Received: 28 January 2019 | Revised: 30 August 2019 | Accepted: 30 August 2019

DOI: 10.1002/jhet.3746

WILEY

ARTICLE

Synthesis of imidazo[1, 2-a]pyridines via the silver acetate-catalyzed Groebke-Blackburn-Bienayme reaction with ethylene glycol as a biodegradable and sustainable solvent

Mustafa Hussain[1] | **Jianhui Liu**[1,2] | **Lu Fu**[2] | **Mehdi Hasan**[3]

[1]State key laboratory of fine chemical, Dalian University of Technology, Dalian, People's Republic of China

[2]School of Petroleum and Chemical Engineering, Dalian University of Technology, Panjin Campus, Panjin, Liaoning Province, People's Republic of China

[3]Department of Chemistry, University of Baltistan, Skardu, Pakistan

Correspondence
Jianhui Liu, School of Petroleum and Chemical Engineering, Dalian University of Technology, Panjin Campus, Panjin, Liaoning Province 124221, People's Republic of China.
Email: liujh@dlut.edu.cn

Funding information
National Key Research and Development Program of China, Grant/Award Number: 2016YFA0602900; National Natural Science Foundation of China

Abstract

An efficient, silver-based catalytic system has been designed for the synthesis of biologically important 3-aminoimidazo-fused heterocycles via the Groebke-Blackburn-Bienayme reaction, in which AgOAc was used as a catalyst and ethylene glycol as a solvent from isocyanides, various aryl aldehydes and an 2-amino heterocycle were also used. Good to excellent yields, high atomic economy and environmentally friendly conditions are the potential features of this one-pot process.

1 | INTRODUCTION

Over the past two decades, significant advances have been achieved using the multicomponent reaction (MCR) for the synthesis of pharmaceuticals and natural products.[1–3] The catalytic Groebke-Blackburn-Bienayme reaction (GBBR) is a synthetically useful MCR to establish the 3-aminoimidazo-fused heterocyclic scaffold by a one-pot formation of the C—N and C—C bonds with good atomic economy.[4–7] This reaction has been widely used for the synthesis of bioactive compounds with a broad spectrum of pharmacological and biological applications, such as antiviral, antibacterial, fungicidal, and anti-inflammatory properties.[8–12] Because of these properties, the imidazo[1,2-a]pyridine (IPY) scaffold was used as an important moiety in many commercially available drugs, such as zolpidem (insomnia treatment drug), alpidem (anxiolytic drug), olprinone (acute heart failure treatment), zolimidine (an anti-peptic ulcer drug), and the optically active drug GSK812397 (anti-HIV infection)[13–17] (Figure 1). In addition, some of the imidazo [1, 2-a] pyridines show fluorescence under the ultraviolet light, which interfered with the enzymatic assay; therefore, this moiety could also be used in fluorescent dyes.[18–20] Due to the wide medicinal utility of such a bicyclic structure, different methods of synthesis based on isocyanides, aldehydes, and 2-aminoazides have been developed in the presence of various catalysts such as ionic liquids ([bmim]Br), $ZnCl_2$, $ZrCl_4$, $RuCl_3$, KF, $BiCl_3$, $LaCl_3{\cdot}7H_2O$, Yb $(OTf)_3$, Sc $(OTf)_3$, Yb $(OTf)_3/Ag_2CO_3$, CuI, NH_4Cl, AcOH, $InCl_3$, and AgOTf.[21–35] Besides

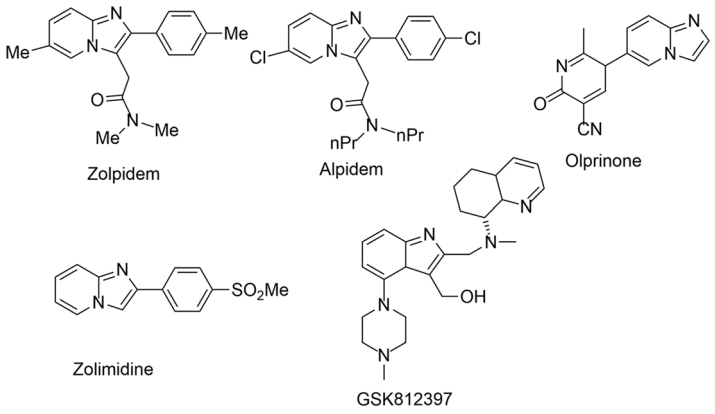


FIGURE 1 Selected biologically and medicinally active molecules of imidazo[1, 2-a]pyridines

GBBR, IPYs were also synthesized by different other methods in the absence of isonitrile. For examples, Pd $(OAc)_2$-catalyzed three-component reaction of 2-aminopyridine, 2-bromo-1-phenylethanone, and 1-bromo-4-nitrobenzene under microwave irradiation.[36] Zeng et al reported the efficient method for construction of IPY skeleton by intermolecular oxidative diamination of alkynes via copper (II) and iron (III) cocatalyzed C—N bond formation.[37] Chen et al reported a metal-free efficient synthesis of IPYs by a cyclization reaction of 2-aminopyridines and alkynoates.[38] CuBr catalyzed aerobic oxidative coupling of 2-aminopyridines with cinnamaldehydes, which help in the formation of 3-formyl-2-phenyl-imidazo[1,2-a]-pyridines was reported by Jaideep group in 2015.[39] These IPY scaffolds were synthesized by the reaction of 2-aminopyridines with β-keto esters by CBr_4 mediated oxidative C—N bond formation.[40] Molecular iodine used as an excellent catalyst for α, β-diamination of cyclohexanones with 2-aminopyrimidines by aerobic oxidative were also reported.[41]

However, many of these methods still suffer from several drawbacks and limitations such as low yields, long reaction time, and tiresome work-up procedures as well as the use of expensive and toxic metal catalysts. To overcome these limitations, different methods have been developed with environmental friendly solvents, especially in a deep eutectic solvent[42] and water without any catalysts[43] or with fluconazole functionalized magnetic nanoparticles as a catalyst.[44] They also have some disadvantages as difficulties in handling, the solubility of organic materials and lack of sustainability. Although various methods have been developed for the synthesis of this imidazopyridine scaffold, there has been no report date for the synthesis of these types of compounds by using silver acetate as the catalyst in ethylene glycol (EG) used as a promoter solvent. This new protocol has unique features due to green reaction conditions, nontoxic, economical catalyst, reduced pollution, and operational simplicity. In continuation of our research program on the development of MCRs with a greener method,[45] herein, we develop the green synthesis of 3-aminoimidazo-fused heterocycles via the GBBR by using 2-amino substituted heterocycles, aldehydes, and isocyanides with AgOAc catalyst having coordination capability with unsaturated bonds and activate isocyanide (—NC).[46–48] Furthermore, EG was used as the promoter, with a high boiling point, low viscosity, high specific energy, and easily miscible with many other organic solvents.[49–53]

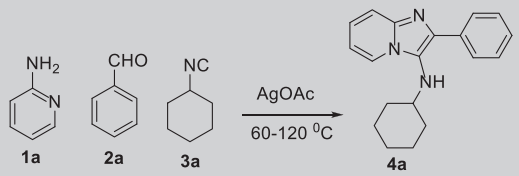
2 | RESULTS AND DISCUSSION

Initially, we performed this reaction starting from 2-aminopyridine, benzaldehyde, and cyclohexyl isocyanide with different solvents at different temperatures in the presence of silver catalysts (Table 1). We initially screened two different silver catalysts, AgOAc and Ag_2CO_3, in three different solvents, including toluene, DMSO, and EG (Table 1, entries 1-12).

