Synthesis of Some New Polyfunctionalized Pyridines

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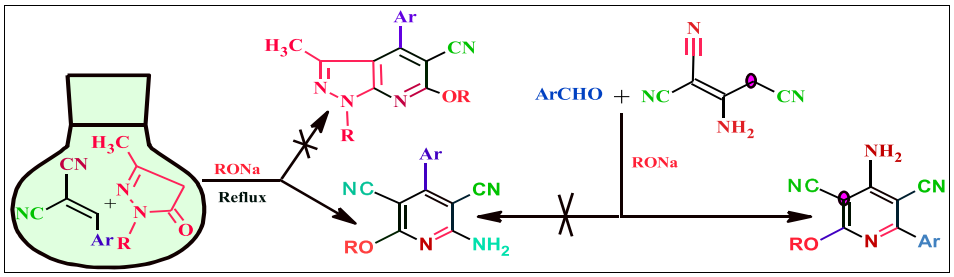

5-Methyl-2,4-dihydro-3*H*-pyrazol-3-one and/or 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one was reacted with arylidenemalononitrile in the presence of sodium alkoxide to give 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4a–e** instead of the reported pyrazolo[3,4-*b*]pyridine-5-carbonitriles. The same products **4a–e** were prepared *via* reaction of arylidenemalononitrile with sodium alkoxide in an appropriative alcohol. However, the new synthetic route for preparation of their positional isomer 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile **7a–j** has been achieved *via* reaction of 2-aminoprop-1-ene-1,1,3-tricarbonitrile with different aromatic aldehydes under the same conditions.

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INTRODUCTION

The pyridine ring is fundamental heterocyclic fragment of naturally occurring biomolecules and synthetic compounds. Within the last few decades, many efforts have been made to design diverse synthetic approaches for pyridine derivatives [1]. Among a wide range of pyridines, cyanopyridines acquired a special attention due to their great therapeutic importance. They act as anticonvulsant [2], antihypertensive [3], anti-inflammatory [4], antimicrobial [5], antiviral [6], antibacterial [7], anti-alzaheimer [8], antihistamine [9], and antitumor [10] drugs. Therefore, synthesis of cyanopyridine derivatives is the current interest owing to their enormous occurrence in diverse biologically active compounds. On the other hand, 2-aminoprop-1-ene-1,1,3-tricarbonitrile is a versatile synthon, and hence it was extensively used in many reactions to prepare the many heterocyclic compounds that have diverse pharmaceutical activities [11–15].

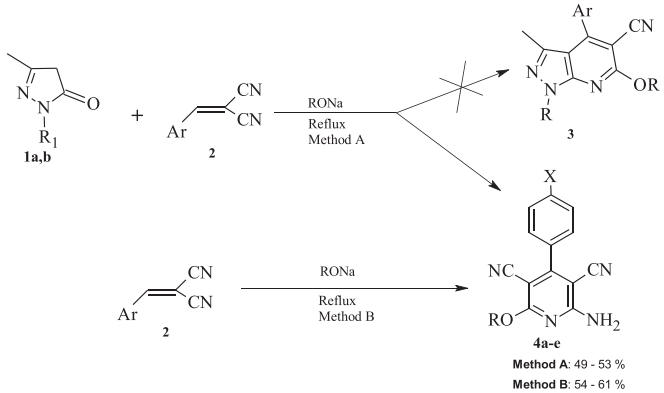
Looking to these multifold properties exhibited by cyanopyridines, we report herein the uses of the 2-aminoprop-1-ene-1,1,3-tricarbonitrile as a convenient synthon for preparation of new polyfunctionalized 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile in the hope that they may possess different biological activities.

