Microwave-Assisted Expedite Synthesis of 2-Phenylimidazo[1,2-*a*] pyridylquinoxalin-2(1*H*)-ones

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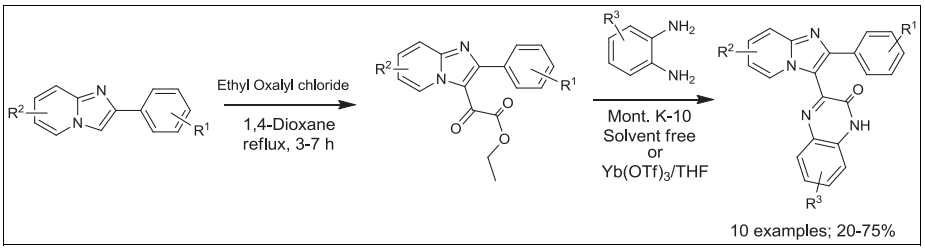

An efficient methodology has been developed for the synthesis of quinoxalin-2(1*H*)-one derivatives of 2-phenylimidazo[1,2-*a*]pyridines by microwave-irradiated Hinsberg heterocyclization between 2-phenylimidazo [1,2-*a*]pyridine-3-glyoxalates and *o*-phenylenediamine using either montmorillonite K-10 or $Yb(OTf)_3$ as catalysts. Montmorillonite K-10 was proven to be an efficient catalyst for the heterocyclization reaction between sterically hindered glyoxalate and *o*-phenylenediamine only under microwave conditions. The use of $Yb(OTf)_3$/tetrahydrofuran was also found to be an effective catalyst for the above chemical transformation among a series of Lewis acids screened under microwave conditions; however, comparatively lesser yields were obtained as compared with the use of montmorillonite K-10.

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INTRODUCTION

Quinoxalines represent an important class of azaheterocycles possessing versatile biological activities, such as antibacterial [1], antihistaminic [2], antitrypanosomal [3], antiplasmodial [4], and anti-inflammatory [5]. In addition, quinoxaline derivatives are reported for their application in dyes, efficient electroluminescent materials, organic semiconductors, and DNA cleaving agents [6]. 1,2-Dihydroquinoxaline-2-ones represent a subfamily with interesting applications in drug discovery. One such application is their antagonism behavior toward glutamate α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors, which have been reported to be effective in the therapy of neurodegenerative disorders such as ischemic stroke, epilepsy, head trauma, and Alzheimer's disease, without showing any side effects such as schizophrenia [7]. GRA-293 (**I**) is an example of imidazole-based 1,2-dihydroquinoxaline-2-one compound (Figure 1) that shows excellent third generation AMPA receptor antagonist activity *in vitro* and *in vivo* as compared with the known first and second generation AMPA receptor antagonists possessing quinoxaline–diones structures such as YM-90K, YM-872 (**II**) [8]. Ladouceur *et al*. reported 3-(indol-2-yl)quinoxalin-2-ones (**III**) as an anti-angiogenesis agents, that showed a potent inhibitory activity toward the VEGF-induced proliferation of human mesangial cells and the VEGF-induced autophosphorylation of human umbilical vein endothelial cells (Figure 1) [9].

Ruthenium(II) arene complexes of 3-(1*H*-benzimidazol-2-yl)-1*H*-quinoxalin-2-one have been reported to possess antiproliferative activity in three human cancer cell lines (A549, CH1, SW480) [10]. Few more 1-({[4-(1*H*-benzimidazol-2-yl)phenyl]amino}methyl)-3-methylquinoxaline-2(1*H*)-ones have been recently reported as antimicrobial agents [11]. Thus, in order to expand the range of the two privileged [12] scaffolds, the imidazo[1,2]heterocycles and quinoxaline systems, we turned our attention to the preparation of 1,2-dihydroquinoxalin-2-one derivatives of 2-phenylimidazo[1,2-*a*]pyridine of potentially biological importance. To the best to our knowledge, there is only one patent that describes only few compounds possessing quinoxaline moiety attached to imidazo[1,2-*a*] pyridine system, as selective inhibitors of platelet-derived growth factor and inhibitors of human ileal bile acid transporter [13]. Recently, Mamedov *et al*. have synthesized a series of pyridylimidazo[1,5-*a*]quinoxaline derivatives possessing antibacterial and antifungal activities [14].

Several methods for the synthesis of 1,2-dihydroquinoxalin-2(1*H*)-ones have been reported in the literature, and among these, the Hinsberg reaction [15] is a straightforward high yielding method that involves the heterocyclization of *o*-phenylenediamine with α-ketoesters in the presence of a catalyst such as acetic acid [16], sulfuric acid [17], citric acid [18], gallium triflate [19], and polyaniline sulfate salt [6]. The general applicability of catalyst for different alkyl/aryl/heteroaryl α-ketoesters substrates remains doubtful, and thus, synthesizing novel heterocyclic quinoxalin-2(1*H*)-ones via Hinsberg reaction remains a challenging task. To our best knowledge, no

