Synthesis of 4-Hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones in the Presence of DABCO as an Efficient Organocatalyst

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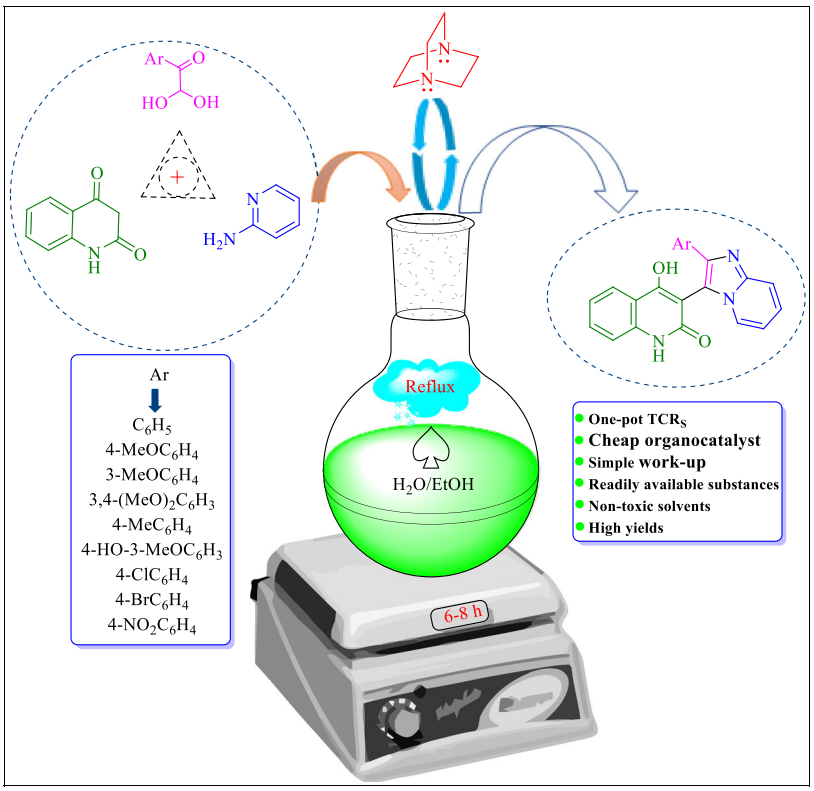


The one-pot, three-component, synthesis of a new series of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones in the presence of DABCO as a catalyst has been achieved using aryl glyoxal monohydrates, quinoline-2,4(1*H*,3*H*)-dione, and 2-aminopyridine in H_2O/EtOH under reflux conditions. The cheapness of organocatalyst, simple workup, operational simplicity, regioselectivity, and high yields are some advantages of this protocol.

INTRODUCTION

Chemical compounds with imidazopyridine scaffolds are an important class of bridgehead nitrogen heterocycle frameworks with privileged pharmaceutical applications [1]. Indeed, imidazo-fused heteroaromatics are the key structure in many marketed drugs, including saripidem, zolpidem, zolimidine, alpidem, soraprazan, olprinone, minodronic acid, miroprofen, necopidem, and cefozopran, or optically active GSK812397 [2] (Fig. 1).

Over the past years, a broad range of useful pharmacological compounds possessing imidazo[1,2-*a*] pyridine backbone have been reported as anticancer [3], antifungal [4], antibacterial [5], antiviral [6], antimalarial agents [7], antiprotozoal [8], anti-inflammatory [9], and inhibitors of mycobacterial adenosine triphosphate synthesis [10].

Current approaches for the synthesis of imidazo[1,2-*a*] pyridine structures include cyclocondensations of 2-aminopyridines to acetophenones [11], 1,3-dicarbonyl compounds [12], α,β-unsaturated ketones [13], α-halocarbonyl compounds [14], propargylic alcohols [15], or nitroolefins [16] and also one-pot, multicomponent reaction of 2-aminopyridines with aryl glyoxals and cyclic 1,3-dicarbonyls [17]. In addition, the coupling of aldehydes with 2-aminopyridines and alkynes or isonitriles (Gröbcke–Blackburn–Bienaymé reaction) in one-pot protocol was found to be a suitable process for the preparation of imidazo[1,2-*a*]pyridine compounds [18]. In recent years, some other novel synthetic strategies have

