3.1 Introduction

The use of renewable sources in developing efficient and particular chemical transformations has received much attention due to rising awareness of the importance of protecting our environment and considerable progress in sustainable and green chemistry.[1] In recent years, visible light has been used to design a broad range of organic reactions with low-energy irradiation and mild reaction conditions as a clean, safe, pollution-free, cheap, widespread, and sustainable energy source, with impressive results.[2–9] Light, like a chemical reagent, acts as a reagent in a photo-induced organic synthetic chemical reaction to facilitate the conversion of a compound.[10]

Photoredox processes triggered by visible light have gained a lot of interest as a strong tool for developing sustainable synthetic processes.[11–18] Metal complexes, especially ruthenium and iridium, are frequently used as photocatalysts for visible light.[19] Despite their remarkable photophysical characteristics in visible light photocatalysis, ruthenium, and iridium polypyridyl complexes are costly and hazardous.[20] In photoredox catalysis, organic dyes become an appealing alternative to transition-metal complexes.[21–23] They're usually less costly, less hazardous, and easier to work with[24–26] Eosin Y, which has been frequently employed in synthetic transformations as an organo-photocatalyst.[27–33]

Compared to conventional reaction strategies, multicomponent reactions (MCRs) have emerged as an intriguing and effective synthetic method in organic synthesis, combinatorial chemistry, and medicinal chemistry, involving the one-pot reaction of three or more than

three different starting components to construct complex molecules with reduced reaction time, improved yield, lesser side products, and easy procedure for workup.[34–45]

Imidazopyrimidines, imidazopyrazines, and imidazopyridines, which are imidazo-fused bicyclic heterocycles, are privileged pharmacophores in the field of organic and medicinal chemistry. These moieties can be used to treat cancer[46], inflammation[47], bacterial infection[48], HIV[49], cancer-induced osteoporosis[50], Alzheimer's disease[51], and diabetes[52,53]. Many commercially available drugs based on this moiety have been developed, including an anxiolytic drug (alpidem)[54], a hypnotic drug (zolpidem)[55], an anti-ulcer drug (zolimidine)[56,57], sedative agents (saripidem & necopidem)[58], and used in the treatment of HIV infection (GSK812397).[59] (**Figure 3.1**)

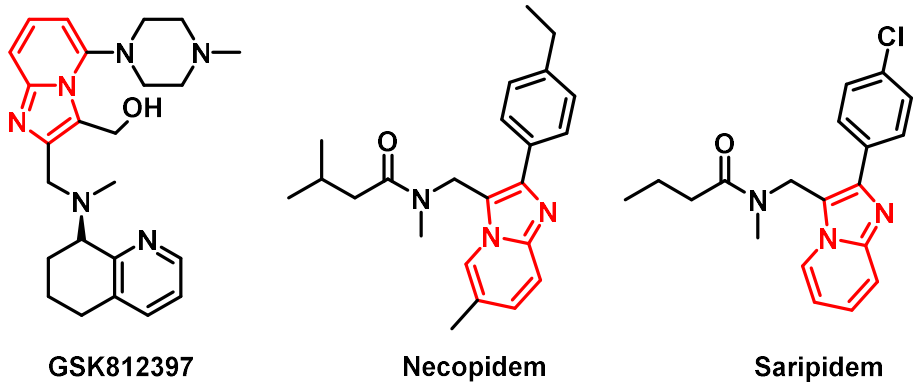
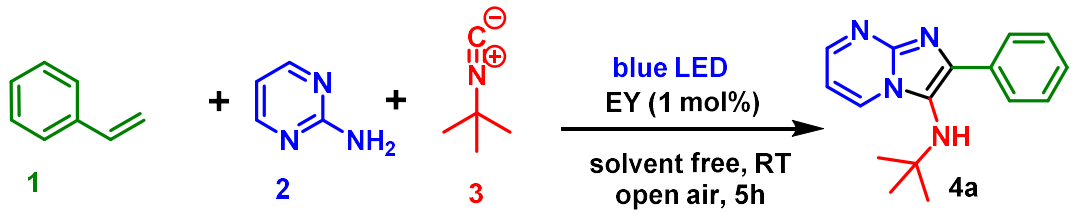


Figure 3.1 Examples of biologically relevant imidazo[1,2-a]pyridines

Besides, several therapeutic probes and approved drug molecules, such as KA1407[60] (anti-malarial probe) and olprinone[61] (cardiotonic), have imidazo-fused rings within their core heterocyclic framework. Given the significance of this structure, a scalable, sustainable,

robust, and efficient approach to fused heterocycles containing imidazole and its derivatives would be extremely beneficial to the larger community of scientists desiring new therapeutic agents.

Despite considerable progress in synthesizing 3-aminoimidazo heterocycles, a practical, environmentally sustainable process with high generality that avoids impractical and environmentally harmful reaction conditions remains highly desirable. As a part of our ongoing research in medicinally and visible-light photochemistry, the development of environmentally friendly approaches to organic transformations has been a major focus of our laboratory.[62,63] In the presence of an organic photocatalyst Eosin Y, we report first time, a convenient and green protocol for the synthesis of 3-aminoimidazo heterocycles by irradiating styrene **(1)**, 2-aminopyrimidine **(2)**, and *t*-butyl isocyanide **(3)** under solvent-free condition (**Scheme 3.1**).



Scheme 3.1 Synthesis of 3-Aminoimidazo[1,2-a]pyrimidines via one-pot multicomponent Reaction

3.2 Results and Discussion

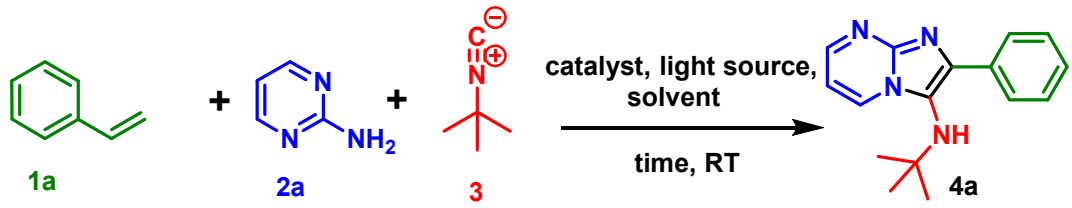
As a model substrate, we used styrene **(1a)**, 2-aminopyrimidine **(2a)**, and tert-butylisonitrile **(3)** in visible light under diverse reaction conditions. First, metal-free photocatalysts such as

Eosin B, Rhodamine B, Acridine Red, Rose Bengal, Na_2-Eosin Y, and Eosin Y were examined as a catalyst in DMSO at room temperature under air (Table 3.1, entries 1-7). The reaction occurred under 3W blue LED (light emitting diode) lamps. Among these photocatalyst examined, Eosin Y was found to be the most effective one in giving the desired product **4a** in 51% (Table 3.1, entry 7). Increasing the amount of Eosin Y to 5 mol% did not improve the reaction efficiency (Table 3.1, entry 8). Notably, the desired product **4a** (64%) was slightly improved by reducing the amount of Eosin Y to 1% (Table 3.1, entry 9). Without a photocatalyst, only a trace amount of the desired product was found (Table 3.1, entry 10).

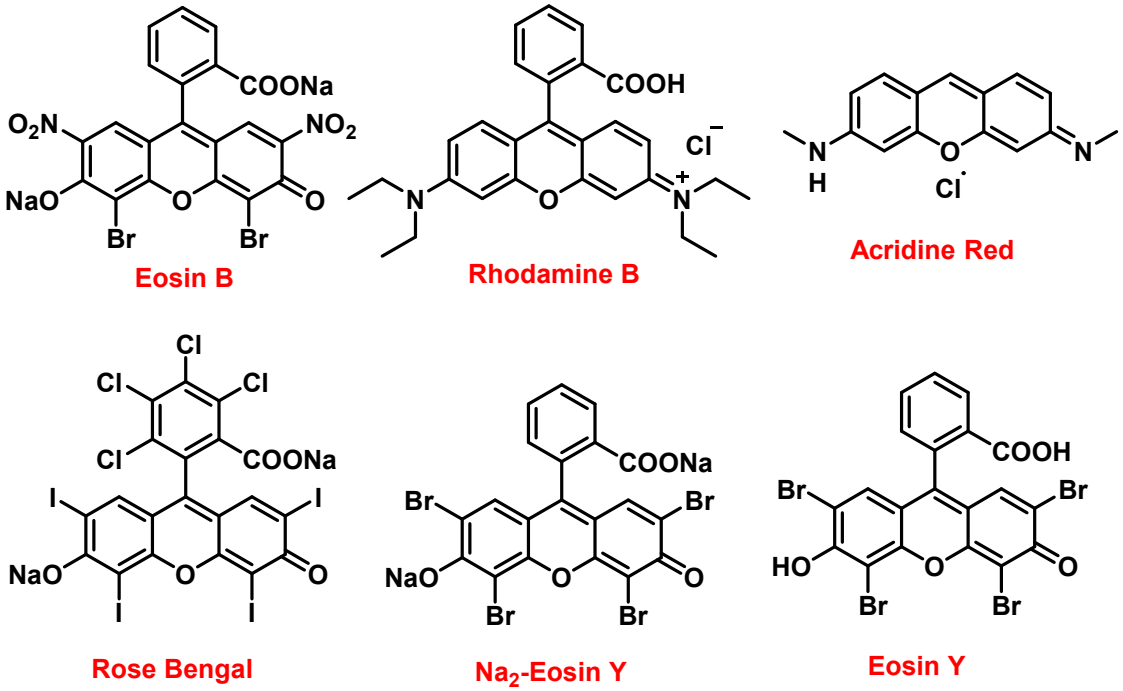
Next, various solvents (green and conventional solvents) were screened by using Eosin Y (1 mol %) as the catalyst. When the reaction was carried out with DCM, CH_3CN, EtOAc, and EtOH solvents for 12 hours at room temperature in the presence of photocatalyst Eosin Y, only a trace amount of product was obtained (Table 3.1 entries 12-15). When the reaction was carried out in DMF for 12 h, a slightly increased amount of product was detected (Table 3.1, entry 11). Further investigations revealed that the solvent-free system was superior in terms of increasing the yield of the target product. The reaction was carried out in solvent-free conditions, which resulted in a marginal increase in yield (86%) and in a shorter reaction time (6 h) (Table 3.1, entry 16). This reaction was carried out under solvent-free conditions because one of the reactants (*t*-butyl- isocyanide) is a liquid that can allow the others to dissolve into it and also with the help of visible light, where visible light used as an activator and promoted chemical reaction. As soon as the catalyst loading was reduced to 1 mol% and the reaction time was reduced to 5h, the desired product 4a was obtained in 92% yield (Table

