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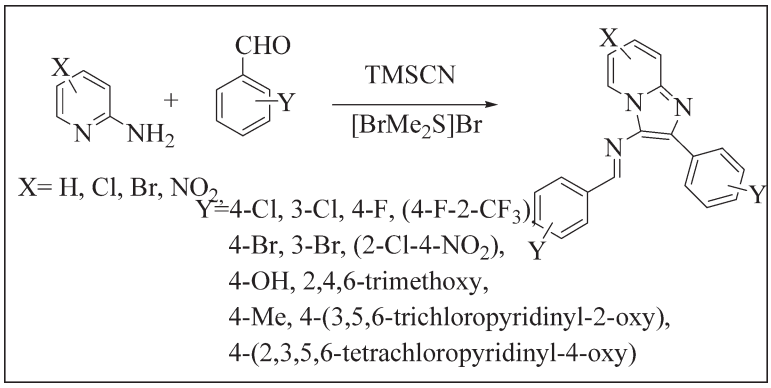

(Bromodimethylsulfonium) bromide–catalyzed one-pot multicomponent reaction of 2-aminopyridine with aromatic aldehyde(s) and TMSCN yielding *N*-benzylidene-2-phenylimidazo[1,2-a]pyridines exclusively has been described. The reaction is solvent free, versatile, and takes significantly short time.

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INTRODUCTION

Multicomponent reactions (MCRs) are defined, in general, as reactions with more than two reactants incorporating all the atoms present in the constituent reactants to form the product [1]. They have received considerable interest due to their high efficiency and atom economy [2]. With focus now on development of small molecule libraries of bioactives and pharmaceuticals, a special stress is laid on development of efficient synthetic methodologies for their construction. Of the MCRs, a recently reported variation of Ugi reaction [3] has found wide applications in construction of fused *N*-heterocycles [4].

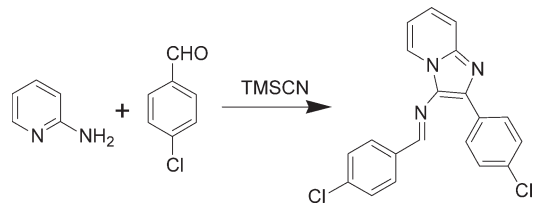
Our current interest in construction of novel fused *N*-heterocycles for potent applications as agrochemicals and pharmaceuticals led us to a class of imidazo[1,2-a] *N*-heterocycles possessing pyridine, pyrazine, and pyrimidine units. These imidazo[1,2-a] heterocycles have found applications as novel pharmaceuticals like antibacterial agents [5], gastric secretion regulators [6], antiulcer agents [7], anti-inflammatory actives [8], calcium channel blockers [9], uterine-relaxing, antibronchospastic, cardiac-stimulating agent [10], etc. Broad range of therapeutic drugs have also been developed like Zolmidine, Zolpidem, Alpidem, and Kifuensine [11]. Classical synthesis of these imidazo[1,2-a]pyridines involves addition of α-haloketones to the corresponding 2-aminoazine, according to Tschitschibabin conditions [12]. However, this reaction has drawbacks. First, it involves lachrymatric α-haloketones and second, it restricts the diversity of these molecules. A 3-component condensation involving aminoazine, formaldehyde, and sodium cyanide [13] has also been reported, which again suffers from limited diversity of products. Isocyanide-based [14] MCRs have been reported with several modifications [15] using montmorillonite K-10 [16], microwave [17], etc. However, the approach involves nasty chemicals, i.e., the isonitriles. An alternate method utilizing ionic liquids has also been reported [18]. Recent reports [19] use TMSCN as an isonitrile equivalent but the methods are known to give more than one product.

RESULTS AND DISCUSSION

This letter deals with the application of TMSCN-based one-pot three-component synthetic protocol using a versatile catalyst (bromodimethylsulfonium) bromide as an improvised method for imidazo[1,2-a]pyridines.