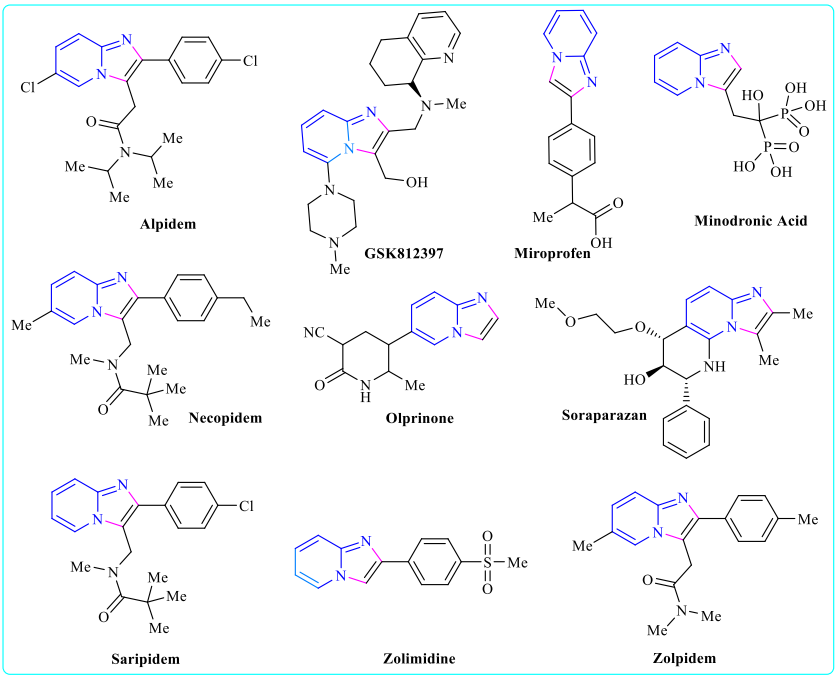


Figure 1. The drugs possessing an imidazo[1,2-*a*]pyridine moiety. [Color figure can be viewed at wileyonlinelibrary.com]

been developed. For instance, the transition metal-catalyzed C–H functionalization methods *via* direct cross-coupling reactions have been established by some chemists [19].

Although excessive progress has been attained, nevertheless, there is still a fundamental strategy need to announce new techniques for synthesis of imidazopyridines for drug development.

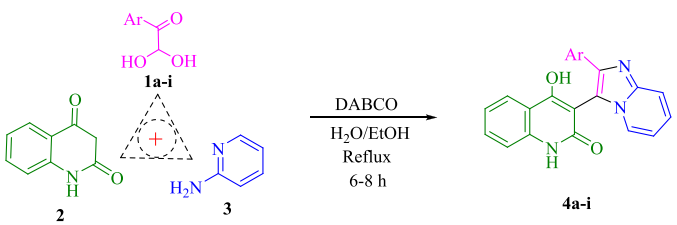
One-pot, multicomponent reaction strategy (MCRs) is a synthetic procedure in which several dissimilar starting reactants in one pot and single step combine together in a reaction vessel by several bond breaking and bond making to form a new heterocyclic compound. Among the most important advantages of MCRs is the generating of highly functionalized molecules without separating intermediary moiety, purification, workup steps, or swapping the solvents and no byproducts, which makes MCRs a tremendously ideal and eco-friendly reaction technique. Multicomponent reactions in green solvents and using green catalysts can be an incredible and important protocol in organic synthesis [20].

The catalysts play a key role in the synthesis of heterocyclic compounds toward green chemistry goals. In the catalyzed reaction, increasing the rate of chemical reaction by reducing the activation energy in the presence of only a very small amount of catalyst is possible. Appropriately catalyzed reactions can be performed at a shorter time, middle condition, requiring less hazardous substances and organic solvents [21].

We used DABCO as an organocatalyst in this work. Some of the advantages of this catalyst are the cheapness, impressively, readily availability, noncorrosive nature, nontoxic, and nonpolluting property [22].

According to our previous studies on the synthesis of a series of heterocyclic compounds through one-pot, multicomponent reactions [23], herein, we report the synthesis of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-

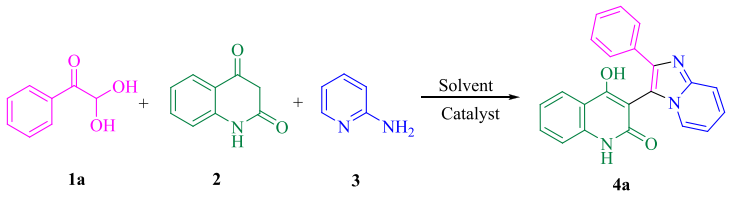
Scheme 1. Synthesis of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a–i**. [Color figure can be viewed at wileyonlinelibrary.com]



Ar = C_6H_5, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-MeC_6H_4, 4-HO-3-$MeOC_6H_3$, 4-ClC_6H_4, 4-BrC_6H_4, 4-$NO_2C_6H_4$

Table 1

Optimization of the reaction conditions for the synthesis of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a**.[a]



