Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 3761–3768

TETRAHEDRON

# Synthesis of nicotinonitrile derivatives as a new class of NLO materials

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Received 22 January 2003; revised 4 March 2003; accepted 27 March 2003

**Abstract**—4,6-Diaryl-2-(pyrrolidin-1-yl)-nicotinonitriles **2a**–**k** and 3-amino-2,4-dicyano-5-aryl-biphenyls **3a**–**c** were synthesized from 1,3-diaryl-prop-2-en-1-ones **1a**–**k** and malononitrile by a convenient one-pot method. Likewise, the reaction of aromatic aldehydes with malononitrile afforded 6-amino-4-aryl-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitriles **6a**–**f**. The reaction of mesityl oxide with malononitrile gave 5-amino-7-(pyrrolidin-1-yl)-2,4,4-trimethyl-1,4-dihydro-1,6-naphthyridine-8-carbonitrile **8**. The NLO studies of the pyridinedinitrile derivatives **6a**, **b**, **f** showed a high value while that of nicotinonitrile **2b** was weak. 

## 1. Introduction

The pyridine ring is one of the most well known systems among the naturally occurring heterocycles.[1] Pyridine and fused pyridine moieties are present in numerous natural products such as quinoline and isoquinoline alkaloids,[2] and nicotine and its analogues.[3–5] They have a vast range of potential biological activities as herbicides[6] and have been used for enrichment of cereals,[7] and for regulation of arterial pressure[8] and cholesterol levels in blood.[9] Some polysubstituted pyridines are used as non-linear optical materials,[10] electrical materials,[11] chelating agents in metal–ligand chemistry[12] and as fluorescent liquid crystals.[13] Thus pyridine derivatives have become increasingly important and hence numerous synthetic methods of pyridine rings have been reviewed.[14–17] The formation of pyridine compounds from α,β-unsaturated ketones and malononitrile in the presence of ammonium acetate has been reported.[18] The reaction of β-aminoenones with malononitrile, furnishing 2(1*H*)-pyridinones (pyridones), is known.[19] Photochemical synthesis of 2-aryl and 2,6-diaryl pyridines have also been reported.[20] In continuation of our work on the synthesis of laser dyes[21–23] and non-linear optical materials,[24] we have reported the synthesis of 1,6-naphthyridine[25] and terphenyl[26] systems, from α,β-unsaturated ketones and malononitrile; the formation of these compounds varied according to the experimental conditions, depending upon the amount of malononitrile and pyrrolidine, which were used for the reaction. Herein, we report a simple, one-pot synthesis of nicotinonitriles, pyridinedinitriles and biaryl derivatives as well as the 1,4-dihydro-1,6-naphthyridine system.

## 2. Results and discussion

The reaction of enones **1a**–**k**, (Table 1) with 1 equiv. each of malononitrile and pyrrolidine in ethanol furnished the nicotinonitriles **2a**–**k** in 40–69% yields. The formation of the nicotinonitriles could be rationalized by Michael addition, enamine formation followed by condensation and aromatization. The reaction of the thienyl and pyridyl enones **1i**–**k** with 2 equiv. each of malononitrile and pyrrolidine in ethanol furnished the nicotinonitriles **2i**–**k** along with the thienyl/pyridyl substituted biphenyl derivatives **3a**–**c** (Scheme 1). When morpholine was used in place

**Table 1**. Reaction of enones **1a**–**k** with malononitrile and pyrrolidine

| 1,2 | 3 | R | Ar |
|---|---|---|---|
| **a** | – | $CH_3$ | 4-$NMe_2$–$C_6H_4$– |
| **b** | – | $OCH_3$ | 4-$NMe_2$–$C_6H_4$– |
| **c** | – | Cl | 4-$NMe_2$–$C_6H_4$– |
| **d** | – | H | 4-$NMe_2$–$C_6H_4$– |
| **e** | – | H | 4-$NEt_2$–$C_6H_4$– |
| **f** | – | $OCH_3$ | 4-$NEt_2$–$C_6H_4$– |
| **g** | – | $OCH_3$ | $C_6H_5$– |
| **h** | – | $OCH_3$ | 4-$OCH_3$–$C_6H_4$– |
| **i** | **a** | H | 2-Thienyl |
| **j** | **b** | $CH_3$ | 2-Thienyl |
| **k** | **c** | H | 2-Pyridyl |

*Keywords*: pyridines; naphthyridines; electronic spectra.

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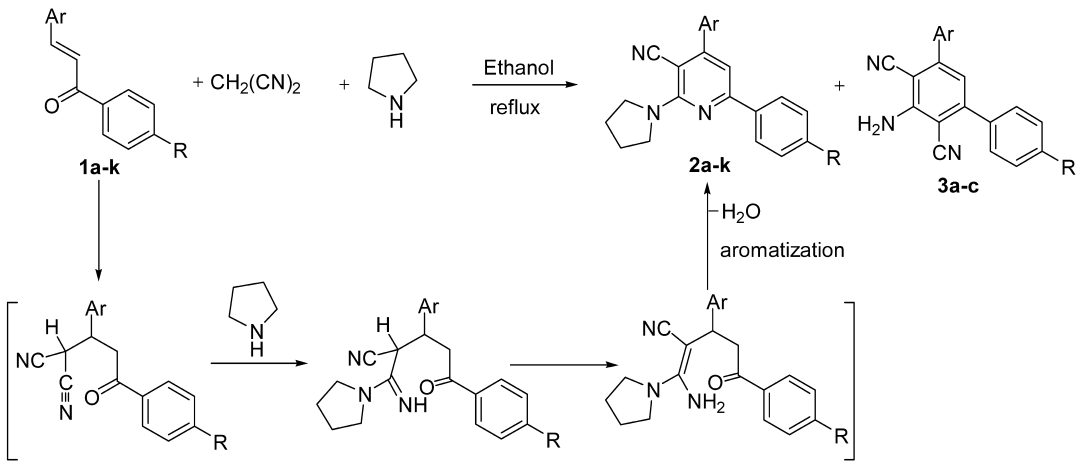
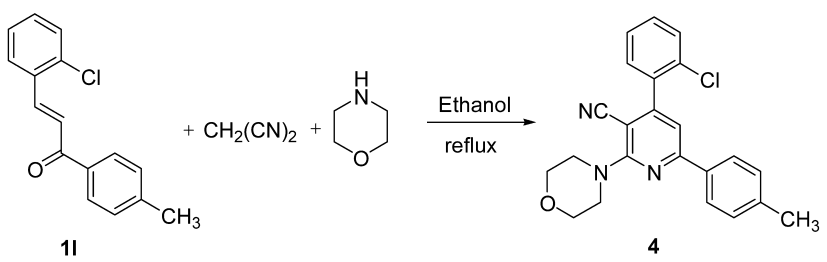
0040–4020/03/$ - see front matter 
doi:10.1016/S0040-4020(03)00507-6




