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Graphical Abstract

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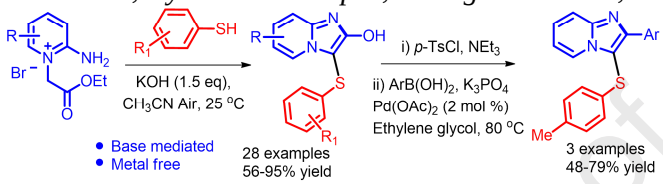

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KOH-mediated intramolecular amidation and sulfenylation: A direct approach to access 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols

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ABSTRACT

A simple and facile method for the synthesis of 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols has been developed by a KOH-mediated reaction of 2-aminopyridinium bromides with aryl thiols. The method afforded a wide range of 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols in moderate to excellent (56-95%) yields with excellent functional group tolerance. Synthetic utility of the protocol was demonstrated by gram-scale reaction and preparation of 2-aryl-3-(*p*-tolylthio)imidazo[1,2-*a*]pyridines from 3-(*p*-tolylthio)imidazo[1,2-*a*]pyridin-2-ol.

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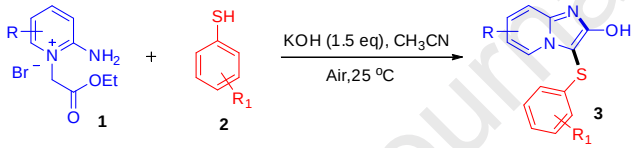
1. Introduction

Compounds with imidazo[1,2-*a*]pyridine scaffold are reported to exhibit a wide range of biological activities.[1,2] This core structure is found in various clinical drugs such as zolpidem, alpidem, necopidem, saripidem, zolimidine, olprinone, soraprazan, miroprofen, and minodronic acid.[3] GSK812397 is an optically active drug derived from imidazo[1,2-*a*]pyridine motif used for the treatment of HIV infections.[4] Imidazo[1,2-*a*]pyridine derivatives have also been extensively utilized in the area of organometallics[5] and field of optics (fluorescence sensors, laser dyes and molecular switches). Owing to their importance, synthesis and functionalization of imidazo[1,2-*a*]pyridines have received significant attention during the past decades.[6-11]

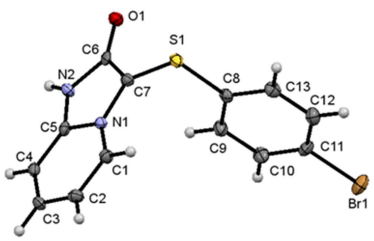
On the other hand, sulfenylation of heterocyclic compounds has emerged as an intriguing strategy for the development of biologically active molecules.[12-14] In this regard, sulfenylation of imidazo[1,2-*a*]pyridines has been extensively elaborated in the literature by various research groups.[15-19] The C-3 sulfenylation of imidazo[1,2-*a*]pyridine is accomplished using various reagents such as thiols,[20] sulfonyl chlorides,[21] sulfonyl hydrazines[22,23] or S□phenyl benzenesulfonothioate,[24] disulfides[25] thiosulfate salts[26] and dithiocarbamates[27] by employing activators such as silica-supported $CeCl_3{\cdot}7H_2O$/NaI,[28] DMSO-$POCl_3$,[29] iodine reagents,[30-32] copper catalyst,[33,34] and *N*-chlorosuccinimide.[35] Most of the existing methods rely on sulfenylation of pre-existing imidazo[1,2-*a*]pyridine ring. Thus, a one-pot method that invole generation of imidazo[1,2-*a*]pyridine skeleton and sulfenylation is worth exploring. As part of our continued interest toward the use of 2-aminopyridinium salts in organic synthesis,[36-38] herein, we wish to report a novel and simple method for the synthesis of 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols by the reaction of 2-aminopyridinium salts with aryl thiols in the presence of KOH under mild conditions (Scheme 1).



Scheme 1: 3-(Arylthio)imidazo[1,2-*a*]pyridin-2-ols from 2-aminopyridinium salts

2. Results and discussion

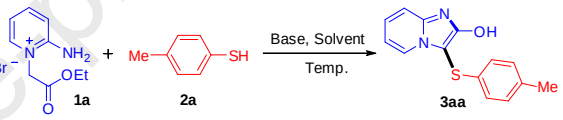
The reaction of 2-amino-1-(2-ethoxy-2-oxoethyl)pyridinium bromide (**1a**, 1 equiv.) and *p*-thiocresol (**2a**, 1.5 equiv.) with NaOH (1.5 equiv.) in acetonitrile at 60 °C for 12 h in open air afforded 3-(*p*-tolylthio)imidazo[1,2-*a*]pyridin-2-ol (**3aa**) in 51% yield after column chromatographic separation. The structure of **3aa** was elucidated by IR, ^{1}H, ^{13}C NMR, HRMS analysis. Further, single-crystal X□ray crystallographic analysis unambigously confirmed the structure of **3aa** (Figure 1, CCDC No 1882988). The probability of hydrogen migration from oxygen to nitrogen was observed leading to a zwitterionic molecule that was susceptible to form a dimer *via* hydrogen bonding with another molecule during the crystallization process (See Supp. Material, Figure S1).



50% probability level.

Encouraged by the formation of **3aa**, the reaction conditions were further optimized by varying various bases, solvents, and reaction temperature (Table 1). Among different inorganic and organic bases screened (Table 1 entries 1-10), KOH was found to give the best yield (61%) of **3aa** under otherwise identical conditions (Table 1, entry 2). Next, the reaction of **1a** and **2a** was studied in different solvents such as THF, 1,4-dioxane, water and toluene (Table 1 entries 11-14). The reaction worked in polar solvents (THF, 1,4-dioxane and water) but the yield of **3aa** was lower than that obtained in acetonitrile. However, in non-polar solvent toluene reaction did not work. Poor yield in toluene may be attributed to the insolubility of the base. Further, when the reaction of **1a** and **2a** was performed at higher temperatures (80 ºC and 100 ºC), the yield of **3aa** decreased to 52% and 35%, respectively (Table 1, 15-16). On the other hand, the yield of **3aa** increased to 73%, when the reaction was performed at 25 ºC under otherwise identical reaction conditions (Table 1, entry 17). It is worth mentioning that the product **3aa** was not observed in the absence of base (Table 1, entry 18). Thus, it was concluded that the best yield of **3aa** was achieved using KOH (1.5 equiv.) in acetonitrile at 25 °C for 12 h in the open air.