At the outset, the protocol was carried out mixing the reactants, TMSCN, aromatic aldehyde, 2-aminopyridine in the ratio of 1:1:1 all added simultaneously followed by catalyst, (bromodimethylsulfonium) bromide in solvent (Scheme 1). 2-Aminopyridine was added to a prestirred mixture of TMSCN and 4-chlorobenzaldehyde

Scheme 1



(entry 1, Table 1) (*in situ* cyanohydrin formation) takes 3 h at room temperature using methanol as solvent. At the end of 8 h, TLC indicated the consumption of reactants and the product formed was characterized by spectral means as an imine derivative, i.e., *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine. The reaction under solvent-free conditions resulted in the formation of same imine derivative without any difference in yield or reaction time. The reaction was found to be very low yielding. Therefore, we thought it fit to modify the conditions and see the effect on yield and course of reaction.

Alternately, it was thought to form Schiff's base (aldehyde and 2-aminopyrine) first and treat with TMSCN later, with a view to ascertain whether the product formed would be same or different. Accordingly, a mixture of 2-aminopyridine and aldehyde was stirred at room temperature for about 3 h and then TMSCN was added, wherein the same *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine was obtained. Interestingly, it was found that the reaction proceeds to give in higher yields and in shorter reaction times compared with the cyanohydrin approach (entry 3, Table 1). Even low temperature has no impact on the type of product formed (entry 4, Table 1) but has lowering effect on yields. It is clear from the above reactions that the yields formed in either case were low as the aldehyde, which is in equimolar stoichiometry to amino compound becomes limiting reagent for the formation of *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine. The reactant ratio was then appropriately increased to 1:2:1 (2-aminopyridine, aldehyde, TMSCN). As a consequence, the yield of the reaction improved considerably (entry 5, Table 1).

Having established the general reaction conditions wherein optimum yield of the product formed (entry 5, Table 1), the scope of the protocol was tested with different aldehydes and substituted 2-aminopyridines (Scheme 2). The yields were higher with electron-donating substituents present on aromatic aldehyde as well as 2-aminopyridine. Electron-withdrawing groups and meta substitutions have the negative impact and resulted in lower yields. Napthaldehyde yielded the corresponding benzylidine product in moderate yield (entry 9, Table 2). Thiophene carboxaldehyde was very effective and 80% yield of product was obtained (entry 10, Table 2).

However, hydroxy substitution resulted in lower yields. No reaction occurred when the aldehydes were replaced by ketones. The yields were poor with aliphatic aldehydes. Nitro substitution on aminopyridine ring did not yield any product. 2-Aminopyrazines were found to yield a complex mixture of products.

Thus, a diverse library of *N*-benzylidene-2-phenylimidazo[1,2-a]pyridines could be made by this procedure indicating its generality. It was found that the method was broadly applicable and compatible with various substitutions on the aromatic rings of both aldehyde and aminopyridine.

The reaction can be visualized to occur via two possible mechanisms. When TMSCN and aldehyde are mixed first, the *in situ* cyanohydrin thus formed undergoes Strecker reaction with 2-aminopyridine. (Bromodimethylsulfonium) bromide being mildly acidic catalyzes both the cyanohydrin formation as well as the

Scheme 2

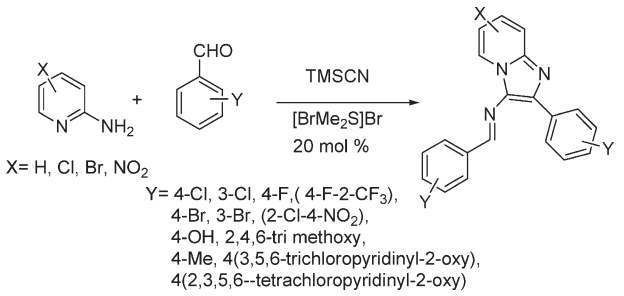


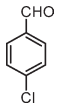
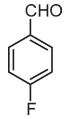
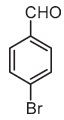
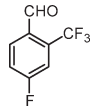
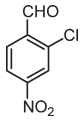
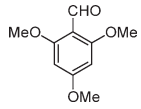
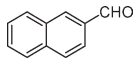
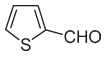
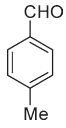
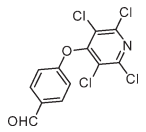
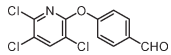
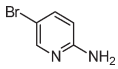
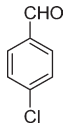
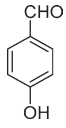
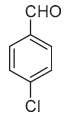
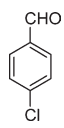
Table 1

The reaction conditions for the 3-component condensation with 20-mol % catalyst.

