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Article

Eosin Y-Catalyzed Synthesis of 3-Aminoimidazo[1,2-*a*]Pyridines via the HAT Process under Visible Light through Formation of the C−N Bond

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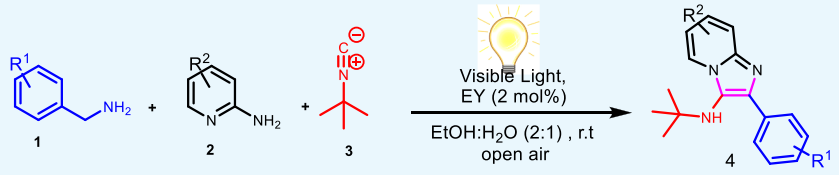

 # Cheap eosin Y as a photocatalyst
 # Hydrogen atom transfer (HAT) catalysis
 # Visible light irradiation, one pot procedure high yield
 # room temperature reaction, environmental friendly solvent,
 # New C-C and C-N bonds are formed

ABSTRACT: A comfortable, environment-friendly, and metal-free approach for synthesizing the biologically important moiety aminoimidazopyridine through the multicomponent reaction of benzylamine, 2-aminopyridine, and *t*-butyl isocyanide under visible light using eosin Y as a photocatalyst has been developed. Inexpensive, nontoxic, the effortless accessibility of starting materials, and nonparticipation of particular glassware and a photoreactor system are important qualities of the current approach. Strangely, the mild conditions, environment-friendly, and enumerating tolerance of an extensive range of both electron-donating and electron-withdrawing groups are additional features of the approach.

INTRODUCTION

Recently, the visible-light-initiated reaction is a flourishing, potent approach for the synthesis of bioactive organic compounds and is an emerging area of research to increase efficacy and synthetic utility. The visible-light-initiated organic reaction has received great devotion because visible light is a pure, inexpensive, benign, easily operational, inexhaustible, and eco-friendly fresh energy source.[1−3] Additionally, photoinduced reactions are relatively accelerated because the reaction vessel catches light from all directions.

Nowadays, photoredox catalysts have been developed as an easy and powerful tool for the activation of organic molecules in visible light and have been used for many unique and valuable chemical reactions.[4] In many cases, visible-light-driven synthetic transformation usually focuses on the excited condition of photocatalysts as they are more reducing and oxidizing than their ground states. Either visible light or photocatalyst with visible light has established unbelievable revolutions in the 21st century and allowed various useful synthetic transformations, which was until that time not approachable by traditional methods.[5] The substrate could be activated by the excited photocatalyst by single-electron transfer (SET) or through transfer of energy,[6a6b6c6d6e6f6g6h] leading to several competent synthetic conversions.[6]

Along with the above approach, a hydrogen atom transfer (HAT) path is another photoactivation mode.[7] In photocatalysis, there are usually three modes of the HAT process.[7a] In the first mode, the activated photocatalyst abstracts a hydrogen atom from the substrate. The catalytic cycle is then turned over to a newly produced intermediate via a reverse HAT (RHAT).[8] Second, one more catalyst is activated by the photocatalyst, which is already excited. After activation, one more catalyst stimulates the reaction through the hydrogen atom transfer pathway.[9] The next (3rd) path is the proton-coupled electron transfer (PCET) process, which involves the coordinated electron transfer and proton transfer from the reagent. This mode generates a radical that might be engaged in many transformation.[10] Meanwhile, the indirect hydrogen atom transfer and proton-coupled electron transfer paths are merely possible in the presence of some additional reagents, and direct

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hydrogen atom transfer catalysis among all these paths is the utmost proficient and economical procedure. However, the main restriction in place of the wide exploitation of the hydrogen atom transfer process is not sufficient for recognized photocatalysts,[7] for example, uranyl cations,[8e] polyoxometalates,[11] and aromatic ketone. Additionally, the aforesaid photocatalyst requires extra additives associated with unwanted side reactions. Hence, there is a need for metal-free and sustainable catalysts that could support direct hydrogen atom transfer routes.

Due to its low cost, easy handling, and environmentally friendly nature, eosin Y has been used as an economically and ecologically superior photocatalyst alternative to transition-metal complexes in organic photochemistry.

In recent times, eosin Y as an HAT photocatalyst has also been exposed[12] for C−H functionalization. On the basis of reported works, we proposed that eosin Y possibly will be the best hydrogen atom transfer photocatalyst and may abstract proton from benzylic C−H from benzylamine (Figure 1).

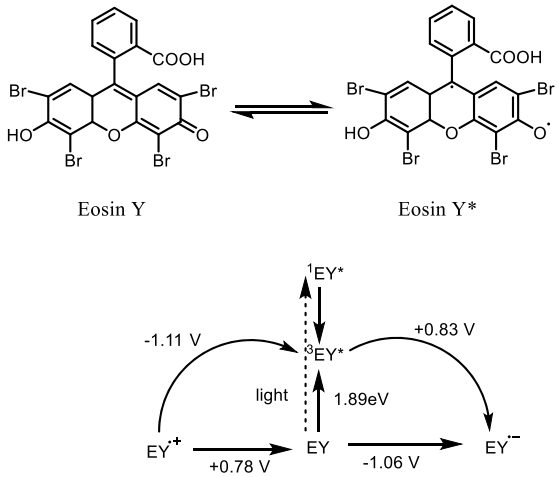

Figure 1. Photochemical and electrochemical properties of eosin Y.

Among the biologically active N-containing heterocyclic moieties, imidazo[1,2-*a*]pyridines attribute substantial devotion in the pharmacological manufacturing because of their extensive bioactivity as well as antifungal,[13a13b] antiviral,[13c13d] antitumor, antiprotozoal, antibacterial,[13e] antiinflammatory,[13f] antipyretic, analgesic, antiapoptotic, anxioselective, and hypnoselective activities.[13g] These compounds are not only of pharmaceutical importance, but they also have significant importance in materials science. In recent times, imidazo[1,2-*a*]pyridine moieties were joined with some commercially available drugs[13h-l] and used for the treatment of insomnia[13j] (zolpidem, A), anxiolytic agent (alpidem, B), and an agent for the treatment of peptic ulcer[13k] (zolimidine, C) (Figure 2). As a result, hard work carries on just before the development of new approaches for the preparation of imidazo[1,2-*a*]pyridines. Several approaches have been established to synthesize imidazo[1,2-*a*]pyridine such as condensation,[14a] oxidative coupling reaction,[14b] multicomponent reaction,[14c] aminooxygenation,[14d] hydroamination reaction,[14e] and tandem reaction.[14f]

Despite the above methods, there is a need for the buildout of effective and viable visible-light-prompted preparation of imidazo[1,2-*a*]pyridines using the photoinitiator eosin Y. As far as we are aware, preparation of imidazo[1,2-*a*]pyridines from multicomponent reaction of benzylamine, 2-aminopyridine, and *t*-butylisocyanide via photocatalysis has not been reported yet.