We found that the yield of target **4** was obviously improved when a silver salt was used as a catalyst but compared with Ag_2CO_3, catalyst AgOAc was superior (Table 1, entries 1, 2, 3 vs entries 4, 5, 7, 8, 9, 10, and 11, respectively). Then, we observed that the reaction showed strong solvent dependence, that is, toluene and DMSO gave lower yields than EG (Table 1, entries 1-2 vs entry 3 and entries 4-5 vs entry 7, 8, 9, and 10).

The catalyst-free reaction in EG gave the desired product with a yield of 58%, which confirmed the power of the EG to promote this conversion (Table 1, entry 6). Next, we perceived that the reaction conditions also

TABLE 1 Optimization of reaction condition[a]



Entry	Catalyst	Solvent	Temp (°C)	Yield %[b]
1	Ag_2CO_3[c]	DMSO	90	50
2	Ag_2CO_3[c]	Toluene	90	55
3	Ag_2CO_3[c]	Ethylene glycol	90	70
4	AgOAc[c]	DMSO	90	65
5	AgOAc[c]	Toluene	90	65
6	—	Ethylene glycol	90	58
7	AgOAc[c]	Ethylene glycol	60	75
8	AgOAc[d]	Ethylene glycol	90	78
9	AgOAc[e]	Ethylene glycol	90	88
10	AgOAc[c]	Ethylene glycol[f]	90	90
11	AgOAc[c]	Ethylene glycol	90	90
12	AgOAc[c]	Ethylene glycol	120	92

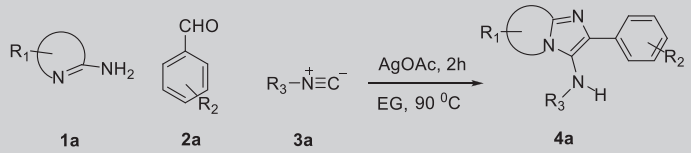
[a]Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), **3a** (1 mmol), and solvent (3.5 mL).
[b]Isolated yield.
[c]Catalyst (30 mol%).
[d]Catalyst (10 mol%).
[e]Catalyst (20 mol%).
[f]EG (1.5 mL).

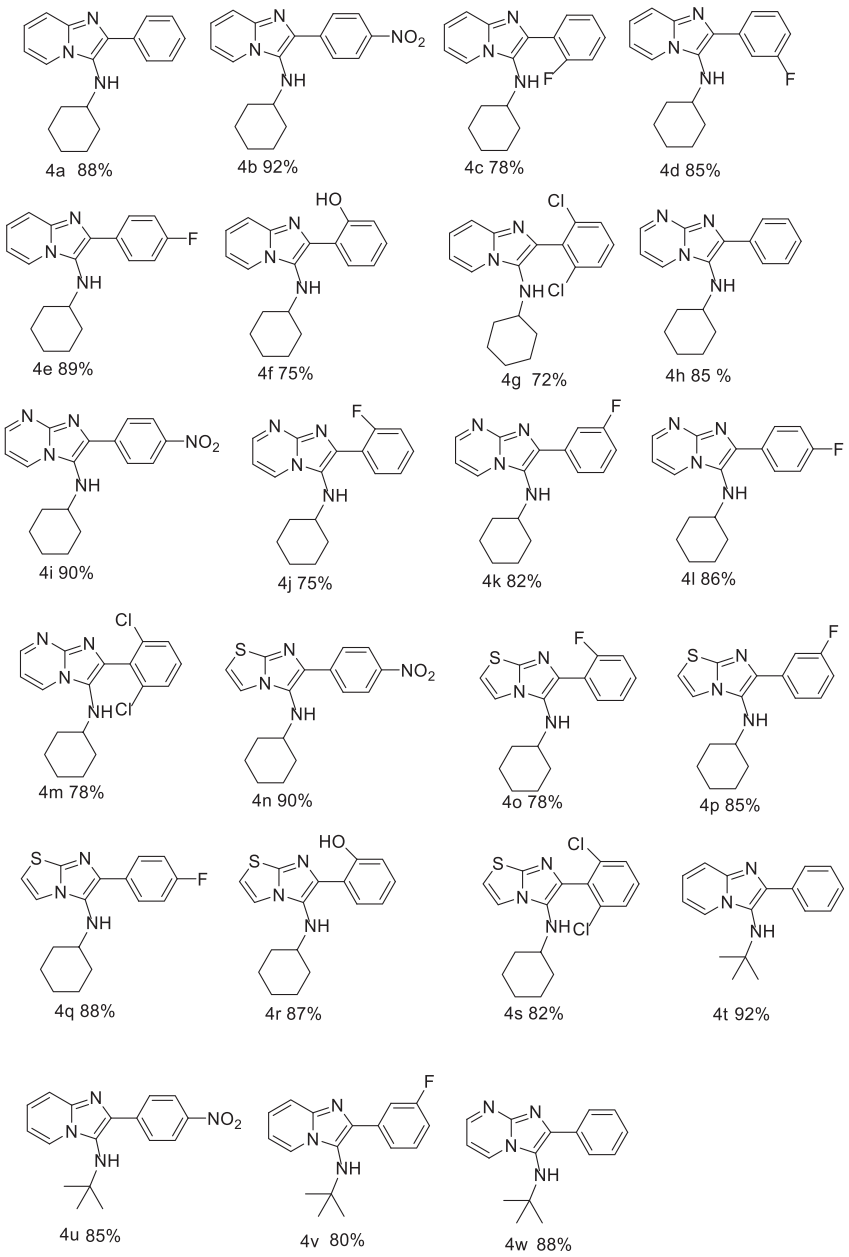
depend on the amount of catalyst. The incremental addition of catalyst from 10% to 30% in EG drove the yield to 90% (Table 1, entries 6-11). Moreover, the study of the temperature effect on yield of product exhibited that our product yield increased from moderate to high with increasing temperature from 60°C to 90°C (Table 1, entries 7-11). Interestingly, if we kept raising the temperature started from 90°C, it had slightly effect on the yield and rate of the reaction (Table 1, entry 12). The best result with a yield of 90% was obtained at an optimum temperature of 90°C, with AgOAc (30 mol%) as the catalyst and EG (1.5 mL) as the solvent. (Table 1, entry 10). However, when we increased the amount of EG solvent (1.5-3.5 mL) with AgOAc (30 mol%) as the catalyst, at an optimum temperature of 90°C, we get the same amount of yield 90% with out any difference. However, when we decreased the amount of catalyst AgOAc from 30 to 10 mol%, the yield of desire product were decreased (Table 1, entry 11 vs entries 8, 9, and 10).

