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Sodium salts (NaI/NaBr/NaCl) for the halogenation of imidazo-fused heterocycles

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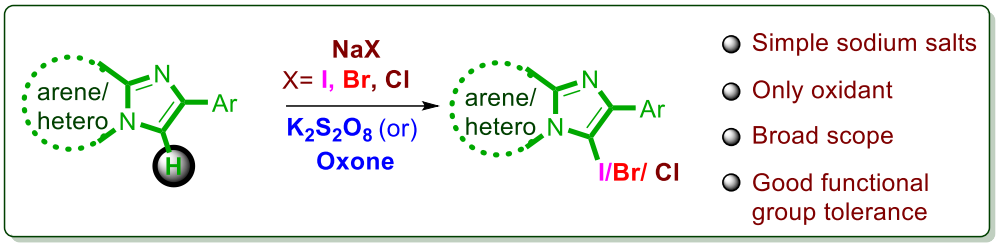

We report herein an effective method for the halogenation of imidazo-fused heterocycles using readily available sodium salts (NaCl/NaBr/NaI) as halogen source and $K_2S_2O_8$ (or) oxone as promoter. A variety of C-3 halogenated imidazo[1,2-a]pyridines and benzo[d]imidazo[2,1-b]thiazoles were obtained in good to excellent yields. The present method of halogenation has been also extended to 2-aminopyridines, 2-aminopyrimidine, indole and isoquinoline with moderate to excellent yields.

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Introduction:

Halogenated (hetero)aromatic compounds are valuable and fundamental building blocks that are being used to construct carbon–carbon and carbon–heteroatom bonds in organic synthesis and drug design.[1] They play pivotal role in drug and natural-product syntheses.[2] Furthermore, (hetero)aromatic bromides and iodides have been extensively used in cross-coupling[3] and in Grignard reactions.[4] The functionalization of (hetero) aromatic compounds with halides through direct activation of C−H bond is a straightforward strategy to obtain halogenated aromatic products.

In recent years, considerable attention has been paid to the development of new routes for the construction of halogenated scaffolds, utilising safe and readily available halide sources such as NH_4X, NaX and HX (X= Br, Cl) have been reported.[5] Particularly, halogenated

imidazofused heterocycles represent an important class of molecules and show unique bioactivities. Particularly, functionalised imidazo[1,2-a]pyridines through halogenations were commercially marketed as drugs. For example, C-3 substituted imidazo[1,2-a]pyridines are well known drug candidates such as zolimidine (pepticulcer), alpidem (anxiolytic), zolpidem (insomnia), saripidem (anxiolytic), olprinone (cardiotonic), necopidem, minodronic acid (antiosteoporosis) and GSK812397 (anti HIV) are basic imidazo[l,2-a]pyridine skeleton are clinically derived (Figure 1).[6]

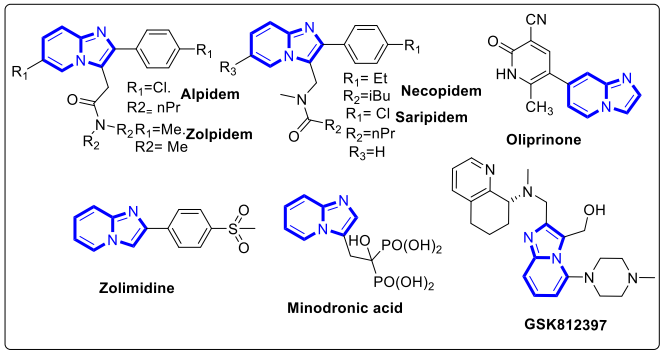
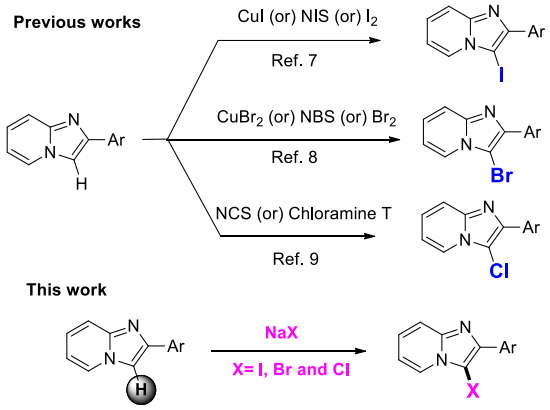


Figure 1. Biological activity of imidazo[1, 2–a]pyridines

In recognition of the importance of these molecules, recently many research groups demonstrated the halogenation of imidazo[1,2-a]pyridines using CuX, NXS and X_2 (X=Br, I) for bromination and iodination,[7,8] NCS and Chloramine- T for chlorination (Scheme 1).[9] Recently, sodium chlorite/bromite has been reported as a halogen source.[10] Even though these methods are efficient, there were no reports for the halogenation of imidazo[1,2-a]pyridines with simple sodium salts as halogenation source. In continuation



Scheme 1. Halogenation of 2-phenylimidazo[1,2-a]pyridine

of our efforts on the functionalization of imidazo[1,2-a]pyridines,[11] and development of eco-friendly halogenation reagents,[12] we report herein the halogenation of imidazo[1,2-a]pyridines and representative other heterocycles using readily available sodium salts (NaI, NaBr and NaCl) as a source for the halogenation under mild reaction conditions.

Results and Discussion:

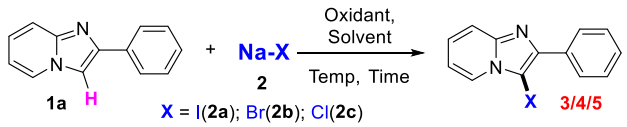
Initially, we focused on the optimization of conditions for the iodination of 2-phenylimidazo[1,2-a]pyridine **1a** using sodium iodide (NaI; **2a**) as iodine source with $Na_2S_2O_8$ as oxidant at 60°C in dichloroethane (DCE) as solvent. To our delight, the desired product 3-iodo 2-phenylimidazo[1,2-a]pyridine **3a** was isolated in 54% yield after 24 h of reaction time (Table 1, entry 1). When the reaction was performed with $K_2S_2O_8$ as oxidant instead of $Na_2S_2O_8$, it resulted in 61% yield of the product **3a** (Table 1, entry 2). The same reaction in acetonitrile (ACN) as solvent the yield of **3a** was increased to 66% (entry 3). To enhance the yield of the iodination, the amount of both NaI and $K_2S_2O_8$ were increased to 0.5 equivalents under these conditions the product yield was raised to 74% (entries 4 and 5).

By decreasing the temperature from 60 to 50°C, the yield of **3a** was increased to 82%, it may be due to the stabilisation of the reactive species generated in-situ (entry 6). Further conducting the reaction at room temperature the yield was decreased to 76% (entry 7). It was observed that, temperature of the reaction was another decisive factor which influence the yield of the product (Table 1, entries 6 & 7). Then, we checked the reaction in dichloromethane (DCM) and diethyl ether (DEE) as solvents, in these cases 75% yield of **3a** and no reaction was observed respectively (Table 1, entries 8 and 9). To check the effect of iodide salt, the reaction was performed with ammonium iodide (NH_4I; 0.5 mmol) in place of NaI, at 50 ℃, under these conditions the yield of desired product was decreased to 60% (entry 10). Based on above studies we fixed the table 1, entry 6 as the best suitable conditions for the extension of iodination for other substrates. Encouraged by the above results on iodination of **1a**, our studies further applied towards optimization of reaction conditions for bromination and chlorination using NaBr (**2b**) and NaCl (**2c**) as corresponding halogen sources.

With the optimized conditions of iodination (entry 6), **1a** was subjected to bromination using NaBr as bromine source. Interestingly, 44% of brominated product **4a** was obtained

(Table 1, entry 11). When the reaction was conducted at room temperature (entry 12) and in DCM as solvent (entry 13) the yield of the bromo product **4a** was marginally increased (53% and 54%). With DCM as solvent, the NaBr amount was increased to 1.0 - 1.25 mmol, the yield of **4a** was obtained in 84% and 95% respectively (entries 14 and 15).

Table 1. Screening of conditions for halogenation of **1a**[a]