Entry	Reaction conditions	Solvent	Temp (°C)	Time (h)	Yield (isolated, %)
1	4-Chlorobenzaldehyde in MeOH, TMSCN, 3 h; followed by catalyst and 2-amino pyridine	CH_3OH	RT	8	41
2	4-Chlorobenzaldehyde in MeOH, TMSCN, 3 h; followed by catalyst and 2-amino pyridine	–	RT	8	40
3	Schiff's base of 4-chlorobenzaldehyde and 2-amino pyridine; then catalyst and TMSCN	–	RT	7	50
4	Schiff's base of 4-chlorobenzaldehyde and 2-amino pyridine in MeOH then catalyst and TMSCN	CH_3OH	0°C RT	7	40
5	Schiff's base of 4-chlorobenzaldehyde, 2-amino pyridine then catalyst and TMSCN (1:2:1)	–	RT	3	91

Table 2

(Bromodimethyl sulphonium) bromide catalyzed synthesis of *N*-benzylidine-2-phenyl imidazo[1,2-a] pyridine.

Entry	Amine	Aldehyde	Time (h)	Yield (isolated, %)	M.p (°C)
1			10	91	170–172
2			11	70	145–148
3			11	60	93–95
4			10	79	184–186
5			10	60	88–90
6			11	70	105–108
7			11	50	200–203
8			10.5	61	244–247
9			10	65	182–185
10			10	80	125–128
11			10.5	82	95–98
12			11	72	205–207
13			11	68	173–175
14			11	55	200–203
15			11	50	278–281
16			>20	–	–
17	 (Excess)		10	–	–

cyclization of the resulting aminonitrile formed. This is followed by 1,3-proton shift to yield 3-amino-2-phenylimidazo[1,2-a]pyridine, which then reacts with another molecule of aldehyde to provide the corresponding *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine. On the other hand, when 2-aminopyridine and aldehyde are reacted first, the reaction proceeds via the imine species, which is attacked presumably by nitrile to form an aminonitrile species. The lone pair of the N-atom on pyridine ring attacks the nitrile carbon and cyclises to bicyclic adduct. 1,3-Proton shift results in aromatization leading to 3-amino-2-phenylimidazo[1,2-a]pyridine. The catalyst plays an important role in enhancing both the imine formation as well as the cyclization. Since imine formation is an equilibration process, the aromatic aldehyde is always available for formation of corresponding *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine, which seems to be the fastest step.

To restrict the imine derivative formation rather than amino derivative, the reaction was carried out with large excess of 2-aminopyridine to shift the equilibrium and product formation. However, the 3-amino-2-phenylimidazo[1,2-a]pyridine could not be isolated due to the formation of an inseparable mixture of products. Nevertheless, the 3-amino-2-phenylimidazo[1,2-a]pyridine could be generated with ease from the *N*-benzylidene-2-phenylimidazo[1,2-a]pyridine by treating with 10% TFA in dichloromethane (DCM).

To conclude, the (bromodimethylsulfonium) bromide catalyzed one-pot, three-component solvent free, high-yielding synthesis of *N*-benzylidene imidazo[1,2-a]pyridines is reported for the first time. Only one other report on direct synthesis of the 3-iminoaryl-phenylimidazo[1,2-a]pyridines, using microwave method, was found in literature [20]. Our transformation occurs at room temperature and is a versatile reaction, taking significantly less time compared with majority of the reported methods for making imidazo[1,2-a]pyridines. Further, it has been demonstrated that 3-amino-2-phenylimidazo[1,2-a]pyridines can be generated from *N*-benzylidene-2-phenylimidazo[1,2-a]pyridines conveniently.