**Scheme 1.**




**Scheme 2.**

of pyrrolidine the respective morpholine derivative **4** was obtained from the enone **1** l in 67% yield (Scheme 2). The formation of the biphenyl ring system from enone on reaction with 2 equiv. of malononitrile in the presence of a catalytic amount of pyrrolidine has been reported earlier.[26]

The IR spectrum of compound **2b** showed a strong absorption band at 2194 $cm^{-1}$ due to cyano group. Proton NMR spectrum of **2b** showed a triplet for *N*-$CH_2$–$CH_2$ at $\delta$ 2.02 (4H) and another triplet for *N*-$CH_2$–$CH_2$ at $\delta$ 3.90 (4H). $^{13}C$ NMR spectrum of the product **2b** showed *N*-$CH_2$–$CH_2$ carbons at $\delta$ 25.94 (t) and *N*-$CH_2$–$CH_2$ carbon at $\delta$ 49.70 (t); the cyano group attached pyridine ring carbon appeared at $\delta$ 86.10 and the cyanocarbon appeared at $\delta$ 114.15. Full data for all compounds are furnished in the experimental section. The structures of **2c**, **2f** and **2g** have been confirmed by X-ray analysis.[27–29]

The biphenyl derivative **3b** was characterized by spectral data and analysis. The IR spectrum showed the amino (3469, 3356 $cm^{-1}$) and cyano (2213 $cm^{-1}$) groups. The proton NMR showed the $NH_2$ at $\delta$ 5.39 (exchanged by $D_2O$), *p*-tolyl moiety at $\delta$ 2.43 (s), $\delta$ 7.32 and $\delta$ 7.47 (2d, $J$=8.3 Hz), the $C_6$ proton at $\delta$ 7.26 (s) and thienyl protons at $\delta$ 7.18, 7.50 and $\delta$ 7.75.

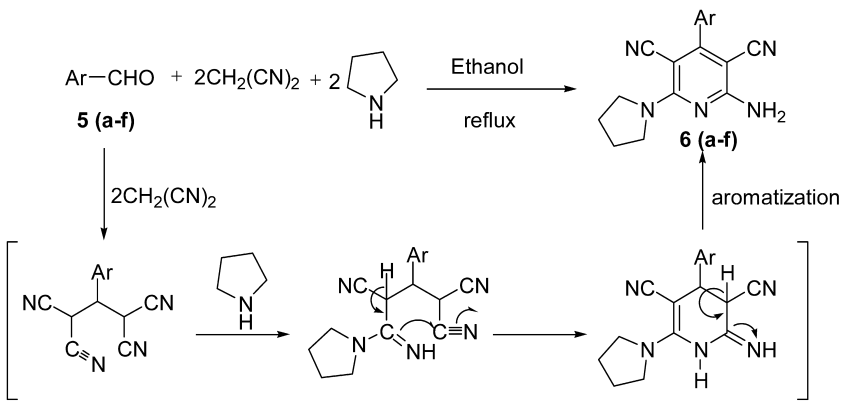
The reaction of aromatic aldehydes **5a–f**, (Table 2) with 2 equiv. each of malononitrile and pyrrolidine in ethanol afforded the pyridine dinitrile derivatives **6a–f**, respectively, in 41–56% yields. The formation of the pyridine ring could be rationalized by Knoevenagel condensation, Michael addition, enamine formation, cyclization and aromatization (Scheme 3). The reaction of benzylidene malononitrile with dimedone giving tetrahydrobenzopyran derivative is reported.[30]

The IR spectrum of product **6c** showed strong absorptions at 3475, 3345 $cm^{-1}$ due to amino group, and at 2206 $cm^{-1}$ due to cyano group. The $^1H$ NMR spectrum of **6c** showed a triplet at $\delta$ 1.94 due to 3′,4′-$CH_2$ and a triplet at $\delta$ 3.75 for *N*-$CH_2$ protons in the pyrrolidine ring and a broad singlet at $\delta$ 5.31 for the $NH_2$ protons (exchanged with $D_2O$). $^{13}C$ NMR spectrum of compound **6c** showed aromatic methyl carbon at $\delta$ 21.42, the 3′, 4′ methylene carbons of the pyrrolidine moiety at $\delta$ 25.36, the nitrogen attached methylene carbons at $\delta$ 49.51, the two cyano attached carbons at $\delta$ 82.09 and 83.21, the two cyano carbons at $\delta$ 116.88 and 118.31. $^{13}C$ NMR, recorded using DEPT-135 technique, showed two inverted signals at $\delta$ 25.36 (↓) for *N*-$CH_2$–$CH_2$ and at $\delta$ 49.51(↓) for *N*-$CH_2$–$CH_2$ of the pyrrolidine ring. Similar procedure furnished the other pyridinedinitriles **6a–f**.

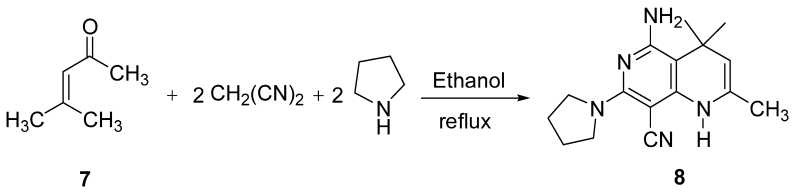
The reaction of mesityloxide **7** with 2 equiv. each of

**Table 2**. Reaction of aromatic aldehydes **5a–f** with malononitrile and pyrrolidine

| **6** | Ar |
|---|---|
| **a** | 4-$Me_2N$–$C_6H_4$– |
| **b** | 4-$Et_2N$–$C_6H_4$– |
| **c** | 4-$CH_3$—$C_6H_4$– |
| **d** | 4-$CH_3O$–$C_6H_4$– |
| **e** | $C_6H_5$– |
| **f** | Indol-3-yl |




**Scheme 3.**




**Scheme 4.**

**Table 3**. SHG efficiency of pyridines

| Compound No. | ΔmV (average) | SHG efficiency (%) |
|---|---|---|
| **Urea** | 328.55 | 100 |
| **2b** | 91.66 | 27.89 |
| **6a** | 599.00 | 182.31 |
| **6b** | 638.33 | 194.28 |
| **6f** | 499.66 | 152.08 |

malononitrile and pyrrolidine, in ethanol afforded the 1,4-dihydro-1,6-naphthyridine **8**, in 32% yield (Scheme 4). Thus, the lack of hydrogen in the β-position of the enone resulted in the formation of the dihydro product **8**, curtailing the dehydrogenation step.[25]