3.1, entry 17). Furthermore, when the reaction was carried out under irradiation with 3 W green and white LED lamps, the desired product **4a** was achieved in 72% and 62% yields, respectively (Table 3.1, entries 19 and 20). No change was observed while the reaction was performed in the dark (Table 3.1, entry 21).

Table 3.1 Optimization of the Reaction Conditions[a]



Structure of photocatalyst :



entry	catalyst (mol%)	light source	solvent	time (h)	yield[b]%
1	Eosin B (1)	Blue LED	DMSO	12	trace
2	Eosin B (2)	Blue LED	DMSO	12	17
3	Rhodamine B (2)	Blue LED	DMSO	12	trace
4	Acridine red (2)	Blue LED	DMSO	12	23
5	Rose bengal (2)	Blue LED	DMSO	8	38
6	Na_2-Eosin Y (2)	Blue LED	DMSO	6	40
7	Eosin Y (2)	Blue LED	DMSO	12	51
8	Eosin Y (1)	Blue LED	DMSO	12	64
9	Eosin Y (5)	Blue LED	DMSO	12	42
10	none	Blue LED	DMSO	24	NR[c]
11	Eosin Y (1)	Blue LED	DMF	12	48
12	Eosin Y (1)	Blue LED	DCM	12	17
13	Eosin Y (1)	Blue LED	CH_3CN	12	trace
14	Eosin Y (1)	Blue LED	EtOAc	12	trace
15	Eosin Y (1)	Blue LED	EtOH	12	trace
16	Eosin Y (2)	Blue LED	None	6	86
17	Eosin Y (1)	Blue LED	None	5	92
18	Eosin Y (5)	Blue LED	None	6	80
19[d]	Eosin Y (2)	Green LED	DMSO	12	72
20[e]	Eosin Y (2)	White LED	DMSO	12	62
21[f]	Eosin Y (2)	Dark	DMSO	12	NR
22[g]	Eosin Y (1)	Blue LED	None	5	92

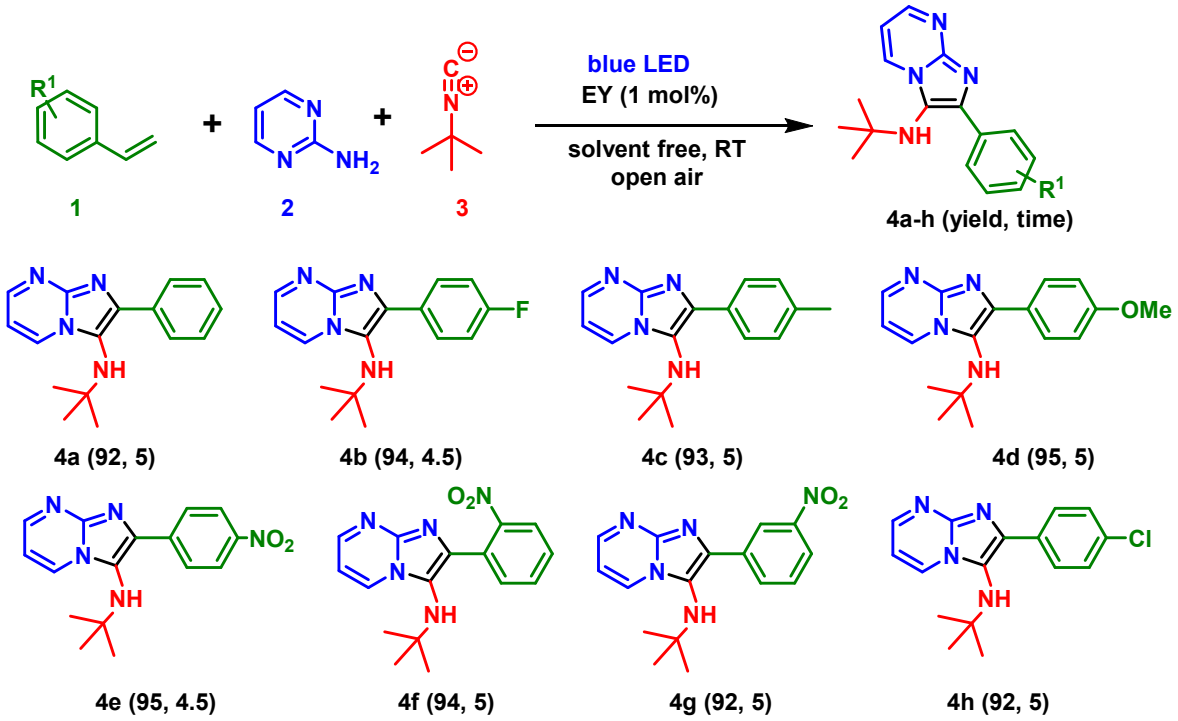
[a]Experimental conditions: Styrene (1 mmol), 2-aminopyrimidine (1 mmol), tert-butylisonitrile (1 mmol), room temperature, Blue LED irradiation (3 W, wavelength in the range of 460-470 nm). [b]Isolated yields. [c]NR = no reaction. [d]Green light (520-525 nm).

[e]White light (380-780 nm). [f]In the dark. [g]The reaction was carried out on the 10 mmol scale.

Additionally, a scale-up reaction was also carried out to demonstrate the methodology's synthetic utility (10 mmol scale). It was observed that the reaction proceeded smoothly and efficiently, emphasizing the synthetic benefits of this procedure (Table 3.1, entry 22).