EXPERIMENTAL

NMR spectra were recorded on Bruker DPX-250 instrument (200 MHz for ^{1}H and 75 MHz for ^{13}C) and $CDCl_3$ and DMSO used as solvent; chemical shifts are reported in δ (ppm) from TMS. Mass spectra were recorded under ESI condition. HRMS data were recorded on QSTAR XL hybrid MS/MS system under ESI condition.

General procedure. To a mixture of 2-aminopyridine (1 mmol) and 4-chlorobenzaldehyde (2 mmol), TMSCN (1 mmol) was added dropwise under stirring followed by addition of (20 mol %) Me_2SBr_2 catalyst. The reaction mixture was stirred at room temperature and monitored by TLC. After the completion of the reaction as indicated by the disappearance of the starting materials, water was added and extracted with DCM. The organic layer was washed with water, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. Addition of ethyl acetate to the residue precipitated the product. Occasionally the product required purification by column chromatography (EtOAc and hexane; 15:85).

N-(4-Chlorobenzylidene)-[2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl]amine. (Entry 1, Table 2), yellow solid, m.p. 170–172°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.73 (d, 1H, J = 4.72 Hz), 8.42 (d, 1H, J = 6.04 Hz), 7.78 (t, 4H, J = 6.04 Hz), 7.50 (d, 1H, J = 8.30 Hz), 7.43–7.36 (m, 4H), 7.24 (t, 1H, J = 7.20 Hz), 6.89 (t, 1H, J = 5.85 Hz). ESI Mass (*m/z*) 366 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{13}N_3Cl_2$) 366.0564; observed *m/z* (amu), 366.0576; IR (KBr, ν, cm^{-1}) 2924, 1347, 1230, 1087, 829, 747.

N-(4-Fluorobenzylidene)-[2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]amine. (Entry 2, Table 2), yellow solid, m.p. 145–148°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 8.69 (s, 1H), 8.40 (d, 1H, J = 6.80 Hz), 7.83–7.74 (m, 4H), 7.56 (d, 1H, J = 9.06 Hz), 7.25 (s, 1H), 7.16–7.09 (m, 4H), 6.86 (t, 1H, J = 6.80 Hz). ESI Mass (*m/z*) 334 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{13}N_3F_2$) 334.1155; observed *m/z* (amu), 334.1164. IR (KBr, ν, cm^{-1}) 1250, 1148, 836, 754, 505.

N-(4-Bromobenzylidene)-[2-(4-bromophenyl)imidazo[1,2-a]pyridin-3-yl]amine. (Entry 4, Table 2), yellow solid, m.p. 184–186°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.79 (s, 1H), 8.49 (d, 1H, J = 6.30 Hz), 7.79 (t, 4H, J = 7.34 Hz), 7.62 (d, 2H, J = 8.40 Hz), 7.56 (d, 2H, J = 8.40 Hz), 7.54 (d, 1H, J = 8.40 Hz), 7.29 (t, 1H, J = 7.34 Hz), 6.95 (t, 1H, J = 7.34 Hz). ESI Mass (*m/z*) 456 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{13}N_3Br_2$), 453.9554; observed *m/z* (amu), 453.9549. IR (KBr, ν, cm^{-1}) 2927, 1344, 1226, 1063, 821, 747.

N-(2-Chloro-4-nitrobenzylidene)-[2-(2-chloro-4-nitrophenyl)imidazo[1,2-a]pyridin-3-yl]amine. (Entry 7, Table 2), pale yellow solid, m.p. 200–203°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 9.09 (d, 1H, J = 2.26 Hz), 8.70 (d, 1H, J = 6.80 Hz), 8.61 (d, 1H, J = 3.02 Hz), 8.52 (s, 1H), 8.29 (dd, 1H, J = 2.26 and 8.30 Hz), 8.18 (dd, 1H, J = 2.26 and 8.30 Hz), 7.68 (dd, 2H, J = 9.06 and 11.33 Hz), 7.54 (d, 1H, J = 9.06 Hz), 7.43 (t, 1H, J = 6.80 Hz), 7.10 (t, 1H, J = 6.80 Hz). ESI Mass (*m/z*) 455 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{11}N_5Cl_20_4$), 456.0266; observed *m/z* (amu), 456.0278. IR (KBr, ν, cm^{-1}) 3093, 1346, 1246, 1042, 834, 739.

