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Synthesis of 2-Aminopyridines via a Base-Promoted Cascade Reaction of *N*-Propargylic *β*-Enaminones with Formamides

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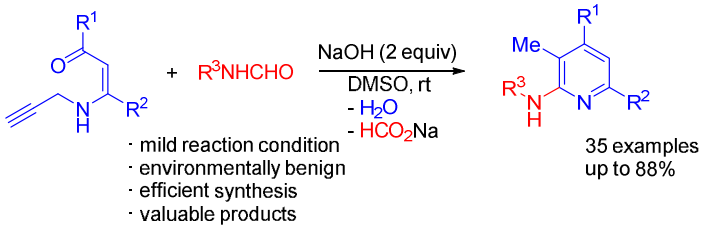
ABSTRACT: *N*-substituted formamides as nucleophiles react with in situ generated 1,4-oxazepines from *N*-propargylic *β*-enaminones, followed by spontaneous *N*-deformylation to deliver densely substituted 2-aminopyridines in good yields (31-88%). The formyl group is found to be a superior traceless activating group of free amines and would ultimately be removed in situ. This reaction proceeds smoothly at room temperature, in the presence of NaOH as sole additive, without protection from the atmosphere, and generating H_2O and sodium formate as byproducts.



■ INTRODUCTION

The 2-aminopyridine moiety represents an important motif in pharmaceuticals and natural products (Figure 1),[1] as well as ligands in organic synthesis and functional materials.[2] Intense efforts have been devoted to developing various methods for the synthesis of 2-aminopyridines and their derivatives. Transition-metal-catalyzed amination of aryl halides , typically including palladium-catalyzed Buchwald-Hartwig amination[3,4] and copper-catalyzed Ullmann-type amination,[5] provide powerful protocols to build such scores (Scheme 1, a). However, sophisticated ligands are always required, and aliphatic amines are not well tolerated in those amination reactions.[6] Ruthenium-[7] and copper-[8] catalyzed cyclization have also been developed for

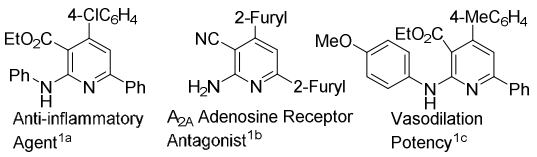
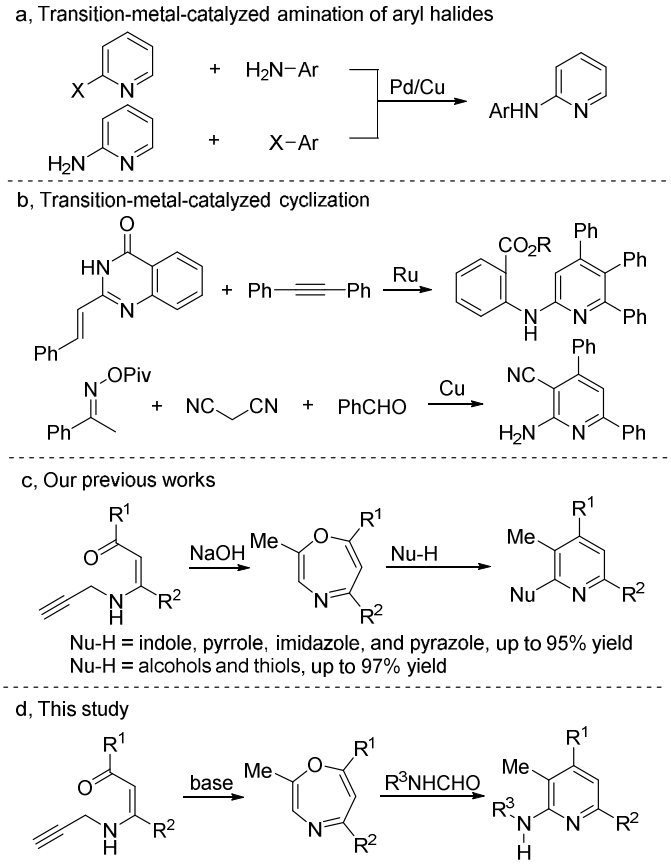


Figure 1. Selected Biologically Active Compounds Containing 2-Aminopyridines

the divergent synthesis of 2-aminopyridines (Scheme 1, b). An important additional drawback of the above mentioned approaches has to do with the toxicity of transition-metals in biological contexts, which seriously limit their applications in biological and medicinal research. Although the 2-aminopyridines could be synthesized by the traditional Chichibabin reaction from sodium amide and pyridines,[9] the nucleophilic addition,[10] and 1,3-dipolar cycloaddition reaction of pyridine derivatives,[11] the functionalized pyridine cores as starting materials are always required. Consequently, developing efficient access to 2-aminopyridines from readily available materials under transition-metal-free conditions is of great significance.

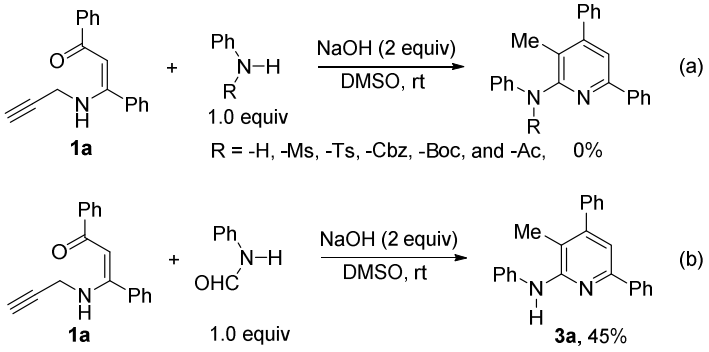
During our ongoing studies on synthesis of heterocyclic compounds,[12] we have recently documented that a variety of *N*-H heteroarenes, alcohols, and thiols could be used as nucleophiles for the capture of 1,4-oxazepine intermediates leading to *N*-substituted heteroarenes (Scheme 1, c) [12a-c] As research continues, herein we disclose a simple and highly efficient cascade approach to multisubstituted 2-aminopyridines from *N*-propargylic *β*-enaminones[13] and formamides (Scheme 1, d). In this scenario, the formyl group would function as a traceless activating group to facilitate nucleophilic addition of formamides to in situ generated 1,4-oxazepines and would spontaneously be released to produce 2-aminopyridines. In contrast to previous work,[3-8] the advantages of our reported reaction includes (i) mild reaction condition (room temperature, and using NaOH as the only additive). (ii) environmentally friendly (transition-metal-free, H_2O and sodium formate are the byproducts). (iii) highly efficiency (cascade reaction in one-pot mode).

