 120.6, 117.0, 114.7 (d, *J* = 11.9 Hz), 114.4, 73.6, 21.7; IR v = 3063, 2925, 1601, 1525, 1448, 1324, 1224, 1089, 858, 768, 690 cm^{-1}; MS (ESI, m/z) 353 $[M+H]^+$, HRMS (ESI) Calcd for $C_{14}H_{11}N_2FI$ $[M+H]^+$ 352.99455; found 352.99445.

1-iodo-5-methyl-3-(p-tolyl)imidazo[1,5-*a*]pyridine (3fj): Green solid (167 mg, 48% yield), mp 124-125 °C; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 5.0 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 2H), 6.73 (dd, *J* = 9.1, 6.5 Hz, 1H), 6.32 (d, *J* = 6.5 Hz, 1H), 2.42 (s, 3H), 2.12 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 139.1, 134.1, 133.7, 130.9, 129.8, 128.1, 120.3, 116.9, 114.4, 73.4, 21.7, 21.4; IR v = 3025, 2924, 2857, 1908, 1745, 1636, 1528, 1449, 1354, 1321, 1258, 1079, 986, 862, 823, 766, 729, 692 cm^{-1}; MS (ESI, m/z) 349 $[M+H]^+$; HRMS (ESI) Calcd for $C_{15}H_{14}N_2I$ $[M+H]^+$ 349.01962; found 349.01958.

1-iodo-5-methyl-3-(*o*-tolyl)imidazo[1,5-*a*]pyridine (3fk): Green solid (146 mg, 42% yield), mp 116-117 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 9.2 Hz, 1H), 7.22 (t, *J* = 8.7 Hz, 2H), 6.73 (dd, *J* = 9.2, 6.5 Hz, 1H), 6.31 (d, *J* = 6.5 Hz, 1H), 2.05 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 139.3, 133.8, 133.5, 132.8, 131.6, 129.6, 129.2, 124.8, 120.3, 117.0, 114.2, 73.1, 20.3, 19.9; IR v = 3025, 2924, 2857, 1908, 1745, 1636, 1528, 1449, 1354, 1321, 1258, 1177, 1079, 986, 862, 823, 766, 729, 692 cm^{-1}; MS (ESI, m/z) 349 $[M+H]^+$; HRMS (ESI) Calcd for $C_{15}H_{14}N_2I$ $[M+H]^+$ 349.01962; found 349.01957.

1-chloro-3-phenylimidazo[1,5-*a*]pyridine (3fl): Green solid (21 mg, 9% yield), mp 157-158 °C; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 7.3 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.49 – 7.42 (m, 2H), 6.79 – 6.75 (m, 1H), 6.60 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.9, 129.3, 129.0, 127.9, 126.4, 121.3, 119.8, 119.2, 117.6, 113.9; IR v = 3064, 2925, 2858, 1746, 1634, 1599, 1513, 1455, 1369, 1281, 1026, 952, 738, 691 cm^{-1}; MS (ESI, m/z) 229 $[M+H]^+$, HRMS (ESI) Calcd for $C_{13}H_{10}N_2Cl$ $[M+H]^+$ 229.05270; found 229.05299.

1-bromo-3-phenylimidazo[1,5-*a*]pyridine (3fm): Green solid (14 mg, 5% yield); mp 120-121 °C; ^1H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 7.3 Hz, 1H), 7.78 – 7.76 (m, 2H), 7.55 – 7.48 (m, 2H), 7.48 – 7.40 (m, 2H), 6.82 – 6.76 (m, 1H), 6.62 – 6.59 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 129.2, 129.0, 128.9, 127.9, 121.5, 119.6, 118.1, 114.0, 106.4; IR v = 3063, 2925, 2857, 1748, 1594, 1469, 1365, 1263, 1123, 1005, 744, 699 cm^{-1}; MS (ESI, m/z) 273 $[M+H]^+$, HRMS (ESI) Calcd for $C_{13}H_{10}N_2Br$ $[M+H]^+$ 273.00219; found 273.00237.