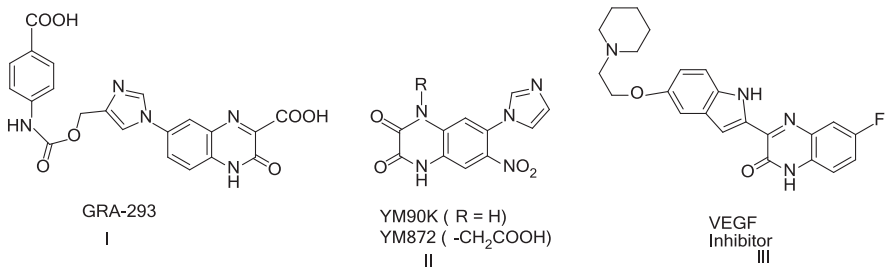


Figure 1. Examples of biologically active 1,2-dihydroquinoxalinones and 1,4-dihydroquinoxalinediones.

regioselectivity of Hinsberg cyclization of sterically hindered substrates of this type to yield biologically active 1,2-dihydroquinoxalines derivatives of imidazo[1,2-*a*] pyridine has been reported.

With a variety of challenges in organic synthesis and the advent of newer technologies, greener methodologies prove valuable additions to existing scientific literature. Thus, the combination of microwave irradiation and solvent-free reactions using either organic or inorganic solid supports for shortening reaction time, and improving yield has increased dramatically using some of these greener methodologies. Montmorillonite K-10 [20,21] and $Yb(OTf)_3$ [22,23] have been used as effective green catalysts in various organic transformations. In this article, we describe a general and efficient synthesis of a series of 3-(2-phenylimidazo[1,2-*a*] pyrid-3-yl)quinoxalin-2(1*H*)-ones from commercially available *o*-phenylenediamine and 2-phenylimidazo[1,2-*a*]pyridine-3-glyoxalates under microwave irradiation using either montmorillonite K-10 under solvent-free conditions or $Yb(OTf)_3$/tetrahydrofuran (THF).

RESULTS AND DISCUSSION

The starting 2-phenylimidazo[1,2-*a*]pyridyl-3-glyoxalates (**3a–i**) required for the present work were synthesized [24] by reacting ethyl oxalyl chloride (**2**) with substituted 2-phenylimidazo[1,2-*a*]pyridines (**1a–i**) in dioxane under reflux conditions for 3–7 h (Table 1). 2-Phenylimidazo[1,2-*a*]pyridines were synthesized by the reaction of substituted phenacyl bromides and 2-aminopyridines in refluxing ethanol using reported literature procedure [25].

Initial examination was aimed at determining the optimal conditions for the heterocyclization reaction between 2-phenylimidazo[1,2-*a*]pyridyl-3-glyoxalate (**3a**) and *o*-phenylenediamine (**4a**), and the results of these experiments are summarized in Table 2. The condensation between **3a** and **4a** to prepare 3-(2-phenylimidazo[1,2-*a*] pyridin-3-yl)quinoxalin-2(1*H*)-one (**5a**) did not proceed on refluxing the substrates in a variety of solvents such as CH_3CN, THF, EtOH, and dimethylformamide (DMF) even up to 5 days (Table 2, entry 1). In the absence of any catalyst in solvents such as CH_3CN, THF, EtOH, and DMF (Table 2, entry 2) under microwave conditions for a period of 2–5 h, formation of **5a** was not observed; however, some of the glyoxalate decomposed to **1a**. With the use of lanthanide triflates $Sc(OTf)_3$ and $Yb(OTf)_3$, not even a trace amount of product was observed by classically refluxing the reactants in THF or CH_3CN even up to 2 days (Table 2, entries 3 and 4). The Lewis acid $Yb(OTf)_3$ (10 mol%) is also fairly effective in this reaction under microwave conditions, giving **5a** in low to moderate yields in a variety of solvents (THF, CH_3CN, and 1,4-dioxane) (Table 2, entry 9). Using other Lewis acids such as In $(OTf)_3$, $Cu(OTf)_2$, $Sc(OTf)_3$, $InBr_3$, and $InCl_3$ in THF under microwave irradiation gave **5a** in lower yields (Table 2, entries 5, 7, and 11–13), and with AgOTf and $Bi(OTf)_3$, only a trace amount of product was observed on thin layer chromatography (TLC; Table 2, entries 6 and 8). The use of $Yb(OTf)_3$ (10 mol%) was found to be the best catalyst for reacting **3a** and **4a** in THF at 90–100°C under microwave irradiation for 1.5 h to give **5a** in 58% yield (Table 2, entry 10). In most cases, increasing the temperature beyond 120°C and prolonging the reaction time lead to decomposition of glyoxalate to **1a**.

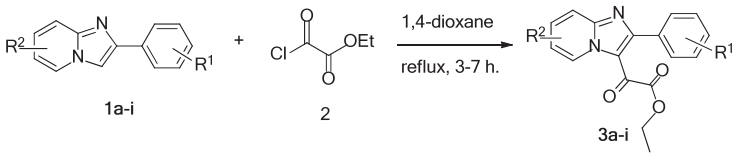
To further increase the yields, we switch to the use of different solid supports such as neutral alumina, acidic alumina, silica gel, and montmorillonite K-10 (Table 2, entries 14–19), among which the use of montmorillonite K-10 support gave 72% of **5a** at 90–100°C for 1.0 h under microwave irradiation (Table 2, entry 16).