Scheme 1. Reported and Present Synthetic Strategy for the Synthesis of 2-Aminopyridines



At the outset of our studies, free alkyl/aryl amines were used to react with *N*-propargylic *β*-enaminone **1a**, however no desired 2-aminopyridine products were observed, probably because of the considerably lower nucleophilicity of free amines. Considering that amides could be deprotonated under strongly basic conditions, and their conjugate bases may serve as nucleophiles. Then, a variety of activating groups, including -Ms, -Ts, -Cbz, -Boc, and -Ac, were screened, still no desired products were formed (Scheme 2, a). Back and co-workers reported that *N*-formyl anilines were more nucleophilic analogues than anilines under basic conditions for the conjugate addition to acetylenic sulfones.[14] When *N*-formyl aniline was subjected to react with **1a**, it was to our delight that the unpredictable *N*-deformylation product **3a** was obtained in 45% isolated yield (Scheme 2, b).

Scheme 2. Screening Activating Groups of Aniline for the Synthesis of 2-(Phenylamino)pyridines

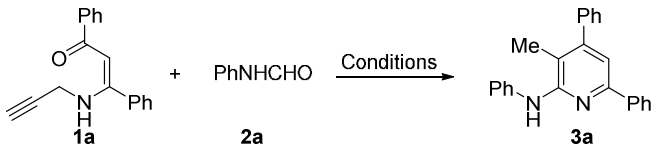


■ RESULTS AND DISCUSSION

(*Z*)-1,3-diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one **1a** and formanilide **2a** were chosen as the model substrates for the optimization of the reaction conditions, and the results were summarized in Table 1. NaOH, KOH, and LiOH were found to be efficient bases for this cascade reaction, among which NaOH gave the best result (Table 1, entries 1–3). The lower yields were encountered for other stronger bases (entries 4–6). Subsequently, various solvents were investigated in the presence of 2 equiv of NaOH as the base (entries 7–9). No better result was obtained than that of DMSO. 70% isolated yield was obtained when the loading of **2a** was decreased to 1.5 equiv (entry 10). Further raising the reaction temperature could improve the yields slightly (entry 13, 14). Therefore, the optimized reaction conditions were found to entail the use of **1a** and **2a** in a molar ratio of 1:1.5, NaOH (2 equiv) as the base at room temperature under air atmosphere (entry 10).

On the basis of the optimized conditions, the generality of this reaction was investigated. As shown in Scheme 3, a variety of substituted formanilides ran smoothly, affording the corresponding products in moderate to good yields (**3a–k**, yields 45–77%). The structure of **3a** was confirmed by single-crystal X-ray diffraction analysis. At first, formanilides with electron-donating groups (Me, OMe) were tested and smoothly converted into the desired products (**3b–e**). The *o*-methyl-substituted substrates, **3b** and **3d**, led to lower yields than *p*-methyl-substituted substrate **3c**,

Table 1. Screening of the Reaction Conditions[a]



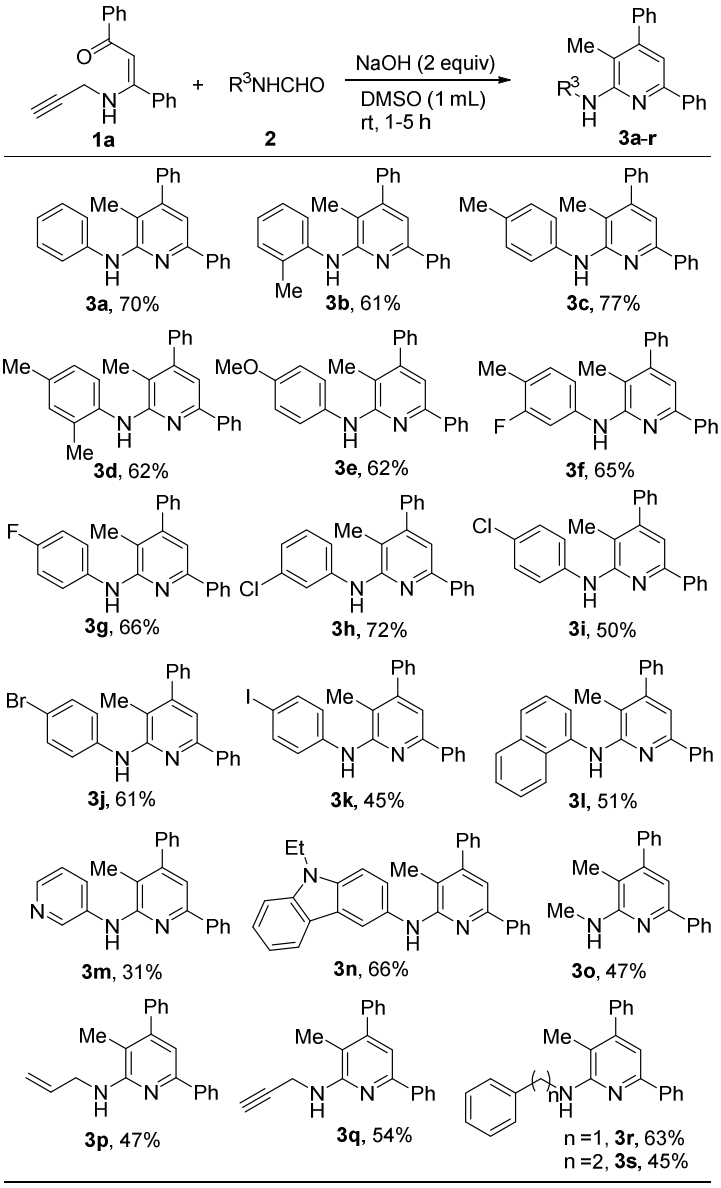
entry	base	solvent	temp (^{o}C)	yield (%)[b]
1	NaOH	DMSO	rt	70
2	KOH	DMSO	rt	67
3	LiOH	DMSO	rt	69
4	KO*t*Bu	DMSO	rt	56
5	NaO*t*Bu	DMSO	rt	53
6	Cs_2CO_3	DMSO	rt	14
7	NaOH	DMF	rt	50
8	NaOH	NMP	rt	49
9	NaOH	CH_3CN	rt	0
10[c]	NaOH	DMSO	rt	75 (70)
11[d]	NaOH	DMSO	rt	48
12[e]	NaOH	DMSO	rt	68
13	NaOH	DMSO	50	76 (70)
14	NaOH	DMSO	80	79 (72)

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), base (0.4 mmol), and solvent (1 mL) at room temperature under air atmosphere.[b]Yields were determined by GC analysis with dodecane as internal standard. Isolated yields in parentheses. [c]1.5 equiv of **2a** was used. [d]1.2 equiv of **2a** was used. [e]1.5 equiv of NaOH was used. DMSO = dimethylsulfoxide, DMF = *N*,*N*-dimethylformamide, NMP = *N*-methyl-2-pyrrolidone.

implying that the steric hindrance of the amides had an obvious effect on the reaction. Formanilides bearing halogen groups (F, Cl, Br, I) at meta- or para- position of the aryl ring afforded the desired products in moderate yields (**3f**–**k**, yields 45–72%), thus the corresponding products are suitable for further functionalization. Remarkably, 1-naphthalenyl amides **3l**, and heterocyclic aromatic amides (**3m**, **3n**) could be compatible with this procedure, providing the desired products in 51%, 31%, and 66% yields, respectively. In addition, various aliphatic formamides, including terminal

alkene and alkyne, furnished the corresponding 2-aminopyridines in moderate yields (**3o**–**s**, yields 45–63%).