RESULTS AND DISCUSSION

It has been reported that reaction of 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one **1a** with arylidenemalononitrile in presence of sufficient amount of alkoxide anion afforded pyrazolo[3,4-*b*]pyridine-5-carbonitrile derivatives **3** [16]. While herein, we found that reaction of 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one **1a** and/or 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one **1b** with arylidenemalononitrile **2** in the presence of sodium alkoxide gave 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4a–e** instead of pyrazolo[3,4-b]pyridine-5-carbonitriles **3** [16]. Furthermore, the same product 4-amino-2-alkoxy-6-arylpyridine-3,5-dicarbonitrile **4** was prepared by refluxing arylidenemalononitrile **2** with sodium alkoxide in the appropriative alcohol for 3 h, this result shows that the pyrazolone **1a,b** do not have any role in this reaction (Scheme 1).

The chemical structures of the synthesized 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4a–e** were confirmed by their spectral (IR, ^{1}H, ^{13}C NMR) and elemental analyses data. For example, the IR spectrum of **4b** showed absorption bands at 3334 and 3232 cm^{-1} characteristic for NH_2 group beside the nitrile stretching vibration bands at 2215 cm^{-1}. ^{1}H NMR spectrum of **4b** exhibited two singlet signals at δ 3.01 and 3.98, which are characteristic for $N(CH_3)_2$ and OCH_3 protons, in addition to two doublet signals at δ 6.83 and 7.39 with coupling constant J = 8 Hz corresponding to aromatic protons, also, it exhibited broad singlet signal at δ 7.69 ppm for the amino group. Its ^{13}C NMR spectrum exhibited data consistent with the established structure in which the methoxide carbon atom appeared at δ 55.03: carbons of $N(CH_3)_2$ group at δ 40.15; the nitrile carbons at δ 111.76, 116.04, while the pyridine C-3 and C-5

Scheme 1. Synthesis of 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4a–e**.



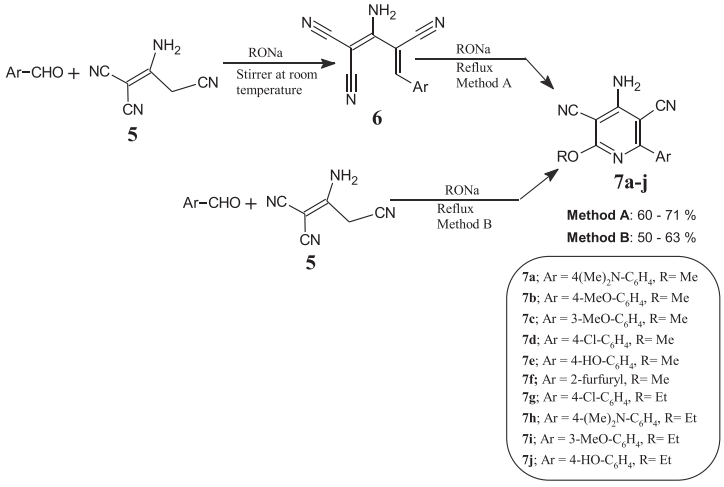
4a; R = Me, X = H, **4b**; R = Me, X= $N(CH_3)_2$, **4c**; R= Me, X= OCH_3, **4d**; R=Et, X = H, **4e**; R=Et, X= OCH_3

appeared at δ 83.11, 83.32, finally, the other aromatic carbons are characterized by peaks at δ 116.57, 120.82, 130.20, 152.00, 161.19, 161.94, and 166.60 ppm.