According to the above results, we then investigated the various substrates to study the scope and limitation for the synthesis of imidazo [1,2-a] pyridines in our screened condition by using various aldehydes, amines, and isocyanates as shown in Table 2. Initially, we treated 2-aminopyridine with various aromatic aldehyde such as benzaldehyde, 4-nitrobenzaldehyde, 2-, 3-, 4-fluoro benzaldehyde, and 2-hydroxy benzaldehyde in combination with cyclohexyl isocyanide (Table 2, **4a**-**4g**). All the products were obtained in good to excellent yield which depended on the electronic environment of amines and aldehydes. An aromatic aldehyde with electron withdrawing group or without any inductive group such as —NO_2, —F, and —Cl gave excellent yield in short reaction time compared to electron-donating group such as OH as shown (Table 2, 92%-85%).

To study the vastness of this reaction, we used 2-aminothiazole and 2-aminopyrimidine with different aromatic aldehydes as shown in Table 2 (**4h**-**4s**). Good results were obtained with yields of 75% to 90%. To further expand the scope of the reaction, we used tertiary butyl isocyanide with different aromatic aldehydes and amines as shown in Table 2 (**4t**-**4w**). It is

TABLE 2 One-pot synthesis of imidazo [1, 2-a] pyridines 4[a,b]





[a]Reaction conditions: 1 (1.0 mmol), 2 (1.0 mmol), 3 (1.0 mmol), and catalyst (20 mol%)..
[b]Isolated yields.
[c]Reactions performed at 90°C in EG (1.5 mL) solvent.
[d]The reaction time was 2 h.

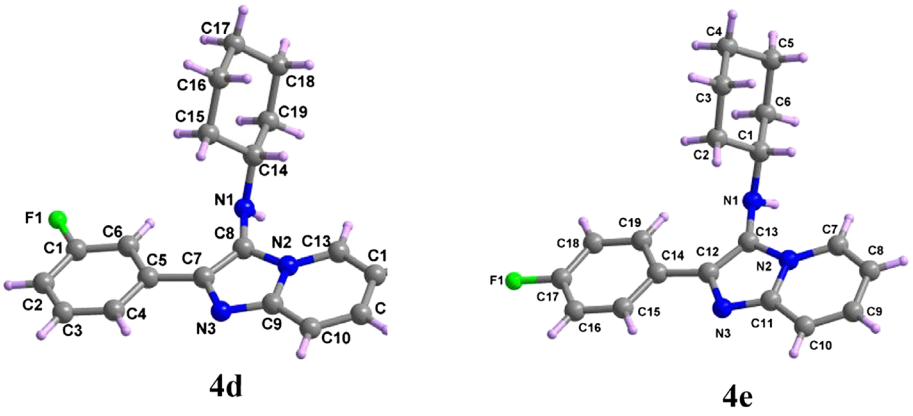
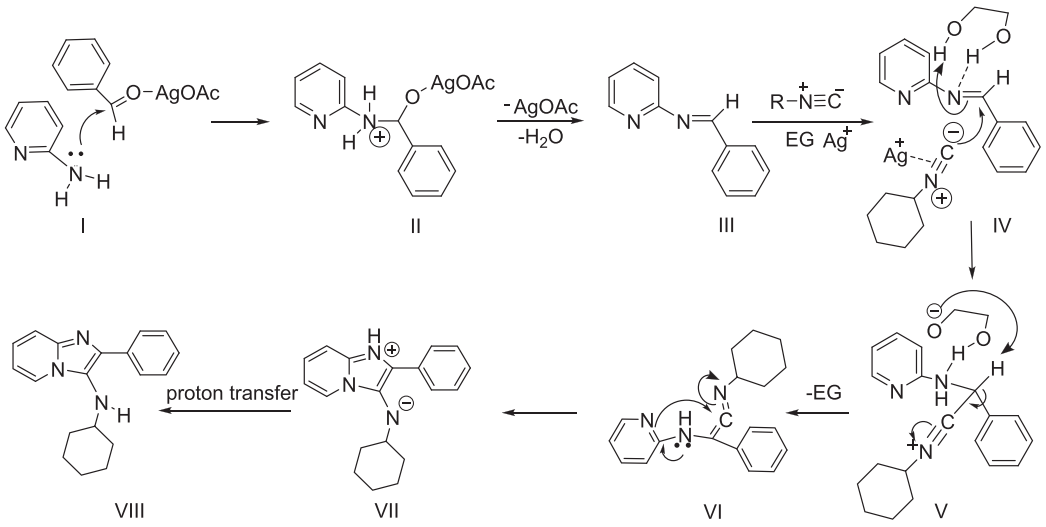


FIGURE 2 ORTEP plot of single crystals of compounds **4d** and **4e** [Color figure can be viewed at wileyonlinelibrary.com]



SCHEME 1 Possible reaction mechanism of AgOAc-catalyzed Groebke-Blackburn-Bienayme reaction (GBBR)

important to mention here that all aryl aldehydes with *ortho*-substituents gave a lower yield of products due to steric hindrance compared to those with *meta*- or *para*-substituents (**4c**, **4f**, **4g**, **4j**, **4m**, **4n**, **4v**, and **4p**).

The structure of the imidazo[1,2-a]pyridines (**4**) was unambiguously supported by the ORTEP plot structure analysis for **4d** and **4e**, as shown in Figure 2.[54,55] The ORTEP analysis showed that these products are monoclinic, with the P21/n space group at the 50% probability level for a thermal ellipsoid.

The possible reaction mechanism is proposed as shown in Scheme 1. Initially, the silver catalyst activated the benzaldehyde through the coordination of the carbonyl oxygen, which then condensed with the amine carbon to give imine intermediate **III**. Next, Ag(I) activates the isocyanide and promotes it to attack imine carbon and formed intermediate **V**, which was activated by amphoteric EG. In addition, EG also helped transfer a proton to form intermediate **VI**. Cyclization and proton transfer with the aid of EG furnished the final product **VIII** by eliminating EG.

3 | EXPERIMENTAL SECTION

3.1 | General information

Chemicals and solvents were purchased from commercial suppliers and used as received. ^{1}H NMR (400 and 500 MHz) and ^{13}C NMR (125 and 100 MHz) spectra were recorded with a Bruker Avance II 500 and 400 NMR spectrometer at 295 K in $CDCl_3$. Chemical shifts are reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: ^{1}H (chloroform δ 7.26) and ^{13}C (chloroform δ 77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), brs (broad singlet). High-resolution mass spectra (HRMS) were recorded with a quadrupole analyzer using an ESI source (Agilent technologies G6224A). TLC was performed on commercially prepared 100 to 400 mesh silica gel GF_{254} plates and visualization was affected at 254 nm.