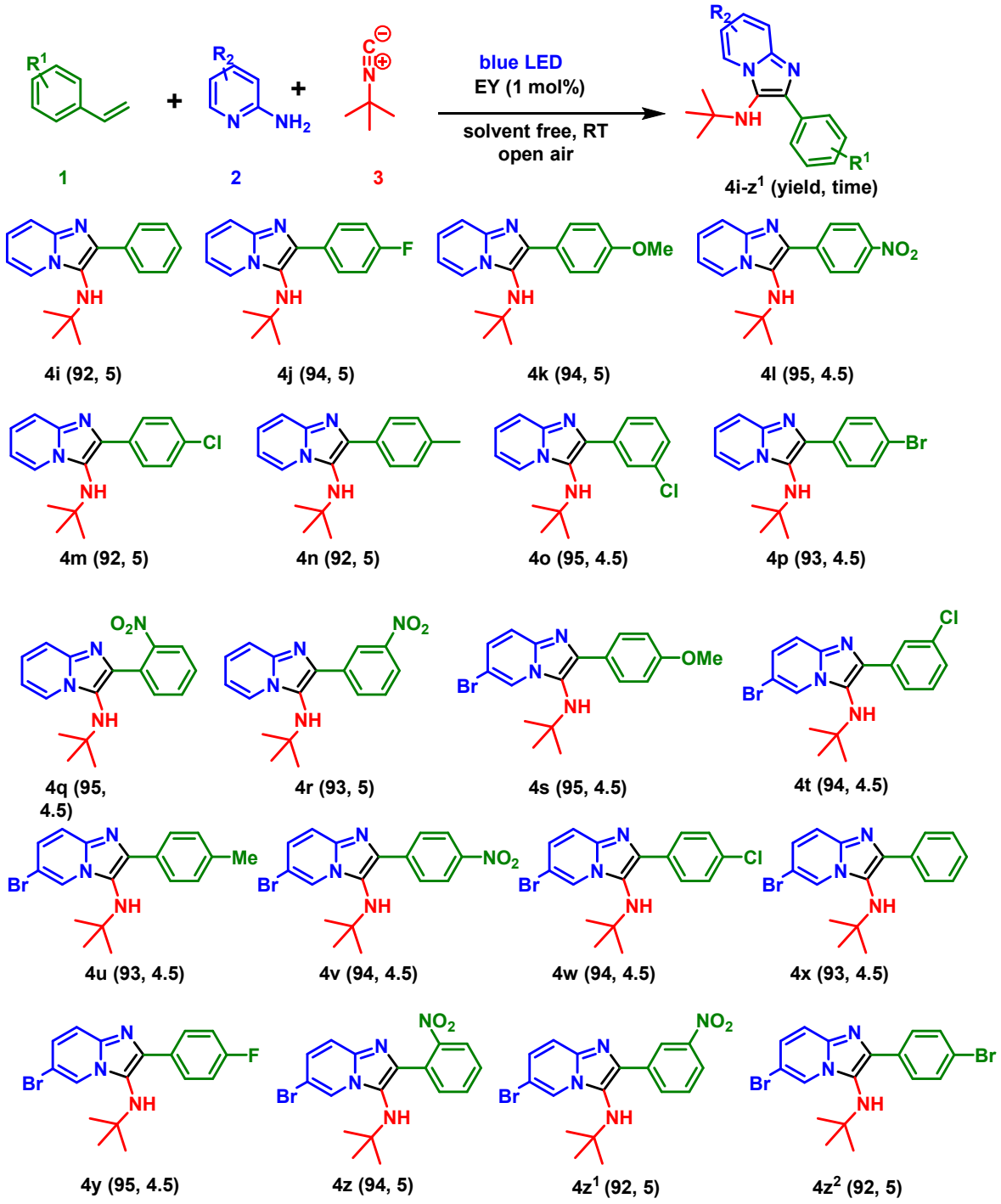
Finally, the reaction's generality and scope were investigated using a variety of styrenes containing various substituents such as -Me, -OMe, -NO_2, -Cl, -Br, and -F. The reaction proceeds satisfactorily in all cases and provides the desired product **4** in good to excellent yields (92–95%). Styrene derivatives having an electron-donating (-OMe) as well as electron-withdrawing group (-NO_2) on the benzene ring were tolerated well in this transition (Table 3.2 and 3.3). The efficiency of the reaction was relatively unaffected by the position of the substituents on the aromatic ring of styrene. The substrate with a nitro substituent at the C-4 position on the styrene backbone reacted readily and generated the corresponding product **4e** in 95% yield.

Table 3.2 Substrate scope and versatility of reaction of 2-aminopyrimidine



Experimental condition: 2- Aminopyrimidine (1 mmol), styrene (1 mmol), tertiary butyl isonitrile (1 mmol), Eosin Y (1 mol%), without solvent, at room temperature, under blue LED.

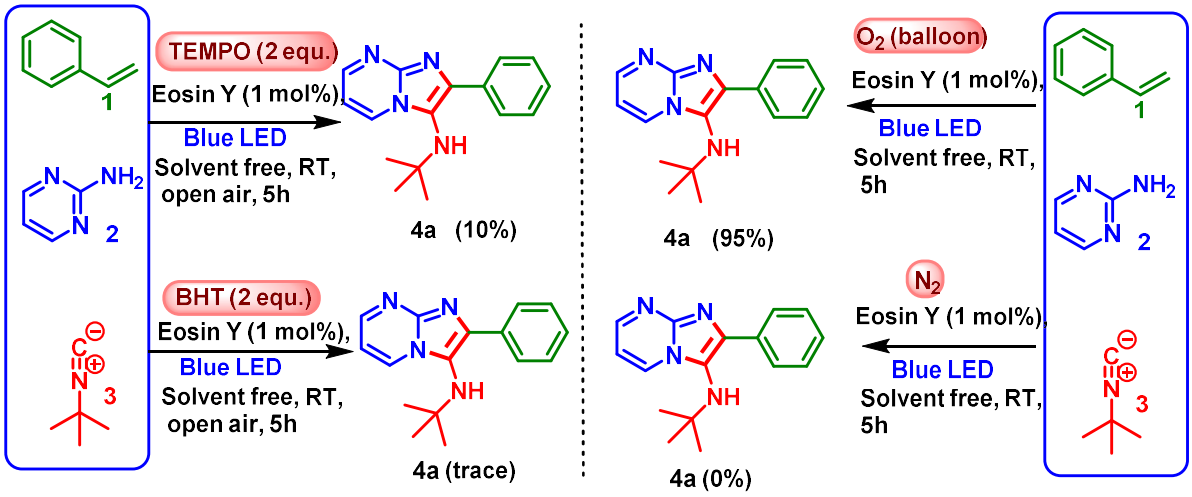
Table 3.3 Substrate scope and versatility of reaction of 2-aminopyridine



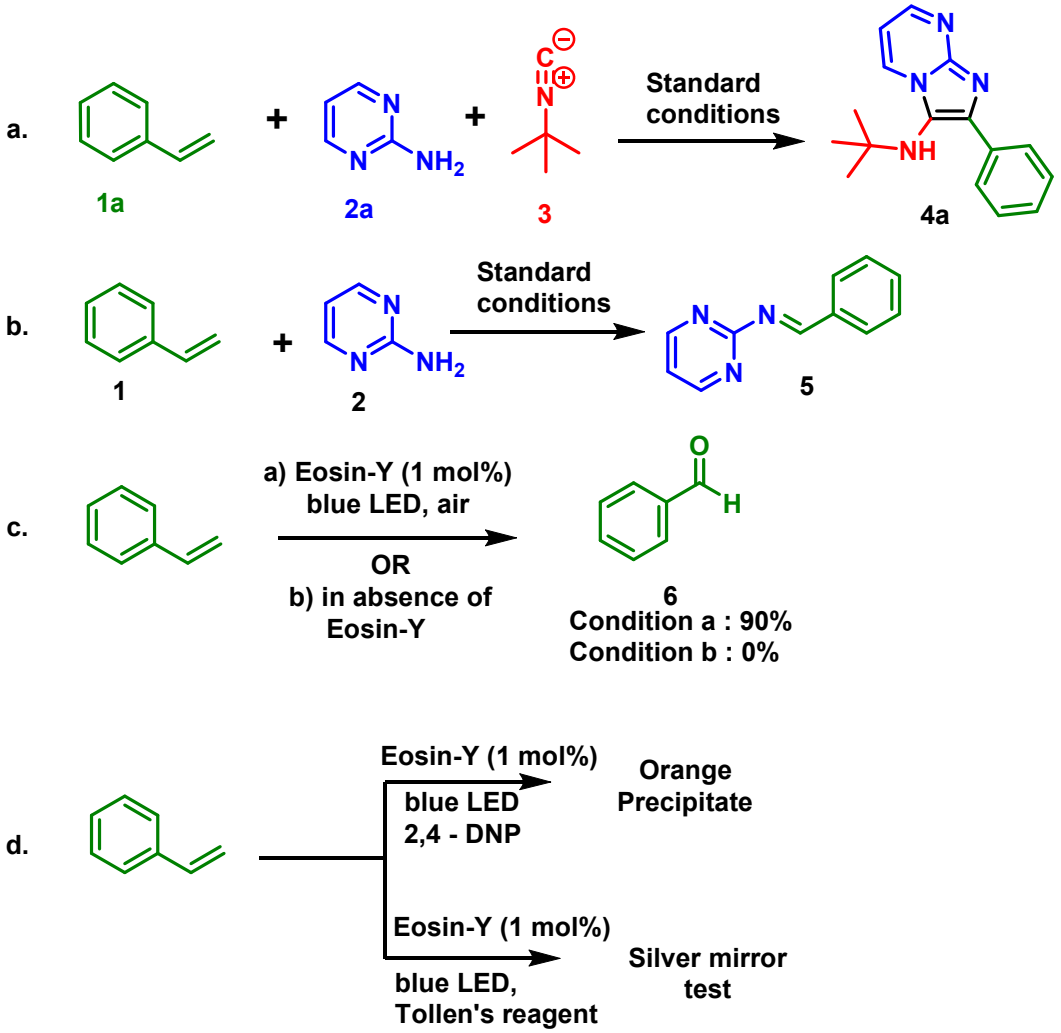
Experimental condition: 2- Aminopyridine (1 mmol), styrene (1 mmol), tertiary butyl isonitrile (1 mmol), Eosin Y (1 mol%), without solvent, at room temperature, under blue LED.