1a **2** **3** **4a**

Entry	Catalyst	Solvent (v/v, %)	Temperature (°C)	Time (h)	Yield (%)[b]
1	—	H_2O	RT	48	—
2	—	EtOH	RT	48	—
3	—	H_2O/EtOH (1:1)	RT	48	—
4	—	H_2O/EtOH (1:1)	Reflux	48	—
5	TPAB	H_2O/EtOH (1:1)	Reflux	24	Trace
6	SBA-15	H_2O/EtOH (1:1)	Reflux	24	Trace
7	$ZnCl_2$	H_2O/AcOH (1:1)	Reflux	24	28
8	*p*-TSA	H_2O/EtOH (1:1)	Reflux	24	Trace
9	*p*-TSA	H_2O	Reflux	24	Trace
10	*p*-TSA	AcOH	Reflux	10	37
11	L-Cysteine	H_2O	Reflux	24	Trace
12	L-Proline	H_2O/AcOH (1:1)	Reflux	24	Trace
13	L-Proline	H_2O/EtOH (1:1)	Reflux	24	—
14	Sulfamic acid	H_2O/EtOH (1:1)	Reflux	24	—
15	Et_3N	H_2O/EtOH (1:1)	Reflux	24	—
18	K_2CO_3	H_2O	Reflux	24	—
17	K_2CO_3	EtOH	Reflux	24	—
18	DABCO	Dioxane	Reflux	18	—
19	DABCO	DMF	Reflux	18	—
20	DABCO	EtOH	Reflux	8	49
21	DABCO	H_2O	Reflux	8	55
22	**DABCO**	**H_2O/EtOH (1:1)**	**Reflux**	**8**	**74**
23	DABCO	H_2O/EtOH (1:1)	RT	10	63

The optimum condition for choosing the reaction condition is shown in bold text. "—" indicate no reaction.
RT, room temperature.
[a]Reaction was performed with **1a** (1 mmol), **2** (1 mmol), **3** (1 mmol), and catalysts (30 mol %).
[b]Isolated yield.

yl)quinolin-2(1*H*)-ones **4a–i** *via* a one-pot, three-component reaction of aryl glyoxal monohydrates **1a–i**, quinoline-2,4(1*H*,3*H*)-dione (**2**), and 2-aminopyridine (**3**) in H_2O/EtOH using DABCO as an efficient organocatalyst under reflux conditions. The synthesized new heterocyclic products **4a–i** may have biological and pharmaceutical activities (Scheme 1).

RESULTS AND DISCUSSION

Our investigation, for the synthesis of various 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-one scaffolds through a one-pot, three-component strategy, started with phenyl glyoxal monohydrate **1a** (1 mmol), quinoline-2,4(1*H*,3*H*)-dione (**2**, 1 mmol), and 2-

Table 2

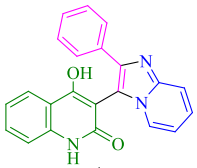
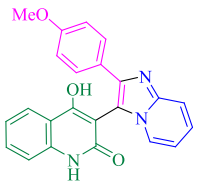
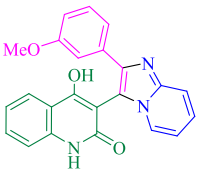
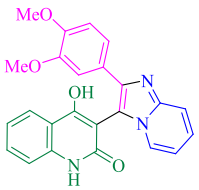
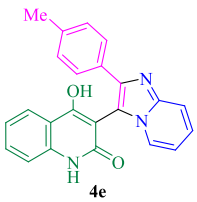
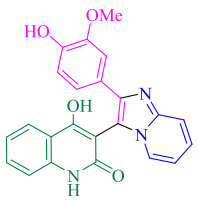
Investigating the effect of various molar ratio of catalyst DABCO for the synthesis of compound **4a**.

Entry	Catalyst (mol %)	Solvent (v/v, %)	Temperature (°C)	Time (h)	Yield (%)
1	DABCO (40)	H_2O/EtOH (1:1)	—	6	68
2	DABCO (35)	H_2O/EtOH (1:1)	—	6	73
3	DABCO (25)	H_2O/EtOH (1:1)	—	6	79
4	**DABCO (20)**	**H_2O/EtOH (1:1)**	**—**	**6**	**82**
5	DABCO (15)	H_2O/EtOH (1:1)	—	6	77
6	DABCO (10)	H_2O/EtOH (1:1)	—	6	75

"—" indicate reflux condition.
The optimum condition for choosing the reaction condition is shown in bold text.

Table 3

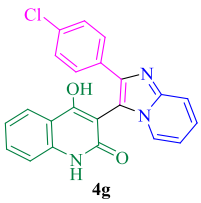
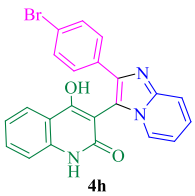
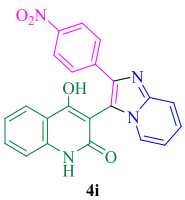
Synthesis of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a–i**.[a]

Entry	Imidazo[1,2-*a*]pyridin	Reaction time (h)	Yield (%)[b]	mp (°C)	Color
1	 **4a**	6	82	337–338	White
2	 **4b**	6	90	312–313	White
3	 **4c**	6	85	325–326	White
4	 **4d**	7	93	331–332	White
5	 **4e**	6	84	311–312	White
6	 **4f**	8	90	228–229	White

(*Continues*)

Table 3

(*Continued*)

Entry	Imidazo[1,2-*a*]pyridin	Reaction time (h)	Yield (%)[b]	mp (°C)	Color
7	 **4g**	7	88	349–350	White
8	 **4h**	7	87	356–357	White
9	 **4i**	8	84	329–330	Yellow

[a]Molar ratio of reactants: **1a–i** (1 mmol), **2** (1 mmol), **3** (1 mmol), and DABCO (20 mol %) in H_2O/EtOH (1:1) (8 mL) under reflux condition for 6–8 h.
[b]Isolated yield after washing with water and cold ethanol.

aminopyridine (**3**, 1 mmol), as model substrates in various reaction conditions (Table 1).