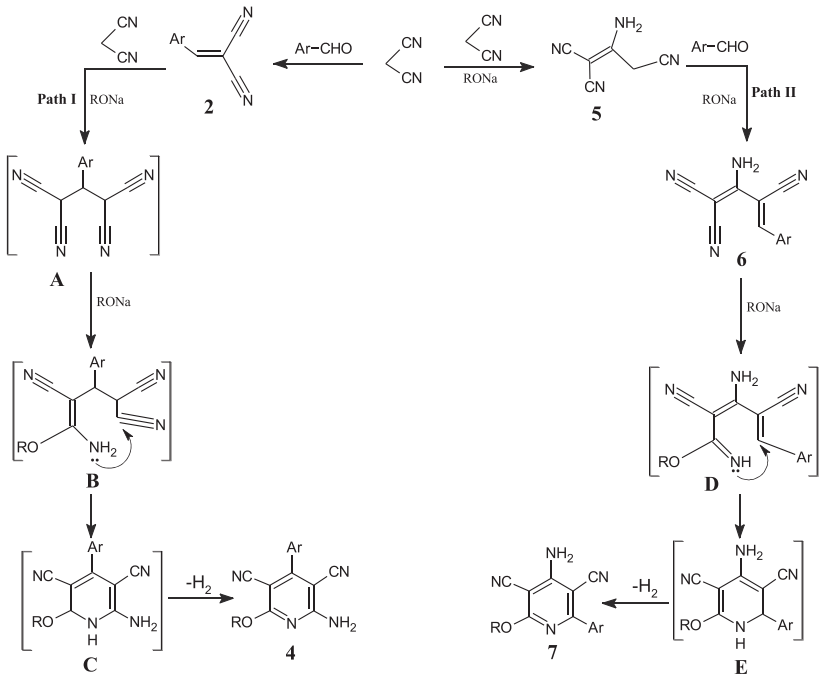
There are many reported procedures for the synthesis of 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4** *via* multi-components reaction between aldehyde and two equivalent moles of malononitrile [17–20], but there is not anyone for synthesis of their positional isomer 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile **7**. While searching for possible synthesis of 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile **7**, we found out that 2-aminoprop-1-ene-1,1,3-tricarbonitrile **5** has not been previously studied in such reactions. However, it was found that stirring of malononitrile dimer **5** with aromatic aldehyde at room temperature in presence of sodium alkoxide afforded 2-amino-4-arylbuta-1,3-diene-1,1,3-tricarbonitrile **6**, which was refluxed with sodium alkoxide to give the targeted products **7a–j** (Method A, Scheme 2). Also, the same products **7a–j** were directly prepared *via* refluxing of malononitrile dimer **5** with aromatic aldehydes under the same reaction conditions (Method B, Scheme 2).

The chemical structures of the new products **7a–j** were established by their spectral (IR, ^{1}H, ^{13}C NMR) and elemental analyses data. The IR spectrum of **7a** contains bands assignable for the amino stretching vibration absorption appeared at 3336, 3238 cm^{-1} beside the nitrile stretching vibration bands at 2204 cm^{-1}. ^{1}H NMR spectrum of **7a** showed the presence of two singlet signals at δ 3.03 and δ 4.02 characteristic of $N(CH_3)_2$ and OCH_3 groups, respectively, also, it exhibited singlet signal at δ 7.30 for the amino group and two doublet signals at δ 7.81 and 7.89 ppm for aromatic protons. ^{13}C NMR spectrum of **7a** exhibited data consistent with the established structure in which the methoxy carbon is characterized by peak at δ 54.84, in addition to the $N(CH_3)_2$ at δ 40.13, while nitrile carbons appears at δ114.28, 111.55. Finally, the pyridine C-3 and C-5 appeared at δ 75.19 and 84.78, while the other aromatic carbon are

Scheme 2. Synthesis of 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile **7a–j**.



Scheme 3. Plausible mechanism for the formation of **4** and **7**.



characterized by peaks at δ 116.99, 123.72, 130.69, 152.61, 160.35, 163.16, and 165.94 ppm.

The formation of **4** was assumed to take place through hydrolysis of arylidenemalononitrile **2** giving aromatic aldehyde and malononitrile, then a Knoevenagel condensation and Michael addition between aromatic aldehyde and two equivalent malononitrile afforded a tetracyano intermediate **A**. Subsequently, cyclization took place due to alkoxide nucleophilic attack at one of the nitrile groups through path **I** to give 2-amino-6-alkoxy-4-arylpyridine-3,5-dicarbonitrile **4**. While the formation of their positional isomer **7** was assumed to take place through dimerization of malononitrile giving malononitrile dimer **5**, which was condensed with aromatic aldehydes to afford **6** followed by alkoxide addition to nitrile group and cyclization to dihydropyridine **E**, which underwent aromatization by air oxidation to produce 4-amino-6-alkoxy-2-arylpyridine-3,5-dicarbonitrile **7** (Path **II**, Scheme 3).