Scheme 3. Scope of Formamides[a]

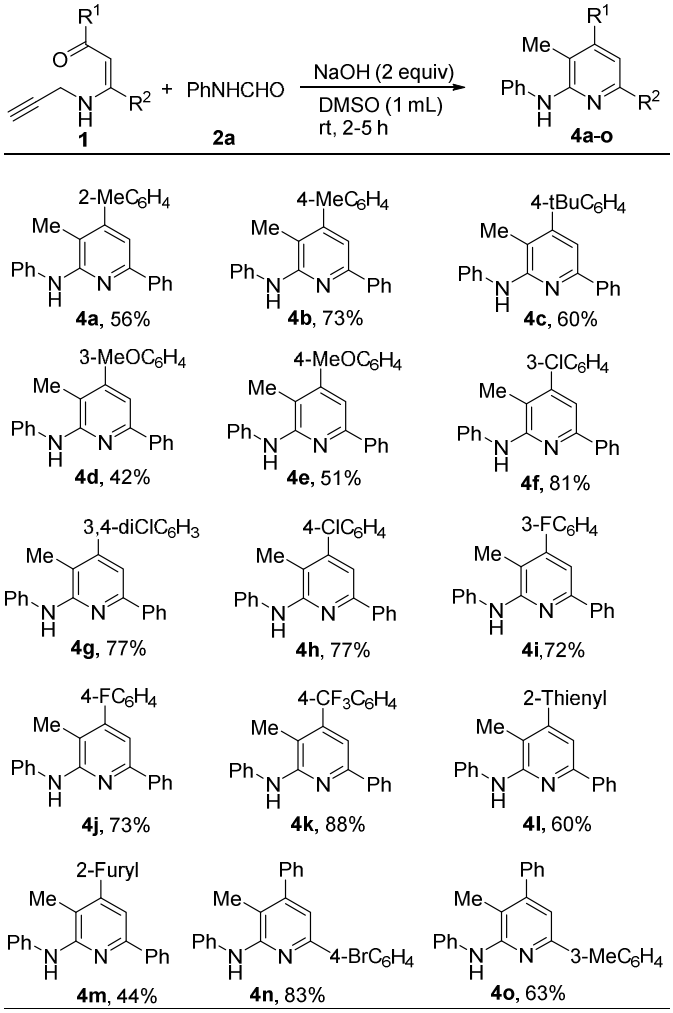


[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol), and NaOH (2 equiv) in DMSO (1 mL) at room temperature under air atmosphere. Yields based on **1a**.

Furthermore, the scope of *N*-propargylic *β*-enaminones was also explored (Scheme 4). The steric hindrance of the *N*-propargylic *β*-enaminones also had an obvious effect on the reaction (**4a**, yield 56%). In general, enaminone components bearing electron-donating substituents (**4b**−**e** and **4o**, yields 42−73%) tended to give slightly lower yields than those bearing electron-withdrawing substituents (**4f**−**k**, **4n**, yields

72−88%). Remarkably, when R^1 was 2-thienyl and 2-furyl, the desired products **4l** and **4m** were obtained in 60% and 44% yields, respectively.

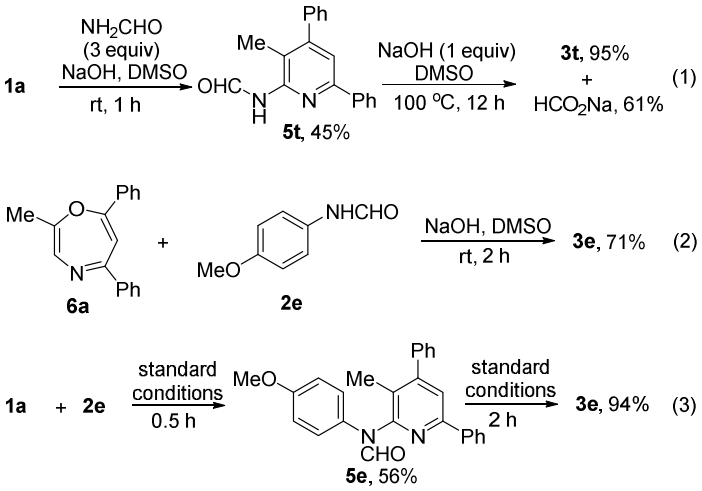
Scheme 4. Scope of *N*-Propargylic *β*-Enaminones[a]



[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), and NaOH (2 equiv) in DMSO (1 mL) at room temperature under air atmosphere. Yields based on **1**.

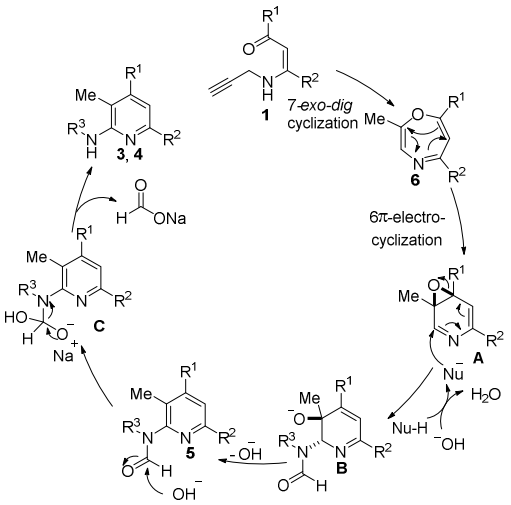
When **1a** was treated with methanamide under the standard reaction conditions, interestingly, *N*-(3-methyl-4,6-diphenylpyridin-2-yl) formamide **5t** was obtained instead of the decarboxylative product **3t**. Then **5t** was treated with 1 equivalent of NaOH at 100 ^{o}C for 12 h, **3t** and sodium formate were obtained in 95% and 61% yields, respectively. Those results indicated that the intermediates **5** could proceed through a base-promoted decarbonylation to produce sodium formate (eq 1). Our previous work[12a-c] had indicated that the active intermediate 1,4-oxazepines were generated from base-promoted 7-*exo-dig* cyclization of *N*-propargylic *β*-enaminones,

which could be used as pyridylation reagents of various *N*-heteroarenes, alcohols and thiols. Then the intermediate 1,4-oxazepine **6a** was treated with formamide **2e** under the standard reaction, the **3e** was obtained in 71% yield (eq 2). To further clarify the reaction mechanism, the reaction of **1a** with *N*-(4-methoxyphenyl) formamide **2e** was quenched with water after stirring at room temperature for 0.5 h, the formamide intermediate **5e** was isolated in 56% yield, which could be further transformed to **3e** at standard conditions for 2 h (eq 3).