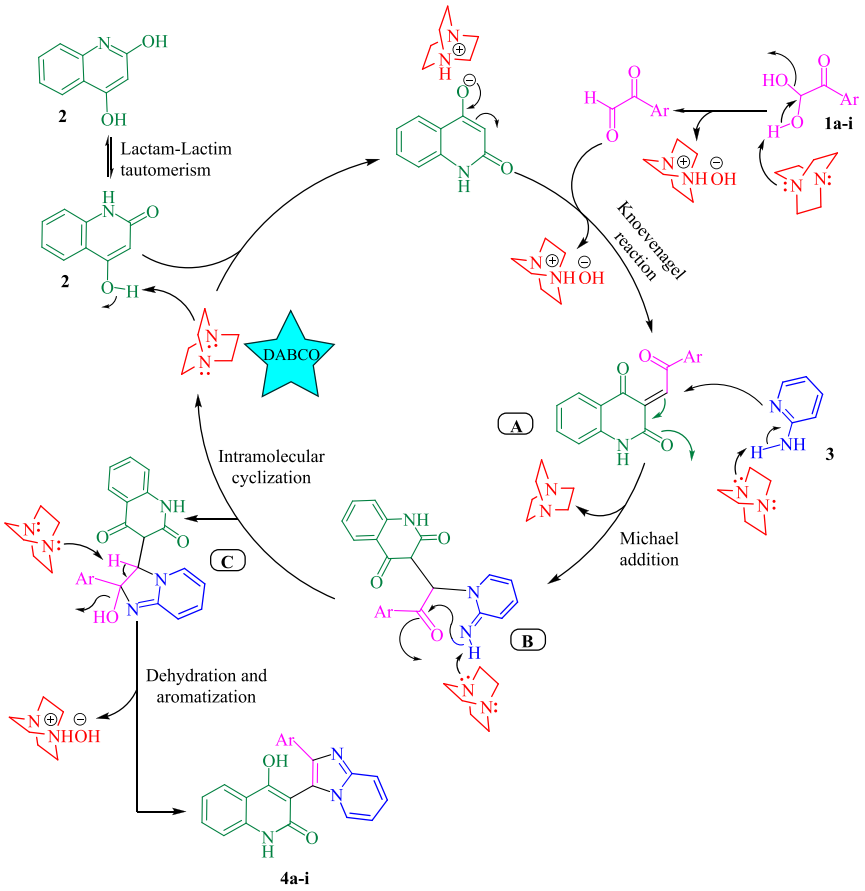
Firstly, in order to find the optimal reaction conditions, we examined this condensational reaction in the absence of a catalyst with different solvents, but no product formation was stirred at room temperature to reflux conditions observed even after 48 h (Table 1, entries 1–4). The model reaction was carried out in the presence of catalysts such as SBA-15 and TPAB (tetrapropylammonium bromide) in H_2O/EtOH as a solvent under reflux for 24 h, which gave a trace amount of desired product (Table 1, entries 5 and 6). Then, the reaction was repeated in the presence of several common acidic catalysts such as $ZnCl_2$, *p*-TSA (*p*-toluene sulfonic acid), L-cysteine, L-proline, and sulfamic acid using various solvents under reflux conditions for 24 h, which gave the desired product in 0–37% (Table 1, entries 7–14). Using basic catalysts such as Et_3N, K_2CO_3, and DABCO in different solvents under reflux conditions gave no product (Table 1, entries 15–19). When the reaction was carried out in EtOH or H_2O in the presence of DABCO as a catalyst under reflux conditions, the desired product was formed in 49 and 55%, respectively, after 8 h (Table 1, entries 20 and 21). The best result was obtained in terms of yield (74%) and reaction time (6 h) when the reaction was performed using DABCO in H_2O/EtOH (1:1) under reflux conditions (Table 1, entry 22). Also, when the reaction was carried out at room temperature, the desired product was formed in 63% yield (Table 1, entry 23).

Using the different molar ratio of catalyst was also studied, which gave the product in 68–82% yield (Table 2, entries 1–6). Changing the molar ratio of catalysts had a high effect on the efficiency of the reaction. The best result in terms of yield (82%) and reaction time (6 h) was obtained using DABCO (20 mol %) as a catalyst in H_2O/EtOH (1:1) under reflux conditions (Table 2, entry 4).