Table 1: Optimization of reaction conditions.[a]



S. No.	Base	Solvent	Temp. (°C)	% Yield of **3aa**[b]
1.	NaOH	CH_3CN	60	51
2.	KOH	CH_3CN	60	61
3.	K_2CO_3	CH_3CN	60	25
4.	K_3PO_4	CH_3CN	60	51
5.	Cs_2CO_3	CH_3CN	60	<5
6.	NaOAc	CH_3CN	60	10
7.	DBU	CH_3CN	60	-[c]
8.	NEt_3	CH_3CN	60	51
9.	Piperidine	CH_3CN	60	<5
10.	DMAP	CH_3CN	60	<5
11.	KOH	THF	60	52
12.	KOH	1,4-dioxane	60	48
13.	KOH	Toluene	60	-[c]
14.	KOH	H_2O	60	50
15.	KOH	CH_3CN	80	52
16.	KOH	CH_3CN	100	35
17.	KOH	CH_3CN	25	73
18.	-	CH_3CN	25	-[c]

[a]Reaction conditions: **1a** (1.2 mmol), **2a** (1.0 mmol.), base (1.5 equiv.), solvent (5 mL) under air for 12 h.

[b]Isolated yields.

[c]No reaction.

With optimized reaction conditions in hand, we next probed the substrate scope and generality of the developed protocol (Table 2). Initially, different substituted aryl thiols (**2a-g**) were reacted with **1a** to give corresponding 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols (**3aa-3ag**) in moderate to good yields. Aryl thiols with electron-withdrawing substituents afforded slightly higher yields of corresponding products as compared to those with electron releasing substituents (**3af** *vs* **3ag**). The 4-chlorobenzenethiol and 4-bromobenzenethiol**,** reacted with **1a** to afford **3ac** and **3ad** in 79% and 77% yields, respectively. Further, the reaction scope was studied by using various substituted 2-aminopyridinium bromides (**1b-1i**). The reaction of 2-

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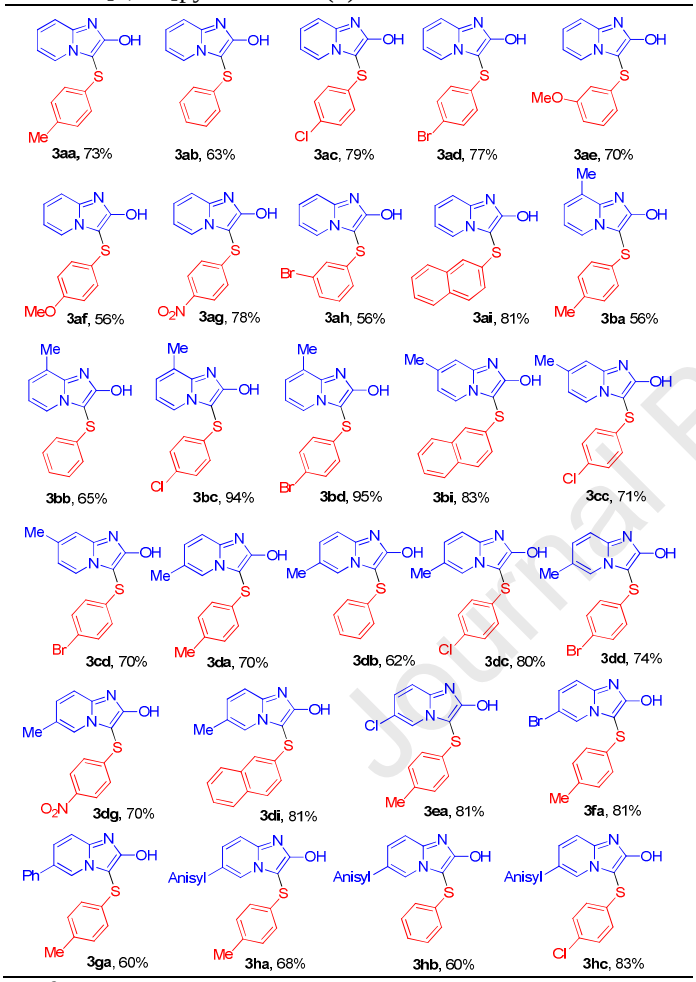
substituents on C-3, C-4 and C-5 positions reacted smoothly to provide corresponding 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols (**3ba-3hc**) in moderate to excellent yields. The position of substituents on pyridine ring influenced the reaction outcome. For example, slightly lower yields of the desired product were obtained from the C-5 methyl or phenyl substituted 2-aminopyridinium bromides compared to other 2-aminopyridinium bromides. Similarly, C-5 halogen-substituted 2-aminopyridinium bromides led to better yields of desired products compared to unsubstituted or C-5 methyl-substituted 2-aminopyridinium bromides. Disappointingly, reaction with alkyl thiols failed to provide the desired product under these conditions.

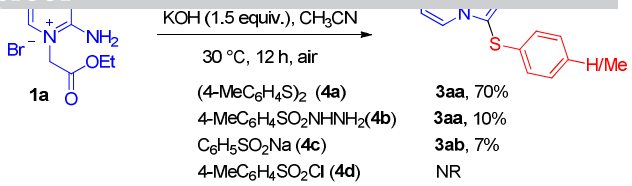
Table 2: Substrate scope for the Synthesis of 3-(arylthio)-imidazo[1,2-*a*]pyridin-2-ols (**3**).[a,b]



[a]Reaction conditions: **1** (1.2 mmol), **2** (1.0 mmol.), KOH (1.5 equiv.), CH_3CN (5 mL) at 25 °C under air for 12 h.