3.3 Control Experiment

Some control experiments were carried out better to understand the mechanistic study. **(Scheme 3.2)** The yield of the intended product **4a** was substantially decreased to 6-10% in the presence of radical scavengers such as TEMPO (2,2,6,6-Tetramethyl-1-piperidinyloxy) or butylated hydroxyl toluene, showing the radical path. The model reaction was carried out under oxygen-purging conditions to check the role of oxygen in this reaction. There was no improvement in the reaction's outcome. Furthermore, just a small amount of product was identified when the reaction was carried out under N_2. This finding suggests that dioxygen is required for the current transformation. **(Scheme 3.2)**



Scheme 3.2 Control reaction experiments



Scheme 3.3 Control experiments

To find out the route of the reaction, some more control experiments were carried out (**Scheme 3.3**). Product **4a** was obtained under standard reaction conditions by the multicomponent reaction of styrene (1.0 mmol), 2-aminopyrimidine (1.0 mmol), and *tert*-butylisonitrile (1.0 mmol) **(eq a).** The intermediacy of imine was suspected in this reaction. When the reaction of 2- aminopyrimidine (1.0 equiv.) with styrene (1.0 equiv.) was carried

out, product **5** was obtained under optimized conditions. (**Scheme 3.3**, **eq b)** We also suspected the intermediacy of aldehyde (obtained by oxidation of Styrene), which upon reaction with 2- aminopyrimidine formed **5** (imine). In order to check the formation of aldehyde as an intermediate in this reaction, the styrene was subjected to a reaction with Eosin Y (1%) in blue LED, which produced aldehyde in good yield. (**Scheme 3.3**, **eq c)** When a similar reaction was carried out in the presence of 2,4- DNP and Tollen's reagent under the same reaction condition, the formation of orange precipitate and silver mirror confirmed the intermediacy of aldehyde. (**Scheme 3.3, eq d)**

3.3.1 ON/OFF Experiments

Furthermore, the On/Off visible-light irradiation experiments were conducted under ideal conditions, indicating that continuous visible-light irradiation is required for this reaction (**Figure 3.2**).

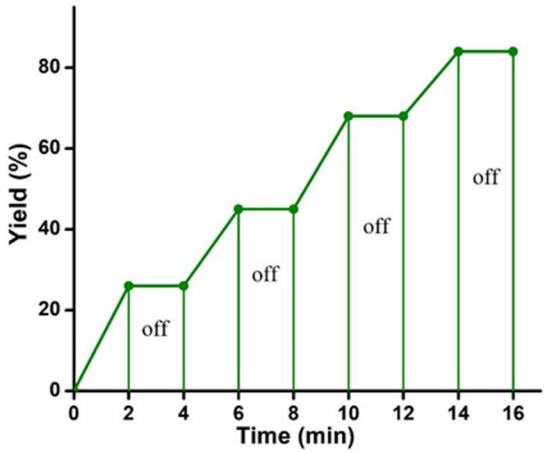
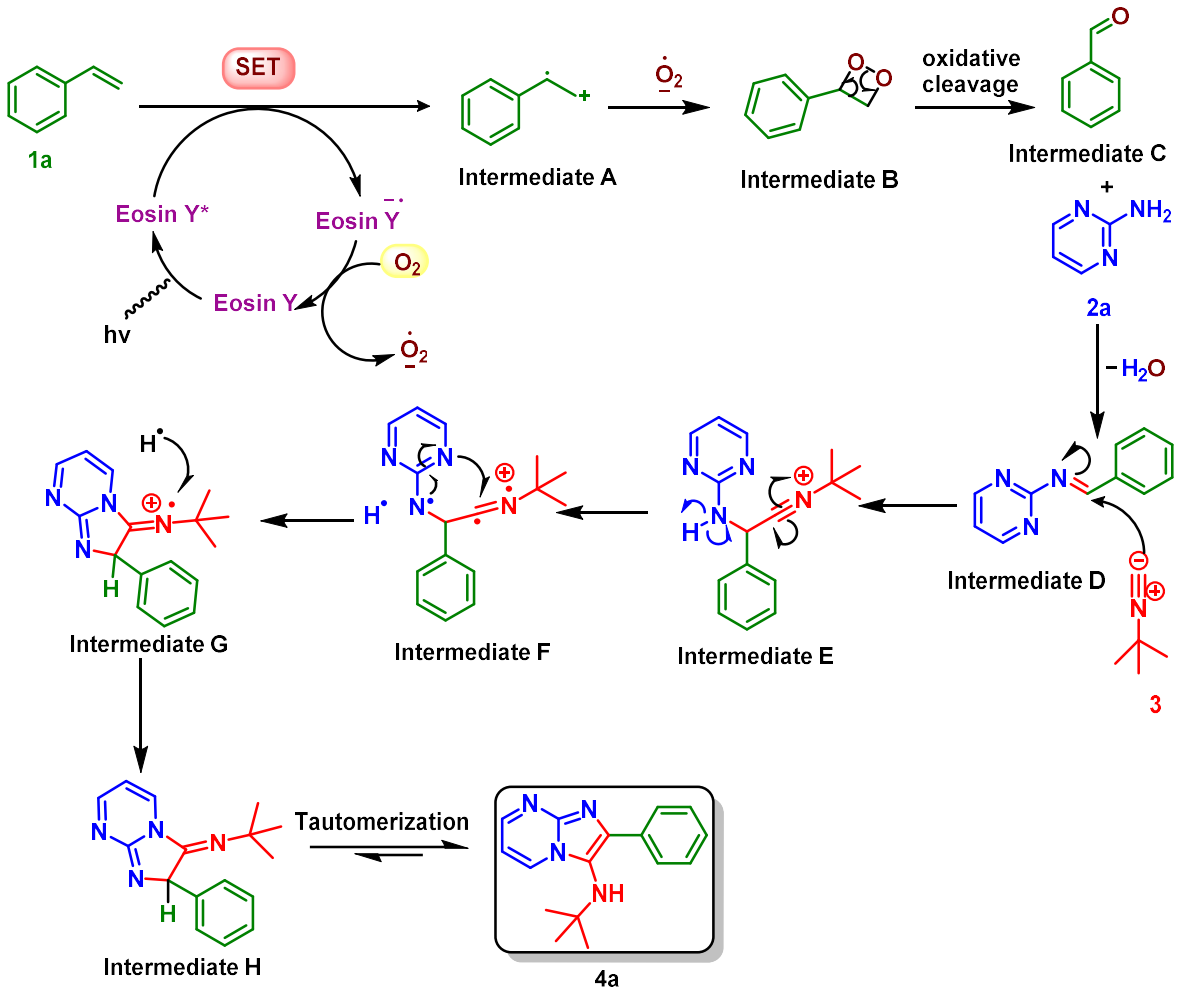


Figure 3.2 Visible-light irradiation on/off experiment

3.4 Proposed Mechanism

On the basis of our control experiments and previous literature,[62–67] a plausible mechanism for the formation of 3-aminoimidazopyrimidines (**scheme 3.4**). Initially, in the presence of blue LED light, Eosin Y is photoexcited to produce the excited-state Eosin Y*. Excited-state Eosin Y* receives an electron from styrene **1a**, resulting in the radical anion Eosin Y•- and the styrene radical cation Intermediate **A**. After which Eosin Y•- is oxidized by dioxygen (air) to produce the ground state Eosin Y and superoxide radical anion ($O_2^{\bullet-}$). The resultant styrene radical cation (Intermediate **A**) conducts [2+2] cycloaddition with the superoxide radical anion ($O_2^{\bullet-}$), yielding a dioxetane (Intermediate **B**), which eventually undergoes oxidative cleavage to produce benzaldehyde (Intermediate **C**). When benzaldehyde **C** reacts with 2-aminopyrimidine **2**, water is liberated, resulting in the formation of imine intermediate **D**, which is then attacked by the isocyanide **3** to yield intermediate **E**. Visible light causes this intermediate **E** to form free radicals, which is then cyclized and followed by a 1,3-H shift to produce the desired product (**4a**).



Scheme 3.4 Plausible mechanism

3.5 Conclusions

In conclusion, solvent-free, metal-free, and visible light-initiated multicomponent reactions of styrene, 2-aminopyrimidine, and *t*-butylisocyanide have been developed for the synthesis of fused imidazo heterocycle through a single electron transfer approach. The reaction goes smoothly at milder conditions using eco-friendly organic dye Eosin Y as photocatalyst and reasonably yields the desired products. A wide-ranging scope of the substrate with different substitution patterns worked splendidly in these processes.

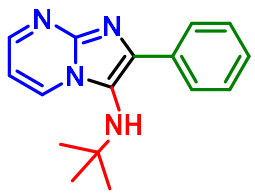
3.6 Experimental Procedures

3.6.1 General Procedure for Synthesis of 3-Aminoimidazo-fused Heterocycles

Styrene **1** (1 mmol), 2-Aminoheterocycle **2** (1 mmol), Isocyanide **3** (1 mmol), and Eosin Y (1 mol%) were loaded into a 5 mL oven-dried round-bottom flask, and the reaction mixture was stirred for 5 hours under blue LED irradiation in ambient air. The product was extracted with ethyl acetate when the reaction (monitored by TLC) was completed. Then, the organic layer was washed with saturated brine solution, dried with anhydrous Na_2SO_4, and the solvents were evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (100-200 mesh) (ethyl acetate/hexane: 20/80) to provide pure product **4** in excellent yields.