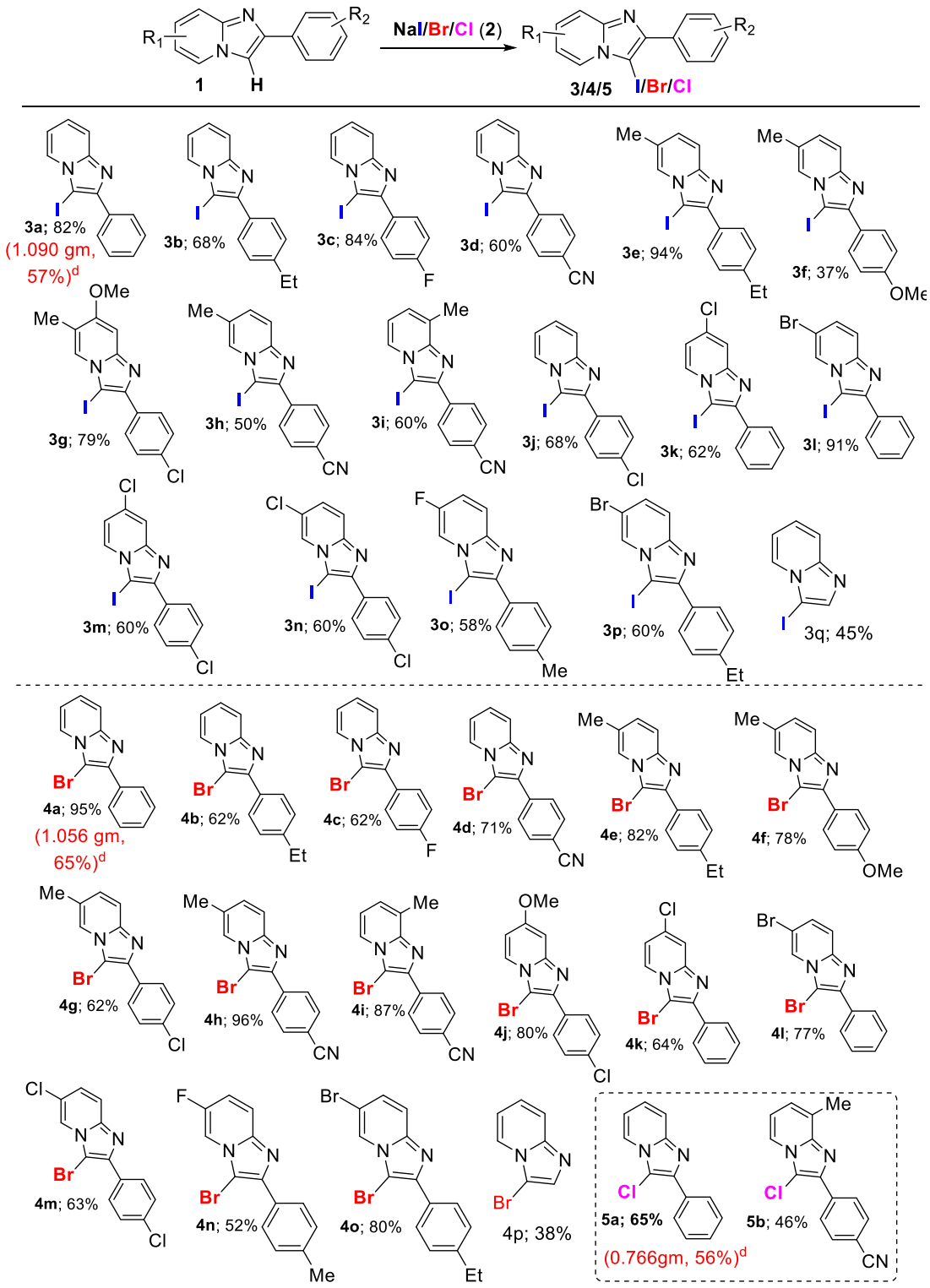
S.No	MX (mmol)	Oxidant (mmol)	Solvent (1 mL)	Temp (°C)	Yield (%)
1	NaI (0.25)	$Na_2S_2O_8$ (0.25)	DCE	60	54
2	NaI (0.25)	$K_2S_2O_8$ (0.25)	DCE	60	61
3	NaI (0.25)	$K_2S_2O_8$ (0.25)	ACN	60	66
4	NaI (0.5)	$K_2S_2O_8$ (0.25)	ACN	60	70
5	NaI (0.5)	$K_2S_2O_8$ (0.5)	ACN	60	74
6	**NaI (0.5)**	**$K_2S_2O_8$ (0.5)**	**ACN**	**50**	**82**
7	NaI (0.5)	$K_2S_2O_8$ (0.5)	ACN	RT	76
8	NaI (0.5)	$K_2S_2O_8$ (0.5)	DCM	RT	75
9	NaI (0.5)	$K_2S_2O_8$ (0.5)	DEE	RT	nr
10	NH_4I (0.5)	$K_2S_2O_8$ (0.5)	ACN	50	60
11	NaBr(0.5)	$K_2S_2O_8$ (0.5)	ACN	50	44
12	NaBr(0.5)	$K_2S_2O_8$ (0.5)	ACN	RT	53
13	NaBr(0.5)	$K_2S_2O_8$ (0.5)	DCM	RT	54
14	NaBr(1)	$K_2S_2O_8$ (0.5)	DCM	RT	84
15	**NaBr(1.25)**	**$K_2S_2O_8$ (0.5)**	**DCM**	**RT**	**95**
16	NaBr(1.25)	$K_2S_2O_8$ (0.5)	Acetone	RT	73
17	NH_4Br(1.25)	$K_2S_2O_8$ (0.5)	DCM	RT	50
18	NaCl (1.25)	$K_2S_2O_8$ (0.5)	DCM	RT	Traces
19	NaCl (1.25)	$K_2S_2O_8$ (0.5)	ACN	RT	33
20	NaCl (1.25)	$K_2S_2O_8$ (0.5)	ACN	60	40
21	NaCl (1.25)	$Na_2S_2O_8$ (0.5)	ACN	60	Traces
22	NaCl (1.25)	$(NH_4)_2S_2O_8$ (0.5)	ACN	60	50
23	NaCl (1.25)	Oxone (0.5)	ACN	60	55
24	NaCl (1.25)	Oxone (0.5)	ACN	80	60
25	NaCl (1.25)	Oxone (0.5)	ACN	100	53
26	**NaCl (1.25)**	**Oxone (0.5)**	**ACN+H_2O**	**80**	**65**
27	NaCl (1.25)	Oxone (0.5)	DCE+H_2O	80	60
28	NaCl (1.25)	Oxone (0.5)	DMF+H_2O	80	42
29	NaCl (1.25)	Oxone (0.75)	ACN+H_2O	80	49
30	NaCl (2)	Oxone (0.5)	ACN+H_2O	80	62
31	NH_4Cl (1.25)	Oxone (0.5)	ACN+H_2O	80	55

[a]Reaction conditions: **1a** (0.25 mmol), **2**, oxidant, solvent (1.0 mL), 24 h, isolated yields. For entries 26-31 the 2:1 ratio of mixture of solvents. DCE (dichloroethane), DCM (dichloromethane), ACN (acetonitrile), DEE (diethyl ether)

Interestingly, the reaction works moderately with acetone as solvent (entry 16). Also, we performed the reaction with NH_4Br as a brominating reagent, but the yield was reduced to 50% (entry 17). We then, extended the methodology for the chlorination of **1a** under the same conditions using NaCl (**2c**) as chlorine source (entry 18). By screening the various conditions such as solvent, temperature and oxidant, the desired product 3-chloro-2-phenylimidazo[1,2-a]pyridine **5a** was obtained up to 60% yield (Table 1, entries 18-25). Further we screened the reaction with, aqueous mixture of solvents, ammonium chloride NH_4Cl and varying the amount of oxidant (oxone) at 80°C (entries 26-31), the best yield of chlorinated product was obtained under the conditions of; 1.25 mmol of NaCl, 0.5 mmol of oxone, 2:1 mixture of acetonitrile and water (ACN+H_2O) as solvent at 80 ℃ (Table 1, entry 26).

With the above optimised conditions, we explored the substrate scope for the halogenation (I/Br/Cl) of different imidazopyridines (Table 2). First, we examined the C-3 iodination of *para* substituted 2-phenylimidazo[1,2-a]pyridines using NaI as iodine source (with the conditions of Table 1, entry 6). To our delight, the protocol tolerated the presence of electron-rich and electron-deficient groups (i.e., Et, F, and CN) and proceeded smoothly under the optimized conditions to give good yields (60–84 %) of selectively C-3 iodinated products **3b**–**3d**. The presence of electron-rich and electron-deficient groups (i.e., Me, Et, OMe, Cl, Br, and CN) at different positions of the phenyl as well as pyridyl ring of the 2-phenylimidazo[1,2-a]pyridines were underwent to these conditions smoothly to afford the corresponding C-3 iodinated imidazo-[1,2-a]pyridines **3e**–**3l** in low to good yields (37–94 %). Dichloro, halo and alkyl substituted imidazopyridines also gave the corresponding iodinated products **3m**–**3p** in moderate yields. The iodination of unsubstituted imidazo(1,2-a)pyridine offered 45% yield of selective C-3 mono-iodinated product **3q**.

Table 2. Scope of halogenation of imidazo[1,2-a]pyridines [a,b,c]



Reaction conditions for products (**3a-q**)[a]: **1** (0.25 mmol), **2a** (0.5 mmol, 2.0 equiv.), $K_2S_2O_8$ (0.5 mmol, 2.0 equiv.), ACN (1 mL), 50°C, 24 h. For (**4a-p**)[b]: **1** (0.25 mmol), **2b** (1.25 mmol, 5.0 equiv.), $K_2S_2O_8$ (0.5 mmol, 2.0 equiv.), DCM (1 mL), RT, 24 h. For (**5a-b**)[c]: **1** (0.25 mmol), **2c**

(1.25 mmol, 5.0 equiv.), oxone (0.5 mmol, 2.0 equiv.), [ACN+ H_2O] (1 ml), 80°C, 24 h. [d] Gram scale synthesis (all reaction are performed at 6.0 mmol w.r.t. **1**). All the reported products are isolated yields after column chromatographic separation.

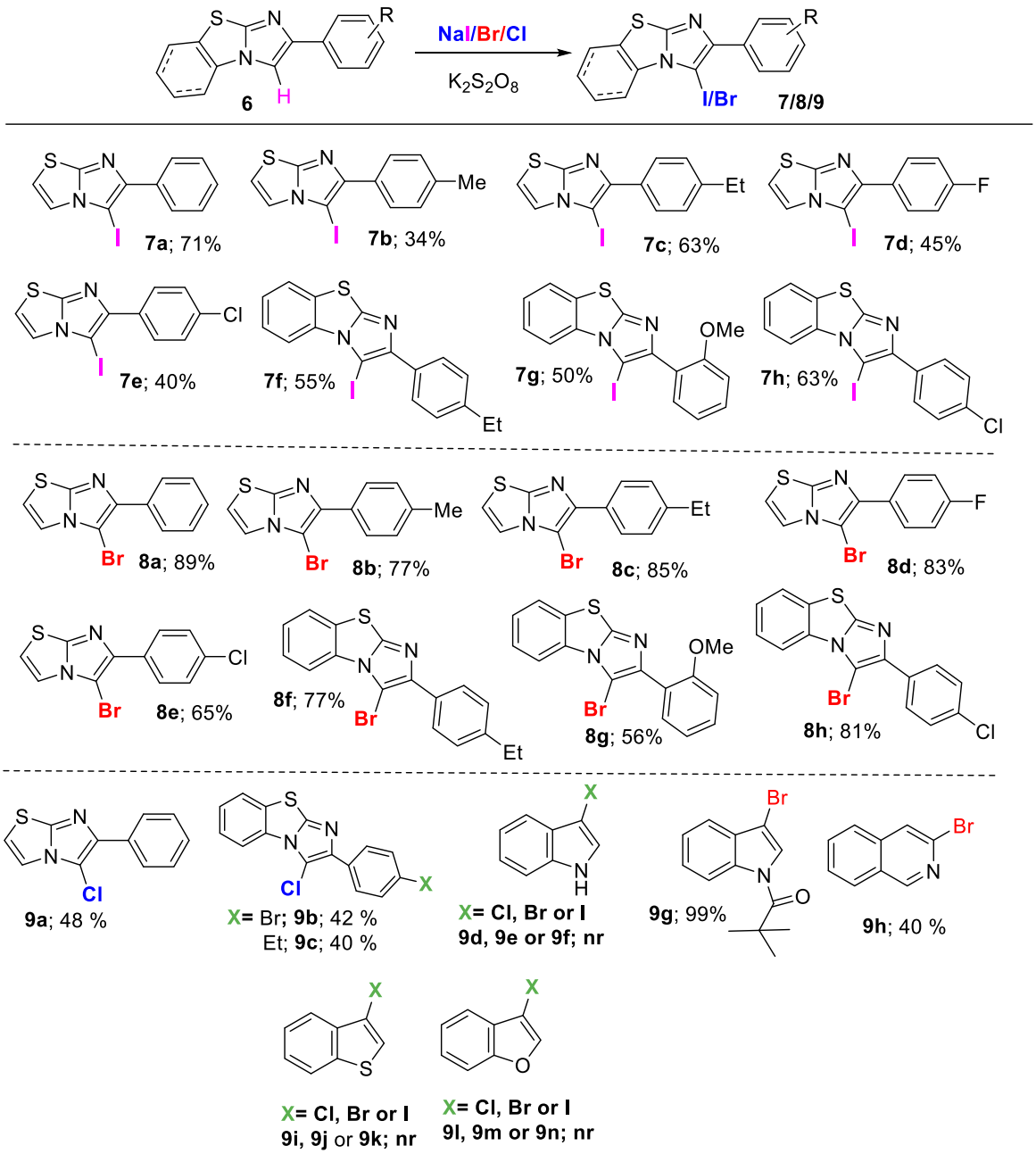
Then we focused on the bromination of substituted 2-phenylimidazo[1,2-a]pyridines (with the conditions of Table 1, entry 15). Similar to iodination, the bromination also underwent smoothly with electron-rich and electron-deficient groups (i.e., Me, Et, OMe, Cl, Br, F and CN) at different positions of the phenyl as well as pyridyl ring of **1**, and afford the corresponding C-3 brominated products **4b**–**4l** in good to excellent yields (62–96%). Even dichloro, halo, alkyl substituted and unsubstituted imidazopyridines gave the corresponding brominated products **4m**-**4p** in moderate to good yields respectively under the same conditions.