To show the generality of this new method, the reactions were performed using various aryl glyoxal monohydrates **1a–i**, quinoline-2,4(1*H*,3*H*)-dione (**2**), and 2-aminopyridine (**3**) to give the desired 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a–i** under the optimized reaction conditions (Table 3).

The aryl glyoxal monohydrates as a starting compound in this text were all prepared by oxidation of the corresponding acetophenones with SeO_2 in H_2O : dioxane under reflux condition [24].

Scheme 2. Proposed mechanism for the synthesis of imidazo[1,2-*a*]pyridines scaffolds **4a–i**. [Color figure can be viewed at wileyonlinelibrary.com]



The plausible mechanisms for the formation of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a–i** are shown in Scheme 2.

In the first step, DABCO converted the aryl glyoxal monohydrates **1a–i** to the aryl glyoxals and quinoline-2,4(1*H*,3*H*)-dione (**2**) to its enolate ion by dehydration and removing a water molecule in each case. The Knoevenagel condensation between previously mentioned reactants leads to the formation of intermediate **A**. The regioselective Michael addition of 2-aminopyridine (**3**) to the intermediate **A** in the presence of catalyst leads to the formation of intermediate **B**, which was converted to intermediate **C** by intramolecular cyclization. Finally, the desired products **4a–i** were obtained by loss of a water molecule from intermediate **C** in the presence of the catalyst (Scheme 2).

Elucidation of the structures of all target molecules **4a–i** was achieved using their ^{1}H-NMR, ^{13}C-NMR, Fourier transform infrared (FTIR), mass, and high-resolution mass spectrometry (HRMS) spectral data.

The FTIR spectra of **4a–i** showed absorption bonds due to vibrations of the NH and OH group at 3450–3160 cm^{-1}. The absorptions at 1635–1617 cm^{-1} belong to the secondary amid carbonyl groups. The ^{1}H-NMR spectra showed sharp singlets for the hydroxyl groups of products at δ = 11.51–11.68 ppm, which were disappeared by addition of D_2O. Unfortunately, the NH group of products could not be recognized because of overlap by impurity peaks of the solvent. The aromatic protons were located at δ = 6.69–8.23 ppm. In the ^{13}C-NMR spectra, the peaks at δ = 162.9–163.6 and δ = 162.3–162.7 ppm are due to the secondary amid carbonyl and C–OH groups, respectively. The signals located around δ = 92.3–151.0 ppm were assigned to the aromatic carbons. Mass spectra showed the molecular ions for all products except **4h**.

CONCLUSIONS

In conclusion, we have reported a green, facile, and remarkable protocol for the synthesis of a new series of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones **4a–i**, by one-pot, three-component reaction of aryl glyoxal monohydrates, quinoline-2,4(1*H*,3*H*)-dione, and 2-aminopyridine by using DABCO (20 mol %) as an organocatalyst in water/ethanol under reflux in high

yields. Some significant advantages of this procedure are the use of cheap and efficient organocatalysts, available material, simple workup approach, and high regioselectivity.

EXPERIMENTAL

All chemicals used in this text were obtained from Sigma-Aldrich (St. Louis, MO) and Merck (Kenilworth, NJ) companies and were used without further purification. Melting points were determined on a Philip Harris C4954718 apparatus (2 Gregory St, Hyde SK14 4TH, UK) and are uncorrected. The progress of the reactions was monitored by thin-layer chromatography on Merck's silica gel plates. Infrared spectra were recorded on a Thermo Nicolet Nexus 670 FTIR instrument (University of Colorado Boulder, Benson Earth Sciences, USA) using KBr discs. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Advance AQS 300-MHz spectrometer (Bruker Corp., Billerica, MA) at 300 and 75.5 MHz, respectively. Chemical shifts were measured in DMSO-d_6 as solvent relative to tetramethylsilane (TMS) as the internal standard. Mass spectra and high-resolution mass spectra were recorded on a Kratos MS 25RF spectrometer (Kratos Analytical Ltd, UK), and relative abundance of fragments is quoted in parentheses after the *m*/*z* values.

General procedure for the synthesis of 4-hydroxy-3-(2-arylimidazo[1,2-*a*]pyridin-3-yl)quinolin-2(1*H*)-ones 4a–i. To a suspension of quinoline-2,4(1*H*,3*H*)-dione (**2**, 1 mmol) in H_2O : EtOH (1:1) (8 mL), DABCO (20 mol %) was added. The reaction mixture was stirred under reflux condition for 10 min to dissolve the reactant. Then aryl glyoxal monohydrates **1a–i** (1 mmol) and 2-aminopyridine (**3**, 1 mmol) were added to the reaction mixture, which was stirred under reflux for appropriate times as shown in Table 3. The development of the reaction was controlled by thin-layer chromatography ($CHCl_3$: MeOH/10:1 as eluent). After completion of the reaction, the residue was filtered and washed with water and cold ethanol to give the desired products **4a–i** in high yields (82–93%).