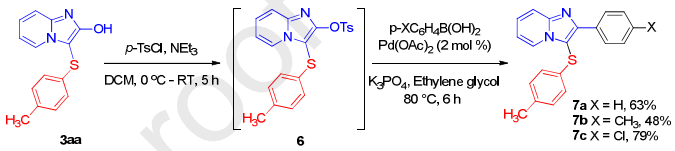
[b]Isolated yields.

We then turned our attention towards the comparative study of other sulfenylation agents (**4**) over thiophenol (**2**) under optimized reaction conditions (Scheme 2). Among studied agents, the reaction of **1a** with *p*-tolyl disulfide (**4a**) provided **3aa** in a 70% yield. On the other hand, a reaction of **1a** with 4-methylbenzene-sulfonohydrazide (**4b**) and sodium benzenesulfinate (**4c**) delivered **3aa** and **3ab** in 10 and 7% yield, respectively, while the reaction of **1a** with *p*-toluenesulfonyl chloride (**4d**) failed to deliver the desired product.



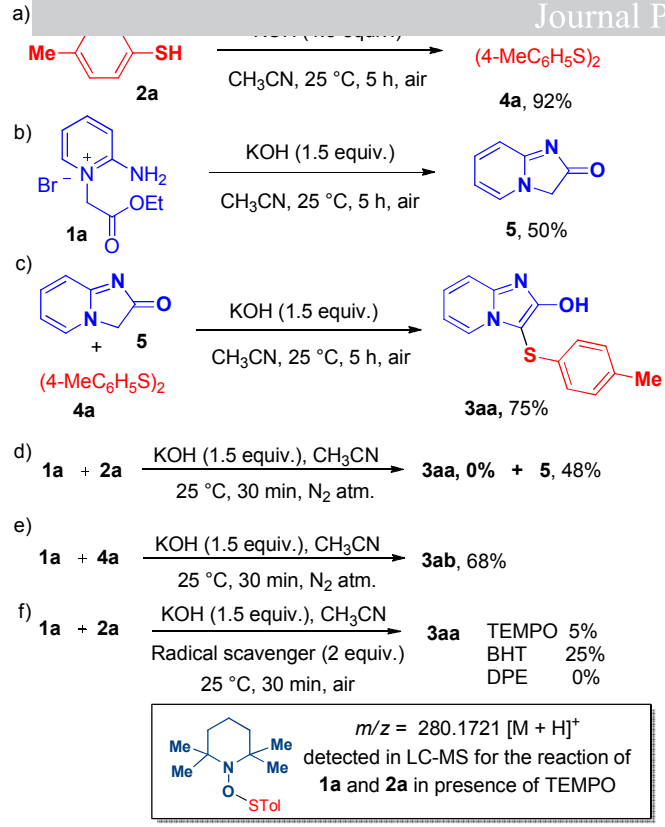
Scheme 2: Comparative study of sulfenylation agents.

The practical utility of this protocol was demonstrated by synthesizing **3aa** from **1a** at 6 mmol scale. In this case, compound **3aa** was obtained in 72% yield. Further, **3aa** was transformed to 2-aryl-3-sulfenylimidazo[1,2-*a*]pyridines in modertae to good yields (Scheme 3). Initially, tosylation of **3aa** produced 3-(*p*-tolylthio)imidazo[1,2-*a*]pyridin-2-yl 4-methylbenzenesulfonate (**6**) which was then subjected to Suzuki reaction with different aryl boronic acids to give corresponding 2-aryl-3-(*p*-tolylthio)-imidazo[1,2-*a*]pyridines (**7a-c**) in good yields.



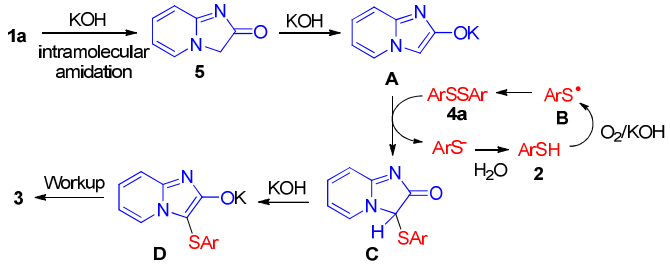
Scheme 3: Synthesis of 2-aryl-3-sulfenylimidazo[1,2-*a*]-pyridines **7** from **3aa**.

To explore the mechanism involved in this transformation, we executed a set of control experiments (Scheme 4). The reaction of **2a** in the absence of **1a** under the standard reaction conditions resulted in the formation of **4a** in a 93% yield (Scheme 4a). Similarly, a reaction of **1a** in the absence of **2a** led to the formation of **5** in a 50% yield through base-catalyzed intramolecular amidation reaction (Scheme 4b). Next, a reaction of **5** with **4a** under optimized reaction condition produced **3aa** in 75% yield (Scheme 4c) indicating the possibility of **4** and **5** as reaction intermediates. Interestingly, the reaction of **1a** and **2a** under a nitrogen atmosphere under otherwise identical conditions failed to yield **3aa** and resulted on **5** in 48% yield (Scheme 4d), while the reaction of **1a** with **4a** under similar conditions provided a 68% yield of **3aa** (Scheme 4e). Further, the formation of **3aa** was substantially quenched when radical scavengers such as TEMPO, BHT, and DPE were added in the reaction (Scheme 4f). These results suggested that compounds **4a** and **5** are the intermediates of this reaction which are formed *in situ* and reaction involves radical pathway. Finally, HRMS analysis of the crude reaction mixture between **1a** and **2a** in the presence of TEMPO revealed a peak at *m*/z 280.1721, which corresponded to the $C_{16}H_{26}NOS^+$ ion. It was conceivable that the 4-$MeC_6H_4S^{\cdot}$ radical generated from **2a** was caught by the TEMPO.