Two representative imidazopyridines, 2-phenylimidazo[1,2-a]pyridine and 4-(8-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile were also subjected to chlorination (under the conditions of table 1, entry 26) and obtained moderate to good yields of C-3 chlorinated products **5a** and **5b**. Compared to iodination and bromination, fewer yields of corresponding chlorination products were observed. The unsubstituted imidazo(1,2-a)pyridine was subjected to chlorination but, corresponding chlorinated product was not observed. It may be due to the low reactivity of chlorine species under the present conditions. It may be noted that, the poly halogenated imidazopyridine derivatives **3m**, **3n**, **4m** and **4n** were well tolerated, and these products could be further useful in traditional cross-coupling reactions. To validate the present protocol for industrial/commercial preparation of such products, the halogenation (I, Br, and Cl) of **1a** was carried out at gram scale using **2a**, **2b** and **2c** under the optimised conditions and obtained the corresponding halogenated 2-phenyl imidazopyridines i.e. **3a**, **4a**, **5a** in moderate to good yields (See Table 2, footnotes).

To further ascertain the scope of the present halogenation method, different fused heterocycles such as 6-phenylimidazo[2,1-b]thiazole[13] and 2-phenylbenzo[d]imidazo[2,1-b]thiazole were studied with the optimised conditions of table 2, and results are presented in Table 3. Initially, the iodination of 6-phenylimidazo[2,1-b]thiazole **6** having various substituents (Me, OMe, Et, Br, Cl and F) at the phenyl ring, was subjected to the iodination and obtained the corresponding 5-iodo-6-phenylimidazo[2,1-b]thiazole derivatives (**7a**–**7e**)

in moderate to good yields. Further, the iodination of 2-phenylbenzo[d]imidazo[2,1-b]thiazoles offered the corresponding 3-iodo-2-phenylbenzo[d]imidazo[2,1-b]thiazole derivatives (**7f**–**7h**) in moderate yields (50-63%). Similarly, the bromination of 6-phenylimidazo[2,1-b]thiazole and 2-phenylbenzo[d]imidazo[2,1-b]thiazole derivatives provided the corresponding bromo products **8a**–**8h** in 56-89% yields. As observed in Table 2, fewer yields of chloro derivatives **9a**–**9c** were observed (Table 3). The halogenation of indole under the present conditions, didn't proceed to yield the desired products (**9d**-**9f**). However, bromination of N-pivaloyl indole under the optimised conditions gave the desired product **9g** in quantitative yield (99%). The product **9g** was obtained in pure form by NMR, without separation by column chromatography, but by solvent extraction and removal of solvent. It may be noted that, indole derivatives are promising scaffolds for drug development.[14] Interestingly, 3-bromoisoquinoline **9h** was also obtained in 40% yield. Unfortunately, benzothiazole and benzofuran completely declined to yield the halogenated products (**9i**–**9n**).

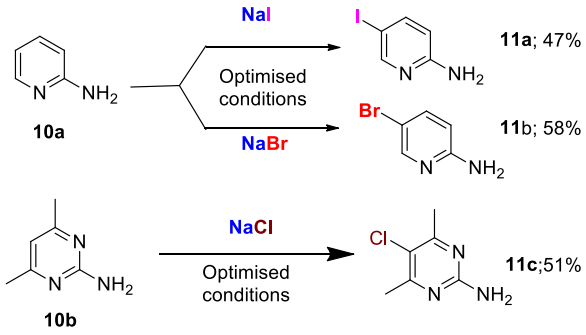
Table 3. Halogenation of other fused heterocycles[a,b,c]



[a]Reaction conditions for product (**7a-h**): **6** (0.25 mmol), **2a** (0.5 mmol, 2.0 eqv.), $K_2S_2O_8$ (0.5 mmol, 2.0 eqv.), ACN (1 mL), 50°C, 24 h. [b]For (**8a-h & 9g-h**): **6** (0.25 mmol), **2b** (1.25 mmol, 5.0 eqv.), $K_2S_2O_8$ (0.5 mmol, 2.0 eqv.), DCM (1 mL), RT, 24 h. [c] For (**9a-c**): **6** (0.25 mmol), **2c** (1.25 mmol, 5.0 eqv.), oxone (0.5 mmol, 2.0 eqv.), ACN+ H_2O (2:1, 1 mL), 80°C, 24 h. All yields of products are isolated except **9g**.

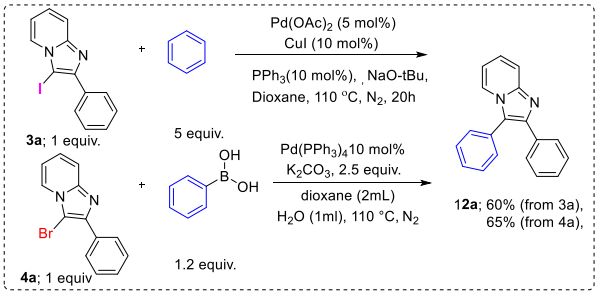
Finally for our curiosity, we applied the same optimised conditions for the iodination and bromination of 2-aminopyridine **10a**, and obtained 5-iodo-2-aminopyridine **11a** and 5-bromo-2-

aminopyridine **11b** in 47% and 58% yields respectively (Scheme 2). Halogenation of 2- and 3-aminopyridines did not undergo under the present conditions. Further the chlorination of biological active compound such as pyrimidine[15] **10b** gave desired product 5-chloro-4, 6-dimethylpyrimidin-2-amine **11c** in 51% isolated yield (Scheme 2).



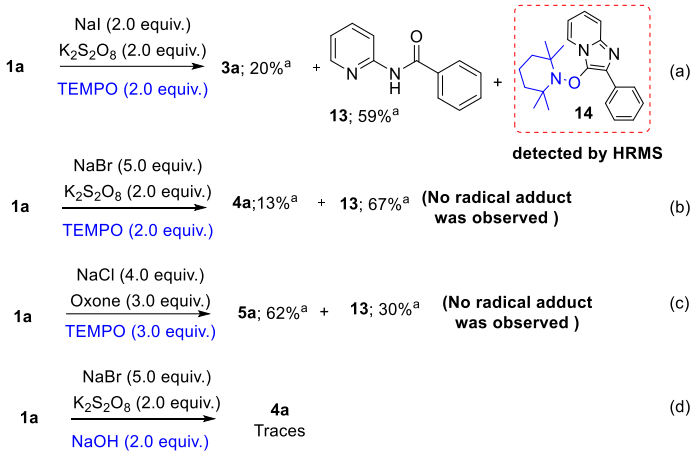
Scheme 2. Halogenation of aminopyridine and aminopyrimidine

To explore the importance of these halogenated fused heterocycles, we further subjected to the cross coupling reactions for making C-C bonds under the conditions of known procedure. Compounds **3a** and **4a** reactions with benzene and phenylboronic acid with palladium catalytic conditions afford the desired product 2, 3-diphenylimidazo[1,2-a]pyridine **12a** in 60% and 65% respectively (Scheme 3). The cross coupled product **12a**, displays significance biological activity towards anti-apoptotic, antiprotozoal, and antiviral activities, and also shows significance reactivity towards kinase inhibitors as well as liver X receptor agonists (Scheme 3). [16]



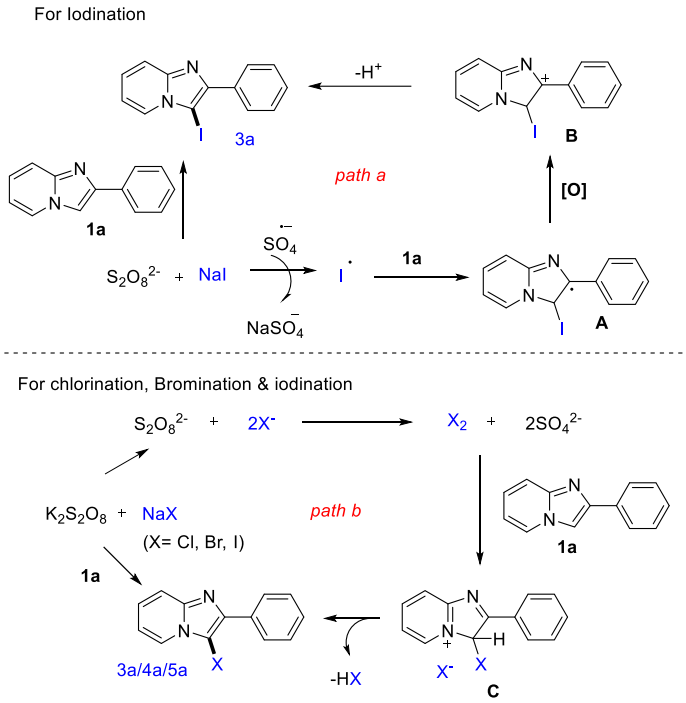
Scheme 3. Applications of halogenated heterocycles for cross coupling reactions.