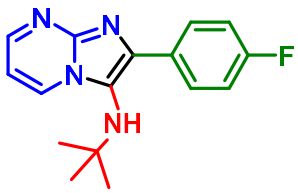
3.7 Characterization of products

N-(tert-butyl)-2-phenylimidazo[1,2-a]pyrimidin-3-amine (4a)



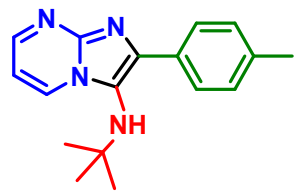
White solid (92%), mp 167°C. IR (KBr, cm^{-1}): 3320 (NH), 2977 (sp^2-CH), 2943 (sp^3-CH), 1619, 1518, 1451, 1365, 1321, 1226, 1017, 767.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 – 8.48 (m, 2H), 7.98 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 6.89 – 6.81 (m, 1H), 3.20 (s, 1H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.48, 145.00, 141.11, 134.50, 131.06, 128.51, 128.23, 128.00, 121.84, 107.71, 56.48, 30.28. Anal. calcd for $C_{16}H_{18}N_4$: C, 72.15; H, 6.81; N, 21.04; found: C, 72.13; H, 6.79; N, 21.02.

N-(tert-butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyrimidin-3-amine (4b)



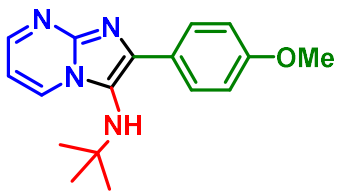
Off -white solid (95%), mp 162°C. IR (KBr, cm^{-1}): 3328 (NH), 2968 (sp^2-CH), 2929 (sp^3-CH), 1632, 1513, 1438, 1369, 1341, 1219, 1028, 725. ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 – 8.45 (m, 2H), 8.00 (dd, *J* = 8.8, 5.5 Hz, 2H), 7.12 (t, *J* = 8.7 Hz, 2H), 6.87 – 6.80 (m, 1H), 3.12 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.49, 161.49, 149.48, 144.97, 140.26, 131.05, 130.02, 121.84, 115.04, 107.52, 56.48, 30.07. Anal. calcd for $C_{16}H_{17}FN_4$: C, 67.59; H, 6.03; N, 19.70; found: C, 67.55; H, 6.01; N, 19.72.

N-(tert-butyl)-2-(p-tolyl)imidazo[1,2-a]pyrimidin-3-amine (4c)



Brown solid (93%), mp 195°C. IR (KBr, cm^{-1}): 3311 (NH), 2948 (sp^2-CH), 2897 (sp^3-CH), 1639, 1549, 1439, 1321, 1319, 1310, 1037, 769. ^1H NMR (500 MHz, $CDCl_3$) δ 8.55 – 8.50 (m, 1H), 8.50 – 8.46 (m, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 2H), 6.83 (dd, *J* = 6.8, 4.1 Hz, 1H), 3.22 (s, 1H), 2.40 (s, 3H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.16, 144.99, 140.99, 137.67, 131.56, 130.97, 129.04, 128.25, 121.62, 107.72, 56.62, 30.30, 21.42. Anal. calcd for $C_{17}H_{20}N_4$: C, 72.83; H, 7.19; N, 19.98; found: C, 72.82; H, 7.14; N, 19.94.

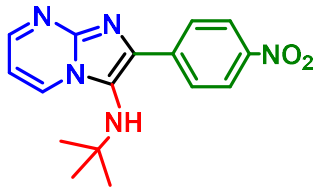
N-(tert-butyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidin-3-amine (4d)



Yellow solid (95%), mp 188°C. IR (KBr, cm^{-1}): 3333 (NH), 2963 (sp^2-CH), 2929 (sp^3-CH), 1619, 1491, 1419, 1369 (CN), 1329, 1229, 1029, 768. ^1H NMR (500 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 24.9, 4.4 Hz, 2H), 7.94 (d, *J* = 8.9 Hz, 2H), 6.96 (d, *J* = 6.6 Hz, 2H), 6.80 (t, *J* = 6.6 Hz,

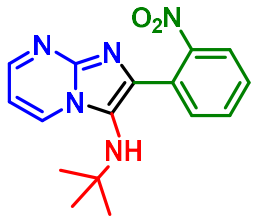
1H), 3.85 (s, 3H), 3.17 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.23, 149.03, 144.98, 140.91, 130.92, 129.63, 126.93, 121.23, 113.69, 107.69, 56.50, 55.24, 30.33. Anal. calcd for $C_{17}H_{20}N_4O$: C, 68.90; H, 6.80; N, 18.90; found: C, 68.95; H, 6.84; N, 18.93.

N-(tert-butyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyrimidin-3-amine (4e)



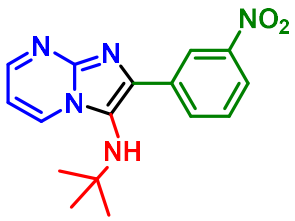
Light Brown solid (95%), mp 171°C. IR (KBr, cm^{-1}): 3291 (NH), 3029 (sp^2-CH), 2998 (sp^3-CH), 1594, 1499, 1428, 1311, 1316, 1226, 1027, 779. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (dd, J = 4.0, 2.0 Hz, 1H), 8.53 (dd, J = 6.8, 2.0 Hz, 1H), 8.31 (dd, J = 5.1, 3.5 Hz, 4H), 6.91 (dd, J = 6.8, 4.0 Hz, 1H), 3.11 (s, 1H), 1.11 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.52, 147.03, 145.35, 141.04, 138.61, 131.23, 128.82, 127.34, 123.67, 108.47, 56.99, 30.48. Anal. calcd for $C_{16}H_{17}N_5O_2$: C, 61.72; H, 5.50; N, 22.49; found: C, 61.75; H, 5.54; N, 22.44.

N-(tert-butyl)-2-(2-nitrophenyl)imidazo[1,2-a]pyrimidin-3-amine (4f)



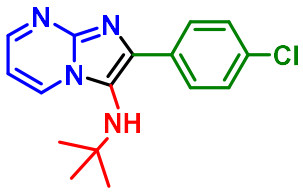
Off -white solid (94%), mp 142°C. IR (KBr, cm^{-1}): 3335 (NH), 2968 (sp^2-CH), 2938 (sp^3-CH), 1622, 1523, 1438, 1367, 1349, 1219, 1026, 736. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 8.6 Hz, 2H), 7.93 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 6.93 – 6.85 (m, 1H), 2.98 (s, 1H), 0.93 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.00, 149.99, 149.26, 145.18, 137.70, 133.12, 132.70, 129.41, 128.86, 124.33, 123.27, 108.41, 55.71, 29.98. Anal. calcd for $C_{16}H_{17}N_5O_2$: C, 61.72; H, 5.50; N, 22.49; found: C, 61.76; H, 5.55; N, 22.43.

N-(tert-butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyrimidin-3-amine (4g)



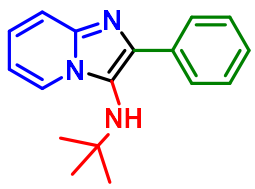
Reddish brown solid (92%), mp 183°C. IR (KBr, cm^{-1}): 33016 (NH), 2951 (sp^2-CH), 2923 (sp^3-CH), 1583, 1477, 1433, 1359 (CN), 1313, 1185, 1027, 763. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.53 (dd, J = 23.1, 7.2 Hz, 3H), 8.17 (s, 1H), 7.60 (t, J = 8.0 Hz, 1H), 6.93 – 6.86 (m, 1H), 3.22 (s, 1H), 1.12 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.23, 150.27, 148.07, 145.24, 138.46, 136.10, 134.13, 131.22, 129.34, 122.78, 122.45, 108.40, 56.76, 30.55. Anal. calcd for $C_{16}H_{17}N_5O_2$: C, 61.72; H, 5.50; N, 22.49; found: C, 61.73; H, 5.51; N, 22.50

N-(tert-butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyrimidin-3-amine (4h)



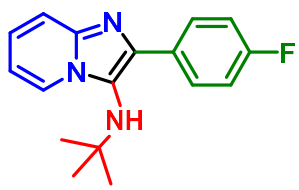
Light orange solid (92%), mp 163-165°C. IR (KBr, cm^{-1}): 3315 (NH), 2961 (sp^2-CH), 2923 (sp^3-CH), 1618, 1517, 1433, 1371 (CN), 1311, 1213, 1027, 749. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 – 8.40 (m, 2H), 8.04 – 7.94 (m, 2H), 7.17 – 7.07 (m, 2H), 6.88 – 6.77 (m, 1H), 3.14 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.63, 145.12, 140.38, 131.05, 130.63, 130.15, 130.02, 121.61, 115.39, 115.27, 108.03, 56.77, 30.29. Anal. calcd for $C_{16}H_{17}ClN_4$: C, 63.89; H, 5.70; N, 18.63; found: 63.94; H, 5.75; N, 18.68