Based on the above results and our previous researches,[12a] a possible mechanism is proposed (Scheme 5). Initially, the active intermediate 1,4-oxazepine **6** was formed by base-promoted cyclization from **1**. Subsequent **6** was isomerized to provide epoxide intermediate **A** undergoing 6π-electrocyclization. Then nucleophilic addition of formamide to epoxide **A** generated 2,3-dihydropyridine intermediates **B**, which subsequently aromatized to intermediate **5**. Finally, *N*-deformylation occurred leading to the final 2-aminopyridine products **3** and **4**.

Scheme 5. Plausible Mechanism for the Synthesis of 2-Aminopyridines



■ CONCLUSION

In summary, we have developed a concise and efficient protocol for the synthesis of a variety of 2-aminopyridine derivatives from *N*-propargylic *β*-enaminones at room temperature. In this reaction, the formyl group was used as a traceless activating group of amines, which would ultimately be released without any other process followed.

■ EXPERIMENTAL SECTION

General Information. All reagents were used directly without further purification. All melting points were determined on a Beijing Science Instrument Dianguang Instrument Factory XT4B melting point apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. HRMS-APCI spectra were obtained on Agilent 6450 Q-TOF spectrometer. IR data were recorded on a Nicolet iS10 spectrometer. The products listed below were determined by ^{1}H, ^{13}C NMR. PE is petroleum ether (60–90 ^{o}C). The 2-methyl-5,7-diphenyl-1,4-oxazepine **6a** was prepared according to the litertures.[12a-b]

Preparation of *N*-propargylic *β*-enaminones 1.[13c] A mixture of propargylamine (1.1 g, 20 mmol), propynones (20 mmol), and CH_3OH (50 mL) was stirred at room temperature under air overnight. After propynones was exhausted completely (monitored by TLC), the solvent was evaporated and the residue was purified by

chromatography (silica gel, 5% EtOAc in PE) to give **1**.

Preparation of formamides 2.[15] A mixture of amide or aniline (10 mmol), methanamide (10 mmol) and *L*-proline (115 mg, 1 mmol) was stirred in sealed tubes at indicated temperature for indicated reaction time (See reference 15). After being cooled to room temperature, 20 ml of water was added and extracted with DCM (20 mL x 3). After removal of solvent, the crude reaction mixture was purified by recrystallization or chromatography.

Preparation of 3-methyl-4,6-diphenylpyridin-2-amine 3t and sodium formate. A mixture of *N*-(3-methyl-4,6-diphenylpyridin-2-yl)formamide **5t** (144 mg, 0.5 mmol) and NaOH (20 mg, 0.5 mmol) in DMSO (1 mL) was stirred at 100 ^{o}C for 12 h. Then DCM (10 mL) was poured into the reaction mixture and the resulting solution was stirred for additional 5 min. Subsequently, the mixture was allowed to cool to 0 ^{o}C overnight, the resulting white solid was filtered off, washed with DCM and dried *in vacuo* to give sodium formate (21 mg, 61%). The organic residue was concentrated and purified by chromatography (silica gel, 5% EtOAc in PE) to give **3t** (123 mg, 95%).

Sodium formate. ^{1}H NMR (400 MHz, D_2O) δ 8.3 (s, 1H); ^{13}C NMR (100 MHz, D_2O) δ 171.1.

Preparation of *N*-(4-methoxyphenyl)-3-methyl-4,6-diphenylpyridin-2-amine 3e. A mixture of 2-methyl-5,7-diphenyl-1,4-oxazepine **6a** (52 mg, 0.2 mmol), *N*-(4-methoxyphenyl)formamide **2e** (45 mg, 0.3 mmol), NaOH (16 mg, 0.4 mmol) in DMSO (1 mL) was stirred at room temperature for 2 h. Then the reaction was quenched with H_2O (4 mL) and extracted with EtOAc (5 mL x 3). The combined EtOAc extracts were dried over Na_2SO_4 and concentrated. Then solvent was evaporated and the residue was purified by chromatography (silica gel, 5% EtOAc in PE) to give **3e** (52 mg, 71%).

Preparation of multisubstituted 2-aminopyridines 3, 4. A mixture of *N*-propargylic *β*-enaminones **1** (0.2 mmol), formamides **2** (0.3 mmol), NaOH (16 mg, 0.4 mmol) in DMSO (1 mL) was stirred at room temperature. After *N*-propargylic *β*-enaminones **1** was exhausted completely (monitored by TLC), the reaction was

quenched with H_2O (4 mL) and extracted with EtOAc (5 mL x 3). The combined EtOAc extracts were dried over Na_2SO_4 and concentrated. Then solvent was evaporated and the residue was purified by chromatography (silica gel, 5% EtOAc in PE).

*3-Methyl-N,4,6-triphenylpyridin-2-amine (**3a**).* Reaction time: 1 h; 47 mg (70%); white solid; m.p. 151–154 °C; IR (KBr): ν 1603, 1529, 1492, 1368, 751, 689, 491 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.73 (d, *J* = 7.7 Hz, 2H), 7.49–7.40 (m, 5H), 7.39–7.34 (m, 5H), 7.21 (s, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.39 (s, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.1, 151.1, 141.2, 140.5, 139.5, 128.9, 128.8, 128.6, 128.4, 128.4, 127.7, 126.6, 121.7, 119.4, 114.0, 113.4, 13.9; HRMS m/z (APCI) calcd for $C_{24}H_{21}N_2$ $(M + H)^+$ 337.1699, found 337.1705.

*3-Methyl-4,6-diphenyl-N-(o-tolyl)pyridin-2-amine (**3b**).* Reaction time: 2 h; 43 mg (61%); pale green solid; m.p. 157–160 °C; IR (KBr): ν 1597, 1530, 1482, 1455, 1368, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 2H), 7.50–7.25 (m, 9H), 7.24–7.21 (m, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.21 (s, 1H), 2.36 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.1, 151.1, 140.5, 139.5 (2C), 130.3, 128.9, 128.5, 128.4, 127.7, 127.2, 126.6, 122.1, 120.5, 114.4, 113.3, 18.2, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1866. (Note that three carbon peaks overlap with other peaks)

*3-Methyl-4,6-diphenyl-N-(p-tolyl)pyridin-2-amine (**3c**).* Reaction time: 2 h; 54 mg (77%); white solid; m.p. 143–146 °C; IR (KBr): ν 1608, 1529, 1401, 1370, 772, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08–7.99 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.47–7.30 (m, 8H), 7.20–7.13 (m, 3H), 6.29 (s, 1H), 2.34 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 152.0, 150.9, 140.6, 139.7, 138.6, 131.2, 129.4, 128.9, 128.6, 128.4, 127.7, 126.7, 119.8, 113.8, 113.1, 20.9, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1864. (Note that two carbon peaks overlap on each other)

*N-(2,4-Dimethylphenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3d**)*. Reaction time: 2 h; 45 mg (62%); white solid; m.p. 148–152 °C; IR (KBr): ν 1609, 1530, 1493, 1398, 1373, 772, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 1H), 7.99 (d,

J = 7.5 Hz, 2H), 7.49–7.29 (m, 8H), 7.18 (s, 1H), 7.08 (d, *J* = 8.3 Hz, 1H), 7.05 (s, 1H), 6.11 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 152.0, 150.9, 140.5, 139.5, 136.8, 131.7, 131.0, 128.8, 128.4, 128.3, 128.3, 127.7, 127.6, 126.9, 126.5, 121.2, 113.9, 112.9, 20.8, 18.1, 13.9; HRMS m/z (APCI) calcd for $C_{26}H_{25}N_2$ $(M + H)^+$ 365.2012, found 365.2019.