1,3-diphenylimidazo[1,5-*a*]quinoline (4aa): Pale yellow solid (256 mg, 80% yield), mp 134−135 °C; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 7.1 Hz, 2H), 7.72 – 7.66 (m, 3H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.47 (t, *J* = 7.7 Hz, 3H), 7.38 – 7.27 (m, 2H), 7.18- 7.12 (m, 1H), 7.08 (d, *J* = 9.5 Hz, 1H). ^{13}C NMR (101 MHz) δ 142.1, 134.4, 133.8, 133.6, 132.5, 129.8, 129.4, 128.9, 128.7, 128.4, 127.5, 127.0, 126.5, 125.7, 125.2, 122.1, 120.1, 117.5, 115.4. IR v = 2923, 1519, 843, 696; MS (ESI, m/z) 321 $[M+H]^+$, HRMS (ESI) Calcd for $C_{23}H_{17}N_2$ $[M+H]^+$ 321.13863; found 321.13944.

Acknowledgements

MS thank UGC-India for financial support in the form of senior research fellowship (SRF). Dr.KRR thanks Director, CSIR-IICT for financial support.

Communication No: IICT/Pubs./2018/110

Keywords: 2-methyl azarenes • Aliphatic amines • Phenylglycine • Copper salts • C-H functionalization

References

[1] D. Kim, L. Wang, J. J. Hale, C. L. Lynch, R. J. Budhu, M. M. Coss, S. G. Mills, L. Malkowitz, S. L. Gould, J. A. D. Martino, M. S. Springer, D. Hazuda, M. Miller, J. Kessler, R. C. Hrin, G. Carver, A. Carella, K. Henry, J. Lineberger, W. A. Schleif, E. A. Emini*, Bioorg. Med. Chem. Lett.* **2005**, *15*, 2129-2134.

[2] M. S. Malamas, Y. Ni, J. Erdei, H. Stange, R. Schindler, H. –J. Lankau, C. Grunwald, K. Y. Fan, K. Parris, B. Langen, U. Egerland, T. Hage, K. L. Marquis, S. Grauer, J. Brennan, R.Navarra, R. Graf, B. L. Harrison, A. Robichaud, T. Kronbach, M. N. Pangalos, N. Hoefgen, N. J. Brandon, *J. Med. Chem.* **2011**, *54*, 7621-7638.

[3] A. Kamal, G. Ramakrishna, P. Raju, A. V. S. Rao, A. Viswanath, V. L. Nayak, S. Ramakrishna**,** *Eur. J. Med. Chem,* **2011,** *46***,** 2427-2435.

[4] N. F. Ford, L. J. Browne, T. Campbell, C. Gemenden, R. Goldstein, C. Gude, J. W. F. Wasley*, J. Med. Chem.* **1985**, *28*, 164-170.

[5] a) G. R. Pettit, J. C. Collins, J. C. Knight, D. L. Herald, R. A. Nieman, M. D. Williams, R. K. Pettit, *J. Nat. Prod.* **2003**, *66*, 544-547. For recent total syntheses of cribrostatin 6, see: b) M. Mohamed, T. P. GonÅalves, R. J. Whitby, H. F. Sneddon, D. C. Harrowven, *Chem. Eur. J.* **2011**, *17*, 13698-13705. c) D. Knueppel, S. F. Martin, *Angew. Chem. Int. Ed*. **2009**, *48*, 2569-2571. d) M. D. Markey, T. R. Kelly, *J. Org. Chem.* **2008**, *73*, 7441-7443.

[6] a) M. Nakatsuka, T. Shimamura, Jpn. Kokai Tokkyo Koho, JP2001035664, 2001; *Chem. Abstr*., **2001**, *134*, 170632. b) G. Tominaga, R. Kohama, A. Takano, Jpn. Kokai Tokkyo Koho, JP2001006877, 2001; *Chem. Abstr*., **2001**, *134*, 93136. c) D. Kitazawa, G. Tominaga, A. Takano, Jpn. Kokai Tokkyo Koho, JP2001057292, 2001; *Chem. Abstr*., **2001**, *134*, 200276. d) L. Salassa, C. Garino, A. Albertino, G. Volpi, C. Nervi, R. Gobrtto, K. I. Hardcastle, *Organometallics*, **2008**, *27*, 1427-1435.

[7] H. Nakamura, H. Yamamoto, *PCT Int. Appl*., WO2005043630**, 2005**; *Chem. Abstr*., **2005**, *142*, 440277.