N-(tert-butyl)-2-phenylimidazo[1,2-a]pyridin-3-amine (4i)



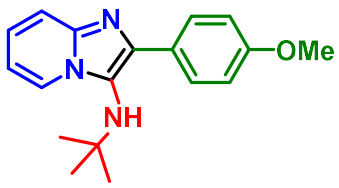
White solid (92%), mp 160– 163°C. IR (KBr, cm^{-1}): 3320 (NH), 2976 (sp^2-CH), 2940 (sp^3-CH), 1610, 1508, 1449, 1360, 1311, 1216, 1037, 766.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.9 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.55 (s, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 6.2 Hz, 1H), 7.16 (m, 1H), 6.80 (t, *J* = 6.8 Hz, 1H), 3.23 (s, 1H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.90, 139.21, 135.00, 129.91, 128.37, 128.24, 127.53, 124.40, 123.65, 117.22, 111.58, 56.55, 30.47. Anal. calcd for $C_{17}H_{19}N_3$: C, 76.95; H, 7.22; N, 15.84; found: C,76.94; H,7.23; N, 15.88

N-(tert-butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine (4j)



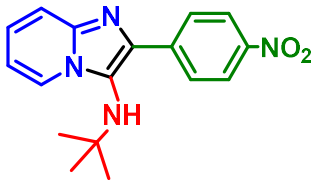
White solid (94%), mp 163-165°C. IR (KBr, cm^{-1}): 3298 (NH), 2970 (sp^2-CH), 2938 (sp^3-CH), 1615, 1516, 1443, 1351, 1323, 1226, 1047, 758. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 9.2 Hz, 1H), 7.94 (dd, *J* = 8.8, 5.5 Hz, 2H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.22 – 7.15 (m, 1H), 7.15 – 7.08 (m, 2H), 6.82 (t, *J* = 6.8 Hz, 1H), 3.12 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.34, 141.79, 138.09, 129.92, 129.78, 124.64, 123.49, 116.97, 115.31, 115.24, 111.64, 56.19, 30.56. Anal. Calcd for $C_{17}H_{18}FN_3$; C, 72.06; H, 6.40; N, 14.83 found: C, 72.10; H, 6.47; N, 14.88

N-(tert-butyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (4k)



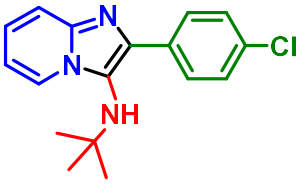
Off -white solid (94%), mp 142°C. IR (KBr, cm^{-1}): 3325 (NH), 2965 (sp^2-CH), 2928 (sp^3-CH), 1632, 1513, 1433, 1366, 1340, 1209, 1027, 726. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 35.3 Hz, 1H), 7.86 (d, J = 9.7 Hz, 2H), 7.54 (d, J = 9.0 Hz, 1H), 7.18 – 7.07 (m, 1H), 6.97 (d, J = 11.6 Hz, 2H), 6.77 (t, J = 6.3 Hz, 1H), 3.88 (s, 3H), 3.12 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.02, 141.77, 139.13, 129.35, 127.57, 124.20, 123.41, 122.91, 116.97, 113.70, 111.30, 55.91, 54.84, 30.57. Anal. Calcd for $C_{18}H_{21}N_3O$; C, 73.19; H, 7.17; N, 14.23 found: C, 73.26; H, 7.19; N, 14.28.

N-(tert-butyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4l)



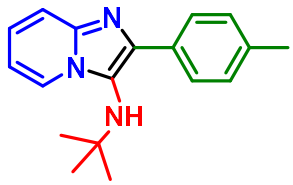
Reddish brown solid (95%), mp 205°C. IR (KBr, cm^{-1}): 3305 (NH), 2948 (sp^2-CH), 2917 (sp^3-CH), 1584, 1476, 1429, 1349 (CN), 1315, 1197, 1007, 769. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 4H), 8.21 (d, J = 15.3 Hz, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.26 – 7.18 (m, 1H), 6.91 – 6.77 (m, 1H), 3.15 (s, 1H), 1.10 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.74, 142.44, 141.40, 136.63, 128.46, 125.58, 125.02, 123.59, 123.41, 117.58, 112.34, 57.05, 30.85. Anal. Calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.87; H, 5.89; N, 18.13.

N-(tert-butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (4m)



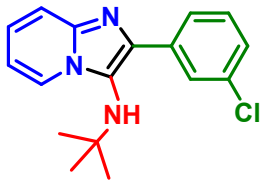
Light orange solid (92%), mp 160-163°C. IR (KBr, cm^{-1}): 3325 (NH), 2966 (sp^2-CH), 2927 (sp^3-CH), 1609, 1516, 1447, 1368 (CN), 1331, 1209, 1027, 746. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 13.6 Hz, 2H), 7.55 (dt, *J* = 9.0, 1.0 Hz, 1H), 7.39 (d, *J* = 9.8 Hz, 2H), 7.20 – 7.13 (m, 1H), 6.80 (t, *J* = 6.2 Hz, 1H), 3.10 (s, 1H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.96, 138.07, 133.47, 133.16, 131.10, 129.35, 129.04, 128.46, 124.69, 123.63, 123.40, 117.25, 111.77, 56.75, 30.84. Anal. Calcd for $C_{17}H_{18}ClN_3$; C, 68.11; H, 6.05; N, 14.02 found: C, 68.09; H, 6.11; N, 14.08.

N-(tert-butyl)-2-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (4n)



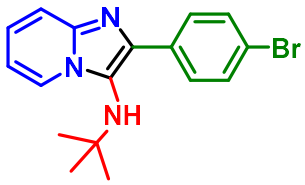
White solid (92%), mp 170°C. IR (KBr, cm^{-1}): 3325 (NH), 2963 (sp^2-CH), 2928 (sp^3-CH), 1610, 1516, 1449, 1369 (CN), 1339, 1208, 1037, 749. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 17.6 Hz, 1H), 7.81 (d, *J* = 29.3 Hz, 2H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.24 (d, *J* = 19.4 Hz, 2H), 7.13 (t, *J* = 12.5 Hz, 1H), 6.80 – 6.70 (m, 1H), 3.15 (s, 1H), 2.39 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.88, 139.24, 137.08, 132.16, 129.00, 128.08, 124.01, 123.47, 123.18, 117.20, 111.21, 56.42, 30.31, 21.32. Anal. Calcd for $C_{18}H_{21}N_3$; C, 77.38; H, 7.58; N, 15.04 found: C, 77.39; H, 7.63; N, 15.11.

N-(tert-butyl)-2-(3-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (4o)



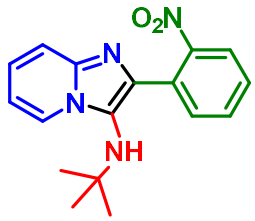
Orange solid (95%), mp 148°C. IR (KBr, cm^{-1}): 3323 (NH), 2958 (sp^2-CH), 2919 (sp^3-CH), 1617, 1489, 1439, 1368 (CN), 1328, 1223, 1028, 758.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 19.4 Hz, 1H), 8.03 (t, *J* = 1.8 Hz, 1H), 7.87 (d, *J* = 10.2 Hz, 1H), 7.56 (d, *J* = 23.8 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.29 (dd, *J* = 5.5, 4.4 Hz, 1H), 7.16 (t, *J* = 11.7 Hz, 1H), 6.86 – 6.76 (m, 1H), 2.91 (s, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.01, 137.90, 136.80, 134.20, 129.51, 128.10, 127.32, 126.19, 124.61, 123.41, 117.40, 111.61, 56.60, 30.28. Anal. Calcd for $C_{17}H_{18}ClN_3$; C, 68.11; H, 6.05; N, 14.02 found: C, 68.19; H, 6.09; N, 14.11.

2-(4-bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine (4p)



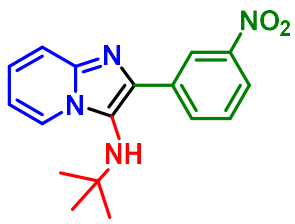
Yellow solid (93%), mp 143-148°C. IR (KBr, cm^{-1}): 3323 (NH), 2965 (sp^2-CH), 2928 (sp^3-CH), 1610, 1516, 1448, 1363 (CN), 1331, 1206, 1027, 766. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 6.9 Hz, 1H), 7.87 (d, *J* = 9.1 Hz, 2H), 7.54 (d, *J* = 16.8 Hz, 3H), 7.19 – 7.12 (m, 1H), 6.84 – 6.74 (m, 1H), 3.07 (s, 1H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.00, 138.17, 134.11, 131.40, 129.66, 124.62, 123.59, 123.50, 121.50, 117.25, 111.64, 56.52, 30.28. Anal. Calcd for $C_{17}H_{18}BrN_3$; C, 59.31; H, 5.27; N, 12.21 found: C, 59.38; H, 5.34; N, 12.28.