*N-(4-Methoxyphenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3e**).* Reaction time: 2 h; 38 mg (52%); white solid; m.p. 162–165 °C; IR (KBr): ν 1530, 1506, 1241, 1036, 824, 772, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–7.96 (m, 2H), 7.66–7.58 (m, 2H), 7.50–7.25 (m, 8H), 7.16 (s, 1H), 6.99–6.84 (m, 2H), 6.23 (s, 1H), 3.82 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 154.2, 151.9, 150.8, 140.5, 139.6, 134.4, 128.8, 128.5, 128.3, 127.6, 126.5, 121.7, 114.0, 113.3, 112.8, 55.6, 13.8; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2O$ $(M + H)^+$ 367.1805, found 367.1811. (Note that two carbon peaks overlap on each other)

*N-(3-Fluoro-4-methylphenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3f**).* Reaction time: 2 h; 48 mg (65%); yellow solid; m.p. 101–104 °C; IR (KBr): ν 1607, 1509, 1372, 1262, 1103, 1027, 803, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 2H), 7.74 (dd, *J* = 12.4, 1.8 Hz, 1H), 7.49–7.31 (m, 8H), 7.17–7.22 (m, 2H), 7.10 (t, *J* = 8.4 Hz, 1H), 6.36 (s, 1H), 2.25 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.30 (d, *J* = 242.0 Hz), 153.5, 152.1, 151.1, 140.4, 140.3, 139.4, 131.0 (d, *J* = 6.7 Hz), 128.8, 128.6, 128.5, 128.4, 127.7, 126.6, 117.4 (d, *J* = 17.7 Hz), 114.5 (d, *J* = 2.7 Hz), 113.9, 113.5, 106.5 (d, *J* = 27.5 Hz), 14.0 (d, *J* = 2.8 Hz), 13.8; HRMS m/z (APCI) calcd for $C_{25}H_{22}FN_2$ $(M + H)^+$ 369.1762, found 369.1766.

*N-(4-Fluorophenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3g**).* Reaction time: 2 h; 47 mg (66%); white solid; m.p. 141–145 °C; IR (KBr): ν 1610, 1503, 1398, 1371, 1202, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–7.97 (m, 2H), 7.69–7.63 (m, 2H), 7.50–7.33 (m, 8H), 7.20 (s, 1H), 7.11–7.01 (m, 2H), 6.30 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (d, *J* = 240.3 Hz), 153.9, 152.0, 151.1, 140.4, 139.5, 137.1 (d, *J* = 2.6 Hz), 128.8, 128.6, 128.5, 128.4, 127.8, 126.6, 121.4 (d, *J* = 7.6 Hz), 115.3 (d, *J* = 22.2 Hz), 113.6, 113.4, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}FN_2$ $(M + H)^+$ 355.1605, found 355.1612.

*N-(3-Chlorophenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3h**).* Reaction time: 2 h; 53 mg (72%); yellow solid; m.p. 100–105 °C; IR (KBr): ν 1601, 1532, 1480, 1396, 1371, 768, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.1 Hz, 2H), 7.99 (s, 1H), 7.52–7.32 (m, 9H), 7.27–7.21 (m, 2H), 6.98 (d, J = 7.9 Hz, 1H), 6.39 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 152.1, 151.3, 142.3, 140.2, 139.24, 134.4, 129.6, 128.8, 128.6, 128.6, 128.4, 127.8, 126.6, 121.4, 119.3, 117.1, 114.2, 113.9, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}ClN_2$ $(M + H)^+$ 371.1310, found 371.1301.

*N-(4-Chlorophenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3i**).* Reaction time: 2 h; 37 mg (50%); white solid; m.p. 153–156 °C; IR (KBr): ν 1605, 1527, 1489, 1397, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06–7.97(m, 2H), 7.72–7.64 (m, 2H), 7.49–7.28 (m, 10H), 7.22 (s, 1H), 6.35 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 152.1, 151.2, 140.3, 139.8, 139.4, 128.8, 128.7, 128.6, 128.6, 128.4, 127.8, 126.6, 126.3, 120.7, 114.0, 113.7, 13.9; HRMS m/z (APCI) calcd for $C_{24}H_{20}ClN_2$ $(M + H)^+$ 371.1310, found 371.1278.

*N-(4-Bromophenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3j**).* Reaction time: 2 h; 51 mg (61%); white solid; m.p. 173–175 °C; IR (KBr): ν 1604, 1524, 1486, 1393, 1369, 1029, 799 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.52–7.29 (m, 10H), 7.22 (s, 1H), 6.35 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 152.0, 151.2, 140.2 (2C), 139.3, 131.6, 128.8, 128.6, 128.5, 128.4, 127.8, 126.5, 121.0, 114.0, 113.7, 113.7, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}BrN_2$ $(M + H)^+$ 415.0804, found 415.0784. (Note that two carbon peaks overlap on each other)

*N-(4-Iodophenyl)-3-methyl-4,6-diphenylpyridin-2-amine (**3k**).* Reaction time: 5 h; 42 mg (45%); white solid; m.p. 194–196 °C; IR (KBr): ν 1603, 1520, 1484, 1392, 1369, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06–7.96 (m, 2H), 7.68–7.60 (m, 2H), 7.54–7.52 (m, 2H), 7.49–7.33 (m, 8H), 7.23 (s, 1H), 6.36 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 152.1, 151.2, 140.9, 140.2, 139.3, 137.5, 128.8, 128.6, 128.5, 128.4, 127.8, 126.5, 121.3, 114.1, 113.8, 83.7, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}IN_2$ $(M + H)^+$ 463.0666, found 463.0667.