To gain insight into the reaction mechanism, specific control experiments were performed (Scheme 4). We subjected the reaction of **1a** with halogenations (iodo, bromo and chloro) reactions under the optimised conditions by the addition of radical scavenger (2,2,6,6-tetramethylpiperidin- 1-yl)oxyl (TEMPO), under these conditions the desired halogenated products **3a**, **4a** and **5a** were observed in 20%, 13% and 62% yields respectively (Scheme 4, eq. a-c). In addition to the desired products, the ring opening product N-(pyridin-2-yl)benzamide **13** was observed in 59%, 67% and 30% yield respectively (Scheme 4, eq. a-c). The product **13** formation is known in the literature under strong oxidising conditions.[17f] Along with the above products, the TEMPO adduct **14** was detected by HRMS in the case of iodination but no such adduct was observed for bromination and chlorination (Scheme 4, eq. a-c).[18]



Scheme 4. Control experiments ([a] GC-MS yield)

In order to conclude the reactive species for the present transformation, we performed the bromination of **1a** under the optimised conditions along with NaOH (Scheme 4, eq. d). Interestingly, only traces of **4a** formation was observed. It indicates that, the Br_2 may generate *in-situ* and which will be trapped by NaOH. From the equations b-d, (Scheme 4), it concludes the bromination may follow ionic pathway (Scheme 4, eq. d).



Scheme 5. Plausible reaction mechanism

Based on mixed results from the above control experiments and based on the literature reports[17] two plausible reaction paths have been proposed (Scheme 5). The iodination may proceed via both ionic and radical pathways, but the bromination and chlorination may follow ionic pathways (Scheme 5). In path *a*; initially, $K_2S_2O_8$ thermally decomposes into sulphate radical (SO4−•)[17d,e] which in turn reacts with NaI to generate iodine radical (I•). Addition of iodine radical (I•) to the C3 position of **1a** generates radical intermediate **A**. Subsequently, single electron transfer (SET) and oxidative aromatisation may deliver the desired product **3a** through the intermediate **B** (Scheme 5, path *a*). In path *b*; the molecular halogen generated in-situ by the oxidant may attack electrophilically (x+) on the C3 position of **1a** to generate another imidazolonium intermediate **C.**[11d&17] Followed by elimination of HX from **C**, gives the desired halogenated products (Scheme 5, path *b*).

In summary, the present study is an attractive alternative to the previously reported halogenation techniques. The use of simple sodium halide salts (NaI/NaBr/NaCl) for the halogenation are being reported first time in the present study. The present transformation indicates very good functional group tolerance and broad substrate scope of imidazo[1,2-a]pyridines and applicable at gram scale synthesis of desired halogenated compounds. The

method is also applicable for the synthesis of important heterocyclic compounds such as imidazo[2,1-b]thiazoles and benzo[d]imidazo[2,1-b]thiazoles as well as indole, isoquinoline, pyrimidine and 2-aminopyridines with moderate to good yields. Due to the less reactivity of chloride, yields for chlorination are not much excited, nevertheless it represents a significant development for the chlorination of imidazoheterocycles using table salt as chlorine source.

Experimental Section:

General: All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^{1}H and $^{13}C\{H\}$ NMR spectra were recorded at 600, and 150 MHz, respectively. The spectra were recorded in $CDCl_3$ as solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc. and coupling constants (J) were given in Hz. Chemical shifts are reported in ppm relative to TMS as an internal standard. The peaks around delta values of ^{1}H NMR (7.26), and $^{13}C\{H\}$NMR (77.0) are deuterated solvent chloroform, [δ value around (1.5) in 1H NMR is of water]. Mass spectra were obtained using electron impact (EI) ionization method. Progress of the reactions was monitored by thin layer chromatography (TLC). All products were purified through column chromatography using silica gel 100-200 mesh size using hexane/ethyl acetate as eluent, unless otherwise indicated.

General procedure for the synthesis of 2-phenylimidazo[1,2-a]pyridine (1):

470 mg (5.0 mmol) of 2-aminopyridine, 1200 mg (10 mmol) of acetophenone, CuI 5 mol% (47 mg; 0.25 mmol), $BF_3{\cdot}Et_2O$ (45–50% purity); 10 mol%, (0.5 mmol) and DMF (2 mL) were placed in a 25-mL double-necked round-bottomed flask. The mixture was heated in oil bath at 60 ^{o}C for 24 h under an oxygen atmosphere (balloon). After completion of the reaction, it was allowed to attain to room temperature and then the mixture was poured into 20 mL of sodium carbonate solution. The product was extracted with DCM (50 mL X 3) and dried with anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and the leftover residue was purified through column chromatography using silica gel (30% EtOAc/hexane) to afford **1a**; yield: 0.799 g (82%) experimental data also matched with reported literature the same method was applied for all the reported starting substrates (1,6 and their derivatives).[13]

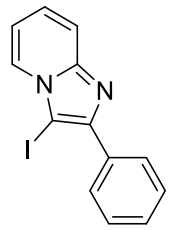
General procedure for the synthesis of 3-iodo-2-phenylimidazo[1,2-a]pyridine (3a): To a reaction tube equipped with a magnetic stir bar, added 2-phenylimidazo[1,2-a]pyridine[13] (**1a**) (48.5 mg, 0.25 mmol), sodium iodide (**2a**) (75mg, 0.5 mmol), and potassium persulfate (135 mg, 0.5 mmol) and 1.0 mL of acetonitrile (ACN). The mixture was heated in an oil bath at 50 ⁰ C in a closed tube. Reaction was monitored by TLC, after completion of the reaction; it was allowed to attain room temperature. Then the mixture was poured into 30 mL of sodium thiosulfate solution and the product was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and solvent was removed under vacuum. The crude residue leftover was purified by column chromatography using 15 % EtOAc/hexane to afford **3a** (65.6 mg; 82% yield).

General procedure for the synthesis of 3-bromo-2-(4-ethylphenyl)benzo[d]imidazo[2,1-b]thiazole (8f): To a reaction tube equipped with a magnetic stir bar, added 2-(4-ethylphenyl)benzo[d]imidazo[2,1-b]thiazole (**6**)[13] (69.5 mg, 0.25 mmol), sodium bromide (**2b**) (127 mg, 1.25 mmol), and potassium persulfate (135 mg, 0.5 mmol) and 1.0 mL of dichloromethane (DCM). The mixture was stirred at room temperature in a closed tube. Reaction was monitored by TLC. The product was extracted with EtOAc and the combined organic layers were dried over Na_2SO_4, concentrated under vacuum. The crude mixture was purified by silica gel column chromatography using 15 % EtOAc/hexane to afford **4a** (68.53 mg; 77% yield).

General procedure for the synthesis of 3-chloro-2-phenylimidazo[1,2-a]pyridine (5a): To a reaction tube equipped with a magnetic stir bar, added 2-phenylimidazo[1,2-a]pyridine (**1a**) (48.5 mg, 0.25 mmol), sodium chloride (**2c**) (72.5mg, 1.25 mmol), and potassium peroxymonosulfate (114 mg, 0.5 mmol) and 1.0 mL of ACN+ H_2O (2:1). The mixture was heated in an oil bath at 80 ⁰ C in a closed tube. Reaction was monitored by TLC. The product was extracted with EtOAc and the combined organic layers were dried over anhydrous Na_2SO_4, the solvent was removed under vacuum. The crude residue leftover was purified by silica gel column chromatography using 15 % EtOAc/hexane to afford **5a** (37.05 mg; 65% yield).

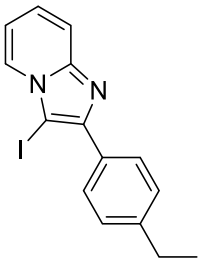
Characterization data :

3-iodo-2-phenylimidazo[1,2-a]pyridine (3a): [25a]



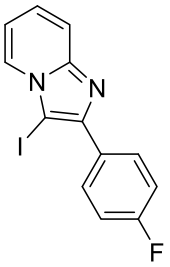
(Eluent: 15% EtOAc/hexane); 82% yield (65.6 mg); yellow solid, Mp: 165 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, *J* = 6.9 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 7.24 – 7.19 (m, 1H), 6.88 (t, *J* = 6.8 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.999, 147.904,133.45, 128.43, 128.27,128.26, 126.42, 125.49, 117.46, 113.08 , 59.50.

2-(4-ethylphenyl)-3-iodoimidazo[1,2-a]pyridine (3b):



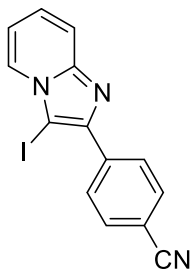
(Eluent: 20% EtOAc/hexane); 68% yield (59.1 mg); yellow solid; Mp: 190 ^{0}C; ^{1}H NMR (600 MHz,$CDCl_3$) δ 8.22 (d, *J* = 6.9 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.25 (dd, *J* = 9.2, 7.2 Hz, 1H), 6.92 (d, *J* = 6.8 Hz, 1H), 2.72 (d, *J* = 7.4 Hz, 2H), 1.29 (t, *J* = 7.5 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.11, 148.06, 144.49, 130.86, 128.41, 127.85, 126.45, 125.41, 117.49, 113.03, 77.00, 59.10, 28.68, 15.41. HRMS-ESI (m/z) $[M+Na]^+$ calcd. For $C_{15}H_{13}IN_2Na$: 371.0021; Found: 371.0019.

2-(4-fluorophenyl)-3-iodoimidazo[1,2-a]pyridine (3c):



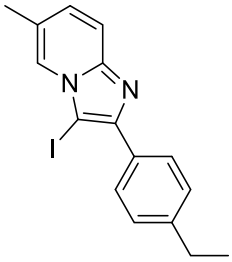
(Eluent: 15% EtOAc/hexane); 84% yield (70.9 mg); yellow solid, Mp: 152 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23(d, J= 7.2 Hz, 1H), 8.05-8.03(m, 2H), 7.61(d, J= 8.4 Hz, 1H), 7.27 (t, J= 9.0 Hz, 1H), 7.18 (t, J= 8.4 Hz, 2H), 6.95 (t, J= 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 163.69, 162.04, 148., 147.29, 130.29 (d, *J* = 8.4 Hz), 129.71, 126.53, 125.69, 117.57, 115.42, 115.28, 113.26, 59.20; HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_9FIN_2$: 338.9794; Found: 338.9799.

4-(3-iodoimidazo[1,2-a]pyridin-2-yl)benzonitrile (3d): [26a]



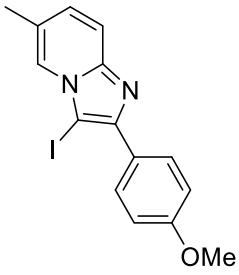
(Eluent: 20% EtOAc/hexane); 60% yield (51.7 mg); white solid, Mp: 120 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, J= 8.4 Hz, 3H), 7.75 (d, J= 7.8 Hz, 2H), 7.62 (d, J= 9.0 Hz, 1H), 7.31 (t, J= 7.8 Hz, 1H), 6.98 (t, J= 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.4, 145.8, 138.2, 132.2, 128.8, 126.7,126.3,117.9, 113.8, 60.6.