Scheme 4: Control experiment

Based on the results of the control experiments and the literature reports,[39] a tentative mechanism for the formation of **3aa** is proposed and shown in Scheme 5. Initially, 2-aminopyridinium bromide (**1a**) undergoes base mediated intramolecular amidation reaction to from **5**, which subsequently on deprotonation of CH_2-proton converts into an electron-rich enolate anion **A.** The thiyl radical **B** generated from the autoxidation of thiol **2** in the presence of KOH and dioxygen undergoes homocoupling to produce disulfide **4a**.[40,41] Subsequently, the reaction of the *in situ* generated enolate **A** with disulfide **4a** affords 3-(arylthio)imidazo[1,2-*a*]-pyridin-2(3H)-one (**C**).[42] Finally, intermediate **C** tautomerizes to enolate anion **D**, which on acidic workup produces **3**.



Scheme 5: Proposed mechanism

3. Conclusion

In conclusion, we have developed an efficient and atom-economical approach to structurally diverse and synthetically useful 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ol *via* a simple base mediated reaction of 2-aminopyridnium bromides with aryl thiols at room temperature. The reaction involves base-mediated intramolecular amidation followed by sulfenylation of the C-H bond through a radical pathway. The protocol is amenable for a scale-up reaction. Given the high pharmaceutical importance of

eful for the synthesis of a variety of 3-sulfenyl-imidazo[1,2-*a*]pyridines under metal-free conditions.

4. Experimental

4.1. General Methods

All reagents and solvents were purchased from commercial sources and used without further purification. Melting points were measured using an automatic capillary point apparatus and are uncorrected. The thin-layer chromatography (TLC) was performed on 0.25 mm silica gel 60-F254, and a UV lamp was used as a visualizing agent. Column chromatography was performed using silica gel (100−200 mesh), and hexane and ethyl acetate were used as eluents. The ^{1}H and ^{13}C NMR spectra were obtained on a 400 and 100 MHz spectrometer. Coupling constants and chemical shifts were reported in hertz (Hz) and parts per million (ppm), respectively, relative to the internal standard of tetramethylsilane (TMS). IR spectroscopy was performed as a neat sample on an FT-IR instrument, and values are expressed in cm^{-1}. The HRMS were analyzed by the electrospray ionization (ESI) method in positive mode on a Q-TOF LC-MS spectrometer. The synthesis of 2-aminopyridinium bromides (**1**) was achieved from the reaction of corresponding 2-aminopyridine and ethyl bromoacetate following our earlier reported method.[37]

4.2. Representative procedure for synthesis of compound 3.

An oven-dried 10 mL round bottom flask was charged with 2-aminopyridinium bromides (0.6 mmol), aryl thiols (0.5 mmol), and KOH (0.042 g, 0.750 mmol) in acetonitrile (5 mL). The resulting reaction mixture was stirred at 25 °C for 12 h. The reaction was monitored by TLC over time. On completion, the acetonitrile was evaporated in the rotatory evaporator to obtain a residue. Water was added to the residue and neutralized with 2N HCl to obtain a solid precipitate. The precipitate was vacuum filtered and dried to obtain crude brown solid which was subjected to column chromatography (50% EtOAc: hexane) to afford **3**.

*4.2.1. 3-(p-Tolylthio)imidazo[1,2-a]pyridin-2-ol (**3aa**)*

Cream colored solid (93 mg, 73%); MP 208 – 210 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (bs, 1H), 8.17 (d, *J* = 6.6 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.02 (d, *J* = 6.7 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 139.3, 135.6, 133.6, 130.3, 127.1, 125.9, 124.0, 114.5, 111.7, 86.8, 20.9; FT-IR ν_{max} (neat) 3364, 3086, 2916, 1612, 1585, 1435, 1265, 1157, 1018, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{13}N_2OS$ $[M + H]^+$ 257.0743, found 257.0725.

*4.2.2. 3-(Phenylthio)imidazo[1,2-a]pyridin-2-ol (**3ab**)*

Brown colored solid (93 mg, 77%); MP 289 – 291 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (bs, 1H), 8.20 (d, *J* = 6.5 Hz, 1H), 7.40 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.18 – 7.11 (m, 1H), 7.04 (td, *J* = 6.8, 1.5 Hz, 1H), 7.02 – 6.96 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 139.3, 137.3, 129.7, 127.3, 126.1, 125.4, 124.1, 114.6, 111.6, 86.1; FT-IR ν_{max} (neat) 3564, 3074, 2916, 1612, 1465, 1327, 1265, 1149, 1018, 887, 732 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{11}N_2OS$ $[M + H]^+$ 243.0587, found 243.0590.

*4.2.3. 3-((4-Chlorophenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3ac**).*

C… …57, (400 MHz, DMSO-d_6) δ 11.90 (bs, 1H), 8.23 – 8.15 (m, 1H), 7.42 (ddd, *J* = 8.4, 7.0, 1.3 Hz, 1H), 7.37 – 7.30 (m, 3H), 7.07 (dd, *J* = 6.8, 1.3 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 139.2, 136.6, 130.7, 129.6, 127.6, 127.2, 124.1, 114.8, 111.4, 85.4; FT-IR ν_{max} (neat) 3356, 3062, 1643, 1612, 1512, 1465, 1327, 1265, 1111, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{10}ClN_2OS$ $[M + H]^+$ 277.0197, found 277.0203.

