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# Regioselective intramolecular electrophilic substitution reactions involving π-deficient pyridine substrates: a new entry to pyridoquinazolines and benzo[*h*][1,6]naphthyridines☆

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ABSTRACT

Regioselective intramolecular electrophilic substitution reactions have been described in π-deficient pyridine substrates tethered at C-2 to the aryl amine. The presence and nature of ring activating groups at C-6 led to the involvement of either N-1 or C-3 of the pyridine ring in the cyclization thereby leading to the regioselective synthesis of pyridoquinazolines and naphthyridines in excellent yields.



## 1. Introduction

1,6-Naphthyridine is an important pharmacophore present in many natural[1] and designed synthetic products of therapeutic importance. They are associated with a wide spectrum of biological activities ranging from anticancer,[2] antiherpes,[3] *anti*-HIV-1,[4] antimicrobial,[5] adrenoceptor blocking[6] to sortase A,[7] HIV-1 integrase inhibitors,[8] and Spleen Tyrosine Kinase[9] inhibitory activities.

Earlier reports for the synthesis of 1,6-naphthyridine skeleton involved Skraup synthesis[10] starting from 4-aminopyridine in 40% yield and a multiple-step synthesis using Heck coupling[11] in 51% yield. The synthesis of benzo[*h*][1,6]naphthyridines has been carried out either via rearrangement of Pyrrolobenzodiazepinones after heating with $POCl_3$[12] or via Friedlander condensation of 4-amino-3-formyl quinolines with either aldehydes or ketones to furnish benzo[*h*][1,6]naphthyridines in 40–56% yields.[13] Recently, Walton et al.[14] described a multistep synthesis of benzo[*h*][1,6]-naphthyridines by irradiating (microwave) oxime ethers of 2-aryl-3-formyl pyridine in 63–68% yield. Photochemical transformation of tertiary amidines has been also used for the synthesis of benzo[*h*][1,6]naphthyridines albeit in 15–30% yields. Thus, the above reported strategies generally suffer from certain disadvantages, such as stringent reaction conditions, low yields and poor generality and limited diversity.

In continuation of our studies of cationic π-cyclization in π-deficient systems tethered to aryl amines,[15] we focused our attention on pyridines for generating naphthyridine based compounds. Structurally, naphthyridine nucleus is a combination of two pyridine (privileged structure[16]) units, which makes it a useful class of compounds in drug discovery. The presence of a multiply bonded nitrogen atom in pyridines not only deactivates the ring toward electrophilic substitution than benzene but also imparts a differentiating effect on the carbons toward electrophilic substitution. The carbons at α- and γ-positions to the doubly bonded nitrogen are more deactivated than β-position.[17] However, when pyridine is exposed to electrophilic substitution, the nitrogen remains the most preferred target by electrophiles, thus preventing C-3 (β-carbon) electrophilic substitution. Indeed, halogenation, nitration, and sulfonation of pyridine not only require drastic conditions; even the yields of C-3 substituted products are exceptionally low.[18] Literature precedence on the involvement of C-3 of pyridine in cationic π-cyclization as nucleophile is scarce.[19] However, the method suffers from limited diversity and involves pyridine substrate tethered to aliphatic amine with exclusive involvement of C-3 in cyclization. In this paper, we describe regioselective intramolecular electrophilic cyclization involving either N-1 or C-3 of the pyridine ring leading to the synthesis of pyridoquinazolines and naphthyridines.

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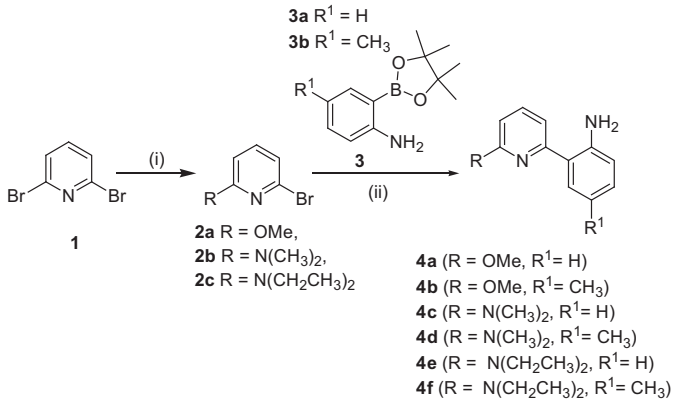
## 2. Results and discussion

Our studies commenced with the design of pyridine-based substrates suitable for cationic π-cyclization. Since inactivated pyridine fails to promote cyclization, we decided to incorporate an electron-donating group at the carbon *ortho* to the nitrogen and introduce an aryl amine as a source for electrophilic component (iminium ion) at the carbon again *ortho* to the nitrogen so as to facilitate π-cyclization using C-3. Though C-4 (*ortho* to C-3) also remains an option for introducing an aryl amine, we initially decided to work with C-2 linked aryl amine due to its synthetic feasibility. Accordingly, the key pyridine-based intermediate required for the synthesis of benzo[*h*][1,6]naphthyridines was identified as the substrate 2-(6-methoxy-pyridin-2-yl)-phenyl-amine **4a**. The latter was synthesized by the Suzuki reaction of 2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine **3a**[20] with 2-Bromo-6-methoxy-pyridine **2a**[21] as shown in Scheme 1. The intermediate **2a** was prepared by selective nucleophilic substitution of 2,6-dibromopyridine **1**.

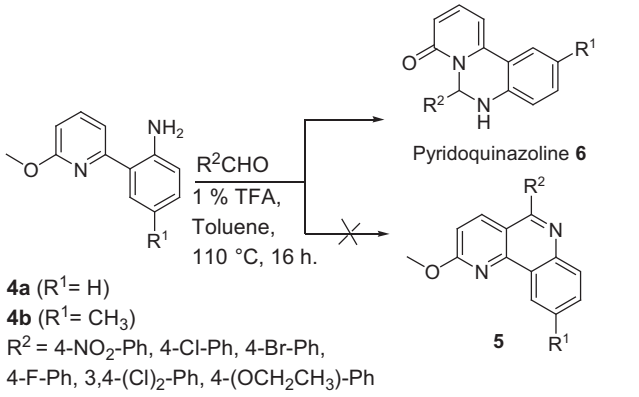



**Scheme 1.** Reagents and conditions: (i) NaOMe, MeOH, 80 °C, 20 h. (ii) $PdCl_2(PPh_3)_2$, $Na_2CO_3$, 80 °C, DMF, 1 h.

Initially, the cationic π-cyclization reaction of the substrate **4a** with *p*-nitrobenzaldehyde was investigated using either 1% TFA/DCM at rt or *p*TsOH in toluene at 80 °C conditions, however, both the protocols failed to give the desired product. Next, the reaction was carried out in the presence of a variety of Bronsted acids (Table 1) and best result involving complete conversion was obtained only when reaction was carried out in 1% TFA in toluene at 110 °C. The crude product exhibiting >98% purity on HPLC was purified using column chromatography furnishing a new product in 95% isolated yield. Surprisingly, the chemical characterization of the isolated product using NMR showed the formation of a product 6-(4-nitrophenyl)-5,6-dihydro-8*H*-pyrido[1,2-*c*]quinazolin-8-one **6a** (Scheme 2) instead of the desired 2-methoxy-5-(4-nitro-phenyl)-benzo[*h*][1,6]naphthyridine **5**. The formation of **6a** appears to have occurred by the attack of the lone pair of electrons present on the pyridyl nitrogen onto the iminium carbon instead of the attack by the C-3 (as π-nucleophile) of the pyridyl ring. Thus, we encountered an intramolecular electrophilic cycloelimination reaction involving N-1 instead of the envisaged cationic π-cyclization involving C-3. Surprisingly, this phenomenon pertaining to the involvement of N-1 was not observed by Padwa and Brodney[19] in their pyridine substrates when tethered with an aliphatic amine. A plausible mechanism for the unexpected formation of the product **6a** (Fig. 1) may be attributed to the attack by the lone pair of electron present on the pyridyl nitrogen onto the iminium carbon in the intermediate **7** followed by demethylation and an intramolecular cyclization thereby leading to the formation of 6-(4-nitrophenyl)-5,6-dihydro-8*H*-pyrido[1,2-*c*]quinazolin-8-one **6a**. Thus, the presence of OMe group at the 2-position of the pyridine ring could be playing an important role in facilitating the regioselective nucleophilic attack by the lone pair of electrons of pyridyl nitrogen instead of C-3 (as π-nucleophile) on to the iminium ion, as initially envisaged by us.