EXPERIMENTAL

Melting points were detected with a Kofler melting points apparatus and uncorrected. Infrared spectra were recorded with a FT-IR-ALPHBROKER-Platinum-ATR spectrometer and are given as cm^{-1}using the attenuated total reflection method. ^1H NMR and ^{13}C NMR spectra for all compounds were recorded in DMSO-$d_6$on a Bruker Bio Spin AG spectrometer at 400 and 100 MHz, respectively. Elemental analyses were obtained on a Perkin-Elmer CHN-analyzer model.

General procedure for the synthesis of compounds 4a–e.

Method A: Pyrazolone **1a**,**b** (3 mmol) was added to a freshly prepared sodium alkoxide solution (4 mmol of sodium in 50 mL of each of absolute ethanol or methanol). Arylidenemalononitrile **2** (2 mmol) was then added and the reaction mixture was heated under reflux for about 3 h. After completion of reaction (monitored with TLC), the reaction mixture was cooled to RT and poured in ice-cold water. The solid deposited was then collected by filtration, washed several times with water, and recrystallized from suitable solvent.

Method B: A mixture of arylidenemalononitrile **2** (2 mmol) and sodium alkoxide (3 mmol of sodium in 50 mL of each of absolute ethanol or methanol) was heated under reflux for about 3 h. After completion of reaction (monitored with TLC), the reaction mixture was cooled to RT and poured in ice-cold water. The solid precipitate was then collected by filtration, washed several times with water, and recrystallized from suitable solvent.

2-Amino-6-methoxy-4-phenylpyridine-3,5-dicarbonitrile (4a). Yield (Method A, 53%; Method B, 61%); mp 263°C (reported 259–261)[17]; FTIR (cm^{-1}) 3408, 3329, 3187, 2970, 2911, 2214, 1647;^1H NMR (400 MHz, DMSO-d_6) δ 7.92 (s. br., 2H, NH_2), 7.57 (s, 3H, $3CH_{arom.}$), 7.53 (s, 2H, $2CH_{arom.}$), 3.99 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.25,

161.66, 161.24, 134.64, 130.69, 129.10, 128.78, 115.83, 115,36, 84.03, 83.82, 55.19; *Anal*. Calcd. for $C_{14}H_{10}N_4O$ (250): C, 67.19; H, 4.03; N, 22.39. Found: C, 67.31; H, 3.91; N, 22.07.

2-Amino-6-methoxy-4-[4-(dimethylamino)phenyl]-pyridine-3,5-dicarbonitrile (4b). Yield (Method A, 49%; Method B, 55%); mp 281°C; FTIR (cm^{-1}) 3471, 3421, 3334, 3232, 2948, 2215, 1642;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.69 (s. br., 2H, NH_2), 7.39 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 6.83 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 3.98 (s, 3H, OCH_3), 3.01 (s, 6H, $N(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.60, 161.94, 161.19,152.00, 130.20, 120.82, 116.57, 116.04, 111.76, 83.32, 83.11, 55.03, 40.15; *Anal*. Calcd. for $C_{16}H_{15}N_5O$ (293): C, 65.52; H, 5.15; N, 23.88. Found: C, 65.60; H, 5.01; N, 23. 56.