2-(4-ethylphenyl)-3-iodo-6-methylimidazo[1,2-a]pyridine (3e):



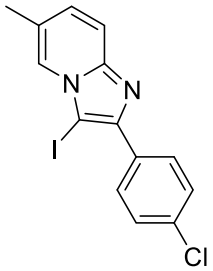
(Eluent: 20% EtOAc/hexane); 94% yield (85.0 mg); white solid, Mp:130 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.94 (m, 3H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.09 (s, 1H), 2.70 (d, *J* = 7.8 Hz, 2H), 2.39 (s, 3H), 1.30 – 1.25 (m, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.85, 147.14, 144.34, 131.06, 128.51, 128.35, 127.81, 124.22, 122.81, 116.85, 77.00, 58.58, 28.69, 18.35, 15.41. HRMS-ESI (m/z) $[M+Na]^+$calcd. For $C_{16}H_{15}IN_2Na$: 385.0178; Found: 385.0179.

3-iodo-2-(4-methoxyphenyl)-6-methylimidazo[1,2-a]pyridine (3f):



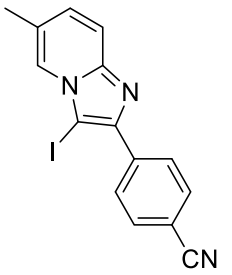
(Eluent: 20% EtOAc/hexane); 37% yield (33.6 mg); yellow solid, Mp:190 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 – 7.93 (m, 3H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 2H), 3.85 (s, 3H), 2.38 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 159.62, 147.60, 147.06, 129.66, 128.47, 126.22, 124.16, 122.74, 116.67, 113.71, 77.00, 58.19, 55.26, 18.31. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{14}IN_2O$: 365.0151; Found: 365.0160.

2-(4-chlorophenyl)-3-iodo-6-methylimidazo[1,2-a]pyridine (3g):



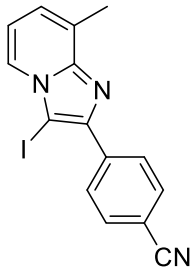
(Eluent: 15% EtOAc/hexane); 79% yield (72.6 mg); yellow solid, Mp:170 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ8.01 (d, J= 8.4 Hz, 2H), 7.97 (s, 1H), 7.50 (d, J= 9.0 Hz, 1H), 7.44 (d, J= 8.4 Hz, 2H), 7.11 (d, J= 9.6 Hz, 1H), 2.39 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.1, 146.5, 134.0, 132.2, 129.6, 128.9, 128.5, 124.2, 123.1, 116.9, 59.9, 18.3. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{14}H_{11}ClIN_2$: 368.9655; Found: 368.9657.

4-(3-iodo-6-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (3h):



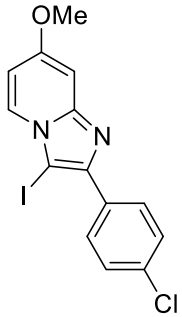
(Eluent:20% EtOAc/hexane); 50% yield (44.87 mg); yellow solid, Mp: 200 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.9 Hz, 2H), 8.00 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 9.1 Hz, 1H), 7.15 (d, *J* = 9.2 Hz, 1H), 2.42 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.36, 145.46, 138.31, 132.11, 129.46, 128.67, 124.31, 123.66, 118.94, 117.17, 111.46, 77.00, 59.94, 18.38. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{11}IN_3$: 359.9998; Found: 359.9987.

4-(3-iodo-8-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (3i):



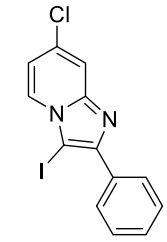
Eluent: 10% EtOAc/hexane); 60% yield (53.8 mg); yellow solid, Mp: 190 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, J= 7.8 Hz, 2H), 8.09 (d, J= 6.6 Hz, 1H), 7.75 (d, J= 8.4 Hz, 2H), 7.09 (d, J= 6.6 Hz, 1H), 6.88 (t, J= 7.2 Hz, 1H), 2.65 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.6, 145.2, 138.4, 132.0, 128.8, 127.9, 124.8, 124.4, 118.9, 113.5, 111.3, 60.7, 56.9, 16.4. HRMS-ESI (m/z) $[M+H]^+$ calcd. For $C_{15}H_{11}IN_3$: 359.9998; Found: 359.9993.

2-(4-chlorophenyl)-3-iodo-7-methoxyimidazo[1,2-a]pyridine (3j):



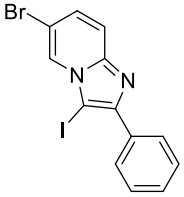
(Eluent: 10% EtOAc/hexane); 68% yield (65.2 mg); yellow solid, Mp:190 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.6, 5.5 Hz, 3H), 7.42 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 2.0 Hz, 1H), 6.63 (dd, *J* = 7.0, 2.1 Hz, 1H), 3.87 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 158.82, 149.18, 146.60, 134.00, 132.18, 129.37, 128.50, 126.80, 108.26, 94.80,56.67, 55.70. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{14}H_{11}ClIN_2O$: 384.9605; Found: 384.9604.

7-chloro-3-iodo-2-phenylimidazo[1,2-a]pyridine (3k):



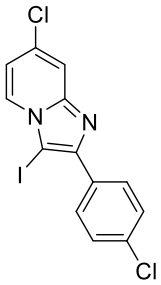
(Eluent: 20% EtOAc/hexane); 62% yield (54.8 mg); yellow solid, Mp: 150 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, J= 7.8,1H), 8.04 (d, J= 7.2 Hz, 2H), 7.63 (s, 1H), 7.49 (t, J= 7.2 Hz, 2H), 7.42 (t, J= 7.2 Hz, 1H), 6.91 (t, J= 1.8 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 149.0, 147.5, 128.5, 128.42, 128.41, 126.7, 117.2, 114.7, 59.5. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_9ClIN_2$: 354.9499; Found: 354.9491.

6-bromo-3-iodo-2-phenylimidazo[1,2-a]pyridine (3l): [26a]



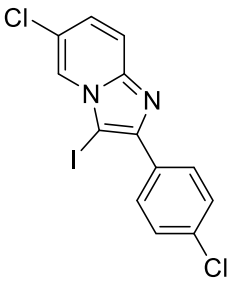
(Eluent: 10% EtOAc/hexane); 91% yield (90.7 mg);yellow solid, Mp: 178 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.04 (d, J= 6.6 Hz, 2H), 7.51-7.47 (m, 3H), 7.42 (t, J= 7.8 Hz, 1H), 7.31 (t, J= 9.0 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.8, 146.6, 133.0, 129.0, 128.5, 128.45, 128.40, 126.7, 118.1, 108.0, 59.8.

7-chloro-2-(4-chlorophenyl)-3-iodoimidazo[1,2-a]pyridine (3m):



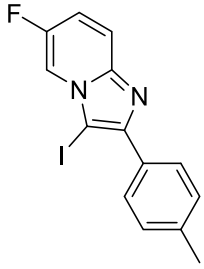
(Eluent: 20% EtOAc/hexane); 60% yield (58.3 mg);white solid, Mp: 175 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, J= 7.2 Hz, 1H), 8.00 (d, J= 9.0 Hz, 2H), 7.62 (s, 1H), 7.46 (d, J = 9.0 Hz, 2H), 6.93 (t, J = 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.9, 147.6, 134.6, 132.3, 131., 129.6, 128.6, 126.78, 116.3, 114.9, 59.5, 29.6 HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_8Cl_2IN_2$: 388.9109; Found: 388.9108.

6-chloro-2-(4-chlorophenyl)-3-iodoimidazo[1,2-a]pyridine (3n):



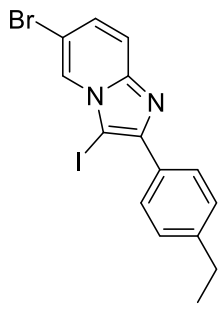
(Eluent: 10% EtOAc/hexane); 60% yield (58.3 mg); yellow solid, 190 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (s,1H), 7.99 (d, J= 8.4 Hz, 2H), 7.55 (d, J= 9.6 Hz, 1H), 7.45 (d, J= 9.0 Hz, 2H), 7.24-7.23 (m, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.8, 146.5, 134.6, 131.6, 129.6, 128.6, 127.2, 124.5, 121.7, 117.9, 60.0. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_8ICl2N_2$:388.9109; Found: 388.9094.

6-fluoro-3-iodo-2-(p-tolyl)imidazo[1,2-a]pyridine (3o):



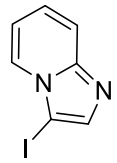
(Eluent: 15% EtOAc/hexane); 58% yield (51.0 mg); yellow solid, Mp: 160 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 – 8.16 (m, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.60 (dd, *J* = 9.6, 5.0 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.17 (ddd, *J* = 10.2, 8.0, 2.2 Hz, 1H), 2.42 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 154.59, 153.01, 149.46, 145.71, 138.43, 130.39, 129.12, 128.25, 117.99 (d, J = 8.9 Hz), 117.42, 117.26, 113.70, 113.42, 21.33. HRMS-ESI (m/z) $[M+Na]^+$calcd. For $C_{14}H_{10}FIN_2Na$: 374.9770; Found: 374.977.

6-bromo-2-(4-ethylphenyl)-3-iodoimidazo[1,2-a]pyridine (3p):



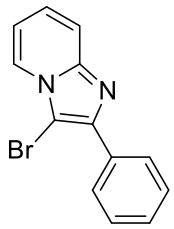
(Eluent: 5% EtOAc/hexane); 60% yield (64.0 mg); yellow solid, Mp: 156 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 9.3 Hz, 1H), 7.31 (t, *J* = 8.7 Hz, 3H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.8 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.89, 146.56, 144.83, 130.38, 128.89, 128.37, 127.93, 127.79, 126.66, 118.06, 107.88, 77.00, 59.48, 36.93, 28.70, 27.94, 15.39, 13.99. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{13}BrIN_2$: 426.9307. Found: 426.9316.

3-iodoimidazo[1,2-a]pyridine (3q): [24]



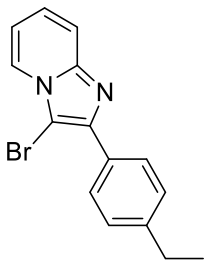
(Eluent: 30% EtOAc/hexane); 45% yield (55.0 mg); Brown solid, Mp: 165 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, J = 6.8 Hz, 2H), 7.58 (d, J = 4.5 Hz, 3H), 7.56 (s, 2H), 7.20 – 7.14 (m, 2H), 6.87 (t, J = 6.8 Hz, 2H). ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.83, 133.60, 124.33, 123.60, 117.88, 112.97, 94.71.