**Table 1**
Optimization of reaction conditions for the conversion of **4a** into **6a**

| Entry | Reaction Conditions | Temp (°C) | Time (h) | Yield of **6a** |
|---|---|---|---|---|
| 1 | 2% TFA in DCM | rt | 24 | 0 |
| 2 | 1% *p*-TsOH in ACN | rt | 24 | 0 |
| 3 | $Yb(OTf)_3$ in $CH_3CN$ | rt | 24 | 0 |
| 4 | 1%Triflic acid in DMF | rt | 24 | 0 |
| 5 | 1% *p*-TsOH in ACN | 80 °C | 24 | 0 |
| 6 | $Yb(OTf)_3$ in $CH_3CN$ | 80 °C | 24 | 0 |
| 7 | 1%Triflic acid in DMF | 80 °C | 24 | 28 |
| 8 | 1% TFA in toluene | 80 °C | 16 | 25 |
| 9 | 1% *p*-TsOH in ACN | 110 °C | 16 | 36 |
| 10 | 1%Triflic acid in DMF | 110 °C | 16 | 42 |
| 11 | 1% TFA in toluene | 110 °C | 16 | 95 |




**Scheme 2.** Synthesis of 6-phenyl-5,6-dihydro-8*H*-pyrido[1,2-*c*]quinazolin-8-one.

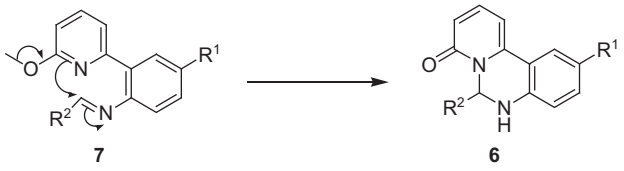



**Figure 1.** Proposed mechanism for the synthesis of **6**.

Quinazoline-based compounds are one of the most crucial heterocyclic skeletons (privileged structure[16]) as they are part of a vast range of therapeutically active molecules. Armed with this observation we set out to explore the application of our strategy for generating quinazoline-based compounds. A careful survey of the literature showed two reports for the synthesis of Pyrido[1,2-*c*]quinazoline template via multiple-step synthesis.[22] However, the strategies suffered from low yields and poor diversity. We studied the scope and limitation of our methodology by treating substrate **4a** (R=OMe; $R^1$=H) with several aryl aldehydes (Table 2) containing either electron withdrawing or electron-donating substituents. Although, reactions of substrate **4** with aldehydes having electron-withdrawing groups, such as nitro, chloro, flouro, bromo furnished **6a–d** and **g** in >90% isolated yields (Table 2), aldehydes with electron-donating group such as $N(Me)_2$ and

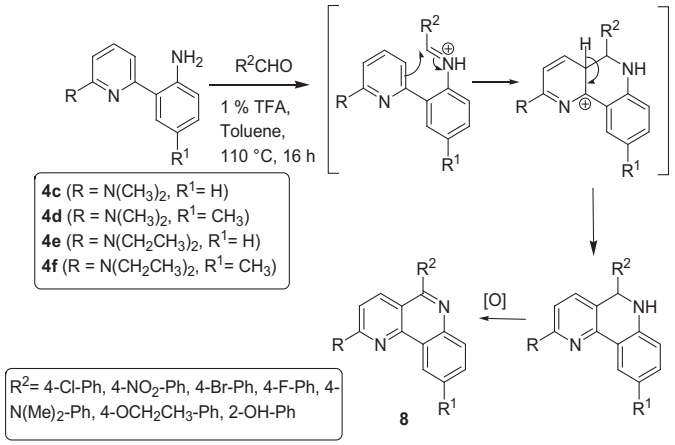
–$OCH_3$ either failed or furnished product (entry 8) in <15% isolated yields. Similar observations were also made with substrate **4b** (R=OMe; $R^1$=$CH_3$), which smoothly underwent cycloelimination reactions when treated with aldehydes having electron-withdrawing substituents to furnish **6i–l** in excellent isolated yields (Table 2). In general the dihydro derivatives **6** were found to be stable and attempts to oxidize them using DDQ/$KMnO_4$ were not successful.

**Table 2**
Synthesis of 8*H*-Pyrido[1,2-*c*]quinazolin-8-one

| Entry | Substrate | $R^2$ | $R^1$ | Product | Yield (%) |
|---|---|---|---|---|---|
| 1 | **4a** | 4-$NO_2$-$C_6H_4$- | H | **6a** | 96 |
| 2 | **4a** | 4-Cl-$C_6H_4$- | H | **6b** | 92 |
| 3 | **4a** | 4-Br-$C_6H_4$- | H | **6c** | 94 |
| 4 | **4a** | 4-F-$C_6H_4$- | H | **6d** | 95 |
| 5 | **4a** | 4-$(CH_3)_2$N-$C_6H_4$- | H | **6e** | NR |
| 6 | **4a** | 3,4-$(OCH_3)_2$-$C_6H_4$- | H | **6f** | NR |
| 7 | **4a** | 3,4-$(Cl)_2$-$C_6H_4$- | H | **6g** | 90 |
| 8 | **4a** | 4-$(OCH_2CH_3)$-$C_6H_4$- | H | **6h** | 15 |
| 9 | **4b** | 4-$NO_2$-$C_6H_4$- | $CH_3$ | **6i** | 95 |
| 10 | **4b** | 4-Cl-$C_6H_4$- | $CH_3$ | **6j** | 93 |
| 11 | **4b** | 4-Br-$C_6H_4$- | $CH_3$ | **6k** | 90 |
| 12 | **4b** | 4-F-$C_6H_4$- | $CH_3$ | **6l** | 89 |

NR=No reaction.

Next, in an attempt to synthesize compounds based on naphthyridines via cationic π-cyclization, we decided to block the attack of pyridyl nitrogen onto the iminium ion by replacing the OMe group with a poorly labile but with ring activating properties such as *N*,*N*-dimethyl group to afford substrate **4c** (Scheme 3). We envisaged that due to the resistant nature of N–C bond to cleavage in $N(CH_3)_2$ group, the attack by the lone pair of electron of the nitrogen of pyridine onto the iminium ion would not be fruitful thereby leaving C-3 as the only option to effect the desired regioselective cationic π-cyclization. Synthesis of **4c** was carried out by treating **1** with dimethylamine to give **2b**, which was then subjected to Suzuki coupling with boronate **3a**. Compound **4c** was then subjected to cationic π-cyclization by treating with *p*-nitrobenzaldehyde in the presence of 1% TFA in toluene at 110 °C, which effected complete conversion of **4c** and afforded a new product >99% purity based on HPLC. The crude product obtained after workup was purified by silica gel column chromatography using EtOAc/hexane as an eluent furnishing **8a** in 97% isolated yield. The latter was characterized using 1D and 2D NMR and ESMS. As reported earlier by us[15], the cationic π-cyclization occurred via protonation of the azomethine bond followed by regioselective intramolecular nucleophilic attack (Pictet–Spengler type) by the pyridyl carbon C-3 to afford an unstable intermediate, which then underwent spontaneous oxidation to *N*,*N*-dimethyl-5-(4-nitrophenyl)benzo[*h*][1,6]naphthyridin-2-amine **8a**. This is in contrast to the formation of dihydropyridoquinazolinones **6** via cycloelimination wherein phenomenon of spontaneous oxidation was not observed. This may be attributed to the high order stability of **6**, which in turn makes it adamant toward oxidation. The scope and limitation of our strategy was then examined by treating substrates **4c** and its derivatives **4d**, **4e**, and **4f** with aryl aldehydes having both electron withdrawing and donating substituents (Table 3). Pleasingly, neither aldehydes ($R^2$) having electron-donating as well as electron-withdrawing group nor substitutions on aryl amine ($R^1$) and pyridine (R) had any adverse effect on the rate of cyclization and benzo[*h*][1,6]naphthyridines **8** in general were obtained in excellent (85–97%) isolated yields. Indeed, aliphatic aldehydes and ketones failed to undergo cationic π-cyclization, which may be attributed to the poor electrophilic nature of the resulting corresponding iminium ions.




**Scheme 3.** Synthesis of benzo[*h*][1,6]naphthyridine **8**.

**Table 3**
Synthesis of benzo[*h*][1,6]naphthyridine **8**

| Entry | Substrate | $R^2$ | $R^1$ | Product | Yield (%) |
|---|---|---|---|---|---|
| 1 | **4c** | 4-$NO_2$-$C_6H_4$- | H | **8a** | 97 |
| 2 | **4c** | 4-Cl-$C_6H_4$- | H | **8b** | 93 |
| 3 | **4c** | 4-Br-$C_6H_4$- | H | **8c** | 95 |
| 4 | **4c** | 4-OH- $C_6H_4$- | H | **8d** | 90 |
| 5 | **4c** | 4-$(CH_3)_2$N-$C_6H_4$- | H | **8e** | 91 |
| 6 | **4c** | 3,4-(O $CH_3)_2$-$C_6H_4$- | H | **8f** | 90 |
| 7 | **4d** | 4-$NO_2$-$C_6H_4$- | $CH_3$ | **8g** | 94 |
| 8 | **4d** | 4-Cl-$C_6H_4$- | $CH_3$ | **8h** | 92 |
| 9 | **4d** | 4-Br-$C_6H_4$- | $CH_3$ | **8i** | 93 |
| 10 | **4d** | 4-F-$C_6H_4$- | $CH_3$ | **8j** | 90 |
| 11 | **4d** | 4-$(CH_3)_2$N-$C_6H_4$- | $CH_3$ | **8k** | 91 |
| 12 | **4d** | 3,4-$(OCH_3)_2$-$C_6H_4$- | $CH_3$ | **8l** | 90 |
| 13 | **4d** | 4-$(OCH_2CH_3)$-$C_6H_4$- | H | **8m** | 88 |
| 14 | **4e** | 4-$NO_2$-$C_6H_4$- | H | **8n** | 95 |
| 15 | **4e** | 4-Cl-$C_6H_4$- | H | **8o** | 93 |
| 16 | **4e** | 4-Br-$C_6H_4$- | H | **8p** | 94 |
| 17 | **4e** | 4-F-$C_6H_4$- | H | **8q** | 91 |
| 18 | **4e** | 4-OH- $C_6H_4$- | H | **8r** | 86 |
| 19 | **4e** | 4-$(CH_3)_2$N-$C_6H_4$- | H | **8s** | 88 |
| 20 | **4e** | 4-$(OCH_2CH_3)$-$C_6H_4$- | H | **8t** | 90 |
| 21 | **4f** | 4-$(CH_3)_2$N-$C_6H_4$ | $CH_3$ | **8u** | 86 |
| 22 | **4f** | 4-Br-$C_6H_4$- | $CH_3$ | **8v** | 90 |
| 23 | **4f** | 4-$NO_2$-$C_6H_4$- | $CH_3$ | **8w** | 95 |
| 24 | **4f** | 4-Cl-$C_6H_4$ | $CH_3$ | **8x** | 93 |
| 25 | **4f** | 4-$(OCH_2CH_3)$-$C_6H_4$- | $CH_3$ | **8y** | 89 |

## 3. Conclusion

In conclusion, we have developed mild and efficient protocol for the regioselective synthesis of benzo[*h*][1,6]naphthyridines and 6-phenyl-5,6-dihydro-8*H*-pyrido[1,2-*c*]quinazolin-8-one via either intramolecular electrophilic or cationic π-cyclization routes using appropriately substituted π-deficient pyridine substrates. The observed regioselectivity, demonstrates the efficacy and versatility of using such electrophilic cyclizations involving π-deficient systems for the synthesis of novel chemprobes.