[8] a) J. D. Bower, G. R. Ramage, *J. Chem. Soc*. **1955**, 2834−2837. For other variants: b) G. Pelletier, A. B. Charette, *Org. Lett.* **2013**, *15*, 2290-2293 and references cited therein..

[9] a) M. Li, Y. Xie, Y. Ye, Y. Zou, H. Jiang, W. Zeng, *Org. Lett***. 2014,** *16***,** 6232-6235. b) H. Wang, W. Xu, Z. Wang, L. Yu, K. Xu, *J. Org. Chem*. **2015**, *80*, 2431-2435. c) Y. Yan, Y. Zhang, Z. Zha, Z. Wang, *Org. Lett.,* **2013**, *15*, 2274-2277. d) D. C. Mohan, S. N. Rao, C.Ravi, S. Adimurthy, *Org. Biomol. Chem*., **2015**, *13*, 5602-5607. e) Z. Li, S. -S. Wu, Z. –G. Luo, W. –K. Liu, C. –T. Feng, S. –T. Ma, *J. Org. Chem*. **2016**, *81*, 4386-4392. f) Z. Tan, H. Zhao, C. Zhou, H. Jiang, M. Zhang, *J. Org. Chem*. **2016**, *81*, 9939-9946.

[10] Selected examples: a) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem. Int. Ed*. **2011**, *50*, 11062-11087. b) Z. Shi, C. Zhang, C. Tanga, Ning Jiao, *Chem. Soc. Rev*., **2012**, *41*,3381-3430. c) S. E. Allen, R. R. Walvoord, R. P.-Salinas, M. C. Kozlowski, *Chem. Rev*. **2013**, *113*, 6234-6458. d) O. Basle´, C.-J. Li, *Green Chem*., **2007**, *9*, 1047-1050. e) X. –X. Guo, D. –W. Gu, Z. Wu, W. Zhang, *Chem. Rev.* **2015**, *115*, 1622-1651. f) X. Xu, M. Zhang, H. Jiang, J. Zheng, Y. Li, *Org. Lett*. **2014**, *16*, 3540-3543. g) R. Gava, A. Olmos, B. Noverges, T. Varea, E. Álvarez, T. R. Belderrain, A. Caballero, G. Asensio, P. J. Pérez, *ACS Catal*. **2015**, *5*, 3726-3730. h) J. Liu, G. Chen, Z. Tanb, *Adv.Synth. Catal***. 2016**, *358*, 1174-1194. i) S. Ranjit, R. Lee, D. Heryadi, C. Shen, J.'E. Wu, P. Zhang, K. –W. Huang, X. Liu, *J. Org. Chem*. **2011**, *76*, 8999-9007. j) M. Wang, Y. Hu, Z. Jiang, H. C. Shen, X. Sun, *Org. Biomol. Chem*., **2016**, *14*, 4239-4246. k) W. –H. Rao, B. –F. Shi, *Org. Chem. Front*., **2016**, *3*, 1028-1047.

[11] a) A. de Meijere, S. Bräse, M. Oestreich, *Metal Catalyzed Cross-Coupling Reactions and More, 3 Volume Set*. (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley, 2014.)) b) I. J. S. Fairlamb, *Chem. Soc. Rev*., **2007**, *36*, 1036-1045.

[12] Selected examples: a) F. Shibahara, E. Yamaguchi, A. Kitagawa, A. Imai, T. Murai, *Tetrahedron*, **2009**, *65*, 5062-5073. b) H. E. Podall, W. E. Foster, *J. Org. Chem*. **1958**, *23*, 280-281. c) G. M. Kosolapoff, *J. Am. Chem. Soc*. **1953**, *75*, 3596-3597. d) N. Iranpoor, M. Shekarriz, *Tetrahedron*, **2000**, *56*, 5209-5211. e) S. M. Bonesi, R. E.-Balsells, *J. Heterocyclic Chem*., **2001**, *38*, 77-87. f) V. K. Chaikovski, V. D. Filimonov, A. Y. Yagovkin, T. S. Kharlova, *Tetrahedron Lett,* **2000**, *41*, 9101-9104.