2-Amino-6-methoxy-4-(4-methoxyphenyl)pyridine-3,5-dicarbonitrile (4c). Yield (Method A, 51%; Method B, 59%); mp 298°C; FTIR (cm^{-1}) 3422, 3327, 3229, 3031, 2985, 2940, 2210, 1634;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (s. br., 2H, NH_2), 7.49 (d, j = 9 Hz, 2H, $2CH_{arom.}$), 7.12 (d, j = 9 Hz, 2H, $2CH_{arom.}$), 3.97 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.34, 161.72, 161.23,160.90, 130.60, 126.50, 116.17, 115.73, 114.51, 83.78, 83.62, 55.81, 55.16; *Anal*. Calcd. for $C_{15}H_{12}N_4O_2$ (280): C, 64.28; H, 4.32; N, 19.99. Found: C, 64.31; H, 4.19; N, 19.62.

2-Amino-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile (4d). Yield (Method A, 49%; Method B, 54%); mp 239–240°C (reported 238–239)[17]; FTIR (cm^{-1}) 3459, 3316, 3214, 2978, 2918, 2213, 1620;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (s. br., 2H, NH_2), 7.57 (s, 3H, $3CH_{arom.}$), 7.53 (s, 2H, $2CH_{arom.}$), 4.45 (q, j = 7 Hz, 2H, CH_2), 1.35 (t, j = 7 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.82, 161.63, 161.26, 134.65, 130.69, 129.11, 128.80, 115.93, 115,48, 84.98, 83.60, 63.83, 14.70; *Anal*. Calcd. for $C_{15}H_{12}N_4O$ (264): C, 68.17; H, 4.58; N, 21.20. Found: C, 68.09; H, 4.29; N, 21.11.

2-Amino-6-ethoxy-4-(4-methoxyphenyl)pyridine-3,5-dicarbonitrile (4e). Yield (Method A, 50%; Method B, 56%); mp 200–202°C (reported 199–200)[17]; FTIR (cm^{-1}) 3412, 3338, 3238, 2967, 2935, 2212, 1650;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.90 (s. br., 2H, NH_2), 7.49 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 7.12 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 4.44 (q, j = 8 Hz, 2H, CH_2), 3.85 (s, 3H, OCH_3), 1.35 (t, j = 8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.96, 161.74, 161.25,160.95, 130.56, 126.64, 116.13, 115.63, 114.54, 84.04, 83.61, 63.75, 55.83, 14.70; *Anal*. Calcd. for $C_{16}H_{14}N_4O_2$ (294): C, 65.30; H, 4.79; N, 19.04. Found: C, 65.53; H, 4.59; N, 18.82.

General procedure for the synthesis of compounds 7a–j.

Method A: 0.4 g (1.6 mmol) of 2-amino-4-(aryl)buta-1,3-diene-1,1,3-tricarbonitrile (**6**) was refluxed in 35 mL methanol containing 0.11 g (2.0 mmol) of sodium methoxide for 3 h. After completion of reaction (monitored with TLC), the reaction mixture was cooled to RT and poured in ice-cold water. The solid deposited was then collected by filtration, washed several times with water, and recrystallized from suitable solvent.

Method B: Equimolar amounts (2 mmol) of aromatic aldehydes, 2-aminoprop-1-ene-1,1,3-tricarbonitrile (0.4 g), and sodium alkoxide solution (4 mmol of sodium in 50 mL of each of absolute ethanol or methanol) were heated at reflux for about 3 h. After completion of reaction (monitored with TLC), the reaction mixture was cooled to RT and poured in ice-cold water. The solid deposited was then collected by filtration, washed several times with water, and recrystallized from suitable solvent.

4-Amino-2-[4-(dimethylamino)phenyl]-6-methoxypyridine-3,5-dicarbonitrile (7a). Yield (Method A, 71%; Method B, 63%); mp 291°C; FTIR (cm^{-1}) 3336, 3238, 3018, 2898, 2858, 2204, 1648;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 7.30 (s, br, 2H, NH_2), 7.81(d, j = 8 Hz, 2H, $2CH_{arom.}$), 4.02 (s, 3H, OCH_3), 3.03 (s, 6H, $N(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.94, 163.16, 160.35, 152.61, 130.69, 123.72, 116.99, 114.28, 111.55, 84.78, 75.19, 54.84, 40.13; *Anal*. Calcd. for $C_{16}H_{15}N_5O$ (293): C, 65.52; H, 5.15; N, 23.88. Found: C, 65.49; H, 5.01; N, 23.53.