4-Hydroxy-3-(2-phenylimidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4a). White powder; yield 82%; mp: 337–338°C; FTIR (KBr) ν_{max}: 3385, 3072, 2963, 2666, 1615, 1579, 1522, 1433, 1407, 1345, 1152, 751 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.58 (s, 1H, exchanged by D_2O addition, OH), 7.95 (d, *J* = 8.4 Hz, 1H, Ar), 7.89 (d, *J* = 6.3 Hz, 1H, Ar), 7.80 (d, *J* = 7.2 Hz, 2H, Ar), 7.66 (d, *J* = 8.7 Hz, 1H, Ar), 7.60 (t, *J* = 6.6 Hz, 1H, Ar), 7.41–7.15 (m, 6H, Ar), 6.85 (t, *J* = 6 Hz, 1H, Ar) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 163.0, 162.5, 145.1, 143.0, 139.7, 135.2, 131.0, 129.7, 128.6, 128.1, 127.8, 126.7, 125.9, 124.4, 122.8, 120.8, 117.9, 115.7, 113.6, 100.2 ppm; LRMS (EI, 70 eV) *m*/*z* (%): 354 $[M + 1]^+$ (39), 353 $[M]^+$ (100), 337 (18), 336 (65), 205 (27), 120 (14), 78 (23); HRMS (ESI): *m*/*z* $[M]^+$ calcd for $C_{22}H_{15}N_3O_2$: 353.1164; found: 353.1188.

4-Hydroxy-3-(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4b). White powder; yield 90%; mp: 312–313°C; FTIR (KBr) ν_{max}: 3366, 3274, 3183, 2913, 2794, 1616, 1578, 1514, 1441, 1249, 1187, 1023, 758 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.55 (s, 1H, exchanged by D_2O addition, OH), 7.92 (d, *J* = 8.7 Hz, 1H, Ar), 7.86 (d, *J* = 6.9 Hz, 1H, Ar), 7.72 (d, *J* = 8.4 Hz, 2H, Ar), 7.62 (d, *J* = 9 Hz, 1H, Ar), 7.57 (t, *J* = 7.8 Hz, 1H, Ar), 7.36 (d, *J* = 8.1 Hz, 1H, Ar), 7.28 (t, *J* = 7.5 Hz, 1H, Ar), 7.21 (t, *J* = 7.5 Hz, 1H, Ar), 6.89 (d, *J* = 8.4 Hz, 2H, Ar), 6.83 (t, *J* = 7.2 Hz, 1H, Ar), 3.71 (s, 3H, OMe) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 163.5, 162.7, 149.1, 144.8, 142.5, 139.8, 130.9, 129.4, 127.5, 127.2, 126.5, 125.4, 124.3, 123.2, 122.7, 120.8, 117.5, 115.3, 113.0, 99.9, 54.5 ppm; LRMS (EI, 70 eV) *m*/*z* (%): 383 $[M]^+$ (10), 324 (12), 267 (12), 230 (16), 205 (17), 193 (22), 153 (12), 134 (16), 120 (20), 119 (46), 104 (16), 79 (25), 78 (100), 77 (45), 51 (12); HRMS (ESI): *m*/*z* $[M]^+$ calcd for $C_{23}H_{17}N_3O_3$: 383.1270; found: 383.1242.

4-Hydroxy-3-(2-(3-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4c). White powder; yield 85%; mp: 325–326°C; FTIR (KBr) ν_{max}: 3414, 3265, 3087, 2944, 2839, 2794, 1625, 1589, 1526, 1492, 1236, 1048, 748 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.61 (s, 1H, exchanged by D_2O addition, OH), 7.94 (d, *J* = 8.4 Hz, 2H, Ar), 7.67 (d, *J* = 9 Hz, 1H, Ar), 7.60 (t, *J* = 7.5 Hz, 1H, Ar), 7.42–7.28 (m, 4H, Ar), 7.27–7.14 (m, 2H, Ar), 6.93–6.76 (m, 2H, Ar), 3.64 (s, 3H, OMe) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6): δ: 163.0, 162.5, 149.5, 145.0, 142.7, 139.8, 136.7, 133.1, 131.0, 130.7, 128.8, 126.4, 125.3, 124.4, 122.8, 120.4,, 118.4, 115.6, 113.8, 113.4, 111.4, 100.2, 56.0 ppm; LRMS (EI, 70 eV) *m*/*z* (%): 384 $[M + 1]^+$ (27), 383 $[M]^+$ (100), 336 (32), 323 (12), 221 (22), 192 (14), 120 (22), 78 (12); HRMS (ESI): *m*/*z* $[M]^+$ calcd for $C_{23}H_{17}N_3O_3$: 383.1270; found: 383.1259.