3.2 | General procedure for the synthesis of *N*-cyclohexyl-2-phenylimidazo[1,2-a] pyridine-3-amine (4a-4s)

A mixture of benzaldehyde (1.5 mmol, 0.15 mL), 2-amino heterocycle (1 mmol, 0.10 mL), and cyclohexyl isocyanide (1.0 mmol, 0.10 mL) in EG (3 mL) in a round-bottom flask was stirred at reflux for 1 to 2 hours at 90°C, and the reaction was monitored by TLC (ethyl acetate/*n*-hexane, 4:6) (as shown in Table 1). After completion of the reaction, the reaction mixture was allowed to cool to room temperature, and the precipitates were filtered. The obtained crude products were purified by recrystallization with ethanol to give products **4** in high yield. Compounds **4c**, **4d**, **4g**, **4j**, **4k**, **4m**, **4o**, **4p**, **4r**, **4t**, **4u**, **4v**, and **4w** were purified by column chromatography using an ethyl acetate/*n*-hexane, 4:6 solvent system. Out of 23 compounds 8 (**4a**, **4b**, **4e**, **4f**, **4h**, **4n**, **4t**, and **4w**) are known and 15 (**4c**, **4d**, **4g**, **4i-4s**, **4u**, and **4v**) are unknown.

***N*-Cyclohexyl-2-phenylimidazo[1,2-a]pyridine-3-amine (4a):** Yield: 88%; greenish solid; mp 178°C to 180°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.0 Hz, 1H, ArH), 8.06 to 8.04 (m, 2H, ArH), 7.58 to 7.55 (m, 1H, ArH), 7.49 to 7.45 (m, 2H, ArH), 7.35 to 7.32 (m, 1H, ArH), 7.16 to 7.12 (m, 1H, ArH), 6.81 to 6.78 (m, 1H, ArH), 3.01 to 2.95 (m, 1H,NH), 1.84 to 1.81 (m, 2H), 1.71 to 1.69 (m, 2H), 1.59 to 1.57 (m, 1H), 1.24 to 1.12 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.60, 136.50, 134.40, 128.56, 127.34, 127.14, 125.02, 124.00, 122.76, 117.31, 111.64, 56.95, 34.17, 25.72, 24.82. HRMS (ESI): m/z calcd for $C_{19}H_{21}N_3$ $[M + H]^+$: 292.3980; found: 292.1812.

***N*-Cyclohexyl-2-(4-nitrophenyl)imidazo[1,2-a]pyridine-3-amine (4b):** Yield: 92%; yellow solid; mp 215°C to 218°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 to 8.30 (m, 4H, ArH), 8.09 (d, J = 8.0 Hz, 1H, ArH), 7.58 (d, J = 8.0 Hz, 1H, ArH), 7.24 to 7.21 (m, 1H, ArH), 6.88 to 6.84 (m, 1H, ArH), 3.12 (d, J = 4.0 Hz, 1H), 3.00 (d, J = 4.0 Hz, 1H), 1.87 to 1.84 (m, 2H), 1.75 to 1.73 (m, 2H), 1.63 to 1.61 (m, 1H), 1.28 to 1.17 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.51, 142.12, 141.16, 134.39, 127.27, 126.55, 124.93, 123.86, 122.70, 117.85, 112.29, 57.11, 34.30, 25.61, 24.83. HRMS (ESI): m/z calcd for $C_{19}H_{20}N_4O_2$ $[M + H]^+$: 337.3950; found: 337.1668.

***N*-Cyclohexyl-2-(2-fluorophenyl)imidazo[1,2-a] pyridine-3-amine (4c):** Yield**:** 78%; yellow solid; mp 170°C to 172°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 5.0 Hz, 1H, ArH), 7.94 to 7.90 (m, 1H, ArH), 7.57 (d, J = 10.0 Hz, 1H, ArH), 7.36 to 7.31 (m, 1H, ArH), 7.29 to 7.21 (m, 1H, ArH), 7.18 to 7.13 (m, 1H, ArH), 6.80 (t, J = 10.0 Hz, 1H, ArH), 3.45 (brs, 1H), 2.68 (brs, 1H), 1.73 to 1.71 (m, 2H), 1.60 (brs, 2H), 1.49 (brs, 1H), 1.29 to 1.21 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.52 (d, J = 243.750 Hz), 142.04, 131.73 (d, J = 2.5 Hz), 131.59 (d, J = 5.0 Hz), 129.18 (d, J = 8.0 Hz), 126.97, 124.69 (d, J = 3.75 Hz), 123.83, 122.97, 122.51 (d, J = 13.75 Hz), 115.63 (d, J = 21.25 Hz), 111.57, 56.68, 41.99, 34.04, 25.66, 24.83. HRMS (ESI): m/z calcd for $C_{19}H_{20}N_3F$ $[M + H]^+$: 310.3884; found: 310.1720.

***N*-Cyclohexyl-2-(3-fluorophenyl)imidazo[1,2-a] pyridine-3-amine (4d)**: Yield: 85%; yellow crystals; mp 208°C to 209°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 to 8.09 (m, 1H, ArH), 7.86 to 7.83 (m, 2H, ArH), 7.57 to 7.54 (m, 1H, ArH), 7.45 to 7.39 (m, 1H, ArH), 7.18 to 7.14 (m, 1H, ArH), 7.05 to 7.00 (m, 1H, ArH), 6.81 (t, J = 10.0 Hz, 1H, ArH), 3.08 to 3.07 (brs, 1H), 3.00 to 2.99 (brs, 1H) 1.91 to 1.83 (m, 2H), 1.73 to 1.71 (brs, 2H), 1.61 to 1.60 (brs, 1H) 1.22 to 1.17 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.1 (d, J = 242.45 Hz), 141.61, 136.78 (d, J = 8.75 Hz), 135.46, 129.93 (d, J = 7.5 Hz), 125.20, 124.22, 122.72, 122.54 (d, J = 3.75 Hz), 117.53, 114.04 (d, J = 20.0 Hz), 113.87 (d, J = 22.5 Hz), 111.78, 56.96, 34.21, 25.69, 24.84. HRMS (ESI): m/z calcd for $C_{19}H_{20}N_3F$ $[M + H]^+$: 310.3884; found: 310.1717.

***N*-Cyclohexyl-2-(4-fluorophenyl)imidazo[1,2-a] pyridine-3-amine (4e)**: Yield: 89%; light yellow crystals; mp 177°C to 180°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, J = 5.0 Hz, 1H, ArH), 8.04 to 8.01 (m, 2H, ArH), 7.59 (d, J = 10.0 Hz, 1H, ArH), 7.21 to 7.19 (m, 1H, ArH), 7.16 to 7.12 (m, 2H, ArH), 2.95 to 2.91 (m, 1H), 1.81 to 1.78 (m, 2H), 1.70 to 1.68 (brs, 3H), 1.58 (brs, 1H) 1.29 to 1.27 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.31 (d, J = 245.0 Hz), 141.20, 135.25, 129.90, 128.88 (d, J = 7.5 Hz), 124.73, 124.61, 122.83, 116.97, 115.49 (d, J = 21.25 Hz), 112.09, 56.84, 34.18, 25.69, 24.80. HRMS

(ESI): m/z calcd for $C_{19}H_{20}N_3F$ $[M + H]^+$: 310.3884; found: 310.1718.