## 4. Experimental

### 4.1. General

All solvents were commercially available and used without purification. All products were characterized by $^1$H NMR, $^{13}$C NMR, ESMS, IR, and HPLC. Analytical TLC was performed using 2.5×5 cm plated coated with a 0.25 mm thickness of silica gel. 60F-254 Merck and visualization was accomplished with UV light and iodine.

Column chromatography was performed using silica gel 60 Thomas Baker (100–200 mesh). $^1$H NMR spectra (200/300 MHz) are reported as follows: chemical shifts in ppm downfield from TMS as internal standard ($\delta$ scale), multiplicity [br=broad, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, o=overlapped, integration and coupling constant (Hz)]. All $^{13}$C NMR spectra (50/75 MHz) were recorded at 25 °C with complete proton decoupling and reported in ppm. Elemental analyses were performed on a Carlo Erba 1108 microanalyzer or Elementar's Vario EL III microanalyzer in the SAIF division of our institute. Analytical HPLC were performed on C-18 reverse-phase column (150 mm×4.8 mm). Mass spectra were recorded on a Merck MS-8000 spectrometer and HR/EI Mass spectra were done on JEOL-600H at 70 eV. Melting points reported were uncorrected.

### 4.2. Procedure for the synthesis of 2-bromo-6-methoxypyridine (2a)

A mixture of 2,6-dibromopyridine **1** (1.0 g, 4.20 mmol) and sodium methoxide (0.39 g, 7.25 mmol) in methanol was heated at 80 °C for 24 h. After completion of the reaction as evident by TLC analysis, methanol was distilled off, water (20 mL) was added and compound was extracted with ethyl acetate (15 mL×3). The organic layer washed with brine, dried over $Na_2SO_4$ and then concentrated in vacuo. The reaction mixture was then subjected to column chromatography (100–200 silica gel) using ethyl acetate:hexane (98:2, v/v) as eluent. Yield=0.65 g (81%), colorless oil, $R_f$=0.50 (Hexane), IR (Neat) $\nu_{max}$ 2972, 1590, 1464, 1409 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=7.44–7.38 (1H, m, ArH), 7.05 (1H, d, $J$=7.4 Hz, ArH), 6.69 (1H, d, $J$=8.2 Hz, ArH), 3.93 (3H, s, $OCH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$=163.8, 140.4, 138.7, 120.3, 109.9, 54.1; mass ($ES^+$) $m/z$ 187.9 ($M^+$+1); Anal. Calcd for $C_6H_6BrNO$: C, 38.33; H, 3.22; N, 7.45. Found: C, 38.28; H, 3.25; N, 7.39.

### 4.3. Procedure for the synthesis of 6-bromo-*N*,*N*-dimethylpyridin-2-amine (2b)

To a solution of 2,6-dibromopyridine **1** (1.0 g, 4.20 mmol) and dimethylamine (5.6 M) in ethanol (1.5 mL) was heated at 80 °C in a sealed tube for 16 h. Reaction mixture was allowed to come to room temperature, ethanol was distilled off, water (20 mL) was added and compound was extracted with ethyl acetate (15 mL×3). The organic layer washed with brine, dried over $Na_2SO_4$ and then concentrated in vacuo. The crude mixture was then subjected to column chromatography (100–200 silica gel) using ethyl acetate:-hexane (95:5, v/v) as eluent. Yield=0.73 g (85%), colorless oil, $R_f$=0.50 (1:9 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3305, 2906, 1598, 1174 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$=7.28–7.20 (1H, m, ArH), 6.66 (1H, d, $J$=11.1 Hz, ArH), 6.37 (1H, d, $J$=12.5 Hz, ArH), 3.06 (6H, s, $N(CH_3)_2$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=159.3, 140.2, 139.1, 114.2, 103.9, 37.9; mass ($ES^+$) $m/z$ 201.2 ($M^+$+1); Anal. Calcd for $C_7H_9BrN_2$: C, 41.82; H, 4.51; N, 13.93. Found: C, 41.80; H, 4.54; N, 13.91.

### 4.4. Procedure for the synthesis of 6-bromo-*N*,*N*-diethylpyridin-2-amine (2c)

To a solution of 2,6-dibromopyridine **1** (1.0 g, 4.20 mmol) in DMF (5 ml) was added diethylamine (0.45 ml, 4.20 mmol) in a sealed tube and heated to 100 °C for 12 h. The reaction mixture was allowed to cool, water (25 ml) was added and compound was extracted with ethyl acetate (15 mL×3). The organic layer was washed with brine, dried over $Na_2SO_4$ and then concentrated in vacuo. The crude mixture was then subjected to column chromatography (100–200 silica gel) using ethyl acetate:hexane (95:5, v/v) as eluent. Yield=0.72 g (75%), yellow oil, $R_f$=0.50 (Hexane), IR (Neat) $\nu_{max}$ 2969, 1583, 1493, 1450, 1115 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=7.22–7.16 (1H, m, ArH), 6.60 (1H, d, $J$=7.4 Hz, ArH), 6.34 (1H, d, $J$=8.4, ArH), 3.47 (4H, q, $J$=7.0 Hz, $CH_2$), 1.16 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=158.1, 140.6, 139.2, 113.3, 104.2, 42.8, 13.2; mass ($ES^+$) $m/z$ 229.2 ($M^+$+1); Anal. Calcd for $C_9H_{13}BrN_2$: C, 47.18; H, 5.72; N, 12.23. Found: C, 47.15; H, 5.74; N, 12.21.

### 4.5. General procedure for the synthesis of 2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (3)

The solution of 2-bromoaniline (2.0 g, 11.62 mmol), bis[pinaclolato]diboron (3.24 g, 12.78 mmol), potassium acetate (1.7 g, 17.43 mmol), and tricyclohexyl phosphine (0.39 g, 1.39 mmol) in dry dioxane (15 ml) was purged with nitrogen for 15 min followed by the addition of tris[dibenzylideneacetone]dipalladium(0) (0.53 g, 0.58 mmol). The reaction mixture was heated at 80 °C for 16 h, filtered through Celite, washed with ethyl acetate and concentrated to get the product, which was used without further purification.

### 4.6. General procedure for the synthesis of 2-pyridin-2-ylaniline (4a–e)

The solution of 2-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)-phenylamine **3a** (0.87 g, 4.0 mmol) and 2-bromo-6-methoxypyridine **2a** (0.5 g, 2.67 mmol) in DMF (5 mL) was degassed with nitrogen for 15 min followed by addition of $Na_2CO_3$ (5.0 mL, 2 M) under continuous flow of nitrogen. $PdCl_2$ $(PPh_3)_2$ (0.30 g, 0.26 mmol) were added to the reaction mixture under a nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 2 h. The solution was diluted with $H_2O$ (5 mL), and then the product was extracted three times with EtOAc (10 mL). The combined organic layer was dried over $Na_2SO_4$ and the solvent was removed in vacuo. The crude product was purified on a silica gel column using hexane:ethyl acetate (90:10, v/v) as eluent to afford 2-(6-methoxypyridin-2-yl)aniline **4a**.

*4.6.1. 2-(6-Methoxypyridin-2-yl)aniline (**4a**).* Yield=0.43 g (80%), yellow solid, mp 42–44 °C, $R_f$=0.50 (1:9 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3344, 3039, 2938, 1256 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=7.66 (1H, t, $J$=7.9 Hz, ArH), 7.50 (1H, dd, $J$=1.3, 7.7 Hz, ArH), 7.24–7.14 (2H, m, ArH), 6.81–6.74 (2H, m, ArH), 6.66 (1H, d, $J$=8.2 Hz, ArH), 5.56 (2H, br s, $NH_2$), 3.95 (3H, s, $OCH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=162.7, 157.0, 146.3, 139.5, 129.8, 129.6, 122.6, 117.9, 117.3, 115.1, 108.1, 53.4; mass ($ES^+$) $m/z$ 201.2 ($M^+$+1); Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.95; H, 6.07; N, 13.97.

*4.6.2. 2-(6-Methoxypyridin-2-yl)-4-methylaniline (**4b**).* Yield=0.66 g (82%), yellow oil, $R_f$=0.30 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3310, 3007, 2929, 1257 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=7.64 (1H, t, $J$=7.9 Hz, ArH), 7.3 (1H, s, ArH), 7.22 (1H, t, $J$=8.0 Hz, ArH), 6.98 (1H, d, $J$=8.0 Hz, ArH), 6.69–6.63 (2H, m, ArH), 5.36 (2H, s, $NH_2$), 3.94 (3H, s, $OCH_3$), 2.28 (3H, s, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=162.7, 157.1, 143.7, 139.5, 130.6, 130.1, 127.0, 122.9, 117.4, 115.8, 108.1, 53.4, 20.6; mass ($ES^+$) $m/z$ 215.3 ($M^+$+1); Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.07. Found: C, 72.85; H, 6.61; N, 13.08.