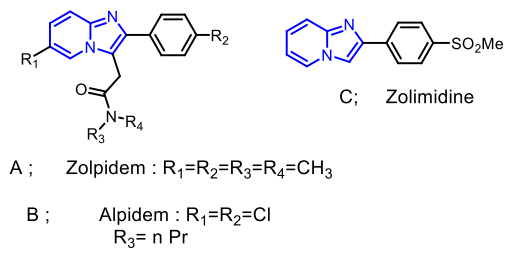

Figure 2. Some of the biologically active compounds containing the imidazo[1,2-*a*]pyridine framework.

In view of the above and as a part of our continuing research interest in the establishment of green and sustainable approaches for the production of biologically active compounds,[15] herein, we report for the first time a visible-light-promoted preparation of 3-aminoimidazo[1,2-*a*]pyridines via one-pot multicomponent reaction of benzylamine (**1**), 2-aminopyridine (**2**), and *t*-butylisocyanide (**3**) (Scheme 1).

RESULTS AND DISCUSSION

We started our observations using a visible-light-initiated multicomponent reaction of 2-aminopyridine (**2a**), benzylamine (**1a**), and *tert*-butylisonitrile (**3**) as a model substrate under various reaction conditions. First of all, various solvents (green as well as conventional solvents) were examined for model reaction with a 22 W white LED (light-emitting diode) under visible light in the presence of eosin Y (2 mol %). Only a trace amount of product was obtained when the reaction was carried out with dichloromethane, CH_3CN, DMF, and DMSO solvents for 12 h at RT (room temperature) in the presence of photocatalyst eosin Y (Table 1, entries 1−4). Pleasingly, the desired product **4a** was obtained in 45 and 51% yields with MeOH and EtOH, respectively (Table 1, entries 5 and 6). When the reaction was carried out in a mixture of a solvent such as EtOH/H_2O (1:1) and MeOH/H_2O (1:1), it led to a marginal increase in yield (81 and 63%, respectively) as well as the reduction in reaction time (6 h) (Table 1, entries 11 and 12). At this juncture, we thought of carrying out this reaction under the various ratios of ethanol and water solvents. To our surprise, this led to a noticeable increase in yield (95%) when the ratio (EtOH/H_2O) is 2:1 (Table 1, entry 13). The control examination showed that the dye is an inevitable component for this transformation (Table 1, entries 10).

Various organic photocatalysts such as rhodamine B, acridine red, and rose bengal were screened, but none of them would match the catalytic efficacy of eosin Y (Table 1, entries 7−9). The desired product was not obtained when the reaction was carried out at room temperature in the dark (Table 1, entry 19). This result indicates that visible light is a critical feature for this transformation. The energy source and intensities of visible light for the reaction were also optimized, and it was concluded that blue and green light were not able to give the desired yield of the product (Table 1, entries 15−18).

Additionally, to confirm the synthetic efficacy of the reaction, a gram-scale reaction was carried out (10 mmol scales), and it was found that reaction proceeded smoothly with the same efficiency, which emphasized the synthetic rewards of this procedure (Table 1, entry 20).

Now, we carried out this experiment using light of different intensities (8, 13, 15, 18, 22, and 32 W) to find the optimal intensity of visible light needed for this reaction. It was observed that the yields and reaction times were the same when 22 and 32

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Scheme 1. Synthesis of 3-Aminoimidazo[1,2-*a*]pyridines via One-Pot Multicomponent Reaction

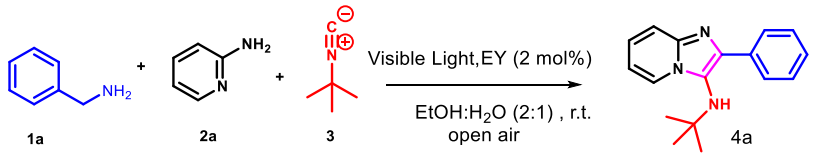
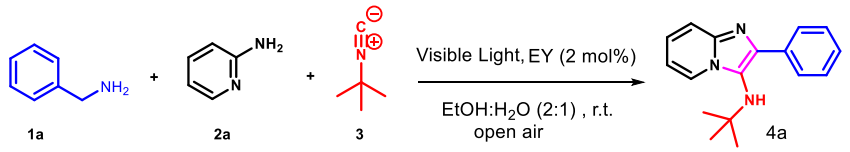


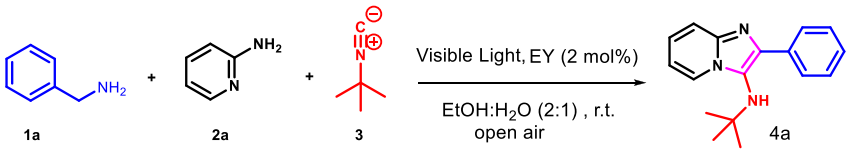
Table 1. Initial Optimization of the Reaction Conditions for the Synthesis of Compound 4a[a]



entry	catalyst (mol %)	light source	solvent	time (h)	yield[b]
1	eosin Y (2)	white light	DCM	12	trace
2	eosin Y (2)	white light	DMSO	12	trace
3	eosin Y (2)	white light	CH_3CN	12	trace
4	eosin Y (2)	white light	DMF	12	trace
5	eosin Y (2)	white light	MeOH	8	45
6	eosin Y (2)	white light	EtOH	6	51
7	rhodamine B (2)	white light	EtOH	12	32
8	rose bengal (2)	white light	EtOH	12	38
9	acridine red (2)	white light	EtOH	12	42
10	none	white light	EtOH	24	NR[c]
11	eosin Y (2)	white light	MeOH/H_2O (1:1)	6	63
12	eosin Y (2)	white light	EtOH/H_2O (1:1)	6	82
13	**eosin Y (2)**	**white light**	**EtOH/H_2O (2:1)**	**3**	**95**
14	eosin Y (2)	white light	EtOH/H_2O (5:1)	6	90
15[d]	eosin Y (2)	blue light	EtOH/H_2O (1:1)	12	54
16	eosin Y (2)	blue light	EtOH/H_2O (2:1)	6	56
17[e]	eosin Y (2)	green light	EtOH/H_2O (1:1)	12	78
18	eosin Y (2)	green light	EtOH/H_2O (2:1)	6	80
19	eosin Y (2)	dark	EtOH/H_2O (2:1)	12	trace
20[f]	eosin Y (2)	white light	EtOH/H_2O (2:1)	3	95