3-bromo-2phenylimidazo[1,2-a]pyridine (4a): [8b]



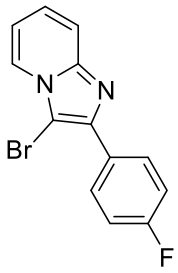
(Eluent: 15%EtOAc/hexane); 95 % yield (64.8 mg); yellow solid, Mp: 85 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 13.8, 7.4 Hz, 3H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.18 – 7.10 (m, 1H), 6.80 (t, *J* = 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.14, 142.22, 132.41, 128.38, 127.82, 125.36, 123.90, 117.37, 113.18, 91.7.

3-bromo-2-(4-ethylphenyl)imidazo[1,2-a]pyridine (4b): [28a]



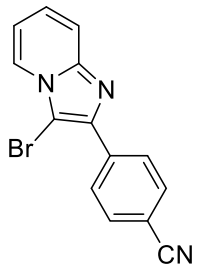
(Eluent: 15% EtOAc/hexane); 62% yield (46.6 mg);white solid, Mp:105 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.9 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.22 (m, 1H), 6.92 (d, *J* = 6.8 Hz, 1H), 2.71 (d, *J* = 7.7 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.37, 144.47, 142.75, 130.19, 127.96, 127.79, 124.92, 123.87, 117.50, 112.89, 91.35, 77.00, 28.68, 15.41.

3-bromo-2-(4-fluorophenyl)imidazo[1,2-a]pyridine (4c): [8b]



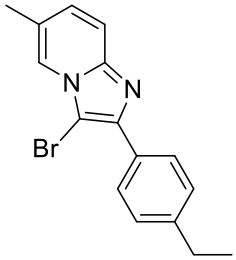
(Eluent: 5% EtOAc/hexane); 62% yield (45.1 mg); white solid, Mp: 110 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13-8.12 (m, 3H), 7.63 (d, J= 6.0 Hz, 1H), 7.26-7.17 (m, 3H), 6.92 (d, J= 3.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 163.5 (d, J= 246.6 Hz), 145.3, 141.7, 129.6 (d; J= 68.7 Hz), 128.9, 125.1, 123.8, 117.4, 115.4 (d, J= 17.7 Hz), 113.0, 91.3.

4-(3-bromoimidazo[1,2-a]pyridin-2-yl)benzonitrile (4d): [27c]



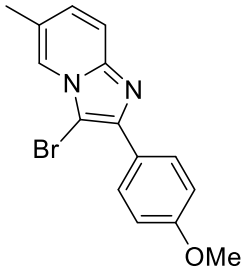
(Eluent: 5% EtOAc/hexane); 71% yield (52.8 mg);white solid, Mp: 175 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, J= 7.8 Hz, 2H), 8.18 (d, J= 7.2 Hz, 1H), 7.74 (d, J= 7.8 Hz, 2H), 7.64 (d, J= 9.0 Hz, 1H), 7.31 (t, J= 7.8 Hz, 1H), 6.98 (t, J= 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.6, 140.4, 137.3, 132.2, 128.0, 125.8, 124.0, 118.8, 117.8, 113.6, 111.4, 92.8.

3-bromo-2-(4-ethylphenyl)-6-methylimidazo[1,2-a]pyridine (4e):



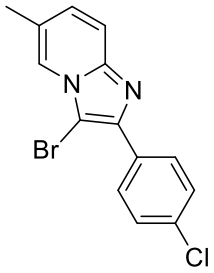
(Eluent: 5% EtOAc/hexane); 82% yield (64.5 mg); white solid, Mp: 120 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.87 (s, 1H), 7.49 (d, *J* = 9.1 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 9.2 Hz, 1H), 2.68 (q, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.29 – 1.24 (m, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 144.32, 144.19, 142.34, 130.31, 127.96, 127.83, 127.62, 122.61, 121.46, 116.68, 90.79, 77.00, 28.60, 18.22, 15.35. HRMS-ESI (m/z) $[M+Na]^+$calcd. For $C_{16}H_{15}BrN_2Na$: 337.0316; Found: 337.0308.

3-bromo-2-(4-methoxyphenyl)-6-methylimidazo[1,2-a]pyridine (4f): [28b]



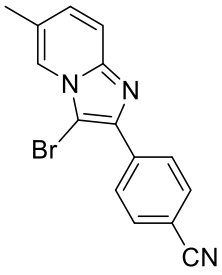
(Eluent: 15% EtOAc/hexane); 78% yield (61.8 mg); yellow solid, Mp: 135 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.3 Hz, 2H), 7.87 (s, 1H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 2.32 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 159.51, 144.31, 142.16, 128.97, 128.58, 127.97, 125.53, 122.59, 121.46, 116.57, 113.77, 90.35, 77.00, 55.20, 18.24.

3-bromo-2-(4-chlorophenyl)-5-methyl-3aH-indene (4g):



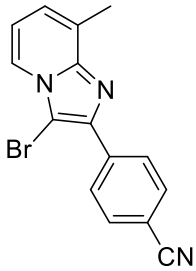
(Eluent: 15% EtOAc/hexane); 62% yield (49.7 mg); yellow solid, Mp: 120 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J= 1.8 Hz, 2H), 7.87 (s, 1H), 7.48 (d, J = 9.0 Hz, 1H), 7.40 (d, J = 2.7 Hz, 2H), 7.07 (d, J = 1.2 Hz, 1H), 2.34 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 144.4, 141.1, 133.9, 131.5, 128.89, 128.5, 128.4, 123.0, 121.5, 116.8, 91.2, 18.3. HRMS-ESI (m/z) $[M+Na]^+$calcd. For $C_{14}H_{10}BrClN_2Na$: 342.9614; Found: 342.9596.

.4-(3-bromo-6-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (4h):



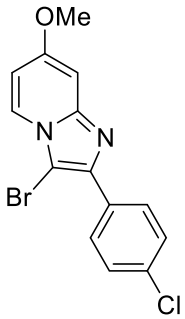
(Eluent: 15% EtOAc/hexane); 96% yield (74.8 mg); yellow solid, Mp: 190 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.4 Hz, 2H), 7.93 (s, 1H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 9.2 Hz, 1H), 7.13 (dd, *J* = 9.2, 1.2 Hz, 1H), 2.39 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 144.70, 140.11, 137.55, 132.14, 129.04, 127.91, 123.55, 121.66, 118.92, 117.15, 111.27, 92.40, 77.00, 18.35. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{11}BrN_3$: 312.0136; Found: 312.012.

4-(3-bromo-8-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (4i): [20]



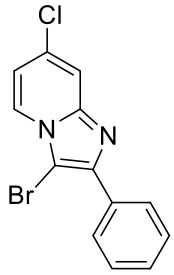
(Eluent: 15% EtOAc/hexane); 87% yield (67.8 mg);white solid, Mp: 185 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, J= 8.4 Hz, 2H), 8.04 (d, J= 7.2 Hz, 1H), 7.73 (d, J= 8.4 Hz, 2H), 7.08 (d, J= 7.2 Hz, 1H), 6.88 (t, J= 7.2 Hz, 1H), 2.64 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.9, 139.8, 137.6, 132.1, 128.1, 127.9, 124.4, 120.8, 118.9, 113.5, 111.2, 93.1, 16.4.

3-bromo-2-(4-chlorophenyl)-7-methoxyimidazo[1,2-a]pyridine (4j):



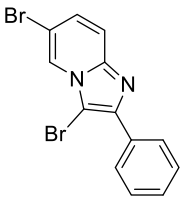
(Eluent: 15% EtOAc/hexane); 80% yield (67.4 mg); white solid, Mp: 158 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J= 8.4 Hz, 2H), 7.93 (d, J= 7.2 Hz, 1H), 7.41 (d, J= 9.0 Hz, 2H), 6.86 (d, J= 1.8 Hz, 1H), 6.62-6.60 (m, 1H), 3.85 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 158.3, 146.6, 133.8, 131.4, 124.2, 108.2, 94.7, 93.8, 89.8, 55.6. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{14}H_{11}BrClN_2O$: 336.9743; Found: 336.9743.

3-bromo-7-chloro-2-phenylimidazo[1,2-a]pyridine (4k):



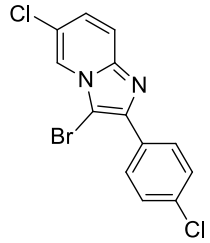
(Eluent: 15% EtOAc/hexane); 64% yield (49.1 mg); yellow solid, Mp: 169 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10-8.06 (m,3H), 7.63 (s, 1H), 7.49 (t, J= 8.4 Hz, 2H), 7.41 (t, J= 7.8 Hz, 1H), 6.90 (t, J= 6.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 145.0, 144.3, 143.5, 133.0, 132.4, 131.6,128.5, 128.4, 127.7, 124.2, 116.3, 115.7, 114.6, 91.9. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_9BrClN_2$: 306.9638; Found: 306.9618.

3,6-dibromo-2-phenylimidazo[1,2-a]pyridine (4l):



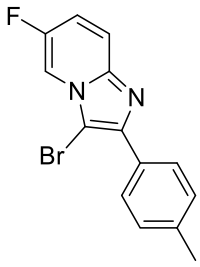
(Eluent: 5% EtOAc/hexane); 77% yield (67.76 mg);white solid, Mp: 155 ^{0}C ; 1H NMR (600 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.14 (d, J= 7.8 Hz, 2H), 7.51 (d, J= 9.0 Hz, 1H), 7.48 (t, J= 7.8 Hz, 2H), 7.40 (t, J= 6.6 Hz, 1H), 7.29 (dd, J= 9.0 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 143.8, 143.4, 132.3, 128.5, 128.4, 127.7, 124.0, 118.1, 107.8, 91.9. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_9Br_2N_2$: 350.9132; Found: 350.9132.

3-bromo-6-chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (4m):



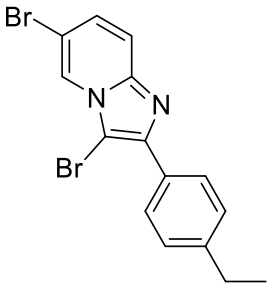
(Eluent: 5%EtOAc/hexane); 63% yield (53.86 mg); white solid, Mp: 160 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$), δ 8.17 (s, 1H), 8.03 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 143.7, 142.4, 134.4, 130.8, 128.9, 128.7, 127.6, 121.9, 121.7, 117.9, 92.1; HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_8BrCl_2N_2$: 340.9248; Found: 340.9233.