*4.2.4. 3-((4-Bromophenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3ad**).*

Off-white solid (123 mg, 77%); MP 245 – 247 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (bs, 1H), 8.19 (d, *J* = 6.6 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.06 (t, *J* = 6.8 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 139.1, 137.2, 132.5, 127.6, 127.5, 124.1, 118.9, 114.8, 111.4, 85.3; FT-IR ν_{max} (neat) 3564, 3062, 1612, 1419, 1327, 1265, 1211, 1111, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{10}BrN_2OS$ $[M + H]^+$ 320.9692, found 320.9667 and 322.964 $[M + H + 2]^+$.

*4.2.5. 3-((3-methoxyphenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3ae**).*

Off-white solid (95 mg, 70%); MP 262 – 264 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.73 (s, 1H), 8.19 (d, *J* = 6.6 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 6.5 Hz, 1H), 6.72 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.55 (s, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 161.1, 160.3, 139.2, 138.8, 130.7, 127.4, 124.1, 117.5, 114.6, 111.5, 111.1, 86.1, 55.5; FT-IR ν_{max} (neat) 3363, 2916, 1609, 1582, 1481, 1327, 1265, 1111, 1084, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{13}N_2O_2S$ $[M + H]^+$ 273.0692, found 273.0670.

*4.2.6. 3-((4-Methoxyphenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3af**).*

Off-white solid (76 mg, 56%); MP 272 – 274 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (bs, 1H), 8.24 (d, *J* = 6.5 Hz, 1H), 7.37 (t, *J* = 8.1 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 3H), 6.85 (d, *J* = 8.3 Hz, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 158.5, 139.1, 128.5, 127.6, 127.0, 124.0, 115.5, 114.5, 111.8, 88.3, 55.6; FT-IR ν_{max} (neat) 3564, 3363, 2916, 1612, 1556, 1481, 1327, 1265, 1111, 1072, 1026, 758 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{13}N_2O_2S$ $[M + H]^+$ 273.0692, found 273.0677.

*4.2.7. 3-((4-Nitrophenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3ag**).*

Yellow solid (112 mg, 78%); MP 214 – 216 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (bs, 1H), 8.19 (dt, *J* = 6.6, 1.1 Hz, 1H), 8.14 – 8.07 (m, 2H), 7.47 (ddd, *J* = 8.5, 7.1, 1.2 Hz, 1H), 7.37 (dt, *J* = 8.7, 1.2 Hz, 1H), 7.25 – 7.18 (m, 2H), 7.08 (td, *J* = 6.9, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 147.8, 145.7, 128.2, 125.5, 124.8, 124.3, 115.1, 111.1, 99.9, 83.3; FT-IR ν_{max} (neat) 3394, 2989, 1612, 1481, 1373, 1265, 1118, 1076, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{10}N_3O_3S$ $[M + H]^+$ 288.0437, found 288.0409.

*4.2.8. 3-((2-Bromophenyl)thio)imidazo[1,2-a]-pyridin-2-ol (**3ah**).*

Off-white solid (90 mg, 56%); MP 287-289 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.90 (bs, 1H), 8.14 (d, *J* = 6.5 Hz, 1H), 7.63 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.50 – 7.41 (m, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.20 (td, *J* = 7.6, 1.3 Hz, 1H), 7.14 – 7.06 (m, 1H), 7.06 (dd, *J* = 7.2, 1.3 Hz, 1H), 6.44 (dd, *J* = 7.8, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 139.2, 137.9, 133.5, 128.8, 127.9, 127.5, 125.5, 124.2, 119.4, 115.1, 111.2, 84.3; FT-IR ν_{max} 1018, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{10}BrN_2OS$ $[M + H]^+$ 320.9692, found 320.9696 and 322.9675 $[M + H + 2]^+$.

*4.2.9. 3-(Naphthalen-2-ylthio)imidazo[1,2-a]-pyridin-2-ol (**3ai**).*

Off-white solid (118 mg, 81%); MP 245 – 247 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (bs, 1H), 8.22 (d, *J* = 6.6 Hz, 1H), 7.84 (d, *J* = 9.3 Hz, 2H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.50 (s, 1H), 7.45 (t, *J* = 7.1 Hz, 2H), 7.40 (d, *J* = 7.1 Hz, 1H), 7.36 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.03 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 139.2, 134.9, 133.8, 131.7, 129.4, 128.1, 127.4, 127.3, 127.2, 126.0, 124.2, 124.1, 123.2, 114.7, 111.5, 86.0; FT-IR ν_{max} (neat) 3394, 2989, 1643, 1612, 1481, 1373, 1265, 1134, 1076, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{13}N_2OS$ $[M + H]^+$ 293.0743 found 293.0750.

*4.2.10. 8-Methyl-3-(p-tolylthio)imidazo[1,2-a]-pyridin-2-ol (**3ba**).*

Off-white solid (76 mg, 56%); MP 253 – 255 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.71 (bs, 1H), 8.03 (d, *J* = 6.5 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.94 (t, *J* = 6.9 Hz, 1H), 6.90 (d, *J* = 8.2 Hz, 2H), 2.41 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 139.5, 135.6, 133.7, 130.3, 126.7, 126.0, 122.0, 121.9, 114.2, 87.4, 20.9, 16.3; FT-IR ν_{max} (neat) 3564, 3074, 2962, 1643, 1604, 1572, 1442, 1327, 1249, 1180, 1018, 794 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{15}N_2OS$ $[M + H]^+$ 271.0900, found 271.0902.

*4.2.11. 8-Methyl-3-(phenylthio)imidazo[1,2-a]-pyridin-2-ol (**3bb**).*

Off-white solid (83 mg, 65%); MP 225 – 227 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (bs, 1H), 8.05 (d, *J* = 6.6 Hz, 1H), 7.25 (q, *J* = 7.2 Hz, 3H), 7.14 (t, *J* = 7.3 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 7.1 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 139.5, 137.4, 129.7, 126.7, 126.1, 125.4, 121.9, 120.5, 114.2, 86.6, 16.2; FT-IR ν_{max} (neat) 3369, 3093, 1604, 1465, 1256, 1180, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{13}N_2OS$ $[M + H]^+$ 257.0743, found 257.0745.