[a]Experimental conditions: 2-aminopyridine (1 mmol), benzylamines (1 mmol), *tert*-butylisonitrile (1 mmol), solvent (3 mL), room temperature, under visible-light irradiation (22 W, wavelength in the range of 380−780 nm). [b]Isolated yields. [c]NR = no reaction. [d]Blue light (455−660 nm). [e]Green light (520−525 nm). [f]The reaction was carried out on the 10 mmol scale.

Table 2. Effect of the Visible-Light Intensity on the Reaction[a]



entry	visible-light Intensity	time (h)	yield (%)[b]
1	8 W	8	75
2	13 W	6	82
3	15 W	4.5	85
4	18 W	4	89
5	22 W	3	95
6	32 W	3	95

[a]All reaction was carried out using **1** (1 mmol), **2** (1 mmol), and **3** (1 mmol) at room temperature under air. [b]Isolated yield.

W white-light-emitting diodes (LEDs) were used. However, when an LED of lower intensities was used, a marginal decrease in the yield and rate of reaction was observed (Table 2, entries 1−4). The use of an LED of higher wattage (32 W), on the other hand, did not have any substantial increase in the yield of the product or time of reaction (Figure 3).

Once ideal conditions for carrying out this reaction had been identified, the scope and limitations of the developed synthetic strategy were explored for the preparation of various 3-aminoimidazo-fused pyridine derivatives under the optimized conditions by reacting a variety of benzylamines with 2-aminopyridine and 5-bromo-2-aminopyridine and *tert*-butylisonitrile (Table 3). It has been indicated that the use of

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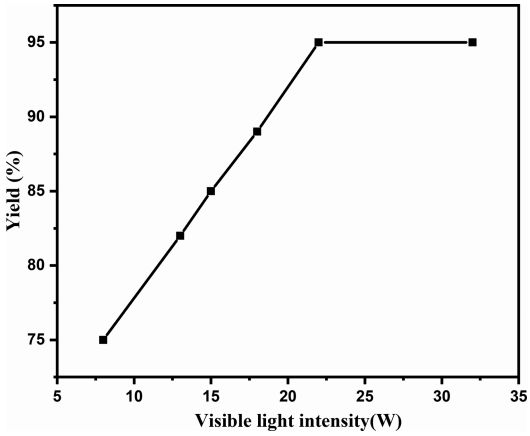

Figure 3. Yield (%) vs visible-light intensity for the preparation of *N*-(*tert*-butyl)-2-phenylimidazo[1,2-*a*]pyridin-3-amine.

benzylamine containing an electron-withdrawing group (−NO_2 and −F) led to higher yields and faster reaction while that of an electron-donating group (−Me and −OMe) on benzylamine slowed down the reaction and led to a reduction in the yield of the product.

In order to recognize the mechanism, some control experiments were carried out with the help of radical scavengers TEMPO and BHT (Scheme 2). There is an extreme reduction in the yield (9−10%) of the desired product **4a** in the presence of radical scavengers, confirming the involvement of the radical mechanism. Further, to examine the effect of O_2 (oxygen), the reaction was carried out under an oxygen balloon. However, there is no significant increase in the yield of the product, and a negligible amount of product was observed while the reaction was performed in the presence of argon, i.e., in the absence of oxygen. This result indicates that oxygen is necessary for this transformation.

To support the path of the reaction, a couple of control experiments were carried out (Scheme 3). The product **4a** was produced by the multicomponent reaction of benzylamine (1 mmol), 2-aminopyridine (1 mmol), and *tert*-butylisonitrile (1 mmol) under standard reaction conditions (eq a). We suspected the intermediacy of imine, and to confirm this, the reaction of 2-aminopyridine (1.0 equiv.) with benzylamine (1.0 equiv.) was carried out, which produced **5** (Scheme 3, eq b) under the optimized reaction conditions. This indicates imine to be a likely intermediate in the formation of product **4a**. To check the formation of the imine intermediate in the reaction, the benzylamine was irradiated with visible light in EtOH/H_2O (2:1) in the presence of eosin Y at room temperature, which gave imine **6** in good yield (Scheme 3, eq c). While a similar experiment was carried out under the same conditions with 2,4-DNP, no orange precipitate was formed (Scheme 3, eq d). This experiment omits the formation of benzaldehyde in the current procedure by using eosin Y as the photoredox catalyst.

According to previous reports[16,17] and on the basis of control experiments, a possible pathway for the overall process was proposed (Scheme 4). From the value of its redox potential, it is clear that eosin Y is not responsible for the oxidation of benzylamine because the SET mode for this reaction was not valid. Initially, excited eosin Y (EY*) was formed from eosin Y (EY) through excitation with visible light, which extracts the hydrogen atom from benzylic amine to generate intermediate A. Subsequently, the oxidation of intermediate A gives benzylimine intermediate B. Reaction of benzylimine B with 2-aminopyridine **2** leads to the formation of imine intermediate C with the liberation of ammonia, which is afterward attacked by the isocyanide **3** to provide intermediate D. This intermediate D is influenced by visible-light radiation to generate free radicals and is further cyclized followed by a 1,3-H shift to give the desired product.