3-bromo-6-fluoro-2-(p-tolyl)imidazo[1,2-a]pyridine (4n):



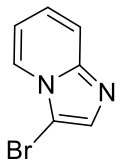
(Eluent: 15% EtOAc/hexane); 52% yield (39.6 mg); yellow solid, Mp:155 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.7 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.61 (dd, *J* = 9.6, 4.9 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.11 (m, 1H), 2.41 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 154.55, 152.97, 144.19, 143.00, 138.42, 129.7, 129.23, 127.64, 118.07 (d, J = 8.8 Hz), 117.04, 116.88, 111.06, 110.78, 92.65, 21.33. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{14}H_{11}BrFN_2$: 305.0090; Found: 305.008.

3,6-dibromo-2-(4-ethylphenyl)imidazo[1,2-a]pyridine (4o):



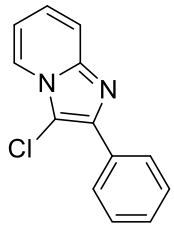
(Eluent: 15% (EtOAc/hexane); 80% yield (76.0 mg); yellow solid, Mp: 130 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 9.5 Hz, 1H), 7.31 (dd, *J* = 12.0, 4.9 Hz, 3H), 2.71 (q, *J* = 7.4 Hz, 2H), 1.29 (t, *J* = 7.5 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 144.85, 143.87, 143.65, 129.76, 128.43, 128.06, 127.80, 124.08, 118.13, 107.79, 91.66, 77.00, 28.71, 15.41. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{13}Br_2N_2$: 378.9445. Found: 378.944.

3-bromoimidazo[1,2-a]pyridine (4p): [23]



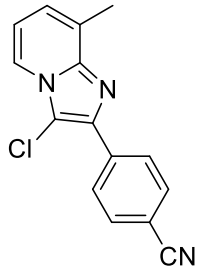
(Eluent: 30% EtOAc/hexane); 38% yield (37.0 mg); Brown solid, Mp: 90 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (t, J = 6.1 Hz, 1H), 7.69 (s, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.21 (t, J = 7.7 Hz, 1H), 6.91 (t, J = 6.5 Hz, 1H). ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.71, 140.21, 125.96, 124.82, 117.83, 113.20, 60.72 .

3-chloro-2-phenylimidazo[1,2-a]pyridine (5a):[25b]



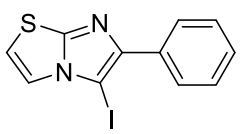
(Eluent: 15% (EtOAc/hexane); 65% yield (37.05 mg) yellow solid, Mp: 115 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (t, *J* = 7.4 Hz, 2H), 8.10 (d, *J* = 6.8 Hz, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 7.49 (t, *J* = 7.9 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.22 (m, 1H), 6.92 (t, *J* = 6.8 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 143.68, 139.75, 132.48, 128.51, 128.21, 127.45, 124.82, 122.65, 117.62, 112.87, 105.66, 77.00.

4-(3-chloro-8-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (5b):



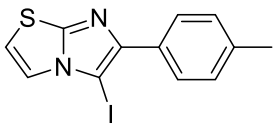
(Eluent: 15% EtOAc/hexane); 46% yield (30.7 mg); yellow solid, Mp: 190 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 6.8 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 6.8 Hz, 1H), 6.88 (t, *J* = 6.8 Hz, 1H), 2.65 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 144.34, 137.37, 137.12, 132.28, 128.09, 127.76, 124.23, 120.62, 119.03, 113.50, 111.19, 77.00, 16.43. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_{11}ClN_3$: 268.0642; Found: 268.0613.

5-iodo-6-phenylimidazo[2,1-b]thiazole (7a): [26a]



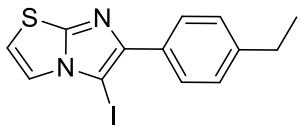
(Eluent: 15% EtOAc/hexane); 71% yield (57.8 mg); yellow solid, Mp: 130 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.45 (dd, *J* = 10.8, 6.1 Hz, 3H), 7.35 (t, *J* = 7.2 Hz, 1H), 6.92 (d, *J* = 4.3 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 150.82, 149.41, 133.61, 128.33, 127.88, 127.45, 119.22, 112.18.

5-iodo-6-(p-tolyl)imidazo[2,1-b]thiazole (7b): [26a]



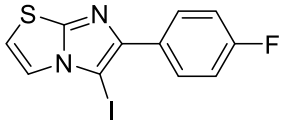
(Eluent: 15% EtOAc/hexane); 34% yield (28.9 mg); white solid, Mp: 135 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 4.6 Hz, 1H), 7.26 (d, *J* = 2.1 Hz, 2H), 6.91 (d, *J* = 4.5 Hz, 1H), 2.40 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 149.56, 137.72, 131.14, 129.05, 127.36, 119.21, 112.42, 111.98, 77.00, 53.72, 21.30.

6-(4-ethylphenyl)-5-iodoimidazo[2,1-b]thiazole (7c):



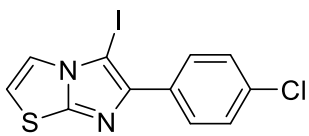
(Eluent: 15% EtOAc/hexane); 63% yield (55.7 mg); yellow solid, Mp: 145 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 4.5 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 4.5 Hz, 1H), 2.70 (d, *J* = 7.5 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 150.69, 149.51, 144.01, 130.99, 127.83, 127.39, 119.20, 111.95, 77.00, 53.70, 28.65, 15.41. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_{12}IN_2S$: 354.9766; Found: 354.9772.

6-(4-fluorophenyl)-5-iodoimidazo[2,1-b]thiazole (7d): [28c]



(Eluent: 15% EtOAc/hexane); 45% yield (38.7 mg); yellow solid, Mp: 145 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.42 (d, *J* = 4.6 Hz, 1H), 7.15 – 7.09 (m, 2H), 6.92 (d, *J* = 4.5 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 163.34, 150.87, 148.66, 129.78, 129.25 (d, J = 7.7 Hz), 119.21, 115.36, 115.21, 112.26, 53.91.

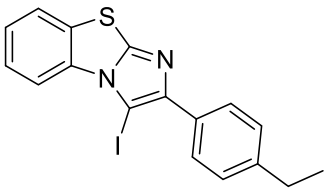
6-(4-chlorophenyl)-5-iodoimidazo[2,1-b]thiazole (7e):



(Eluent: 15% EtOAc/hexane); 40% yield (36.0 mg); yellow solid, Mp: 150 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, J= 9.0 Hz, 2H), 7.42-7.39. (m, 3H), 6.92 (d, J= 4.2 Hz, 1H); ^{13}C{H} NMR (150 MHz,

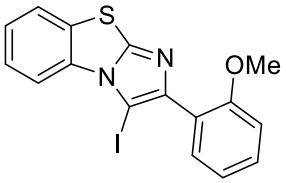
CDCl3) δ 150.9, 148.2, 133.7, 132.1, 128.6, 128.5, 119.1, 112.4, 54.2. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{11}H_7ClIN_2S$: 360.9063; Found: 360.9053.

2-(4-ethylphenyl)-3-iodobenzo[d]imidazo[2,1-b]thiazole (7f):



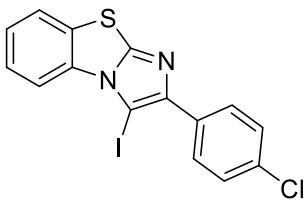
(Eluent: 15% EtOAc/hexane); 55% yield (55.5 mg); yellow solid, Mp: 180 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.9 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 150.94, 150.42, 144.17, 133.76, 132.44, 130.80, 130.54, 130.48, 129.70, 128.01, 127.78, 126.86, 125.38, 125.15, 124.24, 113.83, 77.00, 53.85, 28.68, 15.42. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{17}H_{14}IN_2S$: 404.9922. Found: 404.9916.

3-iodo-2-(2-methoxyphenyl)benzo[d]imidazo[2,1-b]thiazole (7g):



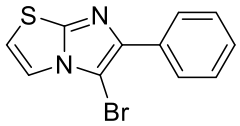
(Eluent: 5% EtOAc/hexane); 50% yield (50.7 mg);white solid, Mp: 145 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.50 (dt, *J* = 16.1, 5.3 Hz, 2H), 7.40 (dt, *J* = 24.3, 7.8 Hz, 2H), 6.93 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.89 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 129.31, 126.56, 125.47, 125.32, 124.83, 124.31, 123.70, 120.57, 114.33, 113.97, 113.13, 77.00, 55.38. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{16}H_{12}IN_2OS$: 406.9715. Found: 406.969.

2-(4-chlorophenyl)-3-iodobenzo[d]imidazo[2,1-b]thiazole (7h): [21a]



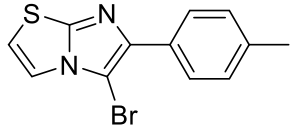
(Eluent: 15% EtOAc/hexane); 63% yield (64.5 mg); white solid, Mp: 130 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (d, *J* = 8.3 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.45 – 7.39 (m, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 133.93, 133.90, 133.67, 133.65, 131.97, 130.53, 129.32, 128.52, 125.53, 125.43, 124.35, 113.91, 77.00.

5-bromo-6-phenylimidazo[2,1-b]thiazole (8a): [21c]



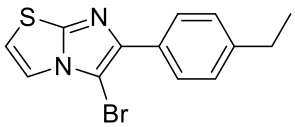
(Eluent: 15% EtOAc/hexane); 89% yield (62.0 mg); white solid, Mp: 100 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (t, *J* = 19.4 Hz, 2H), 7.41 (d, *J* = 22.6 Hz, 3H), 7.33 (s, 1H), 6.89 (s, 1H). ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.75, 143.92, 133.04, 128.41, 127.75, 126.88, 117.49, 112.92, 90.07.

5-bromo-6-(p-tolyl)imidazo[2,1-b]thiazole (8b):



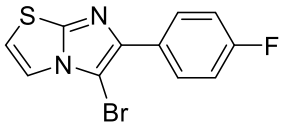
(Eluent: 15% EtOAc/hexane); 77% yield (56.4 mg); yellow solid, Mp: 122 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 4.6 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 4.6 Hz, 1H), 2.38 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.56, 143.90, 137.53, 130.12, 129.08, 126.72, 117.42, 112.71, 89.64, 77.00, 21.23. HRMS-ESI (m/z) $[M+H]_+$calcd. For $C_{12}H_{10}BrN_2S$: 292.9748; Found: 292.975.