*4.6.3. 6-(2-Aminophenyl)-N,N-dimethylpyridin-2-amine (**4c**).* Yield=0.89 g (85%), yellow oil, $R_f$=0.50 (1:1 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3305, 2923, 1600, 1369 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=7.56–748 (2H, m, ArH), 7.16–7.10 (1H, m, ArH), 6.90 (1H, d, $J$=7.5 Hz, ArH), 6.78–6.72 (2H, m, ArH), 6.42 (1H, d, $J$=8.5 Hz, ArH), 5.70 (2H, br s, $NH_2$), 3.10 (6H, s, $N(CH_3)_2$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=158.2, 157.6, 146.4, 138.2, 129.6, 129.4, 123.7, 117.7, 117.1, 110.3,

103.5, 38.4; mass ($ES^+$) $m/z$ 214.3 ($M^+$+1); Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.25; H, 7.03; N, 19.69.

*4.6.4. 6-(2-Amino-5-methylphenyl)-N,N dimethylpyridin-2-amine (**4d**).* Yield=1.32 g (78%), yellow oil, $R_f$=0.37 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3305, 2919, 1604, 1595, 1181 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.56–7.50 (1H, m, ArH), 7.30 (1H, d, $J$=1.2 Hz, ArH), 6.97–6.94 (1H, m, ArH), 6.89 (1H, d, $J$=7.5 Hz, ArH), 6.66 (1H, d, $J$=8.1 Hz, ArH), 6.42 (1H, d, $J$=8.5 Hz, ArH), 5.29 (2H, br s, $NH_2$), 3.10 (6H, s, $N(CH_3)_2$), 2.28 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=158.3, 157.7, 143.9, 138.2, 130.1, 126.9, 124.0, 117.3, 110.4, 103.5, 38.5, 20.7; mass ($ES^+$) $m/z$ 228.3 ($M^+$+1); Anal. Calcd for $C_{14}H_{17}N_3$: C, 73.98; H, 7.54; N, 18.49. Found: C, 73.96; H, 7.58; N, 18.47.

*4.6.5. 6-(2-Aminophenyl)-N,N-diethylpyridin-2-amine (**4e**).* Yield=0.88 g (84%), yellow oil, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3305, 2977, 1598, 1454, 1263 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$=7.58–7.45 (2H, m, ArH), 7.16–7.08 (1H, m, ArH), 6.84 (1H, d, $J$=11.3 Hz, ArH), 6.78–6.70 (2H, m, ArH), 6.37 (1H, d, $J$=12.8 Hz, ArH), 5.67 (2H, br s, $NH_2$), 3.52 (4H, q, $J$=10.6 Hz, $CH_2$), 1.19 (6H, t, $J$=10.6 Hz, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=166.4, 162.6, 158.1, 149.3, 131.1, 128.9, 116.9, 116.6, 115.2, 105.9; mass ($ES^+$) $m/z$ 242.3 ($M^+$+1); Anal. Calcd for $C_{15}H_{19}N_3$: C, 74.65; H, 7.94; N, 17.41. Found: C, 74.63; H, 7.95; N, 17.42.

*4.6.6. 6-(2-Amino-5-methylphenyl)-N,N-diethyl pyridin-2-amine (**4f**).* Yield= 2.80 g (84%), yellow oil, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3294, 2969, 1540 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.51–7.45 (1H, m, ArH), 7.29 (1H, s, ArH), 6.96–6.93 (1H, m, ArH), 6.82 (1H, d, $J$=7.5 Hz, ArH), 6.64 (1H, d, $J$=8.0 Hz, ArH), 6.36 (1H, d, $J$=8.5 Hz, ArH), 3.52 (4H, q, $J$=7.1 Hz, $CH_2$), 2.7 (3H, s, $CH_3$), 1.18 (6H, t, $J$=7.1 Hz, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=158.2, 156.6, 144.1, 138.4, 130.4, 130.3, 127.1, 124.6, 117.5, 110.2, 103.5, 42.9, 21.0, 13.5; mass ($ES^+$) $m/z$ 256.3 ($M^+$+1); Anal. Calcd for $C_{16}H_{21}N_3$: C, 75.26; H, 8.29; N, 16.46. Found: C, 75.24; H, 8.30; N, 16.47.

### 4.7. General procedure for the synthesis of pyrido[1,2-*c*] quinazolin-8-one 6 and benzo[1,6]naphthyridine 8 via cationic π cyclization from substrates (4a–f)

A mixture of **4a**–**f** (1.0 mmol) and aldehyde (1.1 mmol) in toluene (5 mL) was treated with TFA (0.1 mmol) at 110 °C for 8 h. The completion of reaction was monitored by TLC. After that the solvent was evaporated, and the residue so obtained was triturated with aq $NaHCO_3$ (10 mL). It was then extracted with EtOAc (20 mL), washed with brine (10 mL), and dried over $Na_2SO_4$. EtOAc was evaporated to dryness under reduced pressure and the crude product was purified by column chromatography using hexane:ethyl acetate as eluent.

*4.7.1. 6-(4-Nitrophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6a**).* Yield=0.20 g (96%), yellow solid, mp 135–136 °C, $R_f$=0.30 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3289, 2969, 1532, 1341 $cm^{-1}$; $^1H$ NMR (200 MHz, DMSO-$d_6$) $\delta$=8.11 (2H, d, $J$=13.2 Hz, ArH), 7.88 (1H, d, $J$=5.8 Hz, NH), 7.70–7.56 (2H, m, ArH), 7.35 (2H, d, $J$=13.0 Hz, ArH), 7.25–7.21 (2H, m, ArH), 6.91–6.85 (2H, m, ArH, CH), 6.79–6.73 (1H, m, ArH), 6.50 (1H, dd, $J$=13.5 Hz, ArH); $^{13}C$ NMR (75 MHz, DMSO-$d_6$) $\delta$=160.8, 147.6, 142.7, 141.4, 140.9, 132.3, 127.9, 125.3, 124.0, 120.1, 117.3, 116.9, 101.6, 61.3; mass ($ES^+$) $m/z$ 320.2 ($M^+$+1); Anal. Calcd for $C_{18}H_{13}N_3O_3$: C, 67.71; H, 4.10; N, 13.16. Found: C, 67.69; H, 4.13; N, 13.18.

*4.7.2. 6-(4-Chlorophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6b**).* Yield=0.21 g (92%), yellow oil, $R_f$=0.40 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3020, 2928, 1650, 1490, 1216 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.57 (1H, d, $J$=7.9 Hz, ArH), 7.46 (1H, t, $J$=8.1 Hz, ArH), 7.38 (1H, s, CH), 7.27–7.23 (1H, m, ArH), 7.15 (4H, m, ArH), 6.92–6.83 (2H, m, ArH), 6.64–6.60 (2H, m, ArH), 5.12 (1H, br s, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=141.4, 141.2, 139.9, 137.7, 134.0, 131.9, 128.7, 127.9, 124.6, 120.9, 118.2, 117.8, 117.7, 102.0, 61.8; mass ($ES^+$) $m/z$ 309.2 ($M^+$+1); Anal. Calcd for $C_{18}H_{13}ClN_2O$: C, 70.02; H, 4.24; N, 9.07. Found: C, 70.00; H, 4.27; N, 9.04.

*4.7.3. 6-(4-Bromophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6c**).* Yield=0.24 g (94%), yellow solid, mp 187–188 °C, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3386, 3025, 2990, 1532 $cm^{-1}$; $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$=7.77 (1H, d, $J$=3.7 Hz, NH), 7.68 (1H, d, $J$=7.7 Hz, ArH), 7.60–7.55 (1H, m, ArH), 7.46 (2H, d, $J$=8.52 Hz, ArH), 7.24–7.19 (1H, m, ArH), 7.13 (1H, d, $J$=3.7 Hz, CH), 7.06 (2H, d, $J$=8.52 Hz, ArH), 6.89 (1H, d, $J$=7.6 Hz, ArH), 6.83 (1H, d, $J$=7.0 Hz, ArH), 6.78–6.73 (1H, m, ArH), 6.46 (1H, d, $J$=9.5 Hz, ArH); $^{13}C$ NMR (75 MHz, DMSO-$d_6$) $\delta$=160.3, 142.5, 141.1, 140.2, 139.1, 131.8, 131.3, 128.3, 124.7, 121.1, 119.3, 116.7, 116.5, 116.4, 116.3, 100.9, 60.7; mass ($ES^+$) $m/z$ 353.2 ($M^+$+1); Anal. Calcd for $C_{18}H_{13}BrN_2O$: C, 61.21; H, 3.71; N, 7.93; Found: C, 61.15; H, 3.75; N, 7.92.

*4.7.4. 6-(4-Fluorophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6d**).* Yield=0.20 g (95%), yellow solid, mp 150–152 °C, $R_f$=0.38 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3280, 2937, 1647, 1541 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.58 (1H, d, $J$=7.5 Hz, ArH), 7.48–7.43 (1H, m, ArH), 7.38 (1H, d, $J$=3.9 Hz, CH), 7.28–7.18 (3H, m, ArH), 6.91–6.82 (4H, m, ArH), 6.62 (2H, t, $J$=7.6 Hz, ArH) 5.08 (1H, br s, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=160.3, 142.6, 141.1, 140.2, 135.9, 135.8, 131.8, 128.2, 128.1, 124.7, 119.3, 116.6 (d, $J$=69 Hz), 116.3, 115.3, 115.0, 100.9, 60.7; mass ($ES^+$) $m/z$ 293.3 ($M^+$+1); Anal. Calcd for $C_{18}H_{13}FN_2O$: C, 73.96; H, 4.48; N, 9.58. Found: C, 73.95; H, 4.45; N, 9.55.