***N*-Cyclohexyl-2-(2-hydroxyphenyl)imidazo[1,2-a] pyridine-3-amine (4f)**: Yield: 75%; greenish solid; mp 155°C to 158°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (d, J = 5.0 Hz, 1H, ArH), 8.00 (d, J = 10.0 Hz, 1H, ArH), 7.51 (d, J = 8.0 Hz, 1H, ArH), 7.26 to 7.19 (m, 2H, ArH), 7.02 (d, J = 10.0 Hz, 1H, ArH), 6.88 (m, 2H, ArH), 3.02 (brs, 1H), 1.84 to 1.81 (m, 2H), 1.72 to 1.70 (m, 2H), 1.61 to 1.59 (m, 2H) 1.20 to 1.12 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 157.51, 148.99, 139.39, 135.74, 129.16, 126.38, 124.84, 123.49, 122.55, 118.70, 117.71, 116.45, 112.38, 56.97, 34.06, 25.71, 24.85. HRMS (ESI): m/z calcd for $C_{19}H_{21}N_3O$ $[M + H]^+$: 308.3970; found: 308.1760.

***N*-Cyclohexyl-2-(2,6-dichlorophenyl)imid-azo[1,2-a]pyridine-3-amine (4g)**: Yield: 72%; yellow crystal; mp 144°C to 148°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 5.0 Hz, 1H, ArH), 7.65 (d, J = 10.0 Hz, 1H, ArH), 7.44 to 7.42 (m, 2H, ArH), 7.32 to 7.28 (m, 1H, ArH), 7.21 (t, J = 10.0 Hz, 1H, ArH), 2.93 (d, J = 10.0 Hz, 1H), 2.76 to 2.73 (m, 1H), 1.77 to 1.74 (m, 2H), 1.61 to 1.59 (m, 2H), 1.51 to 149 (m, 1H), 1.11 to 1.05 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.43, 136.38, 132.53, 130.10, 128.12, 126.86, 124.11, 122.98, 117.71, 111.91, 56.58, 33.83, 25.66, 24.60. HRMS (ESI): m/z calcd for $C_{19}H_{19}Cl_2N_3$ $[M + H]^+$: 360.3970; found: 360.1035.

***N*-Cyclohexyl-2-(phenyl)imidazo[1,2-a]pyrimidin-3-amine (4h)**: Yield: 85%; yellowish powder; mp 175°C to 176°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (d, J = 5.0 Hz, 1H, ArH), 8.43 (dd, J = 10.0 Hz, 4.0 Hz, 1H, ArH), 8.11 (d, J = 5.0 Hz, 2H, ArH), 7.48 to 7.45 (m, 2H, ArH), 7.36 to 7.33 (m, 1H, ArH) 6.85 to 6.82 (m,1H, ArH), 3.16 (brs, 1H), 2.99 (brs, 1H), 1.82 to 1.80 (m, 2H), 1.71 to 1.69 (m, 3H), 1.29 to 1.16 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.20, 144.47, 137.80, 133.69, 130.40, 128.49, 127.75, 127.33, 123.37, 108.03, 57.02, 34.08, 25.60, 24.71. HRMS (ESI): m/z calcd for $C_{18}H_{20}N_4$ $[M + H]^+$: 293.3860; found: 293.1767.

***N*-Cyclohexyl-2-(4-nitrophenyl)imidazo[1,2-a] pyrimidin-3-amine (4i)**: Yield: 90%; light yellowish solid; mp 275°C to 278°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 to 8.48 (m, 1H, ArH), 8.34 to 8.32 (2H, ArH), 8.28 to 8.25 (m, 2H, ArH), 8.01 (d, J = 10.0 Hz 1H, ArH), 6.85 to 6.82 (m, 1H, ArH), 3.12 (d, J = 5.0 Hz, 1H), 3.09 (d, J = 5.0 Hz, 1H), 2.91 (d, J = 4.0 Hz, 1H) 1.78 to 1.75 (m, 2H), 1.67 to 1.65 (m, 2H), 1.56 (brs, 1H), 1.20 to 1.11 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 158.84, 150.42, 146.92, 146.42, 140.39, 130.74, 130.45, 127.72, 123.92, 108.60, 57.33, 34.32, 25.54, 24.76. HRMS (ESI): m/z calcd for $C_{18}H_{19}N_5O_2$ $[M + H]^+$: 337.3950; found: 337.1668.

***N*-Cyclohexyl-2-(2-fluorophenyl)imidazo [1,2-a] pyrimidin-3-amine (4j)**: Yield: 75%; green solid; mp 156°C to 160°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (s, 1H, ArH), 8.45 (d, J = 5.0 Hz, 1H, ArH), 8.06 to 8.03 (m, 2H, ArH), 7.39 to 7.28 (m, 2H, ArH), 7.19 to 7.15 (t, J = 10.0 Hz, 1H, ArH), 6.87 (dd, J = 10.0 Hz, 5.0 Hz, 1H, ArH), 2.68 (brs, 1H), 1.72 to 1.70 (m, 2H), 1.61 (s, 2H), 1.51 (brs, 1H), 1.26 (s, 1H), 1.10 to 1.08 (m, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.48 (d, J = 243.75 Hz), 149.27, 144.97, 133.40 (d, J = 2.5 Hz), 132.06 (d, J = 3.75 Hz), 130.55, 129.73 (d, J = 8.75 Hz), 125.40, 124.84 (d, J = 2.5 Hz), 121.57 (d, J = 21.25 Hz), 115.58 (d, J = 22.50 Hz) 108.10, 57.01, 33.98, 25.57, 24.74. HRMS (ESI): m/z calcd for $C_{18}H_{19}N_4F$ $[M + H]^+$: 311.374; found: 311.1672.

***N*-Cyclohexyl-2-(3-fluorophenyl) imidazo[1,2-a] pyrimidin-3-amine (4k)**: Yield: 82%; yellow solid; mp 174°C to 178°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 to 8.42 (m, 1H, ArH), 8.34 (d, J = 5.0 Hz, 1H, ArH), 7.84 to 7.80 (m, 2H, ArH), 7.36 to 7.32 (m, 1H, ArH), 6.98 to 6.95 (m, 1H, ArH), 6.79 to 6.77 (m, 1H, ArH), 3.13 (brs, 1H), 3.05 (s, 1H), 2.92 (brs, 1H), 1.76 to 1.74 (m, 2H), 1.65 to 1.63 (m, 2H), 1.54 (brs, 1H), 1.23 to 1.10 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 163.08 (d, J = 243.75 Hz), 149.60, 144.58, 137.01, 136.04 (d, J = 9.0 Hz), 130.39, 130.02 (d, J = 8.0 Hz), 123.57, 122.85 (d, J = 3.0 Hz), 114. 64 (d, J = 21.0 Hz), 114.22 (d, J = 23.0 Hz), 108.20, 57.15, 34.20, 25.61, 24.76. HRMS (ESI): m/z calcd for $C_{18}H_{19}N_4F$ $[M + H]^+$: 311.3764; found: 311.1671.