[13] a) L. Menini, E. V. Gusevskaya, *Chem. Commun*. **2006**, 209-211. b) L. Menini, E. V. Gusevskaya *Applied Catalysis A: General*, **2006**, *309*, 122-128. c) L. Menini, L. A. Parreira, E. V. Gusevskaya, *Tetrahedron Letters*, **2007**, *48,* 6401-6404. d) L. Menini, J. C. da C. Santos, E. V. Gusevskaya, *Adv. Synth. Catal*. **2008**, *350*, 2052-2058. e) L. Yang, Z. Lu, S. S. Stahl, *Chem. Commun*., **2009**, 6460-6462. f) J. Wang, W. Wang, J. –H. Li, *GreenChem*., **2010**,*12*, 2124-2126. g) A. M. Suess, M. Z. Ertem, C. J. Cramer, S. S. Stahl, *J. Am. Chem. Soc*. **2013**, *135*, 9797-9804. h**)** W. Hao, Y. Liu, *Beilstein J. Org. Chem*. **2015**, *11*, 2132-2144. i) N. K. Swamy, A. Yazici, S. G. Pyne, *J. Org. Chem.* **2010**, *75*, 3412-3419.

[14] a) G. S. Kumar, C. U. Maheswari, R. A. Kumar, M. L. Kantam, K. R. Reddy, *Angew. Chem. Int. Ed*. **2011**, *50*, 11748-11751. b) G. S. Kumar, R. A. Kumar, P. S. Kumar, N. V. Reddy, K. V. Kumar, M. L. Kantam, S. Prabhakar, K. R. Reddy, *Chem. Commun.,* **2013**, *49*, 6686-6688. c) R. A. Kumar, G. Saidulu, B. Sridhar, S. T. Liu, K. R. Reddy, *J. Org. Chem*. **2013**, *78*, 10240-10250. d) P. S. Kumar, G. S. Kumar, R. A. Kumar, N. V. Reddy, K. R. Reddy, *Eur. J. Org. Chem*. **2013**, 1218-1222.

[15] a) Q. Wang, S. Zhang, F. Guo, B. Zhang, P. Hu, Z. Wang, *J. Org. Chem*. **2012**, *77*, 11161-11166. b) H. Wang, W. Xu, L. Xin, W. Liu, Z. Wang, K. Xu, *J. Org. Chem*. **2016**, *81*, 3681-3687.

[16] a) A. E. King, L. M. Huffman, A. Casitas, M. Costas, X. Ribas, S. S. Stahl, *J. Am. Chem. Soc.*, **2010**, *132*, 12068-12073. b) Y. Liu, W. Wang, J. Han, J. Sun, *Org. Biomol. Chem*., **2017**, *15*, 9311-9318.

10.1002/ejoc.201800628

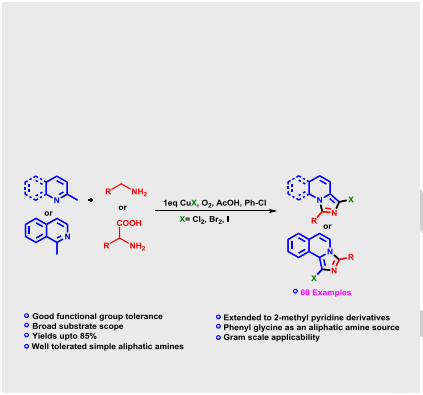
WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

A tandem reaction for the direct access to halogenated fused imidazo[1,5-*a*]*N*-heteroaromatics is developed, with 2-methylazarenes and aliphatic amines or amino acids *via* copper mediated double oxidative C-H amination and halogenation. In this strategy, copper salts serves as catalysts as well as halogen source and molecular oxygen as the sole oxidant.



Key Topic* C-H functionalization, C-H amination.

M. Sandeep, [a],[b] *P. Swati, B. Sravani and K. Rajender Reddy**[a],[b]

Page No. – Page No.

Title
A Direct Access to Halogenated Fused Imidazo[1,5-*a*]*N*-heteroaromatics *via* Copper Promoted Double Oxidative C-H Amination and Halogenation

*one or two words that highlight the emphasis of the paper or the field of the study

Layout 2:

FULL PAPER

((Insert TOC Graphic here; max. width: 11.5 cm; max. height: 2.5 cm; NOTE: the final letter height should not be less than 2 mm.))

Key Topic*

*Author(s), Corresponding Author(s)**

Page No. – Page No.

Title

Text for Table of Contents

*one or two words that highlight the emphasis of the paper or the field of the study