Following optimization of the reaction conditions, the scope of this method was studied for synthesis of substituted imidazo[1,2-*a*]pyridylquinoxalinones **5**, and results are summarized in Table 3. After completion of the reaction, the desired product was isolated either by flash column chromatographic purification or recrystallization with $MeOH/CH_2Cl_2$.

The use of $Yb(OTf)_3$ in THF under microwave irradiation gave the desired products in lesser yields. The reaction tolerated a wide range of electron-donating and electron-withdrawing substituents on imidazo[1,2-*a*]pyridyl system to afford **5a–j** in moderate to good (20–75%) yields. The presence of an electron-withdrawing group on imidazo [1,2-*a*]pyridine system further decreases its reactivity toward this heterocyclization. Thus, 2-(4′-nitrophenyl) imidazo[1,2-*a*]pyridyl-3-glyoxalates (**3e**) (Table 3, entry

Table 1

Synthesis of 2-phenylimidazo[1,2-*a*]pyridyl-3-glyoxalates **3**.



S. No.	Compound	R^1	R^2	Yield %[a]	M. P. (°C)
1	**3a**	H	H	75	177–179[b]
2	**3b**	4-OMe	H	80	131–133
3	**3c**	4-Me	H	84	110–112
4	**3d**	4-Cl	H	85	109–112
5	**3e**	4-NO_2	H	—[c]	—[c]
6	**3f**	H	6-Me	86	179–181
7	**3g**	4-Cl	7-Me	82	135–137
8	**3h**	4-OMe	6-Me	84	117–118
9	**3i**	4-OMe	7-Me	79	131–132

[a]Isolated yield.
[b]Reported [24] as colorless oil.
[c]Obtained as a mixture of glyoxalate and starting material in the ratio 3:2.

5) gave poor yield (20%) of corresponding 3-(2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)quinoxalin-2(1*H*)-one (**5e**), probably because **3e** was not obtained as a pure intermediate and rather was isolated as a mixture along with the starting 2-(4′-nitrophenyl)imidazo[1,2-*a*]pyridine **1e**. The reaction of **3h** with 4-chloro-*o*-phenylenediamine (**4b**) gave a major amount of the **5j** isomer, along with a minor amount of **5j′**, that was inseparable by chromatography techniques.

In the recycling study, both the catalysts $Yb(OTf)_3$ and montmorillonite K-10 could be reused up to three times, without any appreciable loss of catalytic activity. No significant decrease in yield during the three recycles was observed.

The use of montmorillonite K-10 using microwave heating at 90–100°C was finally applied to a mixture of 2-methylimidazo[1,2-*a*]pyridylglyoxalate **6** and *o*-phenylenediamine **4a** to yield the known 3-(2-methylimidazo[1,2-*a*]pyridin-3-yl)quinoxalin-2(1*H*)-one (7) in 82% yield in just 45 min (Scheme 1). The method not only reduced the reaction time from 2 days (conventional refluxing in CH_3CN) [24] to 30 minutes but also gave comparable yield under environmentally friendly reaction conditions.

In summary, we have accomplished the synthesis of 1,2-dihydroquinoxalinone derivatives at sterically hindered third position of 2-alkyl/arylimidazo[1,2-*a*]pyridines using microwave heating (power 80 W) using either montmorillonite K-10 or $Yb(OTf)_3$ as catalysts. Thus, it is possible to apply the tenets of green chemistry to the generation of interesting products using combined approaches of solvent-free, solid-supported reagents under microwave irradiation, that are less expensive and less toxic than those with organic solvents. Moreover, the procedure offers several advantages including operational simplicity, clean reactions, increased safety for small-scale high-speed synthesis, and minimal environmental impact that make it a useful and attractive process for the synthesis of these biologically active compounds.

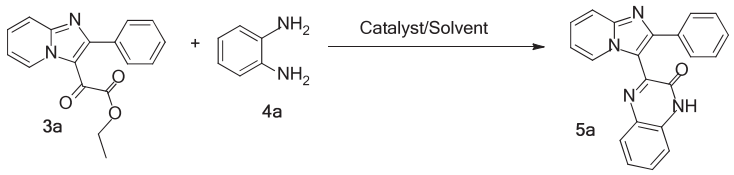
EXPERIMENTAL

General: All chemicals were obtained from commercial suppliers and used without further purification. Melting points were determined in open capillary tubes on an MPA120 automated melting point apparatus Stanford Research Systems, EZ MELT (USA) and are uncorrected. The reactions were carried out in a CEM Discover BenchMate Reactor in 10-mL pressure vials at a power of 80 W. Reactions were monitored by using TLC on 0.2-mm silica gel F254 plates (Merck). The chemical structures of final products and intermediates were characterized by nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR) determined on a Bruker NMR spectrometer (300 MHz, 75 MHz). ^{13}C NMR spectra are fully decoupled. Chemical shifts were reported in parts per million using deuterated solvent peak or tetramethylsilane (internal) as the standard. The chemical structures of final products were confirmed by a high-resolution Biosystems QStar Elite time-of-flight electrospray mass spectrometer.