***N*-Cyclohexyl-2-(4-fluorophenyl) imidazo[1,2-a] pyrimidin-3-amine (4l)**: Yield: 86%; yellow crystals; mp 169°C to 170°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (brs, 1H, ArH), 8.33 (d, J = 10.0 Hz), 8.05 to 8.03 (m, 1H, ArH), 7.09 to 7.06 (m, 1H, ArH), 6.78 to 6.76 (m, 1H, ArH), 3.02 (brs, 1H,), 2.89 (s, 1H), 1.74 to 1.72 (m, 2H), 1.64 to 1.62 (m, 2H), 1.53 (brs, 1H), 1.19 to 1.09 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.52 (d, J = 246.25 Hz), 149.40, 144.52, 137.38, 130.35, 129.81 (d, J = 2.5 Hz), 129.16 (d, J = 8.75 Hz), 122.85, 115. 52 (d, J = 21.25 Hz), 108.17, 57.03, 34.18, 25.62, 24.73. HRMS (ESI): m/z calcd for $C_{18}H_{19}N_4F$ $[M + H]^+$: 311.3764; found: 311.1667.

***N*-Cyclohexyl-2-(2,6-dichlorophenyl)imid-azo[1,2-a]pyrimidin-3-amine (4m)**: Yield: 78%; yellow crystals; mp 148°C to 150°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 to 8.47 (m, 1H, ArH), 8.40 to 8.38 (m, 1H, ArH), 7.38 to 7.36 (m, 2H, ArH), 7.26 to 7.23 (m, 1H, ArH), 6.83 (dd, J = 10.0 Hz, 5.0 Hz, 1H, ArH), 2.66 (brs, 1H), 2.56 (brs, 1H), 1.67 to 1.65 (m, 2H), 1.54 to 1.52 (m, 2H), 1.45 to 141 (m, 1H), 1.07 to 0.96 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 149.32, 144.46, 136.27, 134.62, 132.21, 130.58, 130.28, 128.13, 125.35, 108.20, 56.84, 33.78, 25.57, 24.54.

HRMS (ESI): m/z calcd for $C_{18}H_{18}N_4Cl_2$ $[M + H]^+$: 361.2700; found: 361.0985.

***N*-Cyclohexyl-6-(4-nitrophenyl)imidazo[2,1-b] thiazol-5-amine (4n)**: Yield: 90%; yellow crystals; mp 164°C to 168°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 to 8.19 (m, 4H, ArH), 7.35 (d, J = 4.0 Hz 1H, ArH), 6.84 (d, J = 4.0 Hz, 1H, ArH), 2.98 (brs, 2H), 1.88 (s, 2H), 1.74 (s, 2H), 1.63 to 1.61 (m, 1H), 1.26 to 1.24 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.07, 145.87, 141.36, 135.29, 129.05, 126.12, 123.93, 116.88, 113.10, 57.57, 34.27, 25.61, 24.79. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_4O_2S$ $[M + H]^+$: 343.4170; found: 343.1231.

***N*-Cyclohexyl-6-(2-fluorophenyl)imidazo[2,1-b] thiazol-5-amine (4o)**: Yield: 78%; yellow crystals; mp 155°C to 160°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 to 7.73 (m, 1H, ArH), 7.30 (d, J = 8.0 Hz 1H, ArH), 7.22 to 7.16 (m, 1H, ArH), 7.08 to 7.03 (m, 1H, ArH), 6.70 (d, J = 4.0 Hz,1H, ArH), 2.66 (brs, 1H), 1.70 to 1.67 (m, 3H), 1.51 to 1.55 (m, 2H), 1.46 (brs, 1H), 1.09 to 0.97 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 157.99 (d, J = 242.50 Hz), 144.04, 130.64 (d, J = 2.5 Hz), 130.04 (d, J = 3.75 Hz), 127.54 (d, J = 8.75 Hz), 123.56 (d, J = 2.5 Hz), 121.56 (d, J = 15.0 Hz), 116.19, 114.60 (d, J = 22.5 Hz), 110.79, 56.48, 32.91, 24.64, 23.79. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_3FS$ $[M + H]^+$: 316.4170, found: 316.1273.

***N*-Cyclohexyl-6-(3-fluorophenyl)imidazo[2,1-b] thiazol-5-amine (4p)**: Yield: 85%; yellow crystals; mp 132°C to 138°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 to 7.73 (m, 2H, ArH), 7.34 to 7.32 (m, 2H, ArH), 6.96 to 6.91 (m,1H, ArH), 6.77 to 6.76 (m, 1H), 2.97 (brs, 2H), 1.87 (s, 2H), 1.73 to 1.72 (m,2H), 1.62 to 1.59 (m, 1H), 1.26 to 1.21 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.11 (d, J = 243.0 Hz), 145.15, 137.09, 137.00, 129.84 (d, J = 8.0 Hz), 127.51, 121.52(d, J = 3.0 Hz), 117.01, 113.27 (d, J = 22.0 Hz), 112. 88 (d, J = 23.0 Hz), 112.11, 57.47, 34.18, 25.69, 24.79. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_3FS$ $[M + H]^+$: 316.4104; found: 316.1277.

***N*-Cyclohexyl-6-(4-fluorophenyl)imidazo[2,1-b] thiazol-5-amine (4q)**: Yield: 88%; yellow crystals; mp 122°C to 128°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 to 7.92 (m, 2H, ArH), 7.33 to 7.32 (m, 1H, ArH), 7.11 to 7.09 (m,2H, ArH), 6.76 to 6.75 (m,1H, ArH), 2.94 (brs, 1H), 1.86 (brs, 2H), 1.71 (brs,2H), 1.61 to 1.59 (m, 1H), 1.24 to 1.17 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.71 (d, J = 244.0 Hz), 145.03, 136.82, 130.95 (d, J = 3.0 Hz), 127.81 (d, J = 8.0 Hz), 126.71, 117.05, 115.30 (d, J = 21.0 Hz), 111.80 (d, J = 23.0 Hz), 57.44, 34.16, 25.71, 24.77. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_3FS$ $[M + H]^+$: 316.4104; found: 316.1284.

***N*-Cyclohexyl-6-(2-hydroxyphenyl)imidazo[2,1-b] thiazol-5-amine (4r)**: Yield: 87%; yellow crystals; mp 151°C to 153°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 to 7.96 (m, 1H, ArH), 7.36 to 7.35 (m, 1H, ArH), 7.26 to 7.24 (m,1H, ArH) 7.21 to 7.17 (m,1H, ArH), 7.01 to 6.99 (m,1H, ArH), 6.92 to 6.88 (m, 2H, ArH), 6.80 (d, J = 8.0 Hz 1H), 3.48 to 3.41 (m, 1H), 2.99 to 2.94(m, 1H), 1.87 to 185 (m, 2H), 1.74 to 1.72 (m, 2H), 1.62 to 1.60 (m, 1H), 1.29 to 1.15 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.57, 143.68, 136.90, 130.68, 128.43, 126.32, 125.21, 119.07, 117.59, 117.07, 112.42, 57.60, 33.73, 25.60, 24.75. HRMS (ESI): m/z calcd for $C_{17}H_{19}N_3SO$ $[M + H]^+$: 314.3990; found: 314.0600.