CONCLUSIONS

In brief, an effective procedure to get various types of 3-aminoimidazo[1,2-*a*]pyridines through visible-light-initiated multicomponent reaction of benzylamine, 2-aminopyridine, and *t*-butylisocyanide has been developed using an economical HAT photocatalyst eosin Y dye at room temperature. Strangely, this approach is practically simple, profitable, environment-friendly, and additive-/metal-free and also shows outstanding compatibility with both electron-donating and electron-withdrawing functional groups containing benzylamine. This approach presents a promising alternative to the existing method, accordingly extending the scope of photocatalyzed reaction, which overcomes the problem associated with the environmentally notorious metal-catalyzed reaction.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all the chemicals were bought from E. Merck, Germany, and Sigma-Aldrich Chemicals, USA, and used as received. The progress of the reaction was measured through TLC (thin-layer chromatography) and visualized via UV light. A PerkinElmer FT-IR spectrometer was used to record infrared (IR) spectra. Elemental analysis (C, H, and N) was recorded using a PerkinElmer Microanalyzer. ^{1}H and ^{13}C NMR spectra were recorded through a Bruker Avance 500 MHz spectrometer (^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz), and the chemical shift was indicated in δ ppm, using TMS as an internal reference.

General Procedure for Synthesis of 3-Aminoimidazo-Fused Heterocycles. Benzylamine **1** (1 mmol), 2-amino-heterocycle **2** (1 mmol), isocyanide **3** (1 mmol), and eosin Y (2 mol %) were taken with 2:1 EtOH/H_2O (3 mL) in a 50 mL round bottom flask, which was furnished with a magnetic stirrer bar. This mixture was agitated with 22 W white LEDs under visible light at room temperature. When the reaction was completed (monitored by TLC), water was added to stop the reaction. Subsequently, ethyl acetate was added into it to extract aqueous layer. After that, it was dried over anhydrous $MgSO_4$. The crude product was obtained by evaporation of the solvent under reduced pressure. The purification of the crude product was carried out using column chromatography over silica gel (100−200 mesh) (ethyl acetate/hexane: 20/80) to provide pure products **4** in excellent yields.

*N-(tert-Butyl)-2-phenylimidazo[1,2-a]pyridin-3-amine (**4a**).* White solid (95%), mp 160−162 °C. IR (KBr, cm^{-1}): 3310 (NH), 2966 (sp^2 −CH), 2934 (sp^3 −CH), 1610, 1506, 1441, 1350, 1321, 1216, 1037, 756. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 6.9 Hz, 1H), 7.90 (d, J = 7.1 Hz, 2H), 7.56 (d, J = 9.0 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 6.2 Hz, 1H), 7.16−7.09 (m, 1H), 6.77 (t, J = 6.8 Hz, 1H), 3.16 (s, 1H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.81, 139.13, 134.91, 129.74, 128.29, 128.18, 127.47, 124.32, 123.54, 117.14, 111.48, 56.44, 30.29. Anal. calcd for $C_{17}H_{19}N_3$: C, 76.95; H, 7.22; N, 15.84; found: C,76.93; H,7.20; N, 15.80.

*N-(tert-Butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine (**4b**).* White solid (97%), mp 163−165 °C. IR (KBr,

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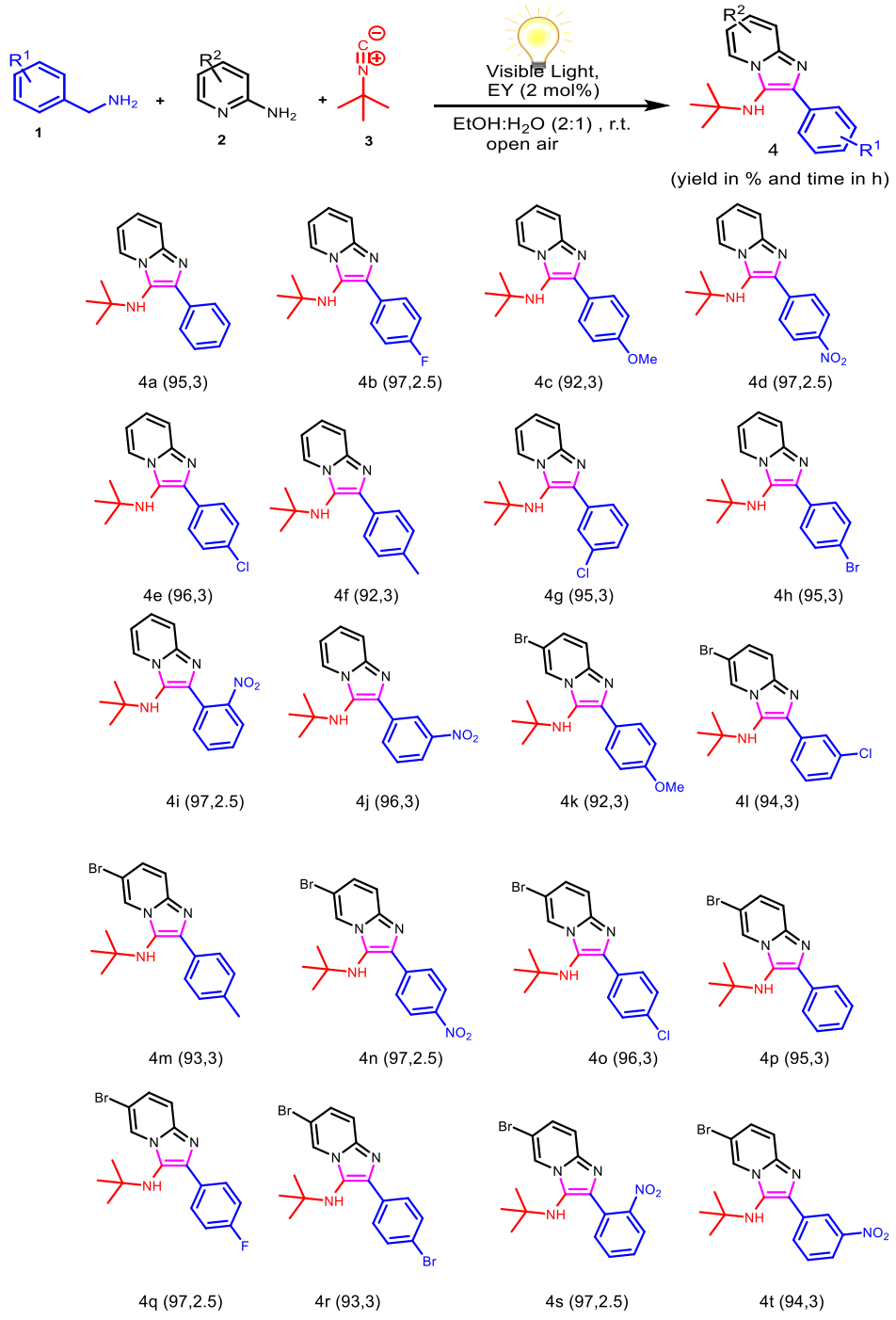
Table 3. Substrate Scope and Versatility of Reaction