2-Phenylimidazo[1,2-*a*]pyridylglyoxalate 3a–i: general procedure. To a solution of substituted 2-phenylimidazo[1,2-*a*]pyridines (**1a–i**, 2 mmol) in 1,4-dioxane (20 mL) was added ethyl oxalyl chloride (**2**, 3.5 mmol) in an inert atmosphere of nitrogen. The mixture was heated at reflux for 5–8 h, then allowed to cool and evaporated. The residue was triturated with water (80 mL), and the resulting precipitate was either removed

Table 2

Optimization of catalyst, solvent, and reaction conditions for the synthesis of **5a**.



Entry	Catalyst	Solvent	Reaction conditions[c]			Yield % (**5a**)[a]
			Heating	Temp. (°C)	Time (h)	
1	—	CH_3CN/THF/EtOH/DMF	Conventional	Reflux	Up to 120	—[b]
2	—	CH_3CN/THF/EtOH/ DMF	MW		2–5	—[b]
3	$Yb(OTf)_3$	THF/CH_3CN	Conventional	Reflux	Up to 48	—[b]
4	$Sc(OTf)_3$	THF/CH_3CN	Conventional	Reflux	Up to 48	—[b]
5	$In(OTf)_3$	THF/CH_3CN	MW	80–90	2	40/46
6	AgOTf	THF/CH_3CN	MW	80–90	2	Trace
7	$Cu(OTf)_2$	THF/CH_3CN	MW	80–90	2	20/trace
8	$Bi(OTf)_3$	THF/CH_3CN	MW	80–90	2	Trace
9	$Yb(OTf)_3$	THF/CH_3CN/Dioxane	MW	80–110	2	55/25/40
10	$Yb(OTf)_3$	THF	MW	90–100	1.5	58
11	$Sc(OTf)_3$	THF/CH_3CN	MW	90–100	2	40/18
12	$InBr_3$	THF/CH_3CN	MW	90–100	2.5	32/trace
13	$InCl_3$	THF/CH_3CN	MW	90–130	2.5	28/trace
14	Neutral alumina	—	MW	100–150	2	50
15	Acidic alumina	—	MW	100–150	2	42
16	Mont. K-10	—	MW	90–100	1.0	72
17	Mont. K-10	—	MW	90–100	2.5	60
18	Mont. K-10	—	MW	120–130	1.5	58
19	Acidic silica gel	—	MW	120–160	2.5	45

M, microwave.
[a]Isolated yield.
[b]Starting material did not react.
[c]Microwave power was varied between 80 and 100 W for the standardization experiments.

by filtration and washed with water (20 mL) or extracted with dichloromethane (3 × 50 mL). In the latter case, the combined organic extracts were dried over sodium sulfate and evaporated to afford the crude product, that were recrystallized from ethanol to give pure **3a–i** (except **3e**).

Ethyl 2-oxo-2-(2-phenylimidazo[1,2-a]pyridin-3-yl)acetate 3a. Yield: 0.440 g (75%); white solid; mp 177–179°C (Lit. [24], reported as colorless oil). ^{1}H NMR ($CDCl_3$): δ = 9.67 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.63 (dd, J = 8.5, 7.2 Hz, 3H), 7.55–7.42 (m, 3H), 7.18 (t, J = 6.9 Hz, 1H), 3.69 (q, J = 7.2 Hz, 2H), 1.00 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 176.78, 163.50, 158.33, 148.14, 133.56, 131.06, 129.62, 129.04, 128.41, 117.95, 117.55, 115.82, 62.10, 13.40. HRMS (TOF MS) calcd for $C_{17}H_{15}N_2O_3^+$ 295.1082, found 295.1068 $[M+H]^+$.

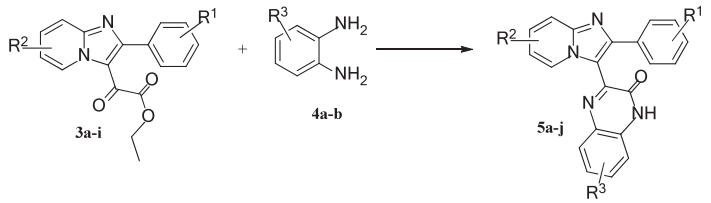
Ethyl 2-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3b. Yield: 0.520 g (80%); yellow solid; mp 131–133°C. ^{1}H NMR ($CDCl_3$): δ = 9.63 (d, J = 6.9 Hz, 1H), 7.79 (d, J = 8.9 Hz, 1H), 7.65–7.53 (m, 3H), 7.15 (td, J = 6.9, 1.2 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 3.78 (q, J = 7.2 Hz, 2H), 1.05 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 176.69, 163.61, 160.87, 158.11, 148.09, 130.99, 128.90, 125.86, 117.66, 117.25, 115.56, 113.84, 62.06, 55.34, 13.42. HRMS (TOF MS) calcd for $C_{18}H_{17}N_2O_4^+$ 325.1189, found 325.1147 $[M+H]^+$.

Ethyl 2-oxo-2-(2-(4-methylphenyl)imidazo[1,2-a]pyridin-3-yl)acetate 3c. Yield: 0.490 g (84%); brown solid; mp 110–112° C. ^{1}H NMR ($CDCl_3$): δ = 9.52 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 7.03 (t, J = 6.7 Hz, 1H), 3.61 (q, J = 7.2 Hz, 2H), 2.30 (s, 3H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 176.76, 163.56, 158.46, 148.13, 139.74, 130.98, 130.66, 129.52, 129.05, 128.95, 117.83, 117.41, 115.66, 62.04, 21.33, 13.38. HRMS (TOF MS) calcd for $C_{18}H_{17}N_2O_3^+$ 309.1239, found 309.1257 $[M+H]^+$.