The IR spectrum of compound **8** showed strong absorption bands at 3492, 3352 and 3211 $cm^{-1}$ due to $NH_2$, NH groups and at 2179 $cm^{-1}$ due to cyano group. The proton NMR spectrum of **8** showed a singlet at $\delta$ 1.37 (6H) for gem-dimethyl protons and a singlet at $\delta$ 1.80 for the C-2 methyl protons; a triplet at $\delta$ 1.91 (4H) and another triplet at $\delta$ 3.68 (4H) confirmed the pyrrolidine moiety; a singlet at $\delta$ 4.21 for the C-3 attached proton, a broad singlet at 4.74 for $NH_2$ protons (exchanged with $D_2O$) and a broad singlet at $\delta$ 5.91 for NH proton were also seen consistent with the structure of **8**. Further, the structure of compound **8** was also confirmed by X-ray crystallographic studies.[31]

### 2.1. Non-linear optical studies

The donor–acceptor substituted compounds have generated interest in recent years since they exhibit unique photophysical, photochemical and optical properties due to charge transfer interaction between the donor and acceptor substituents. Recently several new classes of compounds showing second harmonic generation (SHG) have been studied.[32,33]

We have reported the spectral and photophysical properties of 1,6-naphthyridines derivatives as a new class of compounds for non-linear optics. The NLO efficiency of five 1,6-naphthyridine derivatives ranged from 51 to 91% when compared with urea as standard.[24] On the above lines, we have studied the NLO properties of compounds **2b**, **6a**, **6b** and **6f**. The SHG efficiency of these compounds compared to urea was examined by the Kurtz powder technique using a Nd-YAG pulsed laser (1064 nm, 8 ns pulse), following the experimental conditions described earlier.[24] The data is given in Table 3. Thus the present work has shown that pyridinedinitrile system **6** is a new ring system having better NLO efficiency (152–194%) compared to the standard urea.

## 3. Conclusions

Thus, the reaction of enone with malononitrile depended on the number of equivalents of the malononitrile and the base such as pyrrolidine, piperidine or morpholine used for the reaction, leading to 1,6-naphthyridines and terphenyl/biphenyl system; dihydronaphthyridine was obtained when β-hydrogen was absent in the enone. The pyridinedinitriles **6a**, **6b**, **6f** have been identified as efficient NLO compounds.

## 4. Experimental

### 4.1. General

All melting points are uncorrected. IR spectra were recorded on Shimadzu FT-IR 8300 model. $^1H$ and $^{13}C$ NMR spectra were recorded on Brucker 300 MHz and Jeol GMX 400 MHz spectrometers with $CDCl_3$ and DMSO-$d_6$ as the solvents with tetramethylsilane as the internal standard. Mass spectra were taken on Hewlett–Packard 5985 (70ev)

instrument. Absorption spectra were recorded using Shimadzu UV 260 spectrophotometer. Column chromatography was performed on silica gel (100–200 mesh).

### 4.2. General procedure for the preparation of nicotinonitriles 2a–k

To a solution of enone **1** in absolute ethanol (20 mL), malononitrile (1 equiv.) was added dropwise, followed by the addition of pyrrolidine/morpholine (1 equiv.) at room temperature. The reaction mixture was refluxed on a water bath until the disappearance of the starting material, monitored by TLC; the solvent was removed and the residue obtained was purified by column chromatography using silica gel; elution with hexane/chloroform (1:1) mixture afforded the corresponding nicotinonitrile **2**; the products were recrystallized from ethanol.

**4.2.1. 4-(4-Dimethylaminophenyl)-6-(4-methylphenyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2a).** Following the above general procedure, treatment of 3-(4-dimethylaminophenyl)-1-(4-methylphenyl)-prop-2-en-1-one **1a** (1.0 g, 3.77 mmol) with malononitrile (0.25 g, 3.78 mmol) and pyrrolidine (0.27 g, 3.80 mmol) in absolute ethanol and refluxing for 9 h, gave the compound **2a**. Yield: 0.63 g (44%), yellow solid, mp 164–166°C; IR (KBr): 2198 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 2.01 and 3.91 (2t, 8H, 3′,4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 2.41 (s, 3H, $CH_3$), 3.01 (s, 6H, N$(CH_3)_2$), 6.79 (d, 2H, *J*=8.7 Hz), 7.09 (s, 1H), 7.25 (d, 2H, *J*=7.9 Hz), 7.54 (d, 2H, *J*=8.7 Hz), 7.98 (d, 2H, *J*=7.9 Hz). $^{13}C$ NMR: $\delta$ 21.28, 25.64, 40.15, 49.41, 86.38, 108.58, 111.76, 119.89, 125.15, 127.06, 129.40, 129.68, 135.83, 139.75, 151.07, 157.29, 157.63, 158.71. MS: *m*/*z* (%)=382 ($M^+$, 30), 381 (94), 380 (100), 352 (96), 336 (24), 326 (22), 269 (14), 70 (32). Anal. Calcd for $C_{25}H_{26}N_4$ (382.49): C, 78.49; H, 6.85; N, 14.64. Found: C, 78.72; H, 6.74; N, 14.83.

**4.2.2. 4-(4-Dimethylaminophenyl)-6-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2b).** Treatment of 3-(4-dimethylaminophenyl)-1-(4-methoxyphenyl)-prop-2-en-1-one **1b** (0.5 g, 1.77 mmol) with malononitrile (0.12 g, 1.81 mmol) and pyrrolidine (0.13 g, 1.81 mmol) in absolute ethanol under reflux for 9 h, afforded the compound **2b**. Yield: 0.45 g (64%), yellow solid, mp 182–184°C; IR (KBr): 2194 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 2.02 and 3.90 (2t, 8H, *J*=6.6 Hz, 3′,4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 3.02 (s, 6H, N$(CH_3)_2$), 3.87 (s, 3H), 6.82 (d, 2H, *J*=8.7 Hz), 6.96 (d, 2H, *J*=8.7 Hz), 7.04 (s, 1H), 7.54 (d, 2H, *J*=8.7 Hz), 8.04 (d, 2H, *J*=8.7 Hz). $^{13}C$ NMR: $\delta$ 25.94, 40.46, 49.70, 55.56, 86.10, 108.50, 112.10, 114.15, 120.23, 125.60, 128.89, 129.95, 131.53, 151.41, 157.58, 159.04, 161.32; $^{13}C$ NMR (DEPT-135): $\delta$ 25.94(↓), 49.70(↓). MS: *m*/*z* (%)=398 ($M^+$, 62), 397 (84), 370 (20), 369 (100), 355 (10), 326 (16), 298 (8), 70 (36). Anal. Calcd for $C_{25}H_{26}N_4O$ (398.52): C, 75.34; H, 6.57; N, 14.05. Found: C, 74.94; H, 6.63; N, 13.75.