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cm^{-1}): 3296 (N-H), 2966 (sp^2 −CH), 2934 (sp^3 −CH), 1610, 1506, 1441, 1350, 1321, 1216, 1037, 756. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 6.9 Hz, 1H), 7.94 (dd, J = 8.3, 6.1 Hz, 2H), 7.57 (d, J = 9.0 Hz, 1H), 7.20−7.15 (m, 1H), 7.13 (t, J = 7.7 Hz, 2H), 6.84−6.79 (m, 1H), 3.12 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.25, 141.71, 138.12, 129.88, 129.82, 124.58, 123.42, 117.03, 115.34, 115.17, 111.71, 56.43, 30.35. Anal. calcd for $C_{17}H_{18}FN_3$; C, 72.06; H, 6.40; N, 14.83 found: C, 72.03; H, 6.37; N, 14.80.

*N-(tert-Butyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (**4c**).* Off-white solid (92%), mp 142 °C. IR (KBr, cm^{-1}): 3315 (NH), 2968 (sp^2 −CH), 2925 (sp^3 −CH), 1630, 1513, 1433, 1366, 1339, 1206, 1027, 716. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 6.9 Hz, 1H), 7.87 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 9.0 Hz, 1H), 7.15−7.10 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.77 (t, J = 6.8 Hz, 1H), 3.85 (s, 3H), 3.12 (s, 1H), 1.05 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 159.09, 141.77, 139.13, 129.35, 127.57, 124.04, 123.41, 122.91, 116.97, 113.70, 111.30,

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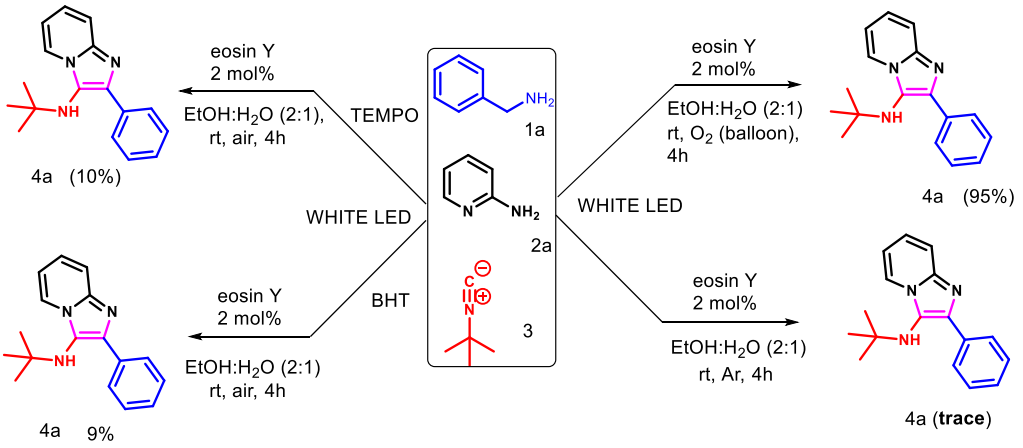
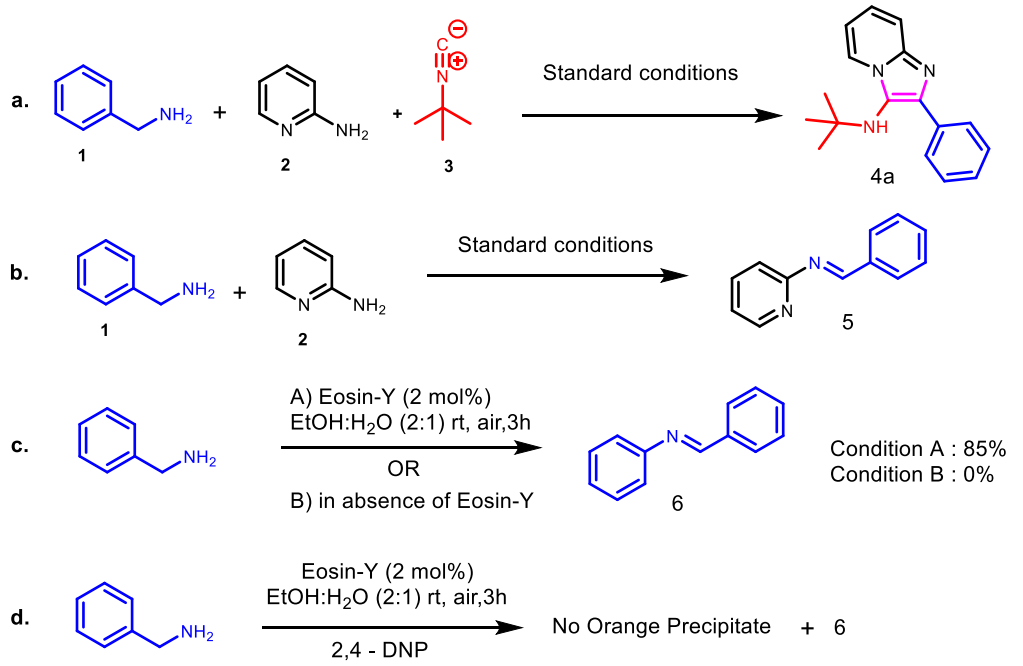
Scheme 2. Control Reaction Experiments



Scheme 3. Control Experiments



56.30, 55.23, 30.34. Anal. calcd for $C_{18}H_{21}N_3O$; C, 73.19; H, 7.17; N, 14.23 found: C, 73.16; H, 7.14; N, 14.21.