Ethyl 2-(2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3d. Yield: 0.530 g (85%); pale brown solid; mp 109–112°C. ^{1}H NMR ($CDCl_3$): δ = 9.67 (d, J = 6.9 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.66 (t, J = 7.9 Hz, 1H), 7.57 (d, J = 9.0 Hz, 2H), 7.47 (d, J = 9.0 Hz, 2H), 7.23 (t, J = 9.0 Hz, 1H), 3.79 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 176.60, 163.45, 157.01, 148.24, 136.04, 132.12, 131.19, 130.95, 129.14, 128.67, 117.99, 117.69, 115.99, 62.31, 13.50. HRMS (TOF MS) calcd for $C_{17}H_{14}ClN_2O_3^+$ 329.0692, found 329.0712 $[M+H]^+$.

Table 3

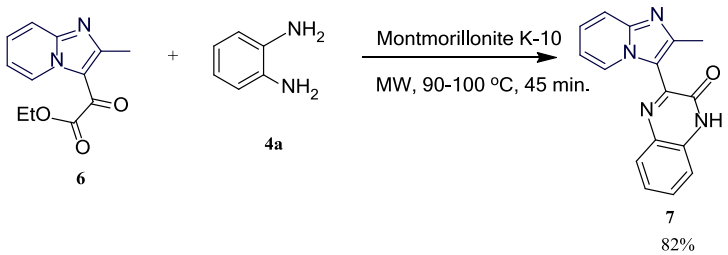
Montmorillonite K-10/$Yb(OTf)_3$ catalyzed synthesis of imidazo[1,2-*a*]pyridylquinoxalinones **5**.



S. No.	R^1	R^2	R^3	*T* (min)	Prod.	Yield %[c] (method A[a])	Yield %[c] (method B[b])
1	H	H	H	60	**5a**	72	58
2	4-OMe	H	H	60	**5b**	75	61
3	4-Me	H	H	75	**5c**	70	56
4	4-Cl	H	H	90	**5d**	65	58
5	4-NO_2	H	H	150	**5e**	20	—
6	H	6-Me	H	60	**5f**	60	49
7	4-Cl	7-Me	H	75	**5g**	58	47
8	4-OMe	6-Me	H	60	**5h**	62	54
9	4-OMe	7-Me	H	60	**5i**	60	48
10	4-OMe	6-Me	4-Cl	90	**5j**	62[d]	52[d]

[a]Montmorillonite K-10 (0.300 g), MW, 90–100°C, 80 W (power).
[b]$Yb(OTf)_3$ (10 mol%)/THF, MW, 80–90°C, 80 W (power).
[c]Isolated yield after flash column chromatography.
[d]Yield of the major isomer; minor isomer could not be separated by column chromatography.

Scheme 1



Ethyl 2-(2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3e. The reaction of 4-nitrophenylimidazo[1,2-*a*] pyridine (**3e**) with ethyl oxalyl chloride did not go to completion even with excess of ethyl oxalyl chloride under refluxing 1,4-dioxane or toluene for longer reaction time (12 h), and the obtained crude product was a mixture of glyoxalate (**4e**) and starting material (**3e**), which showed overlapping spots on TLC and were nonseparable via repeated column chromatography and thus was used as such for the next step. The NMR of the mixture of **4e** and **3e** are given as follows: ^{1}H NMR (DMSO-d_6): $\delta = 9.56$ (dt, $J = 6.7$, 1.2 Hz, 1H), 8.65 (s, 1H), 8.58 (dt, $J = 6.8$, 1.1 Hz, 1H), 8.42–8.35 (m, 2H), 8.34–8.28 (m, 1H), 8.27–8.20 (m, 1H), 8.02 (dt, $J = 8.8$, 1.2 Hz, 1H), 7.93–7.83 (m, 3H), 7.63 (d, $J = 9.2$ Hz, 1H), 7.48 (td, $J = 6.9$, 1.3 Hz, 1H), 7.32 (ddd, $J = 9.1$, 6.7, 1.3 Hz, 1H), 6.96 (td, $J = 6.7$, 1.2 Hz, 1H), 3.69 (q, $J = 7.1$ Hz, 2H), 0.98 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (DMSO-d_6): $\delta = 176.00$, 163.23, 155.37, 148.53, 148.17, 146.91, 145.70, 142.44, 140.95, 140.30, 132.78, 131.28, 129.19, 127.70, 126.73, 126.35, 124.61, 123.89, 118.12, 117.63, 117.44, 113.36, 112.13, 62.60, 13.68.