N-(tert-butyl)-2-(2-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4q)



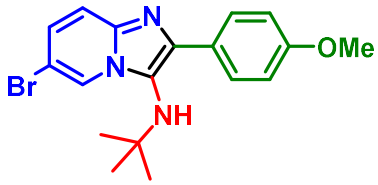
Brown solid (95%), mp 183-185°C. IR (KBr, cm^{-1}): 3314 (NH), 2958 (sp^2-CH), 2926 (sp^3-CH), 1598, 1488, 1459, 1359, 1328, 1199, 1019, 738. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 6.9 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.71 – 7.61 (m, 1H), 7.56 (d, *J* = 14.9 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.23 – 7.10 (m, 1H), 6.88 – 6.75 (m, 1H), 2.75 (s, 1H), 0.95 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.46, 142.53, 136.09, 132.82, 132.44, 130.26, 124.41, 124.27, 123.34, 117.70, 111.74, 55.42, 30.28. Anal. Calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.85; H, 5.88; N, 18.12.

N-(tert-butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4r)



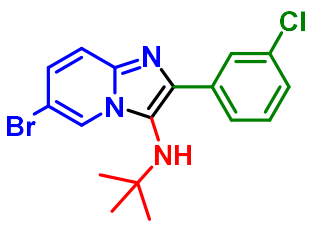
White solid (93%), mp 171°C. IR (KBr, cm^{-1}): 3313 (NH), 2958 (sp^2-CH), 2925 (sp^3-CH), 1598, 1516, 1441, 1368, 1333, 1216, 1018, 737. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (d, *J* = 1.6 Hz, 1H), 8.44 (d, *J* = 7.7 Hz, 1H), 8.20 (d, *J* = 6.9 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.58 (dd, *J* = 23.2, 5.5 Hz, 2H), 7.23 – 7.16 (m, 1H), 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, 142.35, 137.08, 136.97, 133.68, 129.20, 124.85, 124.07, 123.26, 122.51, 121.84, 117.62, 111.94, 56.48, 30.56. Anal. Calcd for $C_{17}H_{18}N_4O_2$; C, 65.79; H, 5.85; N, 18.05 found: C, 65.85; H, 5.88; N, 18.09.

6-bromo-N-(tert-butyl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (4s)



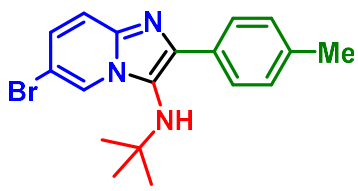
White solid (95%), mp 178°C. IR (KBr, cm^{-1}): 3322 (NH), 2963 (sp^2-CH), 2922 (sp^3-CH), 1611, 1511, 1449, 1358, 1321, 1221, 1029, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 10.0 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 3.09 (s, 1H), 1.01 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.16, 140.59, 140.20, 129.29, 127.12, 123.54, 122.97, 117.90, 113.84, 106.21, 56.47, 55.13, 30.33. Anal. Calcd for $C_{18}H_{20}BrN_3O$; C, 57.76; H, 5.39; N, 11.23 found: C, 57.78; H, 5.44; N, 11.29.

6-bromo-N-(tert-butyl)-2-(3-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (4t)



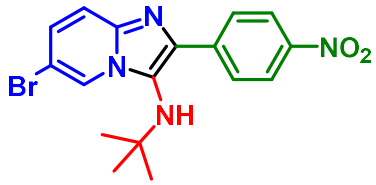
White solid (94%), mp 197-199°C. IR (KBr, cm^{-1}): 3288 (NH), 2959 (sp^2-CH), 2929 (sp^3-CH), 1619, 1493, 1438, 1348, 1319, 1207, 1047, 726. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.99 (t, *J* = 1.6 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.43 (s, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.32 – 7.29 (m, 1H), 7.22 (dd, *J* = 9.4, 1.9 Hz, 1H), 3.08 (s, 1H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.48, 138.78, 136.28, 134.36, 129.65, 128.08, 127.95, 127.72, 126.09, 124.04, 123.67, 118.12, 106.78, 56.47, 30.27. Anal. Calcd for $C_{17}H_{17}BrClN_3$; C, 53.92; H, 4.52; N, 11.10 found: C, 53.97; H, 4.58; N, 11.18.

6-bromo-N-(tert-butyl)-2-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (4u)



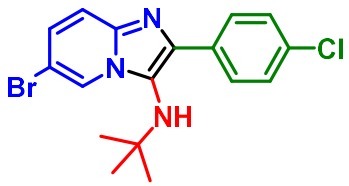
Off-white solid (93%), mp 128-130°C. IR (KBr, cm^{-1}): 3281 (N-H), 2949 (sp^2-CH), 2916 (sp^3-CH), 1618, 1511, 1463, 1368, 1349, 1239, 1069, 716. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 1.1 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 9.4 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.17 (dd, *J* = 9.4, 1.9 Hz, 1H), 3.15 (s, 1H), 2.39 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.44, 140.15, 137.35, 131.72, 129.08, 127.96, 127.20, 123.67, 117.93, 106.33, 56.77, 30.31, 21.42. Anal. Calcd for $C_{18}H_{20}BrN_3$; C, 60.34; H, 5.63; N, 11.73 found: C, 60.36; H, 5.68; N, 11.78.

6-bromo-N-(tert-butyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4v)



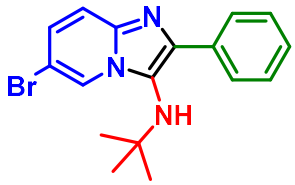
Brown solid (94%), mp 203°C. IR (KBr, cm^{-1}): 3290 (N-H), 3020 (sp^2-CH), 2993 (sp^3-CH), 1592, 1497, 1438, 1318, 1319, 1216, 1017, 769. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 9.7 Hz, 1H), 8.29 (d, *J* = 8.9 Hz, 2H), 8.22 (d, *J* = 8.9 Hz, 2H), 7.46 (d, *J* = 9.4 Hz, 1H), 7.26 (dd, *J* = 9.4, 1.8 Hz, 1H), 3.09 (s, 1H), 1.10 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.91, 141.39, 140.84, 137.77, 128.62, 128.49, 124.91, 123.65, 118.43, 107.18, 57.05, 30.85. Anal. Calcd for $C_{17}H_{17}BrN_4O_2$; C, 52.46; H, 4.40; N, 14.39 found: C, 52.53; H, 4.47; N, 14.46.

6-bromo-N-(tert-butyl)-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-amine (4w)



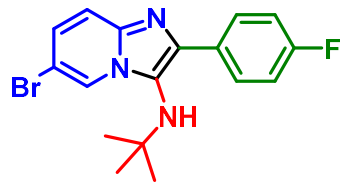
White solid (94%), mp 191°C. IR (KBr, cm^{-1}): 3311 (N-H), 3011 (sp^2-CH), 2988 (sp^3-CH), 1591, 1491, 1434, 1336, 1327, 1219, 1012, 748. ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 1.0 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.37 (t, J = 9.0 Hz, 3H), 7.16 (d, J = 11.2 Hz, 1H), 3.07 (s, 1H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.38, 139.28, 133.45, 133.22, 129.40, 128.49, 127.67, 123.82, 123.60, 117.81, 106.41, 56.77, 30.28. Anal. Calcd for $C_{17}H_{17}BrClN_3$; C, 53.92; H, 4.52; N, 11.10 found: C, 53.97; H, 4.58; N, 11.17.

6-bromo-N-(tert-butyl)-2-phenylimidazo[1,2-a]pyridin-3-amine (4x)



White solid (93%), mp 230°C. IR (KBr, cm^{-1}): 3295 (NH), 3062 (sp^2-CH), 2969 (sp^3-CH), 1609, 1516, 1416, 1357, 1331, 1236, 1038, 776. ^1H NMR (500 MHz, $CDCl_3$) δ 8.36 (dd, J = 1.8, 0.6 Hz, 1H), 7.88 (dd, J = 8.2, 1.2 Hz, 2H), 7.49 – 7.42 (m, 3H), 7.36 – 7.32 (m, 1H), 7.20 (dd, J = 9.4, 1.9 Hz, 1H), 3.18 (s, 1H), 1.04 (s, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.34, 134.53, 129.79, 128.39, 128.15, 127.76, 127.61, 123.89, 123.75, 117.74, 106.19, 56.77, 30.28. Anal. Calcd for $C_{17}H_{18}BrN_3$; C, 59.31; H, 5.27; N, 12.21 found: C, 59.38; H, 5.32; N, 12.28.