*4.7.5. 6-(3,4-Dichlorophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6g**).* Yield=0.16 g (90%), yellow solid, mp 80–82 °C, $R_f$=0.38 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3266, 2938, 1645, 1536 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.58 (1H, dd, $J$=1.0, 7.9 Hz, ArH), 7.50–7.45 (1H, m, ArH), 7.36–7.30 (2H, m, ArH, CH), 7.28–7.22 (2H, m, ArH), 6.05–6.02 (1H, m, ArH), 6.95–6.87 (2H, m, ArH), 6.65–6.60 (2H, m, ArH), 5.07 (1H, br s, NH); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=161.7, 141.1, 140.9, 140.1, 139.6, 132.9, 132.5, 132.1, 130.6, 128.8, 125.9, 124.8, 121.4, 118.6, 118.1, 118.0, 102.2, 61.5; mass ($ES^+$) $m/z$ 243.2 ($M^+$+1); Anal. Calcd for $C_{18}H_{12}Cl_2N_2O$: C, 62.99; H, 3.52; N, 8.16. Found: C, 62.95; H, 3.53; N, 8.13.

*4.7.6. 6-(4-Ethoxyphenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6h**).* Yield=0.04 g (15%), yellow solid, mp 163 °C, $R_f$=0.40 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3258, 2985, 1641, 1536 $cm^{-1}$; $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$=7.71 (1H, d, $J$=3.7 Hz, NH), 7.68 (1H, d, $J$=8.0 Hz, ArH), 7.58–7.53 (1H, m, ArH), 7.23–7.17 (1H, m, ArH), 7.08 (1H, d, $J$=3.6, CH), 7.01 (2H, d, $J$=8.6 Hz, ArH), 6.86 (1H, d, $J$=7.3 Hz, ArH), 6.81–6.71 (4H, m, ArH), 6.44 (1H, dd, $J$=0.8, 9.0 Hz, ArH), 3.91 (2H, q, $J$=7.0 Hz, $CH_2$), 1.24 (3H, t, $J$=7.0 Hz, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=160.3, 158.1, 142.8, 141.3, 139.9, 131.6, 131.4, 127.2, 124.6, 118.9, 116.6, 116.5, 116.2, 114.1, 100.7, 62.9, 60.8, 14.6; mass ($ES^+$) $m/z$ 319.2 ($M^+$+1); Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.53; H, 5.65; N, 8.78.

*4.7.7. 2-Methyl-6-(4-nitrophenyl)-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6i**).* Yield=0.24 g (95%), yellow oil, $R_f$=0.80 (3:7 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3282, 2930, 1533, 1343 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.02 (2H, d, $J$=8.8 Hz, ArH), 7.52–7.37 (5H, m, ArH), 7.01 (1H, d, $J$=8.0 Hz, ArH), 6.85 (1H, d, $J$=8.1 Hz, ArH), 6.65 (2H, d, $J$=8.2 Hz, ArH), 4.94 (1H, d, $J$=4.9 Hz, NH), 2.28 (3H, s, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=161.72, 147.5, 146.5, 141.1, 140.2, 138.4, 133.1, 127.6, 124.7, 123.6, 118.6, 117.6, 102.2, 61.9, 20.9; mass ($ES^+$) $m/z$

334.3 ($M^+$+1); Anal. Calcd for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.41; H, 4.49; N, 12.57.

*4.7.8. 6-(4-Chlorophenyl)-2-methyl-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6j**).* Yield=0.22 g (93%), yellow solid, mp 157–180 °C, $R_f$=0.56 (3:7 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3320, 2922, 1643, 1536 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.47–7.42 (1H, m, ArH), 7.36 (2H, s, ArH), 7.1 (4H, s, ArH), 7.06 (1H, d, $J$=7.9 Hz, ArH), 6.78 (1H, d, $J$=8.1 Hz, ArH), 6.62–6.58 (2H, m, ArH), 4.94 (1H, d, $J$=3.6 Hz, NH), 2.27 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=141.2, 139.8, 138.9, 137.7, 133.8, 132.9, 130.3, 128.5, 128.4, 127.9, 126.3, 124.6, 118.4, 118.1, 117.5, 101.9, 61.9, 20.8; mass ($ES^+$) $m/z$ 323.3 ($M^+$+1); Anal. Calcd for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.67; H, 4.70; N, 8.69.

*4.7.9. 6-(4-Bromophenyl)-2-methyl-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6k**).* Yield=0.25 g (90%), yellow solid, mp 151–153 °C, $R_f$=0.60 (3:7 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3330, 2930, 1644, 1532 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.42 (1H, t, $J$=8.1 Hz, ArH), 7.32 (1H, d, $J$=4.5 Hz, CH), 7.30 (1H, s, ArH), 7.20 (2H, d, $J$=8.4 Hz, ArH), 7.04 (2H, d, $J$=8.4 Hz, ArH), 6.99 (1H, d, $J$=8.1 Hz, ArH), 6.72 (1H, d, $J$=8.1 Hz, ArH), 6.58 (2H, d, $J$=8.7 Hz, ArH), 5.76 (1H, s, NH), 2.22 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=161.7, 141.3, 139.8, 138.9, 138.2, 131.4, 130.2, 128.2, 124.6, 122.0, 118.3, 118.1, 117.4, 101.9, 61.9, 20.8; mass ($ES^+$) $m/z$ 367.2 ($M^+$+1); Anal. Calcd for $C_{19}H_{15}BrN_2O$: C, 62.14; H, 4.12; N, 7.63; O, 4.36. Found: C, 62.16; H, 4.10; N, 7.67.

*4.7.10. 6-(4-Fluorophenyl)-2-methyl-5,6-dihydro-8H-pyrido[1,2-c]quinazolin-8-one (**6l**).* Yield=0.20 g (89%), yellow solid, mp 179–180 °C, $R_f$=0.65 (3:7 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3294, 2922, 1647, 1540 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=7.46–7.43 (1H, m, ArH), 7.37 (2H, s, ArH), 7.21–7.17 (2H, m, ArH), 7.08 (1H, dd, $J$=1.3, 9.4 Hz, ArH), 6.90–6.82 (2H, m, ArH), 6.78 (1H, d, $J$=8.1 Hz, ArH), 6.83 (2H, t, $J$=7.2 Hz, ArH), 4.84 (1H, d, $J$=3.9 Hz, NH), 2.28(3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=161.8, 141.3, 139.8, 138.9, 135.0, 134.9, 132.9, 130.6, 128.4, 128.2, 124.7, 118.7, 118.3, 117.8, 115.6, 115.1, 101.8, 62.0, 20.9; mass ($ES^+$) $m/z$ 307.3 ($M^+$+1); Anal. Calcd for $C_{19}H_{15}FN_2O$: C, 74.50; H, 4.94; N, 9.14. Found: C, 74.53; H, 4.91; N, 9.16.

*4.7.11. N,N-Dimethyl-5-(4-nitrophenyl)benzo[h][1,6]naphthyridin-2-amine (**8a**).* Yield=0.31 g (97%), yellow solid, mp 197 °C, $R_f$=0.35 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3618, 2930, 1610, 1520 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.02 (1H, dd, $J$=1.1, 8.1 Hz, ArH), 8.40 (2H, dd, $J$=1.9, 6.9 Hz, ArH), 8.12 (1H, dd, $J$=0.6, 8.2 Hz, ArH), 7.94–7.87 (3H, m, ArH), 7.80–7.75 (1H, m, ArH), 7.68–7.63 (1H, m, ArH), 6.86 (1H, d, $J$=9.3 Hz, ArH), 3.36 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=159.0, 157.4, 150.0, 148.0, 146.6, 146.2, 136.2, 130.9, 130.2, 129.3, 126.6, 125.0, 124.1, 123.7, 112.3, 108.2, 38.1; mass ($ES^+$) $m/z$ 345.2 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 344.1273 found 344.1291; Anal. Calcd for $C_{20}H_{16}N_4O_2$: C, 69.76; H, 4.68; N, 16.27. Found: C, 69.79; H, 4.69; N, 16.23.

*4.7.12. 5-(4-Chlorophenyl)-N,N-dimethylbenzo[h][1,6]naphthyridin-2-amine (**8b**).* Yield=0.29 g (93%), yellow solid, mp 195 °C, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2930, 1602, 1376, 1131 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.00 (1H, dd, $J$=1.2, 8.1 Hz, ArH), 8.11 (1H, d, $J$=8.2 Hz, ArH), 8.0 (1H, d, $J$=9.3 Hz, ArH), 7.78–7.73 (1H, m, ArH), 7.66–7.60 (3H, m, ArH), 7.53–7.50 (2H, m, ArH), 6.83 (1H, d, $J$=9.3 Hz, ArH), 3.35 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=159.0, 158.8, 150.0, 146.8, 138.3, 136.8, 134.8, 131.2, 129.9, 129.3, 128.7, 126.1, 124.9, 124.0, 112.7, 107.9, 38.0; mass ($ES^+$) $m/z$ 334.4 ($M^+$+1); Anal. Calcd for $C_{20}H_{16}ClN_3$: C, 71.96; H, 4.83; N, 12.59. Found: C, 71.99; H, 4.81; N, 12.58.