Ethyl 2-(6-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3f. Yield: 0.530 g (86%); brown solid; mp 179–181°C. ^{1}H NMR ($CDCl_3$): $\delta = 9.48$ (s, 1H), 7.76 (d, $J = 9.0$ Hz, 1H), 7.62 (dd, $J = 6.5$, 2.8 Hz, 2H), 7.48 (dd, $J = 8.4$, 5.7 Hz, 4H), 3.66 (q, $J = 7.2$ Hz, 2H), 2.46 (s, 3H), 1.00 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$): $\delta = 176.70$, 163.57, 157.92, 146.91, 133.98, 133.43, 129.61, 128.38, 127.06, 126.21, 117.74, 116.68, 62.06, 18.43, 13.40. HRMS (TOF MS) calcd for $C_{18}H_{17}N_2O_3^+$ 309.1239, found 309.1208 $[M+H]^+$.

Ethyl 2-(2-(4-chlorophenyl)-7-methylimidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3g. Yield: 0.560 g (82%); dirty white solid; mp 135–137°C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.37$ (d, $J = 7.1$ Hz, 1H), 7.49–7.40 (m, 3H), 7.33 (d, $J = 8.4$ Hz, 2H), 6.88 (dd, $J = 7.0$, 1.8 Hz, 1H), 3.66 (q, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 0.94 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR ($CDCl_3$):

δ = 176.00, 163.53, 157.09, 148.52, 143.13, 135.77, 132.19, 130.85, 128.49, 128.12, 118.27, 117.62, 116.29, 62.11, 21.61, 13.44. HRMS (TOF MS) calcd for $C_{18}H_{16}ClN_2O_3^+$ 343.0849, found 343.0861 $[M+H]^+$.

Ethyl 2-(2-(4-methoxyphenyl)-6-methylimidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3h. Yield: 0.570 g (84%); brown solid; mp 117–118°C. ^{1}H NMR ($CDCl_3$): δ = 9.45 (s, 1H), 7.81 (d, J = 9.0 Hz, 1H), 7.57 (d, J = 8.7 Hz, 2H), 7.51 (d, J = 9.1 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H), 3.77 (q, J = 7.2 Hz, 2H), 2.45 (s, 3H), 1.05 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 177.43, 164.23, 161.30, 160.67, 160.14, 157.38, 146.87, 134.68, 131.43, 127.71, 126.78, 125.75, 117.99, 116.52, 114.70, 62.12, 55.15, 18.11, 13.06. HRMS (TOF MS) calcd for $C_{19}H_{19}N_2O_4^+$ 339.1344, found 339.1327 $[M+H]^+$.

Ethyl 2-(2-(4-methoxyphenyl)-7-methylimidazo[1,2-a]pyridin-3-yl)-2-oxoacetate 3i. Yield: 0.530 g (79%); brown solid; mp 131–132°C. ^{1}H NMR ($CDCl_3$): δ = 9.52 (d, J = 7.0 Hz, 1H), 7.62 (s, 1H), 7.57 (d, J = 8.6 Hz, 2H), 7.01 (t, J = 6.2 Hz, 3H), 3.86 (s, 3H), 3.77 (q, J = 7.2 Hz, 2H), 2.52 (s, 3H), 1.05 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 176.49, 163.73, 161.46, 160.98, 158.04, 148.30, 143.33, 131.28, 128.24, 125.55, 118.17, 117.46, 116.02, 113.92, 62.12, 55.40, 21.69, 13.48. HRMS (TOF MS) calcd for $C_{19}H_{19}N_2O_4^+$ 339.1344, found 339.1368 $[M+H]^+$.

2-Phenylimidazo[1,2-*a*]pyridylquinoxalin-2-ones 5a–j: general procedure. ***Method A***. A mixture of substituted 2-phenylimidazo [1,2-*a*]pyridylglyoxalate (**3a–i**, 0.6 mmol) and *o*-phenylenediamine (**4a–b**, 0.72 mmol) were dissolved in CH_2Cl_2 (10 mL). Montmorillonite K-10 (300 mg) was added to the mixture, and the solvent was evaporated *in vacuo*. The dry mixture was then transferred to a microwave reaction tube and irradiated in focused microwave oven (CEM) at temperatures 90–100°C at an 80-W power for the specified time mentioned in Table 3. The reaction was monitored via TLC. After the completion of the reaction, the reaction mixture was diluted with CH_2Cl_2 (3 × 50 mL), and the organic layer was separated from the catalyst by filtration. The crude product obtained by evaporating the solvent *in vacuo* was purified by either flash chromatography purification (**5a**, **5c**, **5e–g**, **5j**) or recrystallization with MeOH/CH_2Cl_2 (**5b**, **5d**, **5h**, **5i**) to yield pure quinoxaline-2-ones **5a–j**.

Method B. A mixture of substituted 2-phenylimidazo[1,2-*a*] pyridylglyoxalate (**3a–i**, 0.6 mmol), *o*-phenylenediamine (**4a–b**, 0.72 mmol), and $Yb(OTf)_3$ (0.06 mmol) were dissolved in THF (3 mL) in a microwave reaction tube. The reaction tube was irradiated in focused microwave oven (CEM) at temperatures 80–90°C at an 80-W power for a specified time (1.5–3 h). The reaction was monitored via TLC. After the completion of the reaction, THF was evaporated, and the reaction mixture was diluted with water and extracted with ethyl acetate (3 × 50 mL), and the organic layer was separated. The crude product obtained by evaporating the organic solvent *in vacuo* was purified by flash chromatography to yield pure quinoxaline-2-ones **5a–d** and **5f–j**.