*3-Methyl-N-(naphthalen-1-yl)-4,6-diphenylpyridin-2-amine (**3l**).* Reaction time: 5 h; 39 mg (51%); pale purple solid; m.p. 177–180 °C; IR (KBr): ν 1599, 1537, 1498, 1414, 1372, 769, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.5 Hz, 1H), 8.08–8.03 (m, 1H), 7.94 (d, *J* = 7.9 Hz, 2H), 7.91–7.86 (m, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.56–7.45 (m, 5H), 7.45–7.28 (m, 6H), 7.26 (s, 1H), 6.81 (s, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 152.3, 151.4, 140.4, 139.4, 136.6, 134.4, 128.9, 128.7, 128.5, 128.4, 127.8, 127.2, 126.6, 125.9, 125.7, 125.6, 122.9, 121.2, 117.2, 115.0, 113.9, 14.3; HRMS m/z (APCI) calcd for $C_{28}H_{23}N_2$ $(M + H)^+$ 387.1856, found 387.1858. (Note that two carbon peaks overlap on each other)

*3-Methyl-4,6-diphenyl-N-(pyridin-3-yl)pyridin-2-amine (**3m**).* Reaction time: 2 h; 21 mg (31%); brown solid; m.p. 161–165 °C; IR (KBr): ν 1601, 1525, 1484, 1372, 1261, 1094, 1025, 803, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 2.3 Hz, 1H), 8.42–8.32 (m, 1H), 8.27 (d, *J* = 3.8 Hz, 1H), 8.07–7.95 (m, 2H), 7.53–7.34 (m, 8H), 7.34–7.28 (m, 1H), 7.26 (s, 1H), 6.43 (s, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 152.2, 151.4, 142.6, 141.2, 140.1, 139.2, 137.8, 128.8, 128.6, 128.6, 128.4, 127.9, 126.6, 126.3, 123.4, 114.2, 13.8; HRMS m/z (APCI) calcd for $C_{23}H_{20}N_3$ $(M + H)^+$ 338.1652, found 338.1657. (Note that two carbon peaks overlap on each other)

*9-Ethyl-N-(3-methyl-4,6-diphenylpyridin-2-yl)-9H-carbazol-3-amine (**3n**).* Reaction time: 2 h; 60 mg (66%); brown solid; m.p. 68–72 °C; IR (KBr): ν 1596, 1528, 1489, 1370, 1090, 1025, 802, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.20–8.09 (m, 3H), 7.73–7.67 (m, 1H), 7.54–7.33 (m, 11H), 7.28–7.22 (m, 2H), 6.53 (s, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 2.25 (s, 3H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 151.8, 150.8, 140.7, 140.4, 139.6, 136.2, 133.2, 128.9, 128.5, 128.3, 127.6, 126.5, 125.5, 123.1, 123.1, 120.4, 120.1, 118.4, 113.3, 112.5, 112.5, 108.7, 108.3, 37.6, 13.9; HRMS m/z (APCI) calcd for $C_{32}H_{28}N_3$ $(M + H)^+$ 454.2278, found 454.2280. (Note that two carbon peaks overlap with other peaks)

*N,3-Dimethyl-4,6-diphenylpyridin-2-amine (**3o**).* Reaction time: 2 h; 26 mg (47%); white solid; m.p. 101–105 °C; IR (KBr): ν 1590, 1557, 1509, 1365, 776, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.47–7.30 (m, 8H), 7.02 (s, 1H),

4.35 (brs, 1H), 3.19 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 151.9, 149.6, 140.74, 140.0, 128.8, 128.4, 128.2, 128.1, 127.4, 126.5, 112.5, 110.8, 29.0, 13.3; HRMS m/z (APCI) calcd for $C_{19}H_{19}N_2$ $(M + H)^+$ 275.1543, found 275.1549.

*N-Allyl-3-methyl-4,6-diphenylpyridin-2-amine (**3p**).* Reaction time: 2 h; 28 mg (47%); colourless oil; IR (KBr): ν 1592, 1560, 1510, 1373, 773, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.00 (m, 2H), 7.48–7.29 (m, 8H), 7.03 (s, 1H), 6.20–6.07 (m, 1H), 5.38–5.26 (m, 1H), 5.21–5.13 (m, 1H), 4.44–4.35 (m, 1H), 4.35–4.28 (m, 2H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 151.8, 149.9, 140.7, 139.9, 136.5, 128.8, 128.4, 128.2, 128.1, 127.44, 126.5, 115.6, 112.4, 111.1, 44.5, 13.3; HRMS m/z (APCI) calcd for $C_{21}H_{21}N_2$ $(M + H)^+$ 301.1699, found 301.1705.

*3-Methyl-4,6-diphenyl-N-(prop-2-yn-1-yl)pyridin-2-amine (**3q**).* Reaction time: 2 h; 32 mg (54%); brown solid; m.p. 88–91 °C; IR (KBr): ν 3281, 1594, 1560, 1506, 1070, 1027, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.4 Hz, 2H), 7.48–7.30 (m, 8H), 7.09 (s, 1H), 4.47 (brs, 3H), 2.25 (s, 1H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 151.7, 150.2, 140.4, 139.6, 128.8, 128.4, 128.3, 127.5, 126.5, 112.9, 111.9, 82.2, 70.5, 31.7, 13.3; HRMS m/z (APCI) calcd for $C_{21}H_{19}N_2$ $(M + H)^+$ 299.1543, found 299.1537. (Note that two carbon peaks overlap on each other)

*N-Benzyl-3-methyl-4,6-diphenylpyridin-2-amine (**3r**).* 44 mg (63%); Reaction time: 1 h; white solid; m.p. 79–81 °C; IR (KBr): ν 1592, 1559, 1511, 772, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–7.98 (m, 2H), 7.54–7.25 (m, 13H), 7.06 (s, 1H), 4.88 (d, *J* = 5.2 Hz, 2H), 4.63 (t, *J* = 4.7 Hz, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 151.8, 149.9, 140.7, 140.6, 139.9, 128.8, 128.5, 128.4, 128.2, 128.1, 128.0, 127.5, 127.0, 126.5, 112.4, 111.2, 46.1, 13.4; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1859.

*3-Methyl-N-phenethyl-4,6-diphenylpyridin-2-amine (**3s**).* 33 mg (45%); Reaction time: 2 h; white solid; m.p. 93–97 °C; IR (KBr): ν 1593, 1511, 1028, 774, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–8.06 (m, 2H), 7.47–7.24 (m, 13H), 7.04 (s, 1H), 4.40 (t, *J* = 5.3 Hz, 1H), 3.97–3.86 (m, 2H), 3.06 (t, *J* = 7.0 Hz, 2H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 151.8, 149.8, 140.7, 140.1, 140.0, 129.0, 128.8,

128.5, 128.4, 128.2, 128.1, 127.4, 126.5, 126.2, 112.5, 110.9, 43.3, 36.0, 13.2; HRMS m/z (APCI) calcd for $C_{26}H_{25}N_2$ $(M + H)^+$ 365.2012, found 365.2017.