*4.7.13. 5-(4-Bromophenyl)-N,N-dimethylbenzo[h][1,6]naphthyridin-2-amine (**8c**).* Yield=0.34 g (95%), yellow solid, mp 190 °C, $R_f$=0.45 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3055, 2922, 1598, 1380 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.00 (1H, dd, $J$=1.2, 8.1 Hz, ArH), 8.11 (1H, dd, $J$=0.7, 8.2 Hz, ArH), 7.99 (1H, d, $J$=9.3 Hz, ArH), 7.77–7.68 (1H, m, ArH), 7.68–7.63 (2H, m, ArH), 7.62–7.56 (3H, m, ArH), 6.82 (1H, d, $J$=9.3 Hz, ArH), 3.34 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=159.0, 158.8, 150.0, 146.7, 138.6, 136.8, 131.7, 131.5, 130.0, 129.2, 126.1, 124.9, 123.9, 123.1, 112.6, 107.9, 38.1; mass ($ES^+$) $m/z$ 378.4 ($M^+$+1); Anal. Calcd for $C_{20}H_{16}BrN_3$: C, 63.50; H, 4.26; N, 11.11. Found: C, 63.48; H, 4.29; N, 11.09.

*4.7.14. 4-[2-(Dimethylamino)benzo[h][1,6]naphthyridin-5-yl]phenol (**8d**).* Yield=0.26 g (90%), white solid, mp >250 °C, $R_f$=0.20 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2925, 1601, 1526, 1213 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.82 (1H, s, OH), 8.89 (1H, d, $J$=7.1 Hz, ArH), 8.09 (1H, d, $J$=7.8 Hz, ArH), 7.96 (1H, d, $J$=7.9 Hz, ArH), 7.78–7.72 (1H, m, ArH), 7.63–7.58 (1H, m, ArH), 7.53 (2H, d, $J$=8.5 Hz, ArH), 7.09 (1H, d, $J$=9.4 Hz, ArH), 6.95 (2H, d, $J$=8.5 Hz, ArH), 3.33 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=161.2, 160.1, 158.8, 156.2, 152.0, 138.1, 136.4, 132.7, 132.6, 127.9, 124.3, 123.3, 120.6, 120.3, 116.0, 111.5, 110.8, 38.3; mass ($ES^+$) $m/z$ 316.3 ($M^+$+1); Anal. Calcd for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32. Found: C, 76.15; H, 5.44; N, 13.29.

*4.7.15. 5-[4-(Dimethylamino)phenyl]-N,N-dimethylbenzo[h][1,6]naphthyridin-2-amine (**8e**).* Yield=0.29 g (91%), yellow solid, mp 205 °C, $R_f$=0.25 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3438, 2892, 1607, 1355 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.98 (1H, dd, $J$=1.0, 8.1 Hz, ArH), 8.20 (1H, d, $J$=9.3 Hz, ArH), 8.12 (1H, d, $J$=8.2 Hz, ArH), 7.74–7.69 (1H, m, ArH), 7.64 (2H, d, $J$=8.8 Hz, ArH), 7.59–7.54 (1H, m, ArH), 6.86 (2H, d, $J$=8.8 Hz, ArH), 6.82 (1H, d, $J$=9.3 Hz, ArH), 3.34 (6H, s, $N(CH_3)_2$), 3.04 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=160.3, 158.9, 151.0, 150.1, 147.1, 137.8, 131.1, 129.7, 129.1, 127.9, 125.4, 124.7, 123.9, 113.1, 112.3, 109.8, 107.5, 40.7, 38.1; mass ($ES^+$) $m/z$ 343.4 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 342.1844 found 342.1821; Anal. Calcd for $C_{22}H_{22}N_4$: C, 77.16; H, 6.48; N, 16.36. Found: C, 77.11; H, 6.49; N, 16.40.

*4.7.16. 5-(3,4-Dimethoxyphenyl)-N,N-dimethylbenzo[h][1,6]naphthyridin-2-amine (**8f**).* Yield=0.30 g (90%), yellow solid, mp 180–181 °C, $R_f$=0.30 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2932, 1604, 1519, 1259 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.00 (1H, dd, $J$=1.5, 8.1 Hz, ArH), 8.13–8.10 (2H, m, ArH), 7.77–7.71 (1H, m, ArH), 7.63–7.57 (1H, m, ArH), 7.31–7.21 (2H, m, ArH), 7.02 (1H, d, $J$=8.2 Hz, ArH), 6.83 (1H, d, $J$=9.3 Hz, ArH), 3.97 (6H, s, $(OCH_3)_2$), 3.35 (6H, s, $N(CH_3)_2$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=159.8, 159.0, 150.0, 149.7, 149.2, 146.9, 137.4, 132.6, 129.8, 129.2, 125.8, 124.8, 123.9, 122.7, 113.0, 113.0, 111.0, 107.7, 56.2, 56.2, 38.1; mass ($ES^+$) $m/z$ 360.3 ($M^+$+1); Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.55; H, 5.87; N, 11.73.

*4.7.17. N,N,9-Trimethyl-5-(4-nitrophenyl)benzo[h][1,6]naphthyridin-2-amine (**8g**).* Yield=0.29 g (94%), yellow solid, mp >250 °C, $R_f$=0.45 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2927, 1604, 1515, 1343 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.78 (1H, s, ArH), 8.38 (2H, d, $J$=8.3 Hz, ArH), 8.01 (1H, d, $J$=8.4 Hz, ArH), 7.93–7.87 (3H, m, ArH), 7.60 (1H, d, $J$=8.3 Hz, ArH), 6.85 (1H, d, $J$=9.3 Hz, ArH), 3.37 (6H, s, $N(CH_3)_2$), 2.64 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=159.0, 156.5, 149.8, 147.9, 146.3, 145.1, 136.7, 136.2, 132.1, 130.9, 129.2, 124.8, 123.8, 123.3, 112.4, 108.2, 38.2, 22.1; mass ($ES^+$) $m/z$ 359.3 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 358.1430 found 358.1411; Anal. Calcd for $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 15.63. Found: C, 70.35; H, 5.04; N, 15.66.

*4.7.18. 5-(4-Chlorophenyl)-N,N,9-trimethylbenzo[h][1,6]naphthyridin-2-amine (**8h**).* Yield=0.28 g (92%), white solid, mp 206–208 °C, $R_f$=0.46 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3422, 19.13, 1606,

1379 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.76 (1H, s, ArH), 8.01–7.96 (2H, m, ArH), 7.64 (2H, d, $J$=8.4 Hz, ArH), 7.57 (1H, dd, $J$=2.0, 8.4 Hz, ArH), 7.50 (2H, d, $J$=8.4 Hz, ArH), 6.80 (1H, d, $J$=9.3 Hz, ArH), 3.35 (6H, s, $N(CH_3)_2$), 2.63 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=158.8, 157.7, 149.5, 145.0, 138.2, 136.7, 135.9, 134.6, 131.7, 131.2, 128.9, 128.6, 124.6, 123.1, 112.6, 107.7, 37.9, 21.9; mass ($ES^+$) $m/z$ 348.4 ($M^+$+1); Anal. Calcd for $C_{21}H_{18}ClN_3$: C, 72.51; H, 5.22; N, 12.08. Found: C, 72.48; H, 5.24; N, 12.06.

*4.7.19. 5-(4-Bromophenyl)-N,N,9-trimethylbenzo[h][1,6]naphthyridin-2-amine (**8i**).* Yield=0.32 g (93%), yellow solid, mp 188–200 °C, $R_f$=0.42 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2932, 1610, 1419, 1119 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.72 (1H, s, ArH), 8.35 (1H, d, $J$=8.5 Hz, ArH), 7.98 (1H, d, $J$=9.5 Hz, ArH), 7.74–7.69 (3H, m, ArH), 7.63 (2H, d, $J$=8.3 Hz, ArH), 6.98 (1H, d, $J$=9.5 Hz, ArH), 3.45 (6H, s, $N(CH_3)_2$), 2.65 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=160.3, 154.8, 152.3, 138.8, 137.8, 136.5, 134.4, 132.3, 132.0, 129.8, 126.5, 124.4, 123.7, 122.2, 111.2, 110.4, 38.53, 22.1; mass ($ES^+$) $m/z$ 392.3 ($M^+$+1); Anal. Calcd for $C_{21}H_{18}BrN_3$: C, 64.30; H, 4.62; N, 10.71. Found: C, 64.28; H, 4.63; N, 10.73.

*4.7.20. 5-(4-Fluorophenyl)-N,N,9-trimethylbenzo[h][1,6]naphthyridin-2-amine (**8j**).* Yield=0.26 g (90%), white solid, mp 209–211 °C, $R_f$=0.37 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2914, 1607, 1517, 1380 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.76 (1H, s, ArH), 8.02–7.97 (2H, m, ArH), 7.70–7.65 (2H, m, ArH), 7.57 (1H,, dd, $J$=1.8, 8.4 Hz, ArH), 7.25–7.18 (2H, m, ArH), 6.80 (1H, d, $J$=9.3 Hz, ArH), 3.35 (6H, s, $N(CH_3)_2$), 2.63 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=165.6, 160.6, 158.9, 157.9, 149.6, 145.1, 136.8, 135.9 (d, $J$=12 Hz), 135.8, 131.7, 131.5, 128.9, 124.6, 123.1, 115.6, 115.2, 112.8, 107.7, 38.0, 21.9; mass ($ES^+$) $m/z$ 332.4 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 332.15630 found 332.15616; Anal. Calcd for $C_{21}H_{18}FN_3$: C, 76.11; H, 5.47; N, 12.68. Found: C, 76.13; H, 5.58; N, 12.67.