**4.2.3. 6-(4-Chlorophenyl)-4-(4-dimethylaminophenyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2c).** Treatment of 1-(4-chlorophenyl)-3-(4-dimethylaminophenyl)-prop-2-en-1-one **1c** (1.0 g, 3.50 mmol) with malononitrile (0.23 g, 3.48 mmol) and pyrrolidine (0.25 g, 3.52 mmol) in ethanol under reflux for 10 h, gave the compound **2c**. Yield: 0.69 g (49%), greenish yellow solid, mp 180–182°C; IR (KBr): 2198 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.99 and 3.87 (2t, 8H, 3′, 4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 3.01 (s, 6H, N$(CH_3)_2$), 6.77 (d, 2H, *J*=8.8 Hz), 7.03 (s, 1H), 7.39 (d, 2H, *J*=8.8 Hz), 7.59 (d, 2H, *J*=8.8 Hz), 8.0 (d, 2H, *J*=8.8 Hz). $^{13}C$ NMR: $\delta$ 25.64, 40.15, 49.46, 86.93, 108.55, 111.75, 119.68, 124.81, 128.24, 128.87, 129.70, 135.65, 137.01, 151.16, 156.27, 157.61, 158.59. MS: *m*/*z* (%)=402 (50, M+2), 400 (98), 372 (80), 359 (50), 345 (100), 260 (10), 201 (12), 70 (38). Anal. Calcd for $C_{24}H_{23}N_4Cl$ (402.92): C, 71.54; H, 5.75; N, 13.90. Found: C, 71.52; H, 5.79; N, 13.86.

**4.2.4. 4-(4-Dimethylaminophenyl)-6-phenyl-2-(pyrrolidin-1-yl)-nicotinonitrile (2d).** Following the above general procedure, treatment of 3-(4-dimethylaminophenyl)-1-phenyl-prop-2-en-1-one **1d** (1.0 g, 3.98 mmol) with malononitrile (0.26 g, 3.94 mmol) and pyrrolidine (0.28 g, 3.94 mmol) in absolute ethanol on refluxing for 9 h, gave the compound **2d**. Yield: 0.65 g (46%), greenish yellow solid, mp 180–182°C; IR (KBr): 2198 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 2.00 and 3.91 (2t, 8H, *J*=6.4 Hz, 3′, 4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 3.01 (s, 6H, N$(CH_3)_2$), 6.79 (d, 2H, *J*=8.3 Hz), 7.12 (s, 1H), 7.43–7.57 (m, 5H, Ar-H), 8.06 (d, 2H, *J*=8.2 Hz).$^{13}C$ NMR: $\delta$ 25.60, 40.11, 49.40, 86.64, 108.80, 111.70, 119.78, 124.97, 127.09, 128.42, 129.28, 129.56, 138.53, 151.05, 157.37, 157.55, 158.65. MS: *m*/*z* (%)=368 ($M^+$, 94), 340 (32), 339 (100), 323 (22), 276 (40), 169 (28). Anal. Calcd for $C_{24}H_{24}N_4$ (368.47): C, 78.23; H, 6.57; N, 15.21. Found: C, 78.38; H, 6.64; N, 15.01.

**4.2.5. 4-(4-Diethylaminophenyl)-6-phenyl-2-(pyrrolidin-1-yl)-nicotinonitrile (2e).** Reaction of 3-(4-diethylaminophenyl)-1-phenyl-prop-2-en-1-one **1e** (1.0 g, 3.58 mmol) with malononitrile (0.24 g, 3.63 mmol) and pyrrolidine (0.25 g, 3.52 mmol) in absolute ethanol on refluxing for 9 h, gave the compound **2e**. Yield: 0.62 g (44%), yellow solid, mp 170–172°C; IR (KBr): 2191 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.20 (t, 6H, N$(CH_2CH_3)_2$), 1.99 and 3.86 (2t, 8H, 3′, 4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 3.40 (q, 4H, N$(CH_2CH_3)_2$), 6.73 (d, 2H, *J*=8.7 Hz), 7.04 (s, 1H), 7.37–7.52 (m, 5H, Ar-H), 7.55 (d, 2H, *J*=8.5 Hz).$^{13}C$ NMR: $\delta$ 12.54, 25.64, 44.28, 49.47, 86.80, 108.43, 110.97, 119.76, 23.67, 124.02, 128.66, 129.99, 131.59, 137.52, 148.65, 156.25, 157.58, 158.70. MS: *m*/*z* (%)=396 ($M^+$, 4), 394 (14), 39 (100), 330 (18). Anal. Calcd for $C_{26}H_{28}N_4$ (396.54): C, 78.75; H, 7.11; N, 14.12. Found: C, 79.02; H, 6.94; N, 14.42.

**4.2.6. 4-(4-Diethylaminophenyl)-6-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2f).** Treatment of 3-(4-diethylaminophenyl)-1-(4-methoxyphenyl)-prop-2-en-1-one **1f** (1.0 g, 3.23 mmol) with malononitrile (0.21 g, 3.18 mmol) and pyrrolidine (0.23 g, 3.23 mmol) in absolute ethanol under reflux for 9 h, gave the compound **2f**. Yield: 0.58 g (41%), yellow solid, mp 208–210°C; IR (KBr): 2191 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.20 (t, 6H, N $(CH_2CH_3)_2$), 1.99 and 3.87 (2t, 8H, *J*=6.6 Hz, 3′, 4′-$CH_2$ and *N*-$CH_2$, pyrrolidine), 3.39 (q, 4H, N$(CH_2CH_3)_2$), 3.84 (s, 3H, $OCH_3$), 6.73 (d, 2H, *J*=8.8 Hz), 6.96 (d, 2H, *J*=8.8 Hz), 7.06 (s, 1H), 7.53 (d, 2H, *J*=8.8 Hz), 8.03 (d, 2H, *J*=8.8 Hz). $^{13}C$ NMR: $\delta$ 12.52, 25.64, 44.25, 49.41, 55.24, 85.77, 108.04, 110.94, 113.80, 120.07, 124.07, 128.55, 129.67, 131.20, 148.51, 157.14, 157.19, 158.82, 160.94. Anal. Calcd for $C_{27}H_{30}N_4O$ (426.57): C, 76.03; H, 7.08; N, 13.13. Found: C, 75.92; H, 7.11; N, 13.47.