*4.2.12. 3-((4-Chlorophenyl)thio)-8-methylimidazo-[1,2-a]pyridin-2-ol (**3bc**).*

Off-white solid (138 mg, 94%); MP 238 – 240 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (bs, 1H), 8.05 (d, *J* = 6.5 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.25 (d, *J* = 7.2 Hz, 1H), 7.03 – 6.99 (m, 2H), 6.97 (t, *J* = 6.8 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 139.4, 136.7, 130.7, 129.6, 127.2, 127.1, 122.0, 121.8, 114.5, 86.0, 16.2.; FT-IR ν_{max} (neat) 3564, 3093, 1643, 1612, 1578, 1442, 1318, 1235, 1111, 748 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}ClN_2OS$ $[M + H]^+$ 291.0353, found 291.0354.

*4.2.13. 3-((4-Bromophenyl)thio)-8-methylimidazo-[1,2-a]pyridin-2-ol (**3bd**).*

Off-white solid (159 mg, 95%); MP 246 – 248 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (bs, 1H), 8.04 (d, *J* = 6.4 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 1H), 6.97 (d, *J* = 6.8 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.1, 144.3, 142.0, 137.3, 132.3, 131.8, 126.7, 126.6, 123.7, 119.2, 90.7, 21.0; FT-IR ν_{max} (neat) 3564, 3062, 1620, 1465, 1334, 1249, 1080, 756, 732 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}BrN_2OS$ $[M + H]^+$ 334.9848, found 334.9820, and 336.9799 $[M + H + 2]^+$.

*4.2.14. 8-Methyl-3-(naphthalen-2-ylthio)imidazo-[1,2-a]pyridin-2-ol (**3bi**).*

Yellow solid (127 mg, 83%); MP 265 – 267 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.81 (bs, 1H), 8.08 (d, *J* = 6.5 Hz, 1H), 7.83

(d... Hz, 1H), 7.44 (pd, *J* = 7.0, 1.6 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.17 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.94 (t, *J* = 6.9 Hz, 1H), 2.44 (s, 3H). ; ^{13}C NMR (100 MHz, DMSO) δ 161.3, 139.5, 135.0, 133.8, 131.7, 129.4, 128.1, 127.3, 127.2, 126.9, 126.0, 124.2, 123.3, 122.01, 121.8, 114.3, 86.5, 16.2; FT-IR ν_{max} (neat) 3363, 3070, 2974, 1612, 1597, 1456, 1313, 1256, 1111, 1072, 782 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{18}H_{15}N_2OS$ $[M + H]^+$ 307.0900, found 307.0878.

*4.2.15. 3-((4-Chlorophenyl)thio)-7-methylimidazo-[1,2-a]pyridin-2-ol (**3cc**).*

White solid (102 mg, 71%); MP 244 – 246 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (bs, 1H), 8.07 (d, *J* = 6.7 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.15 (s, 1H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 6.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 139.1, 137.1, 130.5, 129.6, 129.6, 127.0, 123.6, 116.8, 110.1, 83.8, 21.0; FT-IR ν_{max} (neat) 3371, 3047, 2962, 1604, 1597, 1465, 1327, 1265, 1080, 779 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}ClN_2OS$ $[M + H]^+$ 291.0353, found 291.0338.

*4.2.16. 3-((4-Bromophenyl)thio)-7-methylimidazo-[1,2-a]pyridin-2-ol (**3cd**).*

White solid (117 mg, 70%); MP 246 – 248 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.78 (bs, 1H), 8.07 (d, *J* = 6.7 Hz, 1H), 7.62-7.50 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 160.82, 139.16, 137.73, 132.83, 132.46, 129.81, 127.35, 123.63, 118.79, 116.87, 83.71, 21.09; FT-IR ν_{max} (neat) 3365, 3070, 2974, 1643, 1597, 1456, 1313, 1234, 1072, 795 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}BrN_2OS$ $[M + H]^+$ 334.9848, found 334.9819, and 336.9831 $[M + H + 2]^+$.

*4.2.17. 6-Methyl-3-(p-tolylthio)imidazo[1,2-a]-pyridin-2-ol (**3da**).*

White solid (94 g, 70%); MP 221 – 223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.66 (bs, 1H), 8.02 (s, 1H), 7.33 – 7.20 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 2.25 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 142.2, 140.2, 138.8, 135.1, 135.1, 134.1, 130.5, 128.8, 126.8, 115.7, 91.1, 25.6, 22.7; FT-IR ν_{max} (neat) 3535, 3363, 1604, 1558, 1465, 1319, 1242, 1111, 884, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{15}N_2OS$ $[M + H]^+$ 271.0900, found 271.0884.

*4.2.18. 6-Methyl-3-(phenylthio)imidazo[1,2-a]-pyridin-2-ol (**3db**).*

White solid (79 mg, 62%); MP 248 – 250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (bs, 1H), 8.05 (d, *J* = 1.5 Hz, 1H), 7.27 – 7.22 (m, 4H), 7.17 – 7.10 (m, 1H), 7.02 – 6.95 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 137.8, 137.5, 129.7, 129.5, 126.0, 125.3, 124.2, 122.1, 110.9, 85.8, 18.0; FT-IR ν_{max} (neat) 3564, 3055, 1604, 1597, 1465, 165, 1234, 1157, 887, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{13}N_2OS$ $[M + H]^+$ 257.0743, found 257.0729.