*4.7.21. N,N,9-Trimethyl-5-(4-N,N-dimethylphenyl)benzo[h][1,6]naphthyridin-2-amine (**8k**).* Yield=0.28 g (91%), yellow solid, mp 214–215 °C, $R_f$=0.75 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2919, 1603, 1366, 1194 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.6 (1H, s, ArH), 8.37 (1H, d, $J$=8.3 Hz, ArH), 8.16 (1H, d, $J$=9.5 Hz, ArH), 7.69–7.62 (3H, m, ArH), 6.89 (1H, d, $J$=9.5 Hz ArH), 6.80 (2H, d, $J$=8.8 Hz, ArH), 3.39 (6H, s, $N(CH_3)_2$), 3.07 (6H, s, $N(CH_3)_2$), 2.62 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, DMSO-$d_6$) $\delta$=159.5, 156.0, 152.0, 150.9, 137.9, 136.8, 133.4, 131.8, 123.2, 123.1, 121.9, 111.6, 110.6, 110.3, 38.3, 37.8, 21.4; mass ($ES^+$) $m/z$ 357.4 ($M^+$+1); Anal. Calcd for $C_{23}H_{24}N_4$: C, 77.50; H, 6.79; N, 15.72. Found: C, 77.52; H, 6.80; N, 15.69.

*4.7.22. N,N,9-Trimethyl-5-(3,4-dimethoxyphenyl)benzo[h][1,6]naphthyridin-2-amine (**8l**).* Yield=0.29 g (90%), yellow solid, mp 218–219 °C, $R_f$=0.82 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2931, 1607, 1390, 1266 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.72 (1H, s, ArH), 8.36 (1H, d, $J$=4.8 Hz, ArH), 8.13 (1H, d, $J$=9.3 Hz, ArH), 7.67 (1H, d, $J$=6.7 Hz, ArH), 7.40 (1H, s, ArH), 7.26(1H, s, ArH), 7.02 (1H, d, $J$=7.2 Hz, ArH), 6.94 (1H, d, $J$=9.4 Hz, ArH), 3.97 (6H, s, $(OCH_3)_2$), 3.43 (6H, s, $N(CH_3)_2$), 2.64 (3H, s, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=160.1, 156.2, 152.0, 151.8, 149.5, 138.5, 138.0, 134.0, 124.3, 124.2, 123.5, 113.5, 111.6, 111.1, 109.7, 56.4, 56.2, 38.4, 22.1; mass ($ES^+$) $m/z$ 374.4.3 ($M^+$+1); Anal. Calcd for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.99; H, 6.22; N, 11.23.

*4.7.23. 5-(4-Ethoxyphenyl)-N,N,9-trimethylbenzo[h][1,6]naphthyridin-2-amine (**8m**).* Yield=0.27 g (88%), white solid, mp 183–185 °C, $R_f$=0.44 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2922, 1601, 1376, 12539 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.75 (1H, s, ArH), 8.07 (1H, d, $J$=9.3 Hz, ArH), 8.01 (1H, d, $J$=8.4 Hz, ArH), 7.63 (2H, d, $J$=8.6 Hz, ArH), 7.55 (1H, dd, $J$=1.9, 8.4 Hz, ArH), 7.04 (2H, d, $J$=8.6 Hz, ArH), 6.80 (1H, d, $J$=9.3 Hz, ArH), 4.12 (2H, q, $J$=7.0 Hz, $CH_2$), 3.34 (6H, s, $N(CH_3)_2$), 2.62 (3H, s, $CH_3$), 1.34 (3H, t, $J$=7.0 Hz, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=159.4, 158.8, 149.8, 145.2, 137.2, 135.4, 132.3, 131.5, 128.9, 124.5, 123.1, 114.4, 112.9, 107.4, 63.6, 37.9, 21.9, 14.9; mass ($ES^+$) $m/z$ 358.3 ($M^+$+1); Anal. Calcd for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.76. Found: C, 77.25; H, 6.51; N, 11.73.

*4.7.24. N,N-Diethyl-5-(4-nitrophenyl)benzo[h][1,6]naphthyridin-2-amine (**8n**).* Yield=0.29 g (95%), yellow solid, mp 161 °C, $R_f$=0.35 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3063, 2953, 1610, 1341 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=9.00 (1H, dd, $J$=1.2, 8.1 Hz, ArH), 8.40 (2H, dd, $J$=1.9, 7.0 Hz, ArH), 8.10 (1H, d, $J$=8.2 Hz, ArH), 7.91–7.88 (3H, m, ArH), 7.80–7.74 (1H, m, ArH), 7.67–7.62 (1H, m, ArH), 6.80 (1H, d, $J$=9.4 Hz, ArH), 3.78 (4H, q, $J$=7.1 Hz, $CH_2$), 1.35 (6H, t, $J$=7.1 Hz, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=157.7, 157.4, 150.4, 148.0, 146.7, 146.3, 136.2, 130.9, 130.1, 129.3, 126.5, 125.2, 124.1, 123.7, 112.3, 108.3, 43.3, 13.1; mass ($ES^+$) $m/z$ 373.3 ($M^+$+1); Anal. Calcd for $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.91; H, 5.43; N, 15.01.

*4.7.25. N-[5-(4-Chlorophenyl)benzo[h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8o**).* Yield=0.28 g (93%), yellow solid, mp 130 °C, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3071, 2977, 2930, 1598, 1345 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.98 (1H, dd, $J$=1.4, 8.1 Hz, ArH), 8.10 (1H, d, $J$=8.1 Hz, ArH), 7.97 (1H, d, $J$=9.3 Hz, ArH), 7.77–7.71 (1H, m, ArH), 7.66–7.58 (3H, m, ArH), 7.53–7.46 (2H, m, ArH), 6.78 (1H, d, $J$=9.3 Hz, ArH), 3.76 (4H, q, $J$=7.0 Hz, $CH_2$), 1.34 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=158.7, 157.5, 150.3, 146.8, 138.3, 136.8, 134.8, 131.2, 129.9, 129.2, 129.1, 128.7, 126.0, 125.0, 123.9, 112.6, 107.9, 43.2, 13.1; mass ($ES^+$) $m/z$ 362.4 ($M^+$+1),MS (HR EI) $m/z$ calcd for [$M^+$] 361.1346 found 361.1340; Anal. Calcd for $C_{22}H_{20}ClN_3$: C, 73.02; H, 5.57; N, 11.61. Found: C, 73.07; H, 5.58; N, 11.57.

*4.7.26. 5-(4-Bromophenyl)-N,N-diethylbenzo[h][1,6]naphthyridin-2-amine (**8p**).* Yield=0.32 g (94%), yellow oil, $R_f$=0.50 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 2930, 1661, 1606, 1361 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$=9.00 (1H, dd, $J$=2.4, 12.1 Hz, ArH), 8.12–8.07 (1H, m, ArH), 7.94 (1H, d, $J$=13.9 Hz, ArH), 7.69–7.62 (3H, m, ArH), 7.60–7.53 (3H, m, ArH), 6.74 (1H, d, $J$=13.9 Hz, ArH), 3.74 (4H, q, $J$=10.6 Hz, $CH_2$), 1.31 (6H, t, $J$=10.6 Hz, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$=158.7, 157.5, 150.3, 146.7, 138.7, 136.7, 132.8, 131.6, 131.5, 131.0, 129.9, 129.1, 126.0, 124.9, 123.9, 123.0, 112.5, 107.9, 43.2, 13.1; mass ($ES^+$) $m/z$ 406.3 ($M^+$+1); Anal. Calcd for $C_{22}H_{20}BrN_3$: C, 65.03; H, 4.96; N, 10.34. Found: C, 65.01; H, 4.93; N, 10.37.

*4.7.27. N,N-Diethyl-5-(4-fluorophenyl)benzo[h][1,6]naphthyridin-2-amine (**8q**).* Yield=0.26 g (91%), yellow solid, mp 118 °C, $R_f$=0.40 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2971, 2922, 1600, 1351 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$=8.98 (1H, dd, $J$=1.2, 8.1 Hz, ArH), 8.10 (1H, d, $J$=7.6 Hz, ArH), 7.98 (1H, d, $J$=9.3 Hz, ArH), 7.77–7.58 (4H, m, ArH), 7.26–7.19 (2H, m, ArH), 6.78 (1H, d, $J$=9.3 Hz, ArH), 3.76 (4H, q, $J$=7.1 Hz, $CH_2$), 1.33 (6H, t, $J$=7.1 Hz, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$=164.8, 161.8, 158.9, 157.5, 150.3, 146.8, 136.9, 135.9, 129.9, 129.2, 125.9, 125.0, 123.9, 115.7, 115.4, 112.8, 107.9, 43.3, 13.1; mass ($ES^+$) $m/z$ 346.4 ($M^+$+1); Anal. Calcd for $C_{22}H_{20}FN_3$: C, 76.50; H, 5.84; N, 12.17. Found: C, 76.45; H, 5.86; N, 12.21.

*4.7.28. 4-[2-(Diethylamino)benzo[h][1,6]naphthyridin-5-yl]phenol (**8r**).* Yield=0.24 g (86%), yellow solid, mp >250 °C, $R_f$=0.20 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 2985, 2922, 1606, 1353 $cm^{-1}$; $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$=9.81 (1H, s, OH), 8.45 (1H, dd, $J$=1.1, 8.1 Hz, ArH), 8.06 (1H, d, $J$=9.3 Hz, ArH), 7.95 (1H, d, $J$=7.6 Hz, ArH),

7.77–7.72 (1H, m, ArH), 7.64–7.52 (1H, m, ArH), 7.54 (2H, d, $J$=8.5 Hz, ArH), 7.06 (1H, d, $J$=9.3 Hz, ArH), 6.95 (2H, d, $J$=8.5 Hz, ArH), 3.74 (4H, q, $J$=6.9 Hz, $CH_2$), 1.25 (6H, t, $J$=6.9 Hz, $CH_3$); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$=159.0, 157.9, 157.0, 149.2, 146.3, 136.8, 131.0, 129.9, 129.5, 128.6, 125.4, 123.9, 123.3, 114.9, 111.9, 108.5, 42.4, 12.8; mass ($ES^+$) $m/z$ 344.4 ($M^+$+1); Anal. Calcd for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.93; H, 6.18; N, 12.21.