3-Methyl-4,6-diphenylpyridin-2-amine ***(3t)***. This reaction was carried out in 0.5 mmol scale in the presence of 1 equivalent of NaOH; reaction time: 12 h; white solid; 123 mg (95%); m.p. 107–109 °C; IR (KBr): ν 3296, 3174, 1627, 1591, 767, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97–7.90 (m, 2H), 7.45–7.36 (m, 5H), 7.35–7.30 (m, 3H), 7.05 (s, 1H), 4.64 (s, 2H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 152.8, 150.8, 140.2, 139.6, 128.7, 128.4, 128.2, 127.5, 126.6, 113.0, 112.5, 13.7; HRMS m/z (APCI) calcd for $C_{18}H_{17}N_2$ $(M + H)^+$ 261.1386, found 261.1389. (Note that two carbon peaks overlap on each other)

3-Methyl-N,6-diphenyl-4-(o-tolyl)pyridin-2-amine ***(4a)***. Reaction time: 2 h; 39 mg (56%); colourless oil; IR (KBr): ν 1602, 1526, 1495, 1372, 752, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.76 (d, J = 8.1 Hz, 2H), 7.46 – 7.24 (m, 8H), 7.17 – 7.11 (m, 2H), 7.03 (t, J = 7.4 Hz, 1H), 6.37 (s, 1H), 2.13 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 152.0, 150.8, 141.1, 140.0, 139.5, 135.4, 130.0, 128.8, 128.7, 128.5, 128.4, 127.8, 126.5, 125.8, 121.6, 119.3, 114.5, 113.1, 19.7, 13.4; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1850.

3-Methyl-N,6-diphenyl-4-(p-tolyl)pyridin-2-amine ***(4b)***. Reaction time: 4 h; 51 mg (73%); white solid; m.p. 140–142 °C; IR (KBr): ν 1607, 1533, 1495, 1371, 751, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.4 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.47–7.39 (m, 2H), 7.39–7.31 (m, 3H), 7.30–7.23 (m, 4H), 7.20 (s, 1H), 7.01 (t, J = 7.3 Hz, 1H), 6.37 (s, 1H), 2.42 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.0, 151.0, 141.2, 139.6, 137.5, 129.0, 128.8, 128.7, 128.5, 128.3, 126.6, 121.6, 119.3, 114.0, 113.5, 21.2, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1848. (Note that two carbon peaks overlap on each other)

4-(4-(Tert-butyl)phenyl)-3-methyl-N,6-diphenylpyridin-2-amine ***(4c)***. Reaction time: 2 h; 47 mg (60%); white solid; m.p. 159–162 °C; IR (KBr): ν 1604, 1527, 1498, 1372, 747, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.39–7.28 (m, 5H),

7.23 (s, 1H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.38 (s, 1H), 2.21 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.0, 151.0, 150.7, 141.2, 139.6, 137.4, 128.8, 128.6, 128.5, 128.3, 126.6, 125.2, 121.6, 119.4, 114.1, 113.6, 34.6, 31.4, 14.0; HRMS m/z (APCI) calcd for $C_{28}H_{29}N_2$ $(M + H)^+$ 393.2325, found 393.2330.

*4-(3-Methoxyphenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4d**).* Reaction time: 2 h; 31 mg (42%); yellow solid; m.p. 83–85 °C; IR (KBr): ν 1600, 1525, 1494, 1371, 752, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08–8.00 (m, 2H), 7.77–7.69 (m, 2H), 7.46–7.33 (m, 6H), 7.21 (s, 1H), 7.06–6.99 (m, 1H), 6.98–6.92 (m, 2H), 6.91–6.88 (m, 1H), 6.39 (s, 1H), 3.85 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 153.8, 152.0, 150.9, 141.8, 141.1, 139.5, 129.4, 128.8, 128.5, 128.4, 126.6, 121.7, 121.2, 119.4, 114.5, 113.9, 113.2, 113.1, 55.3, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2O$ $(M + H)^+$ 367.1805, found 367.1802.

*4-(4-Methoxyphenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4e**).* Reaction time: 5 h; 37 mg (51%); white solid; m.p. 207–209 °C; IR (KBr): ν 1602, 1519, 1369, 1238, 1026, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–7.98 (m, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.47–7.39 (m, 2H), 7.39–7.33 (m, 3H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.20 (s, 1H), 7.06–6.95 (m, 3H), 6.38 (s, 1H), 3.87 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 153.8, 152.0, 150.7, 141.2, 139.6, 132.7, 130.0, 128.8, 128.5, 128.3, 126.6, 121.6, 119.3, 114.1, 113.8, 113.6, 55.3, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2O$ $(M + H)^+$ 367.1805, found 367.1812.

*4-(3-Chlorophenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4f**).* 60 mg (81%); Reaction time: 2 h; white solid; m.p. 125–128 °C; IR (KBr): ν 1602, 1524, 1496, 1371, 1015, 750, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.46–7.31 (m, 8H), 7.25–7.18 (m, 1H), 7.15 (s, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.37 (s, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.2, 149.5, 142.2, 141.0, 139.3, 134.3, 129.6, 128.9, 128.8, 128.5, 127.8, 127.0, 126.6, 121.8, 119.5, 113.8, 113.0, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}ClN_2$ $(M + H)^+$ 371.1310, found 371.1299. (Note that two carbon peaks overlap on each other)

*4-(3,4-Dichlorophenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4g**).* Reaction time: 2 h; 62 mg (77%); white solid; m.p. 166–170 °C; IR (KBr): ν 1605, 1531, 1495, 752,

692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.3 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.48–7.40 (m, 3H), 7.39–7.30 (m, 3H), 7.21–7.15 (m, 1H), 7.12 (s, 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.37 (s, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.4, 148.5, 140.9, 140.3, 139.1, 132.6, 132.1, 130.7, 130.4, 128.8, 128.6, 128.6, 128.2, 126.6, 122.0, 119.6, 113.6, 112.7, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{19}Cl_2N_2$ $(M + H)^+$ 405.0920, found 405.0929.

*4-(4-Chlorophenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4h**).* Reaction time: 5 h; 57 mg (77%); white solid; m.p. 184–186 °C; IR (KBr): ν 1606, 1533, 1492, 1371, 751, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.48–7.40 (m, 4H), 7.39–7.32 (m, 3H), 7.32–7.26 (m, 2H), 7.15 (s, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.37 (s, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.2, 149.8, 141.0, 139.3, 138.8, 133.8, 130.2, 128.8, 128.6, 128.6, 128.5, 126.6, 121.8, 119.5, 113.8, 113.0, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}ClN_2$ $(M + H)^+$ 371.1310, found 371.1298.

*4-(3-Fluorophenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4i**).* Reaction time: 5 h; 51 mg (72%); white solid; m.p. 110–114 °C; IR (KBr): ν 1604, 1531, 1493, 1373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.48–7.31(m, 6H), 7.17 (s, 1H), 7.15–6.98 (m, 4H), 6.38 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, *J* = 246.9 Hz), 153.8, 152.2, 149.7, 142.5 (d, *J* = 7.6 Hz), 141.0, 139.3, 130.0 (d, *J* = 8.3 Hz), 128.8, 128.6, 128.5, 126.6, 124.6 (d, *J* = 2.7 Hz), 121.8, 119.5, 115.9 (d, *J* = 21.7 Hz), 114.6 (d, *J* = 21.0 Hz), 113.8, 112.9, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}FN_2$ $(M + H)^+$ 355.1605, found 355.1601.