3-(2-(3,4-Dimethoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-4-hydroxyquinolin-2(1H)-one (4d). White powder; yield 93%; mp: 331–332°C; FTIR (KBr) ν_{max}: 3412, 3273, 3083, 2933, 2820, 2320, 1628, 1590, 1521, 1443, 1248, 1161, 760 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.56 (s, 1H, exchanged by D_2O addition, OH), 7.94 (d, *J* = 8.4 Hz, 1H, Ar), 7.09 (d, *J* = 6.3 Hz, 1H, Ar), 7.63 (d, *J* = 8.7 Hz, 1H, Ar), 7.57 (t, *J* = 7.2 Hz, 1H, Ar), 7.48 (s, 1H, Ar), 7.73 (d, *J* = 8.4 Hz, 1H, Ar), 7.35–7.24 (m, 2H, Ar), 7.21 (t, *J* = 7.5 Hz, 1H, Ar), 6.90 (d, *J* = 8.4 Hz, 1H, Ar), 6.83 (t, *J* = 6.9 Hz, 1H, Ar), 3.71 (s, 3H, OMe), 3.23 (s, 3H, OMe) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ:

163.5, 162.7, 148.8, 145.5, 144.7, 142.5, 140.5, 139.8, 133.0, 130.9, 127.8, 126.5, 125.3, 124.4, 122.7, 120.4, 118.4, 115.9, 114.7, 113.2, 100.1, 56.5, 54.5 ppm; LRMS (EI, 70 eV) *m/z* (%): 413 $[M]^+$ (16), 326 (13), 297 (10), 204 (10), 193 (17), 179 (10), 193 (22), 145 (33), 120 (47), 119 (33), 105 (20), 91 (25), 78 (88), 77 (60), 69 (100), 60 (31), 57 (71), 55 (53); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{24}H_{19}N_3O_4$: 413.1376; found: 413.1337.

4-Hydroxy-3-(2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4e). White powder; yield 84%; mp: 311–312°C; FTIR (KBr) ν_{max}: 3386, 3319, 3087, 2921, 2804, 1628, 1617, 1578, 1522, 1445, 1238, 761 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.54 (s, 1H, exchanged by D_2O addition, OH), 7.92 (d, *J* = 8.7 Hz, 1H, Ar), 7.87 (d, *J* = 5.7 Hz, 1H, Ar), 7.68 (d, *J* = 8.5 Hz, 2H, Ar), 7.62–7.56 (m, 2H, Ar), 7.36 (d, *J* = 8.4 Hz, 1H, Ar), 7.35 (t, *J* = 7.8 Hz, 1H, Ar), 7.21 (t, *J* = 6.9 Hz, 1H, Ar), 7.12 (d, *J* = 8.1 Hz, 2H, Ar), 6.83 (t, *J* = 6.6 Hz, 1H, Ar), 2.49 (s, 3H, Me) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 163.1, 162.6, 151.0, 149.9, 148.8, 145.0, 143.1, 139.7, 136.9, 132.5, 130.2, 128.0, 125.9, 124.3, 122.7, 118.1, 115.7, 114.6, 113.3, 100.1, 20.4 ppm; LRMS (EI, 70 eV) *m/z* (%): 368 $[M + 1]^+$ (58), 367 $[M]^+$ (100), 350 (81), 310 (15), 248 (13), 219 (16), 183 (13), 120 (11), 78 (15); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{23}H_{17}N_3O_2$: 367.1321; found: 367.1355.

4-Hydroxy-3-(2-(4-hydroxy-3-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4f). White powder; yield 90%; mp: 228–229°C; FTIR (KBr) ν_{max}: 3434, 3261, 3098, 2947, 2804, 2763, 2661, 1617, 1578, 1522, 1446, 1401, 1238, 749 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.51 (s, 1H, exchanged by D_2O addition, OH), 9.02 (s, 1H, exchanged by D_2O addition, OH), 7.92 (d, *J* = 8.4 Hz, 2H, Ar), 7.86 (d, *J* = 5.7 Hz, 1H, Ar), 7.71–7.49 (m, 2H, Ar), 7.48–7.18 (m, 4H, Ar), 6.82 (t, *J* = 6.6 Hz, 1H, Ar), 6.69 (d, *J* = 8.4 Hz, 1H, Ar), 3.58 (s, 3H, OMe) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 163.6, 162.7, 147.7, 146.6, 144.6, 142.7, 139.8, 138.0, 136.4, 135.1, 130.7, 126.4, 124.4, 122.7, 120.8, 119.0, 116.6, 116.0, 114.7, 113.0, 112.1, 100.0, 58.6 ppm; LRMS (EI, 70 eV) *m/z* (%): 399 $[M]^+$ (11), 310 (10), 236 (10), 218 (16), 193 (13), 168 (11), 146 (16), 120 (51), 105 (11), 92 (34), 78 (100), 57 (27); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{23}H_{17}N_3O_4$: 399.1219; found: 399.1278.