4-Amino-2-methoxy-6-(4-methoxyphenyl)pyridine-3,5-dicarbonitrile (7b). Yield (Method A 69%; Method B 59); mp 291°C; FTIR (cm^{-1}) 3351, 3236, 3008, 3031, 2960, 2916, 2220, 1672;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s. br, 2H, NH_2), 7.47 (s, 2H, $2CH_{arom.}$), 7.11(s, 2H, $2CH_{arom.}$), 4.02 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.25, 163.33, 162.00,160.07, 131.01, 129.53, 116.31, 114.35, 113.87, 86.57, 76.29, 55.94, 55.09; *Anal*. Calcd. for $C_{15}H_{12}N_4O_2$ (280): C, 64.28; H, 4.32; N, 19.99. Found: C, 64.38; H, 4.21; N, 19.72.

4-Amino-2-methoxy-6-(3-methylphenyl)pyridine-3,5-dicarbonitrile (7c). Yield (Method A, 62%; Method B, 57%); mp 268–270°C; FTIR (cm^{-1}) 3412, 3336, 3234, 3011, 2944, 2213, 1653;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (br, 2H, NH_2), 7.48 (t, j = 8 Hz, 1H, $1CH_{arom.}$), 7.14 (d, j = 8 Hz, 1H, $1CH_{arom.}$), 7.08 (m, 2H, $2CH_{phenyl}$) 3.98 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.20, 161.64, 160.97, 159.56, 135.87, 130.29, 120.91, 115.82, 115.17, 115.35, 114.55, 83.97, 79.20, 55.83, 55.17; *Anal*. Calcd. for $C_{15}H_{12}N_4O_2$ (280): C, 64.28; H, 4.32; N, 19.99. Found: C, 64.09; H, 4.19; N, 19.56.

4-Amino-2-(4-chlorophenyl)-6-methoxypyridine-3,5-dicarbonitrile (7d). Yield (Method A, 70%; Method B, 59%); mp 245–246°C; FTIR (cm^{-1}) 3519, 3382, 3326, 3219, 2953, 2221, 1650; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05 (br, 2H, NH_2), 7.66 (d, j = 8 Hz,

2H, $2CH_{arom.}$), 7.57 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 3.98 (s, 3H, OCH_3); *Anal*. Calcd. for $C_{14}H_9ClN_4O$ (284.5): C, 59.06; H, 3.19; N, 19.68. Found: C, 59.16; H, 3.25; N, 19.38.

4-Amino-2-(4-hydroxyphenyl)-6-methoxypyridine-3,5-dicarbonitrile (7e). Yield (Method A, 60%; Method B, 51%); mp 228–230°C dec.; FTIR (cm^{-1}) 3444, 3327, 3222, 2954, 2918, 2214, 1644;^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (br, 1H, OH), 7.76 (s. br, 2H, NH_2), 7.36 (d, j = 7 Hz, 2H, $2CH_{phenyl}$), 6.92 (d, j = 7 Hz, 2H, $2CH_{phenyl}$), 3.98 (s, 3H, OCH_3); *Anal*. Calcd. for $C_{14}H_{10}N_4O_2$ (266): C, 63.15; H, 3.79; N, 21.04. Found: C, 63.01; H, 3.57; N, 20.81.

4-Amino-2-(furan-2-yl)-6-methoxypyridine-3,5-dicarbonitrile (7f). Yield (Method A, 68%; Method B, 57%); mp 268°C; FTIR (cm^{-1}) 3330, 3221, 3007, 2982, 2214, 1651;^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 (s, 1H, CH_{furyl}) 7.44 (s. br, 3H, NH_2 + CH_{furyl}), 6.771(s, 1H, CH_{furyl}), 4.02 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.38, 160.16, 151.44, 150.57, 147,07, 116.55, 115.32, 114.00, 113,30, 83.58, 76.19, 55.01; *Anal*. Calcd. for $C_{12}H_8N_4O_2$ (240): C, 60.00; H, 3.36; N, 23.32. Found: C, 59. 82; H, 3.19; N, 23.07.