*4-(4-Fluorophenyl)-3-methyl-N,6-diphenylpyridin-2-amine (**4j**).* Reaction time: 5 h; 52 mg (73%); white solid; m.p. 150–154 °C; IR (KBr): ν 1607, 1533, 1494, 1216, 839, 753, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.47–7.39 (m, 2H), 7.39–7.27 (m, 5H), 7.20–7.07 (m, 3H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.37 (s, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, *J* = 247.0 Hz), 153.8, 152.1, 150.0, 141.0, 139.4, 136.3 (d, *J* = 3.2 Hz), 130.5 (d, *J* = 8.0 Hz), 128.8, 128.5, 128.5, 126.6, 121.8, 119.4, 115.3 (d, *J* = 21.4 Hz), 113.9, 113.3, 13.8; HRMS m/z (APCI) calcd for $C_{24}H_{20}FN_2$ $(M + H)^+$ 355.1605, found 355.1600.

*3-Methyl-N,6-diphenyl-4-(4-(trifluoromethyl)phenyl)pyridin-2-amine (**4k**).* Reaction time: 2 h; 71 mg (88%); white solid; m.p. 168–170 °C; IR (KBr): ν 1606, 1533, 1496, 1321, 1172, 1126, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.4 Hz, 2H), 7.77–7.67 (m, 4H), 7.50–7.40 (m, 4H), 7.40–7.32(m, 3H), 7.15 (s, 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.38 (s, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 152.3, 149.5, 144.0, 140.9, 139.2, 129.9 (d, *J* = 32.6 Hz), 129.2, 128.8, 128.6, 126.6, 125.4 (d, *J* = 3.6 Hz), 124.1 (d, *J* = 272.2 Hz), 121.9, 119.5, 113.7, 112.8, 13.8; HRMS m/z (APCI) calcd for $C_{25}H_{20}F_3N_2$ $(M + H)^+$ 405.1573, found 405.1577. (Note that two carbon peaks overlap on each other)

*3-Methyl-N,6-diphenyl-4-(thiophen-2-yl)pyridin-2-amine (**4l**).* Reaction time: 2 h; 41 mg (60%); brown solid; m.p. 115–119 °C; IR (KBr): ν 1604, 1534, 1495, 1386, 743, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.49–7.29 (m, 7H), 7.14 (d, *J* = 3.0 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.39 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 152.3, 143.3, 141.3, 141.0, 139.3, 128.8, 128.5, 128.5, 127.5, 127.3, 126.6, 126.2, 121.8, 119.5, 114.5, 113.8, 14.1; HRMS m/z (APCI) calcd for $C_{22}H_{19}N_2S$ $(M + H)^+$ 343.1263, found 343.1262.

*4-(Furan-2-yl)-3-methyl-N,6-diphenylpyridin-2-amine (**4m**).* Reaction time: 2 h; 29 mg (44%); brown solid; m.p. 108–114 °C; IR (KBr): ν 1601, 1525, 1495, 1412, 747, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.59 (s, 1H), 7.55 (s, 1H), 7.48–7.41 (m, 2H), 7.41–7.31 (m, 3H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.70 (d, *J* = 3.3 Hz, 1H), 6.62 – 6.50 (m, 1H), 6.42 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.5, 152.1, 142.9, 141.3, 139.4, 138.9, 128.8, 128.5, 128.5, 126.6, 121.7, 119.3, 113.2, 111.5, 111.0, 110.7, 14.3; HRMS m/z (APCI) calcd for $C_{22}H_{19}N_2O$ $(M + H)^+$ 327.1492, found 327.1490.

*6-(4-Bromophenyl)-3-methyl-N,4-diphenylpyridin-2-amine (**4n**).* Reaction time: 2 h; 69 mg (83%); white solid; m.p. 124–128 °C; IR (KBr): ν 1605, 1531, 1495, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.51–7.30 (m, 9H), 7.15 (s, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.37 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 151.1, 150.8, 141.0, 140.2, 138.0, 134.3, 128.8, 128.8, 128.7, 128.4, 127.8, 127.8, 121.9, 119.5, 114.3, 113.1, 13.8; HRMS m/z (APCI)

calcd for $C_{24}H_{20}BrN_2$ $(M + H)^+$ 415.0804, found 415.0805.

*3-Methyl-N,4-diphenyl-6-(m-tolyl)pyridin-2-amine (**4o**).* Reaction time: 3 h; 44 mg (63%); white solid; m.p. 134–136°C; IR (KBr): ν 1599, 1517, 1448, 1368, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89–7.82 (m, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.50–7.29 (m, 8H), 7.20 (s, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.38 (s, 1H), 2.41 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 152.2, 151.0, 141.2, 140.4, 139.4, 138.0, 129.2, 128.8, 128.7, 128.4, 128.3, 127.7, 127.3, 123.7, 121.6, 119.3, 113.9, 113.4, 21.6, 13.9; HRMS m/z (APCI) calcd for $C_{25}H_{23}N_2$ $(M + H)^+$ 351.1856, found 351.1858.

*N-(4-Methoxyphenyl)-N-(3-methyl-4,6-diphenylpyridin-2-yl)formamide (**5e** , rotameric mixture, ratio of the rotamers = 54/46).* This reaction was carried out in 0.3 mmol scale; reaction time: 0.5 h; 66 mg (56%); white solid; m.p. 148–151 °C; IR (KBr): ν 1683, 1510, 1246, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.98–8.63 (m, 1H), 8.07 (d, *J* = 6.9 Hz, 1H), 7.95 (d, *J* = 6.2 Hz, 1H), 7.72–7.61 (m, 1H), 7.51–7.26 (m, 10H), 6.92 (m, 2H), 3.80 (s, 3H), 2.26–1.92 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 161.7, 158.4, 157.8, 154.6, 154.0, 153.9, 153.2, 153.0, 151.8, 139.1, 138.9, 138.3, 137.8, 133.3, 131.6, 129.2, 128.9, 128.7, 128.4, 128.3, 128.1, 127.2, 126.7, 126.3, 125.9, 125.3, 121.1, 120.5, 114.6, 114.2, 55.4, 15.6, 15.0; HRMS m/z (APCI) calcd for $C_{26}H_{23}N_2O_2$ $(M + H)^+$ 395.1754, found 395.1760.

*N-(3-Methyl-4,6-diphenylpyridin-2-yl)formamide (**5t**).* Reaction time: 2 h; 26 mg (45%); white solid; m.p. 208–212 °C; IR (KBr): ν 1696, 1374, 1262, 1101, 467 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, *J* = 10.2 Hz, 1H), 8.45 (d, *J* = 9.8 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 2H), 7.52–7.37 (m, 7H), 7.37–7.31 (m, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 152.7, 152.7, 149.4, 139.3, 138.2, 129.1, 128.7, 128.7, 128.5, 128.2, 126.6, 117.5, 115.3, 13.3; HRMS m/z (APCI) calcd for $C_{19}H_{17}N_2O$ $(M + H)^+$ 289.1335, found 289.1336.

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^1H NMR and ^{13}C NMR for all synthesized compounds. X-ray crystallographic data of **3a** (CIF). This material is available free of

charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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