N-2-(Naphthalene-2-yl)-N-(naphthalene-2-ylmethylene)imidazo[1,2-a]pyridine-3-amine. (Entry 9, Table 2), yellow solid, m.p. 182–185°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.96 (s, 1H), 8.52 (d, 1H, J = 6.80 Hz), 8.38 (s, 1H), 8.23 (d, 1H, J = 9.82 Hz), 7.89–7.78 (m, 8H), 7.61 (d, 1H, J = 9.06 Hz), 7.51–7.45 (m, 4H), 7.24 (t, 1H, J = 6.80 Hz), 6.89 (t, 1H, J = 5.30 Hz). ESI Mass (*m/z*) 398 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{28}H_{19}N_3$), 398.1657; observed *m/z* (amu), 398.1671. IR (KBr, ν, cm^{-1}) 3043, 2928, 1342, 1230, 823, 746.

N-2-(Thiophen-2-yl)-(thiophen-2-ylmethylene)imidazo[1,2-a] pyridin-3-amine. (Entry 10, Table 2), brown solid, m.p. 125–128°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 9.1 (s, 1H), 8.32 (d, 1H, J = 6.80 Hz), 7.54–7.50 (m, 3H), 7.35 (dd, 2H, J = 3.60 and 5.85 Hz), 7.19 (t, 1H, J = 7.93 Hz), 7.13–7.06 (m, 2H), 6.83 (t, 1H, J = 6.80 Hz). ^{13}C NMR ($CDCl_3$ + DMSO, 75 MHz, δ) 149.38, 142.57, 132.48, 131.32, 130.32, 128.06, 127.39, 126.34, 125.24, 124.16, 116.71, 112.76. ESI Mass (*m/z*) 310 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{16}H_{11}N_3S_2$), 310.0472; observed *m/z* (amu), 310.0484. IR (KBr, ν, cm^{-1}) 3068, 1209, 689.

N-(4-Methylbenzylidene)-2-p-tolylimidazo[1,2-a]pyridin-3-amine. (Entry 11, Table 2), yellow solid, m.p. 95–98°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 8.74 (s, 1H), 8.41 (d, 1H, J = 6.80 Hz), 7.68 (dd, 4H, J = 4.53 and 7.55 Hz), 7.55 (d, 1H, J = 9.06 Hz), 7.23–7.19 (m, 5H), 6.82 (t, 1H, J = 6.04 Hz), 2.41 (d, 6H, J = 4.53 Hz). ^{13}C NMR ($CDCl_3$, 75MHz, δ) 157.30, 142.64, 141.71, 137.43. 133.74, 133.50, 131.79, 129.34, 128.15, 128.00, 124.63, 123.63, 117.10, 112.03. ESI Mass (*m/z*) 326 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{22}H_{19}N_3$) 326.1657; observed *m/z* (amu), 326.1650. IR (KBr, ν, cm^{-1}) 3034, 2928, 1352, 821, 744.

N-(4-(Perchloropyridin-4-yloxy)benzylidene)-2-(4-(perchloropyridin-4-yloxy)phenyl)imidazo[1,2-a]pyridin-3-amine. (Entry 12, Table 2), yellow solid, m.p. 205–207°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.80 (s, 1H), 8.45 (d, 1H, J = 6.00 Hz), 7.88 (d, 6H, J = 7.55 Hz), 7.51 (d, 1H, J = 8.90 Hz), 7.25 (t, 1H, J = 8.12 Hz), 7.03 (d, 2H, J = 7.74 Hz), 6.97 (d, 1H, J = 8.30 Hz). ESI Mass (*m/z*) 755 (M^+) ($C_{30}H_{13}Cl_8N_5O_2$). IR (KBr, ν, cm^{-1}) 2922, 1600, 1500, 1388, 1344, 1196.