*4.2.19. 3-((4-Chlorophenyl)thio)-6-methylimidazo-[1,2-a]pyridin-2-ol (**3dc**).*

White solid (116 mg, 80%); MP 232 – 235 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.73 (bs, 1H), 8.05 (s, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 137.3, 137.1, 130.7, 129.9, 129.6, 127.1, 124.5, 122.2, 110.6, 85.1, 18.0; FT-IR ν_{max} (neat) 3564, 3387, 3070, 2924, 1643, 1604, 1465, 1319, 1273, 1111, 1080, 894, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}ClN_2OS$ $[M + H]^+$ 291.0353, found 291.0353.

*[1,2-a]pyridin-2-ol (**3da**).*

White solid (123 mg, 74%); MP 248 – 250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (bs, 1H), 8.04 (d, *J* = 1.5 Hz, 1H), 7.51 – 7.38 (m, 2H), 7.33 – 7.17 (m, 2H), 6.99 – 6.87 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 137.6, 132.4, 129.8, 127.4, 124.4, 122.2, 118.8, 108.7, 99.9, 89.4, 17.9; FT-IR ν_{max} (neat) 3363, 3070, 2974, 1643, 1597, 1456, 1313, 1234, 1072, 795 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}BrN_2OS$ $[M + H]^+$ 334.9848, found 334.9852 and 336.9831 $[M + H + 2]^+$.

*4.2.21. 6-Methyl-3-((4-nitrophenyl)thio)imidazo-[1,2-a]pyridin-2-ol (**3dg**).*

Yellow solid (105 mg, 70%); MP 275 – 277 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (bs, 1H), 8.11 (d, *J* = 8.5 Hz, 2H), 8.05 (s, 1H), 7.36 – 7.28 (m, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 160.8, 148.3, 145.6, 137.3, 130.4, 125.4, 124.8, 124.8, 122.4, 110.3, 83.0, 17.9; FT-IR ν_{max} (neat) 3448, 3070, 2916, 1643, 1604, 1573, 1504, 1334, 1234, 1080, 840, 740, 663 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}N_3O_3S$ $[M + H]^+$ 302.0594, found 302.0572.

*4.2.22. 6-Methyl-3-(naphthalen-2-ylthio)imidazo-[1,2-a]pyridin-2-ol (**3di**).*

Off-white solid (124 mg, 81%); MP 245 – 247 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (bs,1H), 8.08 (s, 1H), 7.84 (dd, *J* = 8.0, 4.4 Hz, 2H), 7.78 – 7.71 (m, 1H), 7.50 (d, *J* = 1.8 Hz, 1H), 7.45 (td, *J* = 7.4, 1.6 Hz, 2H), 7.27 (m, 2H), 7.19 (dd, *J* = 8.6, 1.9 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 161.6, 135.4, 133.8, 131.7, 129.7, 129.4, 128.1, 127.3, 127.2, 125.9, 124.3, 124.1, 122.9, 122.2, 118.7, 115.8, 86.7, 17.9; FT-IR ν_{max} (neat) 3363, 3070, 2974, 1612, 1597, 1456, 1327, 1256, 1180, 1072, 765 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{18}H_{15}N_2OS$ $[M + H]^+$ 307.0900, found 307.0907.

*4.2.23. 6-Chloro-3-(p-tolylthio)imidazo[1,2-a]-pyridin-2-ol (**3ea**).*

Cream solid (117 mg, 81%); MP 262 – 264 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (bs, 1H), 8.26 (s, 1H), 7.42 (s, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 136.0, 132.8, 130.5, 127.0, 126.3, 121.7, 120.6, 116.0, 114.1, 89.7, 20.9; FT-IR ν_{max} (neat) 3364, 3078, 2924, 1612, 1597, 1465, 1303, 1257, 1211, 1180, 1010, 794 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}ClN_2OS$ $[M + H]^+$ 291.0353, found 291.0357.

*4.2.24. 6-Bromo-3-(p-tolylthio)imidazo[1,2-a]-pyridin-2-ol (**3fa**).*

Cream solid (135 mg, 81%); MP 243 – 245 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.72 (bs, 1H), 8.29 (s, 1H), 7.50 (d, *J* = 9.2 Hz, 1H), 7.36 (d, *J* = 9.4 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 6.94 (d, *J* = 7.9 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.8, 139.4, 136.0, 132.9, 130.5, 129.3, 126.3, 123.6, 116.1, 114.3, 107.4, 89.5, 20.9; FT-IR ν_{max} (neat) 3339, 3065, 2919, 1612, 1585, 1465, 1327, 1256, 1180, 1010, 869,794 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{12}BrN_2OS$ $[M + H]^+$ 334.9848, found 334.9852, and 336.9831 $[M + H + 2]^+$.

*4.2.25. 6-Phenyl-3-(p-tolylthio)imidazo[1,2-a]-pyridin-2-ol (**3ga**).*

Cream solid (132 mg, 80%); MP 239 – 241 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.69 (bs, 1H), 8.29 (s, 1H), 7.71 (d, *J* = 9.1 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 8.2 Hz, 3H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 7.9 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 141.4, 140.5, 138.2, 135.2, 134.4, 133.2, 132.2, 131.7, 131.2, 130.8, 125.3, 117.2, 92.8, 25.6; FT-IR ν_{max} (neat) 3463, 3070, 2974, 1612, 1597, 1456, 1343, 1227, 1180, 1072, 752 cm^{-1}; HRMS

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333.1032.

*4.2.26. 6-(4-Methoxyphenyl)-3-(p-tolylthio)imidazo-[1,2-a]pyridin-2-ol (**3ha**).*

Cream solid (123 mg, 68%); MP 239 – 241 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (bs, 1H), 8.21 (s, 1H), 7.66 (d, *J* = 8.9 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 9.1 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 3.78 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 159.7, 138.6, 135.7, 133.5, 130.4, 129.0, 128.2, 127.3, 126.3, 126.1, 119.9, 115.1, 112.2, 87.9, 55.7, 20.9; FT-IR ν_{max} (neat) 3564, 3362, 2916, 1635, 1604, 1489, 1319, 1242, 1172, 1018, 802, 748 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{21}H_{19}N_2O_2S$ [M + H]$^+$ 363.1162, found 363.1163.