3-(2-Phenylimidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5a. Yield: 0.146 g (72%); brownish yellow solid; mp 273–274°C. ^{1}H NMR ($CDCl_3$ + CD_3OD): δ = 8.75 (d, J = 7.0 Hz, 1H), 7.90 (d, J = 6.9 Hz, 1H), 7.73 (dd, J = 11.4, 8.7 Hz, 3H), 7.51 (t, J = 8.4 Hz, 1H), 7.42–7.25 (m, 5H), 7.02 (d, J = 9.0 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$ + CD_3OD): δ = 154.60, 148.87, 148.71, 146.30, 135.10, 132.72, 131.07, 130.87, 128.78, 128.37, 128.23, 128.10, 126.93, 125.70, 124.47, 117.02, 115.81, 113.19. HRMS (TOF MS) calcd for $C_{21}H_{15}N_4O^+$ 339.1245, found 339.1223 $[M+H]^+$.

3-(2-(4-Methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5b. Yield: 0.152 g (75%); yellow solid; mp 238–240°C. ^{1}H NMR (DMSO-d_6): δ = 12.64 (s, 1H), 8.57 (d, J = 6.9 Hz, 1H), 7.84 (d, J = 7.9 Hz, 1H), 7.68 (t, J = 8.2 Hz, 3H), 7.58 (d, J = 8.0 Hz, 1H), 7.44–7.32 (m, 3H), 6.93 (dd, J = 15.7, 7.8 Hz, 3H), 3.76 (s, 3H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$): δ = 159.57, 154.19, 150.34, 146.66, 145.43, 132.76, 132.63, 131.16, 129.70, 129.21, 127.73, 127.01, 126.55, 123.87, 116.91, 116.24, 115.89, 114.00, 112.73, 55.48. HRMS (TOF MS) calcd for $C_{22}H_{17}N_4O_2^+$ 369.1351, found 369.1323 $[M+H]^+$.

3-(2-(4-Methylphenyl)imidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5c. Yield: 0.148 g (70%); yellow solid; mp 174–175°C. ^{1}H NMR (DMSO-d_6): δ = 12.66 (s, 1H), 8.60 (d, J = 6.9 Hz, 1H), 7.85 (d, J = 7.3 Hz, 1H), 7.72 (d, J = 9.0 Hz, 1H), 7.60 (t, J = 6.4 Hz, 3H), 7.38 (dd, J = 18.3, 7.7 Hz, 3H), 7.15 (d, J = 8.0 Hz, 2H), 6.97 (t, J = 6.4 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$): δ = 154.20, 150.33, 146.78, 145.45, 137.59, 132.79, 132.63, 132.44, 131.28, 129.27, 129.22, 128.37, 127.12, 126.67, 123.92, 117.05, 116.67, 115.91, 112.89, 21.27. HRMS (TOF MS) calcd for $C_{22}H_{17}N_4O^+$ 353.1402, found 353.1423 $[M+H]^+$.

3-(2-(4-Chlorophenyl)imidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5d. Yield: 0.145 g (58%); yellow solid; mp >290°C. ^{1}H NMR (DMSO-d_6): δ = 12.66 (s, 1H), 8.66 (d, J = 6.6 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.73 (t, J = 8.1 Hz, 3H), 7.62 (t, J = 7.4 Hz, 1H), 7.41 (d, J = 7.5 Hz, 5H), 7.01 (t, J = 6.5 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ = 154.14, 149.90, 145.57, 134.22, 132.97, 132.82, 132.62, 131.38, 130.15, 129.31, 128.66, 127.31, 127.12, 123.97, 117.19, 117.08, 115.92, 113.21. HRMS (TOF MS) calcd for $C_{21}H_{14}ClN_4O^+$ 373.0856, found 373.0823 $[M+H]^+$.

3-(2-(4-Nitrophenyl)imidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5e. Yield: 0.046 g (20%); pale yellow solid; mp 240–242°C. ^{1}H NMR ($CDCl_3$): δ = 8.77 (d, J = 7.0 Hz, 1H), 8.24 (d, J = 8.4 Hz, 2H), 7.90 (dd, J = 16.7, 8.2 Hz, 3H), 7.77 (d, J = 9.0 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.13–6.94 (m, 2H). HRMS (TOF MS) calcd for $C_{21}H_{14}N_5O_3^+$ 384.1096, found 384.1125 $[M+H]^+$.

3-(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 5f. Yield: 0.126 g (60%); yellow solid; mp >290° C. ^{1}H NMR (DMSO-d_6): δ = 12.65 (s, 1H), 8.39 (s, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.74–7.58 (m, 4H), 7.44–7.23 (m, 6H), 2.29 (s, 3H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$): δ = 154.27, 150.48, 146.06, 144.42, 135.26, 132.86, 132.69, 131.37, 129.57, 129.38, 128.61, 128.25, 128.10, 124.53, 123.93, 122.23, 116.72, 116.54, 115.91, 18.18. HRMS (TOF MS) calcd for $C_{22}H_{17}N_4O^+$ 353.1402, found 353.1378 $[M+H]^+$.