*N-(tert-Butyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4d**).* Reddish brown solid (97%), mp 205 °C. IR (KBr, cm^{-1}): 3303 (NH), 2935 (sp^2 −CH), 2907 (sp^3 −CH), 1584, 1476, 1424, 1343 (CN), 1315, 1191, 1007, 763. ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 4H), 8.22 (d, J = 6.9 Hz, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.26−7.20 (m, 1H), 6.86 (t, J = 7.2 Hz, 1H), 3.15 (s, 1H), 1.10 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.74, 142.27, 141.48, 136.67, 128.46, 125.41, 124.92, 123.59, 123.49, 117.51, 112.26, 56.85, 30.50. Anal. calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.77; H, 5.83; N, 18.03.

*N-(tert-Butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (**4e**).* Light orange solid (96%), mp 160−163 °C. IR (KBr, cm^{-1}): 3320 (NH), 2962 (sp^2 −CH), 2924 (sp^3 −CH), 1600, 1506, 1441, 1360 (CN), 1331, 1206, 1027, 746. ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 10.0 Hz, 1H), 7.39 (d, J = 11.2 Hz, 2H), 7.19−7.14 (m, 1H), 6.80 (t, J = 6.8 Hz, 1H), 3.10 (s, 1H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.89, 138.03, 133.42, 133.22, 131.05, 129.29, 129.04, 128.40, 124.59, 123.53, 123.45, 117.15, 111.67, 56.51, 30.28. Anal. calcd for $C_{17}H_{18}ClN_3$; C, 68.11; H, 6.05; N, 14.02 found: C, 68.08; H, 6.01; N, 14.00.

*N-(tert-Butyl)-2-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (**4f**).* White solid (92%), mp 170 °C. IR (KBr, cm^{-1}): 3320 (NH), 2962 (sp^2 −CH), 2924 (sp^3 −CH), 1600, 1506, 1441, 1360 (CN), 1331, 1206, 1027, 746. ^1H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 9.0 Hz, 1H), 7.25 (t, J = 14.3 Hz, 2H), 7.12 (t, J = 7.8 Hz, 1H), 6.75 (t, J = 6.7 Hz, 1H), 3.15 (s, 1H), 2.39 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.84, 139.35, 136.98, 132.16, 129.00, 127.99, 124.01, 123.47, 123.28, 117.09, 111.27, 56.19, 30.07, 21.43. Anal. calcd for $C_{18}H_{21}N_3$; C, 77.38; H, 7.58; N, 15.04 found: C, 77.35; H, 7.55; N, 15.01.

*N-(tert-Butyl)-2-(3-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (**4g**).* Orange solid (95%), mp 148 °C. IR (KBr, cm^{-1}): 3313 (NH), 2955 (sp^2 −CH), 2917 (sp^3 −CH), 1607, 1499, 1434, 1363 (CN), 1324, 1213, 1020, 752. ^1H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 6.9 Hz, 1H), 8.03 (t, J = 1.8 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.56 (d, J = 9.0 Hz, 1H), 7.36 (t, J = 7.8 Hz,

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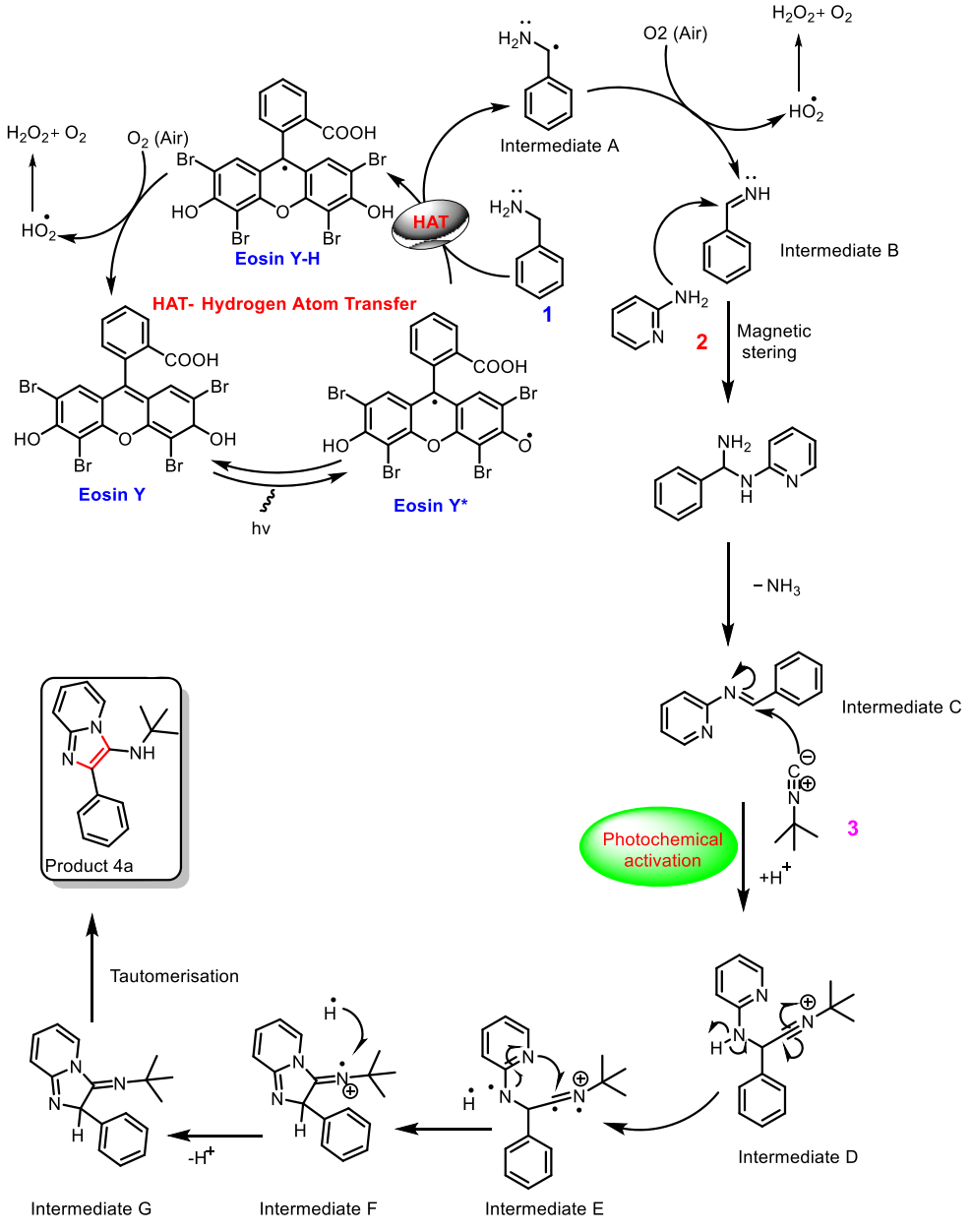
Scheme 4. Plausible Reaction Mechanism