*4.2.27. 6-(4-Methoxyphenyl)-3-(phenylthio)imidazo-[1,2-a]pyridin-2-ol (**3hb**).*

Cream solid (104 mg, 60%); MP 223 – 225 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (s, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.02 (t, *J* = 8.2 Hz, 4H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 159.6, 139.0, 137.4, 129.9, 129.7, 129.0, 128.1, 127.9, 127.6, 127.03, 126.1, 125.6, 119.8, 115.0, 114.9, 112.0, 86.9, 55.6 ; FT-IR ν_{max} (neat) 3348, 3093, 1604, 1566, 1473, 1280, 1172, 1018, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{17}N_2O_2S$ [M + H]$^+$ 349.1005, found 349.1012.

*4.2.28. 3-((4-Chlorophenyl)thio)-6-(4-methoxyphenyl)imidazo[1,2-a]pyridin-2-ol (**3hc**)*

White solid (159 mg, 83%); MP 255 – 257 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (bs, 1H), 8.24 (s, 1H), 7.69 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 159.7, 136.5, 134.9, 130.7, 129.6, 128.8, 128.2, 127.6, 127.3, 126.7, 120.0, 115.1, 111.8, 86.4, 55.7; FT-IR ν_{max} (neat) 3356, 2924, 1635, 1496, 1465, 1319, 1242, 1211, 1080, 802 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{16}ClN_2O_2S$ [M + H]$^+$ 383.0616, found 383.0617.

*4.3. General procedure for synthesis of 2-aryl-3-(arylthio)-imidazo[1,2-a]pyridines (**7**).*

To a round bottom flask (10 mL) containing **3aa** (0.500 g, 1.95 mmol) and DCM (15 mL) was cooled to 0 °C and sequentially added Et_3N (0.295 g, 2.92 mmol) and p-TsCl (0.556 g, 2.95 mmol) dropwise and portion-wise with stirring. The resulting solution was slowly brought to room temperature and stirred for 5 h. The resulting suspension was diluted with DCM (50 mL), stirred for another 30 minutes and filtered. The filtrate was sequentially washed with 10% $NaHCO_3$ solution (2 × 15 mL) and a saturated aq. NaCl solution (30 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated in *vacuo* to obtain crude tosylated product **6** (430 mg, 56%).

A 10 mL round bottom flask was charged with dried **6** (100 mg, 0.25 mmol), aryl boronic acid (0.38 mmol) and K_3PO_4 (134 mg, 0.63 mmol) and $Pd(OAc)_2$ (1 mg, 2 mol %) in ethylene glycol (5 mL). The resulting solution was stirred at 80 °C for 6 h under air. After completion of the reaction, the mixture was poured into water, extracted by ethyl acetate, washed with brine, and dried with anhydrous Na_2SO_4. The organic solvent was removed under reduced pressure to obtain a crude product. The crude residue was subjected to column chromatography (EtOAc: hexane; 3:7 *v/v*) to afford **7**.

*pyridine (**7a**).*

Yellow solid (50 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 8.30 (dt, *J* = 6.8, 1.2 Hz, 1H), 8.29 – 8.20 (m, 2H), 7.75 (dt, *J* = 8.9, 1.1 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.45 – 7.35 (m, 1H), 7.35 (ddd, *J* = 9.0, 6.8, 1.3 Hz, 1H), 7.09 – 7.00 (m, 2H), 6.98 – 6.90 (m, 2H), 6.88 (td, *J* = 6.8, 1.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$-*d*) δ 146.44, 142.27, 131.30, 128.67, 126.75, 125.47, 123.81, 123.67, 123.64, 122.76, 121.84, 121.08, 119.79, 112.87, 108.27, 102.13, 16.15; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{17}N_2S$ [M + H]$^+$ 317.1107, found 317.1120.

*4.3.2. 2-(p-Tolyl)-3-(p-tolylthio)imidazo[1,2-a]-pyridine (**7b**).*

Yellow solid (40 mg, 48%); ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 8.29 (dt, *J* = 6.8, 1.2 Hz, 1H), 8.19 – 8.06 (m, 2H), 7.74 (dt, *J* = 9.0, 1.2 Hz, 1H), 7.34 (ddd, *J* = 8.6, 6.9, 1.4 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.98 – 6.90 (m, 2H), 6.89 – 6.83 (m, 1H), 2.41 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 146.95, 138.5, 135.9, 131.5, 130.4, 130.1, 129.1, 128.2, 126.5, 125.8, 124.5, 117.4, 112.9, 106.5, 21.3, 20.9; HRMS (ESI-TOF, *m/z*): calcd for $C_{21}H_{19}N_2S$ [M + H]$^+$ 331.1263, found 331.1249.

*4.3.3. 2-(4-Chlorophenyl)-3-(p-tolylthio)imidazo-[1,2-a]pyridine (**7c**).*

White solid (70 mg, 79%); ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ 8.29 (d, *J* = 6.9 Hz, 1H), 8.21 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 9.0 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.34 (ddd, *J* = 8.7, 6.8, 1.3 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 6.9 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 146.9, 136.2, 134.5, 131.8, 131.1, 130.3, 129.6, 128.6, 126.9, 125.8, 124.5, 117.5, 113.2, 107.1, 20.92; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{16}ClN_2S$ [M + H]$^+$ 351.0717, found 351.0725.

Declaration of competing interest

Authors declare no competing interest.

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Highlights

- A KOH-mediated tandem intramolecular amidation and sulfenylation.
- Prepared 28 new 3-(arylthio)imidazo[1,2-*a*]pyridin-2-ols
- Synthesis of 2-aryl-3-(*p*-tolylthio)imidazo[1,2-*a*]pyridines
- Transition-metal free reaction conditions
- Gram scale reaction.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.