**4.2.7. 6-(4-Methoxyphenyl)-4-phenyl-2-(pyrrolidin-1-yl)-nicotinonitrile (2g).** Following the above general procedure, treatment of 1-(4-methoxyphenyl)-3-phenyl-prop-2-en-1-one **1g** (0.5 g, 2.10 mmol) with malononitrile (0.14 g, 2.12 mmol) and pyrrolidine (0.15 g, 2.11 mmol) in absolute ethanol and refluxing for 9 h, gave the compound **2g**. Yield: 0.51 g (69%), pale yellow solid, mp 168–170°C; IR (KBr): 2200 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 2.00 and 3.90 (2t, 8H, $J$=6.3 Hz, 3′, 4′-$CH_2$ and $N$-$CH_2$ pyrrolidine), 3.86 (s, 3H, $OCH_3$), 6.96 (d, 2H, $J$=8.8 Hz), 7.02 (s, 1H), 7.46–7.57 (m, 5H, Ar-H), 8.03 (d, 2H, $J$=8.8 Hz). $^{13}C$ NMR: $\delta$ 25.55, 49.28, 55.22, 86.28, 108.44, 113.84, 119.20, 128.32, 128.36, 128.43, 129.08, 130.69, 138.06, 157.16, 157.52, 158.05, 161.15. MS: $m/z$ (%)=355 ($M^+$, 32), 354 (68), 32 (60), 70 (100). Anal. Calcd for $C_{23}H_{21}N_3O$ (355.44): C, 77.72; H, 5.95; N, 11.82. Found: C, 77.70; H, 5.92; N, 11.79.

**4.2.8. 4,6-Di-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2h).** Reaction of 1,3-di-(4-methoxyphenyl)-prop-2-en-1-one **1h** (0.5 g, 1.86 mmol) with malononitrile (0.12 g, 1.82 mmol) and pyrrolidine (0.13 g, 1.83 mmol) in absolute ethanol under reflux for 9 h, gave the compound **2h**. Yield: 0.31 g (43%), brownish yellow solid, mp 174–176°C; IR (KBr): 2202 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 2.00 and 3.90 (2t, 8H, 3′, 4′-$CH_2$ and $N$-$CH_2$, pyrrolidine), 3.85 and 3.87 (2 s, 6H, $(OCH_3)_2$), 6.96 (d, 2H, $J$=8.8 Hz), 7.03 (s, 1H), 7.26 (d, 2H, $J$=8.8 Hz), 7.52 (d, 2H, $J$=8.8 Hz), 8.03 (d, 2H, $J$=8.8 Hz). Anal. Calcd for $C_{24}H_{23}N_3O_2$ (385.46): C, 74.78; H, 6.01; N, 10.90. Found: C, 74.57; H, 6.32; N, 11.14.

**4.2.9. 6-Phenyl-4-(2-thienyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2i).** Following the above general procedure, treatment of 1-phenyl-3-(2-thienyl)-prop-2-en-1-one **1i** (1 g, 4.67 mmol) with malononitrile (0.31 g, 4.67 mmol) and pyrrolidine (0.33 g, 4.67 mmol) in absolute ethanol and refluxing for 9 h, gave the compound **2i**. Yield: 0.80 g (51%), brownish yellow solid, mp 120–122°C; IR (KBr): 2200 (CN), 1562, 1541, 1424, 690 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 2.03 (t, 4H, $J$=6.6 Hz, 3′, 4′-$CH_2$ in pyrrolidine), 3.92 (t, 4H, $J$=6.6 Hz, $N$-$CH_2$ in pyrrolidine), 7.26 (s, 1H, $C_5$-Ar H), 7.18–8.08 (m, 8H, Ar-H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 25.69, 49.63, 108.90, 119.41, 127.25, 127.94, 128.13, 128.63, 128.79, 128.94, 130.05, 138.15, 138.80, 148.84, 158.34. MS (%): $m/z$ 331 ($M^+$, 59), 330 (89), 304 (9), 302 (100), 276 (17), 262 (9), 261 (16), 165 ($M^{++}$, 10), 102 (6), 70 (23). Anal. calcd for $C_{20}H_{17}N_3S$ (331.44): C, 72.42; H, 5.17; N, 12.69. Found: C, 72.20, H, 5.02; N, 12.45.

**4.2.10. 6-(4-Methylphenyl)-4-(2-thienyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2j).** Following the above general procedure, treatment of 1-(4-methylphenyl)-3-(2-thienyl)-prop-2-en-1-one **1j** (1 g, 4.38 mmol) with malononitrile (0.29 g, 4.39 mmol) and pyrrolidine (0.31 g, 4.36 mmol) in absolute ethanol and refluxing for 10 h, gave the compound **2j**. Yield: 0.82 g (54%), yellow solid, mp 130–132°C; IR (KBr): 2199 (CN), 1561, 1541, 1508, 1424, 809, 706 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 2.02 (bs, 4H, 3′ and 4′-$CH_2$ in pyrrolidine), 2.42 (s, 3H, Ar-$CH_3$), 3.91 (t, 4H, $J$=5.8 Hz, $N$-$CH_2$ in pyrrolidine), 7.17 (s, 1H, $C_5$-Ar H), 7.28–7.6 (m, 4H), 7.72 (d, 1H, $J$=1.8 Hz), 7.96 (d, 2H, $J$=7.0 Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 21.38, 25.68, 49.58, 85.34, 108.62, 119.49, 127.17, 127.81, 128.08, 128.85, 129.36, 135.38, 139.03, 140.30, 148.70, 158.32, 158.79. MS (%): $m/z$ 344 ($M^+$-1, 20), 288 (14), 263 (23), 183 (28), 165 (17), 137 (27), 123 (29), 116 (17), 111 (36), 106 (73), 98 (34), 97 (62), 85 (54), 83 (64), 81 (49), 71 (34), 70 (61). Anal. calcd for $C_{21}H_{19}N_3S$ (345.47): C, 73.01; H, 5.54; N, 12.16. Found: C, 72.75, H, 5.45; N, 12.02.