1H), 7.29 (d, J = 7.8 Hz, 1H), 7.19−7.14 (m, 1H), 6.80 (t, J = 6.3 Hz, 1H), 2.98 (s, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.01, 137.84, 136.84, 134.20, 129.51, 128.10, 127.42, 126.12, 124.61, 123.46, 117.31, 111.70, 56.51, 30.42. Anal. calcd for $C_{17}H_{18}ClN_3$; C, 68.11; H, 6.05; N, 14.02 found: C, 68.09; H, 6.02; N, 14.01.

*2-(4-Bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine (**4h**).* Yellow solid (95%), mp 143−148 °C. IR (KBr, cm^{-1}): 3313 (NH), 2955 (sp^2 −CH), 2924 (sp^3 −CH), 1600, 1506, 1441, 1360 (CN), 1331, 1206, 1027, 746. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 6.9 Hz, 1H), 7.87 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.5 Hz, 3H), 7.19−7.13 (m, 1H), 6.80 (t, J = 7.2 Hz, 1H), 3.07 (s, 1H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.00, 138.17, 134.01, 131.40, 129.58, 124.52, 123.54, 123.44, 121.45, 117.25, 111.64, 55.91, 30.41. Anal. calcd for $C_{17}H_{18}BrN_3$; C, 59.31; H, 5.27; N, 12.21 found: C, 59.28; H, 5.24; N, 12.18.

*N-(tert-Butyl)-2-(2-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4i**).* Brown solid (97%), mp 183−185 °C. 3312 (NH), 2954 (sp^2 −CH), 2916 (sp^3 −CH), 1592, 1498, 1449, 1352, 1323, 1199, 1019, 738. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 6.9 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 9.0 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.20−7.13 (m, 1H), 6.81 (t, J = 6.8 Hz, 1H), 2.75 (s, 1H), 0.95 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.46 (s), 142.40 (s), 136.16 (s), 132.82 (s), 130.21 (s), 128.40 (s), 124.67 (s), 124.34 (d, J = 17.5 Hz), 123.34 (s), 117.70 (s), 111.79 (s), 30.04 (s). Anal. calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.76; H, 5.82; N, 18.02.

*N-(tert-Butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4j**).* White solid (96%), mp 171 °C. 3311 (NH), 2953 (sp^2 −CH), 2915 (sp^3 −CH), 1591, 1506, 1441, 1360, 1331, 1206, 1018, 737. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.44 (d, J = 7.7 Hz, 1H), 8.20 (d, J = 6.9 Hz, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.58 (dd, J = 20.1, 8.6 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H),

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6.83 (t, J = 6.5 Hz, 1H), 3.05 (s, 1H), 1.11 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.17 (s), 142.39 (s), 137.00 (d, J = 5.7 Hz), 133.75 (s), 129.20 (s), 124.85 (s), 124.07 (s), 123.37 (s), 122.63 (s), 121.95 (s), 117.62 (s), 111.94 (s), 30.56 (s). Anal. calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.75; H, 5.81; N, 18.01.

*6-Bromo-N-(tert-butyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (**4k**).* White solid (92%), mp 178 °C. IR (KBr, cm^{-1}): 3321 (NH), 2961 (sp^2 −CH), 2921 (sp^3 −CH), 1601, 1501, 1441, 1351, 1311, 1201, 1021, 741. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 1.7 Hz, 1H), 7.81 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 9.4 Hz, 1H), 7.13 (d, J = 9.4 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.09 (s, 1H), 1.01 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.16, 140.32, 140.20, 129.29, 127.22, 127.12, 123.54, 123.24, 117.69, 113.72, 106.09, 56.38, 55.21, 30.33. Anal. calcd for $C_{18}H_{20}BrN_3O$; C, 57.76; H, 5.39; N, 11.23 found: C, 57.72; H, 5.34; N, 11.20.

*6-Bromo-N-(tert-butyl)-2-(3-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (**4l**).* White solid (94%), mp 197−199 °C. IR (KBr, cm^{-1}): 3281 (N−H), 2951 (sp^2 −CH), 2921 (sp^3 −CH), 1609, 1491, 1431, 1341, 1311, 1209, 1037, 716. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 1.7 Hz, 1H), 7.99 (t, J = 1.6 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.44 (d, J = 9.4 Hz, 1H), 7.40−7.26 (m, 2H), 7.22 (d, J = 9.4 Hz, 1H), 3.08 (s, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.35, 138.85, 136.37, 134.30, 129.50, 128.08, 127.95, 127.72, 126.09, 124.04, 123.67, 118.05, 106.71, 56.63, 30.41. Anal. calcd for $C_{17}H_{17}BrClN_3$; C, 53.92; H, 4.52; N, 11.10 found: C, 53.90; H, 4.50; N, 11.08.

*6-Bromo-N-(tert-butyl)-2-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (**4m**).* Off-white solid (93%), mp 128−130 °C. IR (KBr, cm^{-1}): 3280 (N−H), 2946 (sp^2 −CH), 2914 (sp^3 −CH), 1610, 1501, 1461, 1363, 1341, 1231, 1067, 716. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.77 (d, J = 8.1 Hz, 2H), 7.42 (d, J = 9.4 Hz, 1H), 7.23 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 9.4 Hz, 1H), 3.15 (s, 1H), 2.39 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.44, 140.24, 137.44, 131.72, 129.08, 127.96, 127.29, 123.67, 123.63, 117.85, 106.23, 56.53, 30.31, 21.34. Anal. calcd for $C_{18}H_{20}BrN_3$; C, 60.34; H, 5.63; N, 11.73 found: C, 60.32; H, 5.61; N, 11.71.