N-(4-(3,5,6-Trichloropyridin-2-yloxy)benzylidene)-2-(4-(3,5,6-tri chloropyridin-2-yloxy)phenyl)imidazo[1,2-a]pyridin-3-amine. (Entry 13, Table 2), yellow solid, m.p. 173–175°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.85 (s, 1H), 8.51 (d, 1H, J = 6.80 Hz), 8.04 (dd, 2H, J = 2.45 and 6.00 Hz), 7.93 (dd, 4H, J = 8.50 and 14.35 Hz), 7.79 (t, 1H, J = 3.40 Hz), 7.54 (d, 1H, J = 8.90 Hz), 7.25 (dd, 4H, J = 3.02 and 8.70 Hz), 6.94 (t, 1H, J = 6.04 Hz). ESI Mass (*m/z*) 688 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{30}H_{15}N_5O_2Cl_6$), 687.9435; observed *m/z* (amu), 687.9426. IR (KBr, ν, cm^{-1}) 2923, 1569, 1418, 1200.

5-Bromo-N-(4-chlorobenzylidene)-2-(4-chlorophenyl)imidazo [1,2-a]pyridin-3-amine. (Entry 14, Table 2), yellow solid, m.p. 200–203°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.69 (s, 1H), 8.48 (d, 1H, J = 1.51 Hz), 7.77 (d, 2H, J = 8.30 Hz), 7.71 (d, 2H, J = 8.30 Hz), 7.47–7.38 (m, 5H), 7.30 (d, 1H, J = 2.26 Hz). ESI Mass (*m/z*) 443 (M + 1) ($C_{20}H_{12}BrCl_2N_3$). IR (KBr, ν, cm^{-1}) 2924, 1402, 1087, 827, 796.

N-(3-Bromobenzylidene)-[2-(3-bromophenyl)-imidazo[1,2-a] pyridine-3-yl]amine. (Entry 5, Table 2), yellow solid, m.p. 88–90°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 8.73 (s, 1H), 8.48 (d, 1H, J = 6.80 Hz), 8.04 (d, 2H, J = 1.70 Hz), 7.72 (dd, 2H, J = 8.70 and 13.21 Hz), 7.56 (dd, 2H, J = 7.93 and 13.03 Hz), 7.48 (d, 1H, J = 8.12 Hz), 7.37–7.25 (m, 3H), 6.93 (t, 1H, J = 6.80 Hz). ESI Mass (*m/z*) 456 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{13}N_3Br_2$), 453.9554; observed *m/z* (amu), 453.9562. IR (KBr, ν, cm^{-1}) 2819, 1425, 1387, 1066, 778, 728, 673.

N-(3-Chlorobenzylidene)-[2-(3-chlorophenyl)-imidazo[1,2-a] pyridine-3-yl]amine. (Entry 3, Table 2), yellow solid, m.p. 93–95°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.77 (s, 1H), 8.51 (d, 1H, J = 6.80 Hz), 7.90 (d, 2H, J = 5.30 Hz), 7.72 (t, 2H, J = 8.70 Hz), 7.54 (d, 1H, J = 9.06 Hz), 7.44 (d, 2H, J = 4.53 Hz), 7.38–7.26 (m, 3H), 6.95 (t, 1H, J = 6.80 Hz). ESI Mass (*m/z*) 366 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{20}H_{13}N_3Cl_2$) 366.0564; observed *m/z* (amu), 366.0572. IR (KBr, ν, cm^{-1}): 2820, 2683, 1598, 1426, 1069, 779, 726, 674.

N-(2,4,6-Trimethoxybenzylidene)-[2-(2,4,6-trimethoxyphenyl)-imidazo[1,2-a]pyridine-3-yl]amine. (Entry 8, Table 2), yellow solid, m.p. 244–247°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.77 (d, 1H, J = 3.60 Hz), 8.39 (s, 1H), 7.53 (s,1H), 7.24 (s, 1H), 7.12 (dd, 4H, J = 3.00 and 6.23 Hz), 6.91 (s, 1H), 3.93 (t, 6H, J = 1.90 Hz), 3.87 (t, 3H, J = 2.07 Hz), 3.85–3.81 (m, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz, δ) 158.90, 153.66, 142.64, 141.36, 132.69, 129.61, 125.56, 123.09, 117.18, 112.76, 105.17, 77.47, 77.07, 76.63, 60.98, 56.29, 56.12, 21.06. ESI Mass (*m/z*) 478 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{26}H_{27}N_3O_6$), 478.1978; observed *m/z* (amu), 478.1990. IR (KBr, ν, cm^{-1}) 2936, 2836, 1603, 1464, 1330, 1124, 1031, 813, 729.