3-(2-(4-Chlorophenyl)imidazo[1,2-a]pyridin-3-yl)-4-hydroxyquinolin-2(1H)-one (4g). White powder; yield 88%; mp: 349–350°C; FTIR (KBr) ν_{max}: 3215, 3092, 2950, 1630, 1582, 1521, 1410, 1255, 1410, 1255, 1098, 844, 755 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.61 (s, 1H, exchanged by D_2O addition, OH), 7.93 (d, *J* = 8.7 Hz, 1H, Ar), 7.89 (d, *J* = 7.2 Hz, 1H, Ar), 7.79 (d, *J* = 8.1 Hz, 2H, Ar), 7.65 (d, *J* = 9 Hz, 1H, Ar), 7.58 (t, *J* = 7.8 Hz, 1H, Ar), 7.43–7.37 (m, 3H, Ar), 7.32 (t, *J* = 7.5 Hz, 1H, Ar), 7.23 (t, *J* = 7.8 Hz, 1H, Ar), 6.83 (t, *J* = 6.3 Hz, 1H, Ar) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 163.0, 162.4, 145.2, 142.0, 139.8, 134.2, 132.4, 131.1, 129.8, 127.8, 127.5, 124.7, 123.0, 120.9, 118.0, 116.9, 115.5, 113.9, 104.0, 100.0 ppm; LRMS (EI, 70 eV) *m/z* (%): 389 $[M + 2]^+$ (40), 387 $[M]^+$ (100), 372 (14), 370 (47), 330 (16), 294 (12), 248 (17), 239 (20), 221 (33), 205 (33), 193 (32), 154 (23), 120 (64), 92 (43), 79 (43), 78 (99); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{22}H_{14}ClN_3O_2$: 387.0775; found: 387.0721.

3-(2-(4-Bromophenyl)imidazo[1,2-a]pyridin-3-yl)-4-hydroxyquinolin-2(1H)-one (4h). White powder; yield 87%; mp: 356–357°C; FTIR (KBr) ν_{max}: 3306, 3160, 3086, 2956, 2870, 1689, 1635, 1508, 1405, 1267, 1004, 760 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.61 (s, 1H, exchanged by D_2O addition, OH), 7.93 (d, *J* = 8.4 Hz, 1H, Ar), 7.89 (d, *J* = 6 Hz, 1H, Ar), 7.73 (d, *J* = 8.4 Hz, 2H, Ar), 7.60–7.35 (m, 2H, Ar), 7.52 (d, *J* = 8.1 Hz, 2H, Ar), 7.38 (d, *J* = 8.7 Hz, 1H, Ar), 7.31 (t, *J* = 7.8 Hz, 1H, Ar), 7.22 (t, *J* = 8.1 Hz, 1H, Ar), 6.85 (t, *J* = 6 Hz, 1H, Ar) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 162.9, 162.4, 145.2, 142.0, 139.8, 134.7, 132.9, 130.7, 130.1, 127.8, 126.6, 124.6, 122.8, 121.0, 118.1, 115.6, 113.9, 111.1, 100.0, 92.3 ppm; LRMS (EI, 70 eV) *m/z* (%): 279 (10), 167 (43), 149 (100), 113 (15), 85 (98), 83 (99), 71 (33), 70 (30), 57 (41); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{22}H_{14}BrN_3O_2$: 431.0269; found: 431.0211.

4-Hydroxy-3-(2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-yl)quinolin-2(1H)-one (4i). Yellow powder; yield 84%; mp: 329–330°C; FTIR (KBr) ν_{max}: 3437, 3395, 3073, 2964, 2929, 2859, 2360, 1635, 1597, 1516, 1443, 1045, 750 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 11.68 (s, 1H, exchanged by D_2O addition, OH), 8.22 (d, *J* = 8.1 Hz, 2H, Ar), 8.05 (d, *J* = 8.1 Hz, 2H, Ar), 7.82 (d, *J* = 5.1 Hz, 2H, Ar), 7.71 (d, *J* = 8.1 Hz, 1H, Ar), 7.62 (t, *J* = 8.1 Hz, 1H, Ar), 7.43–7.23 (m, 2H, Ar), 7.24 (t, *J* = 8.1 Hz, 1H, Ar), 6.88 (t, *J* = 6.6 Hz, 1H, Ar) ppm; ^{13}C-NMR (75.5 MHz, DMSO-d_6) δ: 162.9, 162.3, 146.6, 145.5, 142.0, 141.0, 140.0, 132.8, 131.2, 128.7, 127.3, 126.6, 126.3, 125.4, 125.2, 123.1, 121.0, 115.9, 115.5, 99.8 ppm; LRMS (EI, 70 eV) *m/z* (%): 398 $[M]^+$ (10), 350 (10), 220 (12), 205 (29), 188 (18), 149 (33), 120 (33), 119 (58), 103 (25), 91 (43), 83 (41), 85 (95), 78 (100), 77 (89), 70 (25), 57 (92); HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{22}H_{14}N_4O_4$: 398.1015; found: 398.1099.

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