**4.2.11. 6-Phenyl-4-(2-pyridyl)-2-(pyrrolidin-1-yl)-nicotinonitrile (2k).** Following the above general procedure, treatment of 1-phenyl-3-(2-pyridyl)-prop-2-en-1-one **1k** (1 g, 4.78 mmol) with malononitrile (0.32 g, 4.84 mmol) and pyrrolidine (0.34 g, 4.78 mmol) in absolute ethanol and refluxing for 9 h, gave the compound **2k**. Yield: 0.82 g (52%), yellowish orange solid, mp 152–154°C; IR (KBr): 2197 (CN), 1547, 1546, 1483, 1245, 776, 761 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 2.03 (bs, 4H, 3′ and 4′-$CH_2$ in pyrrolidine), 3.94 (t, 4H, $J$=6.0 Hz, $N$-$CH_2$ in pyrrolidine), 7.26 (s, 1H, $C_5$-Ar H), 7.35–7.49 (m, 4H), 7.74–7.87 (m, 2H), 8.09–8.12 (m, 2H), 8.78–8.80 (d, 1H, $J$=4.8 Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 25.64, 49.47, 86.59, 109.02, 118.88, 123.84, 123.90, 127.30, 128.55, 129.97, 136.66, 138.14, 149.85, 155.40, 155.45, 158.21, 158.39. MS (%): $m/z$ 326 ($M^+$, 100), 325 (27), 298 (32), 297 (83), 271 (11), 257 (13), 256 (16), 229 (13), 102 (7), 71 (7), 70 (32). Anal. calcd for $C_{21}H_{18}N_4$ (326.40): C, 77.28; H, 5.56; N, 17.16. Found: C, 76.95, H, 5.41; N, 17.02.

**4.2.12. 4-(2-Chlorophenyl)-6-(4-methylphenyl)-2-(morpholin-1-yl)-nicotinonitrile (4).** Following the above general procedure, treatment of 3-(2-chlorophenyl)-1-(4-methylphenyl)-prop-2-en-1-one **1l** (0.5 g, 1.95 mmol) with malononitrile (0.13 g, 1.96 mmol) and morpholine (0.17 g, 1.95 mmol) in absolute ethanol and refluxing for 9 h, gave the compound **4**. Yield: 0.52 g (67%), pale yellow solid, mp 262–264°C; IR (KBr): 2194 (CN) $cm^{-1}$; $^1H$ NMR (300 MHz): $\delta$ 2.17 (s, 3H, $CH_3$), 3.31 (t, 4H), 3.58 (t, 4H), 7.02–7.25 (m, 7H, Ar-H), 7.53 (d, 2H, $J$=7.9 Hz); $^{13}C$ NMR: $\delta$ 20.73, 48.59, 66.14, 114.21, 116.80, 117.61, 123.42, 126.13, 127.64, 129.53, 130.35, 131.47, 136.36, 138.01, 138.36, 147.71, 153.84, 156.89, 165.99. Anal. calcd for $C_{23}H_{20}N_3OCl$ (389.88): C, 70.85; H, 5.17; N, 10.77. Found: C, 71.02; H, 5.20; N, 11.08.

### 4.3. General procedure for the preparation of biphenyls 3a–c

To a solution of enone **1** in absolute ethanol (20 mL), malononitrile (2 equiv.) was added dropwise, followed by the addition of pyrrolidine (2 equiv.) at room temperature. Then, the reaction mixture was refluxed on a water bath for 10–12 h and the solvent was removed. The residue obtained was purified by column chromatography using silica gel and eluted with hexane/ethyl acetate (3:2) mixture to afford biphenyls **3a–c** along with nicotinonitriles **2i–k**, the latter were identified by comparison with the above prepared samples.

**4.3.1. 3-Amino-2,4-dicyano-5-(2-thienyl)-biphenyl (3a).** Following the above general procedure, treatment of 1-phenyl-3-(2-thienyl)-prop-2-en-1-one **1i** (1 g, 4.67 mmol) with malononitrile (0.62 g, 9.39 mmol) and pyrrolidine (0.66 g, 9.29 mmol) in absolute ethanol and refluxing for

12 h, gave the compounds **2i** (yield: 0.49 g (32%)) and **3a**. Yield: 0.69 g (49%), yellow solid, mp 238–240°C; IR (KBr): 3474, 3375 ($NH_2$), 2211 (CN), 1634, 1572, 1421, 1286, 718, 696 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 5.41 (bs, 2H, $NH_2$), 7.00 (s, 1H, $C_6$-Ar H), 7.2 (2d, 1H, $J$=5.0 and 3.6 Hz), 7.50–7.60 (m, 6H), 7.75–7.76 (2d, 1H, $J$=3.7 and 1.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 93.00, 94.64, 115.88, 116.27, 119.34, 128.34, 128.49, 128.78, 128.93, 129.77, 137.22, 138.68, 141.72, 150.19, 153.52. MS (%): *m/z* 301 ($M^+$, 57), 300 (M-1, 100), 273 (14), 272 (9), 255 (7), 228 (6), 150 (11), 136 (12), 88 (6), 77 (4). Anal. calcd for $C_{18}H_{11}N_3S$ (301.38): C, 71.74; H, 3.68; N, 13.94. Found: C, 71.48, H, 3.62; N, 13.75.

**4.3.2. 3-Amino-2,4-dicyano-4′-methyl-5-(2-thienyl)-biphenyl (3b).** Following the above general procedure, treatment of 1-(4-methylphenyl)-3-(2-thienyl)-prop-2-en-1-one **1j** (1 g, 4.38 mmol) with malononitrile (0.58 g, 8.78 mmol) and pyrrolidine (0.62 g, 8.73 mmol) in absolute ethanol and refluxing for 11 h, gave the compounds **2j** (yield: 0.40 g (26%)) and **3b**. Yield: 0.69 g (50%), greenish yellow solid, mp 180–182°C; IR (KBr): 3469, 3356 ($NH_2$), 2213 (CN), 1621, 1595, 1541, 813, 696 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 2.43 (s, 3H, $CH_3$), 5.39 (bs, 2H, $NH_2$), 7.18 (2d, 1H, $J$=4.9 and 3.9 Hz), 7.26 (s, 1H, $C_6$-Ar H), 7.32–7.47 (2d, 4H, $J$=8.30 Hz), 7.50 and 7.75 (2d, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 21.35, 93.00, 95.00, 116.07, 116.35, 119.24, 128.22, 128.47, 128.70, 129.62, 134.33, 138.76, 140.06, 141.61, 150.25, 153.54. MS (%): *m/z* 315 ($M^+$, 100), 314 (M-1, 26), 300 (6), 288 (9), 287 (13), 231 (3), 156.7 ($M^{++}$, 9), 91 (7), 77 (3). Anal. calcd for $C_{19}H_{13}N_3S$ (315.40): C, 72.36; H, 4.15; N, 13.32. Found: C, 72.30, H, 4.11; N, 13.18.