4-Amino-2-(4-chlorophenyl)-6-ethoxypyridine-3,5-dicarbonitrile (7 g). Yield (Method A, 68%; Method B, 55%); mp 193°C; FTIR (cm^{-1}) 3465, 3327, 3220, 2980, 2928, 2215, 1620; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (br, 2H, NH_2), 7.66 (d, j = 9 Hz, 2H, $2CH_{arom.}$), 7.56 (d, j = 9 Hz, 2H, $2CH_{arom.}$), 4.45 (q, j = 7 Hz, 2H, CH_2), 1.36 (t, j = 7 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.75, 161.57, 160.09, 135.64, 133.51, 130.81, 129.29, 115.78, 115,34, 84.01, 80.62, 63.89, 14.68; *Anal*. Calcd. for $C_{15}H_{11}ClN_4O$ (298.5): C, 60.31; H, 3.71; N, 18.76. Found: C, 59.83; H, 3.19; N, 18.07.

4-amino-2-[4-(dimethylamino)phenyl]-6-ethoxypyridine-3,5-dicarbonitrile (7 h). Yield (Method A, 66%; Method B, 50%); mp 239–241°C; FTIR (cm^{-1}) 3430, 3334, 3230, 3001, 2968, 2213, 1637;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77 (s br, 2H, NH_2), 7.39 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 6.83 (d, j = 8 Hz, 2H, $2CH_{arom.}$), 4.43 (q, j = 7 Hz, 2H, CH_2), 301 (s, 6H, $N(CH_3)_2$), 1.35 (t, j = 7 Hz, 3H, CH_3); *Anal*. Calcd. for $C_{17}H_{17}N_5O$ (307): C, 66.43; H, 5.58; N, 22.79. Found: C, 66.57; H, 5.41; N, 22.61.

4-Amino-2-ethoxy-6-(3-methoxyphenyl)pyridine-3,5-dicarbonitrile (7i). Yield (Method A, 62%; Method B, 51%); mp 211°C; FTIR (cm^{-1}) 3425, 3336, 3234, 3064, 2983, 2941, 2214, 1644;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (br, 2H, NH_2), 7.48 (t, j = 7 Hz, 1H, $1CH_{arom}$), 7.10 (m, 3H, $3CH_{arom}$), 4.44 (q, j = 7 Hz, 2H, CH_2) 3.82 (s, 3H, OCH_3), 1.35 (t, j = 7 Hz, 3H, CH_3); *Anal*. Calcd. for $C_{16}H_{14}N_4O_2$ (294): C, 65.30; H, 4.79; N, 19.04. Found: C, 65.07; H, 4.52; N, 18.86.

4-Amino-2-ethoxy-6-(4-hydroxyphenyl)pyridine-3,5-dicarbonitrile (7j). Yield (Method A, 58%; Method B, 51%); mp 198°C dec.; FTIR (cm^{-1}) 3454, 3329, 3227, 2994, 2953, 2217, 1657;^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (br, 1H, OH), 7.76 (br, 2H, NH_2), 7.36 (d, j = 8 Hz, 2H, $2CH_{phenyl}$), 6.92 (d, j = 8 Hz, 2H, $2CH_{phenyl}$), 4.44 (q, j = 7 Hz, 2H, CH_2), 1.35 (t, j = 7 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.00, 161.77, 161.25, 159.79, 130.59, 124.97, 116.24, 115.83, 115.72, 83.91, 77.48, 63.72, 14.69; *Anal*. Calcd. for $C_{15}H_{12}N_4O_2$ (280): C, 64.28; H, 4.32; N, 19.99. Found: C, 63.11; H, 3.80; N, 19.71.

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SUPPORTING INFORMATION

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