N-(4-Fluoro-2-trifluoromethyl benylidene)-[2-(4-fluoro-2-trifluoro methylphenyl)imidazo[1,2-a]pyridin-3-yl]amine. (Entry 6, Table 2), yellow solid, m.p. 105–108°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 8.55 (d, 1H, J = 6.80 Hz), 8.48 (t, 1H, J = 6.04 Hz), 8.30 (s,1H), 7.59 (t, 2H, J = 9.82 Hz), 7.50 (t, 1H, J = 5.30 Hz), 7.39–7.25 (m, 4H), 6.97 (t, 1H, J = 6.80 Hz). ESI Mass (*m/z*) 469 (M+). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition): Calculated *m/z* (amu); ($C_{22}H_{11}N_3F_8$), 470.0903; observed *m/z* (amu), 470.0919. IR (KBr, ν, cm^{-1}) 2852, 1501, 1428, 1321, 1172, 1125, 880, 838.

N-(4-Hydroxybenzylidene)-[2-(4-hydroxyphenyl)imidazo[1,2-a] pyridin-3-yl]amine. (Entry15, Table 2), pale yellow solid, m.p. 278–281°C. ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm) 9.14 (brs, 1H), 8.57 (brs, 1H), 8.03 (s, 1H), 7.73 (d, 1H, J = 6.80 Hz), 7.02 (d, 2H, J = 8.50 Hz), 6.94 (d, 2H, J = 8.30 Hz) 6.80 (d, 1H, J = 8.90 Hz), 6.53 (t, 1H, J = 6.80 Hz), 6.18 (dd, 5H, J = 8.30 and 10.95 Hz). ^{13}C NMR ($CDCl_3$ + DMSO, 75MHz, δ) 161.31, 158.17, 157.50, 142,11, 130.82, 129.57, 128.38, 128.23, 125.64, 125.14, 123.99, 117.08, 116.30, 115.90, 112.89. ESI Mass (*m/z*) 330 (M + 1) ($C_{20}H_{15}N_3O_2$). IR (KBr, ν, cm^{-1}) 3281, 2923, 2479, 1589, 1435, 1266.

Cleavage of benzylidine derivative. To *N*-(4-chlorobenzylidene)-[2-(4-chloro phenyl)imidazo[1,2-a]pyridin-3-yl]amine, TFA in DCM (1:9 mL) was added dropwise and the resulting reaction mixture was stirred at room temperature. The reaction was monitored by TLC. The cleavage was complete by the end of 15 h. The reaction mixture was then neutralized by saturated sodium bicarbonate and extracted with DCM. The organic layer was separated, dried over anhydrous sodium sulphate, filtered and solvent removed. The product 2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine was purified by column chromatography (EtOAc and hexane).

2-(4-Chlorophenyl)imidazo[1,2-a]pyridin-3-amine. Brown solid, m.p. 128–131°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm) 7.92

(dd, 3H, $J = 6.80$ and 8.30 Hz), 7.49 (d, 1H, $J = 9.06$ Hz), 7.36 (d, 2H, $J = 8.30$ Hz), 7.08 (t, 1H, $J = 7.55$ Hz), 6.77 (t, 1H, $J = 6.75$ Hz), 3.27 (brs, 2H, NH_2). ESI Mass (*m/z*) 244 (M + 1). HRMS (QSTAR XL Hybrid MS/MS system under ESI condition); Calculated *m/z* (amu); ($C_{13}H_{10}N_3Cl$), 244.0641; observed *m/z* (amu), 244.0646. IR (KBr, ν, cm^{-1}) 3352, 3292, 3058, 2923, 1487, 1088, 829, 742.

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