*6-Bromo-N-(tert-butyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4n**).* Brown solid (97%), mp 203 °C. IR (KBr, cm^{-1}): 3300 (N−H), 3010 (sp^2 −CH), 2990 (sp^3 −CH), 1590, 1490, 1432, 1328, 1317, 1206, 1007, 766. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.29 (d, J = 8.9 Hz, 2H), 8.22 (d, J = 8.9 Hz, 2H), 7.46 (d, J = 9.4 Hz, 1H), 7.26 (d, J = 9.4 Hz, 1H), 3.08 (s, 1H), 1.10 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.91, 141.28, 140.80, 140.71, 137.87, 128.57, 128.49, 125.03, 123.65, 118.37, 107.18, 56.77, 30.49. Anal. calcd for $C_{17}H_{17}BrN_4O_2$; C, 52.46; H, 4.40; N, 14.39 found: C, 52.43; H, 4.37; N, 14.36.

*6-Bromo-N-(tert-butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (**4o**).* White solid (96%), mp 191 °C. IR (KBr, cm^{-1}): 3301 (N−H), 3001 (sp^2 −CH), 2984 (sp^3 −CH), 1598, 1498, 1424, 1326, 1317, 1210, 1012, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.37 (t, J = 9.0 Hz, 3H), 7.16 (d, J = 9.4 Hz, 1H), 3.07 (s, 1H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.33, 139.28, 133.31, 129.30, 128.49, 127.67, 123.82, 123.60, 117.95, 106.49, 56.49, 30.28. Anal. calcd for $C_{17}H_{17}BrClN_3$; C, 53.92; H, 4.52; N, 11.10 found: C, 53.91; H, 4.51; N, 11.09.

*6-Bromo-N-(tert-butyl)-2-phenylimidazo[1,2-a]pyridin-3-amine (**4p**).* White solid (95%), mp 230 °C. IR (KBr, cm^{-1}): 3290 (N−H), 3052 (sp^2 −CH), 2961 (sp^3 −CH), 1601, 1506, 1436, 1357, 1321, 1226, 1037, 775. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.88 (d, J = 9.4 Hz, 2H), 7.47−7.42 (m, 3H), 7.34 (t, J = 6.8 Hz, 1H), 7.20 (dd, J = 9.4, 1.9 Hz, 1H), 3.18 (s, 1H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.24, 134.53, 129.75, 128.39, 128.15, 127.76, 127.61, 127.45, 123.89, 123.75, 117.91, 56.58, 30.28. Anal. calcd for $C_{17}H_{18}BrN_3$; C, 59.31; H, 5.27; N, 12.21 found: C, 59.29; H, 5.25; N, 12.19.

*6-Bromo-N-(tert-butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine (**4q**).* White solid (97%), mp 215 °C. IR (KBr, cm^{-1}): 3280 (N−H), 2976 (sp^2 −CH), 2940 (sp^3 −CH), 1600, 1505, 1438, 1358, 1291, 1206, 1029, 776. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 2.4 Hz, 1H), 7.89 (dd, J = 8.8, 5.5 Hz, 2H), 7.44 (d, J = 9.8 Hz, 1H), 7.22 (d, J = 9.4 Hz, 1H), 7.13 (t, J = 8.7 Hz, 2H), 3.09 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.46, 140.21, 139.41, 129.82, 127.70, 123.67, 123.59, 117.85, 115.45, 115.28, 106.60, 56.54, 30.35. Anal. calcd for $C_{17}H_{17}BrFN_3$; C, 56.37; H, 4.73; N, 11.60 found: C, 56.33; H, 4.69; N, 11.56.

*6-Bromo-2-(4-bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine (**4r**).* White solid (93%), mp 185 °C. IR (KBr, cm^{-1}): 3313 (N−H), 2914 (sp^2 −CH), 2910 (sp^3 −CH), 1627, 1549, 1493, 1347, 1321, 1229, 1119, 753. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 9.4 Hz, 1H), 7.20 (d, J = 9.4 Hz, 1H), 3.04 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.46, 139.35, 133.71, 131.49, 129.62, 127.74, 123.81, 123.62, 121.75, 118.04, 106.55, 56.63, 30.40. Anal. calcd for $C_{17}H_{17}Br_2N_3$; C, 48.25; H, 4.05; N, 9.93 found: C, 48.22; H, 4.02; N, 9.90.

*6-Bromo-N-(tert-butyl)-2-(2-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4s**).* Brown solid (97%), mp 180 °C. IR (KBr, cm^{-1}): 3290 (N−H), 2967 (sp^2 −CH), 2930 (sp^3 −CH), 1618, 1523, 1451, 1330, 1331, 1286, 1047, 760. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.7 Hz, 1H), 7.65 (t, J = 7.1 Hz, 1H), 7.50 (t, J = 8.3 Hz, 1H), 7.41 (d, J = 9.4 Hz, 1H), 7.21 (d, J = 9.4 Hz, 1H), 2.75 (s, 1H), 0.94 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.37, 140.69, 137.08, 132.72, 132.54, 129.77, 128.73, 127.92, 125.03, 124.37, 123.58, 118.40, 106.95, 55.75, 30.04. Anal. calcd for $C_{17}H_{17}BrN_4O_2$; C, 52.46; H, 4.40; N, 14.39 found: C, 52.42; H, 4.36; N, 14.35.

*6-Bromo-N-(tert-butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (**4t**).* White solid (94%), mp 195 °C. IR (KBr, cm^{-1}): 3310 (N−H), 2950 (sp^2 −CH), 2890 (sp^3 −CH), 1626, 1536, 1421, 1320, 1311, 1296, 1017, 756. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, J = 8.8 Hz, 1H), 8.53−8.47 (m, 1H), 7.99 (d, J = 9.4 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (d, J = 6.4 Hz, 1H), 3.23 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.40, 145.07, 141.06, 134.44, 131.09, 129.69, 128.79, 128.66, 128.42, 128.33, 127.90, 121.88, 107.85, 56.49, 30.28. Anal. calcd for $C_{17}H_{17}BrN_4O_2$; C, 52.46; H, 4.40; N, 14.39 found: C, 52.45; H, 4.39; N, 14.38.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c03941.

^{1}H and ^{13}C NMR spectra of compound **4a**−**4t**, FT-IR spectra of compound **4p**, and UV spectra of 2-aminopyridine, benzylamine, and 4-methoxybenzylamine (PDF)

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Notes

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