5-bromo-6-(4-ethylphenyl)imidazo[2,1-b]thiazole (8c):



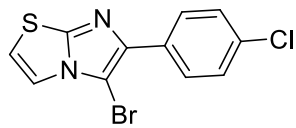
(Eluent: 15% EtOAc/hexane); 85% yield (65.2 mg); white solid, Mp: 167 ^{0}C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 4.6 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 6.87 (d, *J* = 4.4 Hz, 1H), 2.68 (d, *J* = 7.8 Hz, 2H), 1.26 (t, *J* = 7.7 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.62, 144.05, 143.91, 130.44, 127.92, 126.84, 117.48, 112.70, 89.67, 77.00, 28.65, 15.42. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{13}H_{12}BrN_2S$: 306.9905; Found: 306.9900.

5-bromo-6-(4-fluorophenyl)imidazo[2,1-b]thiazole (8d): [21b]



(Eluent: 15% EtOAc/hexane); 83% yield (61.6 mg); yellow solid, Mp: 145 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.2, 5.4 Hz, 2H), 7.39 (d, *J* = 4.3 Hz, 1H), 7.11 (t, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 4.4 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$); δ 163.21, 161.57, 148.78, 143.13, 128.65 (d, J = 8.3 Hz), 117.49, 115.43, 115.29, 112.99.

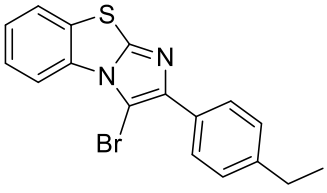
5-bromo-6-(4-chlorophenyl)imidazo[2,1-b]thiazole (8e):



(Eluent: 15% EtOAc/hexane); 65% yield (50.8 mg); yellow solid, Mp: 156 ^{0}C;^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J = 8.9 Hz, 2H), 7.43 – 7.36 (m, 3H), 6.92 (d, J = 4.6 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$

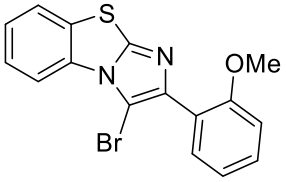
) δ 148.91, 142.89, 134.39, 133.57, 132.57, 131.57, 128.63, 128.08, 117.49, 113.19, 90.21, 77.00. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{11}H_7ClBrN_2S$: 312.9202; Found: 312.919.

3-bromo-2-(4-ethylphenyl)benzo[d]imidazo[2,1-b]thiazole (8f):



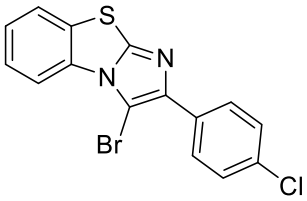
(Eluent: 15% EtOAc/hexane); 77% yield (68.7 mg); yellow solid, Mp: 110 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.5 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.93, 144.44, 144.04, 133.10, 130.20, 130.14, 127.90, 127.15, 125.80, 125.07, 124.16, 113.60, 91.43, 77.00, 28.67, 15.44. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{17}H_{14}BrN_2S$: 357.0061. Found: 357.0056.

3-bromo-2-(2-methoxyphenyl)benzo[d]imidazo[2,1-b]thiazole (8g):



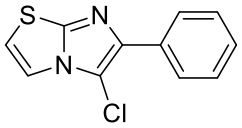
(Eluent: 15% EtOAc/hexane); 56% yield (50.2 mg); white solid, Mp: 135 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.60 – 7.58 (m, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.35 (m, 2H), 6.92 (dd, *J* = 8.2, 2.5 Hz, 1H), 3.89 (s, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 159.65, 148.02, 144.14, 134.11, 133.08, 130.20, 129.40, 125.86, 125.21, 124.20, 119.65, 114.07, 113.71, 112.31, 92.03, 77.00, 55.34. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{16}H_{12}BrN_2OS$: 358.9854. Found: 358.983.

3-bromo-2-(4-chlorophenyl)benzo[d]imidazo[2,1-b]thiazole (8h):

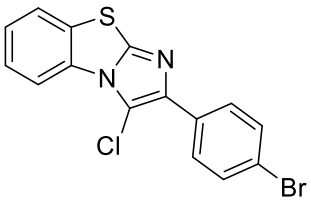


(Eluent: 5% EtOAc/hexane); 81% yield (73.5 mg); yellow solid, Mp: 178 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 8.3, 0.5 Hz, 1H), 8.01 – 7.92 (m, 2H), 7.69 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.45 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.43 – 7.35 (m, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 148.22, 143.19, 133.65, 132.96, 131.31, 130.16, 125.92, 125.31, 124.22, 113.66, 91.94, 77.00, 29.68. HRMS-ESI (m/z) [M+H]+calcd. For $C_{15}H_9BrClN_2S$: 362.9358. Found: 362.9355.

5-chloro-6-phenylimidazo[2,1-b]thiazole (9a): [21c]

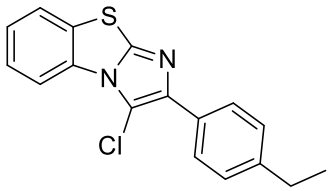
(Eluent: 5% EtOAc/hexane); 48% yield (28.08 mg); yellow solid, Mp:105 ^{0}C; ^{1}H NMR (600 MHz,  $CDCl_3$) δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 4.5 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 4.5 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 147.31, 141.32, 140.92, 132.61, 128.51, 127.73, 126.56, 116.65, 113.34, 77.00.

2-(4-bromophenyl)-3-chlorobenzo[d]imidazo[2,1-b]thiazole (9b):

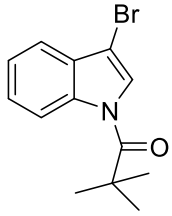


(Eluent: 5% EtOAc/hexane); 42% yield (38.11 mg); yellow solid, Mp: 170 ^{0}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.85 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 140.27, 132.56, 131.71, 131.55, 130.14, 128.22, 126.26, 125.40, 124.33, 121.83, 113.58, 77.00. HRMS-ESI (m/z) $[M+H]^+$calcd. For $C_{15}H_9BrClN_2S$: 362.9358. Found: 362.9350.

3-chloro-2-(4-ethylphenyl)benzo[d]imidazo[2,1-b]thiazole (9c):

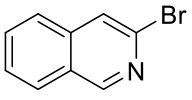
(Eluent: 5% EtOAc/hexane); 40% yield (31.20 mg); yellow solid, Mp: 170 ^{0}C, ^{1}H NMR (600  MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.8 Hz, 3H); ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 143.97, 137.78, 128.02, 127.10, 126.67, 126.07, 125.11, 125.07, 124.58, 124.19, 122.22, 113.46, 77.00, 28.69, 15.47. HRMS-ESI (m/z) [M+H]+calcd. For $C_{17}H_{14}ClN_2S$: 313.0566. Found: 313.0531.

1-(3-bromo-1H-indol-1-yl)-2,2-dimethylpropan-1-one (9g):



99% yield (279.0 mg); yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, J = 8.4 Hz, 1H), 7.81 (s, 1H), 7.54 (d, J = 7.7 Hz, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 1.53 (s, 9H). ^{13}C{H} NMR (150 MHz, $CDCl_3$) δ 176.29, 135.99, 128.27, 126.25, 124.38, 124.05, 119.04, 117.26, 99.25, 41.18, 28.55.HRMS-ESI (m/z) [M+H]+calcd. For $C_{13}H_{15}BrNO$: 280.0322. Found: 280.0349.

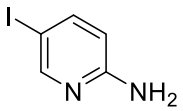
3-bromoisoquinoline 9h [22]



(Eluent: 20% EtOAc/hexane); 40% yield (82.40 mg); Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.70 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.95 (dd, J =

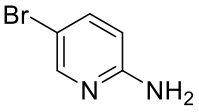
8.0, 3.3 Hz, 1H), 7.79 (t, J = 7.3 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H). $^{13}C\{H\}$ NMR (150 MHz, $CDCl_3$) δ 151.66, 144.57, 134.66, 131.61, 129.65, 128.17, 127.78, 125.82, 119.59.

5-iodopyridin-2-amine (11a): [26b]



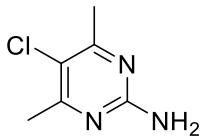
(Eluent: 5% EtOAc/hexane); 47% yield (25.8 mg); off white solid, Mp: 125 ^0C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 6.41 – 6.22 (m, 1H), 4.53 (s, 2H); $^{13}C\{H\}$ NMR (150 MHz, $CDCl_3$) δ 157.26, 153.74, 145.29, 110.83, 77.82, 77.00.

5-bromopyridin-2-amine (11b): [19]



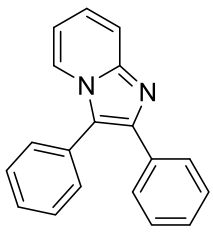
(Eluent: 5% EtOAc/hexane); 58% yield (25.0 mg); white solid, Mp: 135 ^0C; ^1H NMR (600 MHz, $CDCl_3$) δ 8.06 (d, *J* = 2.1 Hz, 1H), 7.46 (dd, *J* = 9.1, 2.3 Hz, 1H), 6.38 (d, *J* = 8.9 Hz, 1H), 4.51 (s, 2H); $^{13}C\{H\}$ NMR (150 MHz, $CDCl_3$,) δ 157.01, 148.65, 140.08, 110.01, 108.23, 77.00.

5-chloro-4,6-dimethylpyrimidin-2-amine 11c [15]



(Eluent: 20% EtOAc/hexane); 51% yield (80 mg); White solid, Mp: 180 ^0C; ^1H NMR (600 MHz,) δ 6.61 (s, 1H), 2.29 (s, 3H). $^{13}C\{H\}$ NMR (150 MHz,) δ 164.00, 161.35, 116.54, 22.42.

2,3-diphenylimidazo[1,2-a]pyridine 12a [25a]



(Eluent: 15% EtOAc/hexane); 60%(16.2 mg)(from 3a), 65%(17.55 mg)(from 4a), yield (16.2 mg); White solid, Mp: 148 ^0C; ^1H NMR (600 MHz,) δ ^1H NMR (600 MHz,) δ 7.96 (d, J = 6.9 Hz, 2H), 7.72 – 7.64 (m, 6H), 7.52 (d, J = 7.0 Hz, 4H), 7.49 (d, J = 7.7 Hz, 2H), 7.46 (d, J = 7.2 Hz, 4H), 7.27 (dt, J = 10.2, 7.2 Hz, 7H), 7.22 – 7.17 (m, 2H), 6.74 (s, 2H).$^{13}C\{H\}$ NMR (150 MHz,) δ 144.78 (s), 142.36 (s), 134.09 (s), 130.71 (s), 129.83 (s), 129.52 (s), 128.86 (s), 128.24 (s), 128.08 (s), 127.45 (s), 124.68 (s), 123.26 (s), 117.51 (s), 112.27 (s).

ASSOCIATED CONTENT

Supporting Information:

Copies of NMR spectra for all compounds and HRMS spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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