**4.3.3. 3-Amino-2,4-dicyano-5-(2-pyridyl)-biphenyl (3c).** Following the above general procedure, treatment of 1-phenyl-3-(2-pyridyl)-prop-2-en-1-one **1k** (1 g, 4.78 mmol) with malononitrile (0.64 g, 9.69 mmol) and pyrrolidine (0.68 g, 9.57 mmol) in absolute ethanol and refluxing for 10 h, gave the compounds **2k** (yield: 0.45 g (29%)) and **3c**. Yield: 0.75 g (53%), pale yellow solid, mp 264–266°C; IR (KBr): 3479, 3382 ($NH_2$), 2213 (CN), 1628, 1580, 1296, 1280, 791, 767, 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 5.45 (bs, 2H, $NH_2$), 7.19 (s, 1H, $C_6$-Ar H), 7.40–7.61 (m, 6H), 7.76–7.92 (m, 2H), 8.80 (d, 1H, $J$=4.8 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 92.58, 93.84, 114.53, 117.08, 121.86, 122.71, 126.95, 127.21, 127.94, 135.63, 136.12, 146.02, 148.03, 148.37, 152.80; $^{13}C$ NMR-DEPT-135: $\delta$ 119.65, 123.09, 124.23, 128.87, 129.70, 137.01, 149.94. MS (%): *m/z* 296 ($M^+$, 85), 295 (M-1, 22), 270 (27), 183 (23), 129 (43), 109 (42), 105 (30), 97 (29), 83 (61), 77 (20). Anal. calcd for $C_{19}H_{12}N_4$ (296.33): C, 77.01; H, 4.08; N, 18.91. Found: C, 76.68, H, 3.95; N, 18.66.

### 4.4. General procedure for the preparation of polysubstituted pyridines 6a–f

To a solution of aromatic aldehyde **5** in absolute ethanol (20 mL), malononitrile (2 equiv.) was added dropwise followed by the addition of pyrrolidine (2 equiv.) at room temperature. The reaction mixture was refluxed on a water bath and monitored by TLC. After the disappearance of the starting material, the solvent was removed under reduced pressure. The residue was purified by column chromatography using silica gel and eluted with hexane/chloroform (1:1) to furnish the corresponding polysubstituted pyridine derivative **6**.

**4.4.1. 6-Amino-4-(4-dimethylaminophenyl)-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6a).** Following the above general procedure, treatment of 4-dimethylaminobenzaldehyde **5a** (0.75 g, 5.03 mmol) with malononitrile (0.66 g, 10 mmol) and pyrrolidine (0.71 g, 10 mmol) in absolute ethanol under reflux for 10 h, furnished the compound **6a**. Yield: 0.92 g (55%), yellow solid, mp 252–254°C; IR (KBr): 3454, 3340 ($NH_2$), 2200 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.97 and 4.11 (2t, 8H, $J$=6.6 Hz, 3′, 4′ $CH_2$ and *N*-$CH_2$, pyrrolidine), 3.02 (s, 6H, $N(CH_3)_2$), 5.28 (bs, 2H, exchanged with $D_2O$), 6.76 (d, 2H, $J$=9.0 Hz), 7.43 (d, 2H, $J$=9.0 Hz).$^{13}C$ NMR: $\delta$ 25.44, 40.06, 49.58, 80.48, 81.36, 111.43, 117.68, 119.01, 121.59, 130.09, 151.62, 158.20, 159.66, 162.15. MS: *m/z* (%)=332 ($M^+$, 100), 331 (62), 303 (34), 287 (16), 260 (31), 219 (21), 151 (28), 70 (21). Anal. Calcd for $C_{19}H_{20}N_6$ (332.41): C, 68.65; H, 6.06; N, 25.25. Found: C, 68.91; H, 6.24; N, 25.03.

**4.4.2. 6-Amino-4-(4-diethylaminophenyl)-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6b).** Following the above general procedure, treatment of 4-diethylaminobenzaldehyde **5b** (1.0 g, 5.61 mmol) with malononitrile (0.74 g, 11.21 mmol) and pyrrolidine (0.71 g, 11.12 mmol) in absolute ethanol and refluxing for 9 h, furnished the compound **6b**. Yield: 1.14 g (56%), pale yellow solid, mp 198–200°C; IR (KBr): 3502, 3369 ($NH_2$), 2198 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.19 (t, 6H, N ($CH_2$–$CH_3$)$_2$), 1.96 and 3.78 (2t, 8H, $J$=6.8 Hz, 3′, 4′-$CH_2$ and *N*-$CH_2$ pyrrolidine), 3.38 (q, 4H, N($CH_2$-$CH_3$)$_2$), 5.28 (bs, 2H, exchanged with $D_2O$), 6.70 (d, 2H, $J$=8.8 Hz), 7.42 (d, 2H, $J$=8.8 Hz). $^{13}C$ NMR: $\delta$ 12.55, 25.43, 44.22, 49.58, 80.21, 81.08, 110.59, 117.83, 119.13, 120.45, 130.44, 149.29, 158.34, 159.74, 162.01. MS: *m/z* (%)=360 ($M^+$, 8), 359 (46), 345 (10), 344 (100), 316 (8), 233 (6), 70 (6). Anal. Calcd for $C_{21}H_{24}N_6$ (360.46): C, 69.97; H, 6.71; N, 23.31. Found: C, 70.14; H, 6.88; N, 23.61.

**4.4.3. 6-Amino-4-(4-methylphenyl)-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6c).** 4-Methylbenzaldehyde **5c** (1.0 g, 8.33 mmol), malononitrile (1.09 g, 16.51 mmol) and pyrrolidine (1.18 g, 16.62 mmol) in absolute ethanol on refluxing for 9 h, furnished the compound **6c**. Yield: 1.30 g (52%), pale yellow solid, mp 278–280°C; IR (KBr): 3475, 3345 ($NH_2$), 2206 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.94 and 3.75 (2t, 8H, 3′, 4′ $CH_2$ and *N*-$CH_2$, pyrrolidine), 2.30 (s, 3H, $CH_3$), 5.31 (bs, 2H, exchanged with $D_2O$), 7.26 (d, 2H, $J$=8.3 Hz), 7.38 (d, 2H, $J$=8.3 Hz); $^{13}C$ NMR: $\delta$ 21.42, 25.36, 49.51, 80.96, 81.84, 116.88, 118.31, 128.39, 129.38, 132.01, 140.36, 157.60, 159.33, 162.18. $^{13}C$ NMR (DEPT-135): $\delta$ 25.36(↓), 49.51(↓). MS: *m/z* (%)=303 ($M^+$, 92), 302 (100), 288 (50), 274 (64), 260 (54), 248 (8), 179 (10). Anal. Calcd for $C_{18}H_{17}N_5$ (303.36): C, 71.26; H, 5.64; N, 23.08. Found: C, 71.48; H, 5.94; N, 23.31.