*4.7.29. N,N-Diethyl-5-(4-N,N-dimethylphenyl)benzo[h][1,6]naphthyridin-2-amine (**8s**).* Yield=0.27 g (88%), yellow oil, $R_f$=0.30 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3422, 2922, 1604, 1355 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.96 (1H, dd, $J$=1.2, 8.1 Hz, ArH), 8.17 (1H, d, $J$=9.3 Hz, ArH), 8.10 (1H, d, $J$=8.1 Hz, ArH), 7.73–7.68 (1H, m, ArH), 7.65–7.63 (2H, m, ArH), 7.60–7.53 (1H, m, ArH), 6.86 (2H, d, $J$=8.8 Hz, ArH), 6.76 (1H, d, $J$=9.3 Hz, ArH) 3.76 (4H, q, $J$=7.0 Hz, $CH_2$), 3.04 (6H, s, $N(CH_3)_2$), 1.33 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$=160.2, 157.4, 150.9, 150.4, 147.1, 137.7, 131.0, 129.6, 129.0, 127.9, 125.3, 123.9, 113.0, 112.2, 107.5, 43.2, 13.2; mass ($ES^+$) $m/z$ 371.4 ($M^+$+1); Anal. Calcd for $C_{24}H_{26}N_4$: C, 77.80; H, 7.07; N, 15.12. Found: C, 77.77; H, 7.08; N, 15.14.

*4.7.30. N,N-Diethyl-5-(4-ethoxyphenyl) benzo[h][1,6 ]naphthyridin-2-amine (**8t**).* Yield=0.28 g (90%), yellow oil, $R_f$=0.38 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3415, 2974, 1604, 1245 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.97 (1H, dd, $J$=2.2, 12.1 Hz, ArH), 8.10 (1H, dd, $J$=1.6, 12.5 Hz, ArH), 8.05 (1H, d, $J$=13.9 Hz, ArH), 7.76–7.53 (4H, m, ArH), 7.07–6.99 (2H, m, ArH), 6.76 (1H, d, $J$=13.9 Hz, ArH), 4.10 (2H, q, $J$=10.4 Hz, $CH_2$), 3.73 (4H, q, $J$=10.5 Hz, $CH_2$), 1.45 (3H, t, $J$=10.4 Hz, $CH_3$), 1.34 (6H, t, $J$=10.5 Hz, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$=159.7, 159.4, 157.3, 150.2, 146.8, 137.2, 132.0, 131.1, 129.6, 128.9, 125.5, 124.8, 123.8, 114.4, 112.8, 107.6, 63.5, 43.1, 14.9, 13.0; mass ($ES^+$) $m/z$ 372.4 ($M^+$+1); Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.57; H, 6.83; N, 11.3.

*4.7.31. N-[5-(4-Dimethylaminophenyl)-9-methylbenzo[h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8u**).* Yield=0.26 g (86%), yellow oil, $R_f$=0.25 (3:7 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3294, 2922, 1601, 1517 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.70 (1H, s, ArH), 8.12 (1H, d, $J$=9.3 Hz, ArH), 8.00 (1H, d, $J$=8.3 Hz, ArH), 7.62 (2H, d, $J$=8.7 Hz, ArH), 7.52 (1H, dd, $J$=1.8, 8.3 Hz, ArH), 6.83 (2H, d, $J$=8.7 Hz, ArH), 6.71 (1H, d, $J$=9.3 Hz, ArH), 3.72 (4H, q, $J$=7.0 Hz, $CH_2$), 2.99 (6H, s, $N(CH_3)_2$), 2.60 (3H, s, $CH_3$), 1.29 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=159.2, 157.2, 150.7, 149.9, 145.2, 137.5, 134.8, 131.3, 130.9, 128.7, 127.7, 124.4, 122.9, 112.9, 112.1, 107.3, 42.9, 40.5, 21.9, 13.1; mass ($ES^+$) $m/z$ 385.4 ($M^+$+1); Anal. Calcd for $C_{25}H_{28}N_4$: C, 78.09; H, 7.34; N, 14.57. Found: C, 78.07; H, 7.35; N, 14.58.

*4.7.32. N-[5-(4-Bromophenyl)-9-methylbenzo[h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8v**).* Yield=0.29 g (90%), white solid, mp 151–152 °C, $R_f$=0.49 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3298, 2922, 1602, 1350 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.72 (1H, s, ArH), 8.00–7.93 (2H, m, ArH), 7.67–7.63 (2H, m, ArH), 7.58–7.54 (3H, m, ArH), 6.76 (1H, d, $J$=9.3 Hz, ArH), 3.76 (4H, q, $J$=7.1 Hz, $CH_2$), 2.62 (3H, s, $CH_3$), 1.33 (6H, t, $J$=7.1 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=157.8, 157.4, 149.9, 145.1, 138.8, 136.7, 135.8, 131.7, 131.6, 131.5, 128.9, 124.7, 123.1, 122.8, 112.6, 107.8, 43.1, 22.0, 13.1; mass ($ES^+$) $m/z$ 420.3 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 420.10753 found 420.10416; Anal. Calcd for $C_{23}H_{22}BrN_3$: C, 65.72; H, 5.28; N, 10.00. Found: C, 65.70; H, 5.29; N, 10.02.

*4.7.33. N-[5-(4-Nitrophenyl)-9-methylbenzo[h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8w**).* Yield=0.29 g (95%), yellow solid, mp 189–190 °C, $R_f$=0.45 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3284, 2969, 1601, 1507 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.74 (1H, s, ArH), 8.48 (2H, d, $J$=8.8 Hz, ArH), 7.99 (1H, d, $J$=8.3 Hz, ArH), 7.88 (3H, m, ArH), 7.58 (1H, dd, $J$=2.0, 8.5 Hz, ArH), 6.80 (1H, d, $J$=9.3 Hz, ArH), 3.78 (4H, q, $J$=7.0 Hz, $CH_2$), 2.64 (3H, s, $CH_3$), 1.34 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=157.5, 156.4, 150.0, 147.8, 146.3, 145.0, 136.4, 136.0, 131.9, 130.8, 129.0, 124.9, 123.6, 123.2, 112.3, 108.1, 43.2, 22.0, 13.1; mass ($ES^+$) $m/z$ 387.2 ($M^+$+1); Anal. Calcd for $C_{23}H_{22}N_4O_2$: C, 71.48; H, 5.74; N, 14.50. Found: C, 71.46; H, 5.76; N, 14.51.

*4.7.34. N-[5-(4-Chlorophenyl)-9-methylbenzo[h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8x**).* Yield=0.27 g (90%), white solid, mp 158–160 °C, $R_f$=0.52 (2:8 EtOAc:Hexane), IR (KBr) $\nu_{max}$ 3287, 2922, 1603, 1509 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.72 (1H, s, ArH), 8.01–7.93 (2H, m, ArH), 7.65–7.62 (2H, m, ArH), 7.56 (1H, dd, $J$=1.9, 8.3 Hz, ArH), 7.51–7.48 (2H, m, ArH), 6.76 (1H, d, $J$=9.3 Hz, ArH), 3.78 (4H, q, $J$=6.9 Hz, $CH_2$), 2.62 (3H, s, $CH_3$), 1.33 (6H, t, $J$=6.9 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=157.7, 157.4, 149.9, 145.1, 138.3, 136.7, 135.8, 134.6, 131.7, 131.2, 128.9, 128.6, 124.7, 123.1, 112.6, 107.8, 43.1, 22.0, 13.1; mass ($ES^+$) $m/z$ 376.3 ($M^+$+1), MS (HR EI) $m/z$ calcd for [$M^+$] 375.1502 found 375.1520; Anal. Calcd for $C_{23}H_{22}ClN_3$: C, 73.49; H, 5.90; N, 11.18. Found: C, 72.49; H, 5.93; N, 11.19.

*4.7.35. N-[5-(4-Ethoxyphenyl)-9-methyl benzo [h][1,6]naphthyridin-2-yl]-N,N-diethylamine (**8y**).* Yield=0.27 g (89%), yellow oil, $R_f$=0.30 (2:8 EtOAc:Hexane), IR (Neat) $\nu_{max}$ 3294, 2922, 1605, 1520 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$=8.71 (1H, s, ArH), 8.04–7.99 (2H, m, ArH), 7.62 (2H, d, $J$=8.7 Hz, ArH), 7.53 (1H, dd, $J$=1.9, 8.4 Hz, ArH), 7.04–6.99 (2H, m, ArH), 6.70 (1H, d, $J$=9.3 Hz, ArH), 4.08 (2H, q, $J$=7.0 Hz, $CH_2$), 3.71 (4H, q, $J$=7.0 Hz, $CH_2$), 2.60 (3H, s, $CH_3$), 1.43 (3H, t, $J$=7.0 Hz, $CH_3$), 1.29 (6H, t, $J$=7.0 Hz, $CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$=159.1, 158.8, 157.3, 149.9, 145.2, 137.2, 135.2, 132.2, 131.4, 131.1, 128.8, 124.6, 123.0, 114.3, 112.9, 107.5, 63.6, 43.0, 21.9, 14.9, 13.0; mass ($ES^+$) $m/z$ 386.3 ($M^+$+1); Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 77.93; H, 7.03; N, 10.92.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.11.115.

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