***N*-Cyclohexyl-6-(2,6-dichlorophenyl)imidazo[2,1-b] thiazol-5-amine(4s):** Yield: 82%; yellow crystals; mp 143°C to 145°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 to 7.31 (m, 3H, ArH), 7.19 (s, 1H, ArH), 6.72 (d, J = 5.0 Hz), 2.79 (brs, 1H), 2.68 to 2.64 (m, 1H), 1.70 to 1.67 (m, 2H,), 1.54 to 1.52 (m, 2H), 1.45 to 1.43 (m, 1H), 1.10 to 0.90 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.49, 136.56, 132.67 (d, J = 8.0 Hz), 129.79, 129.08, 128.05, 117.00, 111.87, 57.07, 33.73, 25.64, 24.59. HRMS (ESI): m/z calcd for $C_{17}H_{17}N_3Cl_2S$ $[M + H]^+$: 366.4170; found: 366.0600.

***N*-(*tert*-Butyl)-2-phenylimidazo[1,2-a]pyridine-3-amine (4t):** Yield: 92%; Greenish crystal; mp 160°C to 165°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.0 Hz, 1H, ArH), 8.06 to 8.04 (m, 1H, ArH), 7.84 to 7.82 (m, 2H, ArH), 7.60 to 7.57 (m, 1H, ArH), 7.38 to 7.34 (m, 3H, ArH), 7.27 to 7.23 (m, 1H, NH), 7.12 to 7.08 (m, 1H, ArH), 6.75 to 6.71 (m, 1H, ArH), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.83, 139.03, 134.74, 124.50, 123.51, 117.09, 111.61, 56.44, 30.26. HRMS (ESI): m/z calcd for $C_{17}H_{19}N_3$ $[M + H]^+$: 266.3600; found: 266.1661.

***N*-(*tert*-Butyl)-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridine-3-amine (4u):** Yield: 85%; yellow solid; mp 155°C to 160°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 to 8.18, (m, 4H, ArH), 8.12 (d, J = 8.0 Hz, 1H, ArH), 7.49 to 7.48 (m, 1H, ArH), 7.14 to 7.13 (m, 1H, ArH), 6.77 to 6.75 (m, 1H, ArH), 2.95 (brs, 1H, NH), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.01, 146.71, 142.58, 142.00, 137.21, 128.43, 124.96, 123.60, 123.38, 117.80, 112.01, 56.84, 30.51. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_4O_2$[M + H]$^+$: 311.3570; found: 311.1508.

***N*-(*tert*-Butyl)-2-(3-fluorophenyl)imidazo[1,2-a] pyridine-3-amine (4v):** Yield: 80%; yellow crystal; mp 210°C to 215°C.^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14, (d, J = 10.0 Hz, 1H, ArH), 7.67 to 7.63 (m, 2H, ArH), 7.48 to 7.46 (m, 1H, ArH), 7.33 to 7.29 (m, 1H, ArH), 7.09 to 7.06 (m, 1H, ArH), 6.95 to 6.92 (m, 1H, ArH), 6.73 to 6.70 (m, 1H, ArH), 2.94 (brs, 1H, NH), 1.00 (s, 9H).^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.88 (d, J = 243.75 Hz), 142.11, 138.38, 137.55, (d, J = 8.75 Hz), 149.01, 129.69 (d, J = 8.75 Hz), 128.43, 124.31, 123.72 (d, J = 3.75 Hz), 123.44, 117.49, 114.96 (d, J = 22.00 Hz), 114.16 (d,

J = 21.05 Hz), 111.52, 56.53, 30.36. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_3F$ $[M + H]^+$: 284.3504; found: 284.1563.

***N*-(*tert*-Butyl)-2-phenylimidazo[1,2-a] pyrimidin-3-amine (4w)**: Yield: 88%; green solid; mp 220°C to 235°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 to 7.90 (m, 2H, ArH), 7.39 to 7.34 (m, 2H, ArH), 7.29 to 7.27 (m, 1H, ArH), 6.78 to 6.76 (m, 2H, ArH), 3.11 (brs, 1H, NH), 0.98 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.27, 149.51, 144.96, 140.84, 134.30, 131.15, 128.37, 127.93, 121.97, 107.92, 56.64, 30.28. HRMS (ESI): m/z calcd for $C_{16}H_{18}N_4$ $[M + H]^+$: 267.3480; found: 266.1600.

4 | CONCLUSION

In conclusion, we have shown that imidazo[1, 2-a]pyridines can be accessed in a one-pot three-component manner starting from isocyanates and different aromatic aldehydes and amines via an AgOAc-catalyzed GBBR with EG as the solvent. The relatively cheap silver catalyst, environmentally friendly conditions, simple work-up procedures, and generation of no side products constituted the unique features for the new protocol.

ACKNOWLEDGMENTS

This work was supported by the National Key Research and Development Program of China (2016YFA0602900) and the National Natural Science Foundation of China.

ORCID

Mustafa Hussain https://orcid.org/0000-0002-1881-4905
Jianhui Liu https://orcid.org/0000-0002-3833-8109