**4.4.4. 6-Amino-4-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6d).** 4-Methoxybenzaldehyde **5d** (1.0 g, 7.35 mmol), malononitrile (0.97 g, 14.69 mmol) and pyrrolidine (1.04 g, 14.64 mmol) in absolute ethanol on

refluxing for 9 h, furnished the compound **6d**. Yield: 0.98 g (41%), brownish yellow solid, mp 242–244°C; IR (KBr): 3444, 3340 ($NH_2$), 2206 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.97 and 3.79 (2t, 8H, $J$=6.8 Hz, 3′, 4′-$CH_2$ and $N$-$CH_2$, pyrrolidine), 3.85 (s, 3H, $OCH_3$), 5.34 (bs, 2H, exchanged with $D_2O$), 7.01 (d, 2H, $J$=8.8 Hz), 7.45 (d, 2H, $J$=8.8 Hz). $^{13}C$ NMR: $\delta$ 25.37, 49.54, 55.26, 80.88, 81.76, 114.08, 117.07, 118.48, 126.98, 130.15, 157.69, 159.39, 161.06, 161.72. MS: $m/z$ (%)=319 ($M^+$, 22), 318 (100), 303 (12), 290 (52), 276 (10), 259 (15), 247 (12), 173 (68), 158 (20), 143 (10), 127 (48), 99 (20), 93 (18), 70 (26), 55 (14). Anal. Calcd for $C_{18}H_{17}N_5O$ (319.36): C, 67.69; H, 5.36; N, 21.93. Found: C, 67.97; H, 5.11; N, 22.14.

**4.4.5. 6-Amino-4-phenyl-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6e).** Following the above general procedure, treatment of benzaldehyde **5e** (1.0 g, 9.43 mmol) with malononitrile (1.24 g, 18.78 mmol) and pyrrolidine (1.34 g, 18.87 mmol) in absolute ethanol and refluxing for 7 h, furnished the compound **6e**. Yield: 1.42 g (52%), pale yellow solid, mp 238–240°C; IR (KBr): 3473, 3321 ($NH_2$), 2204 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.96 and 3.70 (2t, 8H, $J$=6.6 Hz, 3′, 4′ $CH_2$ and $N$-$CH_2$, pyrrolidine), 5.36 (bs, 2H, exchanged with $D_2O$), 7.44–7.51 (m, 5H, Ar-H). $^{13}C$ NMR: $\delta$ 25.37, 49.51, 80.96, 81.85, 116.72, 118.15, 128.41, 128.65, 130.15, 134.92, 157.44, 159.27, 162.04. MS: $m/z$ (%)=289 ($M^+$, 72), 288 (84), 260 (90), 253 (14), 234 (10), 219 (8), 173 (92), 158 (48), 127 (100), 93 (78). Anal. Calcd for $C_{17}H_{15}N_5$ (289.34): C, 70.57; H, 5.22; N, 24.20. Found: C, 70.91; H, 5.28; N, 23.94.

**4.4.6. 6-Amino-4-(indol-3-yl)-2-(pyrrolidin-1-yl)-pyridine-3,5-dicarbonitrile (6f).** Following the above general procedure, treatment of indole-3-carbaldehyde **5f** (1.0 g, 7.5 mmol) with malononitrile (0.99 g, 15.03 mmol) and pyrrolidine (1.06 g, 14.92 mmol) in absolute ethanol under reflux for 9 h, furnished the compound **6f**. Yield: 1.09 g (41%), brownish yellow solid, mp 302–304°C; IR (KBr): 3486, 3342 ($NH_2$), 3221 (NH), and 2205 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.99 and 3.78 (2t, 8H, 3′, 4′-$CH_2$ and $N$-$CH_2$, pyrrolidine), 6.49 (bs, 2H, exchanged with $D_2O$), 7.14–7.65 (m, 5H, Ar-H), 11.50 (s, 1H). $^{13}C$ NMR: $\delta$ 25.15, 49.30, 80.36, 80.57, 109.87, 112.04, 117.65, 118.89, 119.81, 121.89, 124.97, 126.90, 131.91, 136.11, 155.02, 158.26, 160.18. Anal. Calcd for $C_{19}H_{16}N_6$ (328.38): C, 69.49; H, 4.91; N, 25.59. Found: C, 69.28; H, 5.09; N, 25.68.

**4.4.7. 5-Amino-7-(pyrrolidin-1-yl)-2,4,4-trimethyl-1,4-dihydro-1,6-naphthyridine-8-carbonitrile (8).** To a solution of 4-methylpent-3-en-2-one **7** (1.0 g, 10.20 mmol) and malononitrile (1.4 g, 20.30 mmol) in 20 mL of absolute ethanol, pyrrolidine (1.44 g, 20.28 mmol) was added dropwise at room temperature. The reaction mixture was refluxed (17 h), until the disappearance of the starting material, as monitored by TLC, and the solvent removed under reduced pressure. The crude residue was purified by column chromatography using silica gel and eluted with hexane/chloroform (1:2) mixture to furnish the compound **8**. Yield: 0.92 g (32%), white solid, mp 198–200°C (EtOAc/hexane); IR (KBr): 3492, 3352 ($NH_2$), 2179 (CN) $cm^{-1}$; $^1H$ NMR: $\delta$ 1.37 (s, 6H, gem-dimethyl), 1.80 (s, 3H, $CH_3$), 1.91 and 3.68 (2t, 8H, 3′, 4′-$CH_2$ and $N$-$CH_2$, pyrrolidine), 4.21 (s, 1H), 4.74 (bs, 2H, exchanged with $D_2O$), 5.91 (1H, bs). $^{13}C$ NMR: $\delta$ 19.53, 25.89, 31.45, 32.28, 48.76, 66.97, 94.54, 110.64, 120.43, 127.34, 149.56, 158.26. MS: $m/z$ (%)=283 ($M^+$, 8), 269 (14), 268 (100), 251 (8), 234 (6), 70 (10). Anal. Calcd for $C_{16}H_{21}N_5$ (283.37): C, 67.81; H, 7.47; N, 24.71. Found: C, 67.79; H, 7.66; N, 24.90.

## Acknowledgements

We wish to thank University Grants Commission—Special Assistance Program for financial assistance. One of the authors (D. T.) is thankful to CSIR, India for a fellowship. P. R. and V. K. are thankful to DST for financial support.

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