3-(2-(4-Chlorophenyl)-7-methylimidazo[1,2-a]pyridin-3-yl) quinoxalin-2(1H)-one 5g. Yield: 0.134 g (58%); yellow solid; mp >290°C. ^{1}H NMR ($CDCl_3$ + CD_3OD): δ = 8.61 (d, J = 7.1 Hz, 1H), 7.90 (dd, J = 8.1, 1.4 Hz, 1H), 7.64–7.53 (m, 3H), 7.48 (dt, J = 2.0, 1.1 Hz, 1H), 7.41 (ddd, J = 8.3, 7.3, 1.3 Hz, 1H), 7.35–7.30 (m, 2H), 7.26 (dd, J = 8.2, 1.4 Hz, 1H), 6.80 (dd, J = 7.2, 1.7 Hz, 1H), 2.48 (d, J = 1.2 Hz, 3H). ^{13}C NMR ($CDCl_3$ + CD_3OD): δ = 154.24, 148.56, 147.38, 146.67, 138.57, 134.04, 133.63, 132.69, 130.86, 129.55, 128.82, 128.22, 125.06, 124.35, 115.86, 115.50, 115.31, 21.41. HRMS (TOF MS) calcd for $C_{22}H_{16}ClN_4O^+$ 387.1012, found 387.1049 $[M+H]^+$.

3-(2-(4-Methoxyphenyl)-6-methylimidazo[1,2-a]pyridin-3-yl) quinoxalin-2(1H)-one 5h. Yield: 0.142 g (62%); yellow solid; mp 285–287°C. ^{1}H NMR (DMSO-d_6): δ = 12.64 (s, 1H), 8.34 (s, 1H), 7.90–7.82 (m, 1H), 7.68–7.55 (m, 4H), 7.45–7.33 (m, 2H), 7.24 (dd, J = 9.1, 1.7 Hz, 1H), 6.94–6.85

(m, 2H), 3.75 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$): δ = 159.45, 154.22, 150.45, 146.17, 144.40, 132.73, 132.66, 131.19, 129.50, 129.39, 129.25, 127.72, 124.33, 123.89, 122.01, 116.27, 115.87, 115.60, 113.98, 55.46, 18.21. HRMS (TOF MS) calcd for $C_{23}H_{19}N_4O_2^+$ 383.1508, found 383.1542 $[M+H]^+$.

3-(2-(4-Methoxyphenyl)-7-methylimidazo[1,2-a]pyridin-3-yl) quinoxalin-2(1H)-one 5i. Yield: 0.137 g (60%); yellow solid; mp >290°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (d, J = 6.7 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 8.3 Hz, 2H), 7.38 (s, 1H), 7.33–7.26 (m, 1H), 7.07 (dd, J = 16.8, 6.2 Hz, 1H), 6.72 (t, J = 8.6 Hz, 3H), 6.62 (d, J = 7.3 Hz, 1H), 3.47 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): δ = 159.64, 155.23, 148.73, 147.00, 138.04, 132.88, 130.83, 130.37, 129.72, 128.47, 128.31, 125.08, 124.42, 116.09, 115.51, 114.96, 113.53, 55.00, 21.44. HRMS (TOF MS) calcd for $C_{23}H_{19}N_4O_2^+$ 383.1508, found 383.1482 $[M+H]^+$.

6-Chloro-3-(2-(4-methoxyphenyl)-6-methylimidazo[1,2-a] pyridin-3-yl)quinoxalin-2(1H)-one 5j. Yield: 0.155 g (62%); yellow solid; mp 224–225°C. ^{1}H NMR (DMSO-d_6): δ = 12.68 (s, 1H), 8.39 (s, 1H), 7.87 (d, J = 9.0 Hz, 1H), 7.70–7.56 (m, 3H), 7.40 (s, 2H), 7.26 (d, J = 8.9 Hz, 1H), 6.90 (d, J = 8.4 Hz, 2H), 3.75 (s, 3H), 2.29 (s, 3H). ^{13}C NMR ($CDCl_3$ + CD_3OD): δ = 159.51, 154.00, 150.82, 146.46, 144.49, 135.24, 133.85, 131.47, 130.96, 129.60, 127.69, 124.61, 124.00, 122.05, 116.33, 115.77, 115.05, 114.06, 55.51, 18.19. HRMS (TOF MS) calcd for $C_{23}H_{18}ClN_4O_2^+$ 417.1118, found 417.1156 $[M+H]^+$.

3-(2-Methylimidazo[1,2-a]pyridin-3-yl)quinoxalin-2(1H)-one 7. Yield: 82%; yellow solid: mp 222–224°C (Lit. [24], mp > 220° C). ^{1}H NMR (DMSO-d_6): δ = 12.61 (s, 1H), 8.71 (d, J = 6.9 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.56 (dd, J = 12.5, 8.1 Hz, 2H), 7.36 (dd, J = 14.2, 7.1 Hz, 3H), 6.96 (t, J = 6.7 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (DMSO-d_6 + $CDCl_3$): δ = 154.34, 149.60, 147.33, 145.59, 135.42, 132.56, 132.14, 130.50, 128.84, 127.89, 126.33, 123.88, 118.22, 116.36, 115.70, 112.41, 16.21. HRMS (TOF MS) calcd for $C_{16}H_{13}N_4O^+$ 277.1089, found 277.1156 $[M+H]^+$.

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