REFERENCES

[1] V. Nair, *Angew. Chem. Int. Ed.* **2005**, *44*, 5769.
[2] S. K. Guchhait, C. Madaan, B. S. Thakkar, *Synthesis* **2009**, *19*, 3293.
[3] C. De Graaff, E. Ruijter, R. V. A. Orru, *Chem. Soc. Rev.* **2012**, *4*, 3969.
[4] H. Bienayme, K. Bouzid, *Angew. Chem. Int. Ed.* **1998**, *37*, 2234.
[5] K. Groebke, L. Weber, F. Mehlin, *Synlett* **1998**, *6*, 661.
[6] C. Blackburn, B. Guan, P. Fleming, K. Shiosaki, S. Tsai, *Tetrahedron Lett.* **1998**, *39*, 3635.
[7] S. Régnier, W. S. Bechara, A. B. Charette, *J. Org. Chem.* **2016**, *81*, 10348.
[8] C. Enguehard-gueiffier, A. Gueiffier, *Mini-Rev. Med. Chem.* **2007**, *33*, 888.
[9] M. L. Bode, D. Gravestock, S. S. Moleele, C. W. Van Der Westhuyzen, S. C. Pelly, P. A. Steenkamp, H. C. Hoppe, T. Khan, L. A. Nkabinde, *Bioorg. Med. Chem.* **2011**, *19*, 4227.
[10] S. Rostamnia, M. Jafari, *Appl. Organometal. Chem.* **2016**, *3*, 2.
[11] D. B. Salunke, E. Yoo, N. M. Shukla, R. Balakrishna, S. S. Malladi, K. J. Sera, V. W. Day, X. Wang, S. A. David, *J. Med. Chem.* **2012**, *55*, 8137.
[12] G. Martinez-Ariza, J. Nunez-Rios, Y. S. Lee, C. Hulme, *Tetrahedron Lett.* **2015**, *56*, 1038.
[13] A. K. Bagdi, S. Santra, K. Monir, A. Hajra, *Chem. Commun.* **2015**, *51*, 155.
[14] K. Mizushige, T. Ueda, K. Yukiiri, H. Suzuki, *Olprinone: Cardiovas. Drug Rev.* **2002**, *20*, 163.
[15] B. Du, A. Shan, X. Zhong, Y. Zhang, D. Chen, K. Cai, *Am. J. Med. Sci.* **2014**, *347*, 178.
[16] S. Z. Langer, S. Arbilla, S. Tan, K. G. Lloyd, P. George, J. Allen, A. E. Wick, *Pharmacopsychiatry* **1990**, *23*, 103.
[17] A. Maleki, S. Javanshir, M. Naimabadi, *RSC Adv.* **2014**, *4*, 30229.
[18] O. N. Burchak, L. Mugherli, M. Ostuni, J. J. Lacap, M. Y. Balakirev, *J. Am. Chem. Soc.* **2011**, *133*, 10058.
[19] D. Firmansyah, A. I. Ciuciu, V. Hugues, M. Blanchard-desce, L. Flamigni, D. T. Gryko, *Chem. – Asian J.* **2013**, 1279.
[20] N. Nagarajan, G. Velmurugan, A. Prakash, N. Shakti, *Chem. Asian J.* **2014**, *9*, 294.
[21] A. Shaabani, E. Soleimani, A. Maleki, *Tetrahedron Lett.* **2006**, *47*, 3031.
[22] A. L. Rousseau, P. Matlaba, C. Parkinson, *J. Tetrahedron Lett.* **2007**, *48*, 4079.
[23] S. K. Guchhait, C. Madaan, *Tetrahedron Lett.* **2011**, *52*, 56.
[24] S. K. Guchhait, V. Chaudhary, C. Madaan, *Org. Biomol. Chem.* **2012**, *10*, 9271.
[25] S. Rostamnia, A. Hassankhani, *RSC Adv.* **2013**, *3*, 18626.
[26] A. Shahrisa, S. Esmati, *Synlett* **2013**, *24*, 595.
[27] A. H. Shinde, M. Srilaxmi, B. Satpathi, D. S. Sharada, *Tetrahedron Lett.* **2014**, *55*, 5915.
[28] J. Ren, M. Yang, H. Liu, D. Cao, D. Chen, J. Li, L. Tang, J. He, Y. L. Chen, M. Geng, B. Xiong, J. Shen, *Org. Biomol. Chem.* **2015**, *13*, 1531.
[29] B. Maiti, K. Chanda, M. Selvaraju, C. C. Tseng, C. M. Sun, *ACS Comb. Sci.* **2013**, *15*, 291.
[30] H. Sun, H. Zhou, O. Khorev, R. Jiang, T. Yu, X. Wang, Y. Du, Y. Ma, T. Meng, J. Shen, *J. Org. Chem.* **2012**, *77*, 10745.
[31] E. Allahabadi, S. Ebrahimi, M. Soheilizad, M. Khoshneviszadeh, M. Mahdavi, *Tetrahedron Lett.* **2017**, *58*, 121.
[32] M. Kurva, S. G. Pharande, A. Quezada-Soto, R. Gámez-Montaño, *Tetrahedron Lett.* **2018**, *59*, 1596.
[33] S. G. Balwe, Y. T. Jeong, *Org. Biomol. Chem.* **2018**, *16*, 1287.
[34] K. V. Sashidhara, L. R. Singh, D. Choudhary, A. Arun, S. Gupta, S. Adhikary, G. R. Palnati, R. Konwar, R. Trivedi, *RSC Adv.* **2016**, 80037.
[35] K. G. Kishore, U. M. V. Basavanag, A. Islas-jácome, R. Gámez-montaño, *Tetrahedron Lett.* **2015**, *56*, 155.
[36] Y. Wang, B. Frett, H. Li, *Org. Lett.* **2014**, *16*, 3016.
[37] J. Zeng, Y. J. Tan, M. L. Leow, X. Liu, *Org. Lett.* **2012**, *14*, 2286.
[38] Q. Wang, G. Luo, M. Ye, Z. Chen, Y. Wen, *RSC Adv.* **2016**, *6*(89), 8646.
[39] J. B. Bharate, S. Abbat, P. V. Bharatam, R. A. Vishwakarma, S. B. Bharate, *Org. Biomol. Chem.* **2015**, *13*, 7790.

[40] C. Huo, J. Tang, H. Xie, Y. Wang, J. Dong, *Org. Lett.* **2016**, *18*, 1016.
[41] T. B. Nguyen, L. Ermolenko, P. Retailleau, A. Al-mourabit, *J. Org. Chem.* **2016**, *18*, 2177.
[42] N. Azizi, S. Dezfooli, *Environ. Chem. Lett.* **2016**, *14*, 201.
[43] M. Adib, M. Mahdavi, M. A. Noghani, P. Mirzaei, *Tetrahedron Lett.* **2007**, *48*, 7263.
[44] M. Jafarzadeh, E. Soleimani, H. Sepahvand, R. Adnan, *RSC Adv.* **2015**, *5*, 42744.
[45] M. Hussain, J. Liu, Z. Zhang, M. Hu, Y. Li, X. Min, *ChemistrySelect* **2018**, *3*(8), 787.
[46] Y. Wang, R. K. Kumar, X. Bi, *Tetrahedron Lett.* **2016**, *57*, 5730.
[47] Z. Chen, Y. Wen, H. Ding, G. Luo, M. Ye, L. Liu, J. Xue, *Tetrahedron Lett.* **2017**, *58*, 13.
[48] G. Abbiati, E. Rossi, *Beilstein J. Org. Chem.* **2014**, *10*, 481.
[49] H. Yue, Y. Zhao, X. Ma, J. Gong, *Chem. Soc. Rev.* **2012**, *41*, 4218.
[50] R. F. Dye, *Korean J. Chem. Eng.* **2001**, *18*, 571.
[51] C. Bianchini, P. K. Shen, *Chem. Rev.* **2009**, *109*, 4183.
[52] H. Dong, Y. Chen, C. Feldmann, *Green Chem.* **2015**, *17*, 4107.
[53] A. Thakur, P. L. Reddy, M. Tripathi, D. S. Rawat, *New J. Chem.* **2015**, *39*, 6253.
[54] Z. Karimi-Jaberi, E. Ghasemi, *Chem. Biol. Interface* **2017**, *7*, 224.
[55] A. Habibi, Z. Tarameshloo, S. Rostamizadeh, A. M. Amani, *Lett. Org. Chem.* **2012**, *9*, 155.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Hussain M, Liu J, Fu L, Hasan M. Synthesis of imidazo[1, 2-a]pyridines via the silver acetate-catalyzed Groebke-Blackburn-Bienayme reaction with ethylene glycol as a biodegradable and sustainable solvent. *J Heterocyclic Chem*. 2020;1–10. https://doi.org/10.1002/jhet.3746