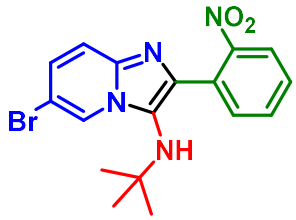
6-bromo-N-(tert-butyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-amine (4y)



White solid (95%), mp 215°C. IR (KBr, cm^{-1}): 3281 (N-H), 2979 (sp^2-CH), 2943 (sp^3-CH), 1610, 1515, 1443, 1362, 1297, 1213, 1037, 778. ^1H NMR (500 MHz, $CDCl_3$) δ 8.34 (dd, J = 1.8, 0.6 Hz, 1H), 7.89 (t, J = 6.1 Hz, 2H), 7.44 (d, J = 9.4 Hz, 1H), 7.21 (dd, J = 9.4, 1.9 Hz,

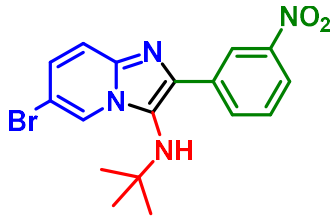
1H), 7.13 (t, *J* = 10.2 Hz, 2H), 3.09 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.43, 140.28, 139.37, 130.75, 129.82, 127.86, 123.67, 123.59, 117.74, 115.45, 115.17, 106.65, 56.48, 30.29. Anal. Calcd for $C_{17}H_{17}BrFN_3$; C, 56.37; H, 4.73; N, 11.60 found: C, 56.41; H, 4.75; N, 11.70.

6-bromo-N-(tert-butyl)-2-(2-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4z)



Brown solid (94%), mp 180°C. IR (KBr, cm^{-1}): 3291 (N-H), 2969 (sp^2-CH), 2937 (sp^3-CH), 1637, 1507, 1457, 1336, 1331, 1286, 1047, 760. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 0.9 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 6.8 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.54 – 7.46 (m, 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 149.26, 140.60, 137.00, 132.72, 132.47, 129.77, 128.73, 127.92, 125.03, 124.43, 123.64, 118.32, 107.01, 55.71, 30.04. Anal. Calcd for $C_{17}H_{17}BrN_4O_2$; C, 52.46; H, 4.40; N, 14.39 found: C, 52.51; H, 4.46; N, 14.43.

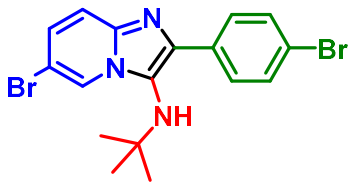
6-bromo-N-(tert-butyl)-2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (4z^1)



White solid (92%), mp 195°C. IR (KBr, cm^{-1}): 3301 (N-H), 2958 (sp^2-CH), 2891 (sp^3-CH), 1636, 1543, 1430, 1329, 1317, 1300, 1027, 766. ^{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 149.26, 145.21, 140.95, 134.56, 131.22, 129.92, 128.42, 128.24, 127.79, 127.27, 122.08,

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, 52.40; H, 4.37; N, 14.35.

6-bromo-2-(4-bromophenyl)-N-(tert-butyl)imidazo[1,2-a]pyridin-3-amine ($4z^2$)



White solid (92%), mp 193°C. IR (KBr, cm^{-1}): 3313 (NH), 3016 (sp^2-CH), 2983 (sp^3-CH), 1595, 1494, 1443, 1342, 1332, 1223, 1017, 753. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.82 (d, J = 33.8 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 38.5 Hz, 1H), 7.20 (dd, J = 9.4, 1.7 Hz, 1H), 3.04 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.40, 139.41, 133.71, 131.57, 129.62, 127.64, 123.78, 123.72, 121.79, 117.98, 106.45, 56.48, 30.27. Anal. Calcd for $C_{17}H_{17}Br_2N_3$; C, 48.25; H, 4.05; N, 9.93 found: C, 48.30; H, 4.15; N, 9.96.

3.8 Spectral Data of few products

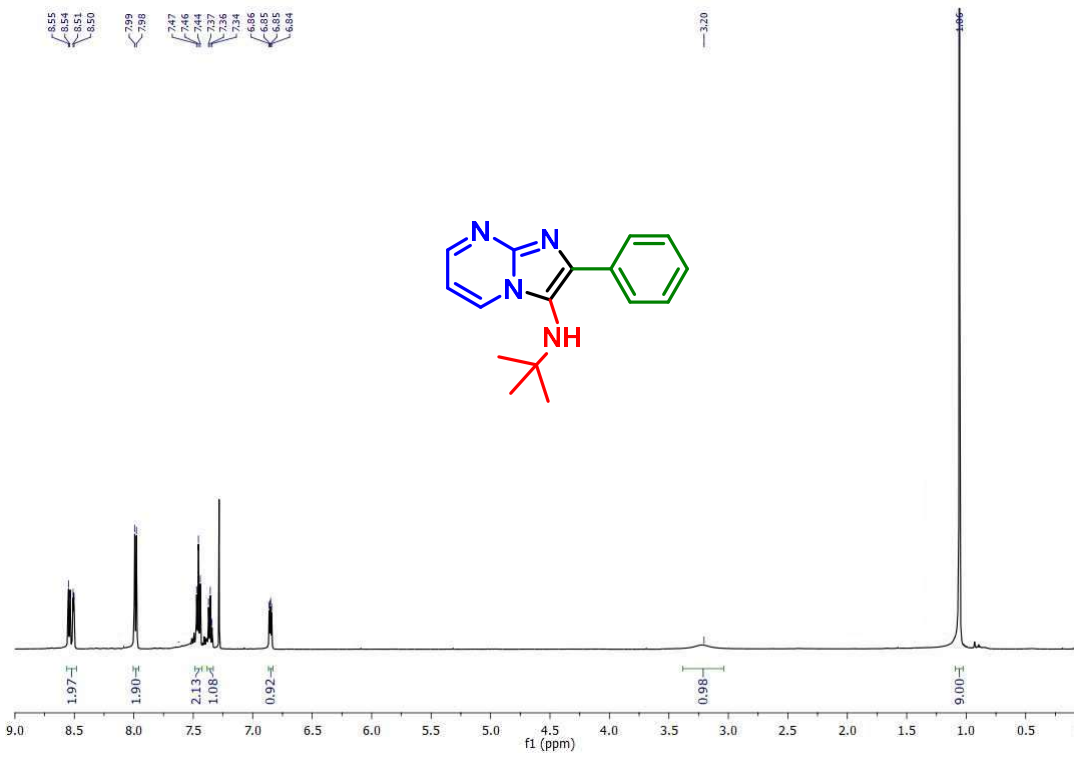


Figure 3.3 ^{1}H NMR of product **4a**

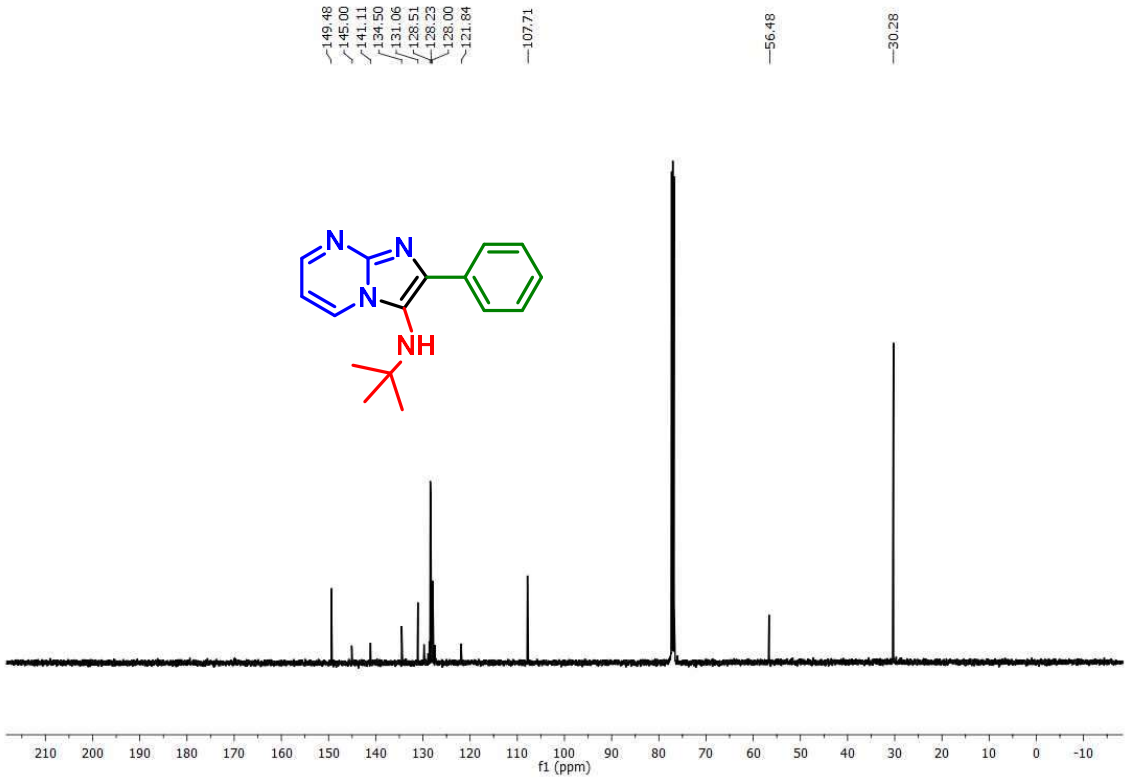


Figure 3.4 ^{13}C NMR of product **4a**

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